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Question # 1

A 2900-g (6.4-lb) male newborn is delivered at term to a 29-year-old primigravid woman. His mother had no routine prenatal care. She reports that the pregnancy was uncomplicated apart from a 2-week episode of a low-grade fever and swollen lymph nodes during her early pregnancy. She has avoided all routine vaccinations because she believes that “natural immunity is better.” The newborn is at the 35th percentile for height, 15th percentile for weight, and 90th percentile for head circumference. Fundoscopic examination shows inflammation of the choroid and the retina in both eyes. A CT scan of the head shows diffuse intracranial calcifications and mild ventriculomegaly. Prenatal avoidance of which of the following would have most likely prevented this newborn's condition?

	Answer	Image
A	Exposure to unvaccinated children	
B	Undercooked pork	The diagram illustrates the life cycle of <i>Toxoplasma gondii</i>. It shows the cycle between a definitive host (cat) and an intermediate host (pork/pig). In the cat, oocysts are shed in feces and sporulate in the environment. In the pig, sporozoites infect cells, developing into bradyzoites and forming cysts. In the human, sporozoites can be ingested from the environment or undercooked pork, leading to infection of cells and development of bradyzoite-filled cysts, which can progress to a chronic stage. A note mentions 'Potential placental colonization and transplacental transmission'.
C	Unprotected sexual intercourse	
D	Mosquito bites	
E	Raw cow milk products	

Hint

Chorioretinitis, diffuse intracranial calcifications, and hydrocephalus (indicated by ventriculomegaly) in a newborn are characteristic of congenital toxoplasmosis.

Correct Answer

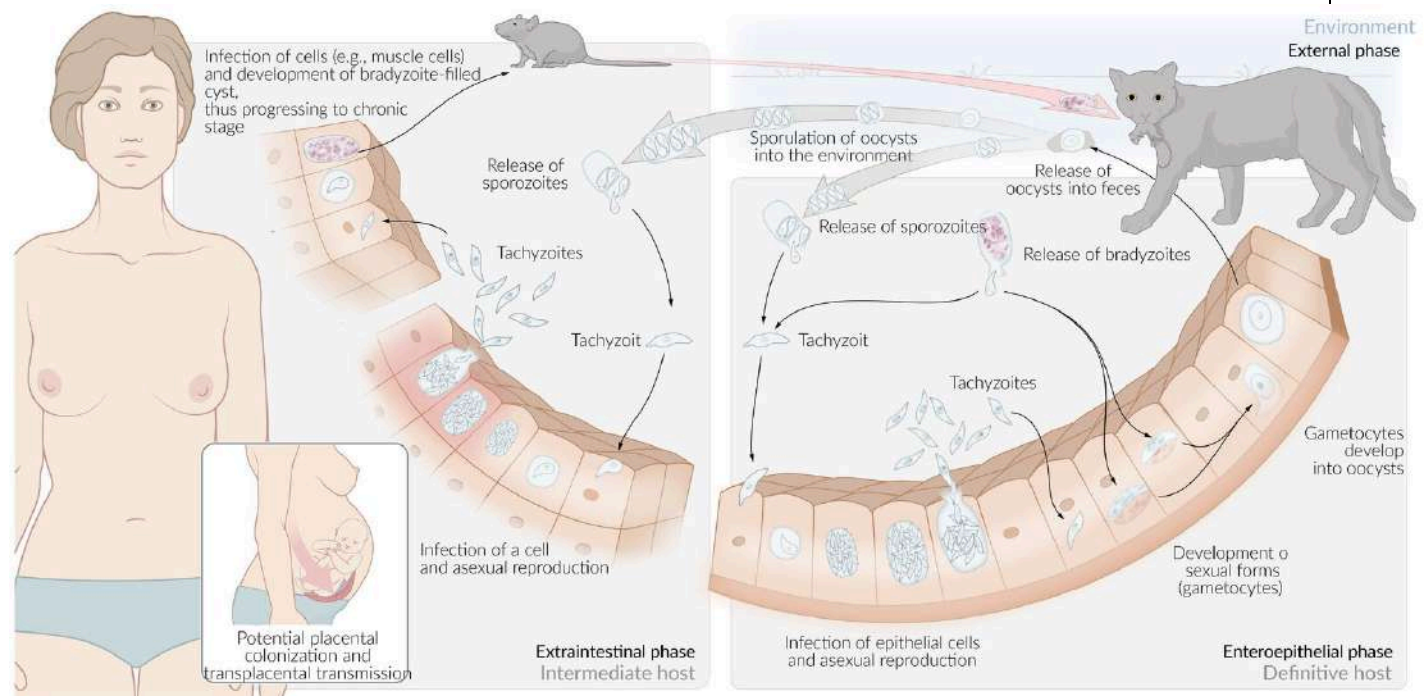
A - Exposure to unvaccinated children

Explanation Why

Exposure of an unvaccinated pregnant woman to unvaccinated children is a [risk factor](#) for maternal infection with [exanthematous](#) diseases of childhood, such as [rubella](#) and [varicella](#). [Congenital rubella syndrome](#) typically manifests with cardiac defects, [cataracts](#), and cochlear defects ([Gregg triad](#)), none of which is seen here. Although [chorioretinitis](#) and ventriculomegaly can be seen in [congenital varicella infection](#), further symptoms, such as [hypertrophic scars](#) and limb [hypoplasia](#), would also be expected. Neither condition is associated with intracranial calcifications. Moreover, the mother has not reported a rash characteristic of either disease.

B - Undercooked pork

Image



Explanation Why

In the US, consumption of contaminated, undercooked meat is the most common cause of [Toxoplasma gondii](#) infection during [pregnancy](#). While the likelihood of transplacental transmission is low in early [pregnancy](#), the risk of symptomatic [toxoplasmosis in the newborn](#) is highest if infection occurs in the [first trimester](#). Maternal [toxoplasmosis](#) is usually asymptomatic but may manifest with general symptoms, such as low-grade [fever](#) and cervical [lymphadenopathy](#), both of which are reported here. Other sources of maternal infection include accidental ingestion of contaminated cat feces and drinking unpasteurized goat's milk.

C - Unprotected sexual intercourse

Explanation Why

Unprotected sexual intercourse during [pregnancy](#) is a [risk factor](#) for [sexually transmitted diseases](#) (e.g., [HIV](#), [CMV](#), [HSV-2](#), [syphilis](#)), which may lead to congenital infections. This [newborn](#) presents with [chorioretinitis](#), intracranial calcifications, and ventriculomegaly, all of which are consistent with [congenital CMV infection](#). Moreover, the mother's symptoms during early [pregnancy](#) (low-grade [fever](#), cervical [lymphadenopathy](#)) are a possible manifestation of [CMV mononucleosis](#). However, intracranial calcifications are usually limited to the periventricular region in [congenital CMV infection](#) unlike the diffuse pattern seen here.

D - Mosquito bites

Explanation Why

Infection with the [Zika virus](#) (e.g., through mosquito bites) during [pregnancy](#) can lead to congenital [birth](#) defects, such as ventriculomegaly and intracranial calcifications. However, congenital Zika infection is not associated with [chorioretinitis](#). Moreover, the mother has not reported typical symptoms of [Zika infection](#), such as a [pruritic maculopapular rash](#) or arthralgia, nor did she travel to an [endemic](#) region.

E - Raw cow milk products

Explanation Why

Consumption of raw cow milk products during [pregnancy](#) is a [risk factor](#) for [Listeria monocytogenes](#) infection, which may lead to [granulomatosis infantiseptica](#) in [newborns](#). This condition is characterized by respiratory distress and [skin](#) lesions, neither of which is seen here. Although the mother's nonspecific febrile illness in early [pregnancy](#) could have been a manifestation of [listeriosis](#), her child's symptoms suggest [congenital toxoplasmosis](#). [Toxoplasma gondii](#) infection has been associated with the ingestion of contaminated raw goat milk rather than cow milk products.

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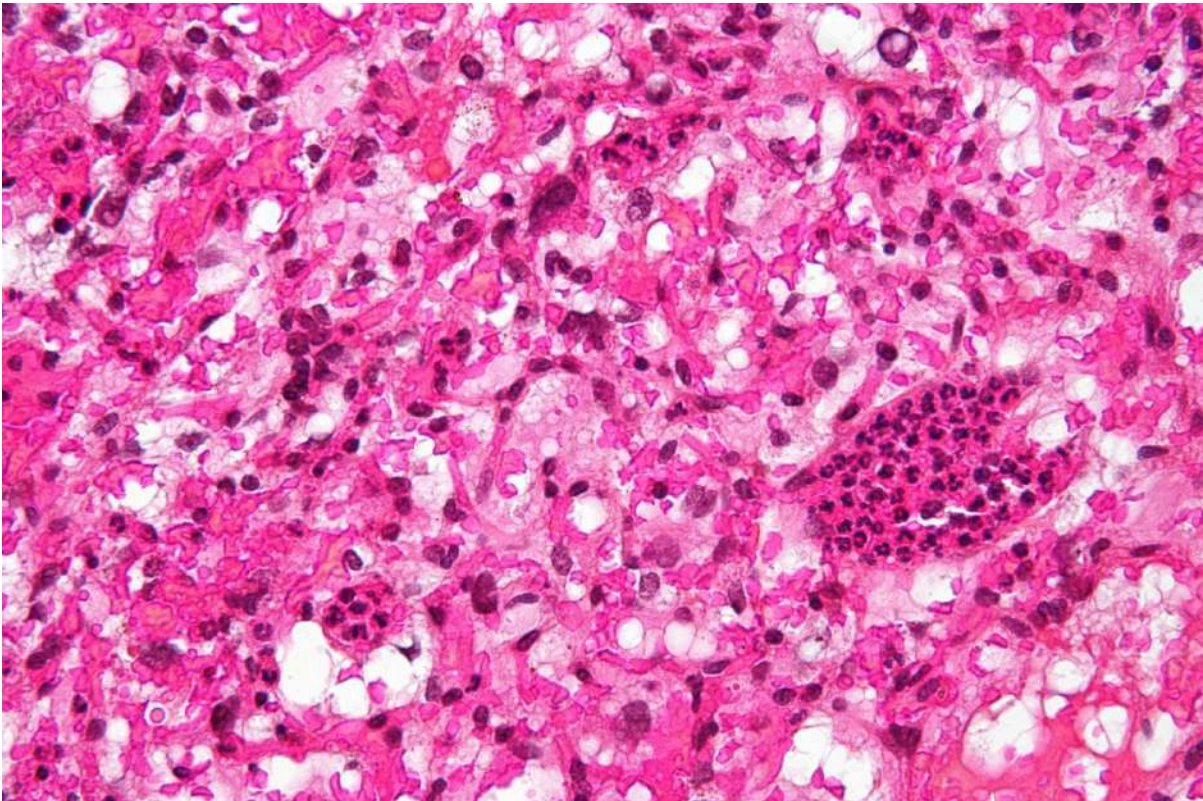
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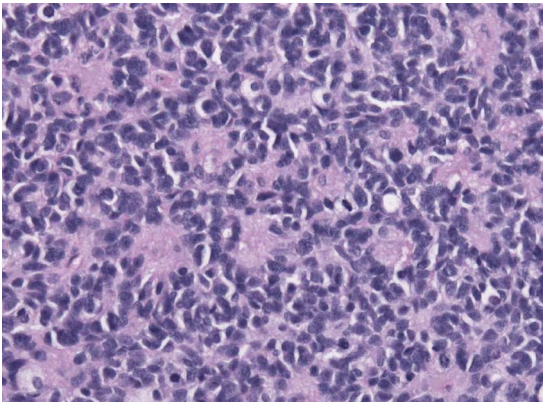
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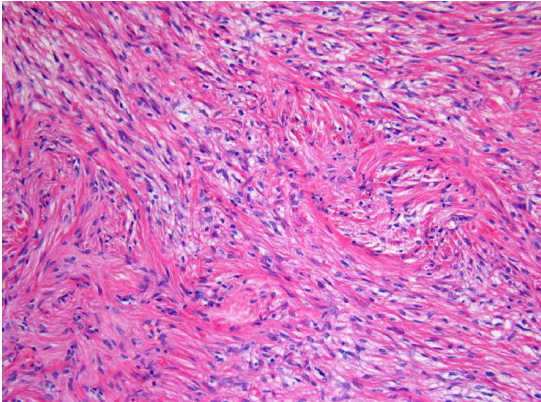
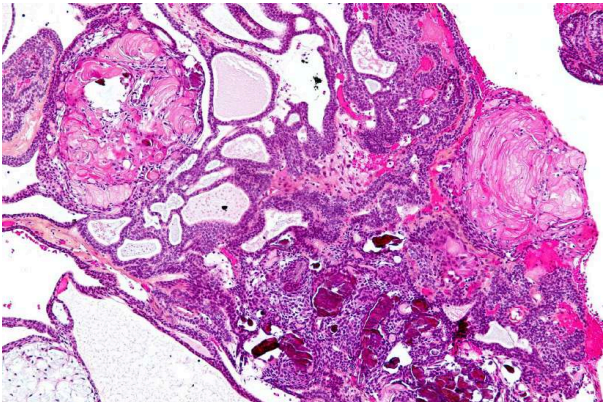
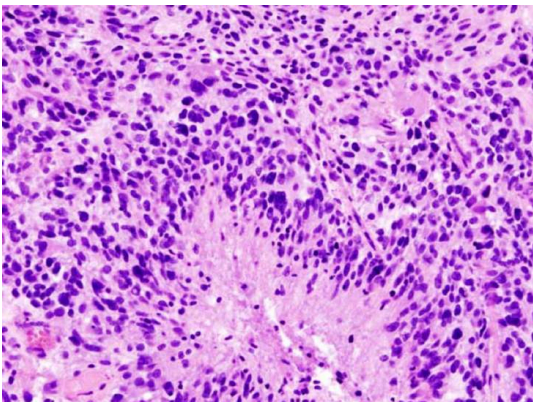
KissPrep: <https://t.me/USMLEKissPrep>

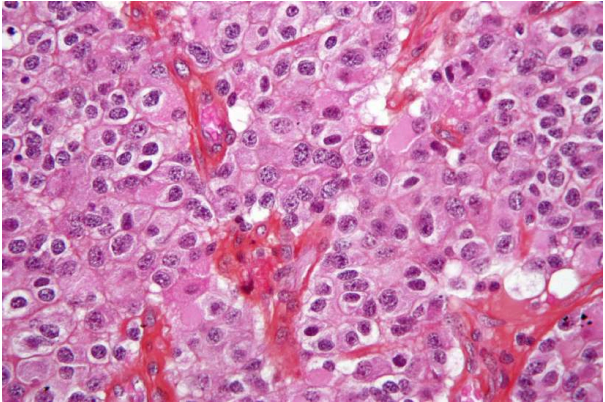
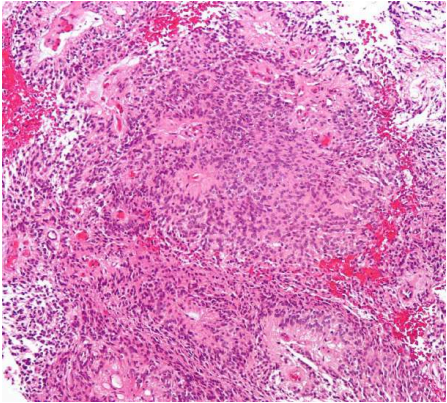
Question # 2

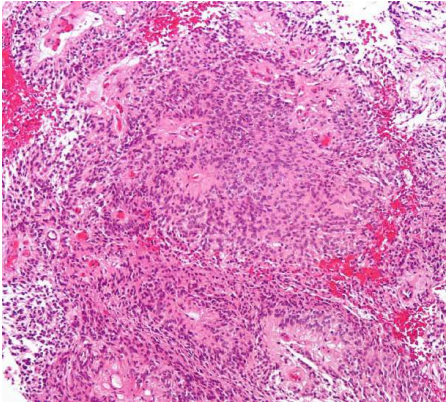
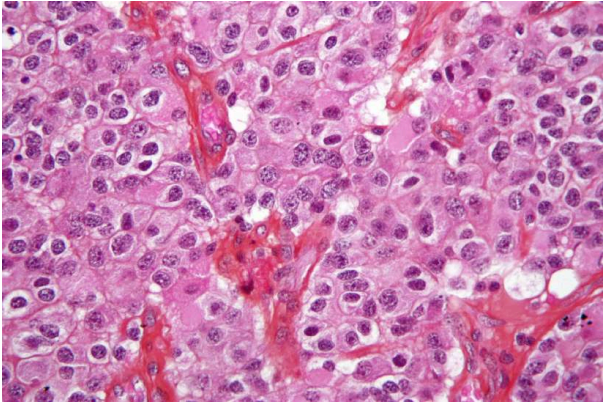
A 22-year-old man comes to the physician because of headaches and blurry vision for the past 6 months. He also reports frequent episodes of vomiting over the last month. His father has died of renal cell carcinoma at the age of 37 years. Examination shows 20/40 vision bilaterally. Fundoscopic examination shows bilateral optic disc swelling and growth of capillary vessels in the temporal peripheral retina. An MRI of the brain shows an infratentorial mass. The patient undergoes surgical resection of the mass. A photomicrograph of the resected specimen is shown. Which of the following is the most likely diagnosis?



	Answer	Image
A	Medulloblastoma	

	Answer	Image
B	Pilocytic astrocytoma	
C	Craniopharyngioma	
D	Glioblastoma	

	Answer	Image
E	Oligodendroglioma	
F	Hemangioblastoma	
G	Ependymoma	



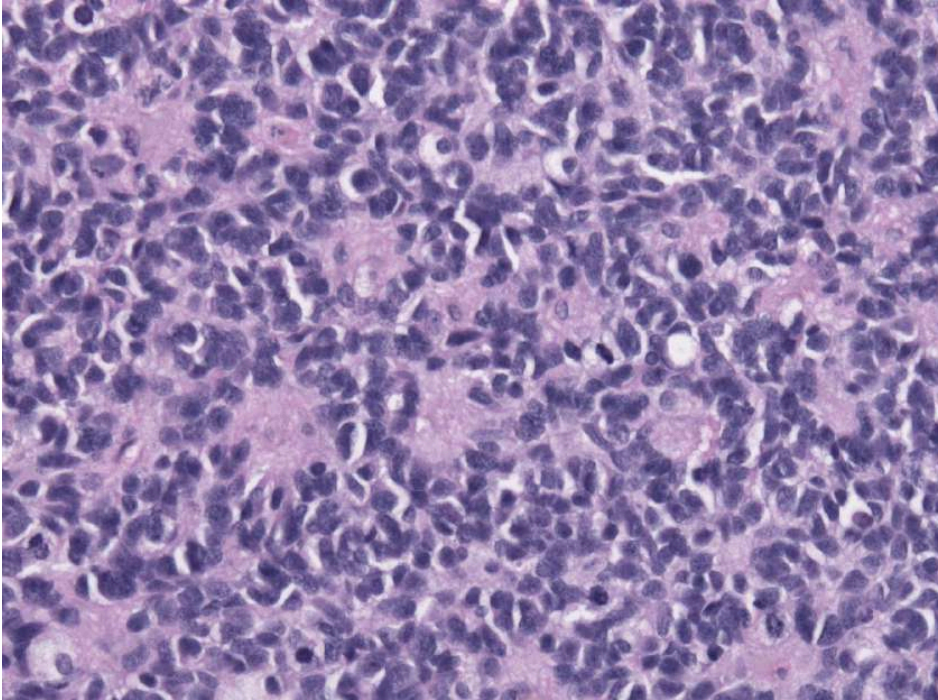
Hint

This patient presents with an infratentorial brain tumor and abnormal capillary growth in the retina. In combination with a family history of renal cell carcinoma, this raises suspicion for von Hippel-Lindau disease.

Correct Answer

A - Medulloblastoma

Image

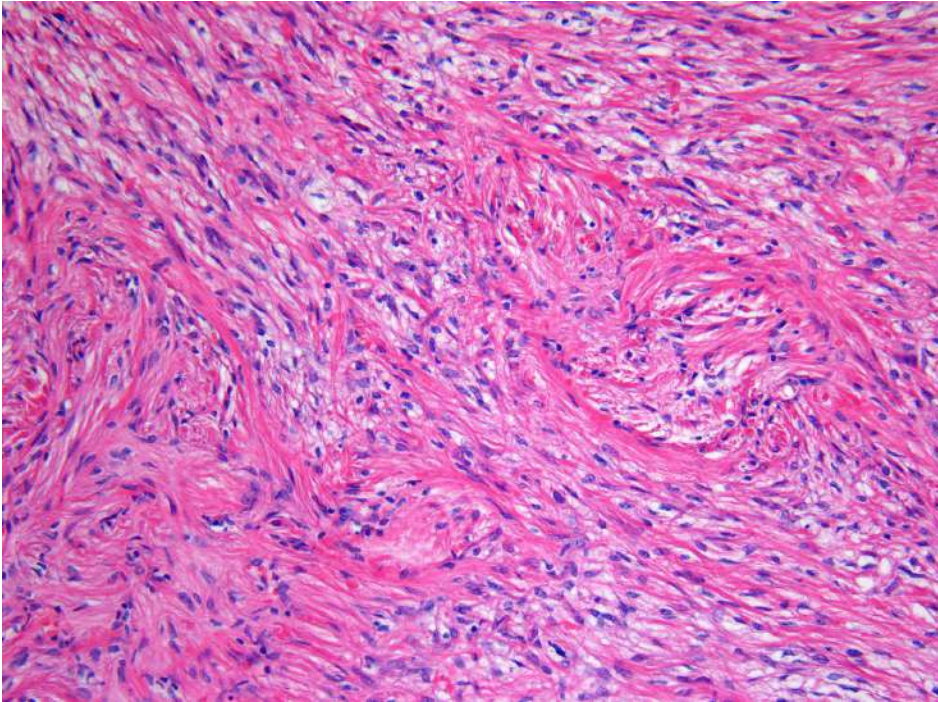


Explanation Why

[Medulloblastomas](#), which are commonly located in the [infratentorial](#) region, may present with [features of increased intracranial pressure](#) (e.g., [headache](#), vomiting, blurred vision, [papilledema](#)), as seen in this patient. However, they are not associated with retinal vascular changes. In addition, this type of [tumor](#) most commonly develops in the first decade of life. [Histology](#) typically shows small round blue cells and [Homer-Wright rosettes](#), which are not seen in this patient's photomicrograph. Finally, [medulloblastomas](#) are not a manifestation of [von Hippel-Lindau](#) disease but instead are associated with [Turcot's syndrome](#).

B - Pilocytic astrocytoma

Image

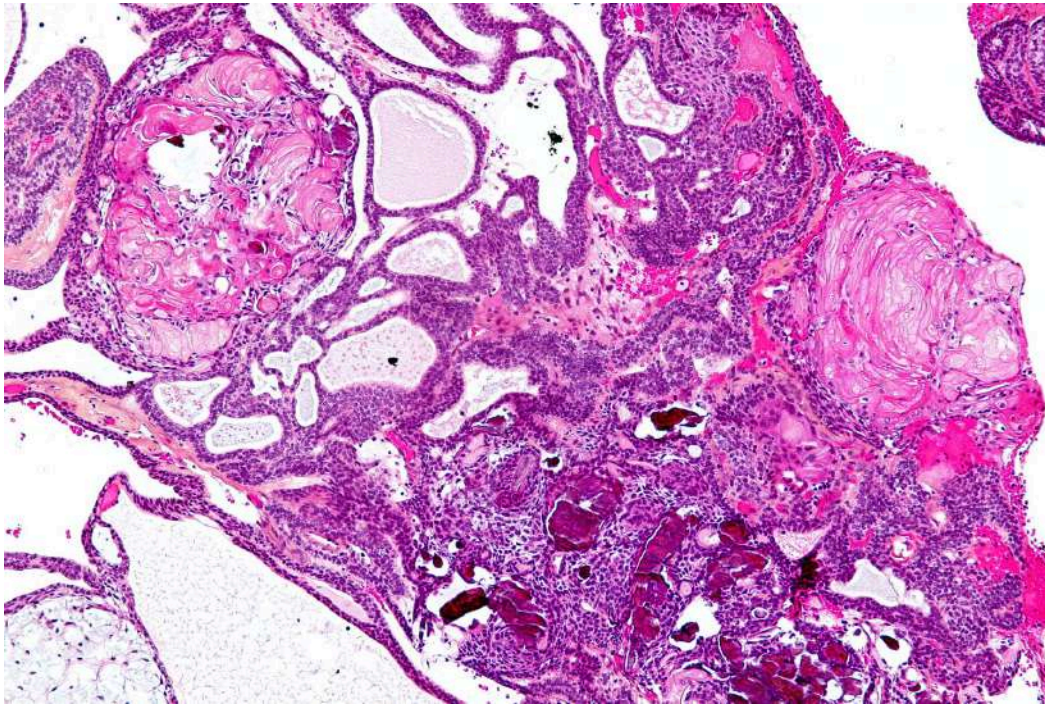


Explanation Why

Pilocytic [astrocytomas](#), which are commonly located in the [infratentorial](#) region, may present with [features of increased intracranial pressure](#) (e.g., [headache](#), vomiting, blurred vision, [papilledema](#)), as seen in this patient. However, they are not associated with retinal vascular changes. Moreover, this type of [tumor](#) most commonly develops in patients younger than 20 years of age. [Histology](#) typically shows [Rosenthal fibers](#) and positive staining for [glial fibrillary acidic protein](#), which are not seen in this patient's photomicrograph. Finally, pilocytic [astrocytomas](#) are not a manifestation of [von Hippel-Lindau](#) disease but instead are associated with [neurofibromatosis type 1](#).

C - Craniopharyngioma

Image

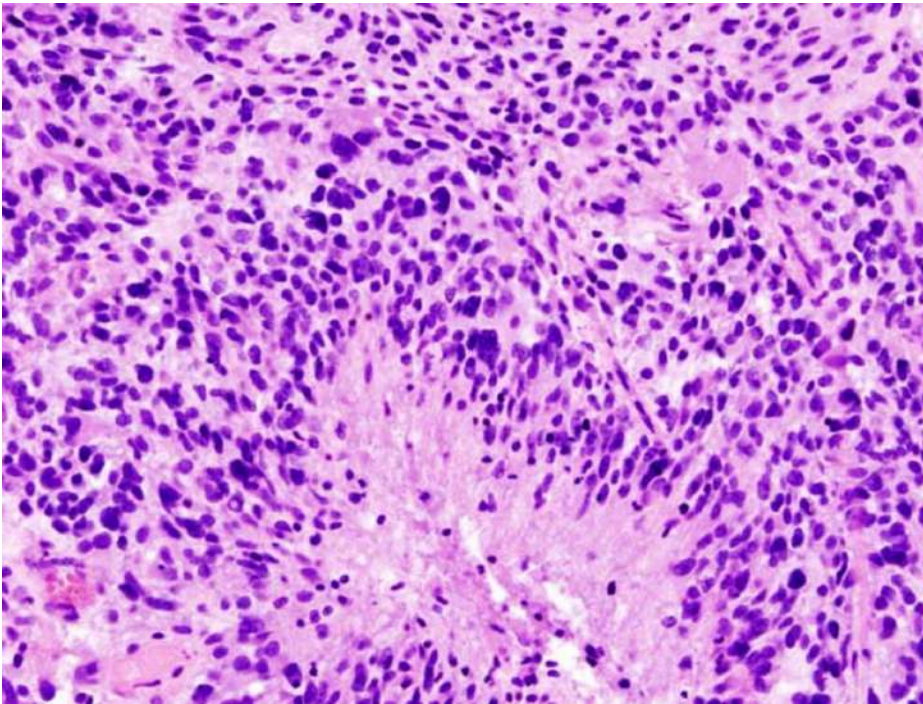


Explanation Why

[Craniopharyngiomas](#) can present with [headache](#) and vomiting, as seen here. However, as opposed to this patient's [tumor](#), this type of neoplasm is located in the [supratentorial](#) (i.e., suprasellar) region. Moreover, [craniopharyngiomas](#) are usually associated with [bitemporal hemianopsia](#), [hyperprolactinemia](#), and [hypopituitarism](#), all of which are absent here. [Histology](#) typically shows [metaplastic](#) squamous cells or reticular [epithelial](#) cells, calcifications, cysts, and [keratin](#) nodules, none of which are seen in this patient's photomicrograph. Finally, [craniopharyngiomas](#) are not a manifestation of [von Hippel-Lindau](#) disease.

D - Glioblastoma

Image

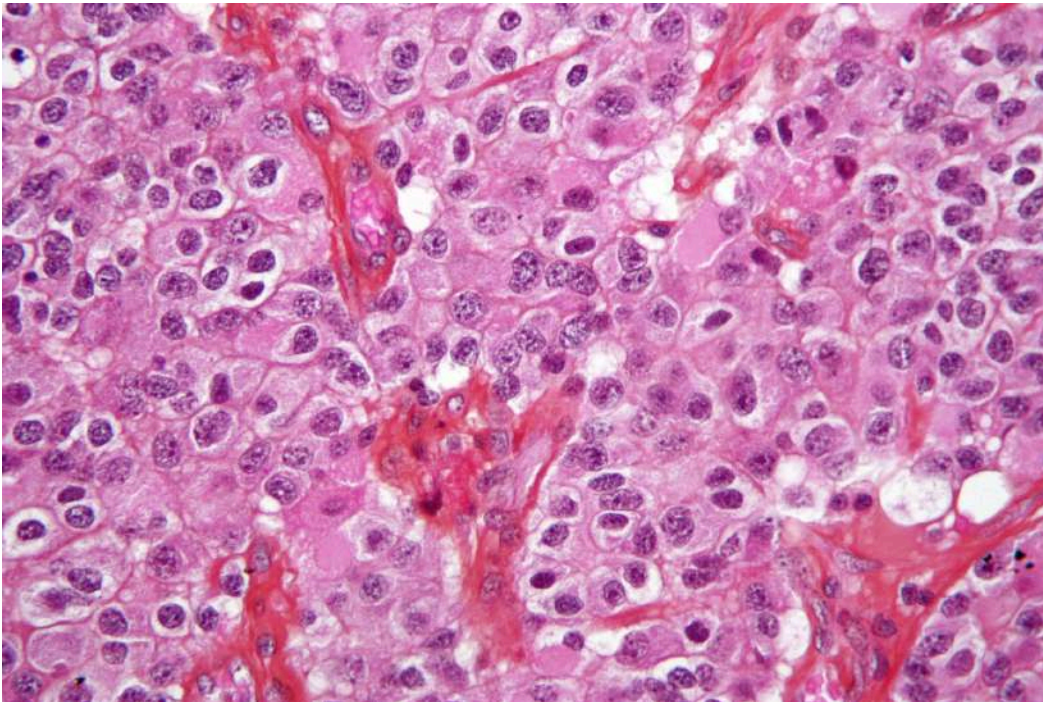


Explanation Why

[Glioblastomas](#) can present with [features of increased intracranial pressure](#) (e.g., [headache](#), vomiting, blurred vision, [papilledema](#)), as seen in this patient. However, as opposed to this patient's [tumor](#), this type of neoplasm is located in the cerebral hemispheres (i.e., [supratentorial](#)). Consequently, symptoms such as [seizures](#), focal neurological deficits, and personality changes are common, none of which are present in this patient. Moreover, the [median](#) age of onset is between 65–75 years of age. [Histology](#) typically shows pleomorphic [anaplastic](#) cells that form pseudopalisades and positive staining for [glial fibrillary acidic protein](#), which are not seen in this patient's photomicrograph. Finally, [glioblastomas](#) are not a manifestation of [von Hippel-Lindau](#) disease.

E - Oligodendroglioma

Image



Explanation Why

[Oligodendrogliomas](#) can present with [headache](#) and vomiting, as seen in this patient. However, as opposed to this patient's [tumor](#), this type of neoplasm is most commonly located in the cerebral hemispheres (i.e., [supratentorial](#)). Consequently, symptoms such as [seizures](#), focal neurological deficits, and personality changes are common, none of which are present in this patient. Moreover, the [median](#) age of onset is between 40–50 years of age. [Histology](#) typically shows fried egg cells and a chicken-wire pattern of [capillary](#) anastomoses, which are not seen in this patient's photomicrograph. Finally, [oligodendrogliomas](#) are not a manifestation of [von Hippel-Lindau](#) disease.

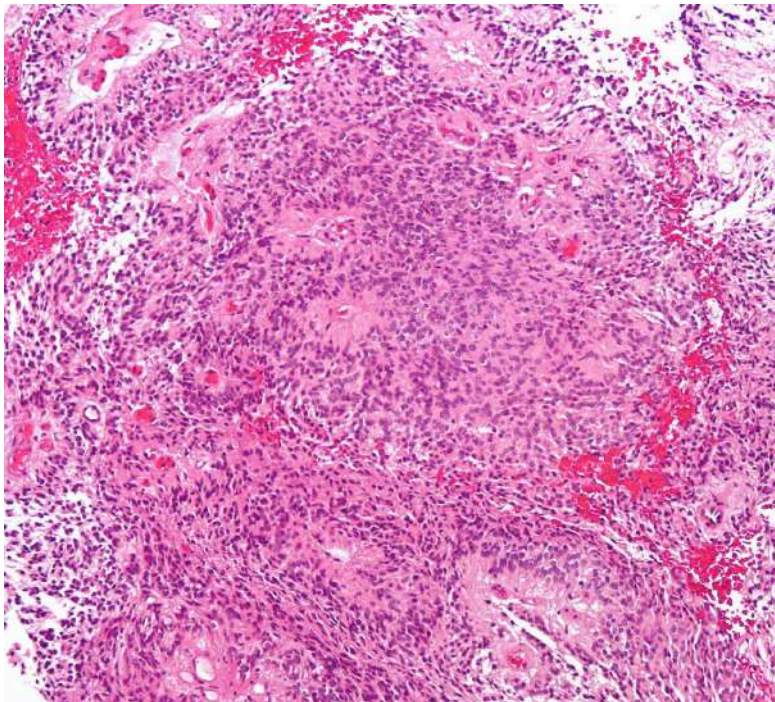
F - Hemangioblastoma

Explanation Why

[Hemangioblastomas](#) are rare, highly vascularized, [infratentorial brain tumors](#), that may occur sporadically or as a manifestation of [von Hippel-Lindau \(VHL\) disease](#). As in this case, patients often present with [features of increased intracranial pressure](#) (e.g., [headache](#), vomiting, blurred vision, [papilledema](#)). [Hemangioblastomas](#) are further associated with [polycythemia](#), caused by [paraneoplastic](#) erythropoietin production. [Histology](#) shows densely packed, thin-walled [capillary](#) vessels surrounded by large stromal cells with intracytoplasmic lipid inclusions, as seen here. [VHL](#)-associated tumors most commonly occur in early adulthood and include [hemangioblastomas](#) of the [spine](#), [cerebellum](#), and [retina](#) (commonly bilateral and peripherally located, as seen here), [renal cell carcinomas](#), [pheochromocytomas](#), and [pancreatic](#) cysts.

G - Ependymoma

Image



Explanation Why

Intracranial [ependymomas](#), which are commonly located in the [infratentorial](#) region, may present with [features of increased intracranial pressure](#) (e.g., [headache](#), vomiting, blurred vision, [papilledema](#)), as seen in this patient. However, they are not associated with retinal vascular changes. Moreover, this type of [tumor](#) most commonly develops in early childhood. [Histology](#) typically shows [perivascular pseudorosettes](#) and rod-shaped blepharoplasts, which are not seen in this patient's photomicrograph. Finally, [ependymomas](#) are not a manifestation of [von Hippel-Lindau](#) disease but instead are associated with [neurofibromatosis type 2](#).

Question # 3

A 52-year-old man is brought to the emergency department 30 minutes after his farmhand found him on the ground sweating profusely. On arrival, he is lethargic and unable to provide any history. His temperature is 37.5°C (99.5°F), pulse is 42/min, and blood pressure is 95/60 mm Hg. Physical examination shows diaphoresis and excessive salivation. The pupils are constricted. There is scattered expiratory wheezing throughout both lung fields. His clothes are soaked with vomit, urine, and feces. A drug with which of the following mechanisms of action is most appropriate for this patient?

	Answer	Image
A	Non-selective α adrenergic receptor antagonism	
B	β_2 adrenergic receptor agonism	
C	Muscarinic acetylcholine receptor antagonism	
D	Acetylcholinesterase enzyme inhibition	
E	Nicotinic acetylcholine receptor agonism	

Hint

This man's symptoms (fecal and urinary incontinence, miosis, bronchospasm, bradycardia, salivation, diaphoresis) suggest organophosphate poisoning.

Correct Answer

A - Non-selective α adrenergic receptor antagonism

Explanation Why

Non-selective alpha blockers such as phentolamine and [phenoxybenzamine](#) are used to treat [pheochromocytoma](#) and [hypertensive crisis](#). They cause [smooth muscle](#) relaxation by exerting an antagonistic effect on [alpha-1 receptors](#). An alpha blocker would exacerbate this patient's [hypotension](#) and is therefore contraindicated.

B - β_2 adrenergic receptor agonism

Explanation Why

[Beta-2 receptor agonists](#) (e.g., [albuterol](#)) are commonly used to treat bronchospasm (e.g., due to [asthma](#), [COPD](#)). While wheezing was heard during this patient's [pulmonary examination](#), use of a [beta-2 receptor agonist](#) would not address his other life-threatening symptoms, nor the underlying etiology of his [cholinergic crisis](#).

C - Muscarinic acetylcholine receptor antagonism

Explanation But

Because [atropine](#) does not act on [nicotinic receptors](#), it cannot reverse any neuromuscular dysfunction caused by [organophosphate poisoning](#). [Pralidoxime](#), a cholinesterase reactivator, is also effective in treating the nicotinic effects of [organophosphates](#) and should be given in addition to [atropine](#).

Explanation Why

[Atropine](#) is a muscarinic acetylcholine receptor antagonist that is considered the [antidote](#) of choice for [organophosphate poisoning](#), which is likely given this patient's symptoms of [cholinergic crisis](#)

and history of farm work. [Organophosphates](#) are commonly used pesticides that cause irreversible inhibition of acetylcholinesterase, resulting in increased [acetylcholine](#) levels and both muscarinic and [nicotinic receptor](#) activation. [Atropine competitively inhibits](#) the effects of [organophosphates](#) at the [muscarinic receptors](#).

D - Acetylcholinesterase enzyme inhibition

Explanation Why

Acetylcholinesterase enzyme inhibition is the mechanism of action of cholinomimetic drugs such as [neostigmine](#) and [physostigmine](#). These agents function similarly to [organophosphates](#) and would lead to increased levels of [acetylcholine](#) and exacerbation of his [cholinergic crisis](#).

E - Nicotinic acetylcholine receptor agonism

Explanation Why

Nicotinic [acetylcholine](#) receptor [agonism](#) is the mechanism of action of [nicotine](#) (e.g., in cigarettes) and neuromuscular-blocking agents such as [succinylcholine](#). Drugs that cause acetylcholine receptor [agonism](#) would further exacerbate the [cholinergic crisis](#) seen in this patient, and are therefore contraindicated.

Question # 4

A 4-year-old boy is brought to the emergency department because of fever, nausea, and headache for 1 day. His temperature is 39.7°C (103.5°F). Examination shows involuntary flexion of the knees and hips when the neck is flexed. A lumbar puncture is performed and cerebrospinal fluid (CSF) analysis shows numerous segmented neutrophils and a decreased glucose concentration. Gram stain of the CSF shows gram-negative diplococci. This patient is at increased risk for which of the following complications?

	Answer	Image
A	Temporal lobe inflammation	
B	Acute pancreatitis	
C	Adrenal insufficiency	
D	Deep neck abscess	
E	Vesicular skin rash	

Hint

Fever, headache, and a positive Brudzinski sign, along with gram-negative diplococci on CSF gram stain are highly suggestive of meningitis caused by *Neisseria meningitidis*.

Correct Answer

A - Temporal lobe inflammation

Explanation Why

[Temporal lobe inflammation](#) is a common complication of [HSV encephalitis](#). Although [HSV encephalitis](#) can also present with [fever](#) and neck stiffness, this patient lacks characteristic features such as focal neurological deficits, behavioral changes, altered mental status, and/or [seizures](#). Furthermore, his [CSF gram stain](#) is not consistent with a viral infection.

B - Acute pancreatitis

Explanation Why

[Pancreatitis](#) is a possible complication of [mumps](#) infection, which can also cause [meningitis](#) and present with similar symptoms to this patient. However, his [CSF gram stain](#) is not consistent with viral infection, making [pancreatitis](#) unlikely to occur.

C - Adrenal insufficiency

Explanation Why

[Waterhouse-Friderichsen syndrome](#) is a rare but potentially lethal complication of [meningococcal meningitis](#). It results from an [endotoxin](#)-triggered [coagulopathy](#), and is characterized by [adrenal hemorrhage](#) and subsequent primary [adrenal insufficiency](#) (low [cortisol](#), elevated [ACTH](#)). In addition to [adrenal insufficiency](#), further signs may include [petechiae](#), [purpura](#), [disseminated intravascular coagulation](#), respiratory failure, and [shock](#).

D - Deep neck abscess

Explanation Why

A deep neck [abscess](#) can occur as a complication of [acute tonsillitis](#), [pharyngitis](#), dental infections, or upper respiratory tract infections. A deep neck [abscess](#) may cause [meningitis](#) if the infection expands into the meningeal space or [CSF](#), but it is not a known sequela of [meningitis](#).

E - Vesicular skin rash

Explanation Why

[Varicella-zoster virus \(VZV\)](#) infection is a common cause of vesicular [skin](#) eruptions in pediatric patients and can also result in [meningitis](#) or encephalitis. However, the vesicular [skin](#) eruption in [VZV](#) infection usually precedes the [CNS](#) infection, rather than being a sequela of the disease. Furthermore, this patient's [CSF gram stain](#) is not consistent with [VZV](#) infection and rather indicates a bacterial infection.

Question # 5

An 8-year-old boy is brought to the physician by his mother because of a 3-week history of irritability and frequent bed wetting. She also reports that he has been unable to look upward without tilting his head back for the past 2 months. He is at the 50th percentile for height and weight. His vital signs are within normal limits. Ophthalmological examination shows dilated pupils that are not reactive to light and bilateral optic disc swelling. Pubic hair development is Tanner stage 2. The most likely cause of this patient's condition is a tumor in which of the following locations?

	Answer	Image
A	Cerebral falx	
B	Dorsal midbrain	
C	Cerebellopontine angle	
D	Fourth ventricle	
E	Sella turcica	
F	Cerebellar vermis	

Hint

This patient presents with vertical gaze palsy and signs of increased intracranial pressure (papilledema). These findings are suggestive of a brain tumor that is causing compression symptoms due to hydrocephalus. Signs of precocious puberty are due to the tumor cell line.

Correct Answer

A - Cerebral falx

Explanation Why

[Meningiomas](#) often arise in the [cerebral falx](#) and are typically asymptomatic due to their slow growth rate. Compression of the adjacent hemisphere can cause [seizures](#) as well as [spastic paraparesis](#) and incontinence. Falcine [meningiomas](#) do not typically cause [hydrocephalus](#) or [precocious puberty](#).

B - Dorsal midbrain

Explanation But

Other causes of [vertical gaze palsy](#) include [stroke](#), [multiple sclerosis](#), and encephalitis.

Explanation Why

[Pinealoma](#) is a childhood [tumor](#) of the [dorsal midbrain](#) that compresses the [pretectal region](#), resulting in [vertical gaze palsy](#). Because of the close proximity to the [cerebral aqueduct](#), [hydrocephalus](#) (due to obstruction of [cerebrospinal fluid](#) outflow pathway) can also develop, which would explain this patient's [increased intracranial pressure](#). The most common type of [pinealoma](#) in children is germinoma, which often secretes [β-hCG](#), stimulating testosterone production and causing [precocious puberty](#) in boys.

C - Cerebellopontine angle

Explanation Why

[Acoustic schwannoma](#) is the most common [tumor](#) of the [cerebellopontine angle](#). Compression of structures adjacent to the [cerebellopontine angle](#) can cause [hydrocephalus](#), but the absence of [vestibulocochlear nerve](#) (CN VIII) involvement (causes unilateral [sensorineural hearing loss](#) and [tinnitus](#), unsteady gait) in this patient and the relatively short clinical course (4 weeks) make [acoustic](#)

[schwannoma](#) (a slow-growing [tumor](#)) an unlikely etiology. Furthermore, the [median](#) age of patients presenting with [acoustic schwannoma](#) is ~ 50 years.

D - Fourth ventricle

Explanation Why

[Ependymomas](#) are childhood tumors that are typically located in the [fourth ventricle](#). This [tumor](#) most commonly presents with [noncommunicating hydrocephalus](#), which can result in compression of a number of [CNS](#) structures and cause [vertical gaze palsy](#) and [central precocious puberty](#). However, in the case of [hydrocephalus](#) due to an [ependymoma](#), symptoms of [hydrocephalus](#) (e.g., irritability, [urinary incontinence](#)) would precede the onset of [vertical gaze palsy](#) unlike this patient who had a [vertical gaze palsy](#) before the onset of [hydrocephalus](#) symptoms.

E - Sella turcica

Explanation Why

[Pituitary tumors](#) arise within the [sella turcica](#). These tumors can cause compression of the [optic chiasm](#) and manifest with [bitemporal hemianopsia](#). Because the [pituitary gland](#) is not in close proximity to the [ventricular system](#), [hydrocephalus](#) does not occur. In addition, [pituitary tumors](#) originating from gonadotropic cells (gonadotroph adenoma) are typically nonsecretory (inactive), resulting in [hypogonadism](#) due to the destruction of functioning gonadotropic cells, instead of [precocious puberty](#).

F - Cerebellar vermis

Explanation Why

[Pilocytic astrocytoma](#) and [medulloblastoma](#) are childhood tumors located in the [cerebellar vermis](#). [Hydrocephalus](#) due to compression of the [fourth ventricle](#) by these tumors can cause [vertical gaze palsy](#) and [central precocious puberty](#). However, in the case of [hydrocephalus](#) due to either of these tumors, symptoms of [hydrocephalus](#) (e.g., irritability, [urinary incontinence](#)) would precede the onset of [vertical gaze palsy](#) unlike this patient who had a [vertical gaze palsy](#) before the onset of

[hydrocephalus](#) symptoms. Additionally, compression of the [cerebellar vermis](#) would cause [truncal ataxia](#), which is not reported in this patient.

Question # 6

A 35-year-old woman comes to the emergency department because of a 3-day history of pain in the left cheek. The pain occurs every few hours, lasts 30–60 seconds, and is aggravated by chewing and brushing. She has a history of pain with a vesicular rash in the right axillary area 1 year ago. She had an upper respiratory infection 2 weeks ago. Physical examination shows no abnormalities. Which of the following is the most likely diagnosis?

	Answer	Image
A	Cluster headache	
B	Paroxysmal hemicrania	
C	Trigeminal neuralgia	
D	Postherpetic neuralgia	
E	Sinus headache	
F	Temporal arteritis	

Hint

The first-line therapy for this patient's condition is carbamazepine.

Correct Answer

A - Cluster headache

Explanation Why

[Cluster headaches](#) usually manifest as attacks of intense unilateral facial [pain](#), occurring ~ 8 times per day and lasting ~ 15 minutes, in contrast to this patient's episodic [pain](#) that lasts 30–60 seconds. The [pain](#) is also usually periorbital or temporal rather than in the cheeks. In addition, autonomic symptoms, such as [conjunctival injection](#), lacrimation, [rhinorrhea](#), and nasal congestion, are often seen in association with [cluster headaches](#).

B - Paroxysmal hemicrania

Explanation Why

[Paroxysmal hemicrania](#) manifests as recurring unilateral periorbital [headaches](#) that occur > 5 times per day and last for 2–45 minutes, in contrast to this patient's episodic cheek [pain](#) that lasts 30–60 seconds. In addition, autonomic symptoms, such as [conjunctival injection](#), lacrimation, [rhinorrhea](#), and nasal congestion, are often seen in association with [paroxysmal hemicrania](#).

C - Trigeminal neuralgia

Explanation But

[Trigeminal neuralgia](#) is a progressive disease (i.e., attacks become more frequent over time) and can cause psychological distress, leading to depression and even suicidal tendencies. In addition, it may be associated with [multiple sclerosis](#) in young women, particularly in cases in which the disease manifests bilaterally.

Explanation Why

[Trigeminal neuralgia](#) is a chronic [pain](#) syndrome characterized by transient (< 1 minute), recurrent,

severe shooting, stabbing, and/or paroxysmal [pain](#) that can occur up to 100 times per day in the distribution of the [trigeminal nerve](#). It most commonly manifests with [pain](#) shooting from the mouth to the angle of the [jaw](#). It can be triggered by a variety of stimuli, including brushing, chewing, cold, and touch. It is not related to this patient's prior rash and upper respiratory infection.

D - Postherpetic neuralgia

Explanation Why

Though this patient may have a history of [shingles](#) in the right [axilla](#), [postherpetic neuralgia](#) manifests with recurrent [pain](#), burning, and/or anesthesia in the same region as a prior [shingles](#) flare, not the episodic unilateral facial [pain](#) seen in this patient.

E - Sinus headache

Explanation Why

Sinus [headaches](#) are caused by bacterial infection of the [maxillary sinuses](#), usually following a viral upper respiratory infection. [Bacterial sinusitis](#) manifests as constant infraorbital [pain](#) and tenderness to palpation over the [maxillary sinuses](#) that is aggravated by leaning forward, which is not seen in this patient. Patients also usually manifest with [fever](#), malaise, and/or [purulent](#) nasal discharge.

F - Temporal arteritis

Explanation Why

[Temporal arteritis](#) can manifest with constant [pain](#) over the temples that is aggravated by chewing, in contrast to this patient's episodic cheek [pain](#) that lasts 30–60 seconds. [Pain](#) associated with [temporal arteritis](#) usually manifests as new-onset, [pulse](#)-synchronous, dull throbbing [headache](#), with associated [jaw claudication](#). Moreover, [temporal arteritis](#) is rarely observed in patients < 50 years of age, and patients often also have scalp tenderness, weight loss, new-onset vision loss, and/or a history of [amaurosis fugax](#).

Question # 7

A 62-year-old woman with type 2 diabetes mellitus comes to the physician because of a 1-year history of progressively worsening paresthesias in her upper limbs. She has accidentally burned her fingers on hot dishes several times. She was involved in a motor vehicle collision 3 years ago. Neurologic examination shows absent temperature sensation with normal fine touch sensation over the upper extremities and chest. Without treatment, this patient is at increased risk of developing which of the following?

	Answer	Image
A	Exaggerated biceps reflex	
B	Decreased Mini-Mental State Examination score	
C	Absent anal wink reflex	
D	Deviation of the jaw	
E	Drooping of the eyelid	
F	Absent knee-jerk reflex	

Hint

This patient's neurologic exam cape-like dissociated sensory loss typical of central cord syndrome, which is most likely the result of syringomyelia secondary to a whiplash injury.

Correct Answer

A - Exaggerated biceps reflex

Explanation Why

[Syringomyelia](#) damages [lower motor neurons](#) in the [anterior horn](#) of the [spinal cord](#), which causes bilateral weakness that can progress to bilateral [flaccid paralysis](#) and muscle [atrophy](#). This would result in decreased or absent [biceps reflex](#). An exaggerated [biceps reflex](#) is present in [upper motor neuron](#) lesions and can be seen in conditions such as [multiple sclerosis](#), [stroke](#), tumors, [vitamin B12 deficiency](#), and [ALS](#).

B - Decreased Mini-Mental State Examination score

Explanation Why

[Syringomyelia](#) does not affect [cognition](#), and therefore, a decreased [MMSE](#) score is not expected in this patient. Conditions associated with [spinal cord](#) involvement and altered [cognition](#) include [subacute combined degeneration](#) due to [vitamin B12 deficiency](#), paralytic dementia, and [tabes dorsalis](#).

C - Absent anal wink reflex

Explanation Why

[Syringomyelia](#) does not affect the [anal wink](#) reflex, even if left untreated and expansion of the [syrinx](#) occurs. The [anal wink](#) reflex is controlled by the [pudendal nerve](#) and nerve fibers arising from the sacral region, specifically at the level of S2 to S4. These fibers are not affected by [syringomyelia](#).

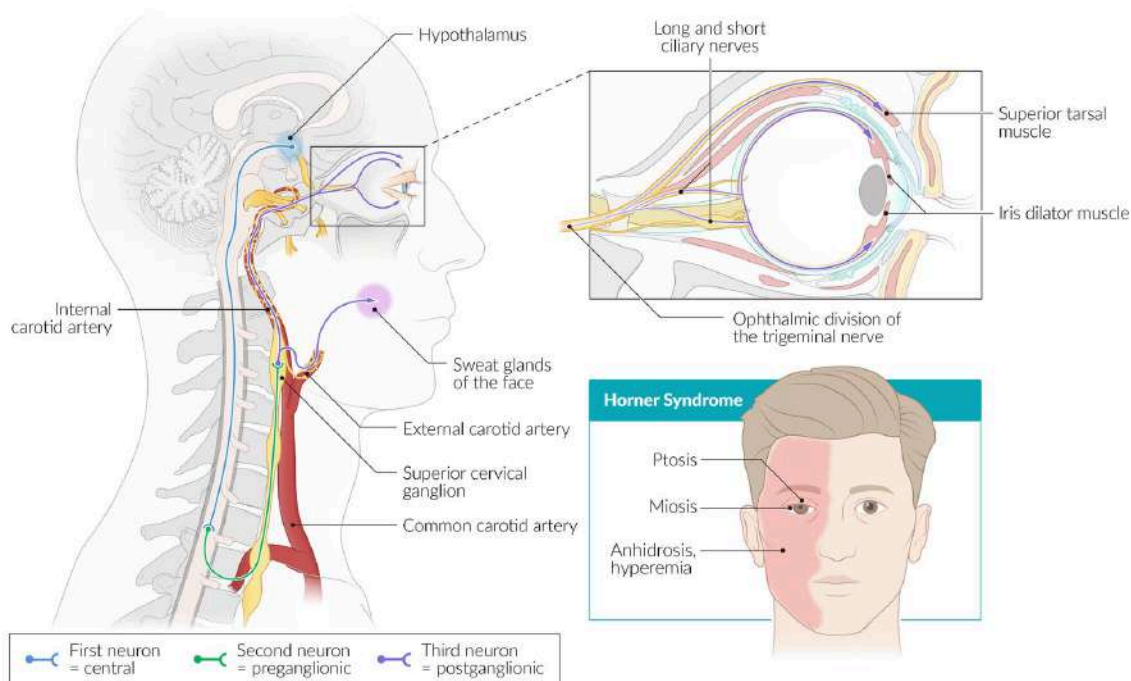
D - Deviation of the jaw

Explanation Why

Because [syringomyelia](#) does not affect the [trigeminal nerve](#), deviation of the [jaw](#) is highly unlikely. The [trigeminal nerve](#) (CN V), specifically the mandibular branch (V3), provides innervation to the [muscles of mastication](#), which include the [masseter](#), [temporalis](#), [medial pterygoid](#), and [lateral pterygoid muscle](#).

E - Drooping of the eyelid

Image



Explanation Why

Drooping of the [eyelid](#) ([ptosis](#)) is part of the [triad of Horner syndrome](#). This patient's presentation ([dysesthetic pain](#), absent temperature sensation, normal fine touch sensation) and history of a motor vehicle accident indicate [syringomyelia](#). Without treatment, expansion of the [syrinx](#) can damage

descending [hypothalamic](#) fibers in the T1 to T4 segments, which carry [sympathetic](#) fibers from the [hypothalamus](#) to the [intermediate horn](#), resulting in central [Horner syndrome](#).

F - Absent knee-jerk reflex

Explanation Why

Expansion of the [syrinx](#) can cause damage to the [corticospinal tract](#), which manifests as a hyperactive (not an absent) [knee-jerk reflex](#). In addition, [spasticity](#) and muscle spasm of the lower extremities can develop due to disruption of descending inhibitory fibers from [upper motor neurons](#). An absent [knee-jerk reflex](#) indicates a [lower motor neuron lesion](#).

Question # 8

A previously healthy 16-year-old girl is brought to the physician by her parents because of behavior changes and involuntary limb movements over the past 2 days. She also has a 2-week history of fever, headache, and fatigue. Her temperature is 38°C (100.4°F), pulse is 110/min, respirations are 20/min, and blood pressure is 102/72 mm Hg. Mental status examination shows impaired speech and a disorganized thought process. Muscle strength is 5/5 in all extremities. Urine toxicology screening is negative.

Cerebrospinal fluid analysis shows a leukocyte count of 70 cells/mm³ (90% lymphocytes) and a protein concentration of 51 mg/dL. Abdominal ultrasound shows a large right adnexal mass. The patient's symptoms are most likely caused by antibodies against which of the following?

	Answer	Image
A	Purkinje cell Yo antigens	
B	GM1 ganglioside	
C	Acetylcholine receptors	The diagram, titled 'Myasthenia Gravis: Autoantibodies', illustrates three mechanisms of autoantibody action on ACh receptors (AChR) at the neuromuscular junction: Blockade of ACh receptors: An antibody binds to the AChR, preventing ACh from binding. This results in 'No muscle activation' and 'Muscle Weakness'. Receptor internalization/degradation: An antibody binds to the AChR, leading to its internalization and degradation. This also results in 'No muscle activation' and 'Muscle Weakness'. Complement activation: An antibody binds to the AChR, activating the complement system. This leads to the formation of the Membrane Attack Complex (MAC), which causes 'Muscle Cell Lysis'. All three pathways ultimately lead to 'Muscle Weakness'.
D	Neuronal Hu antigens	
E	Glutamate receptors	

Hint

This young girl with an adnexal mass has features of paraneoplastic encephalomyelitis such as cognitive defects, personality changes, speech impairment, involuntary limb movements, and autonomic instability (tachycardia, hypotension)

Correct Answer

A - Purkinje cell Yo antigens

Explanation Why

[Autoantibodies](#) against the Yo antigens of [cerebellar Purkinje cells](#) are seen in [paraneoplastic cerebellar degeneration](#) (PCD) due to gynecological malignancies such as [ovarian cancer](#) (adnexal mass). [Cerebellar](#) degeneration can result in impaired [speech](#) due to [dysarthria](#). However, [cerebellar](#) degeneration would not cause features of cognitive defects (e.g., personality change) or autonomic instability (e.g., [tachycardia](#), [hypotension](#)), and patients with [cerebellar](#) degeneration would have loss of coordination ([intention tremor](#), [dysidiadochokinesia](#), [ataxia](#)) and nystagmus rather than involuntary limb movements.

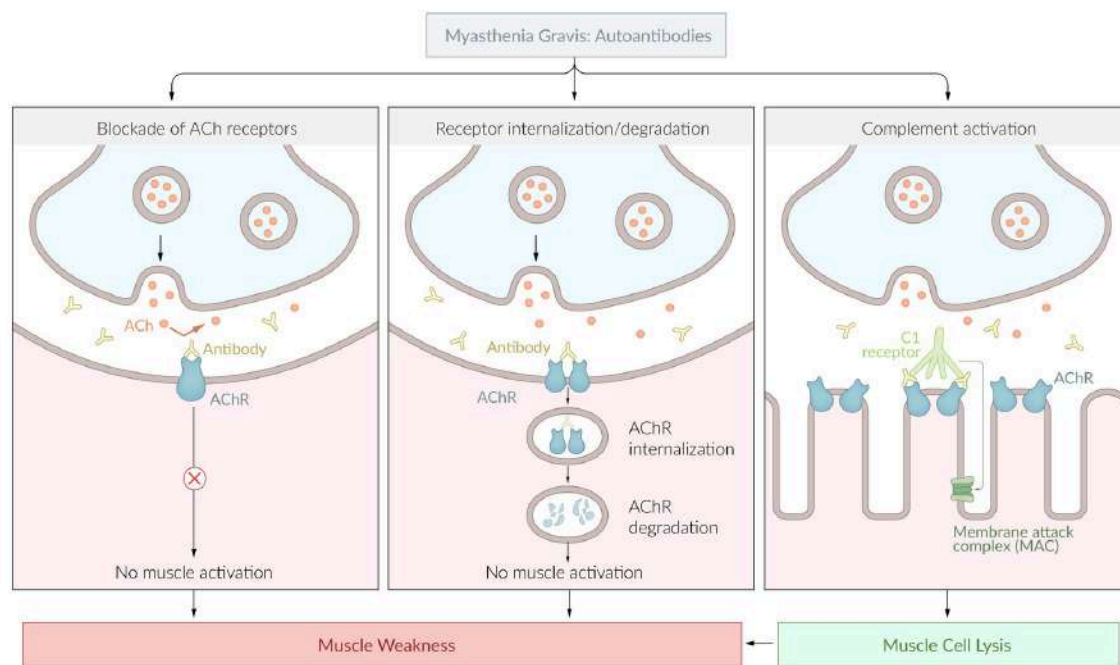
B - GM1 ganglioside

Explanation Why

GM1 ganglioside autoantibodies occur in patients with Guillain-Barré syndrome (GBS). GBS can cause features of autonomic instability (e.g., [tachycardia](#), [hypotension](#)) and [CSF lymphocytic pleocytosis](#), and GBS might be preceded by symptoms of a viral infection (e.g., [fever](#), [headache](#), fatigue). However, patients with GBS would typically have ascending muscle weakness, unlike this patient with 5/5 limb strength in all extremities, and GBS would not cause involuntary limb movements or cognitive defects, which are seen here.

C - Acetylcholine receptors

Image



Explanation Why

[Antibodies](#) targeting acetylcholine receptors cause [myasthenia gravis](#) (MG), which would present with symptoms such as muscle weakness, [diplopia](#), and/or [ptosis](#). MG does not cause cognitive or [speech](#) defects. Moreover, [paraneoplastic](#) MG is typically associated with [thymoma](#). A different [paraneoplastic](#) disorder is more likely in this patient with normal limb strength, cognitive defects, and an adnexal mass.

D - Neuronal Hu antigens

Explanation Why

[Autoantibodies](#) against neuronal Hu antigens can cause [paraneoplastic encephalomyelitis](#), as seen here. However, anti-Hu encephalitis is typically a [paraneoplastic](#) manifestation of [small cell lung](#)

[cancer](#). A different diagnosis is more likely in this patient with an adnexal mass.

E - Glutamate receptors

Explanation Why

NMDA glutamate receptors are targeted by [antibodies](#) in [anti-NMDA encephalitis](#), which is a type of [paraneoplastic encephalomyelitis](#) (PEM) that is typically associated with ovarian [teratoma](#). Patients with PEM can have a [prodrome](#) of [fever](#), [headache](#), and fatigue lasting weeks to months before the onset of features of [CNS](#) damage. [CSF analysis](#) of patients with PEM can show [lymphocytic pleocytosis](#) with increased protein concentration. Another cause of PEM is [autoantibodies](#) against neuronal Hu antigens (anti-Hu encephalitis), which typically occur in patients with [small cell lung cancer](#).

Question # 9

A 26-year-old woman comes to the physician for a follow-up examination 1 week after undergoing rotator cuff repair surgery. Physical examination of the right shoulder shows decreased sensation to pinprick and light touch over the lateral shoulder. There is normal passive range of motion of the shoulder, but she has difficulty externally rotating and abducting her right arm. Which of the following structures was most likely injured during the surgery?

	Answer	Image
A	Radial nerve	
B	Upper trunk of the brachial plexus	
C	Axillary nerve	
D	Lower trunk of the brachial plexus	

	Answer	Image
E	Long thoracic nerve	

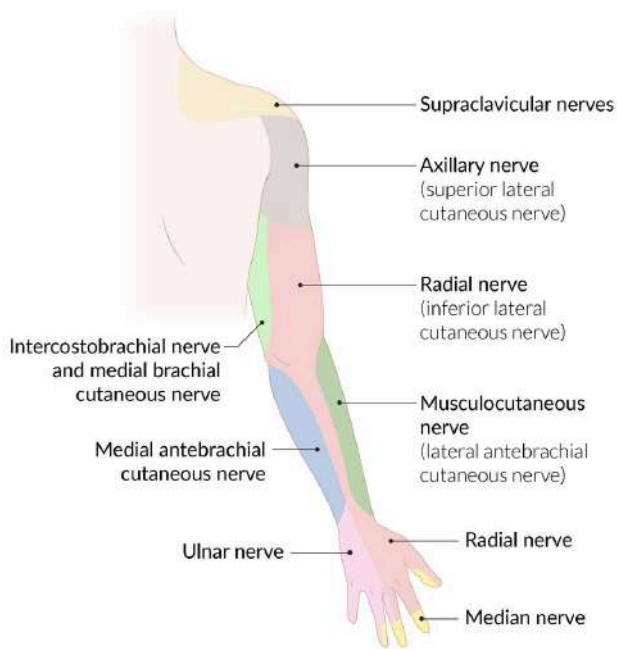
Hint

Injury to this structure can also occur after delayed reduction of an anterior shoulder dislocation.

Correct Answer

A - Radial nerve

Image



Explanation Why

The radial nerve can be injured by compression within the [axilla](#) (e.g., due to crutches), a midshaft [fracture](#) of the [humerus](#), or repeated [pronation/supination](#) of the forearm. In contrast to the features seen in this patient, [radial nerve palsy](#) manifests with impaired [elbow](#), wrist, and finger extension; reduced grip strength; and sensory deficits over the [posterior](#) arm, [posterior](#) forearm, and [dorsal](#) hand.

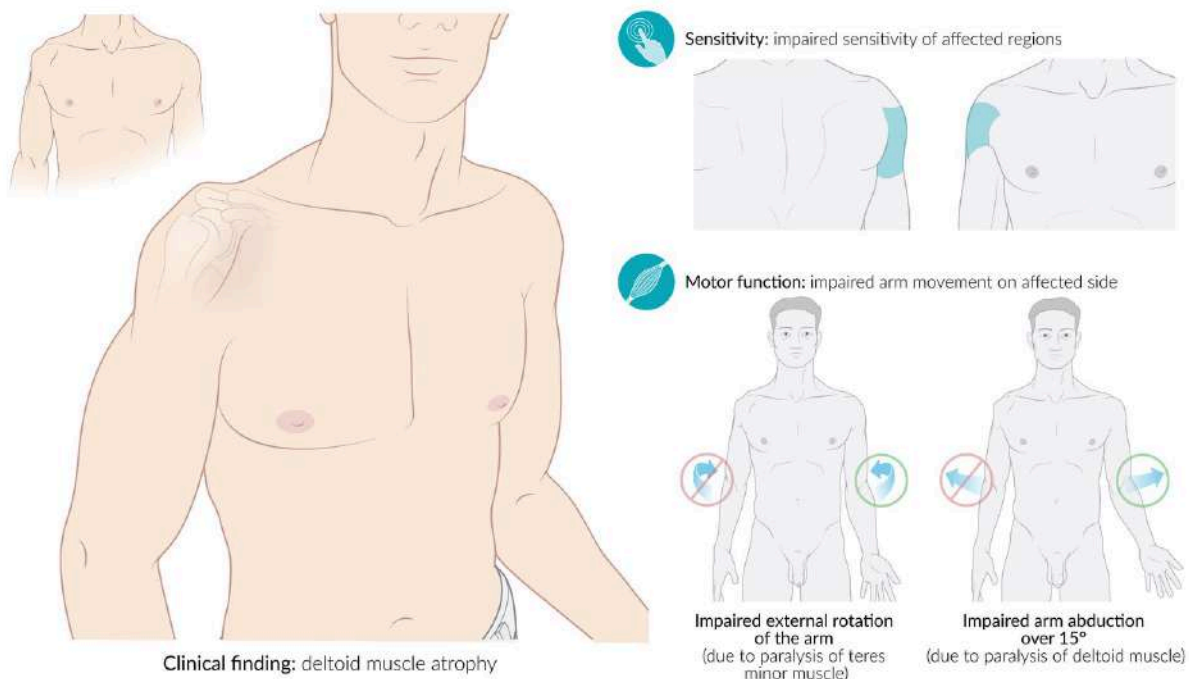
B - Upper trunk of the brachial plexus

Explanation Why

Injury to the [upper trunk of the brachial plexus](#) results in [Erb palsy](#). Paralysis of the deltoid, [supraspinatus](#), and [infraspinatus](#) muscles results in impaired shoulder [abduction](#) and [external rotation](#), which are both seen in this patient. However, the [biceps brachii muscle](#) is also affected, resulting in impaired [flexion](#) and [supination](#). Patients present with an extended, medially rotated, and [pronated](#) arm. In adults, [Erb palsy](#) typically occurs secondary to trauma (excessive traction or tear of the nerves). It occurs most often in [newborns](#) as a result of excessive [lateral flexion](#) of the head during delivery.

C - Axillary nerve

Image



Explanation Why

Injury to the [axillary nerve](#) results in impaired [abduction](#) (from 15–100°) due to deltoid paralysis, limited [external rotation](#) due to [teres minor](#) paralysis, and sensory deficits over the [skin](#) of the [lateral](#) deltoid. Because the [axillary nerve](#) circumflexes the [neck of the humerus](#), injury to the nerve from excessive traction or direct injury can result from [rotator cuff](#) surgery, [fracture](#) of the [surgical neck of the humerus](#), or [anterior](#) dislocation of the [humerus](#).

D - Lower trunk of the brachial plexus

Explanation Why

In adults, injury to the [lower trunk of the brachial plexus](#) typically occurs secondary to trauma (e.g., an attempt to grab an object to break a fall from a height) and leads to [Klumpke palsy](#). In contrast to this patient's features, it manifests as paralysis of the intrinsic hand muscles ([lumbricals](#), [interossei](#), [thenar eminence](#), and [hypothenar muscles](#)) and often [forearm muscles](#) (flexors of the wrist and fingers; sometimes also the pronators), which classically presents as “[claw hand](#).” [Klumpke palsy](#) is uncommon in adults. It is most commonly seen in [newborns](#) following a [birth trauma](#) (i.e., hyperabduction of the arm during delivery).

E - Long thoracic nerve

Explanation Why

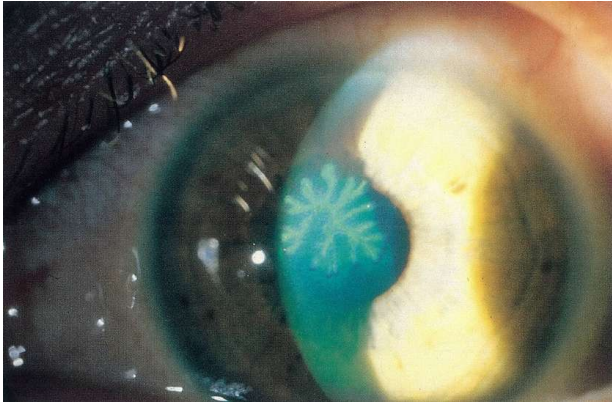
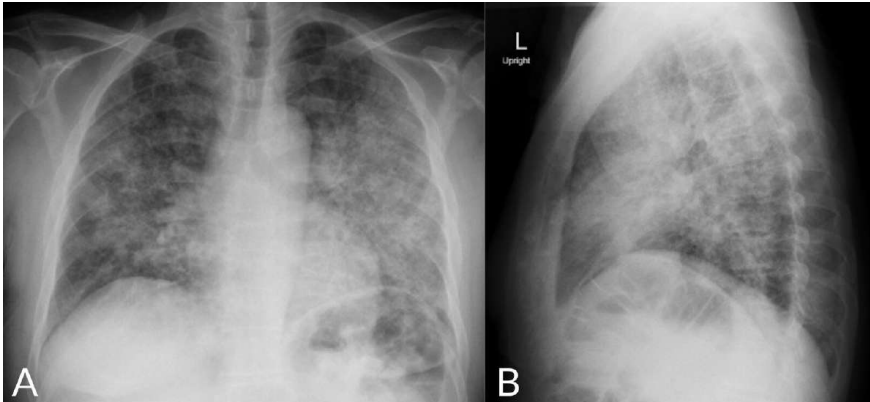
[Long thoracic nerve injury](#) typically occurs secondary to [chest wall injuries](#) and axillary node dissection during [mastectomy](#). Injury to this nerve results in paralysis of the [serratus anterior muscle](#), which causes [medial winging of the scapula](#) and impaired shoulder [abduction](#) beyond 90°. [Long thoracic nerve injury](#) would not, however, account for this patient's sensory deficit over the [lateral](#) shoulder or the impaired [external rotation](#) in her arm.

Question # 10

A 34-year-old man comes to the physician because of a 2-day history of progressively blurred vision. He also reports seeing flashing lights in his visual field. He does not have any pain. The patient has not been examined by a physician in several years. He appears emaciated. Examination shows right conjunctival injection. Visual acuity is 20/20 in the left eye and 20/100 in the right eye. Fundoscopic examination of the right eye is shown. His CD4+ T-lymphocyte count is $46/\text{mm}^3$. Which of the following is the most appropriate pharmacotherapy for this patient's eye condition?



	Answer	Image
A	Valganciclovir	

	Answer	Image
B	Acyclovir	 A clinical photograph of a human eye showing anterior chamber uveitis. The iris is partially obscured by a dense, yellowish-white inflammatory exudate (hypopyon) that has settled at the bottom of the anterior chamber. The visible portion of the iris shows a normal pattern.
C	Penicillin G	
D	Famciclovir	 A clinical photograph of a skin rash on a person's arm. The rash consists of numerous small, red, vesicular lesions (blisters) that are clustered together, characteristic of a herpes zoster (shingles) outbreak.
E	Sulfadiazine and pyrimethamine	
F	Trimethoprim-sulfamethoxazole	 Two chest X-ray images. Image A is a frontal view showing bilateral, patchy, and somewhat confluent opacities in the lung fields, suggesting pneumonia. Image B is a lateral view of the chest, also showing opacities in the lung parenchyma. The label 'L Upright' is visible in the upper right corner of image B, and the letter 'A' is in the bottom left corner of image A.

Hint

Fundoscopy in this patient, whose depressed CD4⁺ T-lymphocyte count is almost certainly secondary to infection with the human immunodeficiency virus (HIV), shows fluffy, hemorrhagic, perivascular retinal lesions that radiate out from the optic disc (pizza-pie appearance). These symptoms and findings are characteristic of cytomegalovirus (CMV) retinitis.

Correct Answer

A - Valganciclovir

Explanation But

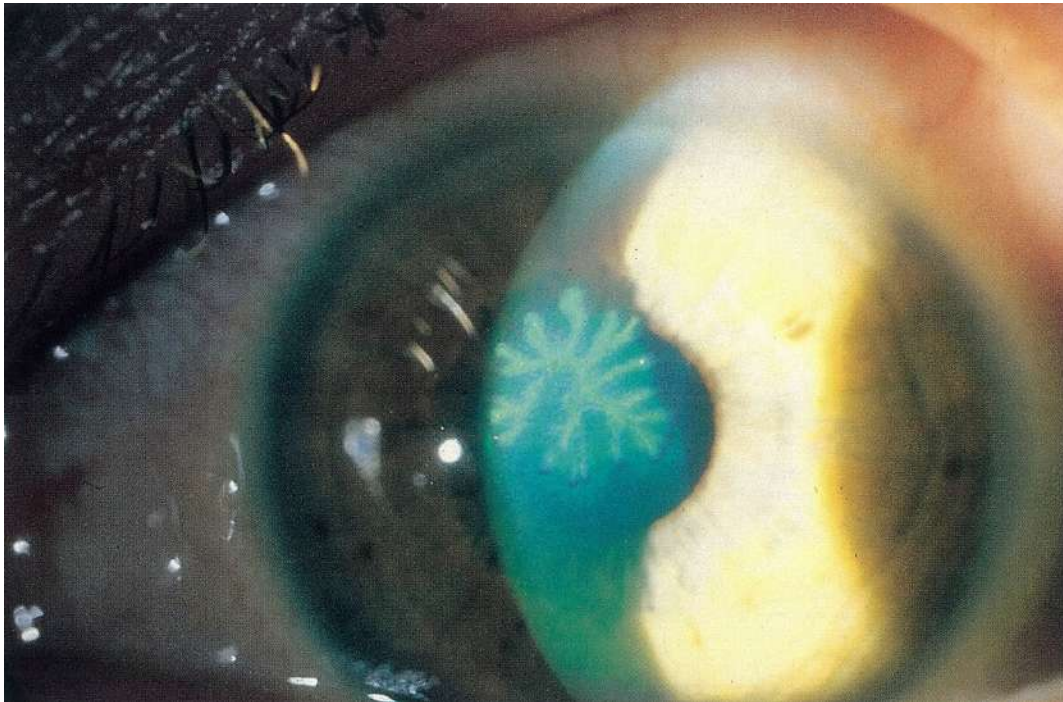
Additionally, this patient should be started on an antiretroviral therapy to increase his [CD4+ T-lymphocyte](#) count.

Explanation Why

[Valganciclovir](#) is a first-line systemic therapy for [CMV retinitis](#), a condition that can cause blurring, vision loss, [floaters](#), and [photopsia](#) (flashing lights). It usually occurs unilaterally (right [eye](#) in this patient) but can affect the other [eye](#) if untreated. Other first-line systemic therapies include [ganciclovir](#), [foscarnet](#), and [cidofovir](#). Patients with acutely sight-threatening disease (e.g., lesions < 1.5 mm from the fovea or adjacent to the [optic nerve](#) head) should also receive intravitreal therapy with [ganciclovir](#) or [foscarnet](#). Other [CMV infections](#) that develop in patients with [CD4+ T-cell](#) count < 50/mm³ include [CMV esophagitis](#), [CMV colitis](#), [CMV pneumonitis](#), and [CMV encephalitis](#).

B - Acyclovir

Image



Explanation Why

[Acyclovir](#) is used to treat herpes simplex virus (HSV) and [varicella-zoster virus \(VZV\)](#) infections, which can affect the eyes and present with visual blurring and [conjunctivitis](#). However, [HSV keratitis](#) and [VZV keratitis](#) both present with corneal ulcers and are typically painful. The extensive hemorrhagic lesions seen in this patient are not common manifestations of HSV or [VZV](#) ocular infections. [Acyclovir](#) is ineffective against [CMV](#).

C - Penicillin G

Explanation Why

[Penicillin G](#) is used to treat [syphilis](#), which can affect the [uvea](#) and [optic nerve](#) (and, less commonly, other ocular structures). Though ocular [syphilis](#) causes [conjunctival injection](#) and decreased visual

acuity, it typically also causes [eye pain](#) and photophobia. Syphilitic [uveitis](#) also causes perivascular retinal [inflammation](#) and depigmentation of the [retina](#), unlike the extensive hemorrhagic lesions seen in this patient. Additionally, isolated ocular findings are rare; patients typically have other findings of primary or [secondary syphilis](#) (e.g., [chancre](#), [condyloma lata](#), or [generalized lymphadenopathy](#)). [Penicillin G](#) is ineffective against [CMV](#).

D - Famciclovir

Image



Explanation Why

[Famciclovir](#) is used to treat [shingles](#) caused by [varicella-zoster virus \(VZV\)](#) as well as genital and labial [herpes simplex virus infections \(HSV\)](#). Though [VZV](#) and HSV can affect the eyes and cause visual blurring and [conjunctivitis](#), these infections both present with corneal ulcers and are typically painful. [Famciclovir](#) is not approved for ocular manifestations of [VZV](#) or HSV, nor is it effective against [CMV](#).

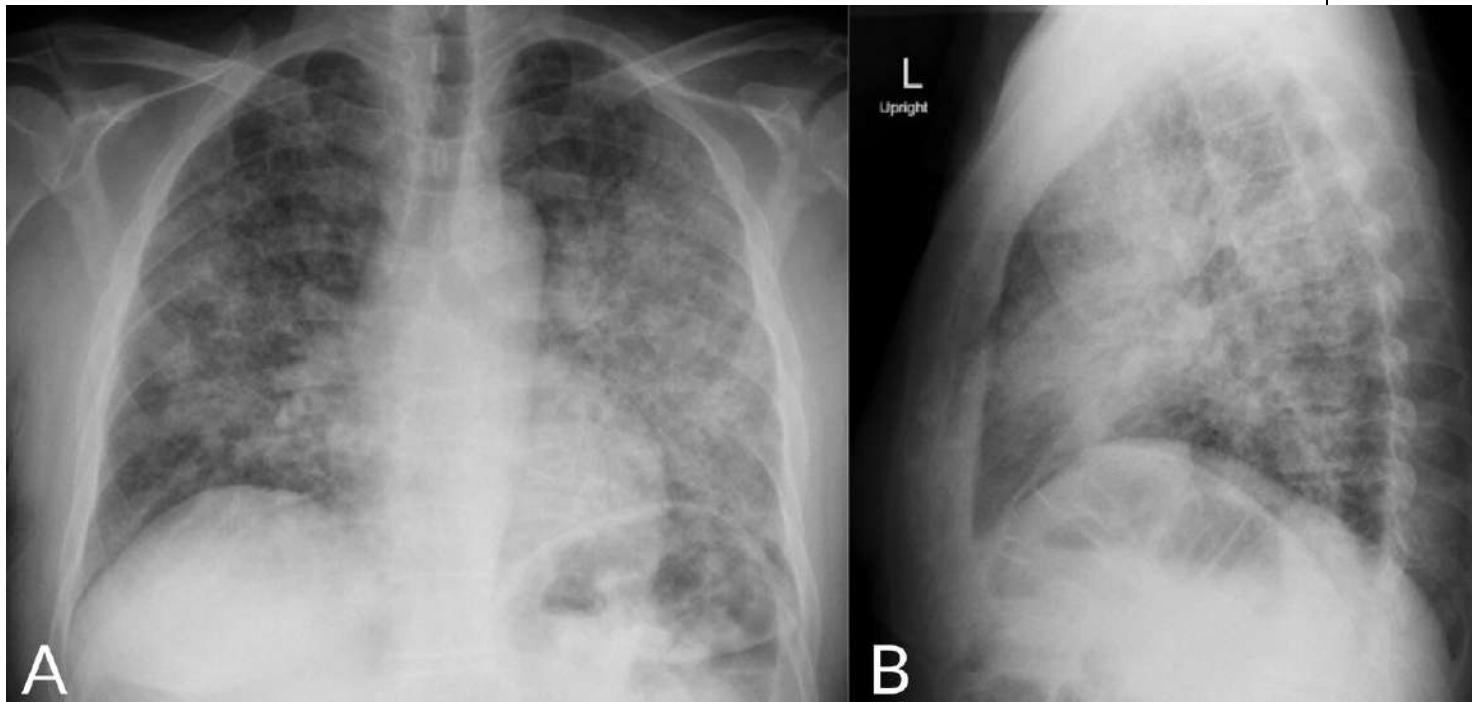
E - Sulfadiazine and pyrimethamine

Explanation Why

[Sulfadiazine](#) and [pyrimethamine](#) are used in combination to treat [toxoplasmosis](#), which can cause [chorioretinitis](#). Though [toxoplasmosis retinochoroiditis](#) results in decreased visual acuity, it typically also causes [eye pain](#). Additionally, unlike the perivascular retinal lesions seen in this patient, toxoplasmic [chorioretinitis](#) causes yellow-white, fluffy lesions in a nonvascular distribution. [Sulfadiazine](#) and [pyrimethamine](#) are ineffective against [CMV](#).

F - Trimethoprim-sulfamethoxazole

Image



Explanation Why

[Trimethoprim-sulfamethoxazole](#) (TMP-SMX) is commonly used for [Pneumocystis jirovecii pneumonia](#) prophylaxis in patients with [CD4+ T-lymphocyte](#) count $< 200/\text{mm}^3$. It is also used to

treat Pneumocystis choroiditis, a condition typically seen in patients with disseminated *Pneumocystis* infections. Pneumocystis choroiditis manifests with multiple, bilateral, yellow-white choroidal lesions that spare the [retina](#). Visual changes are uncommon. [TMP-SMX](#) is ineffective against [CMV](#).

Question # 11

A 21-year-old man comes to the physician's office due to a 3-week history of fatigue and a rash, along with the recent development of joint pain that has moved from his knee to his elbows. The patient reports going camping last month but denies having been bitten by a tick. His past medical history is significant for asthma treated with an albuterol inhaler. His pulse is 54/min and blood pressure is 110/72. Physical examination reveals multiple circular red rings with central clearings on the right arm and chest. There is a normal range of motion in all joints and 5/5 strength bilaterally in the upper and lower extremities. Without proper treatment, the patient is at highest risk for which of the following complications?

	Answer	Image
A	Cranial nerve palsy	Lyme disease Epidemiology Spc approx. 1:41 (1° > 0°) Reported incidence (U.S. total, 2018): 7.2/100,000 Exact incidence unknown. Cases concentrated in the Northeast and upper Midwest. Most common vector-borne disease in the US Etiology Pathogen: <i>Borrelia burgdorferi</i> Vector: Tick species of genus Ixodes (primarily Ixodes scapularis) Risk of infection increases with duration of tick blood meal Diagnosis Two-step serological testing: Initial test (EUSA) + confirmatory test (western blot) Treatment Oral or IV antibiotics Note National notifiable disease Prevention: No vaccine available → avoid exposure, appropriate tick removal Differential diagnosis includes other tick-borne diseases, e.g. RMSF Early localized infection (stage I) Flu-like symptoms: - Fever, fatigue - Mild neck stiffness - Headache, myalgia, arthralgia Erythema chronicum migrans (~80% of patients) Liver function abnormalities Early disseminated infection (stage II) Early neuroborreliosis E.g., meningitis, cranial nerve disorders (most commonly facial nerve palsy), peripheral radiculoneuropathy Lyme carditis (conduction disorders, myocarditis may occur) Late disseminated infection (stage III) Lyme arthritis (monoarthritis/oligoarthritis) Late neuroborreliosis E.g., cognitive impairment, abnormal gait, bladder dysfunction, psychiatric changes, peripheral polyneuropathy. Progressive encephalomyelitis is a rare but severe manifestation.
B	Glomerular damage	
C	Heart valve stenosis	
D	Bone marrow failure	
E	Liver capsule inflammation	

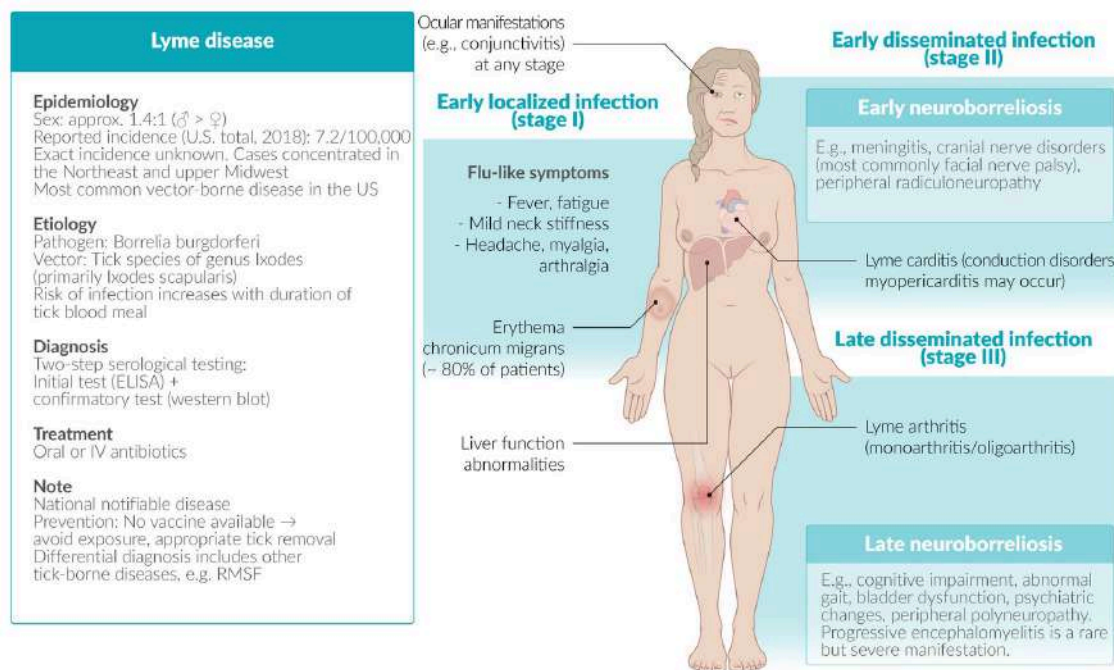
Hint

Lyme disease is caused by *Borrelia burgdorferi*, which is typically transmitted by the bite of the *Ixodes* tick. Camping is, therefore, a risk factor for Lyme disease. Patients typically present with a painless, circular, slowly expanding red ring around the bite site after an incubation period of 7–14 days (early localized Lyme disease). However, in approx. 20% of patients the initial rash at the bite site may not be present. If left untreated, patients will develop early disseminated Lyme disease.

Correct Answer

A - Cranial nerve palsy

Image



Explanation Why

[Cranial nerve](#) palsy, most commonly [Bell palsy](#), is often a finding of early disseminated (stage II) [Lyme disease](#). Other features of this stage of [Lyme disease](#) include migratory arthralgia, [polyneuropathy](#), [meningitis](#), and the risk of developing [cardiac arrhythmia](#) due to an [atrioventricular block](#). This patient should have an urgent [electrocardiogram](#) to evaluate for an [AV block](#) in the setting of his [bradycardia](#).

B - Glomerular damage

Explanation Why

[Glomerular](#) damage can be indicative of Henoch-Schönlein [purpura](#) (HSP), which can manifest with both arthritis and a rash. The rash of HSP, however, is typically described as raised, [erythematous](#), symmetrically distributed [macules](#) or [urticarial](#) lesions which coalesce into palpable [purpura](#) (non-blanching [skin](#) lesions). This patient's rash does not fit this description. In addition, HSP typically presents after an upper respiratory infection; this patient has no history of a recent illness.

C - Heart valve stenosis

Explanation Why

[Heart valve](#) stenosis can be a complication of [rheumatic fever](#) and could present similarly to this patient, with fatigue, migratory arthritis, a circular rash ([erythema marginatum](#)), and possibly, [bradycardia](#). However, this patient does not have the typical history of a prior [Streptococcus pyogenes](#) infection. Additionally, [rheumatic fever](#) is increasingly less common in developed countries because of improved hygiene standards, a decline in infections by rheumatogenic strains of [streptococci](#), and the routine use of [antibiotics](#) for [streptococcal pharyngitis](#). A different diagnosis is much more likely given the recent history of camping.

D - Bone marrow failure

Explanation Why

[Bone marrow](#) failure can be indicative of an [aplastic crisis](#), which is a complication of a [parvovirus B19](#) infection. [Parvovirus B19](#) can manifest with both arthritis and [dermatitis](#); however, children are more likely to develop the “slapped cheek rash” without [joint](#) involvement, while adults often develop symmetrical polyarthritis (fingers, hands, [knees](#), and ankles) without dermatologic manifestations. This patient's migratory, asymmetric arthritis of the large [joints](#) is more likely to have a different cause.

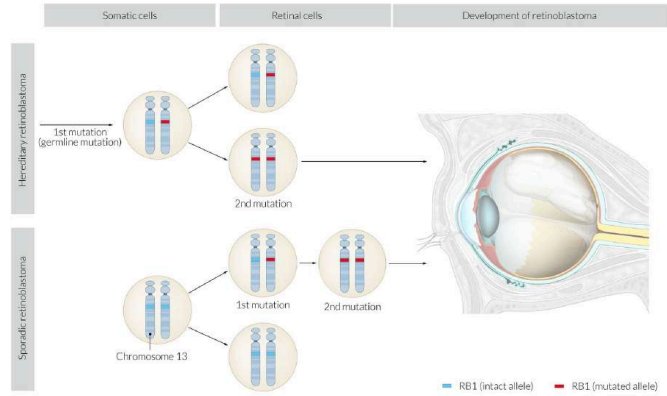
E - Liver capsule inflammation

Explanation Why

[Liver capsule inflammation](#) can be a finding of [Fitz-Hugh-Curtis syndrome](#), a rare complication of [pelvic inflammatory disease](#) secondary to [gonorrhea](#). While [disseminated gonococcal infection](#) can also present with migratory arthritis and [dermatitis](#), the rash is expected to be [pustular](#) or vesicular and accompanied by [tenosynovitis](#). Furthermore, [Fitz-Hugh-Curtis](#) syndrome occurs almost exclusively in women.

Question # 12

A 1-year-old boy is brought to the physician for a well-child examination. He has no history of serious illness. His older sister had an eye disease that required removal of one eye at the age of 3 years. Examination shows inward deviation of the right eye. Indirect ophthalmoscopy shows a white reflex in the right eye and a red reflex in the left eye. The patient is at increased risk for which of the following conditions?

	Answer	Image
A	Neuroblastoma	
B	Acute lymphoblastic leukemia	
C	Basal cell carcinoma	
D	Osteosarcoma	

	Answer	Image
E	Gastric cancer	
F	Wilms tumor	

Hint

This patient has a unilateral white light reflex (leukocoria), which can be a sign of retinoblastoma. The family history of an eye condition that required enucleation strongly suggest a germline mutation in the retinoblastoma gene.

Correct Answer

A - Neuroblastoma

Explanation Why

[Neuroblastoma](#) is the most common [malignancy](#) in [infants](#). About half of the cases are associated with an amplification and overexpression of [oncogene MYCN](#) caused by deletions of the short arm of [chromosome 1](#). A higher [incidence](#) of [neuroblastoma](#) has been described in patients with [Hirschsprung disease](#), [neurofibromatosis type 1](#), and [Turner syndrome](#). However, there is no association with hereditary [retinoblastoma](#).

B - Acute lymphoblastic leukemia

Explanation Why

[Acute lymphoblastic leukemia \(ALL\)](#) is the most common hematologic [malignancy](#) in children. As a secondary [malignancy](#) in patients with hereditary [retinoblastoma](#), however, it is extremely rare. Genetic diseases that increase the risk for development of [ALL](#) include [Down syndrome](#), [neurofibromatosis type 1](#), and [ataxia telangiectasia](#).

C - Basal cell carcinoma

Image

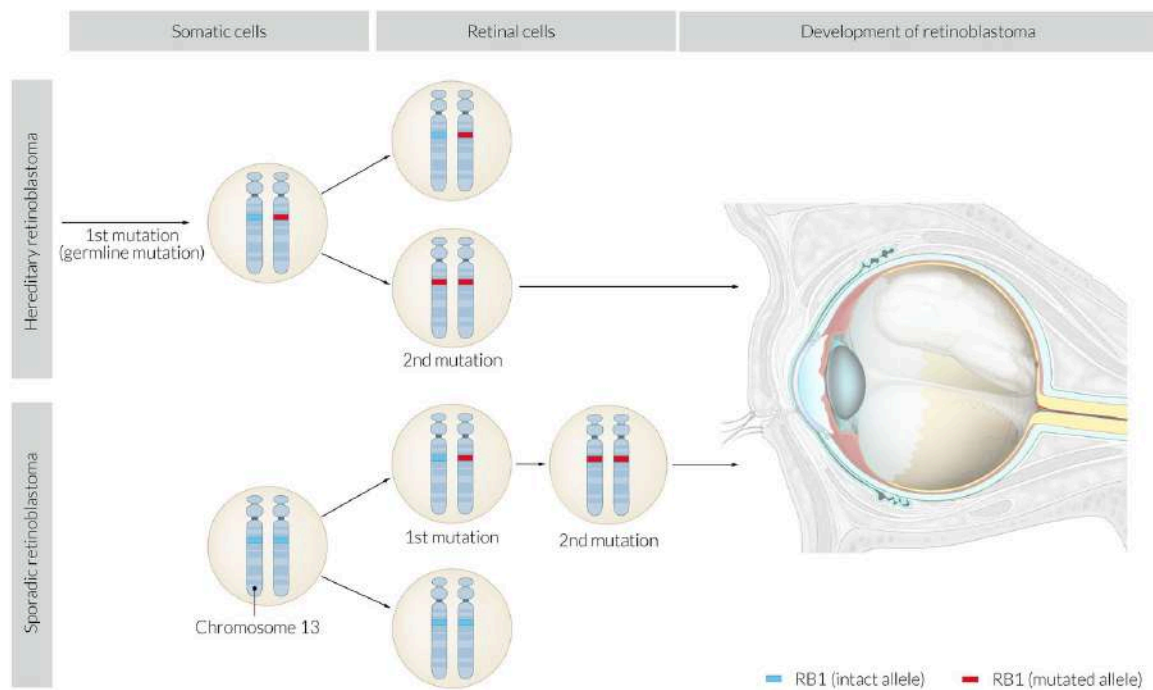


Explanation Why

[Basal cell carcinoma](#) is the most common cutaneous [malignancy](#) and associated with sun exposure. While hereditary [retinoblastoma](#) is associated with a higher risk of [malignant melanoma](#), it is not associated with an increased risk for [basal cell carcinoma](#).

D - Osteosarcoma

Image



Explanation But

[Leukocoria](#) is considered a [retinoblastoma](#) until proven otherwise. A fundus examination of an [infant](#) presenting with [leukocoria](#) should be conducted as quickly as possible.

Explanation Why

Patients with inherited retinoblastoma gene (Rb gene) mutations have a significantly increased risk of developing [osteosarcomas](#). Usually, a [germline mutation](#) takes place in one of the [alleles](#) of the Rb gene only and development of [retinoblastoma](#) does not occur until a spontaneous mutation of the second, priorly functioning [allele](#) results in a non-functioning RB [gene](#) ([two-hit hypothesis](#)). Sporadic [retinoblastomas](#), on the other hand, are caused by two spontaneous mutations in the same retinal cell, affecting both RB [alleles](#).

E - Gastric cancer

Explanation Why

Most [gastric cancers](#) are sporadic, only a minority of cases are associated with hereditary factors (e.g., [hereditary nonpolyposis colon cancer](#)). There is no increased risk for patients with inherited retinoblastoma gene mutations. Moreover, [gastric cancer](#) is extremely rare in children.

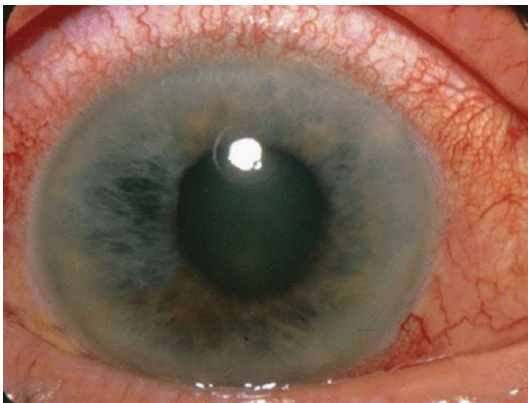
F - Wilms tumor

Explanation Why

[Wilms tumor](#) is the most common renal [malignancy](#) in children. Only a minority of cases are associated with [loss of function mutations](#) (esp. [WT1 gene](#) on [chromosome 11](#)) and specific syndromes (e.g., [WAGR syndrome](#), [Beckwith-Wiedemann syndrome](#)). There is no increased risk for patients with inherited retinoblastoma gene mutations.

Question # 13

A 60-year-old woman is brought to the emergency department because of sudden, painless loss of vision in her right eye that occurred 30 minutes ago while watching TV. She has coronary artery disease, hypertension, and type 2 diabetes mellitus, and has had trouble adhering to her medication regimen. Her blood pressure is 160/85 mm Hg. Examination shows 20/50 vision in the left eye and no perception of light in the right eye. Direct pupillary reflex is present in the left eye but absent in the right eye. Accommodation is intact bilaterally. Intraocular pressure is 16 mm Hg in the left eye and 18 mm Hg in the right eye. Fundoscopic examination of the right eye shows a pale, white retina with a bright red area within the macula. The optic disc appears normal. Which of the following is the most likely diagnosis?

	Answer	Image
A	Central retinal vein occlusion	
B	Retinal detachment	
C	Central retinal artery occlusion	
D	Acute angle-closure glaucoma	
E	Anterior ischemic optic neuropathy	

Hint

Indirect pupillary reflex will likely be absent in the left (not right!) eye, which would be consistent with retinal or optic nerve damage.

Correct Answer

A - Central retinal vein occlusion

Explanation Why

[Hypertension](#), [diabetes](#), and [atherosclerosis](#) are all [risk factors](#) for [ischemic central retinal vein occlusion \(CRVO\)](#). It may present with sudden, painless loss of vision and a [relative afferent pupillary defect](#) as well as severe [edema](#) of the [macula](#) and [optic disc](#). However, fundoscopy would reveal focal retinal hemorrhage instead of a white, pale [retina](#). The most common form of [CRVO](#) is nonischemic and results in a decrease in visual acuity over the course of a few days instead of sudden loss of vision seen here.

B - Retinal detachment

Explanation Why

Both [hypertension](#) and [diabetes mellitus](#) are [risk factors](#) for [retinal detachment](#). Patients with extensive [retinal detachment](#) or [retinal detachment](#) involving the [macula](#) would also present with sudden, painless loss of vision, and an [afferent pupillary defect](#). However, fundoscopy would reveal a gray, detached, freely floating gray [retina](#). Retinal pallor and a cherry red spot within the [macula](#) suggest a different diagnosis.

C - Central retinal artery occlusion

Explanation But

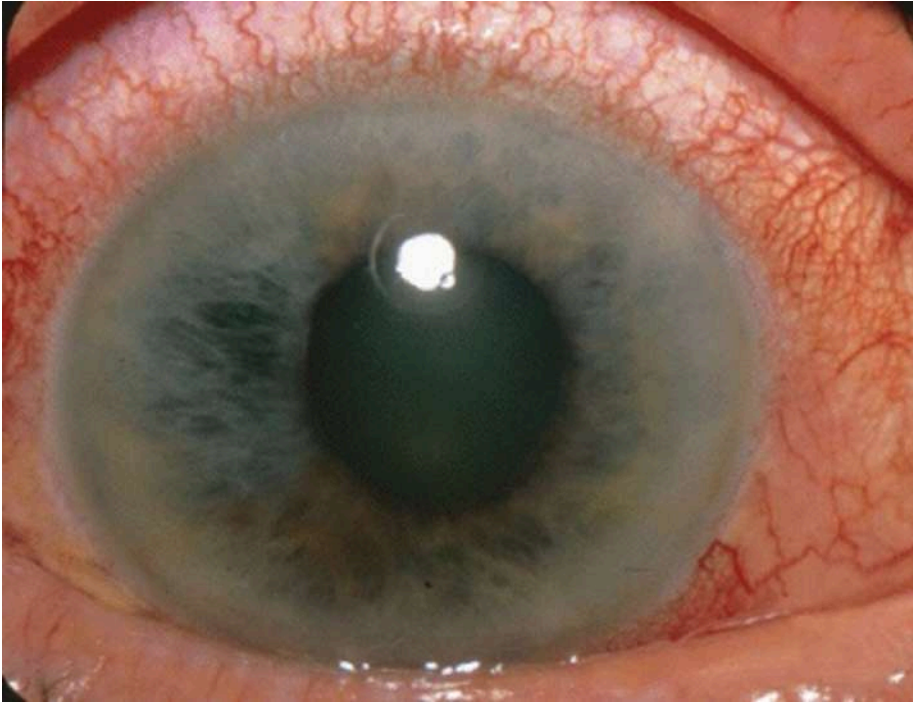
Retinal [artery](#) occlusion is an ophthalmologic emergency. Therapeutic measures include eyeball massage, an inhalation of a mixture of 95% oxygen and 5% carbon dioxide, and arterial [vasodilators](#) (e.g., sublingual [nitroglycerine](#)). A delay in the initiation of therapy can result in permanent loss of vision.

Explanation Why

The patient has multiple [risk factors](#) for retinal [artery](#) disease, including [diabetes](#), [hypertension](#), and [atherosclerosis](#). [Central retinal artery occlusion](#) (CRAO) is characterized by sudden, painless loss of vision and an [afferent pupillary defect](#). Ophthalmoscopy findings of [CRAO](#) include retinal pallor and a cherry-red spot in the foveal region. Narrow retinal vessels with a cattle-truck appearance are another classic finding of retinal [artery](#) occlusion.

D - Acute angle-closure glaucoma

Image



Explanation Why

Patients with acute [angle closure glaucoma](#) may present with sudden loss of vision, and an absent or sluggish [direct pupillary reflex](#). However, the loss of vision in the case of acute [angle closure glaucoma](#) is always associated with severe [pain](#) and increased [intraocular pressure](#) (> 21 mm Hg), as opposed to the normal [intraocular pressure](#) in this patient (18 mm Hg in the right [eye](#)). The [indirect pupillary reflex](#) and the [accommodation reflex](#), which are normal in this patient, would also be impaired. Injection and [chemosis](#) of the [conjunctiva](#), as well as [trigeminal](#) autonomic symptoms such as nausea, vomiting, and lacrimation, which are frequently present in acute [angle closure glaucoma](#),

are absent in this patient. On fundoscopy, the [optic disc](#) would appear [edematous](#) or hyperemic, in contrast to the normal [optic disc](#) in this patient.

E - Anterior ischemic optic neuropathy

Explanation Why

[Anterior ischemic optic neuropathy](#) may also present with sudden, painless loss of vision. However, fundoscopy would reveal a hyperemic or [edematous optic disc](#) and possibly [splinter hemorrhages](#) within the [optic disc](#), as opposed to a normal [optic disc](#) seen in this patient. Retinal and [macular](#) changes would also not be present. Retinal pallor and a cherry red spot within the [macula](#) suggest a different diagnosis.

Question # 14

A 56-year-old man is brought to the emergency department by his neighbor 2 hours after ingesting an unknown substance in a suicide attempt. He is confused and unable to provide further history. His temperature is 39.1°C (102.4°F), pulse is 124/min, respiratory rate is 12/min, and blood pressure is 150/92 mm Hg. His skin is dry. Pupils are 12 mm and minimally reactive. An ECG shows no abnormalities. Which of the following is the most appropriate treatment for this patient's condition?

	Answer	Image
A	Sodium bicarbonate	
B	Naloxone	
C	Physostigmine	
D	N-acetylcysteine	
E	Glucagon	
F	Flumazenil	

Hint

A patient with elevated body temperature, tachycardia, dry skin, mydriasis with cycloplegia, and confusion after ingesting an unknown substance likely has anticholinergic toxicity.

Correct Answer

A - Sodium bicarbonate

Explanation Why

Sodium bicarbonate is used for the treatment of [tricyclic antidepressant](#) (TCA) overdose. Overdose with certain TCAs, such as [amitriptyline](#), can manifest almost identically to an [anticholinergic overdose](#), but with the additional finding of [ECG](#) abnormalities (e.g., [QT prolongation](#), [arrhythmias](#)).

B - Naloxone

Explanation Why

[Naloxone](#) is used for the rapid reversal of an [opioid overdose](#). Though [opioid overdose](#) can also cause altered mental status, it also typically manifests with significantly reduced respiratory drive, [bradycardia](#), [hypotension](#), [hypothermia](#), and [miosis](#).

C - Physostigmine

Explanation Why

[Physostigmine](#) is the first-line treatment for [anticholinergic syndrome](#), as it readily enhances [parasympathetic](#) signaling and is able to cross the [blood-brain barrier](#). In addition to the classic findings seen in this patient, overdose of [anticholinergic drugs](#) can also cause [urinary retention](#), decreased bowel sounds, and [erythematous skin](#) (due to compensatory cutaneous [vasodilation](#) from the hyperthermia).

D - N-acetylcysteine

Explanation Why

[N-acetylcysteine](#) is used for the treatment of [acetaminophen overdose](#) to restore depleted hepatic [glutathione](#), which is needed for the conjugation and excretion of the toxic [acetaminophen](#) metabolites. These patients typically manifest nonspecifically with [nausea and vomiting](#) before eventually progressing to [liver](#) failure (if not treated), in contrast to the acute, severe reaction seen in this patient.

E - Glucagon

Explanation Why

[Glucagon](#) is used in the treatment of [beta blocker overdose](#), as it activates [adenylate cyclase](#) during [depolarization](#), raising intracellular [cAMP](#) levels and improving cardiac contractility. Overdose with these drugs typically manifests with pronounced [bradycardia](#), [cardiogenic shock](#), altered mental status, wheezing (due to bronchoconstriction), and [hypotension](#).

F - Flumazenil

Explanation But

Routine use of [flumazenil](#) for [benzodiazepine overdose](#) is not recommended, as it can potentiate withdrawal symptoms and [seizures](#) in patients with [benzodiazepine dependence](#).

Explanation Why

[Flumazenil](#) may be indicated for severe cases of [benzodiazepine overdose](#), which could explain this patient's signs of [central nervous system](#) depression, such as decreased [respiratory rate](#) and altered mental status. However, [benzodiazepine toxicity](#) typically also causes [hyporeflexia](#) and does not cause [hypertension](#), elevated temperature, dry [skin](#), or [mydriasis](#).

Question # 15

A 65-year-old man comes to the physician because of double vision that began this morning. He has hypertension and type 2 diabetes mellitus. He has smoked two packs of cigarettes daily for 40 years. His current medications include lisinopril, metformin, and insulin. Physical examination shows the right eye is abducted and depressed with slight intorsion. Visual acuity is 20/20 in both eyes. Extraocular movements of the left eye are normal. Serum studies show a hemoglobin A_{1c} of 11.5%. Which of the following additional findings is most likely in this patient?

	Answer	Image
A	Inability to abduct the right eye	
B	Absent consensual light reaction on the right eye	
C	Loss of the right nasolabial fold	
D	Upper eyelid droop on the right eye	
E	Loss of smell	
F	Absent direct light reaction on the right eye	

Hint

The most likely cause of an isolated oculomotor nerve palsy in a patient with uncontrolled diabetes mellitus is diabetic mononeuropathy, which occurs as a result of microangiopathic ischemia.

Correct Answer

A - Inability to abduct the right eye

Explanation Why

This patient has an isolated [oculomotor nerve palsy](#) due to his poorly controlled [diabetes](#), as the right [eye](#) is [abducted](#) with slight [intorsion](#). [Abduction](#) of the [eye](#) is governed by the [abducens nerve \(CN VI\)](#), which is unlikely to be affected by [diabetic microangiopathy](#).

B - Absent consensual light reaction on the right eye

Explanation Why

An absent consensual light reaction on the right [eye](#) would suggest a defect of the [parasympathetic](#) fibers of [CN III](#), which are responsible for pupillary constriction. Because microangiopathy typically involves the vaso nervosum within the [oculomotor nerve](#), the pial blood vessels (which supply the [superficial parasympathetic](#) fibers) are usually spared. Therefore, one would not expect to see a pupillary defect.

C - Loss of the right nasolabial fold

Explanation Why

The [nasolabial fold](#), along with most facial movements, are controlled by branches of the [facial nerve \(CN VII\)](#), which is unlikely to be involved by [diabetic microangiopathy](#).

D - Upper eyelid droop on the right eye

Explanation Why

[Ptosis](#) occurs in patients with [oculomotor nerve palsy](#) because levator palpebrae superioris is innervated by the [oculomotor nerve](#). Whereas patients with [oculomotor nerve palsy](#) due to compression usually show dilated pupils, those with diabetic mononeuropathy normally do not have pupillary involvement because the microangiopathy typically involves the vasa nervorum within the [oculomotor nerve](#), while the pial blood vessels (which supply the [superficial parasympathetic](#) fibers) are usually spared.

E - Loss of smell

Explanation Why

[Anosmia](#) occurs through dysfunction of the [olfactory nerve](#) (CN I). Neither this patient's symptoms nor the likely etiology of his condition ([diabetic microangiopathy](#)) suggests involvement of the [olfactory nerve](#).

F - Absent direct light reaction on the right eye

Explanation Why

Microangiopathy typically involves the vasa nervorum within the [oculomotor nerve](#), while the pial blood vessels (which supply the [superficial parasympathetic](#) fibers) are usually spared. Because both [CN II](#) (responsible for detecting light on the [retina](#)) and the [parasympathetic](#) fibers of [CN III](#) (responsible for pupillary constriction) are intact, there is no pupillary defect when light is shone on the right [eye](#). Of note, if this patient's [oculomotor nerve](#) function had been caused by compression (such as [uncal herniation](#)), the [parasympathetic](#) fibers running superficially along [CN III](#) are actually first to be affected.

Question # 16

A 69-year-old man comes to the physician with a 2-year history of progressive hearing loss. His hearing is worse in crowded rooms, and he has noticed that he has more difficulty understanding women than men. He has no history of serious illness and does not take any medications. A Rinne test shows air conduction is greater than bone conduction bilaterally. This condition is most likely associated with damage closest to which of the following structures?

	Answer	Image
A	External acoustic meatus	
B	Tympanic membrane	
C	Basal turn of the cochlea	
D	Helicotrema	
E	Round window	
F	Base of the stapes	

Hint

Age-related, progressive, bilateral hearing loss at higher frequencies (e.g., women's voices) that worsens in noisy environments is the key feature of presbycusis, the most common type of hearing loss in older adults. Since sound conduction is unaffected, the Rinne test is normal bilaterally (air conduction is greater than bone conduction).

Correct Answer

A - External acoustic meatus

Explanation Why

Abnormalities of the external acoustic meatus (e.g., [cerumen impaction](#)) cause [conductive hearing loss](#) because sound is not able to travel through [the ear](#) canal. However, as in all conductive hearing abnormalities, the [Rinne test](#) would be abnormal (i.e., bone conduction greater than air conduction).

B - Tympanic membrane

Explanation Why

Damage or decreased mobility of the [tympanic membrane](#) causes [conductive hearing loss](#) because it means sound is unable to travel from the external ear to the [middle ear ossicles](#). Causes of [tympanic membrane](#) abnormalities include [otitis media](#) and [acoustic trauma](#) that involves perforation of the [tympanic membrane](#). However, as in all conductive hearing abnormalities, the [Rinne test](#) would be abnormal (i.e., bone conduction greater than air conduction).

C - Basal turn of the cochlea

Explanation But

Since [hearing loss](#) in [presbycusis](#) is typically bilateral and symmetrical, the [Weber test](#) does not usually lateralize to a particular ear.

Explanation Why

Sound waves cause vibrations that resonate with the [basilar membrane](#) of the [cochlea](#), which converts this input into nerve signals that encode the auditory information. The sound wave's point of optimal resonance within the [cochlea](#) depends on the frequency of the sound wave (tonotopy). The base of the [cochlea](#), including the basal turn, responds to higher frequencies. Progressive

degeneration of the [organ of Corti](#) near this region causes [presbycusis](#).

D - Helicotrema

Explanation Why

The [helicotrema](#) is located near the apex of the [cochlea](#). Lower frequency sound waves vibrate the [basilar membrane](#) of the [helicotrema](#), which converts this input into nerve signals that encode the auditory information. This patient with [presbycusis](#) has no difficulty hearing low-frequency sounds (e.g., men's voices), which indicates that the [helicotrema](#) is not damaged.

E - Round window

Explanation Why

When sound waves compress the [oval window](#) through the footplate of the [stapes](#), the communicating [perilymph](#) pushes the [round window](#) membrane outwards, which allows the sound wave to travel through the [cochlea](#) and vibrate the [basilar membrane](#). Acute changes in perilymphatic pressure (e.g., from loud noises or during diving, violent nose-blowing, or lifting heavy weights) can rupture the [round window](#) and manifest as [sensorineural hearing loss](#) (air conduction greater than bone conduction on [Rinne test](#)). However, the onset would be acute, asymmetrical, independent of the sound frequency, and typically associated with [tinnitus](#) and [vertigo](#).

F - Base of the stapes

Explanation Why

Damage to the base of the [stapes](#) causes [conductive hearing loss](#) because it prevents sound from being conducted to the [oval window](#). [Otosclerosis](#), the most common cause of [conductive hearing loss](#) in older adults, causes impaired mobility of the [stapes](#). However, as in all conductive hearing abnormalities, the [Rinne test](#) would be abnormal (i.e., bone conduction greater than air conduction).

Question # 17

A 38-year-old woman undergoes hemithyroidectomy for treatment of localized, well-differentiated papillary thyroid carcinoma. The lesion is removed with clear margins. However, during the surgery, a structure lying directly adjacent to the superior thyroid artery at the upper pole of the thyroid lobe is damaged. This patient is most likely to experience which of the following symptoms?

	Answer	Image
A	Voice pitch limitation	This anatomical diagram illustrates the larynx and thyroid gland. The superior thyroid artery is shown running along the superior border of the thyroid gland. The superior laryngeal nerve is shown running along the superior border of the thyroid gland, just posterior to the superior thyroid artery. Other structures labeled include the superior and inferior parathyroid glands, larynx, right and left tubes, pyramidal lobe, isthmus, trachea, vagus nerve, and the right and left recurrent laryngeal nerves.
B	Perioral paresthesias	
C	Ineffective cough	
D	Weakness of shoulder shrug	
E	Difficulty swallowing	This diagram illustrates the effects of nerve palsy on the larynx during respiration and phonation. It shows a normal larynx and two scenarios of nerve palsy: Paresis of the recurrent laryngeal nerve (Inferior laryngeal nerve) and Paresis of the vagus nerve (Inferior and superior laryngeal nerve). For each scenario, it shows Unilateral and Bilateral involvement. The diagram compares the larynx in a Paramedian position (blue) and an Intermediate position (yellow). The diagram shows that in the normal state, the larynx is in the paramedian position during respiration and the intermediate position during phonation. In the case of unilateral or bilateral nerve palsy, the larynx is unable to move into the intermediate position during phonation, leading to difficulty swallowing.

	Answer	Image
F	Shortness of breath	

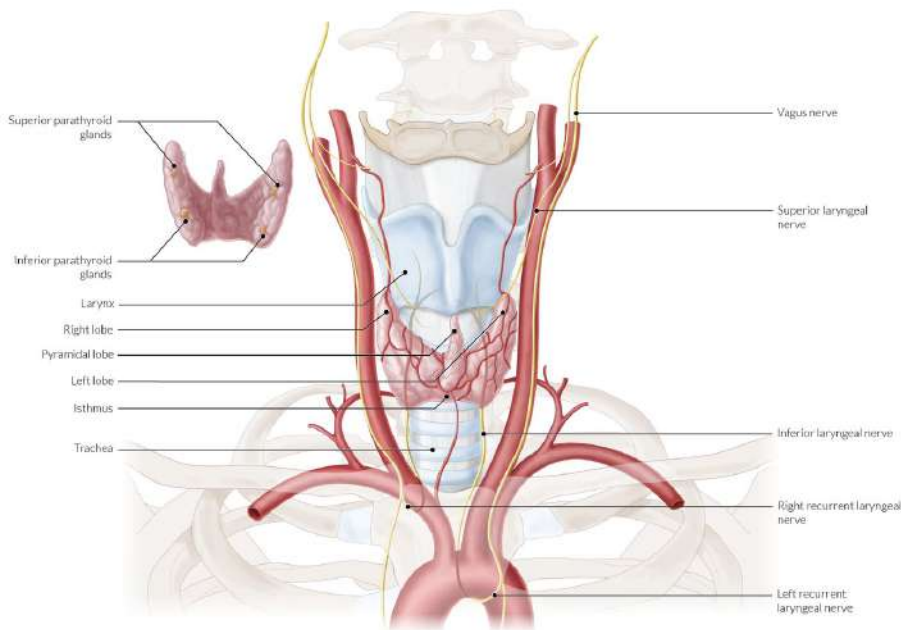
Hint

The external branch of the superior laryngeal nerve lies directly adjacent to the superior thyroid artery at the upper pole of the thyroid lobe. If the artery is ligated during surgery, it may be damaged.

Correct Answer

A - Voice pitch limitation

Image



Explanation Why

Voice pitch limitation is caused by damage to the external branch of the [superior laryngeal nerve](#) (SLN), which occurs in up to 30% of [thyroid](#) dissections. The external branch of the SLN innervates the [cricothyroid muscle](#), which is responsible for lengthening, thinning, and stiffening the [vocal cords](#) and increases the pitch of [phonation](#). The [cricothyroid muscle](#) is the only tensor of the [vocal cord](#), and its denervation results in an inability to increase the pitch of the voice or produce explosive sounds as well as easy voice fatigability.

B - Perioral paresthesias

Explanation Why

Perioral [paresthesia](#) after [thyroid surgery](#) is a result of [hypocalcemia](#) secondary to [hypoparathyroidism](#), usually due to unintentional removal of one or several of the [parathyroid glands](#). [Hypoparathyroidism](#) is the most frequent complication of total or near-total [thyroidectomy](#). However, the superior [parathyroid glands](#) are most commonly found inferior to the superior [thyroid artery](#) and the external branch of the [recurrent laryngeal nerve](#) and are thus less likely to be injured in this patient.

C - Ineffective cough

Explanation Why

Ineffective [cough](#) could result from unilateral [recurrent laryngeal nerve](#) (RLN) injury. This causes the affected [vocal fold](#) to rest in the paramedian or lateralized position. [Coughing](#), which requires transient tight glottic closure, may then become ineffective. While unilateral RLN injury can occur during [thyroid surgery](#), the nerve is unlikely to be damaged during ligation of the superior [thyroid artery](#). Instead, the RLN is at risk during preparation of the inferior pole of the [thyroid gland](#), as it runs close to the [inferior thyroid artery](#).

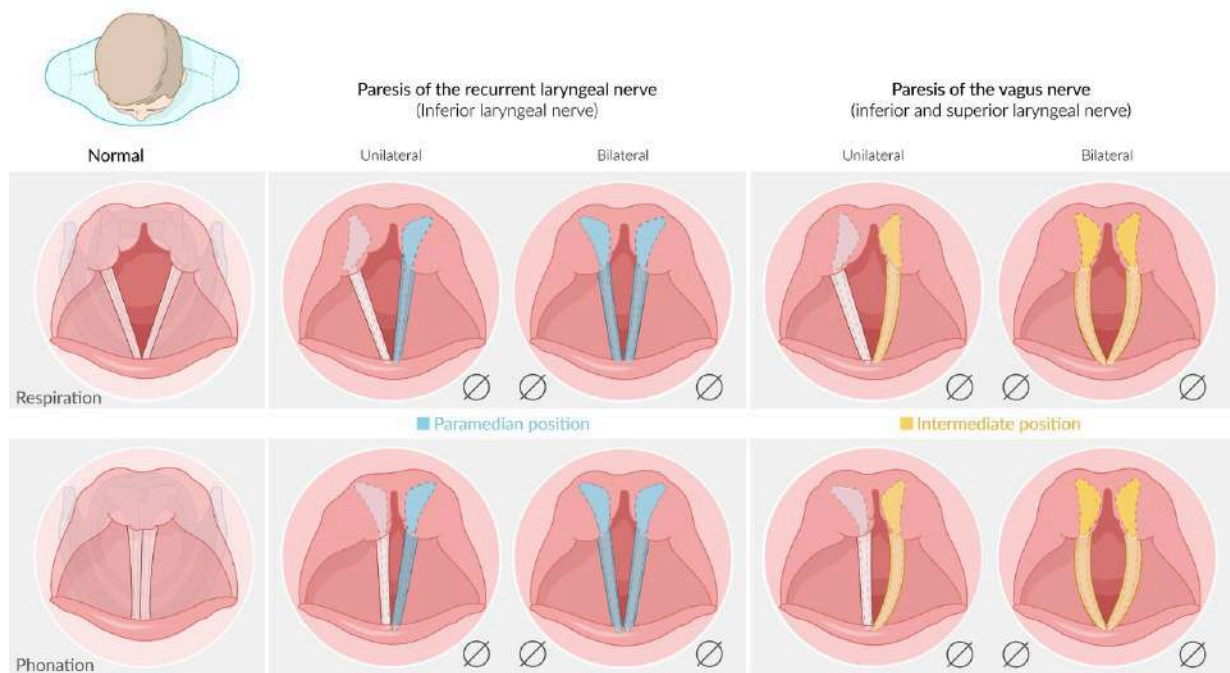
D - Weakness of shoulder shrug

Explanation Why

Weakness of shoulder shrug can occur due to [spinal accessory nerve injury](#) ([cranial nerve XI](#)). The [spinal accessory nerve](#) runs through the [posterior triangle of the neck](#) and supplies the [trapezius muscle](#), which is responsible for shoulder shrugging. However, injury to the [spinal accessory nerve](#) would not be expected during a [hemithyroidectomy](#). The most common causes of [spinal accessory nerve injury](#) include biopsy of the cervical [lymph nodes](#) in the [posterior](#) triangle and radical [neck dissection](#).

E - Difficulty swallowing

Image



Explanation Why

Difficulty [swallowing](#) and increased risk of [aspiration](#) can occur in bilateral injury to the [recurrent laryngeal nerve](#) (RLN), which innervates all the [intrinsic muscles](#) of the [larynx](#) except the [cricothyroid muscle](#). It also carries sensory input from the [larynx](#) below the [vocal cords](#). The RLN can be injured during [thyroid surgery](#) because it passes close to the [inferior thyroid artery](#) on its ascent to the [larynx](#). Unilateral damage to the external branch of the [superior laryngeal nerve](#) is unlikely to cause difficulty [swallowing](#).

F - Shortness of breath

Explanation Why

[Shortness of breath](#) may be caused by bilateral injury to the [recurrent laryngeal nerve](#) (RLN), which

can be injured during [thyroid surgery](#) because it passes [lateral](#) to the [thyroid gland](#), adjacent to the [inferior thyroid artery](#), on its ascent to the [larynx](#). The RLN innervates the [posterior cricoarytenoids](#), which are responsible for [vocal cord abduction](#). In cases of bilateral RLN injury, the [vocal cords](#) are unable to [abduct](#), which restricts air entry into the [trachea](#) and can lead to [shortness of breath](#). Unilateral damage to the external branch of the [superior laryngeal nerve](#) is unlikely to cause [shortness of breath](#).

Question # 18

A 39-year-old man comes to the physician for evaluation of hearing loss. He reports difficulty hearing sounds like the beeping of the microwave or birds chirping, but can easily hear the pipe organ at church. He works as an aircraft marshaller. A Rinne test shows air conduction greater than bone conduction bilaterally. A Weber test does not lateralize. Which of the following is the most likely underlying cause of this patient's condition?

	Answer	Image
A	Perforation of the tympanic membrane	
B	Immobility of the stapes	
C	Compression of the vestibulocochlear nerve	
D	Rupture of the oval window	
E	Destruction of the organ of Corti	The image contains two audiograms side-by-side. The left audiogram (red circles) shows a normal hearing curve up to 2000 Hz, followed by a sharp drop at 4000 Hz to approximately 50 dB, and a slight improvement at 8000 Hz. The right audiogram (black crosses) shows a similar pattern, with a sharp drop at 4000 Hz to approximately 40 dB. Both graphs have frequency on the x-axis (125 to 8000 Hz) and decibels on the y-axis (-10 to 120 dB).
F	Excess endolymphatic fluid pressure	

Hint

Bilateral high-frequency hearing loss in a patient with occupational noise exposure should raise concern for noise-induced hearing loss. The absence of lateralization on Weber tests suggests that both ears are equally affected, while the normal Rinne test suggests that the hearing loss is sensorineural in origin.

Correct Answer

A - Perforation of the tympanic membrane

Explanation Why

Perforation of the [tympanic membrane](#) causes [conductive hearing loss](#) and thus results in an abnormal [Rinne test](#). [Tympanic membrane](#) perforation can be caused by foreign body trauma, [temporal bone fractures](#), [otitis media](#), [barotrauma](#), or blast injury. While this patient's occupation puts him at increased risk of damage to [the ear](#), there is nothing in this patient's history to suggest [tympanic membrane](#) perforation and the [Rinne test](#) was normal, indicating that he does not have [conductive hearing loss](#).

B - Immobility of the stapes

Explanation Why

Immobility of the [stapes](#) is the cause of [otosclerosis](#), which can result in [conductive hearing loss](#). The [stapes](#) lies against the [oval window](#) and transmits sounds from the [tympanic membrane](#). In [otosclerosis](#), the [ossicles](#) are rendered immobile by extensive bony remodeling. Patients usually present with bilateral [conductive hearing loss](#) and have an abnormal [Rinne test](#). [Otosclerosis](#) would not be responsible for the bilateral [sensorineural hearing loss](#) seen in this patient.

C - Compression of the vestibulocochlear nerve

Explanation Why

External compression of the [vestibulocochlear nerve](#) can be caused by tumors such as [acoustic neuromas](#), which are usually unilateral, although they may be bilateral in [neurofibromatosis type 2](#). Compression of this nerve would also result in [sensorineural hearing loss](#). However, [acoustic neuromas](#) are usually accompanied by [dizziness](#) and [ataxia](#), and they are unlikely to cause isolated symmetrical high-frequency [hearing loss](#). Given this patient's history of chronic exposure to loud noises, a different etiology of his [hearing loss](#) is much more likely.

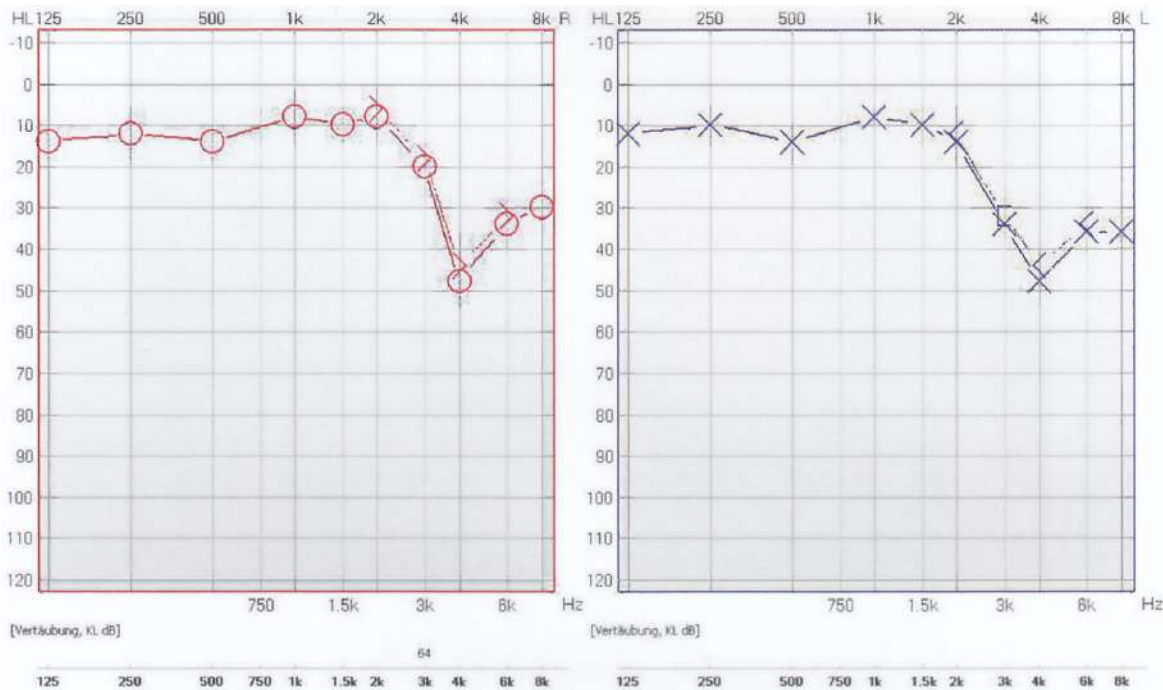
D - Rupture of the oval window

Explanation Why

Rupture of the [oval window](#) is a cause of [hearing loss](#) associated with [barotrauma](#). Sudden decreases in pressure between the inner and [outer ear](#) cause dissolved gasses to be released from the perilymphatic fluid in the [inner ear](#) and results in rupture of the [oval window](#). Patients with [barotrauma](#) will have a recent history of diving or flying, which this patient does not. In addition, the [sensorineural hearing loss](#) resulting from rupture of the [oval window](#) is not limited to high-frequency sounds.

E - Destruction of the organ of Corti

Image



Explanation Why

[Noise-induced hearing loss](#) is caused by the destruction of cochlear [hair](#) cells, also known as the [organ of Corti](#). In a normally functioning ear, sound waves are transmitted mechanically through the [tympanic membrane](#), via the [ossicles](#), and through the [oval window](#) to the [perilymph](#)-filled [inner ear](#). The resulting vibrations are transmitted to the cochlear [hair](#) cells, from where neurologic impulses are transmitted via the [vestibulocochlear nerve](#). Repeated exposure to sounds louder than 85 dB, like those this man experiences at work, or even an isolated exposure to extremely loud sounds greater than 140 dB, can damage the [organ of Corti](#) and result in subsequent [sensorineural hearing loss](#) that typically affects high-frequency hearing first.

F - Excess endolymphatic fluid pressure

Explanation Why

Excess endolymphatic fluid pressure resulting in [sensorineural hearing loss](#) is seen in [Meniere disease](#). Symptoms are usually unilateral and typically include [hearing loss](#), aural fullness, episodic [vertigo](#), and [tinnitus](#), none of which are present in this patient. Additionally, the [sensorineural hearing loss](#) in [Meniere disease](#) usually affects lower-frequency sounds and is unilateral. The patient described in this case has high-frequency [hearing loss](#) that is bilateral, as suggested by the absence of lateralization on the [Weber test](#).

Question # 19

A 2-year-old girl who emigrated from Pakistan 2 weeks ago is brought to the emergency department because of lower limb weakness for one-day. One week ago, she had a 3-day episode of flu-like symptoms that resolved without treatment. She has not yet received any routine childhood vaccinations. Deep tendon reflexes are 1+ in the right lower extremity and absent in the left lower extremity. Analysis of cerebrospinal fluid shows a leukocyte count of 38 cells/mm³ (68% lymphocytes), a protein concentration of 49 mg/dL, and a glucose concentration of 60 mg/dL. Which of the following is the most likely diagnosis in this patient?

	Answer	Image
A	Coxsackie meningitis	
B	Poliomyelitis	
C	HSV encephalitis	
D	Botulism	
E	Tetanus	
F	Guillain-Barre syndrome	

Hint

In this unvaccinated migrant child, the most likely cause of acute flaccid paralysis (weakness with decreased deep tendon reflexes) is anterior horn cell destruction.

Correct Answer

A - Coxsackie meningitis

Explanation Why

The [CSF](#) findings suggestive of a viral infection ([lymphocytic pleocytosis](#), elevated protein, and normal glucose levels) as well as [prodromal flu-like](#) symptoms are consistent with [coxsackievirus meningitis](#). However, [infants](#) with [meningitis](#) typically manifest with non-specific neurological symptoms such as irritability, [lethargy](#), poor feeding, vomiting, and/or [seizures](#). Asymmetric flaccid weakness of the lower limbs is not characteristic of [coxsackievirus meningitis](#).

B - Poliomyelitis

Explanation But

Due to widespread [vaccination](#) measures, [poliomyelitis](#) has been almost eradicated worldwide, with 378 reported cases in 2019 mostly due to outbreaks in Afghanistan and Pakistan, where the virus is still [endemic](#). The [inactivated poliovirus vaccine](#) (IPV) is administered in 4 doses at 2, 4, and 6–18 months, followed by a booster dose at 4–6 years.

Explanation Why

[Poliomyelitis](#), which is caused by the [poliovirus](#), manifests as acute [lower motor neuron](#) weakness that begins asymmetrically in the lower extremities and ascends over hours to days. Patients can have pro-dromal [flu-like](#) symptoms before the onset of weakness. [CSF analysis](#) in [poliomyelitis](#) is typically consistent with viral infection ([lymphocytic pleocytosis](#), normal or slightly increased protein levels, and normal glucose levels), as seen here. Diaphragmatic involvement ultimately results in respiratory failure and death.

C - HSV encephalitis

Explanation Why

The [CSF](#) findings suggestive of a viral infection ([lymphocytic pleocytosis](#), elevated protein, and normal glucose levels) as well as [prodromal flu-like](#) symptoms are consistent with [HSV encephalitis](#). However, [infants](#) with encephalitis typically manifest with non-specific neurological symptoms such as irritability, [lethargy](#), poor feeding, vomiting, and/or [seizures](#). Asymmetric flaccid weakness of the lower limbs is not characteristic of [HSV encephalitis](#).

D - Botulism

Explanation Why

[Botulism](#) can cause acute [flaccid paralysis](#). However, muscle weakness in [botulism](#) typically descends from [proximal](#) to [distal](#) parts of the body, and is not preceded by [prodromal flu-like](#) symptoms. Furthermore, [CSF](#) findings are typically normal in [botulism](#) because it is a toxin-mediated disease.

E - Tetanus

Explanation Why

[Tetanus](#) can occur in an unvaccinated individual following contamination of an injury with [Clostridium tetani](#) spores. However, [tetanus](#) causes [spastic paralysis](#) (spasm, [trismus](#), [risus sardonicus](#), and [opisthotonus](#)), and [prodromal flu-like](#) symptoms would not be expected. Furthermore, [CSF analysis](#) is typically normal in [tetanus](#) because it is a toxin-mediated disease.

F - Guillain-Barre syndrome

Explanation Why

[Guillain-Barre syndrome](#) (GBS) would manifest as acute ascending [flaccid paralysis](#), and is often preceded by a viral upper respiratory tract illness ([flu-like](#) symptoms). However, the paralysis is typically symmetrical unlike this patient with asymmetrical lower extremity weakness, and [CSF analysis](#) would show [albuminocytologic dissociation](#) rather than [lymphocytic pleocytosis](#).

Question # 20

A 70-year-old man is brought to the emergency department with painful discharge from his right ear with difficulty hearing for 3 days. His temperature is 39.5°C (103.1°F) and pulse is 120/minute. Physical examination shows mild facial asymmetry with the right corner of his mouth lagging behind the left when the patient smiles. There is severe ear pain when the right auricle is pulled superiorly. Otoscopic examination shows granulation tissue at the transition between the cartilaginous and the osseous part of the ear canal. Which of the following is most likely associated with this patient's condition?

	Answer	Image
A	Invasive tumor of external auditory canal	
B	Decreased intracranial perfusion	
C	Glucose intolerance	
D	Pus-filled mastoid air cells	
E	Positive streptococcal culture	

Hint

This patient has a history and physical exam findings consistent with malignant otitis externa given his severe ear pain, vital sign abnormalities (i.e., high fever, tachycardia), facial droop (indicating progression to osteomyelitis of the temporal bone with associated CN VII palsy), and the presence of granulation tissue in the ear canal.

Correct Answer

A - Invasive tumor of external auditory canal

Explanation Why

Although an invasive [tumor](#) (e.g., [squamous cell carcinoma](#)) of the [external auditory canal](#) that has extended into the [temporal bone](#) could present with ear [pain](#), this is a rare location for [malignancy](#). Also, this patient's signs of severe systemic infection ([fever](#) and [tachycardia](#)), and the presence of [granulation tissue](#) in [the ear](#) canal suggest an acutely infectious, not malignant, etiology.

B - Decreased intracranial perfusion

Explanation Why

Acutely decreased intracranial perfusion can present with [cranial nerve VII \(CN VII\)](#) palsy, in the setting of acute [ischemic stroke](#). However, other signs of acute [stroke](#) that commonly occur with unilateral [facial nerve palsy](#), including one-sided weakness of the extremities, are absent in this patient. Furthermore, [stroke](#) cannot explain the painful [ear discharge](#) with signs of systemic infection.

C - Glucose intolerance

Explanation Why

There is a strong association between [diabetes mellitus](#) and the development of [malignant otitis externa](#), which is most commonly caused by an infection with [Pseudomonas aeruginosa](#). The specific connection between [diabetes mellitus](#) and [malignant otitis externa](#) is not fully understood but may be related to increased pH in diabetic [cerumen](#). Elderly diabetic patients are especially at risk for this potentially fatal condition. Following blood cultures, high-dose IV [ciprofloxacin](#) should be initiated and [cranial](#) imaging performed.

D - Pus-filled mastoid air cells

Explanation Why

Pus-filled mastoid air cells is a sign of [mastoiditis](#), which can be a complication after acute or chronic infections of the sinus or [middle ear](#). Since the [middle ear](#) communicates with the [mastoid process](#), [otitis media](#) can result in opacification of the mastoid's air cells on imaging. However, this patient likely has an infection of the external ear, which does not have a direct communication with the [mastoid process](#) and is therefore not associated with opacified mastoid air cells.

E - Positive streptococcal culture

Explanation Why

Streptococcus pneumoniae is the most common bacterial causes of [acute otitis media](#). [AOM](#) typically presents with ear [pain](#) and [fever](#), but more serious complications, like [osteomyelitis](#) of the [skull](#) and [cranial nerve palsies](#), are rare. [Otoscopy](#) in [AOM](#) shows bulging of the [tympanic membrane](#), not [granulation tissue](#) in the canal. Also, [AOM](#) most commonly affects young children. This patient is more likely to have an infection with *Pseudomonas aeruginosa* which is responsible for more than 95% of malignant [external otitis](#) cases.

Question # 21

A 26-year-old man comes to the physician for a follow-up examination. Two weeks ago, he was treated in the emergency department for head trauma after being hit by a bicycle while crossing the street. Neurological examination shows decreased taste on the right anterior tongue. This patient's condition is most likely caused by damage to a cranial nerve that is also responsible for which of the following?

	Answer	Image
A	Uvula movement	
B	Facial sensation	
C	Eyelid closure	
D	Tongue protrusion	
E	Parotid gland salivation	

Hint

Taste on the anterior two-thirds of the tongue is mediated by cranial nerve VII.

Correct Answer

A - Uvula movement

Explanation Why

The [vagus nerve \(CN X\)](#) provides the uvula with motor function. It also carries somatosensory and [taste](#) fibers that innervate the [epiglottis](#) and the most [posterior](#) part of the [tongue](#), but not the [anterior](#) two-thirds. [CN X](#) is the most important [parasympathetic](#) nerve in the human body and innervates the intestines up to the [splenic flexure](#) of the [colon](#). In addition, [CN X](#) is responsible for innervating the chemo- and [baroreceptors](#) of the [aortic arch](#), elevating the [posterior tongue](#) and [soft palate](#) during [swallowing](#), and the [cough reflex](#).

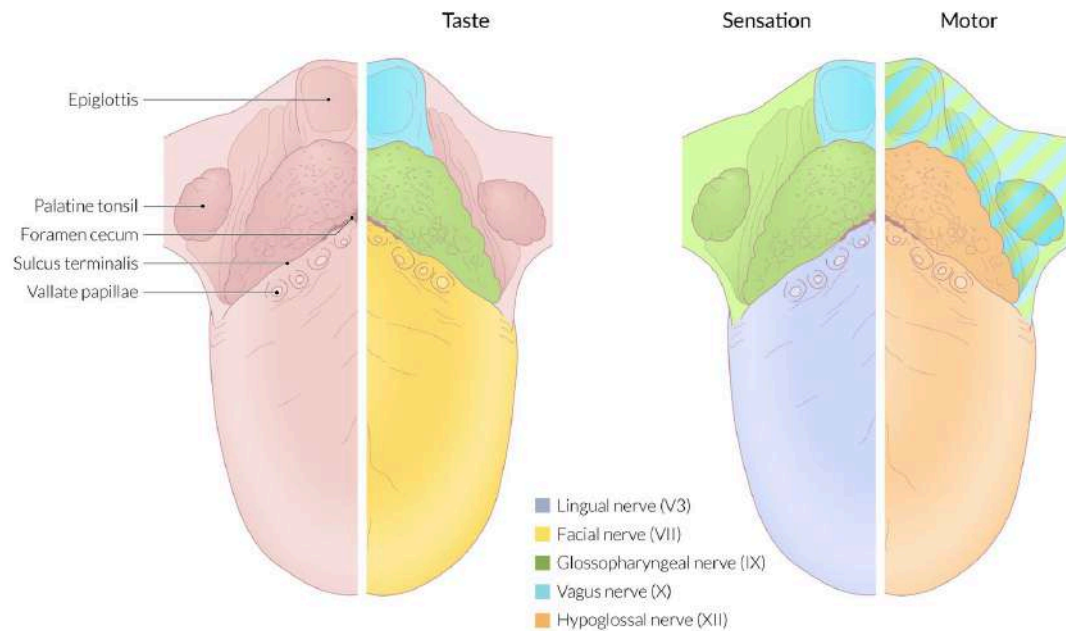
B - Facial sensation

Explanation Why

Sensory innervation of the face is provided by branches of the [trigeminal nerve \(CN V\)](#) – namely the ophthalmic, maxillary, and mandibular nerves. [CN V](#) provides somatosensory innervation to the [anterior](#) two-thirds of the [tongue](#); it does not carry special sensory fibers for [taste](#) perception. [CN V](#) is also responsible for the motor function of the muscles used in [mastication](#) (the [masseter](#), [temporalis](#), [medial](#) and [lateral pterygoid muscles](#)).

C - Eyelid closure

Image



Explanation Why

Closing the eyelids is accomplished through the contraction of the [orbicularis oculi muscle](#), which is, like all facial muscles, innervated by the [facial nerve \(CN VII\)](#). The [chorda tympani](#) branch of the [facial nerve](#) innervates the [taste buds](#) of the [anterior](#) two-thirds of the [tongue](#). The [facial nerve](#) is also responsible for innervation of the [lacrimal gland](#), submandibular and [sublingual glands](#), and the [stapedius muscle](#).

D - Tongue protrusion

Explanation Why

[Tongue](#) protrusion is made possible by the [extrinsic muscles of the tongue](#), which are innervated by the [hypoglossal nerve \(CN XII\)](#). [CN XII](#) is an exclusively motor nerve that also provides the intrinsic

[tongue](#) muscles with motor function. The only [extrinsic tongue muscle](#) that is not innervated by [CN XII](#) is the [palatoglossus muscle](#), which elevates the [posterior tongue](#) when [swallowing](#).

E - Parotid gland salivation

Explanation Why

[Parotid gland](#) salivation is controlled by [parasympathetic](#) fibers of the [glossopharyngeal nerve](#) ([CN IX](#)). While [CN IX](#) carries somatosensory and special sensory [taste](#) fibers, it does so for the [posterior](#) third of the [tongue](#) rather than the [anterior](#) two-thirds. [CN IX](#) is also responsible for transmitting somatosensory information for the [middle ear](#) and [eustachian tube](#), innervating the chemo- and [baroreceptors](#) of the carotid body and sinus, and innervating the pharyngeal muscles and muscles of the upper [GI tract](#).

Question # 22

A 45-year-old man is brought to the emergency department following a motor vehicle collision. He reports right hip pain and numbness along the right thigh. Physical examination shows decreased sensation to light touch over a small area of the medial thigh. X-rays of the pelvis show a displaced pelvic ring fracture. Further evaluation of this patient is most likely to show which of the following findings?

	Answer	Image
A	Sensory deficit of the dorsal foot	
B	Impaired hip extension	
C	Impaired dorsiflexion of the foot	
D	Impaired extension of the knee	
E	Absent cremasteric reflex	
F	Impaired adduction of the hip	

Hint

This man has a pelvic ring fracture with decreased sensation over a small area of the right medial thigh. This is consistent with an obturator nerve injury.

Correct Answer

A - Sensory deficit of the dorsal foot

Explanation Why

Sensory deficits of the [dorsal](#) foot can be caused by injury to the [superficial](#) peroneal branch of the [common peroneal nerve](#), which provides sensory cutaneous innervation to the [lateral](#) lower leg and [dorsal](#) aspect of the foot. However, injury to the [common peroneal nerve](#) or its branches would not cause decreased sensation in the [medial](#) thigh.

B - Impaired hip extension

Explanation Why

Impaired [hip](#) extension can be caused by [sciatic nerve injury](#), which can occur in the setting of [hip](#) dislocation or [hip arthroplasty](#). The [sciatic nerve](#) innervates the [semimembranosus](#), [semitendinosus](#), and long head of the [biceps femoris](#), which are responsible for [hip](#) extension and [knee flexion](#). It does not provide sensory innervation to the [medial](#) thigh.

C - Impaired dorsiflexion of the foot

Explanation Why

Impaired [dorsiflexion](#) of the foot can be seen in [common peroneal nerve injury](#), which typically occurs in the setting of fibular head [fractures](#) or external compression of the [common peroneal nerve](#) at the level of the fibular head. The branches of the [common peroneal nerve](#) provide sensory innervation to the first [dorsal](#) web space and the [lateral](#) lower leg and [dorsal](#) foot. Injury to this nerve would not explain the patient's decreased sensation in the [medial](#) thigh.

D - Impaired extension of the knee

Explanation Why

Impaired extension of the [knee](#) can occur following injury to the [femoral nerve](#), which innervates the [quadriceps](#) muscles. Although [femoral nerve injury](#) can be caused by direct trauma (e.g., [fracture](#), compression from a [hematoma](#)) it is unlikely to be the cause of this patient's sensory deficit on the [medial](#) thigh because sensory fibers from the [femoral nerve](#) also provide cutaneous innervation to the [medial](#) lower leg and foot.

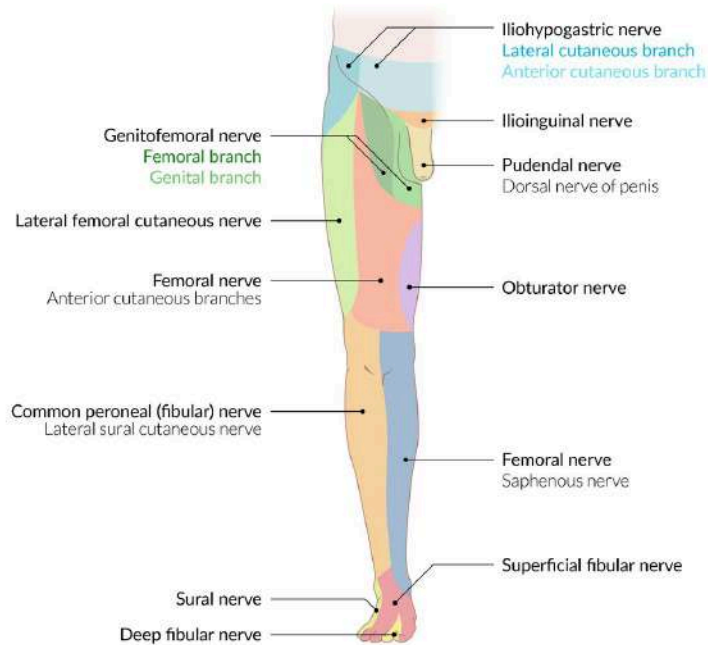
E - Absent cremasteric reflex

Explanation Why

Absence of the [cremasteric reflex](#) is seen in patients with injury to the genitofemoral nerve, as the nerve provides motor innervation to the [cremaster muscle](#). The genitofemoral nerve also provides sensory cutaneous innervation to the [scrotum](#) in men and to the mons pubis and [labia majora](#) in women; there are also cutaneous branches to the [proximal](#) aspect of the anteromedial thigh. This patient presents with decreased sensation to the [medial](#) thigh, which could be seen in [genitofemoral nerve injury](#). However, pelvic ring [fractures](#) are not associated with [genitofemoral nerve injuries](#).

F - Impaired adduction of the hip

Image

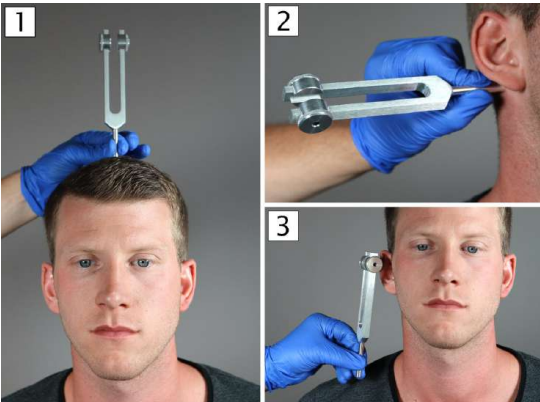


Explanation Why

Pelvic ring [fracture](#) is a common cause of [obturator nerve injury](#). In addition to providing sensory cutaneous innervation to a small area of the [medial thigh](#), the [obturator nerve](#) also provides motor innervation to the [hip](#) adductor muscles in the [medial compartment of the thigh](#). Thus, injury to the nerve can result in impaired [adduction](#) of the [hip](#).

Question # 23

An otherwise healthy 62-year-old woman comes to the physician because of a 3-year history of hearing loss. To test her hearing, the physician performs two tests. First, a vibrating tuning fork is held against the mastoid bone of the patient and then near her ear, to which the patient responds she hears the sound better on both sides when the tuning fork is held near her ear. Next, the physician holds the tuning fork against the bridge of her forehead, to which the patient responds she hears the sound better on the right side than the left. The patient's examination findings are most consistent with which of the following conditions?

	Answer	Image
A	Cerumen impaction on the right	
B	Otosclerosis on the left	
C	Cochlear ischemia on the right	
D	Acoustic neuroma on the left	 The image block contains three sub-images labeled 1, 2, and 3. Image 1 shows a tuning fork being held against the bridge of a patient's forehead (Weber test). Image 2 shows a tuning fork being held behind a patient's ear (Rinne test). Image 3 shows a tuning fork being held near a patient's ear (Rinne test).
E	Presbycusis bilaterally	
F	Cholesteatoma on the right	

Hint

In this patient, the results of the Rinne test are positive, indicating normal conductive hearing. In combination with a Weber test that lateralized to the right, this indicates left-sided sensorineural hearing loss.

Correct Answer

A - Cerumen impaction on the right

Explanation Why

[Cerumen impaction](#) is associated with [conductive hearing loss](#) due to direct obstruction of the [external acoustic canal](#). If [cerumen impaction](#) were present on the right side, the patient would have a negative [Rinne test](#) on the right and a positive test on the left. The [Weber test](#) would lateralize to the right side.

B - Otosclerosis on the left

Explanation Why

[Otosclerosis](#) is characterized by [conductive hearing loss](#) (more in the lower frequencies than in the higher), typically bilateral. It most commonly manifests in the third or fourth decade of life. If [otosclerosis](#) were present on the left side, the patient would have a negative [Rinne test](#) on the left and a positive test on the right. The [Weber test](#) would lateralize to the left.

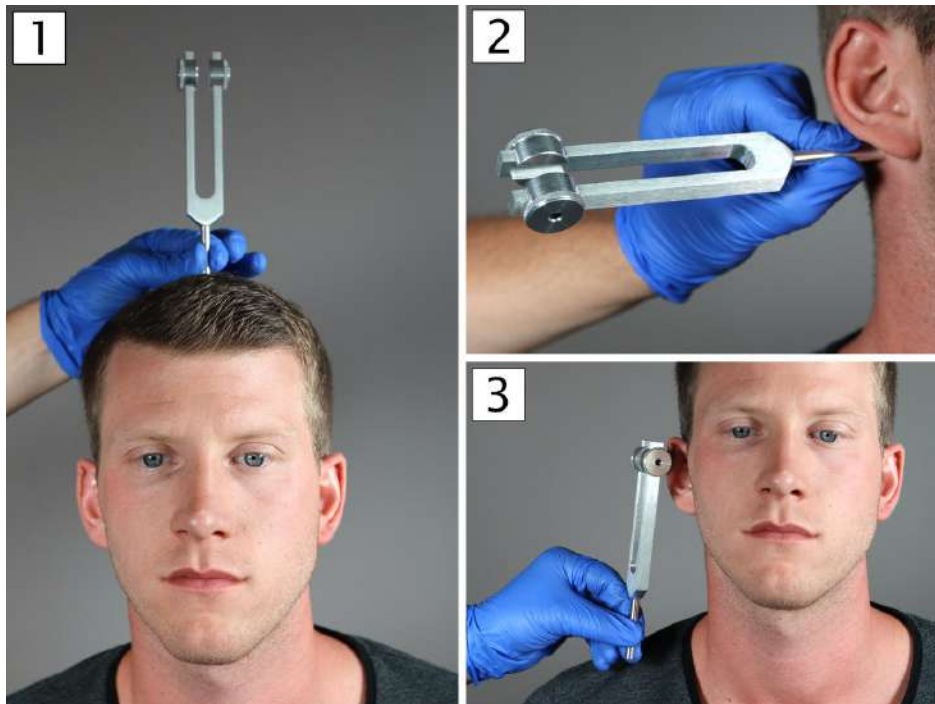
C - Cochlear ischemia on the right

Explanation Why

Cochlear [ischemia](#) can lead to direct cochlear nerve damage and thus cause unilateral [sensorineural hearing loss](#), as seen here. In a patient with right-sided cochlear [ischemia](#), the [Rinne test](#) would be positive on both sides. However, the [Weber test](#) would lateralize to the left because of right-sided nerve damage.

D - Acoustic neuroma on the left

Image



Explanation Why

[Acoustic neuromas](#), which commonly arise from the internal acoustic canal, often exert a [mass effect](#) on the [vestibulocochlear nerve \(CN VIII\)](#). The resulting unilateral [sensorineural hearing loss](#), as seen in this patient, is the most common early symptom of this condition. Other symptoms include [tinnitus](#) due to pressure on [CN VIII](#) as well as [dizziness/vertigo](#) and gait instability due to vestibular deficits.

E - Presbycusis bilaterally

Explanation Why

[Presbycusis](#) is the most common cause of [sensorineural hearing loss](#), with onset most commonly occurring in the sixth decade of life. It typically manifests with difficulty hearing in noisy

environments. If bilateral [presbycusis](#) were present, the patient would have positive [Rinne tests](#) on the right and left. The [Weber test](#) would not lateralize.

F - Cholesteatoma on the right

Explanation Why

[Cholesteatoma](#) does not always present with [hearing loss](#), but would cause [conductive hearing loss](#) due to erosion of the [ossicles](#). In a case of a symptomatic [cholesteatoma](#) on the right side, this patient would have a negative [Rinne test](#) on the right and a positive test on the left. The [Weber test](#) would lateralize to the right side.

Question # 24

A 69-year-old man undergoes modified radical neck dissection for an oropharyngeal tumor. During the procedure, he requires multiple blood transfusions. Four hours after the surgery, examination shows that the right and left pupils do not constrict when a light is shone into the left eye. When light is shone into the right eye, both pupils constrict. Fundoscopic examination shows no abnormalities. Which of the following is the most likely location of the lesion?

	Answer	Image
A	Optic nerve	
B	Pretectal nuclei	
C	Superior cervical ganglion	
D	Ophthalmic nerve	
E	Edinger-Westphal nucleus	

	Answer	Image
F	Lateral geniculate body	The diagram illustrates the visual pathway. At the top, the visual fields of the left (L) and right (R) eyes are shown, with nasal and temporal fields indicated. Light enters the eyes at the retina. The optic nerves exit the eyes and meet at the optic chiasm. From there, the optic tracts lead to the lateral geniculate nucleus. The optic radiations then carry the signals to the primary visual cortex at the back of the brain.
G	Ciliary ganglion	

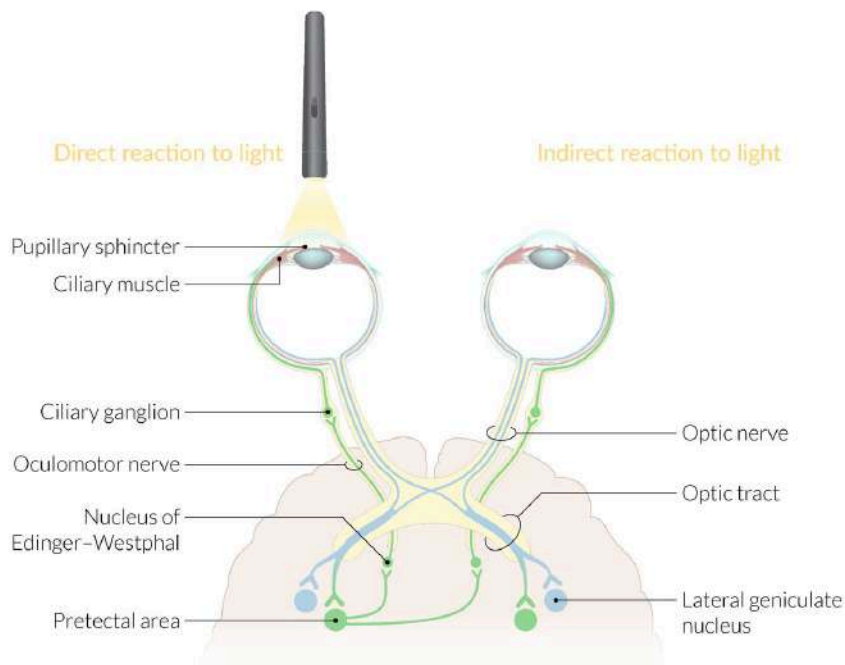
Hint

The patient presents with a relative afferent pupillary defect (RAPD). Given his need for multiple blood transfusions during surgery, the patient presumably had an episode of intraoperative blood loss. This blood loss could have resulted in hypotension and subsequent ischemic damage to a CNS structure involved in the pupillary response.

Correct Answer

A - Optic nerve

Image



Explanation Why

A [relative afferent pupillary defect \(RAPD\)](#) typically occurs because of unilateral damage to the [retina](#) and/or [optic nerve \(CN II\)](#). In this patient damage to the [optic nerve \(CN II\)](#) due to [ischemic](#) optic neuropathy has resulted in [RAPD](#). Complete damage to [CN II](#) would also result in loss of vision on the affected side.

B - Pretectal nuclei

Explanation Why

The [pretectal region](#) receives afferent fibers of the pupillary pathway from both eyes. Unilateral

damage can, therefore, be compensated by the innervation from the contralateral side. Bilateral damage to the [pretectal region](#), on the other hand, manifests with absent [direct pupillary reflexes](#) and [indirect pupillary reflexes](#) in both eyes.

C - Superior cervical ganglion

Explanation Why

Damage to the [superior cervical ganglion](#) and its [sympathetic](#) nerve fibers is a potential complication of radical deep [neck dissection](#). However, patients in such cases would present with ipsilateral [miosis](#) and other symptoms of [Horner syndrome](#) (e.g. [ptosis](#), [anhidrosis](#)).

D - Ophthalmic nerve

Explanation Why

Damage to the [ophthalmic nerve](#) (a branch of the [CN V](#)) results in absent [corneal reflex](#). [Ophthalmic nerve](#) damage can also result in sensory deficits in the periorbital region and the ipsilateral forehead. The pupillary response would not be affected.

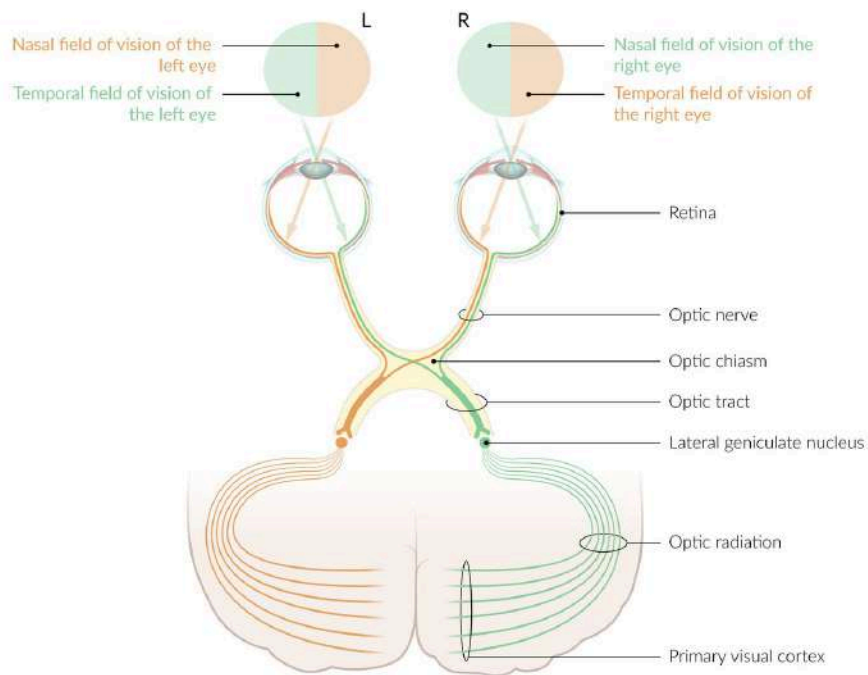
E - Edinger-Westphal nucleus

Explanation Why

Damage to the [parasympathetic Edinger-Westphal nucleus](#), which contains the efferent pupillary response pathway, leads to absent [pupillary reflex](#) (direct and indirect) in the ipsilateral [eye](#), while the [pupillary reflex](#) (direct and indirect) in the contralateral [eye](#) remains intact.

F - Lateral geniculate body

Image



Explanation Why

Damage to the [lateral geniculate body](#) leads to [homonymous hemianopia](#) of the contralateral [visual field](#). The pupillary response pathway does not pass through the [lateral geniculate body](#), and so pupillary reactions to light would not be affected.

G - Ciliary ganglion

Explanation Why

Damage to the [ciliary ganglion](#), which contains the efferent fibers of the [CN III](#), results in paresis of the [sphincter pupillae](#) muscle. Thus, damage to the [ciliary ganglion](#) would manifest with [mydriasis](#) and absent [pupillary reflex](#) (both direct and consensual) in the ipsilateral [eye](#), and normal pupillary response in the unaffected [eye](#).

Question # 25

A 78-year-old left-handed woman with hypertension and hyperlipidemia is brought to the emergency room because of sudden-onset right leg weakness and urinary incontinence. Neurologic examination shows decreased sensation over the right thigh. Muscle strength is 2/5 in the right lower extremity and 4/5 in the right upper extremity. Strength and sensation in the face are normal but she has difficulty initiating sentences and she is unable to write her name. The most likely cause of this patient's condition is an occlusion of which of the following vessels?

	Answer	Image
A	Right anterior cerebral artery	
B	Right vertebrobasilar artery	
C	Right posterior cerebral artery	
D	Left posterior cerebral artery	
E	Left middle cerebral artery	
F	Left vertebrobasilar artery	
G	Right middle cerebral artery	

	Answer	Image
H	Left anterior cerebral artery	The diagram, titled "Arterial supply of the brain", illustrates the major arteries of the brain and their territories. It includes a central "Circle of Willis" diagram and three brain cross-sections: "Caudal view", "Cortical vascular territories", and "Oblique-frontal view". Internal carotid artery circulation (Anterior): - Anterior communicating artery - Anterior cerebral artery (ACA) - Internal carotid artery (ICA) - Middle cerebral artery (MCA) Vertebral artery circulation (Posterior): - Posterior communicating artery - Posterior cerebral artery (PCA) - Basilar artery - Vertebral artery (VA) - Anterior spinal artery Other labels in the oblique-frontal view: - ACA - MCA - PCA - ICA - Common carotid artery - VA - Subclavian artery - Aorta

Hint

This patient's lower extremity deficits, urinary incontinence, and aphasia raise concern for a stroke in a specific vascular distribution.

Correct Answer

A - Right anterior cerebral artery

Explanation Why

[Anterior cerebral artery](#) (ACA) [strokes](#) typically manifest with contralateral sensorimotor deficits, language deficits, and [urinary incontinence](#). This woman's sensorimotor deficits are ipsilateral to the right ACA territory, which is inconsistent with a right ACA [stroke](#).

B - Right vertebrobasilar artery

Explanation Why

Vertebrobasilar [artery strokes](#) can manifest with [vertigo](#), [tinnitus](#), visual deficits, gait [ataxia](#), and ipsilateral [cranial nerve](#) deficits with contralateral [paresthesias](#) and [hemiplegia](#). Rarely, it can cause [locked-in syndrome](#). Although this patient presents with sensorimotor deficits, there is no evidence of [cranial nerve](#) or [cerebellar](#) involvement.

C - Right posterior cerebral artery

Explanation Why

[Posterior cerebral artery](#) (PCA) [strokes](#) typically manifest with [visual field](#) defects, contralateral hemisensory loss, and [vertigo](#). Right-sided PCA [strokes](#) may also cause visual recognition deficits ([prosopagnosia](#)). Although this patient does have sensory deficits, a PCA occlusion would not explain her [hemiparesis](#), incontinence, or [aphasia](#). Her sensory deficits are also right-sided, as opposed to the left-sided symptoms expected in a right PCA [stroke](#).

D - Left posterior cerebral artery

Explanation Why

[Posterior cerebral artery](#) (PCA) [strokes](#) typically manifest with [visual field](#) defects, contralateral hemisensory loss, and [vertigo](#). Left-sided PCA [strokes](#) can also cause language deficits ([alexia](#), [anomic aphasia](#)). Although this patient has right-sided sensory deficits, a PCA occlusion would not explain her [hemiparesis](#) or incontinence. She also lacks the visual deficits and [vertigo](#) typically seen in PCA [strokes](#).

E - Left middle cerebral artery

Explanation Why

[Middle cerebral artery](#) (MCA) [strokes](#) typically manifest with contralateral sensorimotor deficits (face and upper extremities more pronounced than lower extremities), gaze deviation, [aphasia](#) (or [hemineglect](#)), and contralateral [homonymous hemianopia](#). Although this patient has right-sided sensorimotor deficits and [aphasia](#), the pattern of weakness (i.e., legs > arms) is the opposite of what would be expected in [MCA stroke](#).

F - Left vertebrobasilar artery

Explanation Why

Vertebrobasilar [artery strokes](#) can manifest with [vertigo](#), [tinnitus](#), visual deficits, gait [ataxia](#), and ipsilateral [cranial nerve](#) deficits with contralateral [paresthesias](#) and [hemiplegia](#). Rarely, it can cause [locked-in syndrome](#). Although this patient presents with right sensorimotor deficits, there is no evidence of [cranial nerve](#) or [cerebellar](#) involvement.

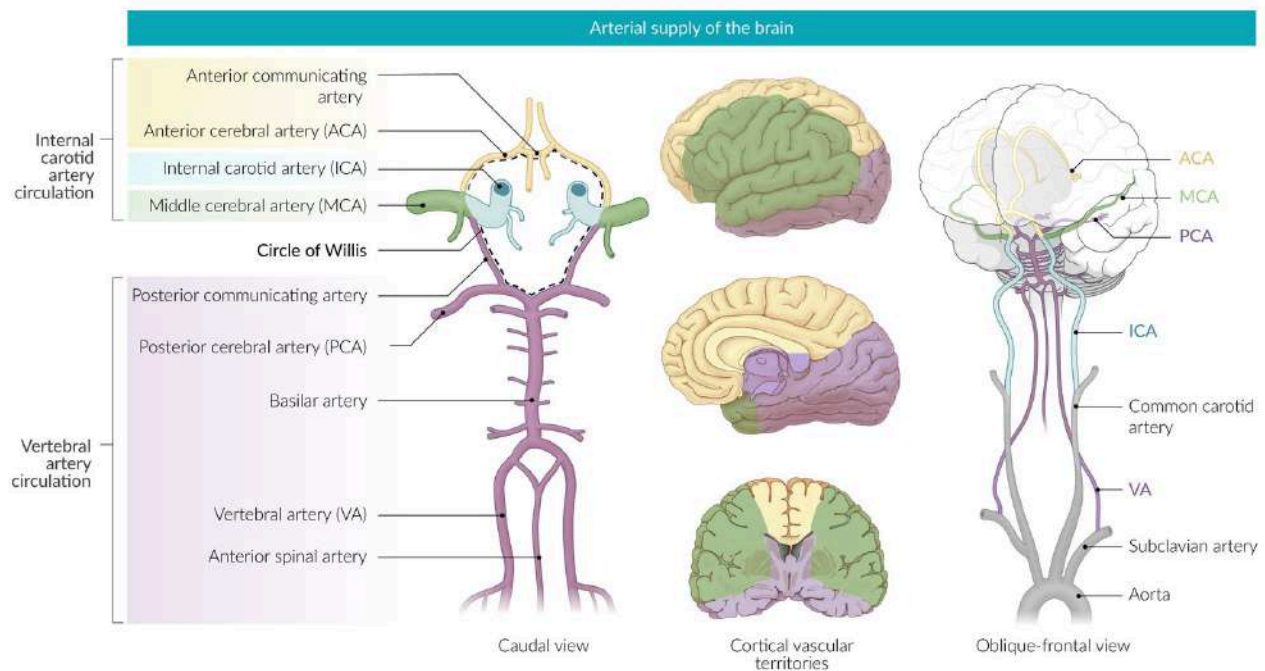
G - Right middle cerebral artery

Explanation Why

[Middle cerebral artery \(MCA\) strokes](#) typically manifest with contralateral sensorimotor deficits (face and upper extremities more pronounced than lower extremities), gaze deviation, [aphasia](#) (or [hemineglect](#)), and contralateral [homonymous hemianopia](#). Although this patient has sensorimotor deficits and [aphasia](#), the pattern of weakness (right legs > right arms) is the opposite of what would be expected in a right [MCA stroke](#).

H - Left anterior cerebral artery

Image



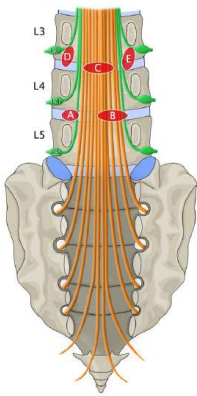
Explanation Why

[Anterior cerebral artery \(ACA\) strokes](#) manifest with contralateral sensorimotor deficits (more pronounced in the lower extremity than in the upper extremity), [urinary incontinence](#), and, less

commonly, [speech](#) and language deficits (typically [transcortical motor aphasia](#)). Limb [apraxia](#) and [abulia](#) can also be seen. This patient's right-sided sensorimotor deficits, incontinence, and [aphasia](#) are consistent with a left ACA [stroke](#).

Question # 26

A 75-year-old man comes to the physician because of a 2-week history of sharp, stabbing pain in the lower back that radiates to the back of his left leg. He also has had a loss of sensitivity around his buttocks and inner thighs as well as increased trouble urinating the last week. Two years ago, he was diagnosed with prostate cancer and was treated with radiation therapy. Neurologic examination shows reduced strength and reflexes in the left lower extremity; the right side is normal. The resting anal sphincter tone is normal but the squeeze tone is reduced. Which of the following is the most likely diagnosis?

	Answer	Image
A	Brown-sequard syndrome	
B	Anterior spinal cord syndrome	
C	Central cord syndrome	
D	Conus medullaris syndrome	
E	Cauda equina syndrome	

Hint

Two key factors that differentiate this diagnosis are the strong unilateral radicular pain and asymmetrical weakness.

Correct Answer

A - Brown-sequard syndrome

Explanation Why

[Brown-Sequard syndrome](#) in the thoracic [spinal cord](#) segments would present with unilateral lower limb weakness, as seen here. However, the affected side would also present with loss of vibration and [proprioception](#) and the contralateral side would show loss of [pain](#) and temperature sensation, features which are absent in this patient.

B - Anterior spinal cord syndrome

Explanation Why

[Anterior spinal cord syndrome](#) may lead to difficulty voiding because the descending pathways that control sphincter function are located ventrally in the [spinal cord](#). However, it would also cause symmetrical lower limb weakness and loss of [pain](#) and temperature sensations in all areas below the level of the lesion.

C - Central cord syndrome

Explanation Why

[Central cord syndrome](#) in the thoracic [spinal cord](#) segments would produce symmetrical lower limb weakness, as well as loss of [pain](#) and temperature sensation, which is not reported in this patient. Sensation around the buttocks, inner thighs, and genitalia, as well as anal sphincter tone are classically spared in [central cord syndrome](#).

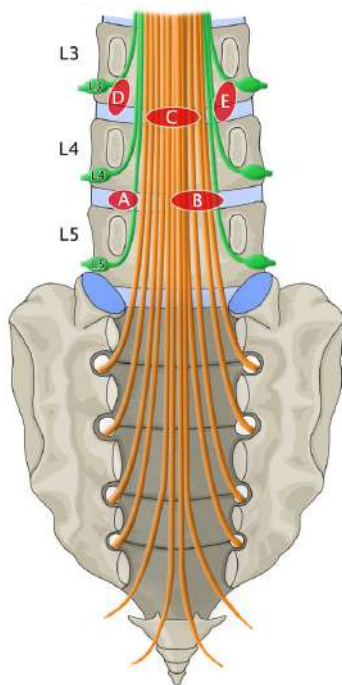
D - Conus medullaris syndrome

Explanation Why

[Conus medullaris syndrome](#) may cause the similar symptoms as seen in this patient, although they usually occur symmetrically with a sudden onset. This patient's symptoms developed over the course of 2 weeks and are asymmetric. Additionally, the [knee-jerk](#) reflexes are often spared and numbness is primarily limited to the perianal region, since [conus medullaris syndrome](#) typically involves sacral [spinal cord](#) segments, and not L3 and L4 (which control the [knee-jerk](#) reflex and innervate the saddle region beyond the perianal area). Radiating [radicular pain](#) also tends to be less severe in patients with [conus medullaris syndrome](#).

E - Cauda equina syndrome

Image



Explanation Why

The gradual development of asymmetrical lower limb weakness, reduced reflexes in both the [knees](#) and ankles, [saddle anesthesia](#), difficulty voiding, a decreased anal tone, and severe back [pain](#) with radiation to the lower limb is the classic clinical picture of [cauda equina syndrome](#). [Cauda equina syndrome](#) is typically caused by traumatic injury, [disc herniation](#), or a [tumor](#) below the level of the L2 [vertebra](#). Given the history of [prostate cancer](#) in this patient, [spinal](#) imaging is needed to rule out [vertebral](#) or epidural [metastases](#).

Question # 27

A 60-year-old man is brought to the emergency room because of fever and increasing confusion for the past 2 days. He has paranoid schizophrenia treated with chlorpromazine. He appears diaphoretic. His temperature is 40°C (104°F), pulse is 130/min, respirations are 29/min, and blood pressure is 155/100 mm Hg. Neurologic examination shows psychomotor agitation and incoherent speech. There is generalized muscle rigidity. His deep tendon reflexes are decreased bilaterally. Serum laboratory analysis shows a leukocyte count of 11,300/mm³ and serum creatine kinase concentration of 833 U/L. The most appropriate drug for this patient acts by inhibiting which of the following?

	Answer	Image
A	Cholinesterase	
B	Postsynaptic dopamine D2 receptors and serotonin 2A receptors	
C	Ryanodine receptor on the sarcoplasmic reticulum	
D	Histamine H1 receptor and serotonin 2 receptors	
E	Beta adrenergic receptors	
F	Bacterial cell wall synthesis	

Hint

This schizophrenic patient's presentation of fever, altered mental status, muscle rigidity, decreased DTRs, autonomic instability (hypertension, tachycardia, diaphoresis), and elevated serum creatine kinase is indicative of neuroleptic malignant syndrome (NMS). Initial treatment of NMS should target the patient's rigidity and hyperthermia to prevent progression into rhabdomyolysis.

Correct Answer

A - Cholinesterase

Explanation Why

[Physostigmine](#) is a [cholinesterase inhibitor](#) that decreases the total breakdown of [acetylcholine](#), thereby increasing [parasympathetic](#) activity. It can be used to treat [anticholinergic toxicity](#), which can also cause [fever](#), confusion, and agitation in affected patients. However, [anticholinergic toxicity](#) causes dry [skin](#), not [diaphoresis](#), and would not lead to muscle [rigidity](#).

B - Postsynaptic dopamine D2 receptors and serotonin 2A receptors

Explanation Why

[Clozapine](#) is an [atypical antipsychotic](#) used primarily for treatment-refractory [schizophrenia](#) that acts by postsynaptic blockade of [dopamine D2 receptors](#) and also inhibition of [serotonin 2](#), [α-adrenergic](#), and [histamine H1 receptors](#). There is no evidence that this patient's [schizophrenia](#) is poorly controlled. Furthermore, this patient has [NMS](#), which requires immediate treatment. The addition of another [antipsychotic](#) may worsen this patient's [NMS](#) given its antidopaminergic properties.

C - Ryanodine receptor on the sarcoplasmic reticulum

Explanation Why

[Dantrolene](#) is a [muscle relaxant](#) that prevents the release of calcium into the [myocyte cytoplasm](#) by inhibiting the [ryanodine receptor](#) on the [sarcoplasmic reticulum](#). After discontinuation of the offending drug (i.e., [chlorpromazine](#)), [dantrolene](#) is indicated in the treatment of [NMS](#) because it decreases muscle [rigidity](#) and thereby body temperature and the risk of [rhabdomyolysis](#). Although [dantrolene](#) is most commonly given, alternative pharmacotherapy includes [bromocriptine](#), [amantadine](#), and possibly [apomorphine](#). [Benzodiazepines](#) are also usually given to patients suffering from [NMS](#) with psychomotor agitation, as seen here.

D - Histamine H1 receptor and serotonin 2 receptors

Explanation Why

[Cyproheptadine](#) is a [first-generation H1 antihistamine](#) that is indicated in the treatment of [serotonin syndrome](#) because of its nonselective antiserotonergic activity. This condition has a similar presentation to [NMS](#); but [serotonin syndrome](#) also tends to cause [hyperreflexia](#), myoclonus, nausea, vomiting, and [diarrhea](#). In addition, [serotonin syndrome](#) generally occurs in the context of polypharmacy with drugs that increase [serotonin](#) levels (e.g., [SSRI](#), [MAOI](#), [SNRI](#)), none of which are taken by this patient.

E - Beta adrenergic receptors

Explanation Why

[Propranolol](#) is a [nonselective beta blocker](#) that decreases [sympathetic](#) activation. It can be used for symptom reduction caused by increased adrenergic tone in patients with [thyroid storm](#), which shares some clinical features with [NMS](#) ([fever](#), [hypertension](#), [tachycardia](#), and altered mental status). However, [thyroid storm](#) usually causes [hyperreflexia](#) and occurs in patients with [hyperthyroidism](#). It would not explain this patient's muscle [rigidity](#) or [hyporeflexia](#).

F - Bacterial cell wall synthesis

Explanation Why

Inhibition of [bacterial cell wall](#) synthesis by forming a complex with [murein](#) is the mechanism of [vancomycin](#), a broad-spectrum [antibiotic](#) that may be indicated if gram-positive [sepsis](#) is suspected. Although [sepsis](#) can also cause altered mental status, [tachycardia](#), [tachypnea](#), and [fever](#), it would not typically cause [hypertension](#), [hyporeflexia](#), or hypertonia.

Question # 28

A 51-year-old woman comes to the physician because of progressively worsening lower back pain. The pain radiates down the right leg to the lateral side of the foot. She has had no trauma, urinary incontinence, or fever. An MRI of the lumbar spine shows disc degeneration and herniation at the level of L5–S1. Which of the following is the most likely finding on physical examination?

	Answer	Image
A	Difficulty walking on heels	
B	Exaggerated patellar tendon reflex	
C	Diminished sensation of the anus and genitalia	
D	Weak achilles tendon reflex	
E	Diminished sensation of the anterior lateral thigh	

Hint

In the lumbar and sacral spinal column, a disc herniation usually affects the spinal nerve below the level of the lesion. So a lumbar disc herniation between vertebral bodies L5 and S1 would most likely result in an S1 radiculopathy.

Correct Answer

A - Difficulty walking on heels

Explanation But

This patient is more likely to show impaired toe walking rather than impaired heel walking.

Explanation Why

Difficulty walking on heels (e.g., foot drop) may be seen in patients with an injury to the L4 or L5 [nerve roots](#). Both the L4 and L5 nerve roots exit the [spinal canal](#) above the level of where this patient's lumbar disc herniation is located (L5 and S1) and are unlikely to be affected. In addition, [L5 radiculopathy](#) would cause [pain](#) extending along the dorsolateral thigh, the [lateral](#) side of the [knee](#), lower leg, and dorsum of the foot and big toe. [L4 radiculopathy](#) would also cause [pain](#) over the patella up to the inner side of the lower leg. This patient describes [pain](#) in neither of these regions.

B - Exaggerated patellar tendon reflex

Explanation Why

An exaggerated [patellar reflex](#) is seen in [UMN](#) lesions affecting the L4 [spinal](#) nerve (e.g., [L4 radiculopathy](#)). [Disc herniations](#), on the other hand, typically cause [LMN](#) lesions, resulting in reduced [deep tendon reflexes](#). Furthermore, involvement of the L4 [spinal](#) nerve is unlikely in this patient with a [disc herniation](#) between the L5–S1 [vertebrae](#) since the nerve exits the [spinal canal](#) above the level of this lesion.

C - Diminished sensation of the anus and genitalia

Explanation Why

Diminished sensation of the [anus](#) and the genitalia is seen in [cauda equina syndrome](#). Although patients typically present with asymmetric, unilateral [radicular pain](#) in the lower limb [dermatomes](#)

(due to a lesion below the level of L2), there are usually numerous [spinal nerves](#) (L3–S5) involved rather than an isolated [nerve root](#) (S1 [dermatome](#)) as seen in this patient. Furthermore, other expected findings (e.g., [saddle block](#) anesthesia, fecal incontinence, and/or [urinary incontinence](#) or retention) are lacking in this patient.

D - Weak achilles tendon reflex

Explanation Why

A lumbar disc herniation between the [vertebral bodies](#) L5 and S1 is a common cause of [S1 radiculopathy](#), which can manifest with a weak [achilles tendon](#) reflex due to compression of the S1 [spinal nerve](#) root. The S1 [spinal nerve](#) is also responsible for sensation of the [lateral](#) aspect of the calf and foot, which explains this patient's radiating [pain](#), as well as for [plantar flexion](#) and [eversion](#), which can result in impaired toe walking.

E - Diminished sensation of the anterior lateral thigh

Explanation Why

Diminished sensation of the [anterior lateral](#) thigh is consistent with an injury to the L3 [nerve root](#) (e.g., [L3 radiculopathy](#)), which could be seen with an L2–L3 [disc herniation](#). The L3 [spinal nerve](#) exits the [spinal canal](#) above the level of this patient's lumbar disc herniation (L5–S1) and is, therefore, unlikely to be affected.

Question # 29

A 29-year-old man comes to the physician for a follow-up examination. He has had numbness and tingling of his legs for the past 10 days. Three months ago, he was diagnosed with pulmonary tuberculosis and started on antituberculosis therapy. Examination shows dry scaly lips and cracks at the corner of the mouth. Sensation to pinprick and light touch is decreased over the lower extremities. His hemoglobin concentration is 10.4 g/dL and mean corpuscular volume is $76 \mu\text{m}^3$. Administration of which of the following is most likely to have prevented this patient's current symptoms?

	Answer	Image
A	Iron	
B	Vitamin E	
C	Folic acid	
D	Vitamin B12	
E	Pyridoxine	
F	Intravenous immunoglobulins	

Hint

This patient's sensory neuropathy and microcytic anemia are the result of isoniazid toxicity.

Correct Answer

A - Iron

Explanation Why

While [iron deficiency](#) is the most common cause of [anemia](#) and could explain the patient's [microcytic anemia](#) and [cheilosis](#), it is not associated with neurologic symptoms.

B - Vitamin E

Explanation Why

[Vitamin E](#) deficiency may present with [peripheral neuropathy](#) (tingling and decreased sensation to pinprick/light touch), but the patient here does not have muscle weakness, [ataxia](#), or [hemolytic anemia](#), which are also typical features of [vitamin E](#) deficiency. In addition, this diagnosis is usually associated with conditions that cause fat [malabsorption](#) (e.g., [pancreatic exocrine insufficiency](#), [cholestatic liver](#) disease), which is not suggested by the patient's history.

C - Folic acid

Explanation Why

[Folate deficiency](#) causes [megaloblastic anemia](#) – not [microcytic anemia](#). It also does not result in sensory neuropathy.

D - Vitamin B12

Explanation Why

Although [vitamin B12 deficiency](#) may present with [peripheral neuropathy](#), as seen in this patient, it is usually accompanied by further neurological abnormalities ([subacute combined degeneration](#)). Additionally, it causes [megaloblastic anemia](#), not [microcytic anemia](#).

E - Pyridoxine

Explanation But

[Isoniazid](#) also commonly causes hepatotoxicity, which presents with elevated [liver](#) enzymes and symptoms such as nausea, vomiting, abdominal [pain](#), and [jaundice](#). Mild hepatotoxicity is usually self-limiting, and treatment should be continued, whereas more severe involvement is an indication for discontinuing the drug.

Explanation Why

Since [pyridoxine](#) ([vitamin B6](#)) is an essential [cofactor](#) in the synthesis of [neurotransmitters](#) and [heme](#), patients with a chronic [pyridoxine deficiency](#) typically present with sensory [peripheral neuropathy](#) and hypochromic, [microcytic anemia](#) ([sideroblastic anemia](#)), as seen here. While [vitamin B6 deficiency](#) is rare in the general population, it is commonly seen in association with [isoniazid](#) ([INH](#)) use in antituberculosis treatment, because [INH](#) competes with [pyridoxine](#) in [neurotransmitter](#) synthesis. To prevent [peripheral neuropathy](#), supplemental [pyridoxine](#) should therefore be added to every treatment regimen that includes [INH](#).

F - Intravenous immunoglobulins

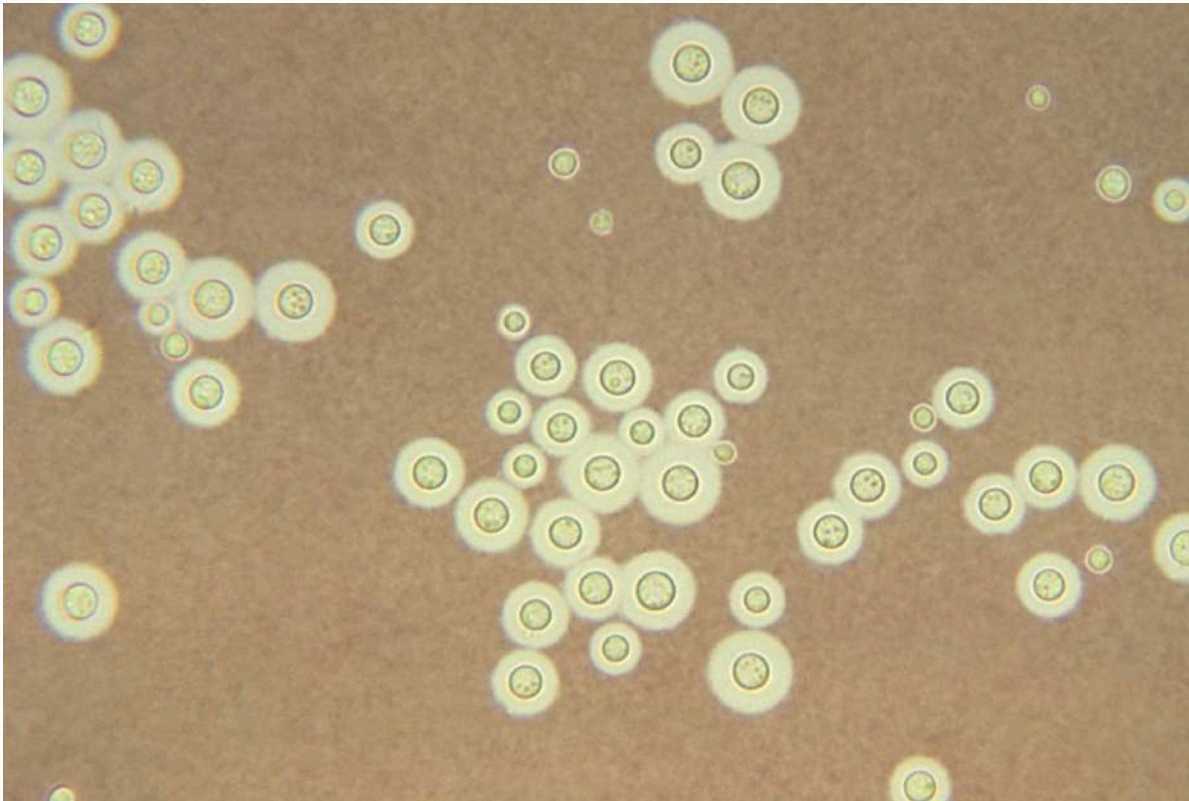
Explanation Why

Intravenous [immunoglobulins](#) are used to treat diseases such as [Guillain-Barré syndrome](#) (GBS). While GBS can also cause [paresthesias](#) of the [distal](#) extremities, these are usually mild and

accompanied by [pain](#), rather than frank loss of sensation. Furthermore, in the case of GBS, muscle reflexes would be absent and bilateral ascending paralysis would be expected.

Question # 30

A 40-year-old woman with HIV infection comes to the emergency department because of a 4-week history of progressively worsening fatigue and headache. Her temperature is 38.1°C (100.6°F). On mental status examination, the patient is somnolent and oriented only to person. Her CD4⁺ lymphocyte count is 80/mm³. Analysis of this patient's cerebrospinal fluid (CSF) shows a leukocyte count of 30/mm³ (60% lymphocytes), a protein concentration of 52 mg/dL, and a glucose concentration of 37 mg/dL. An India ink stain of the CSF is shown. Which of the following is the most appropriate pharmacotherapy for this patient's neurological symptoms?



	Answer	Image
A	Pyrimethamine, sulfadiazine, and folinic acid	
B	Isoniazid, rifampin, pyrazinamide, and ethambutol	

	Answer	Image
C	Cefotaxime and ampicillin	
D	Amphotericin B and flucytosine	
E	Fluconazole	

Hint

This patient presents with fever, headache, and altered mental status, all of which suggests the presence of a CNS infection. Lymphocytic pleocytosis and the detection of a yeast with a prominent halo on Indian ink stain suggest meningitis due to infection with *Cryptococcus neoformans*.

Correct Answer

A - Pyrimethamine, sulfadiazine, and folinic acid

Explanation Why

The combination of [pyrimethamine](#), [sulfadiazine](#), and [folinic acid](#) is the treatment of choice for [cerebral toxoplasmosis](#) in [immunocompromised](#) patients. [Cerebral toxoplasmosis](#) typically presents with altered mental status, [headache](#), focal neurologic deficits, [seizures](#), and [fever](#). Although this patient has signs and symptoms of [CNS](#) infection, and [HIV](#) infection, the [CSF](#) findings suggest a fungal infection, which makes the diagnosis of [cerebral toxoplasmosis](#) unlikely.

B - Isoniazid, rifampin, pyrazinamide, and ethambutol

Explanation Why

The combination of [isoniazid](#), [rifampin](#), [pyrazinamide](#), and [ethambutol](#) is used to treat an active [Mycobacterium tuberculosis](#) infection, which should be suspected in patients who present with constitutional symptoms and pulmonary symptoms. [M. tuberculosis](#) can also spread to the [central nervous system](#) and cause [tuberculous meningitis](#), which may present with [headache](#), [fever](#), and an altered mental status, as seen in this patient. While this patient's [CSF](#) findings suggest a fungal infection, [M. tuberculosis](#) would appear as acid-fast, pink rods on [Ziehl-Neelsen stain](#).

C - Cefotaxime and ampicillin

Explanation Why

The combination of [cefotaxime](#) and [ampicillin](#) is used as an [empiric treatment](#) for community-acquired [meningitis](#) in [neonates](#) < 1 month old. Adult patients < 50 years of age should receive an [empiric treatment](#) with [vancomycin](#) and [ceftriaxone](#). However, this patient has an infection with [Cryptococcus neoformans](#), against which bacterial [antibiotics](#) are of no use.

D - Amphotericin B and flucytosine

Explanation Why

The combination of intravenous [amphotericin B](#) and oral [flucytosine](#) is used to treat [cryptococcal meningitis](#). This combination is administered during the induction phase to achieve rapid [sterilization](#) of the [CSF](#), followed by maintenance therapy with [fluconazole](#). [Cryptococcal meningitis](#) can develop following initial respiratory infection and may lead to death within weeks if left untreated.

E - Fluconazole

Explanation Why

[Fluconazole](#) monotherapy is indicated for the maintenance therapy of [cryptococcal meningitis](#) once the induction phase has been completed. [Fluconazole](#) alone is not sufficient to treat active [cryptococcal meningitis](#).

Question # 31

A 5-day-old boy is brought to the emergency department because of a 1-day history of poor feeding, irritability, and noisy breathing. The mother did not receive any prenatal care. His respirations are 26/min. Physical examination shows sunken fontanelles, tightly clenched fists, and erythema around the umbilical cord stump. Which of the following best describes the pathogenesis of the disease process in this patient?

	Answer	Image
A	Decreased release of acetylcholine	
B	Inhibition of voltage-gated sodium channels	
C	Destruction of Schwann cells	
D	Decreased release of glycine	
E	Destruction of anterior horn cells	

Hint

This newborn has several risk factors (lack of maternal prenatal care, umbilical cord stump infection) that should raise concern for neonatal tetanus.

Correct Answer

A - Decreased release of acetylcholine

Explanation Why

[Infant botulism](#) is due to ingestion of [botulinum toxin](#) produced by [Clostridium botulism](#). The toxin inhibits the release of [acetylcholine](#) from the [neuromuscular junction](#) (NMJ) and causes muscle paralysis. Although [infant botulism](#) also presents with breathing difficulty, poor feeding, and irritability, it causes descending [flaccid paralysis](#), while this patient has [spastic paralysis](#).

B - Inhibition of voltage-gated sodium channels

Explanation Why

Inhibition of voltage-gated sodium channels in the nervous system can occur shortly after ingestion of seafood that is contaminated with [tetrodotoxin](#) or ciguatoxin. These [neurotoxin](#) blocks the formation of [action potentials](#) in [neurons](#) and thereby blocks neural signals from passing to muscles. [Tetrodotoxin](#) or ciguatoxin [poisoning](#) would not be expected in this 5-day old [neonate](#) who has not yet been weaned!

C - Destruction of Schwann cells

Explanation Why

[Guillain-Barré syndrome](#) (GBS) is a postinfectious autoimmune reaction in which [molecular mimicry](#) results in formation of antiganglioside antibodies and subsequent destruction of [Schwann cells](#). GBS causes ascending [flaccid paralysis](#) rather than [spastic paralysis](#) (tightly clenched fists).

D - Decreased release of glycine

Explanation But

The most effective measure to prevent [neonatal tetanus](#) is [immunization](#) of women who are pregnant or of childbearing age. Vaccinated women produce [antibodies](#) against [tetanospasmin](#) that can cross the [placenta](#), which provided [passive immunity](#) for the [neonate](#).

Explanation Why

[Neonatal tetanus](#) is caused by [tetanospasmin](#), which is produced by ubiquitous [Clostridium tetani](#) spores that then contaminate wounds (e.g., [umbilical cord](#)). The toxin reaches the [CNS](#) via retrograde axonal transport and blocks the release of [glycine](#) and [GABA](#) from inhibitory interneurons ([Renshaw cells](#)). This causes uncontrolled activation of [alpha motor neurons](#), which results in tonic and clonic spasms (difficulty opening the mouth and feeding due to [trismus](#), clenched hands).

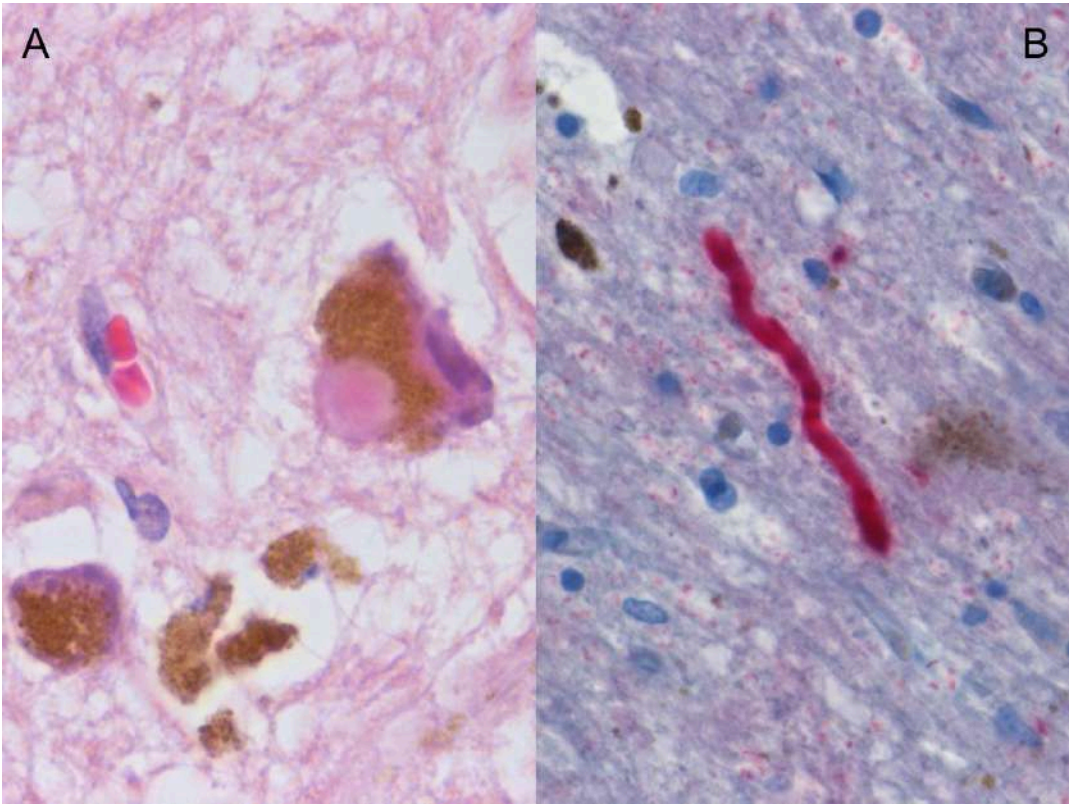
E - Destruction of anterior horn cells

Explanation Why

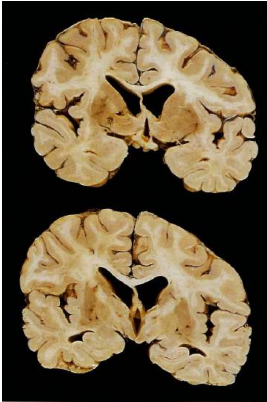
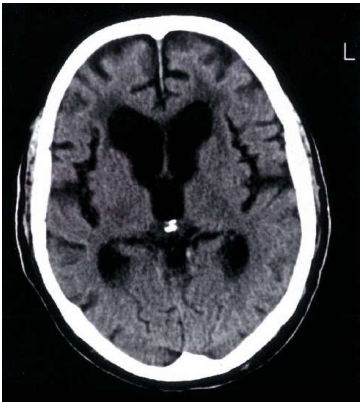
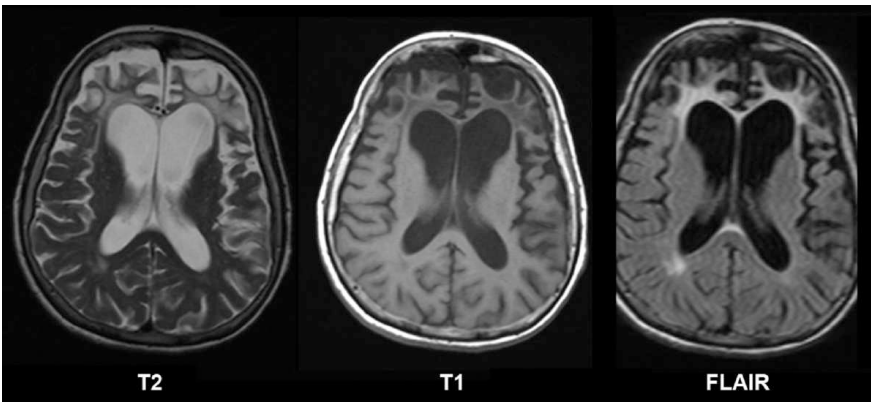
[Poliomyelitis](#) is a viral disease that causes destruction of [anterior horn cells](#). Although difficulty breathing, poor feeding, and irritability are clinical features of [poliomyelitis](#), it causes ascending [flaccid paralysis](#) rather than the [spastic paralysis](#) (tightly clenched fists) seen in this patient. Furthermore, [poliomyelitis](#) has been eradicated from the United States and most other countries due to widespread [vaccination](#).

Question # 32

An 81-year-old man is brought to the physician by his daughter after he was found wandering on the street. For the last 3 months, he often has a blank stare for several minutes. He also claims to have seen strangers in the house on several occasions who were not present. He has hypertension and hyperlipidemia, and was diagnosed with Parkinson disease 8 months ago. His current medications include carbidopa-levodopa, hydrochlorothiazide, and atorvastatin. His blood pressure is 150/85 mm Hg. He has short-term memory deficits and appears confused and disheveled. Examination shows bilateral muscle rigidity and resting tremor in his upper extremities. He has a slow gait with short steps. Microscopic examination of the cortex of a patient with the same condition is shown. Which of the following is the most likely diagnosis?



	Answer	Image
A	Lewy body dementia	
B	Creutzfeldt-Jakob disease	

	Answer	Image
C	Vascular dementia	
D	Normal pressure hydrocephalus	
E	Frontotemporal dementia	

Hint

Histopathological findings show intracellular eosinophilic inclusions composed of α -synuclein. This finding with visual hallucinations is a common combination in this patient's condition.

Correct Answer

A - Lewy body dementia

Explanation Why

Histopathological findings of intracellular [Lewy bodies](#) in the cortex are found in patients with [Parkinson disease](#) or some [Parkinson-plus syndromes](#). New-onset [dementia](#), early onset of gait abnormalities, and a poor response to [levodopa](#) in a patient with [Parkinsonism](#) should raise suspicion of a Parkinson-plus syndrome. This patient's [visual hallucinations](#) are especially consistent with [Lewy body dementia](#), the second most common form of neurodegenerative [dementia](#). Another Parkinson-plus syndrome associated with [Lewy bodies](#) is [multiple system atrophy](#).

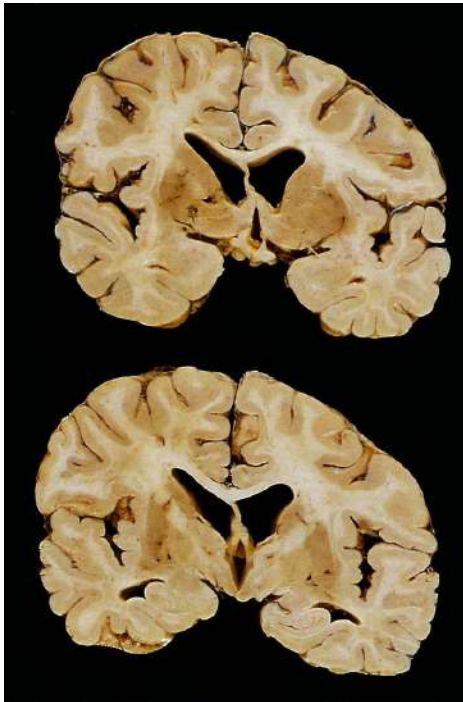
B - Creutzfeldt-Jakob disease

Explanation Why

[Creutzfeldt-Jakob disease](#) is a [prion disease](#) that causes [dementia](#) and [visual hallucinations](#), as seen in this patient. However, the disease progresses extremely rapidly and other findings, such as myoclonus and [seizures](#), would be expected as well. In addition, the biopsy shown in this case does not show [prions](#).

C - Vascular dementia

Image



Explanation Why

Patients with [vascular dementia](#) may present with [dementia](#) and loss of cognitive function (e.g., [disorientation](#)), but the onset is typically abrupt with stepwise deterioration. Moreover, [vascular dementia](#) does not cause [visual hallucinations](#), and focal neurologic deficits (e.g., [hemiparesis](#), [dysarthria](#)) would be expected. [Vascular dementia](#) also does not explain the biopsy findings.

D - Normal pressure hydrocephalus

Image

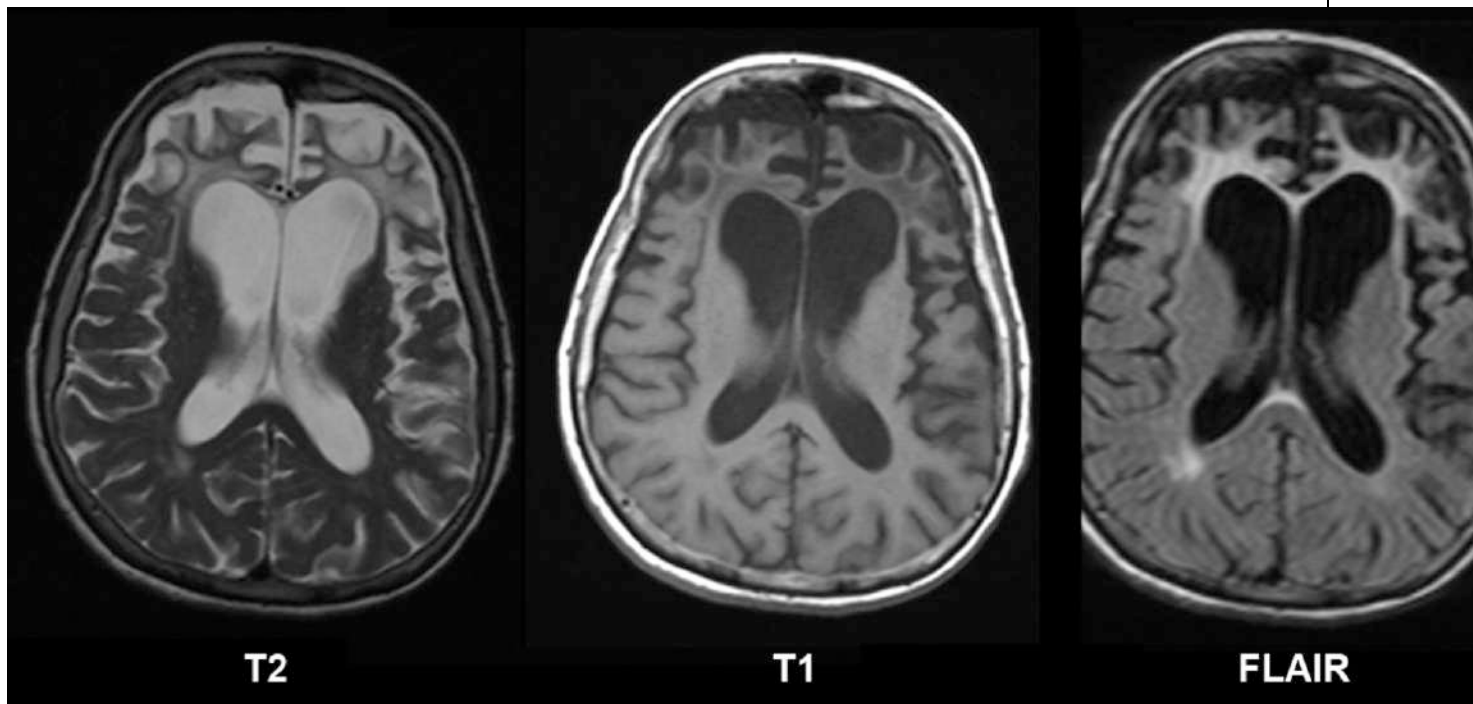


Explanation Why

[Normal pressure hydrocephalus](#) (NPH) is caused by impaired absorption of [CSF](#) and resulting ventriculomegaly. This condition is characterized by [dementia](#) and gait abnormalities. However, another typical feature is [urinary incontinence](#), which this patient lacks. Moreover, the biopsy and [visual hallucinations](#) are inconsistent with NPH.

E - Frontotemporal dementia

Image



Explanation Why

[Frontotemporal dementia](#) also causes [dementia](#) and [parkinsonism](#). However, unlike in this patient, these findings typically manifest in the late stages of disease. Instead, early changes in behavior and personality (e.g., irritability, failure to observe social etiquette) and primary progressive [aphasia](#), which are cardinal signs of [frontotemporal dementia](#), would be expected. Biopsy findings of [frontotemporal dementia](#) would also show inclusions of hyperphosphorylated [tau proteins](#) (called [Pick bodies](#)) or ubiquitinated [TDP-43](#). In addition, [frontotemporal dementia](#) typically manifests between the ages of 40–69.

Question # 33

A 53-year-old woman is brought to the physician by her husband for the evaluation of progressive memory loss, which he reports began approximately 2 weeks ago. During this time, she has had problems getting dressed and finding her way back home after running errands. She has also had several episodes of jerky, repetitive, twitching movements that resolved spontaneously. She is oriented only to person and place. She follows commands and speaks fluently. She is unable to read and has difficulty recognizing objects. Which of the following is the most likely underlying cause of this patient's symptoms?

	Answer	Image
A	Extracellular senile plaques	
B	Copper accumulation	
C	Mutant prion accumulation	
D	Severe cerebral ischemia	
E	Increased number of CAG repeats	
F	Substantia nigra degeneration	

Hint

This patient has Creutzfeldt-Jakob disease, which causes myoclonus (jerky, repetitive, twitching movements) and rapidly-progressive dementia associated with aphasia and agnosia.

Correct Answer

A - Extracellular senile plaques

Explanation Why

Extracellular [senile plaques](#) made of [A \$\beta\$ protein](#) are associated with [Alzheimer disease](#) (AD), which manifests with progressive [memory](#) loss, language deficits, and temporal and spatial [disorientation](#). The [memory](#) loss seen in patients with AD is gradual and affects short-term [memory](#) first. This patient's rapid progression within the past 2 weeks and associated myoclonus are inconsistent with AD.

B - Copper accumulation

Image



Explanation Why

[Wilson disease](#) is characterized by [copper](#) accumulation in the [liver](#), [cornea](#), and [central nervous system](#); particularly within the [basal ganglia](#), [brain stem](#), and [cerebellum](#). Neurologic symptoms include [parkinsonism](#), drooling, and behavioral changes such as depression, irritability, and [psychosis](#). Patients also present with [liver](#) disease (e.g., [cirrhosis](#), hepatitis, [acute liver failure](#)), [dysarthria](#), and almost always [Kayser-Fleischer](#) rings on [slit-lamp examination](#). While this patient has some [speech](#) difficulties and motor anomalies, she does not have signs of [liver](#) disease or [Kayser-Fleischer](#) rings, and she is older than the typical age of onset for [Wilson disease](#) (5–35 years).

C - Mutant prion accumulation

Explanation Why

[Creutzfeldt-Jakob disease](#) ([CJD](#)) is a [neurodegenerative disorder](#) caused by cerebral accumulation of misfolded protein particles called [prions](#). Normal [prion proteins](#) (PrP^c) are found on the surface of cortical [neurons](#) and are protective against [free radicals](#). Misfolded [prion proteins](#) (PrP^{Sc}) have more [beta-sheets](#) in their [secondary structures](#), which changes their conformation. These misfolded [proteins](#) accumulate into plaques, causing neuronal [cell death](#) and spongiform encephalopathy. As there is no curative treatment for [CJD](#), management is supportive and most patients die within 12 months of diagnosis.

D - Severe cerebral ischemia

Explanation Why

Severe cerebral [ischemia](#) (i.e., [stroke](#)) causes irreversible neurologic deficits, and multiple [strokes](#) can cause [vascular dementia](#) (VD). Patients with VD typically present with a stepwise decline in function (following each [ischemic](#) event), as well as focal deficits such as [hemiparesis](#), unilateral [visual field](#) deficits, [urinary incontinence](#), and behavioral changes. This patient's rapid, nonstepwise progression of symptoms and myoclonus are not typical of VD.

E - Increased number of CAG repeats

Explanation Why

An increased number of CAG repeats in the [huntingtin gene](#) on [chromosome 4](#) causes [Huntington disease](#) (HD), an [autosomal dominant](#) hereditary disorder that most commonly manifests around 40 years of age. Patients present with [dementia](#), depression, and/or anxiety, along with [choreiform](#) movements (more irregular than the myoclonus motions seen in this patient). [Dementia](#) in HD usually first occurs in advanced stages of the disease. Also, this patient is older than the typical age of onset and has no [family history](#) of [neurodegenerative disorders](#).

F - Substantia nigra degeneration

Explanation Why

[Substantia nigra](#) degeneration occurs in [Parkinson disease](#) (PD). [Dementia](#) associated with PD is insidious and unlikely to progress rapidly within 2 weeks, as seen in this patient. In addition, the motor symptoms associated with PD are [bradykinesia](#)/akinesia, a [resting tremor](#), [rigidity](#), [postural instability](#), and a [Parkinsonian gait](#) and not myoclonus, which is seen in this patient.

Question # 34

A 66-year-old man is brought to the emergency department 1 hour after the abrupt onset of painless loss of vision in his left eye. Over the last several years, he has noticed increased blurring of vision; he says the blurring has made it difficult to read, but he can read better if he holds the book below or above eye level. He has smoked 1 pack of cigarettes daily for 40 years. Fundoscopic examination shows subretinal fluid and small hemorrhage with grayish-green discoloration in the macular area in the left eye, and multiple drusen in the right eye with retinal pigment epithelial changes. Which of the following is the most appropriate pharmacotherapy for this patient's eye condition?

	Answer	Image
A	Ustekinumab	
B	Ruxolitinib	
C	Cetuximab	
D	Aldesleukin	
E	Etanercept	
F	Ranibizumab	

Hint

The patient's acute, painless, unilateral loss of central vision (central scotoma), together with his history of gradual loss of central vision and fundoscopic findings of a subretinal hemorrhage and grayish-green retinal discoloration, are characteristic of wet age-related macular degeneration.

Correct Answer

A - Ustekinumab

Explanation Why

[Ustekinumab](#) is a human [monoclonal antibody](#) that acts as an antagonist of both [interleukin-12 \(IL-12\)](#) and [interleukin-23 \(IL-23\)](#). Both of these [proteins](#) play a role in immune-mediated disorders; [IL-12](#) induces [Th1](#)-cell differentiation and [IFN- \$\gamma\$](#) production, whereas IL-23 plays a role in controlling TH17 development. [Ustekinumab](#) is used in the treatment of [psoriasis](#), [psoriatic arthritis](#), and [Crohn disease](#) but not wet [age-related macular degeneration](#).

B - Ruxolitinib

Explanation Why

[Ruxolitinib](#) is a [tyrosine kinase inhibitor](#) that acts as a JAK1/2 inhibitor. It is used in the treatment of [polycythemia vera](#); it is not indicated for wet [age-related macular degeneration](#).

C - Cetuximab

Explanation Why

[Cetuximab](#) is an [epidermal growth factor receptor \(EGFR\)](#) inhibitor that is used in the treatment of stage IV [colorectal cancer](#), and head and neck cancers. It is not used for the treatment of wet [age-related macular degeneration](#).

D - Aldesleukin

Explanation Why

[Aldesleukin](#) is a recombinant [cytokine](#) that acts as an [interleukin-2 \(IL-2\)](#) analog. It is used in the immunotherapy of [renal cell carcinoma](#) and [metastatic melanoma](#). However, it is not used for the treatment of wet [age-related macular degeneration](#).

E - Etanercept

Explanation Why

[Etanercept](#) is a [tumor necrosis factor \(TNF\)](#) inhibitor that acts as a [TNF- \$\alpha\$](#) decoy receptor. It is mainly used in the treatment of systemic inflammatory illnesses like [rheumatoid arthritis](#), [inflammatory bowel disease \(IBD\)](#), and [ankylosing spondylitis](#). It has no role in the treatment of wet [age-related macular degeneration](#).

F - Ranibizumab

Image



Explanation But

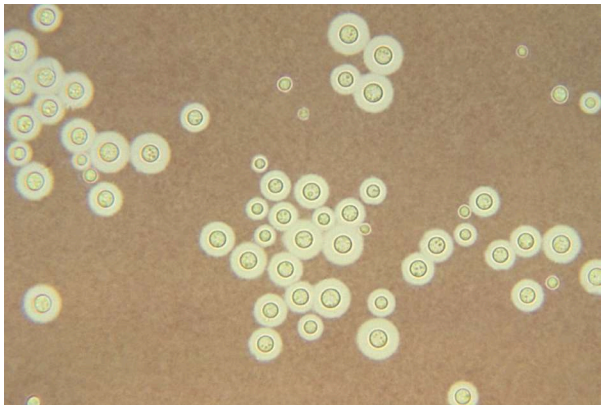
Dry [AMD](#), the most common form of [AMD](#), involves the deposition of [drusen](#) in and under the [retinal pigment epithelium](#). These depositions cause progressive [atrophy](#) of the central and/or pericentral [retinal pigment epithelium](#), resulting in painless central and/or pericentral visual impairment.

Explanation Why

[Ranibizumab](#) is a [vascular endothelial growth factor \(VEGF\)](#) inhibitor. [VEGF](#) release in wet [age-related macular degeneration](#) (wet [AMD](#) or neovascular [AMD](#)) causes growth of new, friable blood vessels in the choriocapillaris, which are [prone](#) to bleeding and leaking. [VEGF](#) inhibitors delivered intravitreally are the first-line treatment for wet [AMD](#) and have become the mainstay of treatment due to their efficacy and safety profile.

Question # 35

A 52-year-old woman with HIV infection is brought to the emergency department 20 minutes after she had a generalized tonic-clonic seizure. She appears lethargic and confused. Laboratory studies show a CD4+ count of 89 cells/ μ L ($N > 500$). A CT scan of the head with contrast shows multiple ring-enhancing lesions in the basal ganglia and subcortical white matter. An India ink preparation of cerebrospinal fluid is negative. Which of the following is the most likely diagnosis?

	Answer	Image
A	HIV encephalopathy	
B	Progressive multifocal leukoencephalopathy	
C	Primary CNS lymphoma	
D	Cryptococcal encephalitis	

	Answer	Image
E	Cerebral toxoplasmosis	

Hint

In a patient with HIV with a CD4⁺ count < 100 cells/μL, multiple ring enhancing lesions are pathognomonic features of this condition.

Correct Answer

A - HIV encephalopathy

Explanation Why

[HIV encephalopathy](#) is a complication of advanced [HIV](#) infection. However, patients typically have evidence of cerebral atrophy and non-enhancing lesions, unlike this patient's [ring-enhancing](#) lesions. Additionally, the most common clinical features of [HIV encephalopathy](#) include [memory](#) losses, depression, gait disturbances, and movement disorders, none of which are seen here.

B - Progressive multifocal leukoencephalopathy

Explanation Why

[PML](#) is a rapidly progressive [HIV](#)-associated [CNS](#) disease caused by reactivation of [JC virus](#). Unlike this patient's lesions which are [ring-enhancing](#), [PML](#) associated [CNS](#) lesions are typically non-enhancing.

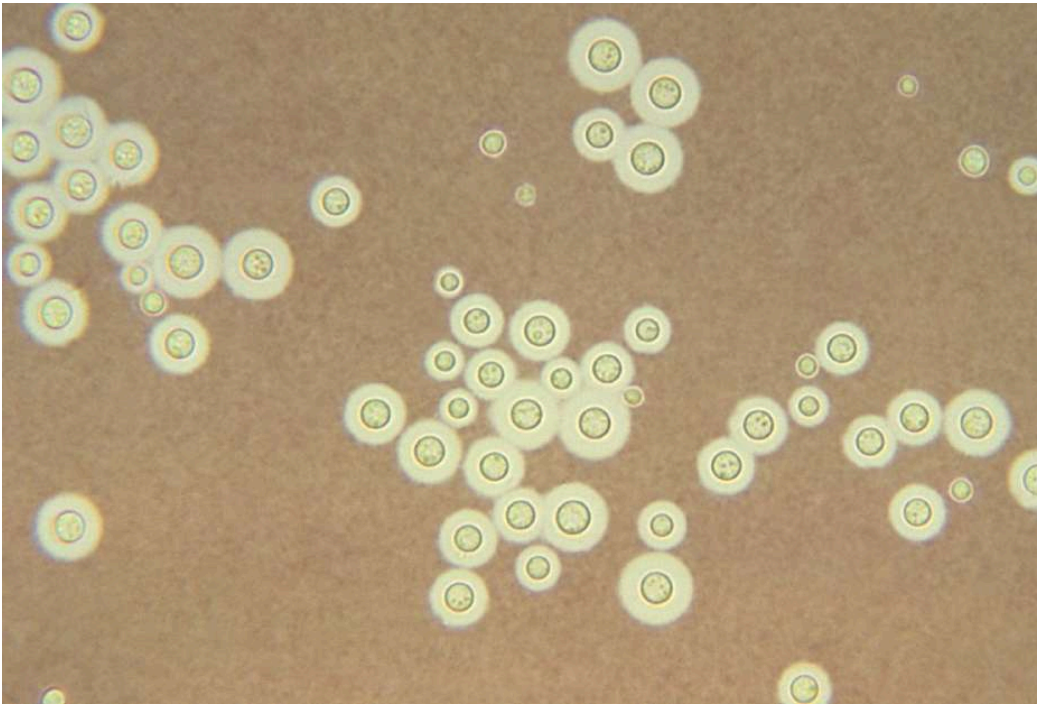
C - Primary CNS lymphoma

Explanation Why

[Primary CNS lymphoma \(PCNSL\)](#), a type of extranodal [non-Hodgkin lymphoma](#) associated with [HIV](#) infection, can cause [seizures](#) and a [ring-enhancing](#) lesion on brain imaging. However, patients usually have a solitary lesion (unlike the multiple lesions in this patient) located in periventricular white regions or the corpus callosum.

D - Cryptococcal encephalitis

Image

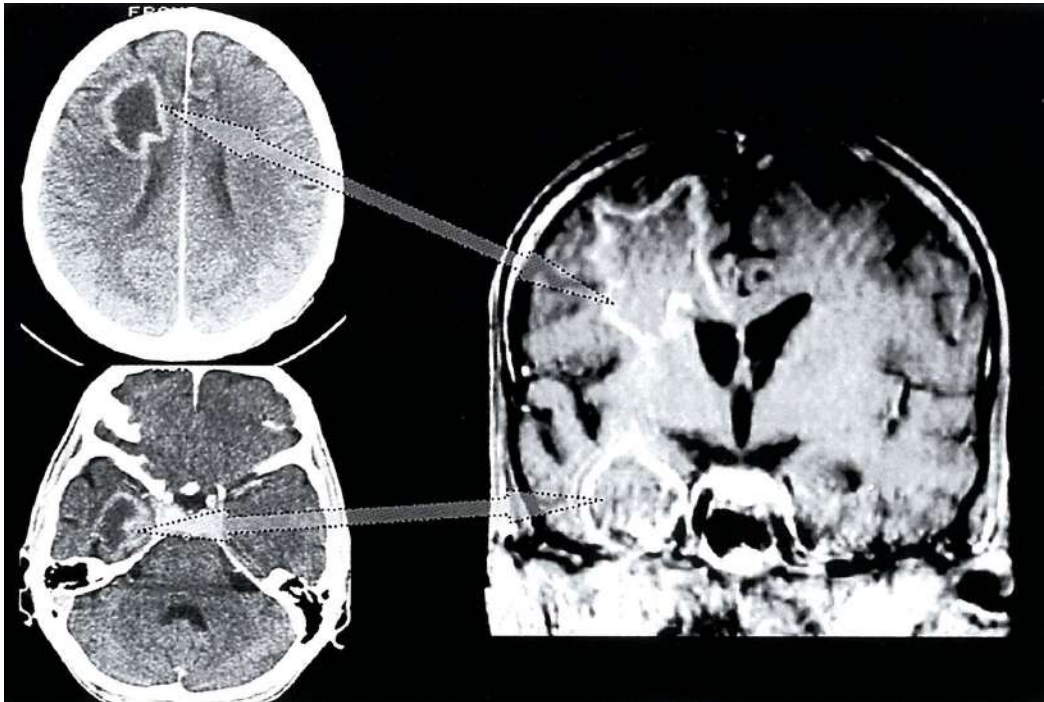


Explanation Why

[Cryptococcal meningoencephalitis](#) can cause [seizures](#) in [immunocompromised](#) patients (e.g., [AIDS](#) patients) and present with partially [ring-enhancing](#) lesions in the [basal ganglia](#). However, an [India-ink preparation](#) of the [CSF](#) would have been positive for [yeast](#) cells with halos.

E - Cerebral toxoplasmosis

Image

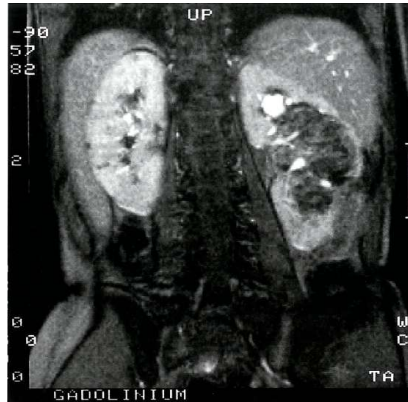


Explanation Why

In an [immunocompromised](#) patient, multiple [ring enhancing lesions](#) within the subcortical [white matter](#), [basal ganglia](#), and/or [thalamus](#) are highly suggestive of [cerebral toxoplasmosis](#). *Toxoplasma gondii* is an obligate intracellular parasite, contracted via ingestion of cysts in raw meat or cat feces. In immunocompetent patients, the presentation is usually asymptomatic. [Cerebral toxoplasmosis](#) is treated with a combination of [sulfadiazine](#) and [pyrimethamine](#).

Question # 36

A 6-year-old boy is brought to the physician by his parents because of right lower extremity weakness, worsening headaches, abdominal pain, dark urine, and a 5-kg (11-lb) weight loss for the past 2 months. His teachers report that he has not been paying attention in class and his grades have been worsening. He has a history of infantile seizures. Physical examination shows a palpable abdominal mass and left costovertebral angle tenderness. Neurological exam shows decreased strength of the right lower limb. He has several acne-like angiofibromas around the nose and cheeks. Further evaluation is most likely to show which of the following?

	Answer	Image
A	Port wine stain	
B	Pheochromocytoma	
C	Lisch nodules	
D	Subependymal giant cell astrocytoma	
E	Vestibular schwannoma	

Hint

This boy's combination of facial angiofibromas (adenoma sebaceum), signs of angiomyolipomas (abdominal mass, macrohematuria), a history of infantile seizures, and signs of a potential brain tumor (i.e., focal neurologic deficits indicated by decreased limb strength, declining performance, poor attention) indicates tuberous sclerosis.

Correct Answer

A - Port wine stain

Explanation Why

A [port wine stain](#) in the V1-V2 [trigeminal nerve](#) distribution is characteristic of [Sturge-Weber syndrome \(SWS\)](#), which also causes neurologic disturbances such as [seizures](#), [intellectual disability](#), and focal neurological deficits (e.g., paresis, [visual field](#) defects). Although this patient's history of [seizures](#), poor attention and declining performance at school could represent neurological manifestations of [SWS](#), [angiofibromas](#) on the nose and cheeks and renal involvement (as indicated by [hematuria](#)) would not be expected.

B - Pheochromocytoma

Explanation Why

[Pheochromocytoma](#) is a [tumor](#) associated with [Von Hippel-Lindau disease \(VHL\)](#). Other tumors that can occur in [VHL](#) include [hemangioblastomas](#) (most often in the [cerebellum](#), [spinal cord](#), and/or [retina](#)), [renal cell carcinoma](#), and [pancreatic](#) cysts and tumors. Although this patient has clinical features that can be caused by [VHL](#) ([headaches](#), [hematuria](#), abdominal mass, and left [costovertebral angle tenderness](#)), [angiofibromas](#) on the nose and cheeks would not be expected.

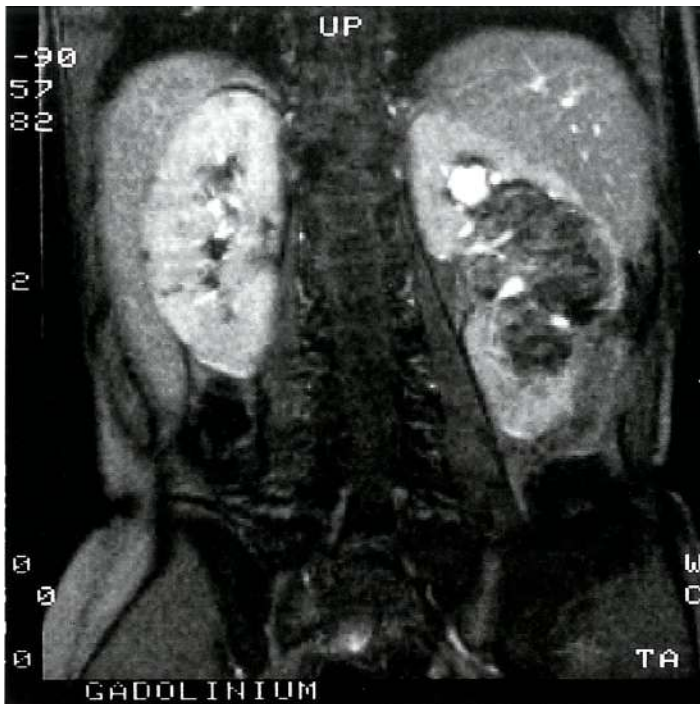
C - Lisch nodules

Explanation Why

[Lisch nodules](#) are an ophthalmologic finding associated with [Neurofibromatosis type 1 \(NF1\)](#). This condition is characterized by café-au-lait spots, [neurofibromas](#), and optic pathway [gliomas](#). It may be accompanied by [seizures](#), cognitive deficits, and soft tissue [sarcomas](#) such as [gastrointestinal stromal tumors](#). This patient's [seizures](#), weight loss, declining performance, poor attention, and abdominal fullness may be consistent with [NF1](#). However, [angiofibromas](#) of the nose and cheeks would not be expected. In addition, his flank [pain](#) and [hematuria](#) point to a renal rather than gastrointestinal origin of his abdominal [pain](#) and fullness.

D - Subependymal giant cell astrocytoma

Image



Explanation But

This patient's infantile [seizures](#) were likely caused by “[tubers](#)” (cortical tumors) in the brain.

Explanation Why

Subependymal giant cell astrocytoma is a [brain tumor](#) associated with [tuberous sclerosis \(TSC\)](#). Other common manifestations of [TSC](#) that this patient could develop include [shagreen patches](#), [ash-leaf spots](#), benign cysts, and [renal cell carcinoma](#).

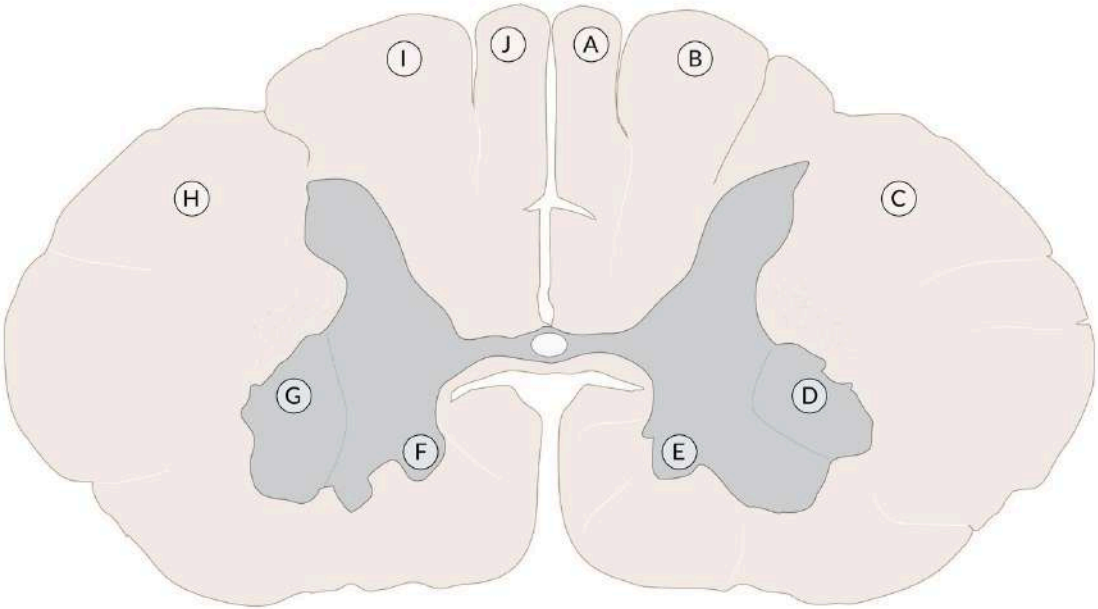
E - Vestibular schwannoma

Explanation Why

[Vestibular schwannoma](#) is a [brain tumor](#) that is associated with [neurofibromatosis type 2 \(NF2\)](#), particularly if there is bilateral involvement. The condition is typically diagnosed when tumors appear in late [adolescence](#) or early adulthood. While subcutaneous lesions (usually [schwannomas](#) or neurilemmomas) can be present in [NF2](#), this patient's [angiofibromas](#) around the nose and cheeks would not be expected. Moreover, this patient's findings indicate renal, behavioral, and cognitive abnormalities, which are inconsistent with a diagnosis of [NF2](#).

Question # 37

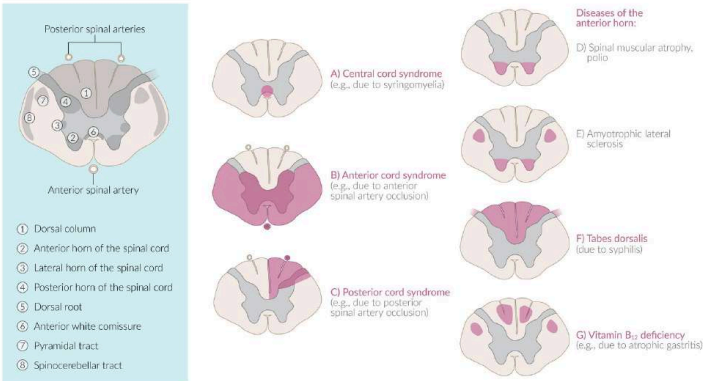
A 44-year-old man comes to the physician because of weakness in his right hand for the past 3 months. He works as a violinist in a professional orchestra. Physical examination shows atrophy of the thenar and dorsal interosseus muscles of the right hand. Sensation to pinprick and vibration is normal. A cross-section of the spinal cord at the level of C6 is shown. The most likely cause of this patient's symptoms is damage to which of the following labeled structures?



Right

Left

	Answer	Image
A	A	
B	B	
C	C	

	Answer	Image
D	D	
E	E	
F	F	
G	G	 Posterior spinal arteries Anterior spinal artery 1 Dorsal column 2 Anterior horn of the spinal cord 3 Lateral horn of the spinal cord 4 Posterior horn of the spinal cord 5 Dorsal root 6 Anterior white commissure 7 Pyramidal tract 8 Spinocerebellar tract A) Central cord syndrome (e.g., due to syringomyelia) B) Anterior cord syndrome (e.g., due to anterior spinal artery occlusion) C) Posterior cord syndrome (e.g., due to posterior spinal artery occlusion) Diseases of the anterior horn: D) Spinal muscular atrophy, polio E) Amyotrophic lateral sclerosis F) Tabes dorsalis (due to syphilis) G) Vitamin B₁₂ deficiency (e.g., due to atrophic gastritis)
H	H	
I	I	
J	J	

Hint

Muscle atrophy and weakness are signs of lower motor neuron damage.

Correct Answer

A - A

Explanation Why

Structure A is the left [fasciculus gracilis](#). Damage to this structure leads to a loss of sensory functions (pressure, vibration, fine touch, and [proprioception](#)) of the left lower body and legs. This loss of function is seen in conditions such as [tabes dorsalis](#) and [subacute combined degeneration](#). Muscle [atrophy](#) and weakness would not be expected. Moreover, the patient's preserved sensation to pinprick and vibration rules out this possibility.

B - B

Explanation Why

Structure B is the left [fasciculus cuneatus](#). Damage to this structure leads to a loss of sensory functions (pressure, vibration, fine touch, and [proprioception](#)) in the left upper body and arm, which is seen in conditions such as [tabes dorsalis](#) and [subacute combined degeneration](#). Muscle [atrophy](#) and weakness would not be expected. Moreover, the patient's preserved sensation to pinprick and vibration rules out this possibility.

C - C

Explanation Why

Structure C is the left [lateral corticospinal tract](#). Damage to this structure would lead to signs of [upper motor neuron damage](#) on the left side of the body (e.g., increased muscle tone and reflexes). This patient presents with [lower motor neuron](#) symptoms of the right side of the body, ruling out this possibility.

D - D

Explanation Why

Structure D is the left dorsolateral column in the [anterior horn](#). Damage to this structure would lead to signs of [lower motor neuron damage](#) (e.g., muscle weakness, reduced muscle tone, loss of reflexes) of the [distal](#) portion of the left limbs. This patient's [lower motor neuron signs](#) are on the right side of his body, not the left.

E - E

Explanation Why

Structure E is the left dorsomedial column in the [anterior horn](#). Damage to this structure would lead to signs of [lower motor neuron damage](#) (e.g., muscle weakness, reduced muscle tone, loss of reflexes) on the left side of the body in the region of the shoulder and the [proximal](#) extensor muscles. This patient presents with signs of [lower motor neuron damage](#) in the right hand, not in the left [proximal](#) arm or shoulders.

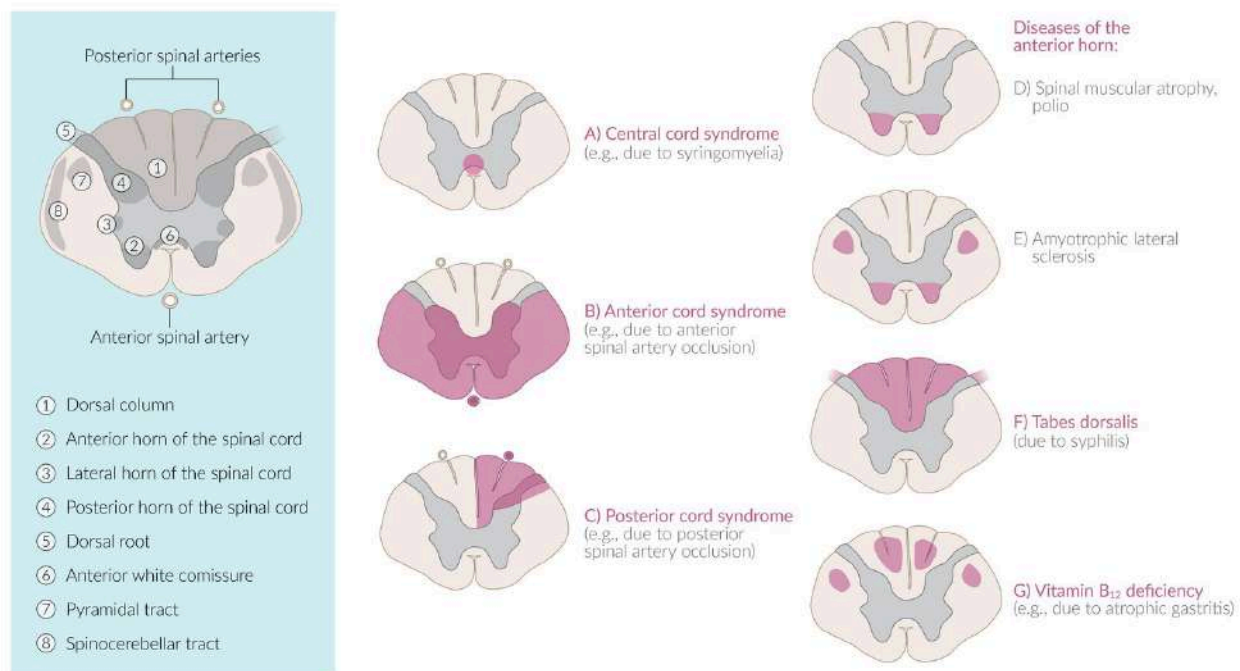
F - F

Explanation Why

Structure F is the right dorsomedial column in the [anterior horn](#). Damage to the right [medial](#) group of the [anterior horn](#) would lead to signs of [lower motor neuron damage](#) (e.g., muscle weakness, reduced muscle tone, loss of reflexes) on the right side of the body in the region of the shoulder and the [proximal](#) extensor muscles. This patient presents with signs of [lower motor neuron damage](#) in the hand, not in the [proximal](#) arm or shoulders.

G - G

Image



Explanation But

[Median nerve palsy](#) leads to similar [atrophy](#), but it also manifests with associated sensory deficits.

Explanation Why

Structure G, the right dorsolateral column in the [anterior horn](#), is responsible for this patient's symptoms. This patient's presentation of [atrophy](#) restricted to the [thenar eminence](#) is a common early sign of [amyotrophic lateral sclerosis \(ALS\)](#), known as split-hand syndrome. While the [corticospinal tracts](#) (structures C and H) are also often damaged in [ALS](#), this patient has no signs of [upper motor neuron damage](#) (e.g., increased muscle tone and reflexes).

H - H

Explanation Why

Structure H is the right [lateral corticospinal tract](#). Damage to this structure would lead to signs of [upper motor neuron damage](#) (e.g., increased muscle tone and reflexes) on the right side of the body. The patient's presentation with [lower motor neuron](#) symptoms rules out this possibility.

I - I

Explanation Why

Structure I is the right [fasciculus cuneatus](#). Damage to this structure leads to a loss of the sensory functions (pressure, vibration, fine touch, and [proprioception](#)) of the right upper body and arm, which is seen in conditions such as [tabes dorsalis](#) and [subacute combined degeneration](#). Muscle [atrophy](#) and weakness would not be expected. Moreover, the patient's preserved sensation to pinprick and vibration rules out this possibility.

J - J

Explanation Why

Structure J is the right [fasciculus gracilis](#). Damage to this structure leads to a loss of sensory functions (pressure, vibration, fine touch, and [proprioception](#)) of the right lower body and leg, which is seen in conditions such as [tabes dorsalis](#) and [subacute combined degeneration](#). Muscle [atrophy](#) and weakness would not be expected. Moreover, the patient's preserved sensation to pinprick and vibration rules out this possibility.

Question # 38

A 67-year-old man is brought to the physician by his daughter because he frequently misplaces his personal belongings and becomes easily confused. His daughter mentions that his symptoms have progressively worsened for the past one year. On mental status examination, he is oriented to person, place, and time. He vividly recalls memories from his childhood but can only recall one of three objects presented to him after 5 minutes. His affect is normal. This patient's symptoms are most likely caused by damage to which of the following?

	Answer	Image
A	Substantia nigra	
B	Amygdala	
C	Ventral posterolateral nucleus	
D	Nucleus accumbens	
E	Hippocampus	
F	Superior temporal gyrus	

Hint

Short-term memory loss is often the earliest sign of Alzheimer disease, the most common cause of progressive dementia in the United States.

Correct Answer

A - Substantia nigra

Explanation Why

The [substantia nigra](#) is part of the [basal ganglia](#) and plays a role in initiation of voluntary movements. Damage to this region occurs in [Parkinson disease](#), which presents with [bradykinesia](#), [tremor](#), and/or [rigidity](#). This patient has [memory](#) deficits, which are unlikely to be caused by damage to the [substantia nigra](#).

B - Amygdala

Explanation But

Bilateral damage to the [amygdala](#) results in Klüver-Bucy syndrome, which is characterized by emotional lability, anxiety, hypersexuality, [hyperorality](#), and [hyperphagia](#).

Explanation Why

The [amygdala](#) is a structure of the [limbic system](#) that plays a role in the processing of emotions. Involvement of the [amygdala](#) in [Alzheimer disease](#) causes emotional lability, depression, and/or [anhedonia](#). Damage to a different structure would more likely explain the short-term [memory](#) loss in this patient with a normal affect.

C - Ventral posterolateral nucleus

Explanation Why

The [ventral posterolateral nucleus](#) is a structure of the [thalamus](#) involved in relaying sensory input from the [spinothalamic tract](#) and [dorsal column](#) to the [primary somatosensory cortex](#). This nucleus does not play a role in [memory](#) formation and is not affected in early [Alzheimer disease](#). The [medial dorsal nucleus](#) of the [thalamus](#) and the [anterior thalamic nucleus](#) are involved in [memory](#) formation.

D - Nucleus accumbens

Explanation But

Decreased [GABA](#) secretion by the nucleus accumbens is seen in [Huntington disease](#) and [anxiety disorders](#).

Explanation Why

The nucleus accumbens is a basal forebrain structure that has a role in the reward pathway. This structure does not play a major role in semantic (factual) recall. Degeneration of other basal forebrain structures such as the [nucleus basalis of Meynert](#) can cause [memory](#) loss and cognitive decline in [Alzheimer disease](#).

E - Hippocampus

Explanation Why

The earliest sites of neurodegeneration in [Alzheimer disease](#) are structures in the [medial temporal lobe](#) such as the [hippocampus](#) and parahippocampal cortex, which are critical for [memory](#) formation.

F - Superior temporal gyrus

Explanation Why

The [superior temporal gyrus](#) of the dominant hemisphere contains the [primary auditory cortex](#) and the [Wernicke area](#). Damage to this structure would result in [sensory aphasia](#). Early [Alzheimer disease](#) can cause [atrophy](#) of the [medial temporal lobe](#) structures but typically has little impact on the [superior temporal gyrus](#).

Question # 39

A 62-year-old man with hypertension and atrial fibrillation is brought to the emergency department because of sudden onset visual changes. He stopped taking all of his medications 2 months ago. Blood pressure is 170/90 mm Hg and pulse is 108/min. He is alert and oriented to person but does not follow commands. His speech is fluent with normal cadence, but he uses frequent non-existent words and the content of his speech is nonsensical. He appears unaware of his speech impairment. He is unable to read a text out loud. Peripheral vision is diminished in the right upper visual fields bilaterally. This patient's presentation is most consistent with injury to which of the following labeled areas?



	Answer	Image
A	A	
B	B	
C	C	

	Answer	Image
D	D	
E	E	

Hint

This patient's receptive aphasia, right upper homonymous quadrantanopsia, and CVA risk factors are concerning for stroke secondary to occlusion of the inferior division of the left MCA.

Correct Answer

A - A

Explanation Why

Region A corresponds with the [hippocampus](#), which is involved in the [limbic system](#) and is important for [memory](#) formation; it is supplied by the [posterior cerebral artery](#) and is particularly vulnerable to [ischemia](#). [Ischemic stroke](#) involving the [hippocampus](#) would result in [anterograde amnesia](#) rather than the fluent [aphasia](#) and [visual field](#) defects seen in this patient.

B - B

Explanation Why

Region B corresponds with the [internal capsule](#) and is a common site of [lacunar infarcts](#), which classically present with contralateral [hemiparesis](#) or [hemiplegia](#); [dysarthria](#) and [dysphagia](#) may also be present. This patient has significant [risk factors](#) for a [lacunar infarct](#) (e.g., age and unmanaged [hypertension](#)), but his [receptive aphasia](#) and right upper [homonymous quadrantanopsia](#) are not consistent with an [internal capsule infarct](#).

C - C

Explanation Why

Region C corresponds with the [insula](#), a complex structure involved in perception, somatosensory processing, visceromotor functions, and [cognition](#). [Ischemic](#) injury to this region is extremely rare and can have variable presentation, including vestibular, motor, somatosensory, [speech](#), and/or cardiac conduction abnormalities. Insular [strokes](#) are most commonly associated with [nonfluent aphasia](#); the combination of a fluent, [receptive aphasia](#) and right upper [homonymous quadrantanopsia](#) in this patient is not consistent with an insular [stroke](#).

D - D

Explanation Why

Region D corresponds with the inferior frontal [gyrus](#), which is an important region for language and comprehension and is supplied by the superior division of the [MCA](#). [Ischemic stroke](#) involving the inferior frontal [gyrus](#) classically presents with [Broca aphasia](#), which is characterized by nonfluent [speech](#) deficits and relative sparing of comprehension. This patient has evidence of fluent [aphasia](#), making injury to the inferior frontal [gyrus](#) unlikely.

E - E

Explanation Why

The patient's presentation of [Wernicke aphasia](#) and right upper [homonymous quadrantanopsia](#) is most consistent with an [ischemic](#) injury to the [superior temporal gyrus](#) (region E) due to an [ischemic stroke](#) involving the inferior division of the left [MCA](#). His [visual field](#) deficits are the result of the involvement of the inferior fascicle of the left [optic radiations](#) (Meyer loop) in the [temporal lobe](#). His [atrial fibrillation](#) and medical nonadherence suggest a [thromboembolic stroke](#) as the underlying cause.

Question # 40

A 59-year-old man with Parkinson disease is brought to the emergency department 1 hour after he had a syncopal episode. Over the past two weeks, the patient has felt light-headed upon standing and has noticed that his legs have been swollen. He was started on a medication for early symptoms of Parkinson disease one month ago. Vital signs show blood pressure 114/70 mm Hg when supine and 92/38 mm Hg upon standing. Examination of the lower extremities shows a lacy, purple rash and 2+ pitting edema. Neurologic examination shows an ataxic gait. The physician decreases the dose of medication. The patient is most likely experiencing adverse effects caused by a drug that works through which of the following mechanisms of action?

	Answer	Image
A	Increased dopamine release from central neurons	The diagram illustrates the synthesis, release, and metabolism of dopamine. In the substantia nigra, dopamine is synthesized from L-tyrosine by the enzyme tyrosine decarboxylase (DDC). Dopamine precursors (L-DOPA) can be converted to dopamine by COMT (catechol-O-methyltransferase) in the blood or by COMT in the brain. COMT inhibitors (Tolcapone (peripheral), Entacapone (peripheral)) block this conversion. In the brain, COMT is also inhibited by Selegiline (MAO-B inhibitor). Dopamine is released from the presynaptic terminal into the synaptic cleft, where it can bind to dopamine receptors on the postsynaptic neuron. Dopamine is also metabolized by MAO-B in the glial cell. Dopamine agonists (Ropinirole (nonergot), Bromocriptine (ergot)) bind to dopamine receptors. The diagram also shows the striatum where dopamine acts on M-cholinergic receptors (inhibited by anticholinergic drugs like Benztropine) and NMDA receptors (inhibited by NMDA antagonists like Amantadine).
B	Inhibition of acetylcholine activity in the basal ganglia	
C	Selective inhibition of monoamine oxidase type B	
D	Decreased peripheral conversion of levodopa to dopamine	

	Answer	Image
E	Inhibition of central methylation of dopamine	

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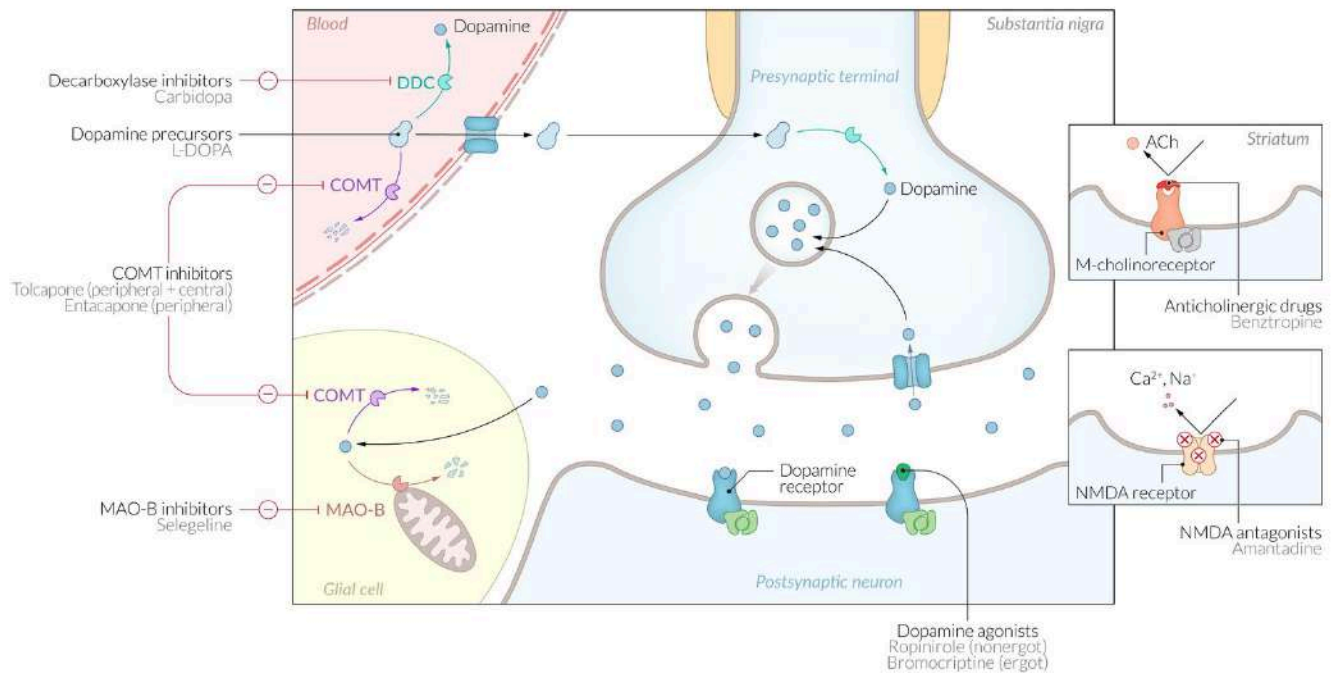
Hint

This patient shows signs of amantadine toxicity, including orthostatic hypotension, livedo reticularis, peripheral edema, and ataxia.

Correct Answer

A - Increased dopamine release from central neurons

Image



Explanation Why

[Amantadine](#) increases [dopamine](#) release, decreases [dopamine](#) reuptake, and inhibits the [N-methyl-D-aspartate](#) (NMDA) receptor. It can be used as initial short-term monotherapy in patients with mild [symptoms of Parkinson disease](#), mainly for those with prominent [tremor](#). In addition to the side effects seen in this patient, [amantadine](#) is associated with [anticholinergic](#)-like side effects (e.g., dry mouth, [constipation](#)), [prolonged QT interval](#), and psychological disorders (e.g., [hallucinations](#), anxiety).

B - Inhibition of acetylcholine activity in the basal ganglia

Explanation Why

Inhibition of [acetylcholine](#) activity in the [basal ganglia](#) is the mechanism of action of [muscarinic antagonists](#) (e.g., [benztropine](#)). [Muscarinic antagonists](#) can be used as initial monotherapy in patients with [Parkinson disease](#), particularly in those with a prominent [tremor](#). Although [muscarinic antagonists](#) can lead to [hypotension](#), they would not explain this patient's [livedo reticularis](#), peripheral [edema](#), or [ataxia](#). [Anticholinergic side effects](#) such as dry mouth, confusion, and [constipation](#) would occur instead.

C - Selective inhibition of monoamine oxidase type B

Explanation Why

Selective [monoamine oxidase](#) type B ([MAO-B](#)) inhibitors (e.g., [selegiline](#)) increase [dopamine](#) availability by preventing its breakdown. [MAO-B inhibitors](#) can be used for short-term monotherapy in the early stages of [Parkinson disease](#). Although patients can experience [orthostatic hypotension](#) from [MAO-B inhibitor](#) therapy, [livedo reticularis](#) and peripheral [edema](#) are not typical. Other adverse effects of [MAO-B inhibitors](#) include [headaches](#), [dizziness](#), psychological disorders (e.g., [hallucinations](#)), and [hypertensive crisis](#) (when ingested with foods containing [tyramine](#)).

D - Decreased peripheral conversion of levodopa to dopamine

Explanation Why

By decreasing the peripheral conversion of [levodopa](#) to [dopamine](#), [carbidopa](#) increases the amount of [levodopa](#) that can cross the [blood-brain](#) barrier and enter the [central nervous system](#). [Carbidopa](#) is only used in combination with [levodopa](#) and would not be administered as monotherapy. Furthermore, [carbidopa](#) reduces the risk of side effects due to increased peripheral [dopamine](#) (e.g., [orthostatic hypotension](#)) and would not explain this patient's [livedo reticularis](#), peripheral [edema](#), or [ataxia](#).

E - Inhibition of central methylation of dopamine

Explanation Why

By inhibiting central [methylation](#) of [dopamine](#) to 3-methoxytyramine, [catechol-O-methyltransferase \(COMT\)](#) inhibitors (e.g., [tolcapone](#)) increase [dopamine](#) availability. [COMT inhibitors](#) are typically used in combination with [carbidopa/levodopa](#); they should not be used as monotherapy. Although [COMT inhibitors](#) can cause [orthostatic hypotension](#), they would not cause this patient's [livedo reticularis](#), peripheral [edema](#), or [ataxia](#).

Question # 1

A 3-week-old male infant is brought to the physician for follow-up. He was delivered at 30 weeks' gestation via cesarean section and was cyanotic at birth, requiring resuscitation and a neonatal intensive care unit hospitalization. His mother received no prenatal care; she has diabetes mellitus type II and hypertension. She was not tested for sexually transmitted infections during the pregnancy. The infant appears well. Ophthalmologic examination shows tortuous retinal vessels. There are well-demarcated areas of nonvascularized retina in the periphery. This patient's retinal findings are most likely a result of which of the following?

	Answer	Image
A	Retinal malignancy	
B	Oxygen toxicity	
C	Glucocorticoid deficiency	
D	Hyperglycemia	
E	Syphilis infection	
F	Non-accidental trauma	
G	Chlamydia infection	

Hint

This infant's ophthalmologic examination revealed areas of nonvascularized retina with tortuous vessels, which are consistent with retinopathy of prematurity (ROP).

Correct Answer

A - Retinal malignancy

Explanation Why

[Retinoblastoma](#) is an important cause of ocular disease in [infants](#) and is caused by mutations in the RB1 tumor suppressor gene that are often inherited. However, this patient has no [family history](#) of [malignancy](#) and the ophthalmologic findings are not consistent with [retinoblastoma](#).

B - Oxygen toxicity

Explanation Why

This [premature infant](#) likely received supplemental oxygen at [birth](#), which is a major contributing factor in the development of [ROP](#). Higher arterial oxygen tension in a [premature infant](#) inhibits the production of [VEGF](#), leading to [apoptosis](#) of [endothelial](#) cells and cessation of normal retinal vascular formation. Switching to room air results in relative [hypoxia](#) due to the lower oxygen concentration, increased metabolic demand of the growing [retina](#), and poor vascular network, leading to the production of proangiogenic growth factors (e.g., [VEGF](#)) and uncontrolled [neovascularization](#). The formation of new blood vessels can cause hemorrhages, form fibrovascular membranes, and ultimately lead to [retinal detachment](#) or blindness.

C - Glucocorticoid deficiency

Explanation Why

[Glucocorticoid](#) deficiency is associated with an increased risk of [neonatal respiratory distress syndrome](#), as [glucocorticoids](#) play a vital role in promoting fetal [lung](#) maturity by stimulating the production of [surfactant](#). However, [glucocorticoid](#) deficiency is not a [risk factor](#) for the development of [ROP](#).

D - Hyperglycemia

Explanation Why

Maternal [diabetes](#) may lead to a wide range of complications in the [infant](#), including [macrosomia](#), respiratory distress, [hyperbilirubinemia](#), and congenital cardiac anomalies. Maternal [diabetes](#) also increases the risk of prematurity, which is the greatest [risk factor](#) for [ROP](#). While this [infant's](#) prematurity may be related to maternal [diabetes](#), there is another factor that more directly contributes to the development of [ROP](#).

E - Syphilis infection

Explanation Why

[Syphilis](#) is one of several congenital infections ([TORCH infections](#)) that can cause ocular abnormalities in affected [infants](#). [Congenital syphilis](#) can manifest with [uveitis](#), [keratitis](#), [glaucoma](#), and congenital [cataracts](#). However, this [infant's](#) funduscopy findings are highly indicative of [ROP](#), and, although infection may worsen the course of [ROP](#), it is not a contributing factor to the development of this condition.

F - Non-accidental trauma

Explanation Why

[Head trauma](#) as a result of rotational and shearing forces can cause [shaken baby syndrome](#). This condition manifests with retinal and [intracranial hemorrhages](#) but does not contribute to the development of [ROP](#).

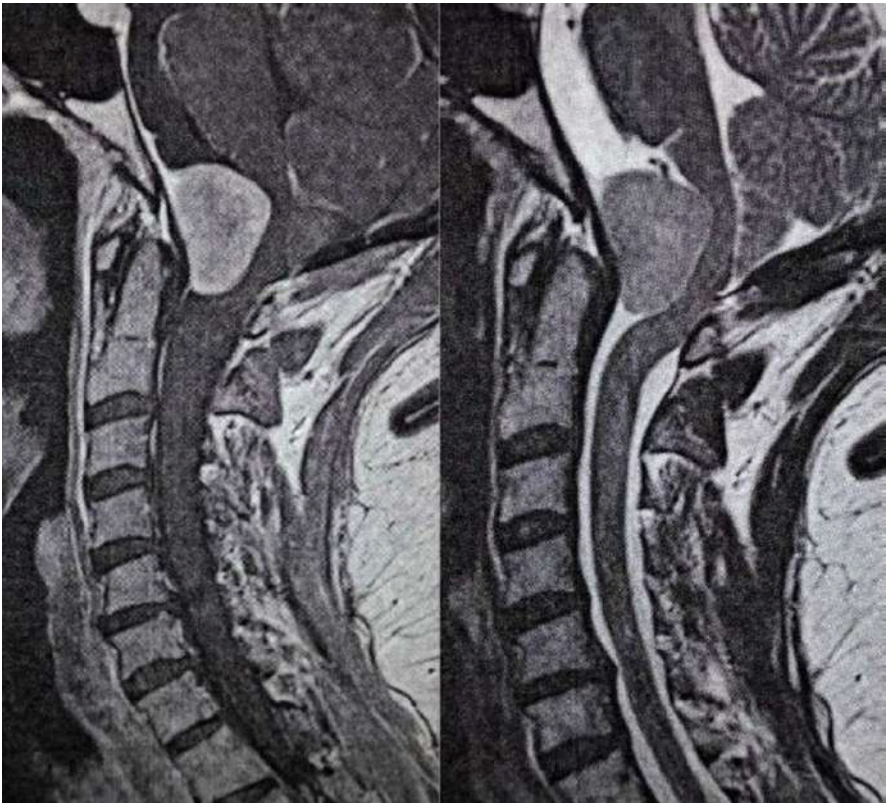
G - Chlamydia infection

Explanation Why

Mothers receiving routine [prenatal care](#) are screened for [chlamydia](#) infection to eliminate the risk of [chlamydial conjunctivitis](#) in the [newborn](#). This mother's lack of [prenatal care](#) puts the [infant](#) at risk of this disease, which often manifests 1–2 weeks after [birth](#). However, ocular findings include mucopurulent or watery discharge, [eyelid](#) swelling, and [chemosis](#). This disease does not affect the [retina](#).

Question # 2

A 63-year-old woman comes to the office because of a 2-year history of upper and lower extremity weakness and neck pain that is worse with sneezing. She has had difficulty swallowing and speaking for the past 8 months. Musculoskeletal examination shows spasticity and decreased muscle strength in all extremities. There is bilateral atrophy of the trapezius and sternocleidomastoid muscles. Neurologic examination shows an ataxic gait and dysarthria. Deep tendon reflexes are 4+ bilaterally. Babinski sign is positive. Sensation is decreased below the C5 dermatome bilaterally. An MRI of the neck and base of the skull is shown. Which of the following is the most likely cause of this patient's symptoms?



	Answer	Image
A	Foramen magnum meningioma	
B	Cerebral glioblastoma multiforme	
C	Cerebellar astrocytoma	

	Answer	Image
D	Amyotrophic lateral sclerosis	
E	Syringomyelia	

Hint

The pattern of this patient's presentation is suggestive of CNS compression in a location that affects both long tracts (cortical) and bulbar tracts.

Correct Answer

A - Foramen magnum meningioma

Explanation But

[Meningiomas](#) are slow-growing tumors, patients usually present after several months to years of slowly progressive symptoms, as seen in this patient that progressed in the course of 2-years.

Explanation Why

This patient most likely has a [foramen magnum meningioma](#), as indicated by the [MRI](#). Although the [falx cerebri](#), the [supratentorial](#) convex surface, and the sphenoidal wings are the most common locations of [meningiomas](#), in rare cases they also occur at the [foramen magnum](#). Early features include neck [pain](#), which is typically worse with neck [flexion](#) and maneuvers that increase ICP (e.g., sneezing). Later, patients present with long tract signs (e.g., sensory and motor deficits that progress from one extremity to the others). Other late findings include [spasticity](#) ([hyperreflexia](#)), positive [Babinski sign](#), gait disturbances, and lower [cranial nerve palsies](#) (CN IX–XII), which most likely accounts for this patient's [dysarthria](#) and [atrophy](#) of the [sternocleidomastoid](#) and [trapezius](#) muscles. Microscopic examination shows [psammoma bodies](#) and concentrically arranged spindle cells.

B - Cerebral glioblastoma multiforme

Explanation Why

A [glioblastoma multiforme](#) is most commonly located in the [white matter](#) of the cerebral hemispheres and therefore most frequently manifests with [signs of increased intracranial pressure](#) (e.g., [headache](#), [seizures](#)). The symptoms develop over a short period of time (several weeks) due to rapid growth of the [tumor](#). While the condition can present with motor weakness, the pattern of symptom progression over 2 years seen in this patient is not consistent with [glioblastoma multiforme](#).

C - Cerebellar astrocytoma

Explanation Why

Pilocytic [astrocytomas](#) are grade I (benign) [astrocytomas](#) that are often localized in the [cerebellum](#) and most frequently occur in children and young adults. Signs of [cerebellar](#) masses include [symptoms of increased intracranial pressure](#) (e.g., [headache](#), nausea, and vomiting), [ataxia](#), and possibly [failure to thrive](#). While an [ataxic gait](#) could be caused by a [cerebellar tumor](#), the patient's age, muscle weakness, sensory symptoms, and [dysarthria](#) suggest another diagnosis.

D - Amyotrophic lateral sclerosis

Explanation Why

[Amyotrophic lateral sclerosis](#) manifests with signs of [UMN](#) (e.g., [hyperreflexia](#), [spastic paresis](#)) as well as [LMN](#) involvement (e.g., [atrophy](#), [fasciculations](#), and [flaccid paresis](#)), both of which are present in this patient. [ALS](#) may initially present with bulbar symptoms (e.g., [dysarthria](#), [dysphagia](#)) and/or asymmetric limb weakness, which often begins unilaterally in an upper extremity and progresses during the course of disease. However, her only [LMN](#) deficit is the result of a lower [cranial nerve](#) lesion ([sternocleidomastoid muscle atrophy](#) due to [CN XI](#) involvement), whereas other typical [LMN lesions](#) are missing (muscle [atrophy](#) of the extremities and [fasciculations](#)). Also, [ALS](#) is usually a rapidly progressive disease that leads to life-threatening symptoms such as respiratory failure (due to paralysis of respiratory muscles) or weight loss and [malnutrition](#) (due to [dysphagia](#)) within three years, making [ALS](#) an unlikely diagnosis in this patient.

E - Syringomyelia

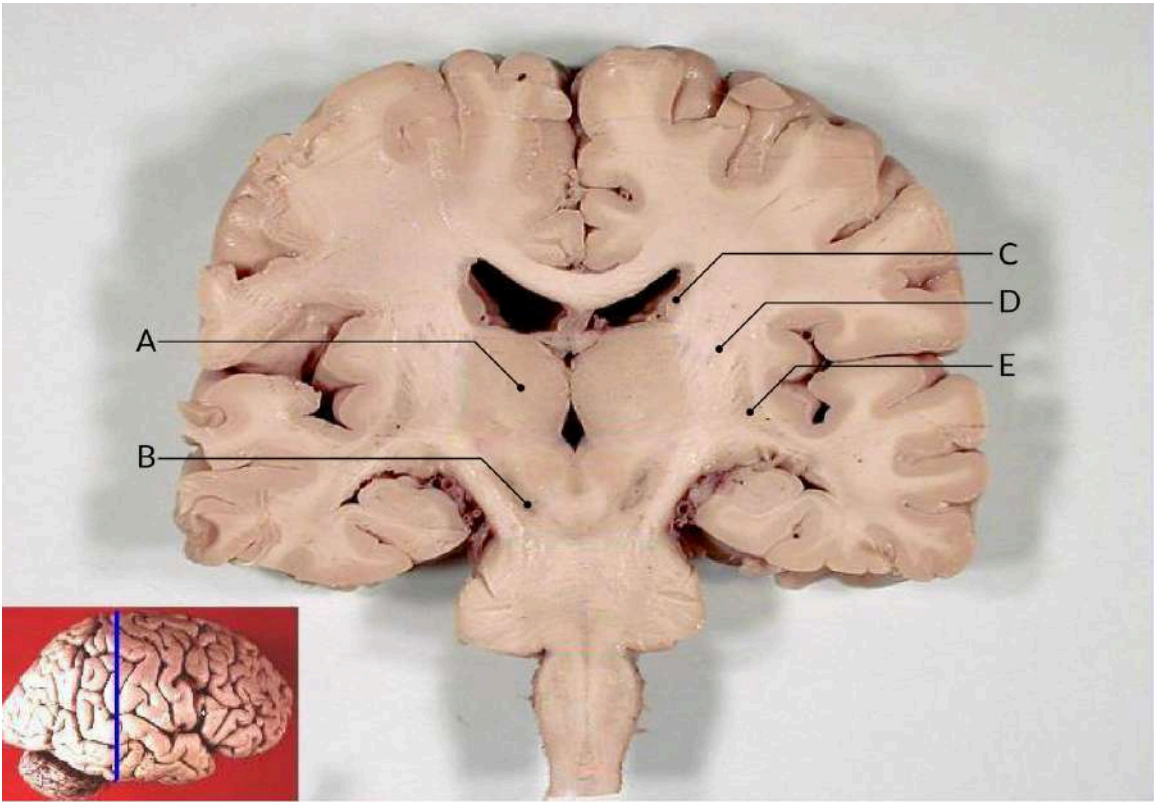
Explanation Why

In [syringomyelia](#), the compression from the fluid-filled cavity within central [spinal cord](#) results in neck [pain](#) and a cape-like distribution (neck, shoulders, arms) of [dissociated sensory loss](#) that develops over years. The sensory symptoms in [syringomyelia](#) are often exacerbated by maneuvers that increase the intramedullary pressure (e.g., [coughing](#), sneezing), as in this patient. Muscle [atrophy](#) is another common feature of [syringomyelia](#) and most commonly affects the small muscles of the

hand. Other [LMN signs](#), such as [fasciculations](#) and areflexia (rather than this patient's [hyperreflexia](#)), may also be present. While [spastic paraparesis](#) of the limbs is a possible feature of [syringomyelia](#) (involvement of the [pyramidal tract](#) and first motor [neuron](#)), quadriparesis would be uncommon.

Question # 3

A 71-year-old man comes to the physician because of involuntary shaking and gait abnormalities for the past year. He also reports depressed mood and diminished smell and taste. Examination shows a shuffling gait, resting tremor in the left hand, and rigidity in both arms. This patient most likely has structural changes in which of the following labeled areas of the brain?



	Answer	Image
A	A	

	Answer	Image
B	B	Parkinson disease Etiology Degeneration of dopaminergic neurons in the substantia nigra (motor inhibition) Epidemiology Sex: ♀ = ♂ Peak age: 50–60 years Cardinal symptoms T - Tremor (resting) R - Rigidity A - Akinesia P - Postural instability Common early symptoms Myalgia and arthralgia Hyposmia Depression Obstipation Life expectancy Normal with treatment Patients often become dependent on care in later stages
C	C	
D	D	
E	E	

Hint

This patient's depressed mood, sensory deficits (hyposmia), and motor findings are characteristic of Parkinson disease.

Correct Answer

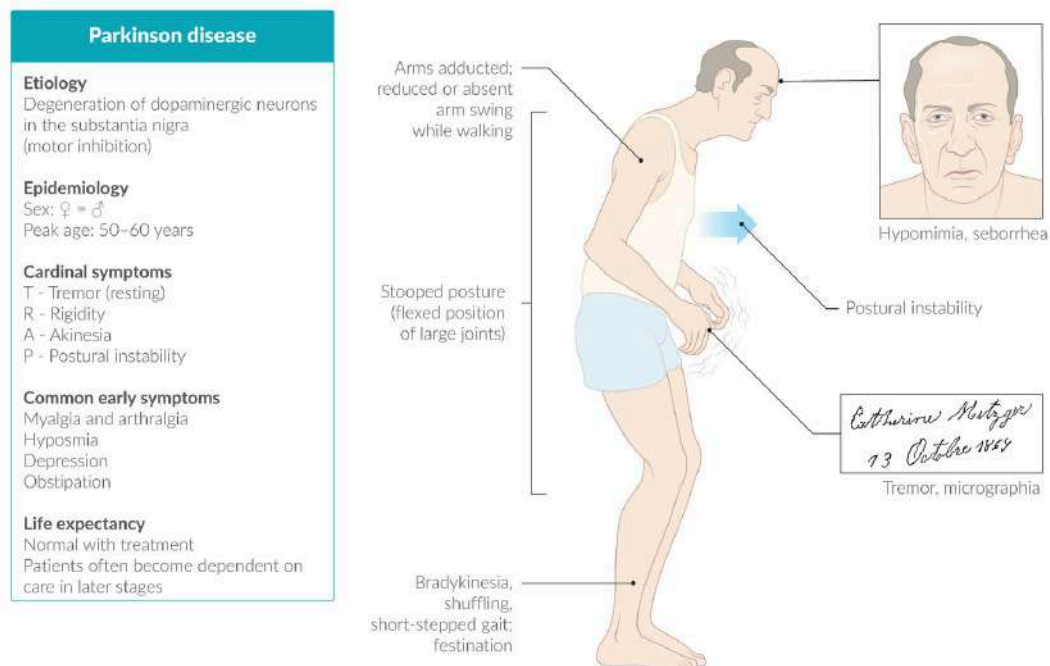
A - A

Explanation Why

The [thalamus](#) serves as a relay station for motor and somatosensory information between subcortical structures and the [cerebral cortex](#). [Hemorrhagic stroke](#) is the most common cause of thalamic dysfunction and can manifest acutely with [hemiparesis](#), [paresthesia](#), imbalance, and autonomic and cognitive impairment. The [thalamus](#) is not involved in [Parkinson disease](#). Moreover, afferent stimuli for every sensory system are relayed via a thalamic nucleus, except for the olfactory system. Hence, [anosmia](#) is unlikely to occur due to a lesion in the [thalamus](#).

B - B

Image



Explanation But

[Melanin](#) pigments in cells of the [substantia nigra](#) are responsible for its black/dark brown appearance.

Explanation Why

The [substantia nigra](#) pars compacta contains [dopaminergic neurons](#) that transmit signals involved in movement regulation and is the part of the [basal ganglia](#) affected in [Parkinson disease](#). Progressive degeneration of these [neurons](#) results in a clinical syndrome characterized by [bradykinesia](#)/akinesia, [resting tremor](#), [rigidity](#), and gait abnormalities, as seen in this patient. Additional findings include sensory deficits, personality changes, and [dementia](#).

C - C

Explanation Why

The [caudate nucleus](#) is a component of the [striatum](#) that is affected in [Huntington disease](#). Although [caudate nucleus atrophy](#) can also occur in [Parkinson disease](#), significant degeneration of [neurons](#) in this region would result in hyperkinetic symptoms (e.g., [chorea](#), nystagmus, [hyperreflexia](#)) and [autonomic dysfunction](#) (e.g., hyperhidrosis, [urinary incontinence](#)), neither of which are reported here.

D - D

Explanation Why

The [internal capsule](#) is a subcortical structure located between the [basal ganglia](#). It contains motor and somatosensory fibers that can be damaged as a result of an [ischemic](#) or [hemorrhagic stroke](#). [Hemiparesis](#), [paresthesia](#), and [ataxia](#) commonly manifest after an injury to the [internal capsule](#). The [internal capsule](#) is not involved in the pathophysiology of [Parkinson disease](#).

E - E

Explanation Why

The [putamen](#) is a component of the [striatum](#) that is involved in the regulation of movement and learning. [Hemorrhagic stroke](#) secondary to [hypertension](#) is the most common cause of putaminal dysfunction, which can manifest with acute-onset contralateral [hemiplegia](#), sensory loss, gaze palsy, ipsilateral deviation of the eyes, [stupor](#), and [coma](#). [Parkinson disease](#) is not associated with structural changes in the [putamen](#).

Question # 4

Two weeks after starting chemotherapy with etoposide, a 66-year-old man with small cell lung cancer comes to the physician because of persistent nausea and vomiting. His symptoms improve significantly after the administration of metoclopramide. This patient's symptoms were most likely due to the effect of chemotherapy on which of the following structures?

	Answer	Image
A	Vestibular nerve	
B	Intestinal smooth muscle	
C	Vagus nerve	
D	Cerebral cortex	
E	Area postrema	

Hint

Chemotherapy induces nausea by acting on the chemoreceptor trigger zone, which responds to certain chemicals in the blood. Metoclopramide is a dopamine receptor antagonist that is especially effective in chemotherapy-induced nausea and vomiting.

Correct Answer

A - Vestibular nerve

Explanation Why

The vestibular branch of the [vestibulocochlear nerve](#) sends input to the [nucleus tractus solitarius](#) (NTS), which is part of the vomiting center of the medulla. Conditions such as Ménière disease, [labyrinthitis](#), and motion sickness can overstimulate the vestibular nerve and cause vomiting. The vestibular nerve is not directly involved in [chemotherapy](#)-induced nausea.

B - Intestinal smooth muscle

Explanation But

[Metoclopramide](#) can enhance the effects of [acetylcholine](#) on intestinal [smooth muscle](#), thereby promoting motility and accelerating gastric emptying.

Explanation Why

Intestinal [smooth muscle cell](#) function is required to maintain normal bowel motility and digestion. Conditions that impair intestinal motility, such as [paralytic ileus](#), chronic [dyspepsia](#), and [Hirschsprung disease](#), can lead to [nausea and vomiting](#). However, this is not a common site involved in [chemotherapy](#)-induced nausea and [etoposide](#) is not known to have any effect on intestinal [smooth muscle cells](#).

C - Vagus nerve

Explanation Why

The [vagus nerve](#) carries afferent input from the [gastrointestinal tract](#) to the [nucleus tractus solitarius](#) (NTS), which is part of the vomiting center of the medulla. The NTS responds to [serotonin](#) release from the [GI tract](#), which sensitizes the [vagus nerve](#) and causes vomiting. This pathway is blocked

both centrally and peripherally by [serotonin receptor antagonists](#) such as [ondansetron](#) and [metoclopramide](#) (at high doses). [Chemotherapy](#)-induced nausea occurs due to effects on a different structure.

D - Cerebral cortex

Explanation But

Anticipatory emesis can usually be treated with [anxiolytics](#) such as [lorazepam](#). [Metoclopramide](#) is not typically used for psychogenic or stress-induced vomiting

Explanation Why

The [cerebral cortex](#) sends input to the [nucleus tractus solitarius](#) (NTS) in the vomiting centers of the medulla. The [cerebral cortex](#) is involved in psychogenic vomiting, which can result from psychiatric disorders and/or emotional distress, and includes anticipatory emesis (which is commonly seen in patients receiving [chemotherapy](#)). However, the [cerebral cortex](#) is not directly affected in [chemotherapy](#)-induced nausea.

E - Area postrema

Explanation Why

The [area postrema](#) is an area of the medulla that contains the chemoreceptor trigger zone (CTZ) and is one of the primary sites involved in [chemotherapy-induced nausea and vomiting](#), along with the [nucleus tractus solitarius](#). The [area postrema](#) of the [brainstem](#) has [fenestrated capillaries](#), which allows input from substances in the blood such as drugs (e.g., [chemotherapy](#)) and/or [hormones](#). [Metoclopramide](#) is a D2 [dopamine receptor antagonist](#) that acts primarily by inhibiting the vomiting centers of the [area postrema](#).

Question # 5

A 27-year-old man is brought to the emergency department because of a knife wound to his back. His pulse is 110/min, respirations are 14/min, and blood pressure is 125/78 mm Hg. Examination shows a 5-cm deep stab wound at the level of T9. He withdraws the right foot to pain but is unable to sense vibration or whether his right toe is flexed or extended. Sensation in the left leg is normal. Motor strength is 5/5 in all extremities. Rectal tone is normal. Which of the following spinal column structures was most likely affected?

	Answer	Image
A	Dorsal root	
B	Posterior spinal artery	
C	Central spinal cord grey matter	
D	Lateral corticospinal tract	
E	Artery of Adamkiewicz	

Hint

A unilateral loss of proprioception and vibration with preservation of motor function and pain sensation indicates isolated damage to this patient's dorsal column.

Correct Answer

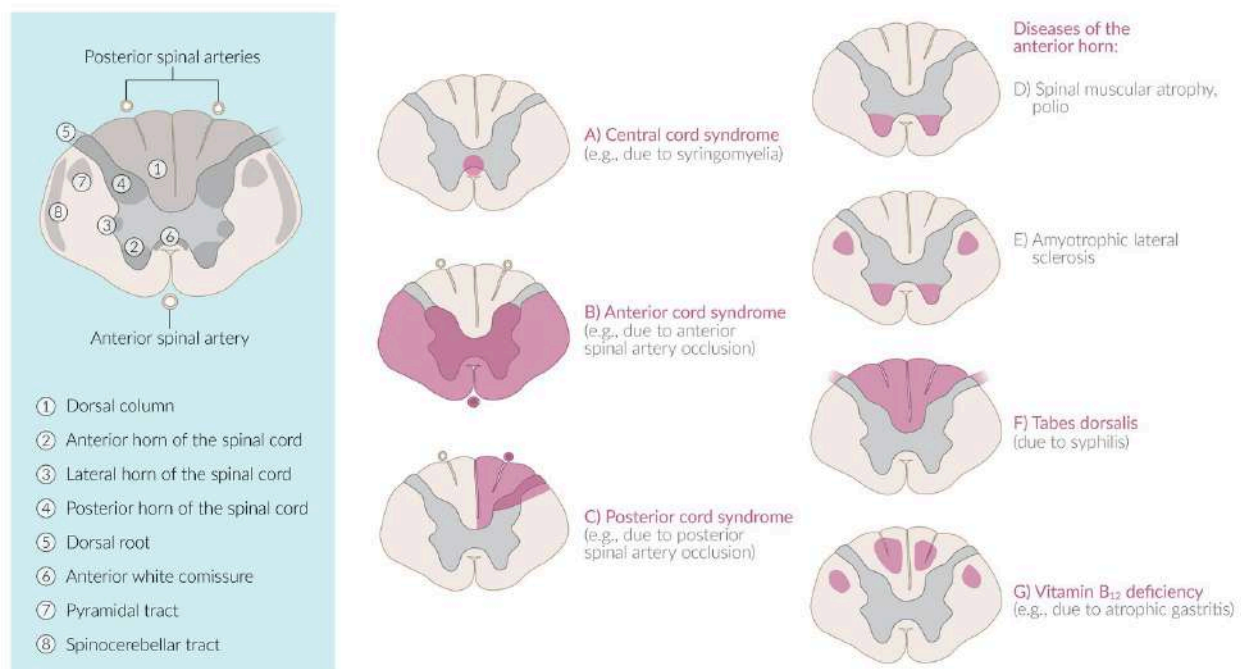
A - Dorsal root

Explanation Why

Injury to the [dorsal root ganglion](#) at the level of T9 would lead to complete loss of sensory function in the corresponding T9 [dermatome](#), which this patient does not have. Furthermore, this would not explain the loss of [proprioception](#) or vibration sensation in his right toe.

B - Posterior spinal artery

Image



Explanation Why

Injury to the right [posterior spinal artery](#) leads to posterior spinal artery syndrome due to [ischemia](#) and subsequent [infarction](#) of the [posterior column](#), which is directly supplied by this [artery](#). Affected

patients present with absent ipsilateral [proprioception](#) and vibration sensation below the level of the wound. In most cases, sensation to light touch is preserved. This patient's normal motor function and sensation to [pain](#) rule out any further injury to the [corticospinal tract](#) and [spinothalamic tract](#).

C - Central spinal cord grey matter

Explanation Why

Damage to the central [spinal cord gray matter](#), which most typically results from hyperextension injury, [spinal cord compression](#), and [syringomyelia](#), leads to [central cord syndrome](#) (CCS). Unlike this patient, patients with CCS present with both sensory symptoms (e.g., loss of [pain](#)/temperature sensation bilaterally) and motor symptoms (weakness). CCS is most commonly caused by injuries in the cervical region, the involvement of the upper extremities is typically more prominent than in the lower extremities.

D - Lateral corticospinal tract

Explanation Why

Injury to the [lateral corticospinal tract](#) would cause ipsilateral weakness below the level of the lesion. This patient instead presents with isolated sensory findings and full motor strength.

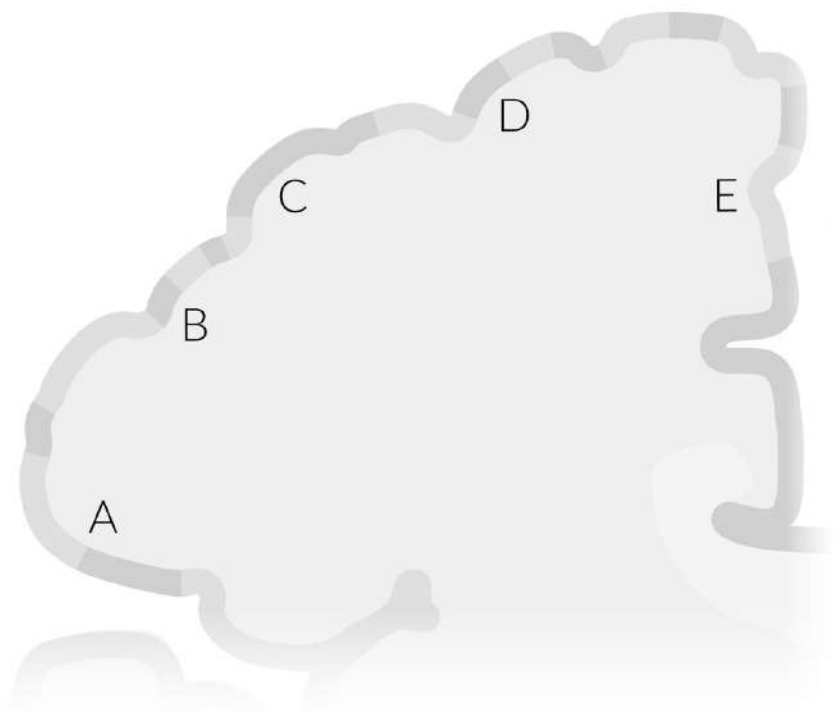
E - Artery of Adamkiewicz

Explanation Why

Injury to the [artery of Adamkiewicz](#) leads to [anterior cord syndrome](#) and can also be accompanied by urinary and fecal incontinence from [infarction](#) of the lumbosacral [anterior spinal cord](#). Since an injury to this [artery](#) typically spares the [dorsal columns](#), loss of [proprioception](#) and [vibratory sense](#), as seen in this patient, would be unexpected.

Question # 6

A 71-year-old man with hypertension and hyperlipidemia is brought to the emergency department after the sudden onset of slurred speech 1 hour ago. Physical examination shows drooling and hypernasal speech. His face is symmetric and strength is 5/5 in all extremities. This patient's presentation is most consistent with injury to which of the labeled areas of the primary motor cortex?



	Answer	Image
A	A	

	Answer	Image
B	B	
C	C	
D	D	
E	E	

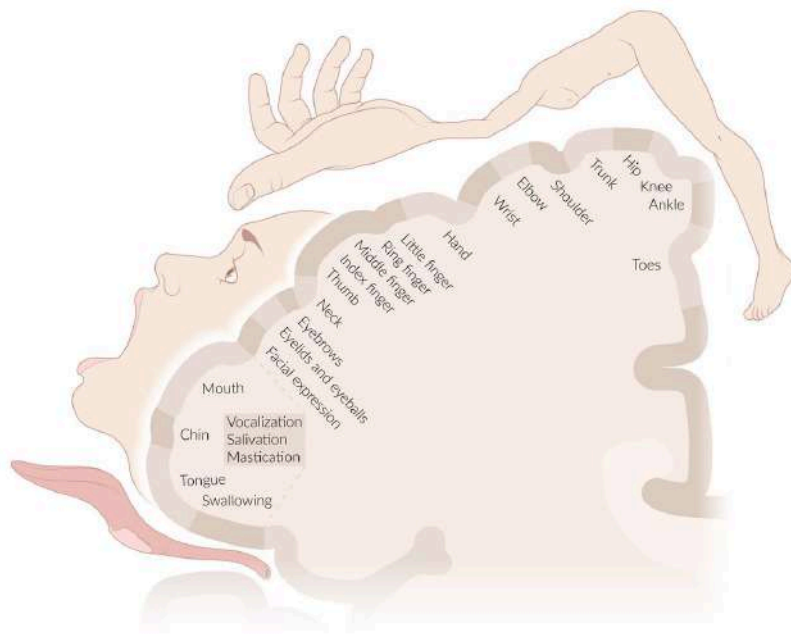
Hint

This patient presents with signs of an ischemic stroke. His slurred speech and drooling indicate pathological changes in the cortical area responsible for the central control of swallowing and vocalization. The motor homunculus represents all parts of the body arranged medially to laterally.

Correct Answer

A - A

Image



Explanation Why

This area of the [motor homunculus](#) corresponds with the motor innervation of the muscles of the throat involved in [swallowing](#), as well as the [tongue](#), [mastication](#), and vocalization. Slurred [speech](#) and drooling are signs of injury to this area, most likely due to an [ischemic stroke](#).

B - B

Explanation Why

This corresponds to the region of the [motor homunculus](#) that is responsible for facial expressions. This patient's face is symmetric, and his drooling and hypernasal [speech](#) suggest the involvement of a

different labeled area.

C - C

Explanation Why

This corresponds to the region of the [motor homunculus](#) that is responsible for the movement of the index finger. This patient does not present with impaired index finger function.

D - D

Explanation Why

This corresponds to the region of the [motor homunculus](#) that is responsible for the movement of the wrist. This patient does not present with impaired wrist [flexion](#)/extension or [adduction](#)/[abduction](#)

E - E

Explanation Why

This corresponds to the region of the [motor homunculus](#) that is responsible for the movement of the toe. This patient does not present with toe or foot paralysis.

Question # 7

A 31-year-old woman with multiple sclerosis comes to the physician because of a 4-day history of cramps in her left leg. Physical examination shows flexion of the left hip and increased tone in the thigh muscles. A local anesthetic block of which of the following nerves would most likely improve this patient's condition the most?

	Answer	Image
A	Obturator nerve	
B	Sciatic nerve	
C	Inferior gluteal nerve	
D	Femoral nerve	
E	Superior gluteal nerve	

Hint

This patient is showing signs of spasticity, a common clinical feature of multiple sclerosis, of the hip flexors. The nerve that innervates these muscles originates from spinal roots L₂–L₄ and lies below the inguinal ligament.

Correct Answer

A - Obturator nerve

Explanation Why

The [obturator nerve](#) (L2–L4 [nerve roots](#)) primarily innervates most of the [hip](#) adductors. Blocking it would not improve this patient's [spastic hip flexion](#).

B - Sciatic nerve

Explanation Why

The [sciatic nerve](#) (L4–[S3 nerve roots](#)) innervates much of the lower extremity musculature directly (the [adductor magnus](#) and the [hamstring muscles](#): [biceps femoris](#), [semitendinosus](#), [semimembranosus](#)) or via the [common peroneal nerve](#) and its subsequent branches. The [hamstring muscles](#) function as flexors and rotators of the [knee](#) and extensors of the [hip](#). Blocking the [sciatic nerve](#) would decrease countering [hip](#) extension and thus exacerbate this patient's [spastic hip flexion](#).

C - Inferior gluteal nerve

Explanation Why

The [inferior gluteal nerve](#) (L5–S2 [nerve roots](#)) primarily innervates the [gluteus maximus](#), which functions as a [hip](#) extensor and [external rotator](#). Blocking it would decrease countering [hip](#) extension and thus exacerbate [spastic hip flexion](#).

D - Femoral nerve

Explanation Why

Motor fibers of the [femoral nerve](#) (L2–L4 [nerve roots](#)) innervate the [hip](#) flexors. Selectively blocking the [femoral nerve](#) would improve [hip](#) flexor [spasticity](#). One adverse effect, though, would be a loss of [knee](#) extension because the nerve also innervates the [quadriceps femoris](#) muscles. Since the [femoral nerves](#) also provide sensory-only fibers, another adverse effect would be a loss of feeling of her anteromedial thigh via blocking of the [anterior](#) cutaneous branches, as well as the [medial](#) lower leg and foot via a [saphenous nerve](#) deficit, respectively.

E - Superior gluteal nerve

Explanation Why

The [superior gluteal nerve](#) (L4–S1 [nerve roots](#)) innervates the [gluteus minimus](#) and [gluteus medius](#), which function primarily as [hip](#) abductors, internal rotators, and external rotators of the thigh (if the [hip](#) is extended). The nerve also innervates the [tensor fascia latae](#), which does indeed participate in [hip flexion](#). Although blocking the [superior gluteal nerve](#) could minimally improve this patient's [spastic hip flexion](#), blocking another nerve would improve this patient's condition more since the nerve plays a much more dominant role in [hip flexion](#).

Question # 8

An investigator is developing a drug that selectively inhibits the retrograde axonal transport of rabies virus towards the central nervous system. To achieve this effect, this drug must target which of the following?

	Answer	Image
A	Tubulin	The diagram illustrates the structure of a microtubule. At the top, individual α-tubulin and β-tubulin subunits are shown forming a tubulin dimer. A γ-tubulin ring is shown at the minus end, with a capping protein also indicated. The microtubule is composed of tubulin dimers, with GTP-tubulin dimers at the plus end. A cross-section shows 13 tubulin molecules arranged in a ring, with a diameter of 25 nm. The microtubule is labeled with 'Minus end' and 'Plus end'.
B	Kinesin	
C	Dynein	The diagram shows a neuron with various organelles and transport pathways. The cell body (soma) contains the nucleus, Nissl bodies, Golgi apparatus, and mitochondrion. Dendrites and dendritic spines are shown. The axon is covered by a Schwann cell and contains a Node of Ranvier. Presynaptic terminals are shown at the end of the axon. Arrows indicate 'Anterograde transport' (from soma to terminals) and 'Retrograde transport' (from terminals to soma).
D	Nidogen	
E	Acetylcholine	

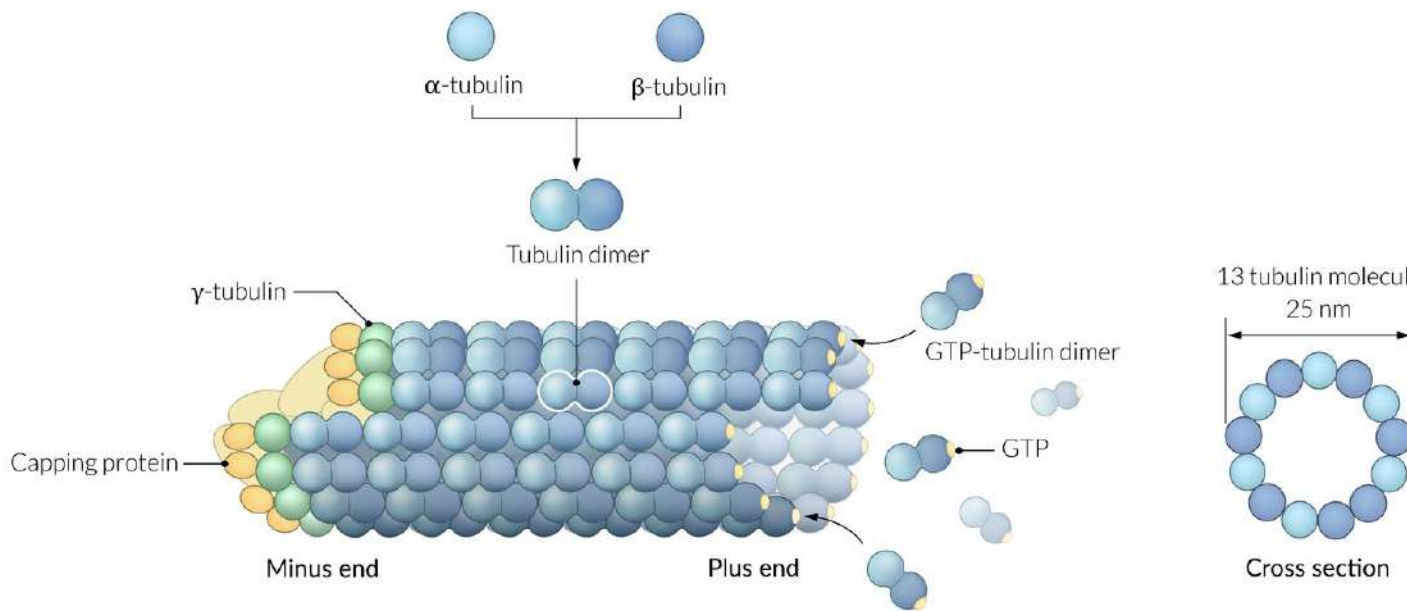
Hint

Rabies virus travels from the site of inoculation to the central nervous system (CNS) with the aid of motor proteins that facilitate the movement of cargo proteins across axons.

Correct Answer

A - Tubulin

Image



Explanation Why

[Tubulin](#) is a globular protein that polymerizes into filaments of heterodimers (pairs of α - and β -[tubulin](#)) to form [microtubules](#). As a structural component of [microtubules](#), [tubulin](#) is involved in spreading the [rabies](#) virus to the [CNS](#) via retrograde transport. However, drugs that inhibit polymerization into [microtubules](#) by binding [tubulin](#) (e.g., [colchicine](#), [vincristine](#), and [vinblastine](#)) would not only inhibit retrograde transport, but also anterograde transport and impair the structural stability of the [neuron](#).

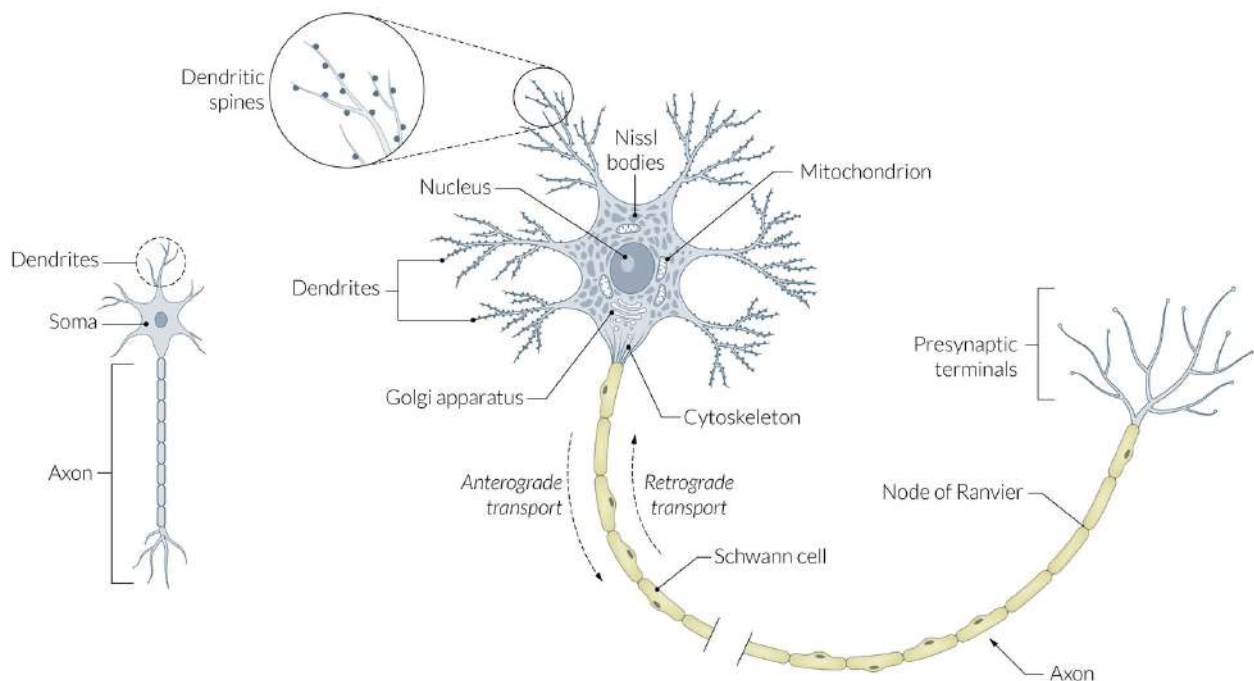
B - Kinesin

Explanation Why

[Kinesin](#) is an [ATP](#)-dependent motor protein responsible for the anterograde migration and movement of cellular organelles and [proteins](#) along [microtubules](#) (especially important in [axons](#)). Disrupting the integrity of [kinesin](#) would impair the transport of [proteins](#) from the cell body ([soma](#)) of [neurons](#) to the [axon](#) tip. [Rabies virus](#) does not use the [kinesin](#) motor system to spread to the [CNS](#).

C - Dynein

Image



Explanation Why

[Dynein](#) is an [ATP](#)-dependent motor protein responsible for the retrograde migration and movement of cellular organelles and [proteins](#) along [microtubules](#) in [axons](#). After [rabies](#) exposure, the [rabies](#) virus binds to acetylcholine receptors and enters the motor and sensory nerves of the [peripheral](#)

[nervous system](#), spreading in a retrograde direction to the [CNS](#). To inhibit the migration of the virus and subsequent brain infection, the new drug must therefore target [dynein](#) motors.

D - Nidogen

Explanation Why

Nidogen (also known as entactin) is a ubiquitous glycoprotein that constitutes an intrinsic component of the [basement membrane](#). It is found in high concentrations near [neuromuscular junction synapses](#) and has been identified as binding site of [tetanus](#) toxin to [neurons](#), which is required for retrograde transport of [tetanus](#) toxin towards the axonal [soma](#). However, nidogen does not relate to the transport of [rabies](#) virus within [axons](#).

E - Acetylcholine

Explanation Why

Nicotinic acetylcholine receptors (not [acetylcholine](#) itself) have been implicated as the binding site of the [rabies](#) virus to [axons](#). A drug targeting these receptors could inhibit the entry of [rabies virus](#) into [neurons](#), but it would not selectively impair the retrograde axonal transport towards the [CNS](#).

Question # 9

An investigator is studying central nervous system neurotransmitters in mice. He injects the spinal cord with a protease that cleaves SNARE proteins, thereby blocking the release of neurotransmitters from the Renshaw cells in the spinal cord. Which of the following consequences would be expected?

	Answer	Image
A	Disinhibited behavior	
B	Hydrophobia	
C	Positive Kernig sign	
D	Spastic paralysis	
E	Ascending flaccid paralysis	

Hint

Some neurotoxins released by bacteria are proteolytic enzymes that cause a disruption of neuronal function. This particular neurotoxin also causes risus sardonicus and opisthotonus.

Correct Answer

A - Disinhibited behavior

Explanation Why

Disinhibited behavior can occur in several neurological diseases, including [HSV encephalitis](#) or [frontotemporal dementia](#). Disinhibited behavior is not related to the cleavage of SNARE proteins.

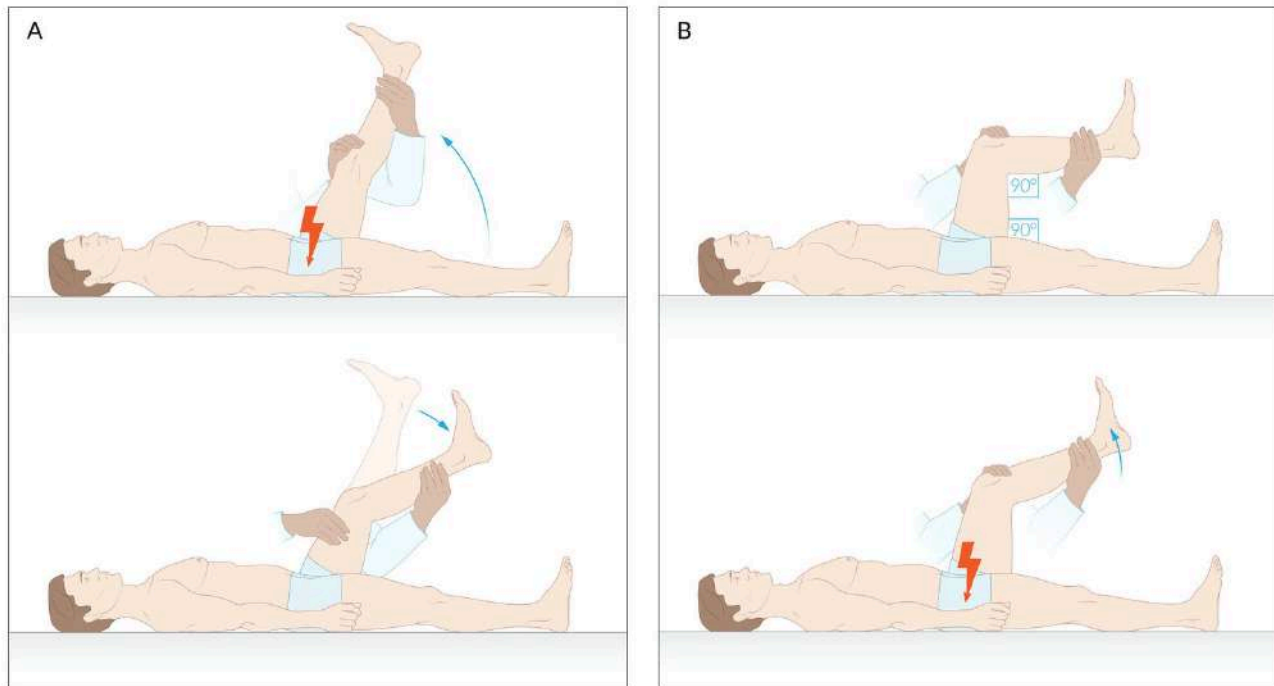
B - Hydrophobia

Explanation Why

[Hydrophobia](#) is a classic symptom of [rabies](#). The [rabies virus](#) travels from the bite wound retrograde along the peripheral nerves towards the [CNS](#). The pathogenesis of [rabies](#) is not fully understood, but [experimental studies](#) have postulated a potential involvement of acetylcholine receptors. There is no known association with SNARE proteins or [proteases](#).

C - Positive Kernig sign

Image



Explanation Why

A positive [Kernig sign](#) can be caused by meningeal irritation, a typical feature of [meningitis](#). Other symptoms of [meningitis](#) include [headache](#), [fever](#), and altered mental status. It is most commonly caused by a viral or bacterial infection (e.g., [Streptococcus pneumoniae](#) and [Neisseria meningitidis](#) in adult patients). There is no known association with SNARE proteins or [proteases](#).

D - Spastic paralysis

Explanation Why

The mechanism of action of the substance described is consistent with [tetanospasmin](#), which cleaves SNARE proteins (e.g., synaptobrevin, syntaxin) and thereby prevents the release of inhibitory [neurotransmitters](#) from [Renshaw cells](#). Injection with [protease](#) would lead to uncontrolled activation

of [alpha motor neurons](#), causing [spastic paralysis](#), [trismus](#), [risus sardonicus](#), and [opisthotonus](#). Another [neurotoxin](#) that acts through the cleavage of SNARE proteins is [botulinum toxin](#), which acts peripherally at the neuromuscular junctions and prevents the release of [neurotransmitters](#) into the [synaptic cleft](#). The resulting clinical manifestation is a peripheral flaccid muscle paralysis that descends [caudally](#).

E - Ascending flaccid paralysis

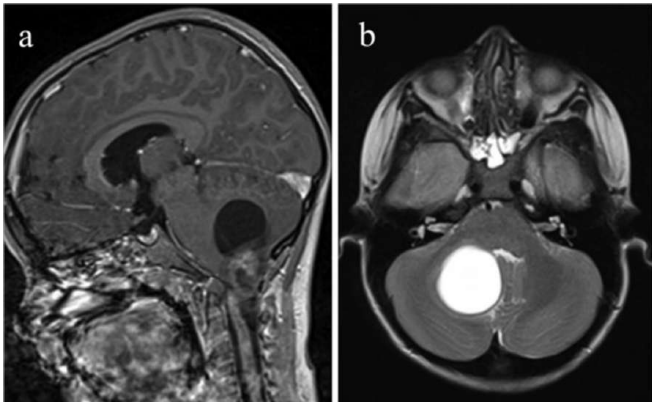
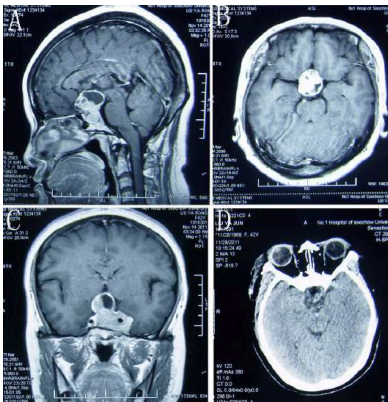
Explanation Why

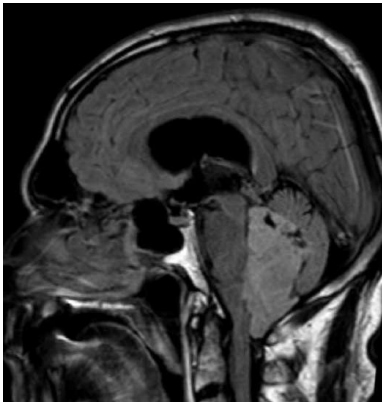
An ascending [flaccid paralysis](#) is a typical finding in [Guillain-Barré syndrome](#), which results from an autoimmune reaction mediated by cross-reactive [antibodies](#) against [Schwann cells](#) (e.g., following an infection with *C. jejuni*) and subsequent [demyelination](#). No [proteases](#) are involved in ascending [flaccid paralysis](#), and it is not related to the cleavage of SNARE proteins.

Question # 10

A 9-year-old boy is brought to the physician for evaluation of 2 months of progressive clumsiness, falls, and increased urinary frequency. Physical examination shows bilateral temporal visual field loss. An MRI of the head shows a small calcified suprasellar mass. The patient undergoes surgery with complete removal of the mass. Pathological examination of the specimen shows a lobular tumor composed of cysts filled with oily, brownish-yellow fluid. This mass is most likely derived from which of the following structures?

	Answer	Image
A	Rathke pouch	
B	Primitive neuroectoderm	

	Answer	Image
C	Arachnoid cells	
D	Astroglial cells	
E	Lactotroph cells	

	Answer	Image
F	Ventricular ependyma	

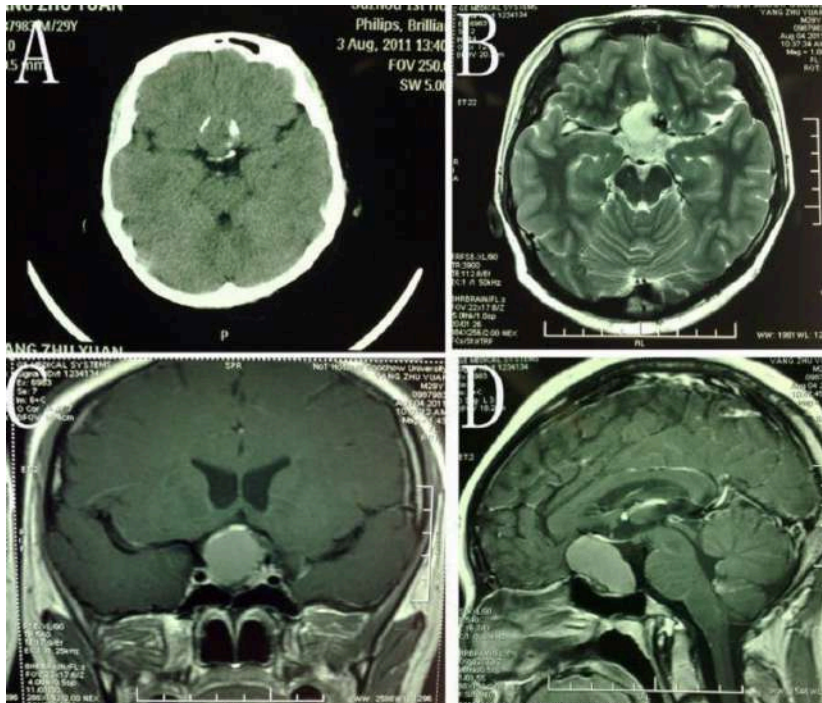
Hint

This child's bitemporal hemianopia and the MRI showing a calcified suprasellar mass are highly suggestive of craniopharyngioma, the most common supratentorial tumor in children. The histopathologic findings of a cystic mass filled with dark, oily fluid (“motor oil-like”) confirm this diagnosis.

Correct Answer

A - Rathke pouch

Image

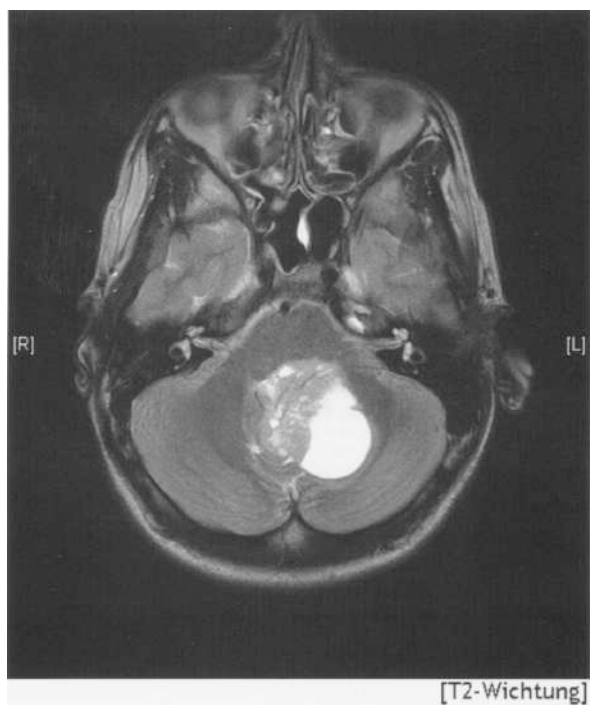


Explanation Why

[Craniopharyngiomas](#) are derived from remnants of the Rathke pouch, which is an ectodermal outpouching of the pharyngeal roof that develops into the [anterior pituitary gland](#). Compression of the [optic chiasm](#) by the [craniopharyngioma](#) would cause [bitemporal hemianopsia](#) and possibly, clumsiness or frequent tripping due to the [visual field](#) defect. Destruction of the [posterior pituitary](#) by the [tumor](#) would result in [central diabetes insipidus](#), which explains the increased [urinary frequency](#) in this patient.

B - Primitive neuroectoderm

Image



Explanation Why

[Medulloblastomas](#), which are the most common malignant [brain tumor](#) in children, originate from the primitive [neuroectoderm](#) and can cause clumsiness, frequent falls, and urinary symptoms (e.g., frequency, incontinence). However, [medulloblastomas](#) typically occur in the [cerebellum](#), unlike the suprasellar [tumor](#) that is seen here. Also, [bitemporal hemianopsia](#) would not be expected and patients with urinary symptoms due to a [medulloblastoma](#) would also have evidence of raised [intracranial pressure](#) (e.g., [headache](#), vomiting, [papilledema](#)) and ventriculomegaly on imaging due to [obstructive hydrocephalus](#). Biopsy of a [medulloblastoma](#) would show small blue cells arranged around a neuropil ([Homer-Wright rosettes](#)).

C - Arachnoid cells

Image

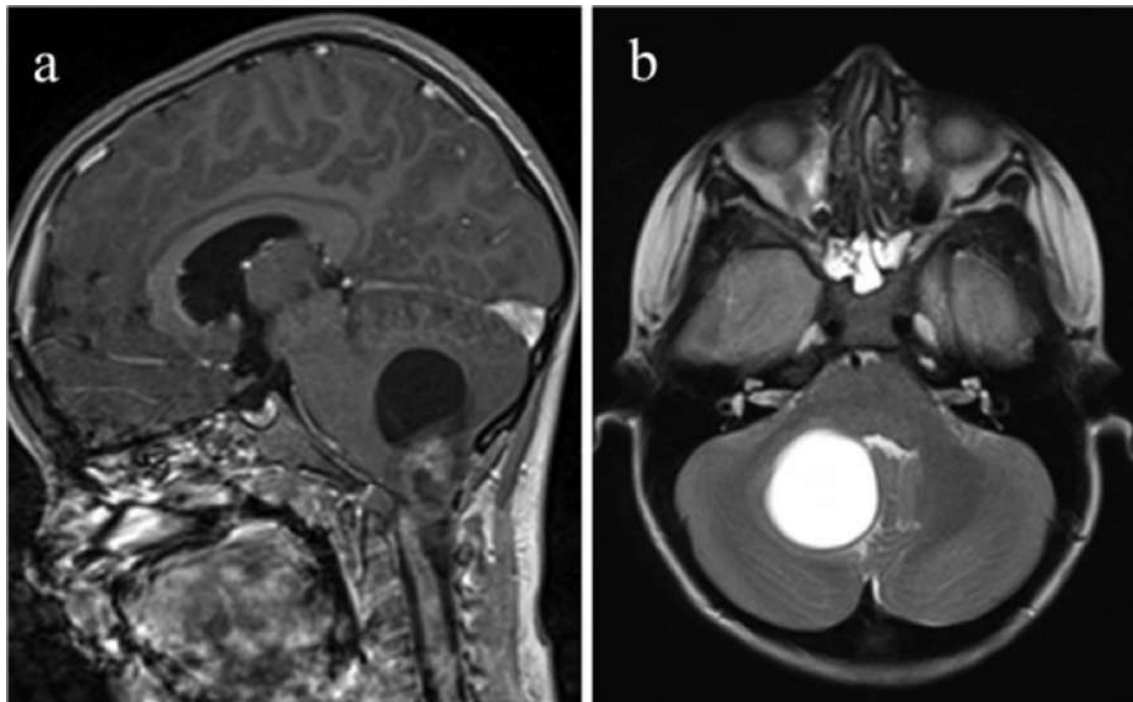


Explanation Why

Arachnoid cells give rise to [meningiomas](#). A parasagittal [meningioma](#) can cause falls and clumsiness (due to [spastic](#) lower limb weakness) and urinary symptoms (e.g., frequency, incontinence). However, [meningiomas](#) typically occur in adults; they are extremely rare in children. Moreover, [meningiomas](#) are characterized on [histopathology](#) by layers of densely packed syncytial [tumor](#) cells, often arranged in whorls, interspersed spindle cells, and [psammoma bodies](#).

D - Astroglial cells

Image

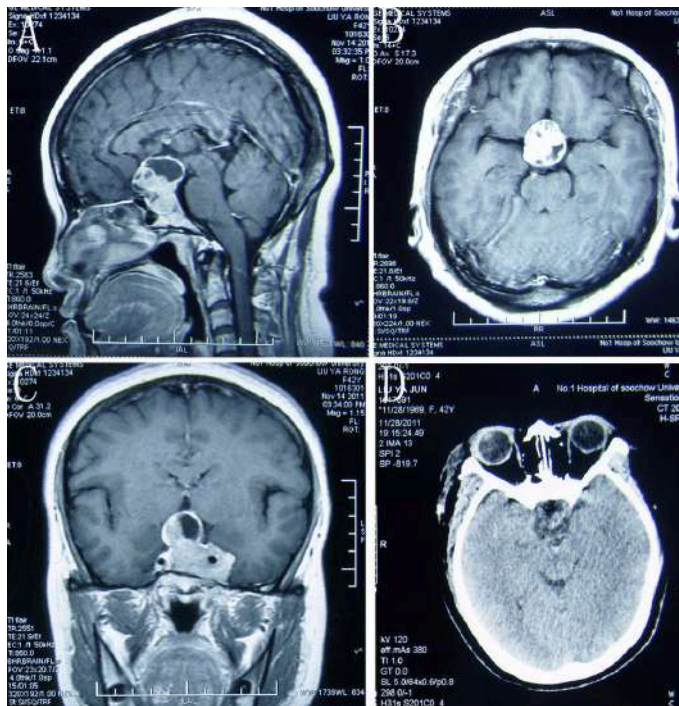


Explanation Why

[Astrocytomas](#) arise from [astroglial cells](#). A [pilocytic astrocytoma](#), which is the most common primary [brain tumor](#) in childhood, can cause clumsiness, frequent falls, and urinary symptoms (e.g., frequency, incontinence). However, a [pilocytic astrocytoma](#) is typically located in the posterior cranial fossa (e.g., [cerebellum](#)), unlike the suprasellar [tumor](#) that is seen here. Also, [bitemporal hemianopsia](#) would not be expected and patients with urinary symptoms due to a [pilocytic astrocytoma](#) would also have evidence of raised [intracranial pressure](#) (e.g., [headache](#), vomiting, [papilledema](#)) and ventriculomegaly on imaging due to [obstructive hydrocephalus](#). Biopsy of a [pilocytic astrocytoma](#) would show [Rosenthal fibers](#), which stain positive for glial fibrillary acid protein ([GFAP](#)).

E - Lactotroph cells

Image

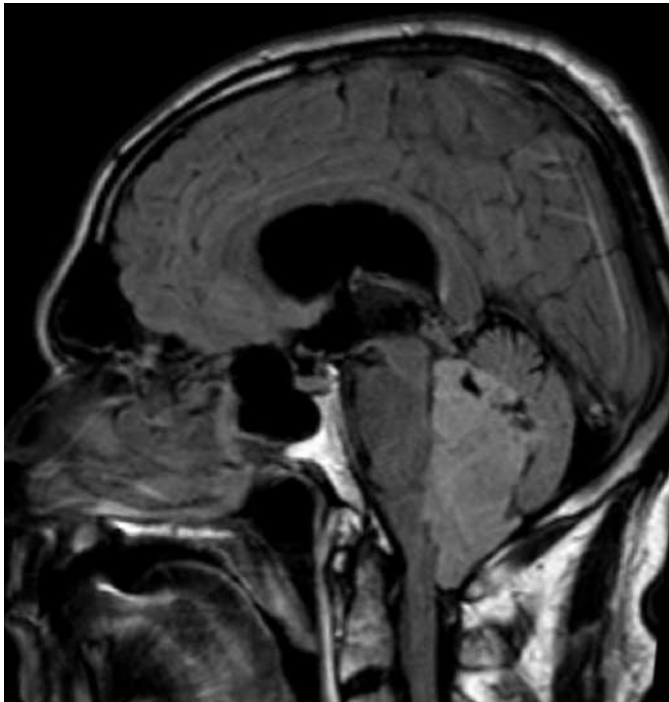


Explanation Why

[Lactotroph](#) cells can give rise to [prolactinomas](#), which could also manifest with [urinary frequency](#) (due to [central diabetes insipidus](#)), [bitemporal hemianopsia](#), and a history of clumsiness or frequent tripping due to the [visual field](#) defect. However, [prolactinomas](#) arise within the [sella turcica](#) unlike the suprasellar mass that is seen here and this patient does not have any features of [hyperprolactinemia](#) (e.g., [gynecomastia](#)). Moreover, [prolactinomas](#) are usually seen in adults (35–60 years), not in children, and [histopathology](#) would show acidophilic [lactotrophs](#) displacing the other endocrine [pituitary](#) cells, not a cystic mass filled with dark, oily fluid.

F - Ventricular ependyma

Image



Explanation Why

[Ependymomas](#) can arise from the modified [ependymal cells](#) that line the walls of cerebral ventricles. An [ependymoma](#) can cause [hydrocephalus](#), which could present with clumsiness, frequent falls, and urinary symptoms (e.g., frequency, incontinence). However, [ependymomas](#) typically arise [infratentorially](#) within the [4th ventricle](#). The [3rd ventricle](#), which is located in the suprasellar region, is an unusual location for an [ependymoma](#). Moreover, [bitemporal hemianopsia](#) would not be expected. Instead, patients would have evidence of raised [intracranial pressure](#) (e.g., [headache](#), vomiting, [papilledema](#)) and ventriculomegaly on imaging. [Histopathology](#) would show [perivascular pseudorosettes](#) and rod-shaped blepharoplasts (basal [ciliary bodies](#)).

Question # 11

A 30-year-old woman comes to the physician because of numbness, fatigue, and blurry vision for 1 week. The symptoms are worse after a hot shower or bath. She had an episode of right arm weakness 2 years ago that resolved without intervention. She recently returned from a hiking trip in upstate New York. Her temperature is 37.1°C (100°F) and blood pressure is 100/66 mm Hg. Physical examination shows decreased sensation to light touch in the left hand, right thigh, and right flank. Strength is normal. There is left-sided photophobia and pupillary constriction in the left eye is decreased compared to the right eye. Which of the following best describes the pathogenesis of the disease process in this patient?

	Answer	Image
A	Spirochete protein cross-reactivity in the meninges	
B	Osmotically-mediated Schwann cell damage	
C	Th1 cell-mediated nerve sheath damage	
D	Antibody binding at the neuromuscular junction	
E	Immune complex deposition in the arterial endothelium	
F	Lymphocytic infiltrate of the endoneurium	

Hint

This patient presents with characteristic findings of multiple sclerosis including optic neuritis (impaired vision), Uhthoff's phenomenon (worsening of symptoms in response to increased body temperature), as well as episodes of sensory and motor deficits followed by periods of remission.

Correct Answer

A - Spirochete protein cross-reactivity in the meninges

Explanation Why

[Spirochete](#) protein [cross-reactivity](#) in the [meninges](#) is characteristic of aseptic [meningitis](#) caused by late-stage [Lyme disease](#) ([neuroborreliosis](#)). This patient has no history of [tick bite](#) or [erythema migrans](#) to suggest [Lyme disease](#) infection. Symptoms of [meningitis](#) include [headache](#), neck stiffness, [fevers](#), and altered mental status, none of which are present in this patient.

B - Osmotically-mediated Schwann cell damage

Explanation Why

Osmotically-mediated [Schwann cell](#) damage is observed in [diabetic neuropathy](#) due to chronic [hyperglycemia](#). [Diabetic neuropathy](#) has a stocking-glove distribution and is associated with [dysesthesias](#) and loss of sensation. This patient lacks a history of [diabetes mellitus](#) and her sensory changes have a different distribution.

C - Th1 cell-mediated nerve sheath damage

Explanation Why

[Multiple sclerosis](#) is an immune-mediated [demyelinating](#) disease with a predilection for young, white females. Although the pathophysiology is not fully understood, it is believed that [Th1 cells](#) react to [myelin](#) basic [proteins](#) and initiate an inflammatory response, leading to focal [demyelination](#) of [white matter](#) in the brain and [spinal cord](#). Typical clinical features include transient, isolated episodes of [optic neuritis](#), [diplopia](#), limb weakness, sensory deficits, and [ataxia](#) that fully or partially resolve in days to weeks.

D - Antibody binding at the neuromuscular junction

Explanation Why

The pathophysiology of [myasthenia gravis](#) involves binding of [acetylcholine receptor antibodies](#) to the postsynaptic [neuron](#), resulting in impaired neuromuscular transmission. Symptoms of MG typically begin with vision changes due to ocular muscle weakness before progressing to generalized muscle weakness. Although this patient has visual changes and fatigue, the isolated nature of her right arm weakness is not characteristic of MG. Furthermore, MG symptoms are exacerbated by physical activity and improve with rest and do not typically change in response to warm temperatures.

E - Immune complex deposition in the arterial endothelium

Explanation Why

[Vasculitis](#) due to deposition of [immune complexes](#) in the arterial [endothelium](#) can be seen in [systemic lupus erythematosus](#) and Henoch-Schönlein [purpura](#). [Vasculitides](#) may cause neurological involvement, such as [mononeuritis multiplex](#), which typically presents with painful sensory and/or motor deficits. This patient lacks classic findings of [vasculitis](#), including palpable [purpura](#), renal involvement (glomerulonephritis), and arthralgias.

F - Lymphocytic infiltrate of the endoneurium

Explanation Why

[Lymphocytic](#) infiltrate of the [endoneurium](#) leading to [myelin](#) damage is seen in [Guillain-Barré syndrome](#). This syndrome causes [polyneuropathy](#) and ascending [flaccid paralysis](#) and typically follows a viral or bacterial gastrointestinal infection (most commonly [Campylobacter jejuni](#)). This patient has no history of recent infection and lacks the characteristic features of GBS.

Question # 12

A 78-year-old right-handed man with hypertension and hyperlipidemia is brought to the emergency department for sudden onset of nausea and vertigo one hour ago. Physical examination shows 5/5 strength in all extremities. Sensation to light touch and pinprick is decreased in the right arm and leg. A CT scan of the brain shows an acute infarction in the distribution of the left posterior cerebral artery. Further evaluation of this patient is most likely to show which of the following findings?

	Answer	Image
A	Left-sided hemineglect	
B	Right-sided homonymous hemianopia	Site of injury Visual field defects 1 Left optic nerve L R 2 Medial portion of the optic chiasm L R 3 Left optic tract L R 4 Lower bundle (Meyer's loop) of the left optic radiation L R 5 Upper bundle of the left optic radiation L R 6 Anterior portion of the calcarine sulcus and adjacent visual cortex L R 7 Left occipital pole L R Nasal field of vision of the left eye Temporal field of vision of the left eye Nasal field of vision of the right eye Temporal field of vision of the right eye
C	Left-sided gaze deviation	
D	Prosopagnosia	
E	Right-sided superior quadrantanopia	

Hint

The posterior cerebral artery supplies the occipital lobe.

Correct Answer

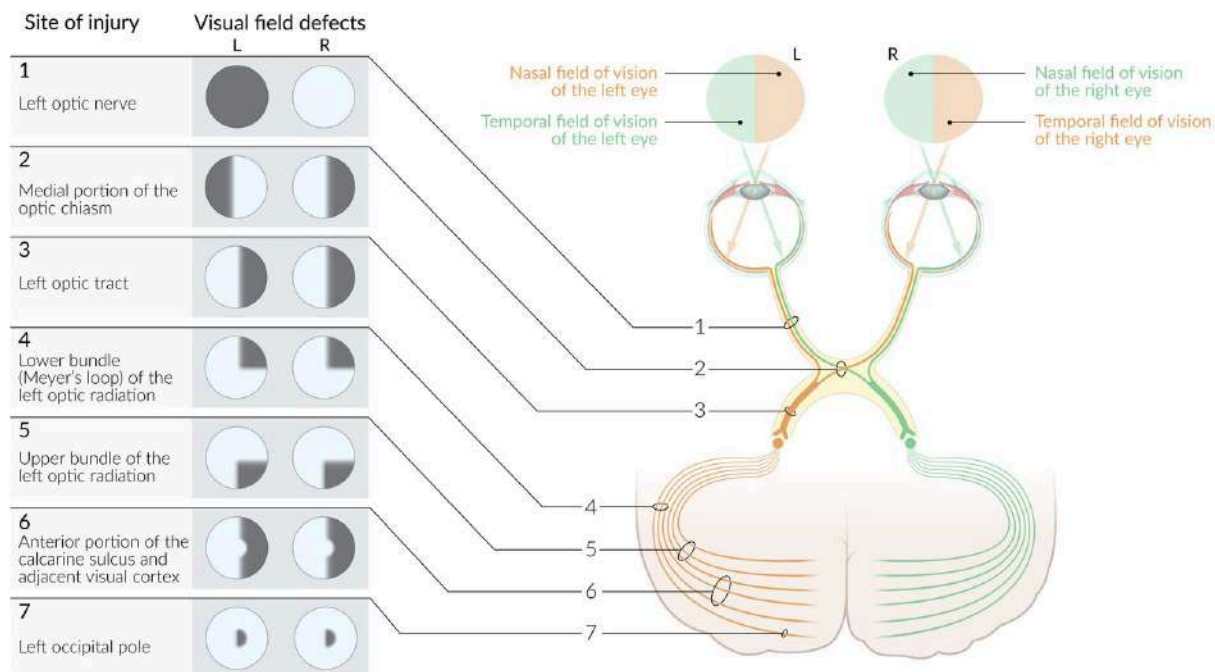
A - Left-sided hemineglect

Explanation Why

Left-sided [hemineglect](#) would be consistent with damage to the right [parietal lobe](#) (e.g., due to a right [middle cerebral artery stroke](#)), which is usually associated with contralateral motor and sensory deficits. In this patient, a [posterior cerebral artery stroke](#) was diagnosed and no motor deficits are present.

B - Right-sided homonymous hemianopia

Image



Explanation Why

The [posterior cerebral artery](#) supplies parts of the [thalamus](#) and the visual cortex within the [occipital](#)

[lobe](#). In addition to contralateral hemisensory loss due to [lateral](#) thalamic [infarction](#) (as seen in this patient), occlusion to the [posterior cerebral artery](#) causes damage to the visual cortex that results in contralateral [homonymous hemianopia](#) with [macular sparing](#). Central vision is not impaired in [posterior cerebral artery infarction](#) since the corresponding cortical area of the [macula](#) is supplied by the [middle cerebral artery](#).

C - Left-sided gaze deviation

Explanation Why

Gaze deviation towards the side of [infarction](#) (in this case: left-sided gaze deviation) combined with contralateral sensory loss, as seen in this patient, would be consistent with [infarction](#) of the left [middle cerebral artery](#), which supplies the [frontal eye field](#). Affected patients are also likely to present with right-sided motor dysfunction and [aphasia](#). This patient, however, presents with [posterior cerebral artery stroke](#).

D - Prosopagnosia

Explanation Why

[Prosopagnosia](#) is most commonly seen with right [posterior cerebral artery strokes](#) (e.g., [infarction](#) of the right occipitotemporal lobe). This would not be an expected finding in a patient with a left [posterior cerebral artery stroke](#), as seen here.

E - Right-sided superior quadrantanopia

Explanation Why

Right upper [homonymous quadrantanopia](#) would suggest a lesion in the left [optic radiation](#) and can be seen in [strokes](#) involving the left [middle cerebral artery](#). This finding would not be expected in a patient with a [posterior cerebral artery stroke](#).

Question # 13

A 24-year-old woman in graduate school comes to the physician for recurrent headaches. The headaches are unilateral, throbbing, and usually preceded by blurring of vision. The symptoms last between 12 and 48 hours and are only relieved by lying down in a dark room. She has approximately two headaches per month and has missed several days of class because of the symptoms. Physical examination is unremarkable. The patient is prescribed an abortive therapy that acts by inducing cerebral vasoconstriction. Which of the following is the most likely mechanism of action of this drug?

	Answer	Image
A	Inhibition of β_1 - and β_2 -adrenergic receptors	
B	Activation of μ -opioid receptors	
C	Activation of 5-HT ₁ receptors	
D	Inhibition of 5-HT and NE reuptake	
E	Inhibition of voltage-dependent Na ⁺ channels	
F	Inactivation of GABA degradation	

Hint

Triptans are the standard abortive therapy for primary migraines.

Correct Answer

A - Inhibition of β 1- and β 2-adrenergic receptors

Explanation Why

Inhibition of [\$\beta\$ 1 receptors](#) and [\$\beta\$ 2 receptors](#) is the mechanism of action of non-selective [\$\beta\$ -blockers](#) (e.g., [propranolol](#)), which can be used for the long-term prophylaxis of [migraine headaches](#). [\$\beta\$ -blockers](#) inhibit [norepinephrine](#) release, which stabilizes neuronal membranes, reducing their activity and excitability. However, vasoconstriction of intracranial vessels has not been described among their effects in the treatment of [migraine](#).

B - Activation of μ -opioid receptors

Explanation Why

Activation of [\$\mu\$ -opioid receptors](#) is the mechanism of action of [opiates](#), which cause inhibition of ascending [pain](#) impulses and alter the perception of [pain](#). [Butorphanol](#) is an [opioid analgesic](#) that can be used for the treatment of severe [migraine headaches](#). However, [opiates](#) induce [vasodilation](#) rather than vasoconstriction.

C - Activation of 5-HT₁ receptors

Explanation Why

Selective activation of 5-HT₁ receptors on cerebral blood vessels and sensory fibers of the [trigeminal nerve](#) is the mechanism of action of [triptans](#), which are considered first-line abortive therapy for the treatment of acute [migraine headaches](#) and [cluster headache](#) attacks. [Triptans](#) induce vasoconstriction by inhibiting the release of vasoactive [peptide](#) and reduce neurogenic inflammation associated with [migraine](#). They are especially effective if taken early at the onset of an attack. Adverse effects of [triptans](#) include coronary vasospasm, [serotonin syndrome](#), and [paresthesias](#).

D - Inhibition of 5-HT and NE reuptake

Explanation Why

Inhibition of [5-HT](#) and [norepinephrine](#) (NE) reuptake is the mechanism of action of [amitriptyline](#), a [tricyclic antidepressant](#) used for the prophylaxis of [migraine headaches](#). Vasoconstriction has not been identified as one of [amitriptyline](#)'s effects and it is not used as an abortive therapy.

E - Inhibition of voltage-dependent Na⁺ channels

Explanation Why

Inhibition of voltage-dependent sodium channels is the mechanism of action of [topiramate](#), an [antiepileptic drug](#) used for prevention of [migraine](#) attacks. In addition to sodium and calcium channel blockade, [topiramate](#) suppresses [glutamate](#) neurotransmission and enhances [GABA](#) activity. However, it does not induce cerebral vasoconstriction, nor is it used for abortive therapy of [migraines](#).

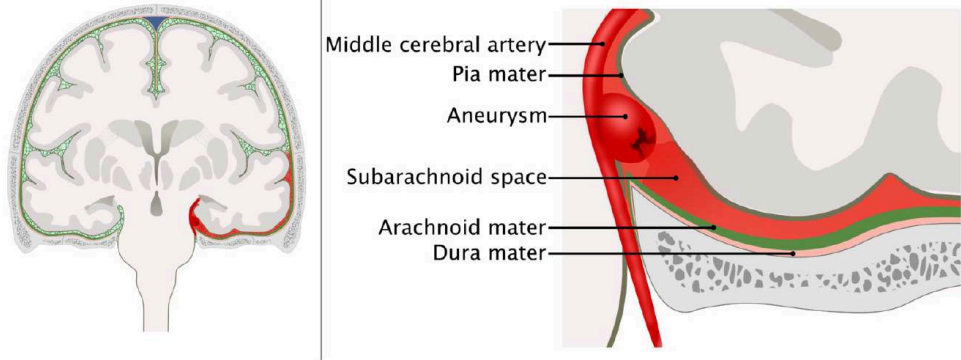
F - Inactivation of GABA degradation

Explanation Why

[Valproate](#) is an [antiepileptic drug](#) that increases the levels of the [neurotransmitter GABA](#) by inhibiting GABA transaminase. It is used for prophylactic treatment of [migraine headaches](#) but would not be used in the abortive treatment of [migraine headache](#).

Question # 14

A 44-year-old woman with recurrent urinary tract infections is brought to the emergency department by ambulance after sudden onset of severe headache 30 minutes ago. She has a history of occasional, mild headaches in the morning. There is no other history of serious illness. Both her father and her paternal grandmother died of chronic kidney disease. Her temperature is 37.2°C (99.1°F) and blood pressure is 145/90 mm Hg. Physical examination shows neck stiffness. When her hip is flexed, she is unable to fully extend her knee because of pain. Lumbar puncture performed 12 hours after headache onset yields 10 mL of yellow-colored fluid with no leukocytes. Which of the following is the most likely predisposing factor for this patient's current condition?

	Answer	Image
A	Arterial atherosclerosis	
B	Bacterial infection	
C	Hypercoagulable state	
D	Cerebral atrophy	
E	Saccular aneurysm	 The diagram illustrates a saccular aneurysm. On the left, a coronal section of the brain shows the location of the aneurysm in the middle cerebral artery. On the right, a detailed cross-section of the aneurysm shows the middle cerebral artery, the pia mater, the aneurysm itself, the subarachnoid space, the arachnoid mater, and the dura mater.

Hint

Signs of arterial hypertension (e.g., morning headaches), frequent UTIs, and a family history of renal failure are concerning for autosomal dominant polycystic kidney disease (ADPKD), whereas a positive Kernig's sign indicates meningeal or nerve root irritation.

Correct Answer

A - Arterial atherosclerosis

Explanation Why

While [chronic kidney disease](#) (e.g., [polycystic kidney disease](#)) increases the risk of [atherosclerosis](#), which in turn is a [risk factor](#) for [ischemic stroke](#), this patient does not have focal neurologic findings suggestive of a [stroke](#). [Ischemic stroke](#) typically presents with sudden painless neurological impairments that may be accompanied by a mild [headache](#), unlike this patient who presented with a sudden severe [headache](#). A sudden-onset severe [headache](#) indicates [subarachnoid hemorrhage](#), which can cause [hemorrhagic stroke](#) instead of [ischemic stroke](#).

B - Bacterial infection

Explanation Why

While this patient has meningismus, she does not have a [fever](#) or [leukocytes](#) on [CSF](#) suggestive of [meningitis](#). She is also not in a high-risk group for contracting [meningitis](#) (unvaccinated, college age and living in close quarters, or [immunocompromised](#)). In addition, there is no association between [polycystic kidney disease](#) and [meningitis](#).

C - Hypercoagulable state

Explanation Why

While a [hypercoagulable state](#) can increase the risk of a [thromboembolic stroke](#), this patient does not have focal neurologic findings suggestive of a [stroke](#). [Ischemic stroke](#) typically presents with sudden painless neurological impairments that may be accompanied by a mild [headache](#), unlike this patient who presented with a sudden severe [headache](#). A sudden-onset severe [headache](#) indicates [subarachnoid hemorrhage](#), which can cause [hemorrhagic stroke](#) instead of [ischemic stroke](#). In addition, [polycystic kidney disease](#) does not increase the risk of [hypercoagulability](#).

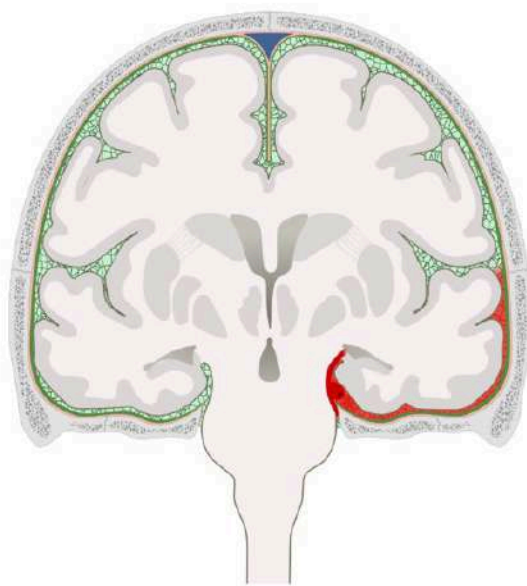
D - Cerebral atrophy

Explanation Why

Cerebral atrophy increases the risk of a [subdural hemorrhage \(SDH\)](#), which can manifest with worsening [headache](#). This patient, however, has no [risk factors](#) for cerebral atrophy (advanced age, [dementia](#), preceding trauma), and there is no link between [polycystic kidney disease](#) and cerebral atrophy or [SDH](#). Moreover, [SDH](#) usually does not have a sudden onset. Instead, it tends to manifest with [headache](#) and confusion over hours to weeks that is possibly accompanied by impaired consciousness and focal neurological deficit.

E - Saccular aneurysm

Image



Middle cerebral artery

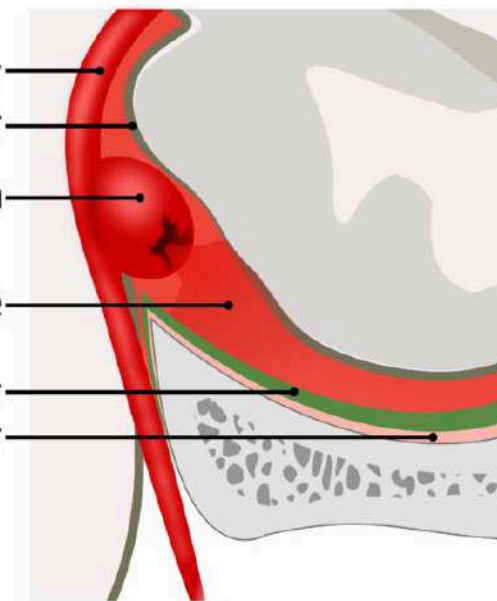
Pia mater

Aneurysm

Subarachnoid space

Arachnoid mater

Dura mater



Explanation Why

Patients with [ADPKD](#) have an increased risk of developing [saccular aneurysms](#). This patient

presented with symptoms of a [subarachnoid hemorrhage](#) resulting from rupture of one of these [aneurysms](#). The sudden onset of a severe [headache](#) (“worst [headache](#) of my life”) should raise suspicion for [SAH](#). Other signs of [SAH](#) include [fever](#), [xanthochromia](#) (yellow-colored [CSF](#)), and meningismus (neck stiffness and [Kernig's sign](#)) caused by irritation of the [meninges](#) by blood.

Question # 15

A 61-year-old woman comes to the physician for a follow-up examination 1 week after undergoing right-sided radical mastectomy and axillary lymph node dissection for breast cancer. She says that she has been unable to comb her hair with her right hand since the surgery. Physical examination shows shoulder asymmetry. She is unable to abduct her right arm above 90 degrees. When she pushes against a wall, there is protrusion of the medial aspect of the right scapula. Injury to which of the following nerves is the most likely cause of this patient's condition?

	Answer	Image
A	Upper trunk of the brachial plexus	
B	Axillary nerve	
C	Long thoracic nerve	
D	Suprascapular nerve	
E	Thoracodorsal nerve	

Hint

This woman has a winged scapula caused by paralysis of the serratus anterior muscle.

Correct Answer

A - Upper trunk of the brachial plexus

Explanation Why

The upper trunk of the [brachial plexus](#) can be injured by trauma (e.g., [shoulder dystocia](#) during [labor](#)) but is at low risk for injury during axillary lymph node dissection. This nerve injury manifests with an [adducted](#), extended, [pronated](#), and medially rotated arm ([Erb palsy](#)). It does not cause a [winged scapula](#).

B - Axillary nerve

Explanation Why

The [axillary nerve](#) can be injured by trauma (e.g., [anterior shoulder dislocation](#)) or [iatrogenic](#) damage (e.g., [rotator cuff](#) surgery) but is at low risk for injury during axillary lymph node dissection. [Axillary nerve injury](#) impairs arm [abduction](#) due to paralysis of the [deltoid muscle](#). However, it also impairs [external rotation](#) of the arm (due to paralysis of the [teres minor muscle](#)) and leads to a sensory deficit over the lower half of the deltoid region (due to injury to the superior [lateral](#) cutaneous nerve of the arm). It does not cause a [winged scapula](#).

C - Long thoracic nerve

Explanation But

Injury of the [dorsal scapular nerve](#) also causes [winging of the scapula](#), but it causes [lateral](#) winging (not [medial](#) winging).

Explanation Why

This patient has evidence of a [long thoracic nerve injury](#), which is a common complication of axillary lymph node dissection. The [long thoracic nerve](#) innervates the [serratus anterior muscle](#);

injury to the nerve typically results in [medial winging of the scapula](#) and impaired [abduction](#) of the arm beyond 90°.

D - Suprascapular nerve

Explanation Why

The [suprascapular nerve](#) is not located in the axillary region and thus is at low risk for injury during axillary lymph node dissection. [Suprascapular nerve injury](#) causes paralysis of the [infraspinatus](#) and [supraspinatus](#) muscles, which limits [adduction](#), [abduction](#), and [external rotation](#) of the arm and causes shoulder instability (due to paralysis of [rotator cuff](#) muscles). It does not cause a [winged scapula](#).

E - Thoracodorsal nerve

Explanation Why

The [thoracodorsal nerve](#), which innervates the [latissimus dorsi](#) and [teres major](#) muscles, can also be injured during axillary lymph node dissection. However, this nerve injury impairs shoulder [retraction](#) and [adduction](#) and [internal rotation](#) of the arm. It does not cause a [winged scapula](#).

Question # 16

A 49-year-old man is brought to the emergency department after being discovered unconscious in a field near the county fair. Several empty bottles of vodka were found near him. On arrival, he is mumbling incoherently. He is malodorous and appears disheveled. Serum studies show:

Na ⁺	150 mEq/L
K ⁺	3.3 mEq/L
Cl ⁻	115 mEq/L
HCO ₃ ⁻	13 mEq/L
Urea nitrogen	30 mg/dL
Glucose	75 mg/dL
Creatinine	1.4 mg/dL
Lactic acid	6 mmol/L (N < 2)

Which of the following changes to enzyme activity best explains this patient's laboratory findings?

	Answer	Image
A	Decreased activity of glucose-6-phosphate dehydrogenase	
B	Increased activity of α -ketoglutarate dehydrogenase	

	Answer	Image
C	Increased activity of phenylalanine hydroxylase	
D	Decreased activity of phosphofructokinase-2	
E	Decreased activity of pyruvate dehydrogenase	

Hint

The patient presents with altered mental status and lactic acidosis, most likely due to ethanol intoxication.

Correct Answer

A - Decreased activity of glucose-6-phosphate dehydrogenase

Explanation Why

[Glucose-6-phosphate dehydrogenase \(G6PD\)](#) is an initial step in the [pentose phosphate pathway](#), which is a prominent metabolic pathway in [erythrocytes](#) and is important for the production of [NADPH](#) and ribose. Decreased activity of [G6PD](#) leads to decreased [NADPH](#) levels, which has several effects including a disruption in the reduction of [glutathione](#). Without [reduced glutathione](#), [hydrogen peroxide](#) and [free radicals](#) cannot be eliminated. While [G6PD deficiency](#) is asymptomatic most of the time, it can become symptomatic due to stimuli such as stress, infection, and classically fava beans when poorly countered [hydrogen peroxide](#) and [free radicals](#) accumulate and damage [RBC](#) membrane, thereby causing [hemolytic anemia](#). Clinical findings include yellow-tinted [skin](#), dark [urine](#), and fatigue. However, [lactic acidosis](#) is not seen in these patients.

B - Increased activity of α -ketoglutarate dehydrogenase

Explanation Why

The [\$\alpha\$ -ketoglutarate dehydrogenase](#) reaction is a key step of the [citric acid cycle](#), during which [NADH](#) is generated from [NAD⁺](#) and [\$\alpha\$ -ketoglutarate](#). This reaction therefore has no role in the production of [lactic acid](#) in this intoxicated patient.

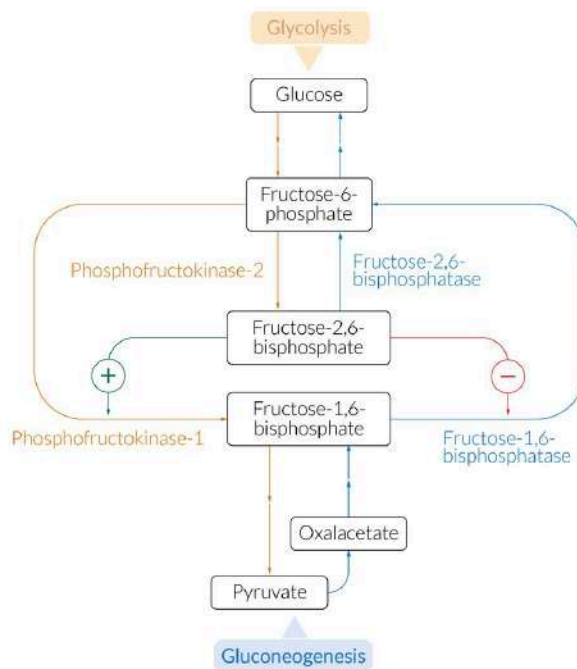
C - Increased activity of phenylalanine hydroxylase

Explanation Why

[Phenylalanine hydroxylase](#) is responsible for the metabolism of [phenylalanine](#). While a deficiency of this enzyme leads to [phenylketonuria](#), increased activity would not lead to the [lactic acidosis](#) seen in this intoxicated patient.

D - Decreased activity of phosphofructokinase-2

Image

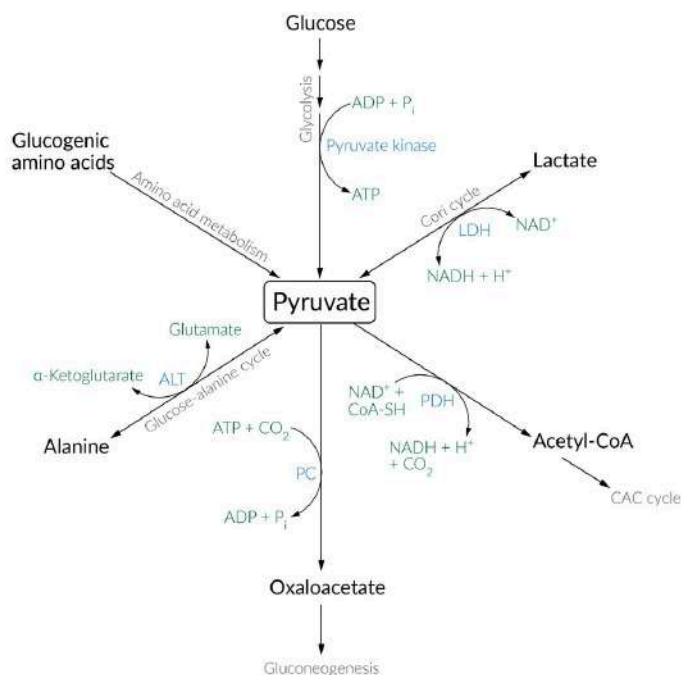


Explanation Why

[Phosphofructokinase-2 \(PFK2\)](#) converts fructose 6-phosphate to [fructose 2,6-bisphosphate](#), an important regulator of [glycolysis](#). Decreased [PFK2](#) activity would not lead to [lactic acidosis](#) as seen in this patient but favors utilization of [pyruvate](#) in [gluconeogenesis](#). Ethanol consumption, in contrast, inhibits [gluconeogenesis](#).

E - Decreased activity of pyruvate dehydrogenase

Image

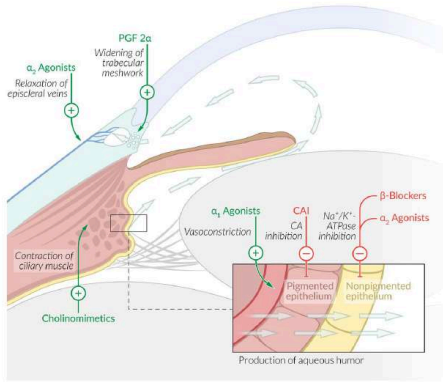


Explanation Why

The increased [lactic acid](#) levels in this patient suggest that his body has shifted from [aerobic cellular respiration](#), the first step of which involves the transformation of [pyruvate](#) to [acetyl-CoA](#) by [pyruvate dehydrogenase complex](#) (PDC), to [anaerobic](#) cellular respiration that includes conversion of [pyruvate](#) to [lactate](#). [Alcohol dehydrogenase](#) breaks down ethanol by reducing [NAD⁺](#) to [NADH](#). This increased [ratio](#) of [NADH/NAD⁺](#) inhibits the [citric acid cycle](#), which results in an accumulation of [acetyl-CoA](#). [NADH](#) and [acetyl-CoA](#) are both [pyruvate dehydrogenase](#) reaction products and thus inhibit [PDC](#) activity. [NAD⁺](#) is replenished by the reduction of [pyruvate](#) to [lactate](#) by [lactate dehydrogenase](#), which has led to the [lactic acidosis](#) seen in this patient.

Question # 17

A 62-year-old woman is brought to the emergency department because of the sudden onset of severe left eye pain, blurred vision, nausea, and vomiting. She has had an upper respiratory tract infection for the past 2 days and has been taking phenylephrine to control her symptoms. Examination shows a rock-hard, injected left globe and a fixed, mid-dilated pupil on the left. Gonioscopy shows that the iris meets the cornea at an angle of 10° ($N = 20\text{--}45^\circ$). Systemic pharmacotherapy is initiated with a drug that decreases the secretion of aqueous humor from the ciliary epithelium. The next day, her serum potassium concentration is slightly decreased. Which of the following additional adverse effects is most likely to occur in this patient?

	Answer	Image
A	Epithelial keratopathy	
B	Xerostomia	
C	Bradycardia	
D	Metabolic acidosis	 The diagram illustrates the production and regulation of aqueous humor. It shows the ciliary body with pigmented and nonpigmented epithelium. Key regulatory points include: PGF 2α: Promotes widening of the trabecular meshwork. α₁ Agonists: Cause vasoconstriction of episcleral veins and contraction of ciliary muscle. Cholinergics: Cause contraction of ciliary muscle. CAI (Carbonic Anhydrase Inhibitors): Inhibit the production of aqueous humor by the ciliary epithelium. Na⁺/K⁺ ATPase: Inhibited by α₁ agonists, affecting ion transport across the epithelium. β-Blockers: Inhibit the production of aqueous humor.
E	Diaphoresis	

Hint

The patient's sudden-onset eye pain and blurred vision along with a rock-hard left globe on exam are highly suggestive of acute primary angle-closure glaucoma. A narrow iridocorneal angle confirms the diagnosis. The patient received treatment with acetazolamide.

Correct Answer

A - Epithelial keratopathy

Explanation Why

[Epithelial](#) keratopathy is a possible adverse effect of the topical [prostaglandin latanoprost](#), which is a first-line treatment for open-angle [glaucoma](#). This patient, however, has acute closed-angle [glaucoma](#) and is being treated with a systemic medication. In addition, [latanoprost](#) increases [aqueous humor](#) drainage through the [uveoscleral pathway](#), whereas this patient was treated with a medication that decreases the secretion of [aqueous humor](#) by the ciliary [epithelium](#). Finally, [latanoprost](#) does not affect potassium levels.

B - Xerostomia

Explanation Why

[Xerostomia](#) is associated with drugs that suppress secretion from the salivary glands, like α_2 -adrenergic [agonists](#). [Apraclonidine](#), a topical ophthalmic α_2 -adrenergic [agonist](#), is often used to treat acute [angle-closure glaucoma](#) by decreasing synthesis of [aqueous humor](#) by the ciliary [epithelium](#), similar to the medication used here. However, this patient is receiving systemic pharmacotherapy and α_2 -adrenergic [agonists](#) do not cause a decrease in potassium levels.

C - Bradycardia

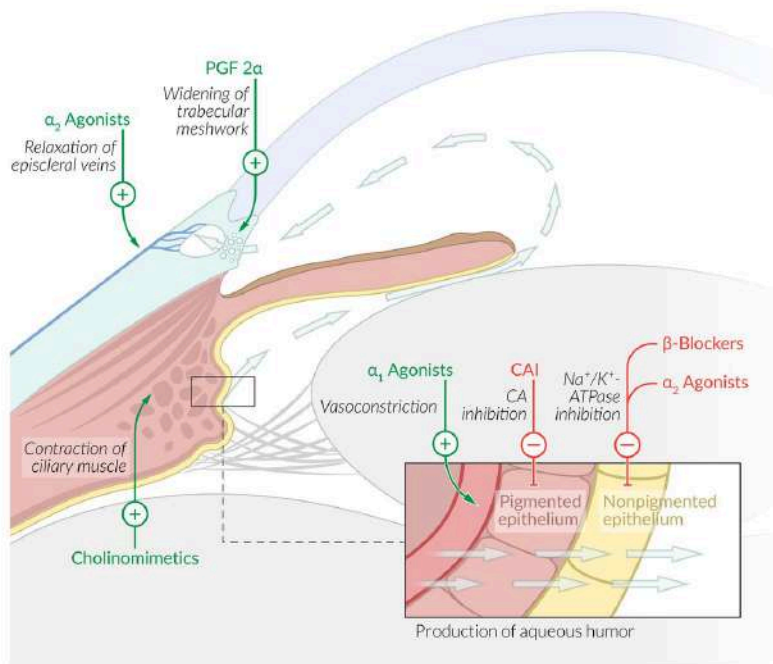
Explanation Why

[Beta-blockers](#) (e.g., [timolol](#)) and [parasympathomimetics](#) (e.g., [pilocarpine](#)) can cause [bradycardia](#). While these medications can be used in the treatment of acute primary angle-closure [glaucoma](#), they are given as topical formulations whereas this patient is receiving systemic treatment. While [beta-blockers](#) also improve the symptoms of [glaucoma](#) by decreasing [aqueous humor](#) synthesis, they are associated with [hyperkalemia](#), in contrast to this patient who developed [hypokalemia](#) after starting the medication. [Parasympathomimetics](#), on the other hand, increase [aqueous humor](#) drainage via

[ciliary muscle](#) contraction and [trabecular meshwork](#) opening

D - Metabolic acidosis

Image



Explanation Why

[Acetazolamide](#), a [carbonic anhydrase inhibitor](#), improves the symptoms of [glaucoma](#) by decreasing [aqueous humor](#) synthesis by the ciliary [epithelium](#). It is a first-line treatment for acute primary angle-closure [glaucoma](#), which can be precipitated by [mydriasis](#) due to darkness, fear, stress, or certain medications (e.g., [phenylephrine](#)). However, [acetazolamide](#) can impair [bicarbonate](#) reabsorption in the [proximal](#) tubule, which may cause non-anion gap metabolic acidosis as a result of [type 2 renal tubular acidosis](#). Other important adverse effects of [acetazolamide](#) include [hypokalemia](#), sulfa [allergy](#), and [hyperammonemia](#) with [paresthesias](#).

E - Diaphoresis

Explanation Why

[Diaphoresis](#) can be an adverse effect of [parasympathomimetic drugs](#), including the topical ophthalmic formulations (e.g., [pilocarpine](#)) given in the treatment of acute primary angle-closure [glaucoma](#). This patient, however, is receiving systemic treatment. In addition, parasympathomimetics increase [aqueous humor](#) drainage via [ciliary muscle](#) contraction and [trabecular meshwork](#) opening, whereas this patient was treated with a medication that decreases the secretion of [aqueous humor](#) by the ciliary [epithelium](#).

Question # 18

A 53-year-old woman with hypertension is brought to the emergency department 30 minutes after having a generalized, tonic-clonic seizure. She has had recurrent headaches and dizziness in the last 3 months. One year ago, she had diarrhea after a trip to Ecuador that resolved without treatment. She has not received any medical care in the last five years. She has smoked 1 pack of cigarettes daily for 20 years. Her temperature is 36°C (96.8°F) and blood pressure is 159/77mm Hg. Physical examination shows dysarthria and hyperreflexia. She is confused and oriented only to name and place. Four brain lesions are found in a CT scan of the head with contrast; one of the lesions is shown. Which of the following is most likely to have prevented this patient's condition?



	Answer	Image
A	Avoidance of contaminated food	
B	Vaccination against meningococcus	

	Answer	Image
C	Avoidance of cat feces	
D	Smoking cessation	
E	Breast cancer screening	
F	Improved blood pressure control	

Hint

This patient's combination of seizure, headache, dizziness, dysarthria, hyperreflexia, confusion, recent travel to South America, and ring-enhancing, cystic lesions on head CT scan indicates a diagnosis of neurocysticercosis.

Correct Answer

A - Avoidance of contaminated food

Explanation But

[Neurocysticercosis](#) is characterized by [seizures](#), increased [intracranial pressure](#), and focal neurologic deficits. Depending on the stage of disease, multiple [ring-enhancing](#), cystic, and eventually calcified lesions can be seen on brain [CT scan](#), some of which may show a [scolex](#).

Explanation Why

Avoidance of food contaminated by the eggs of *Taenia solium* reduces the risk of [neurocysticercosis](#), which is the most common parasitic disease of the nervous system and the most important cause of adult-onset [seizures](#) in Asia, Africa, Central and South America. [Neurocysticercosis](#) is a fecal-oral transmitted disease that results from ingestion of eggs of [Taenia solium](#), which can be found in food and water contaminated by the feces of people with [intestinal taeniasis](#). Several strategies have been described to prevent the infection, which include washing food prior to consumption, proper hand hygiene, and avoidance of raw pork meat, as well as adequate [freezing](#) and cooking of food to destroy the parasite.

B - Vaccination against meningococcus

Explanation Why

[Vaccination](#) against [meningococcus](#) is routinely recommended in [adolescents](#) 11–18 years old and high-risk groups to reduce the risk of infection with [Neisseria meningitidis](#), a gram-negative diplococcus responsible for most of the cases of community-acquired [meningitis](#) in children and young adults. Although [meningococcal meningitis](#) can also cause neurological deficits as in this patient, other important signs such as neck stiffness and signs of infection (e.g., [fever](#)) are not present. In addition, [meningococcal meningitis](#) does not cause [ring-enhancing](#) lesions but instead presents with inflamed [meninges](#) on imaging. Therefore, [vaccination](#) would not have prevented this patient's condition.

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C - Avoidance of cat feces

Explanation But

[Echinococcus](#) spp. can also be transmitted by ingestion of eggs shed in feline feces. However, the clinical manifestations of [echinococcosis](#) are mostly gastrointestinal and pulmonary rather than neurologic.

Explanation Why

Avoidance of cat feces reduces the risk of infection with [Toxoplasma gondii](#), a ubiquitous intracellular parasite acquired by ingestion of [oocytes](#) from water, fruits, vegetables or contaminated meat. [Cerebral toxoplasmosis](#) can also cause neurological deficits and [ring-enhancing](#) lesions on brain [CT scan](#), it would be very unlikely in this immunocompetent patient. Given the patient's gastrointestinal infection acquired in South America, another diagnosis is more likely. Therefore, avoidance of cat feces would not have prevented this patient's condition.

D - Smoking cessation

Explanation Why

Smoking cessation is the best preventive strategy to reduce the risk of [lung cancer](#), which is the most frequent [malignancy](#) producing [metastasis](#) to the brain. Although this patient with a long history of tobacco use presents with signs and symptoms of [elevated intracranial pressure](#), [ring-enhancing](#) lesions are not characteristic of [metastatic lung malignancy](#). Therefore, smoking cessation would not have prevented this patient's condition.

E - Breast cancer screening

Explanation Why

[Mammography](#) screening is routinely performed in women 50–74 years old with an average risk of [breast cancer](#), the most common malignant disease in [postmenopausal](#) women. Although [breast](#)

[cancer](#) has a high risk of metastasizing, most patients have a previous diagnosis of primary disease and < 5% present with brain involvement. Additionally, [brain metastasis](#) on [CT scan](#) appears as multiple, well-circumscribed lesions at the gray-white matter junction, and not as [ring-enhancing](#), cystic lesions like those observed in this patient. Therefore, [breast cancer](#) screening would not have prevented this patient's condition.

F - Improved blood pressure control

Explanation Why

Improved blood pressure control minimizes the chances of [stroke](#) in patients with elevated cardiovascular risk. Although this patient presents with a history of untreated [hypertension](#), her blood pressure at the time of evaluation is not high enough to produce acute end-organ damage. Additionally, the morphologic features of the lesions on brain [CT scan](#) are not characteristic of [ischemic](#) or [hemorrhagic stroke](#). Therefore, improving blood pressure would not have prevented this patient's condition.

Question # 19

A 2-day-old male newborn is brought to the physician because he became somnolent and felt cold after breastfeeding. Pregnancy and delivery were uncomplicated. He was born at 40 weeks' gestation and weighed 3538 g (7 lb 13 oz); he currently weighs 3311 g (7 lb 5 oz). Examination shows generalized hypotonia. Serum studies show an ammonia concentration of 150 $\mu\text{mol/L}$ ($N < 50$). Fasting serum glucose concentration is normal. Accumulation of which of the following substances is most likely involved in the pathogenesis of this patient's neurological symptoms?

	Answer	Image
A	α -Ketoglutarate	
B	Succinyl-CoA	
C	Urea	
D	Acylcarnitine	
E	Glutamine	

Hint

This neonate's hyperammonemia after feeding is most likely due to a urea cycle disorder. Ammonia is metabolized through the actions of glutamate dehydrogenase and glutamine synthetase.

Correct Answer

A - α -Ketoglutarate

Explanation Why

Under physiological conditions, [\$\alpha\$ -ketoglutarate](#) and [ammonia](#) act in equilibrium with [glutamate](#) in the [central nervous system](#). When there is excess [ammonia](#), however, this equilibrium shifts toward [glutamate](#), reducing levels of [\$\alpha\$ -ketoglutarate](#). Thus, [hyperammonemia](#) causes depletion rather than accumulation of [\$\alpha\$ -ketoglutarate](#). Because [\$\alpha\$ -ketoglutarate](#) is also an important substrate of the [citric acid cycle](#), its depletion can cause impairment of cerebral energy metabolism and subsequent neurologic dysfunction.

B - Succinyl-CoA

Explanation Why

Accumulation of [succinyl-CoA](#), an intermediate of the [citric acid cycle](#) synthesized from [\$\alpha\$ -ketoglutarate](#), is not associated with any disorder presenting with [hyperammonemia](#). In rare cases, neonatal [hyperammonemia](#) is due to [methylmalonic acidemia](#), which is caused by impaired metabolism of [methylmalonic acid](#) and characteristically leads to decreased rather than increased [succinyl-CoA](#) concentrations.

C - Urea

Explanation Why

Increased urea concentration is seen in uremic encephalopathy, which can manifest with [somnolence](#) and muscle weakness (e.g., [hypotonia](#)). However, uremic encephalopathy is caused by advanced [renal failure](#), which would not explain this patient's elevated blood [ammonia](#) level. This patient most likely has a [urea cycle disorder](#), which would cause an impaired ability to convert [amino acids](#) to urea, not an elevation in urea levels.

D - Acylcarnitine

Explanation Why

Acylcarnitines accumulate in [CPT II deficiency](#), a disorder caused by impaired [long-chain fatty acid](#) oxidation in the [mitochondria](#). Possible manifestations include [somnolence](#), [hypotonia](#), and [hyperammonemia](#), all of which are seen here. However, in [CPT II deficiency](#), [fatty acids](#) are not able to be used as substrates for [gluconeogenesis](#), leading to hypoketotic fasting [hypoglycemia](#). Conversely, this patient's serum glucose concentration is normal.

E - Glutamine

Explanation But

While the accumulation of [glutamine](#) is one component of the pathogenesis of [hepatic encephalopathy](#), the process is multifactorial and remains an area of ongoing study. In addition to the osmotic damage to [astrocytes](#) induced by the accumulation of [glutamine](#), the metabolism of other [neurotransmitters](#), including [glutamate](#) and [GABA](#), is also disturbed in states of [hyperammonemia](#). It is thought that these changes in metabolism lead to inhibition of excitatory neurotransmission and activation of inhibitory neurotransmission.

Explanation Why

[Hyperammonemia](#) results in the accumulation of [glutamine](#), which plays an important role in the development of [hepatic encephalopathy](#). Upon activation, [neurons](#) in the brain release [neurotransmitters](#) (e.g., [glutamate](#), [GABA](#)) that are normally taken up from the [synaptic cleft](#) and recycled by [astrocytes](#). In states of [hyperammonemia](#), excess [ammonia](#) crosses the [blood-brain barrier](#) and enters into [astrocytes](#). The [astrocytes](#) detoxify excess [ammonia](#) through the actions of [glutamate dehydrogenase](#) and [glutamine synthetase](#). The consequent production of excess [glutamine](#) creates an osmotic effect that draws water into [astrocytes](#) and causes cellular swelling and dysfunction, resulting in [cerebral edema](#) that manifests with neurological symptoms such as those seen here.

Question # 20

A 28-year-old primigravid woman at 39 weeks gestation is admitted to the hospital in active labor. On examination, the cervix is 100% effaced and 10 cm dilated. After 5 minutes of pushing, there is a prolonged deceleration of the fetal heart rate to 90/min. A decision to perform an episiotomy is made to expedite vaginal delivery. The anesthesiologist locates the ischial spines by palpating the posterolateral vaginal sidewall and administers an anesthetic. Three minutes later, pinching the posterior vulva does not provoke pain. The anesthetized nerve most likely also supplies which of the following structures?

	Answer	Image
A	Obturator externus muscle	
B	Skin of the lateral thigh	
C	Gluteus medius muscle	
D	External anal sphincter	
E	Skin of the mons pubis	
F	Detrusor muscle	

Hint

The anesthesiologist has performed a pudendal nerve block to reduce sensation from the posterior perineum, vulva, and lower vagina.

Correct Answer

A - Obturator externus muscle

Explanation Why

The [obturator externus](#) is innervated by the [obturator nerve](#). This nerve also innervates a small area of [skin](#) on the [medial](#) thigh, as well as the [gracilis](#), [pectineus](#), [obturator externus](#), and [adductor magnus](#), longus, and brevis muscles. [Obturator nerve](#) blocks are achieved with anesthetic injection into the [medial](#) thigh, not intravaginally.

B - Skin of the lateral thigh

Explanation Why

The [skin](#) of the [lateral](#) thigh is innervated by the [lateral femoral cutaneous nerve](#). Anesthetic block of this nerve would not be helpful in performing an [episiotomy](#).

C - Gluteus medius muscle

Explanation Why

The [gluteus medius muscle](#) is innervated by the [superior gluteal nerve](#). This nerve is purely a motor nerve, so injection of local anesthetic would produce muscle paralysis without accompanying anesthesia. Other muscles innervated by the [superior gluteal nerve](#) include the [gluteus minimus](#) and [tensor fascia lata](#).

D - External anal sphincter

Explanation Why

The [external anal sphincter](#), along with the [external urethral sphincter](#), [levator ani](#), [bulbospongiosus](#), and [ischiocavernosus muscles](#) are motor targets of the [pudendal nerve](#). Sensory innervation is to the perineum, [clitoris](#), labia, and [anal canal](#). [Pudendal nerve block](#) is sometimes used to provide anesthesia during surgical procedures involving the perineum (e.g., [episiotomy](#)) or during the [second stage of labor](#) if [epidural anesthesia](#) is no longer feasible. The ischial [spine](#) is usually used as a landmark for injection to locate the [pudendal nerve](#), which runs in close proximity to this bony prominence.

E - Skin of the mons pubis

Explanation Why

The [skin](#) of the mons pubis is innervated by the ilioinguinal nerve and iliohypogastric nerve, as well as by the genital branch of the genitofemoral nerve, but not by the [pudendal nerve](#). The ilioinguinal nerve also innervates the [skin](#) of the [labia majora](#) and, in men, the [skin](#) of the [proximal penis](#) and [scrotum](#). The iliohypogastric nerve also supplies sensation to the [lateral](#) gluteal region and motor signals to the [internal oblique](#) and transverse abdominal muscles. The genitofemoral nerve also supplies sensation to the [proximal](#) and [anterior](#) thigh.

F - Detrusor muscle

Explanation Why

The [detrusor muscle](#) of the [bladder](#) wall is innervated by the [autonomic nervous system](#). The [pudendal nerve](#), however, is a purely somatic nerve. [Sympathetic](#) input is received from the lower thoracic and upper lumbar [spinal cord](#) segments via the [hypogastric nerve](#) while [parasympathetic](#) tone is supplied by the sacral segments of the [spinal cord](#) via the [pelvic splanchnic nerves](#).

Question # 21

A 74-year-old woman is brought to the physician by her daughter for worsening memory for the past 1 month. She can no longer manage her bills and frequently forgets the names of her children. Her daughter is also concerned that her mother has a urinary tract infection because she has had increased urinary urgency and several episodes of urinary incontinence. Vital signs are within normal limits. Physical examination shows poor short-term memory recall and a slow gait with wide, short steps. Which of the following is most likely to improve this patient's condition?

	Answer	Image
A	Cerebral shunt placement	
B	Bromocriptine therapy	
C	Donepezil therapy	
D	Ciprofloxacin therapy	
E	Physical therapy referral	
F	Vaginal pessary placement	

Hint

Apraxic (“magnetic”) gait, dementia, and incontinence are the classic triad of normal pressure hydrocephalus.

Correct Answer

A - Cerebral shunt placement

Explanation Why

[Normal pressure hydrocephalus](#) presents a risk of permanent neurological damage, due to compression of periventricular [white matter](#) from ventricular distention. Even removal of a small amount of [CSF](#) via a [lumbar puncture](#) can be helpful but the definitive treatment of [normal pressure hydrocephalus](#) usually involves the drainage of excess [CSF](#) via a [cerebral shunt](#), usually into the [peritoneum](#) (e.g., [VP shunt](#)).

B - Bromocriptine therapy

Explanation Why

Prescription of [bromocriptine](#) is used in the treatment of [Parkinson disease](#). Though patients with [Parkinson disease](#) may show gait abnormalities, this patient's gait abnormalities (wide, short steps) are inconsistent with the characteristic [Parkinson gait](#) and her triad of symptoms suggest underlying NPH.

C - Donepezil therapy

Explanation Why

Prescription of [donepezil](#), a [cholinesterase inhibitor](#), is an established treatment for mild to moderate [Alzheimer disease](#) or [vascular dementia](#). Although this patient does show signs of [dementia](#), her cognitive symptoms only developed recently and manifest alongside [urinary incontinence](#), which would not be expected until the late stages of [Alzheimer disease](#). In addition, gait abnormalities are not a typical feature of [Alzheimer disease](#).

D - Ciprofloxacin therapy

Explanation Why

Prescription of [ciprofloxacin](#) can be used for the treatment of [UTI](#). Although urinary incontinence can be a symptom of [UTI](#), this diagnosis would not explain this patient's other symptoms of [normal pressure hydrocephalus](#) (e.g., [dementia](#), gait abnormalities).

E - Physical therapy referral

Explanation Why

[Physical therapy](#) can help improve symptoms of incontinence caused by decreased [pelvic floor](#) support and subsequent [pelvic organ prolapse \(POP\)](#), as well as help decrease falls in the elderly. However, [physical therapy](#) alone would not address the underlying etiology of this woman's symptoms due to NPH.

F - Vaginal pessary placement

Explanation Why

Placement of a [vaginal pessary](#) can be helpful in the treatment of urinary incontinence due to [pelvic organ prolapse](#) and could theoretically provide some symptomatic relief for the [urinary incontinence](#) in this [post-menopausal](#) woman. It would not, however, help in the treatment of her other symptoms of [normal pressure hydrocephalus](#) (e.g., [dementia](#), gait abnormalities).

Question # 22

One week after being involved in a bicycling accident, a 32-year-old woman comes to the physician because of intermittent double vision. She reports worsening of symptoms when she tries to type on her computer or while buttoning her shirts. Physical examination shows a slight right-sided head tilt. Her left eye is deviated upwards, which becomes even more prominent when she attempts left eye adduction. This patient's symptoms are most likely due to impaired innervation to which of the following muscles?

	Answer	Image
A	Superior oblique	
B	Superior rectus	
C	Medial rectus	
D	Lateral rectus	
E	Inferior oblique	
F	Inferior rectus	

Hint

This patient's right-sided head tilt, diplopia, upward deviation of the eye that worsens during adduction, and history of blunt trauma to the head suggest palsy of the left trochlear nerve (CN IV).

Correct Answer

A - Superior oblique

Image



Explanation Why

The [superior oblique muscle](#) is innervated by the [trochlear nerve \(CN IV\)](#) and is responsible for [abduction](#), [internal rotation \(incyclotorsion\)](#), and depression of the [eye](#) during [adduction](#). Impairment of this muscle manifests with vertical and torsional [diplopia](#) that worsens when the patient looks down and toward the nose (e.g., while typing on a computer); expected examination findings include mild ipsilateral inward deviation ([esotropia](#)), [external rotation \(excyclotorsion\)](#), and upward deviation ([hypertropia](#)) of the affected [eye](#). Downward gaze is impaired when the affected [eye](#) is [adducted](#). The contralateral tilting of the head in this patient may be conscious or unconscious and serves as a compensatory mechanism.

B - Superior rectus

Explanation Why

The [superior rectus muscle](#) is responsible for elevation, [incyclotorsion](#), and [adduction](#) of the [eye](#) and is innervated by the [oculomotor nerve](#). Impairment in the function of this muscle secondary to nerve injury would cause vertical [diplopia](#), limitation of upgaze in the ipsilateral [eye](#), and downward [eye](#) deviation ([hypotropia](#)).

C - Medial rectus

Explanation Why

The [medial rectus muscle](#) is responsible for [adduction](#) of the [eye](#) and is innervated by the [oculomotor nerve](#). Impairment in the function of this muscle secondary to nerve injury would cause horizontal [diplopia](#), limitation of the ipsilateral [eye](#) to the [medial](#) gaze, and deviation of the [eye](#) outwards ([exotropia](#)).

D - Lateral rectus

Explanation Why

The [lateral rectus muscle](#) is responsible for [abduction](#) of the [eye](#) and is innervated by the [abducens nerve](#). Impairment in the function of this muscle secondary to nerve injury would cause [medial](#) deviation of the [eye](#) ([esotropia](#)) at primary gaze, an ipsilateral [abduction](#) deficit, and horizontal [diplopia](#) that worsens when looking at distant objects.

E - Inferior oblique

Explanation Why

The [inferior oblique muscle](#) is innervated by the [oculomotor nerve](#) and is responsible for [excyclotorsion](#), elevation, and [abduction](#) of the [eye](#). Impairment in the function of this muscle secondary to nerve injury would cause the [eye](#) to deviate downwards ([hypotropia](#)) and rotate inwards ([incyclotorsion](#)).

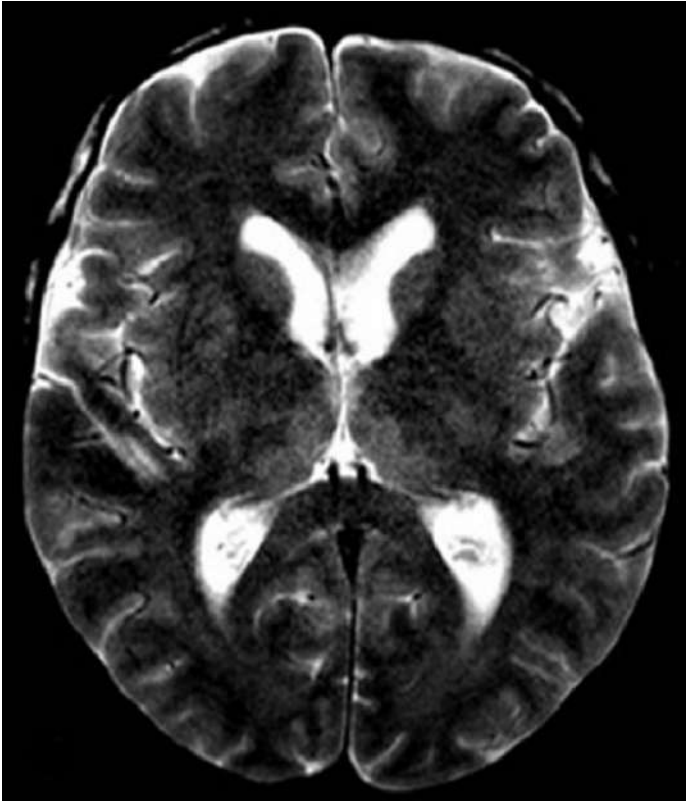
F - Inferior rectus

Explanation Why

The [inferior rectus muscle](#) is responsible for depression, [excyclotorsion](#), and [adduction](#) of the [eye](#) and is innervated by the [oculomotor nerve](#). Impairment in the function of this muscle secondary to nerve injury would cause vertical [diplopia](#), limitation of downgaze in the ipsilateral [eye](#), and upward [eye](#) deviation ([hypertropia](#)).

Question # 23

A 59-year-old man with alcohol use disorder is brought to the emergency department by a friend because of progressively worsening forgetfulness and frequent falls. He appears disheveled. On mental status examination, he is confused and oriented only to person. Neurologic examination shows horizontal nystagmus on lateral gaze. He walks with wide-based, small steps and his gait is unsteady. An MRI of the brain is shown. Supplementation of which of the following is most likely to have prevented this patient's current condition?



	Answer	Image
A	Vitamin B12	
B	Vitamin B1	
C	Vitamin B6	

	Answer	Image
D	Vitamin B3	
E	Vitamin B9	

Hint

This patient with alcohol use disorder presents with confusion, oculomotor dysfunction (e.g., nystagmus), gait ataxia, and a brain MRI showing hyperintensities in the thalamus. These signs and symptoms suggest Wernicke encephalopathy.

Correct Answer

A - Vitamin B12

Explanation Why

[Cobalamin](#) ([vitamin B₁₂](#)) deficiency can be caused by severe [malnutrition](#) associated with [alcohol use disorder](#). It can present clinically with [megaloblastic anemia](#), [subacute combined degeneration](#) of the [spinal cord](#), irritability, [memory](#) loss, and [dementia](#). However, it does not manifest with the symptoms of [Wernicke encephalopathy](#) seen here. Although [cobalamin](#) is also used in the long-term treatment of patients with [malnutrition](#) and [alcohol use disorder](#), supplementation would not have prevented this patient's condition.

B - Vitamin B1

Explanation Why

[Thiamine deficiency](#) leads to neuronal injury and impaired axonal conduction that cause the symptoms of [Wernicke encephalopathy](#) (i.e., confusion, oculomotor dysfunction, and [gait ataxia](#)). [Thiamine](#) ([vitamin B₁](#)) is a [cofactor](#) for critical enzymes involved in cerebral glucose and energy metabolism, which can be depleted in patients with [alcohol use disorder](#) and/or [malnourishment](#). Early supplementation of [thiamine](#) would most likely have prevented this patient's condition.

C - Vitamin B6

Explanation Why

[Pyridoxine](#) ([vitamin B₆](#)) deficiency most commonly occurs due to severe [malnutrition](#) and/or [alcohol use disorder](#) and can cause [cheilosis](#), [glossitis](#), stomatitis, [sideroblastic anemia](#), irritability, [seizures](#), and [peripheral neuropathy](#). It does not manifest with symptoms of [Wernicke encephalopathy](#) and [pyridoxine](#) supplementation would not have prevented this patient's condition.

D - Vitamin B3

Explanation Why

Although [niacin](#) ([vitamin B3](#)) deficiency can be caused by [alcohol use disorder](#) and [malnutrition](#), it typically manifests clinically with [pellagra](#), a clinical syndrome characterized by [dermatitis](#), [diarrhea](#), [glossitis](#), [dementia](#), and, if not treated, death. It does not manifest with the symptoms of [Wernicke encephalopathy](#) seen here. Supplementation would, thus, not have prevented this patient's condition.

E - Vitamin B9

Explanation Why

[Folic acid](#) ([vitamin B9](#)) deficiency may be caused by [alcohol use disorder](#) and/or [malnutrition](#) but typically presents with [megaloblastic anemia](#) and not with [Wernicke encephalopathy](#). [Folic acid](#) replacement is also used for long-term treatment of [Wernicke encephalopathy](#) because it promotes neurogenesis. However, supplementation would not have prevented the development of this condition.

Question # 24

A 75-year-old woman is brought to the emergency department because of a 6-hour history of severe headache, nausea, and 1 episode of vomiting. On arrival, she is lethargic and oriented only to self. Her pulse is 50/min, respirations are 8/min and shallow, and blood pressure is 150/96 mm Hg. Examination shows medial deviation of the left globe and ecchymoses of the upper eyelids. Appropriate pharmacotherapy with an intravenous drug is initiated, and the patient's urine output subsequently increases. The patient is at greatest risk of which of the following adverse effects?

	Answer	Image
A	Drug-induced hypersensitivity syndrome	
B	Hyperuricemia	
C	Tinnitus	
D	Increased intraocular pressure	
E	Pulmonary edema	

Hint

The patient presents with nausea, vomiting, headache, and a decreased level of consciousness. Examination shows the Cushing triad (bradycardia, respiratory depression, and hypertension), cranial nerve VI palsy, and spontaneous bruising of the upper eyelids. These are classic features of elevated intracranial pressure (ICP), which can be treated with mannitol, an osmotic diuretic.

Correct Answer

A - Drug-induced hypersensitivity syndrome

Explanation Why

[Drug-induced hypersensitivity syndrome \(DRESS\)](#) is associated with [sulfa drugs](#), which includes [diuretics](#) such as [furosemide](#), [acetazolamide](#), and [hydrochlorothiazide](#). [Furosemide](#) can be used as an adjunct in cases of acutely [increased intracranial pressure](#) but it is not the first-line drug. [Acetazolamide](#) is used to treat [glaucoma](#) and [idiopathic intracranial hypertension](#) but is not indicated for acutely [increased intracranial pressure](#). [Thiazide diuretics](#) are not indicated for the treatment of [elevated intracranial pressure](#).

B - Hyperuricemia

Explanation Why

[Hyperuricemia](#) can arise following treatment with [hydrochlorothiazide](#) but is not associated with [mannitol](#). [Thiazide diuretics](#) are not indicated for the treatment of [elevated intracranial pressure](#).

C - Tinnitus

Explanation Why

[Tinnitus](#) is a potential side effect of [acetazolamide](#) or [furosemide](#) but is not a side effect of [mannitol](#). [Furosemide](#) can be used as an adjunct in cases of acutely [increased intracranial pressure](#) but it is not the first-line drug. [Acetazolamide](#) is used to treat [glaucoma](#) and [idiopathic intracranial hypertension](#) but is not indicated for acutely [increased intracranial pressure](#).

D - Increased intraocular pressure

Explanation Why

[Mannitol](#) infusions tend to decrease [intraocular pressure](#) by reducing the volume of [vitreous humor](#), which is why they are used for treating acute [angle closure glaucoma](#). Since increased [intraocular pressure](#) is a potential side effect of [corticosteroids](#), they are not recommended in cases of [elevated intracranial pressure](#).

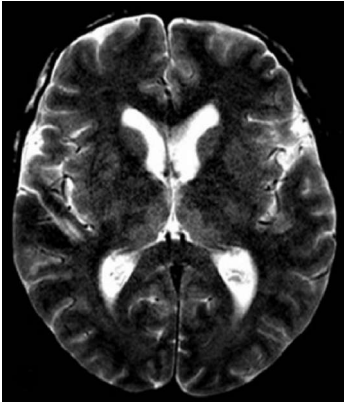
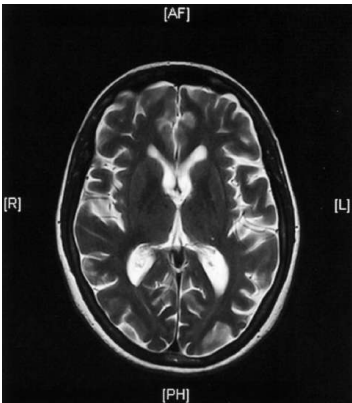
E - Pulmonary edema

Explanation Why

[Mannitol](#) causes an increase in plasma osmolality, resulting in osmotic shifts of water into the intravascular space. This effect decreases [cerebral edema](#) but can lead to [iatrogenic](#) volume overload and [pulmonary edema](#). [Risk factors](#) for this side effect of [mannitol](#) include very high doses and a low [glomerular filtration rate](#).

Question # 25

A 68-year-old man with alcohol use disorder is brought to the physician by his sister for frequent falls and an unsteady gait over the past 2 months. He has not seen a physician in 10 years. He appears emaciated and inattentive. He is oriented to person only. Physical examination shows a wide-based gait with slow, short steps. Eye examination shows lateral gaze paralysis and horizontal nystagmus. One month later, he dies. Which of the following is the most likely finding on autopsy?

	Answer	Image
A	Small vessel hemorrhage in mammillary bodies	
B	Degeneration of the frontotemporal lobe	
C	Depigmentation of the substantia nigra	
D	Widespread atrophy of cerebral cortex	

	Answer	Image
E	Atrophy of the caudate and putamen	

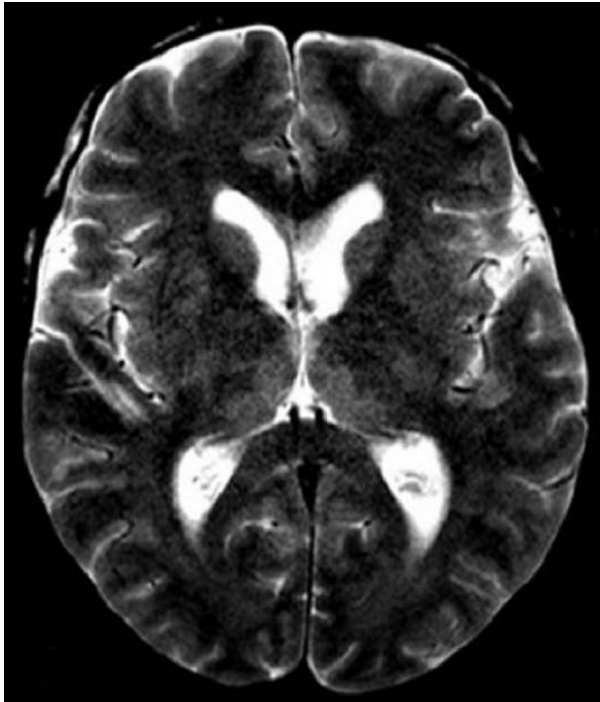
Hint

Confusion, ophthalmoplegia (lateral gaze paralysis), nystagmus, and ataxia in a malnourished patient with alcohol use disorder indicate Wernicke encephalopathy.

Correct Answer

A - Small vessel hemorrhage in mammillary bodies

Image



Explanation But

Treatment with high doses of intravenous [thiamine](#) should be immediately initiated in any patient who presents with [Wernicke encephalopathy](#). This condition must be treated urgently to prevent development and/or progression of [Korsakoff syndrome](#).

Explanation Why

Small vessel hemorrhage and [necrosis](#) in the [mammillary bodies](#) of the [hypothalamus](#) can be found in patients with [Wernicke encephalopathy](#), a sequela of severe [thiamine](#) ([vitamin B1](#)) deficiency. [Thiamine deficiency](#) causes neuronal injury and axonal conduction impairment, which leads to a classic triad of confusion/[memory](#) loss, [ataxia](#), and [ophthalmoplegia](#). [Alcohol use disorder](#), as seen in this patient, decreases intake, absorption, and hepatic storage of [thiamine](#), and is the most important [risk factor](#) associated with [Wernicke encephalopathy](#).

B - Degeneration of the frontotemporal lobe

Explanation Why

Degeneration of the frontotemporal lobe is seen in [frontotemporal dementia \(Pick disease\)](#), a neurodegenerative disease that is associated with mutations of [genes](#) encoding [tau proteins](#). [Frontotemporal dementia](#) can present with confusion, [ophthalmoplegia](#), and movement disorders, as seen in this patient. However, patients with [frontotemporal dementia](#) usually present with changes in personality and behavior early in the course of the disease, while orientation and [memory](#) are initially preserved.

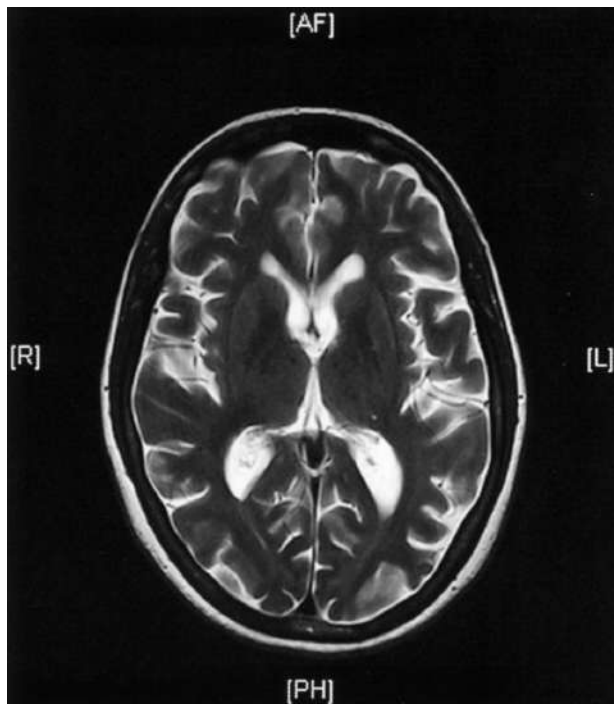
C - Depigmentation of the substantia nigra

Explanation Why

Depigmentation of the [substantia nigra](#) is found in [Parkinson disease](#), a neurodegenerative condition involving progressive depletion of [dopaminergic neurons](#) in the [basal ganglia](#). Although [Parkinson disease](#) typically presents with gait abnormalities and neurocognitive dysfunction, as seen here, other classic findings, such as [rigidity](#), akinesia, and [resting tremor](#) would be expected.

D - Widespread atrophy of cerebral cortex

Image



Explanation Why

Widespread [atrophy](#) of the [cerebral cortex](#) is found in [Alzheimer disease](#), a chronic neurodegenerative condition and the most common cause of [dementia](#). [Alzheimer disease](#) typically presents with confusion and [memory](#) loss. [Ophthalmoplegia](#), nystagmus, and [ataxia](#) in conjunction with a history of [alcohol use disorder](#) suggest a different diagnosis.

E - Atrophy of the caudate and putamen

Explanation Why

[Atrophy](#) of the caudate and [putamen](#) is found in [Huntington disease](#), a neurocognitive disorder caused by an increased number of CAG [trinucleotide repeats](#) in the [huntingtin gene](#). Findings of [Huntington disease](#) include [dementia](#), [ophthalmoplegia](#), and movement disorder, as seen here.

However, this patient lacks other typical findings of [Huntington disease](#), such as [chorea](#), [athetosis](#), and [dystonia](#).

Question # 26

A 25-year-old man is brought to the emergency department 30 minutes after he was involved in a motorcycle collision. Physical examination shows a deep laceration on the volar surface of the distal left forearm. Neurological examination shows loss of abduction and opposition of the left thumb. The radial and ulnar pulses are palpable. Based on these findings, which of the following nerves is most likely injured in this patient?

	Answer	Image
A	Posterior interosseous nerve	
B	Axillary nerve	
C	Radial nerve	
D	Median nerve	
E	Musculocutaneous nerve	
F	Ulnar nerve	

Hint

If this same nerve were injured more proximally (e.g., at or above the elbow), examination would show the hand of benediction sign.

Correct Answer

A - Posterior interosseous nerve

Explanation Why

The [posterior interosseous nerve](#) is a terminal branch of the radial nerve located deep in the [dorsal](#) forearm, making it very unlikely to be injured by a [volar](#) laceration. Injury to this nerve typically causes extension deficits at the wrist and fingers. Injury to the [posterior interosseous nerve](#) does not affect [abduction](#) or opposition of the thumb.

B - Axillary nerve

Explanation Why

The [axillary nerve](#) innervates the deltoid and [teres minor](#) as well as the [skin](#) overlying the [lateral](#) shoulder. Injury to this nerve classically occurs with [anterior](#) shoulder dislocations or [fractures](#) of the [surgical neck of the humerus](#) and causes weak arm [abduction](#) and a characteristically flattened shoulder. [Injury to the axillary nerve](#) does not affect the thumb.

C - Radial nerve

Explanation Why

The radial nerve courses along the [dorsal](#) aspect of the forearm and thus is very unlikely to be injured by a [volar](#) laceration. Patients with radial nerve injuries typically have extension deficits at the [elbow](#), wrist, and fingers. Injury to the radial nerve does not affect [abduction](#) or opposition of the thumb.

D - Median nerve

Explanation Why

Laceration of the median nerve at the wrist causes loss of thumb [abduction](#) and opposition, as seen in this patient. Additional deficits include reduced or absent sensation in the thumb, index, middle, and radial-sided ring fingers. The laceration could be through the median nerve proper or through the recurrent branch of the median nerve. The presence of sensory disturbances would be the determining factor, as the recurrent branch solely provides motor innervation.

E - Musculocutaneous nerve

Explanation Why

The [musculocutaneous nerve](#) is not typically affected by [distal](#) forearm injuries. Injury to this nerve (e.g., from upper trunk compression) causes loss of forearm [flexion](#) and [supination](#) as well as loss of sensation over the [lateral](#) forearm. [Injury to the musculocutaneous nerve](#) does not affect [abduction](#) or opposition of the thumb.

F - Ulnar nerve

Explanation Why

[Distal](#) injuries to the ulnar nerve typically cause sensory deficits in the ulnar-sided ring and small fingers. Motor deficits manifest with hyperextension of the [metacarpophalangeal joints](#) and [flexion](#) of the [distal interphalangeal joints](#) and [proximal interphalangeal joints](#) when the patient is asked to make a fist ([ulnar claw](#)). Injury to the ulnar nerve does not affect the thumb.

Question # 27

A 3-year-old boy is brought to the emergency department after losing consciousness. His parents report that he collapsed and then had repetitive, twitching movements of the right side of his body that lasted approximately one minute. He recently started to walk with support. He speaks in bisyllables and has a vocabulary of almost 50 words. Examination shows a large purple-colored patch over the left cheek. One week later, he dies. Which of the following is the most likely finding on autopsy of the brain?

	Answer	Image
A	Intraparenchymal cyst	
B	Periventricular calcification	
C	Brainstem glioma	
D	Leptomeningeal vascular malformation	
E	Subependymal giant cell astrocytoma	

Hint

This patient's condition is associated with somatic mutation of the GNAQ gene.

Correct Answer

A - Intraparenchymal cyst

Explanation Why

Intraparenchymal cysts are a common finding in [neurocysticercosis](#). While [neurocysticercosis](#) can manifest with [seizures](#), it is not associated with cutaneous findings or [intellectual disability](#). Moreover, [neurocysticercosis](#) takes 3–5 years to develop after initial [Taenia solium infection](#) and therefore would be unlikely in a 3-year-old child.

B - Periventricular calcification

Explanation Why

Periventricular calcifications are a common feature of [congenital CMV infection](#), which can manifest with [seizures](#) and [skin](#) findings. However, [petechiae](#) and blueberry muffin rash would be expected rather than a [port-wine stain](#). Moreover, this patient does not have other features of [congenital CMV infection](#) such as [hearing loss](#) or [chorioretinitis](#).

C - Brainstem glioma

Explanation Why

[Brainstem gliomas](#) are a common finding in [neurofibromatosis type 1](#), which can present with [seizures](#), developmental delay, and [skin](#) findings. However, [café au lait spots](#) and [neurofibromas](#) would be expected rather than a [port-wine stain](#). Moreover, this patient would be expected to have other features of [neurofibromatosis type 1](#) such as [optic gliomas](#), [pheochromocytomas](#), and [Lisch nodules](#).

D - Leptomeningeal vascular malformation

Explanation But

[Sturge-Weber syndrome](#) is also associated with early-onset [glaucoma](#) secondary to abnormal [blood vessels of the eye](#).

Explanation Why

This patient has several characteristics of [Sturge-Weber syndrome](#), a congenital disorder that affects the [capillaries](#) and commonly manifests with developmental delay and [port-wine stain](#). [Sturge-Weber syndrome](#) is associated with vascular [malformations](#) in the [choroid](#) and [CNS](#), including [leptomeningeal angiomas](#), which are typically located ipsilateral to the [port-wine stain](#) and can cause [seizures](#).

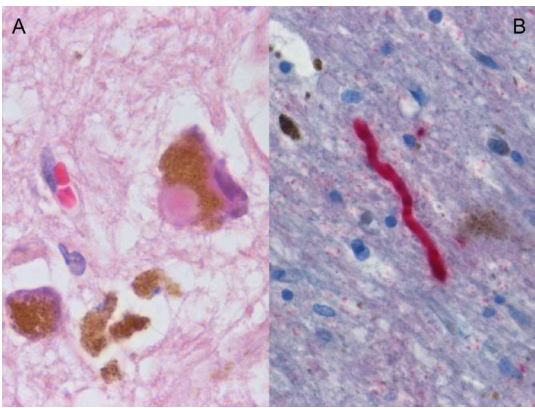
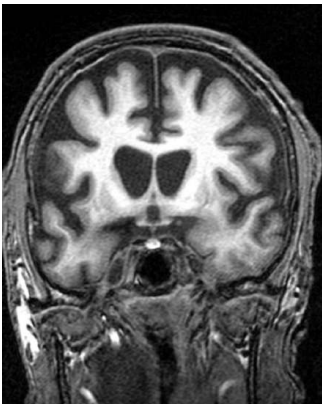
E - Subependymal giant cell astrocytoma

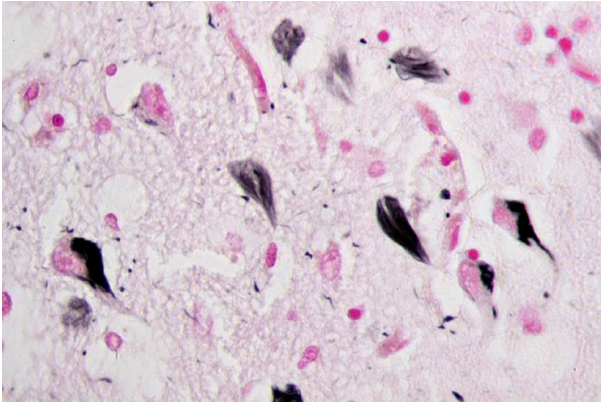
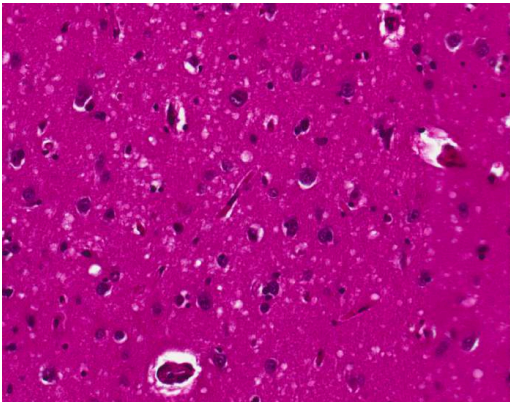
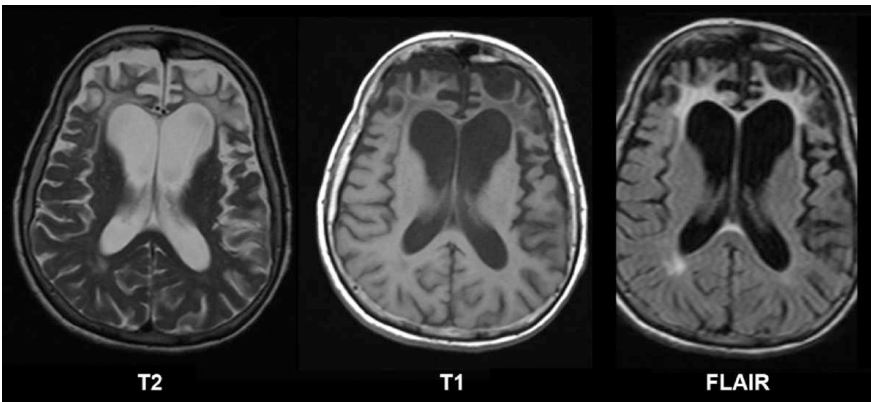
Explanation Why

Small [benign tumors](#) such as subependymal giant cell astrocytomas are commonly found in [tuberous sclerosis](#). [Tuberous sclerosis](#) can manifest with [infantile spasms](#), [seizures](#), [skin](#) findings, and [intellectual disability](#). However, the [skin](#) findings typically consist of [adenoma sebaceum](#), [ash leaf spots](#), and/or [Shagreen patches](#) rather than the [port-wine stain](#) seen in this patient.

Question # 28

A 62-year-old woman comes to the physician because of worsening mental status over the past month. Her husband reports that she was initially experiencing lapses in memory but has recently started having difficulties performing activities of daily living. She appears withdrawn and avoids eye contact. Examination shows diffuse involuntary muscle jerking that can be provoked by loud noises. A cerebrospinal fluid analysis shows elevated concentration of 14-3-3 protein. Four months later, the patient dies. Pathologic examination of the brain on autopsy is most likely to show which of the following findings?

	Answer	Image
A	Degeneration of the substantia nigra pars compacta	
B	Marked atrophy of caudate and putamen	
C	Focal inflammatory demyelination and gliosis	

	Answer	Image
D	Deposits of amyloid beta peptides	
E	Spongiform vacuolation of the cortex	
F	Atrophy limited to the frontal and temporal lobes	

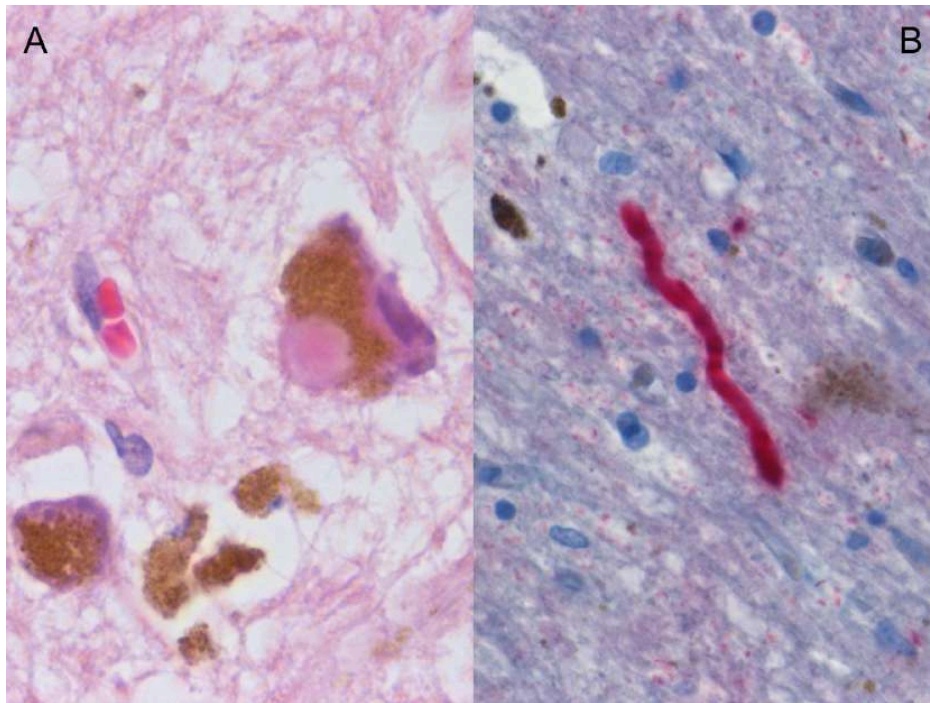
Hint

Rapidly progressive mental deterioration (dementia, behavioral abnormalities, altered mood), startle myoclonus, and elevated 14-3-3 protein concentration in the cerebrospinal fluid are highly suggestive of Creutzfeldt-Jakob disease.

Correct Answer

A - Degeneration of the substantia nigra pars compacta

Image



Explanation Why

Degeneration of the [substantia nigra](#) pars compacta and eosinophilic intracytoplasmic [inclusion bodies](#) ([Lewy bodies](#)) within [neurons](#) are typical histological features of [Parkinson disease](#) (PD). Although PD can manifest with signs of [dementia](#), which is seen in this patient, the hallmark features of [bradykinesia](#), [rigidity](#), and [tremor](#) are absent here. Furthermore, such rapid progression and death within months of symptom onset is not typical of PD. In addition, elevated levels of 14-3-3 protein in [CSF](#) would not be expected in PD.

B - Marked atrophy of caudate and putamen

Image



Explanation Why

[Atrophy](#) and [gliosis](#) in the caudate and [putamen basal ganglia](#) are typical histological features of [Huntington disease](#) (HD). Although HD can lead to neuropsychiatric symptoms like [dementia](#) in late stages of the disease, patients typically initially present with movement abnormalities, e.g., [chorea](#), as well as [hyperreflexia](#), which are absent in this patient. Furthermore, symptoms in HD usually first appear much earlier in life (around 40 years of age), and often progress over decades, as opposed to months, until death. In addition, elevated levels of 14-3-3 protein in [CSF](#) would not be expected in HD.

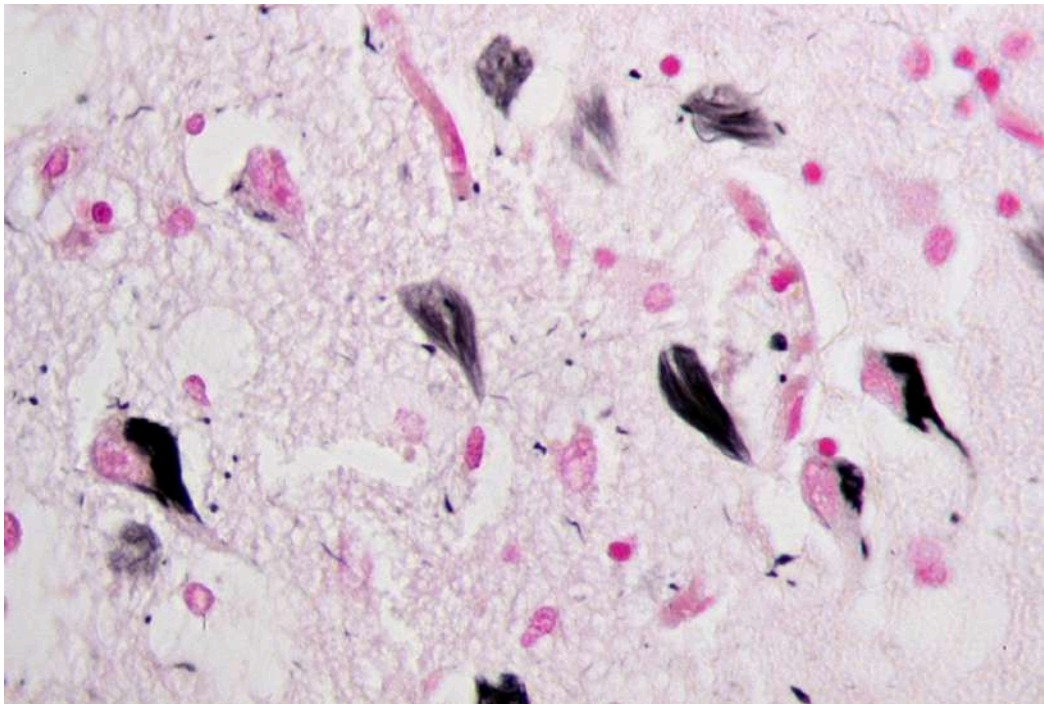
C - Focal inflammatory demyelination and gliosis

Explanation Why

Multifocal areas of [inflammation](#), [demyelination](#), and [gliosis](#) are histological hallmarks of [multiple sclerosis](#) (MS). MS can present with [memory](#) deficits, but this is usually a very late feature. The disease more typically presents with impaired vision, [color blindness](#), the [Lhermitte sign](#), and signs of [upper motor neuron](#) dysfunction (e.g., [spasticity](#), positive [Babinski sign](#)), none of which are present in this patient. Furthermore, MS would not involve such a rapid progression within months of symptom onset. Lastly, elevated levels of 14-3-3 protein in [CSF](#) are not characteristic of MS.

D - Deposits of amyloid beta peptides

Image



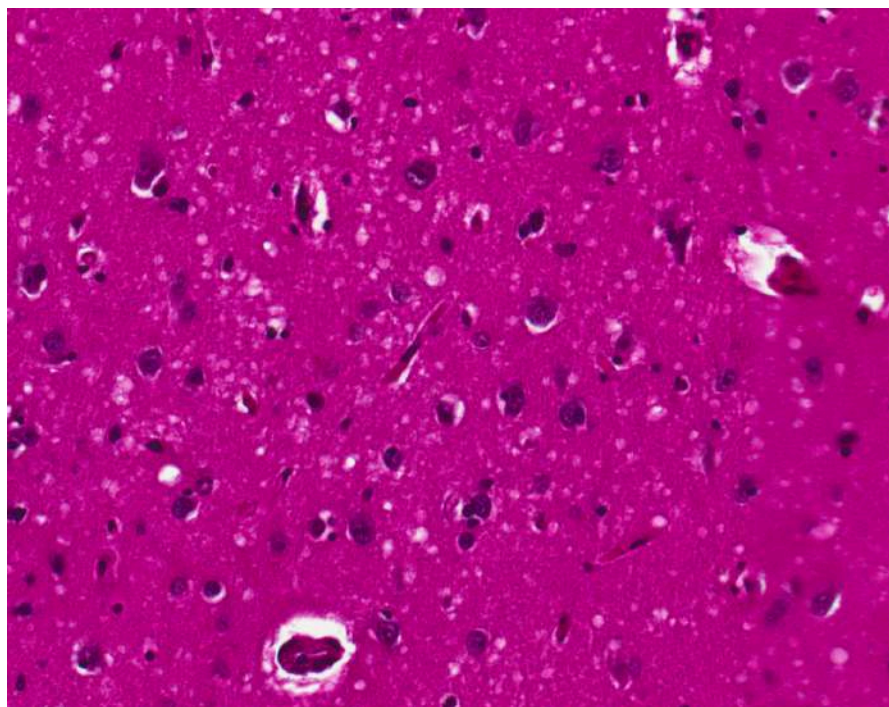
Explanation Why

Extracellular plaques composed of [amyloid beta peptides](#) and intracellular accumulation of

hyperphosphorylated [tau protein](#) ([neurofibrillary tangles](#)) are typical histological features of [Alzheimer disease](#) (AD). Although AD initially manifests with short-term [memory](#) loss, which is seen in this patient, other classic findings are absent here, e.g., impaired naming and language comprehension or temporospatial [disorientation](#). Most importantly, AD has an insidious onset and progresses slowly over several years, whereas this patient's symptoms progressed rapidly within 4 months. In addition, elevated levels of 14-3-3 protein in [CSF](#) are not characteristic of AD.

E - Spongiform vacuolation of the cortex

Image



Explanation But

Electroencephalogram of patients with [CJD](#) typically shows triphasic [periodic sharp wave complexes](#).

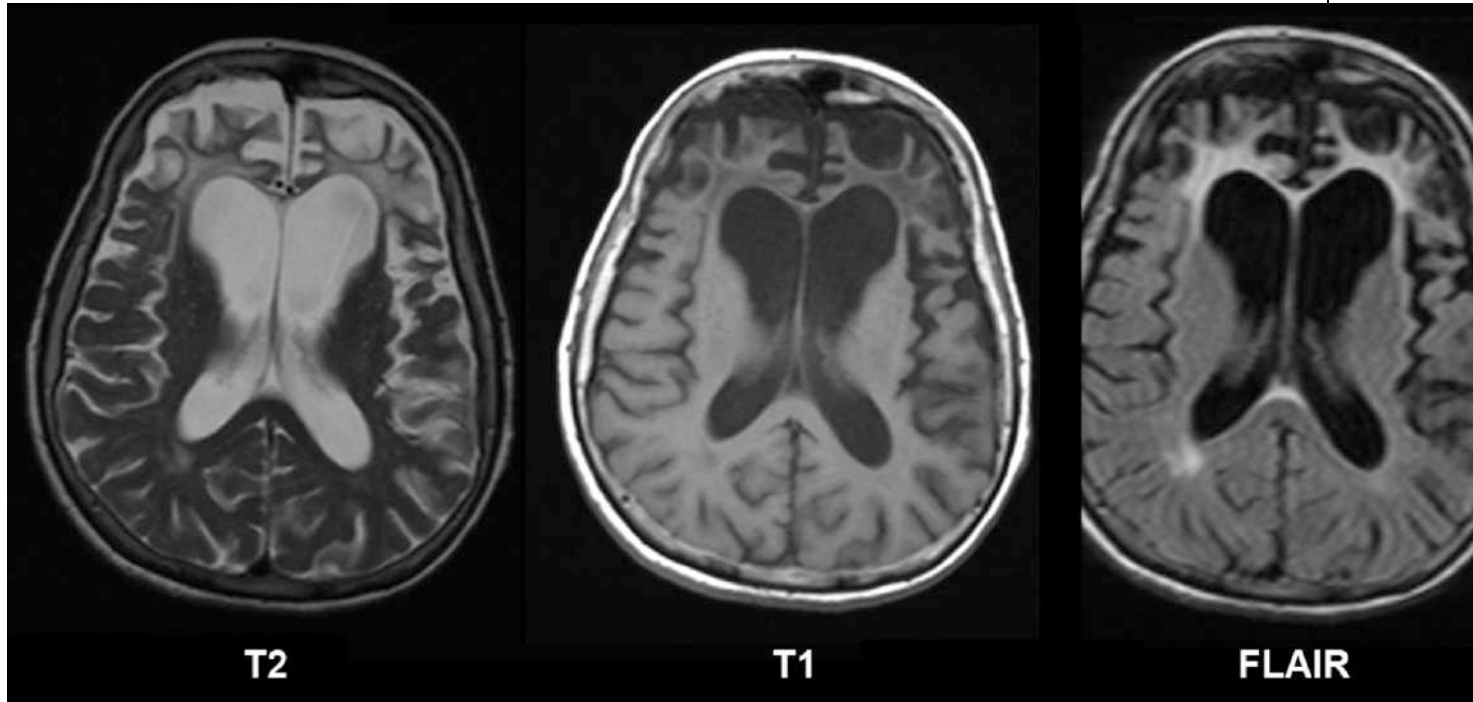
Explanation Why

The presence of intracytoplasmic vacuoles within [neurons](#) of the cerebral and [cerebellar cortex](#) (spongiform encephalopathy) is the characteristic histological feature of [Creutzfeldt-Jakob disease](#) ([CJD](#)) and other [prion diseases](#). In addition to the classic features displayed by this patient, [CJD](#) can also lead to [akinetic mutism](#), [seizures](#), and neuropsychiatric symptoms (e.g., [visual hallucinations](#),

depression). The disease has a rapid course that often leads to death within 12 months.

F - Atrophy limited to the frontal and temporal lobes

Image

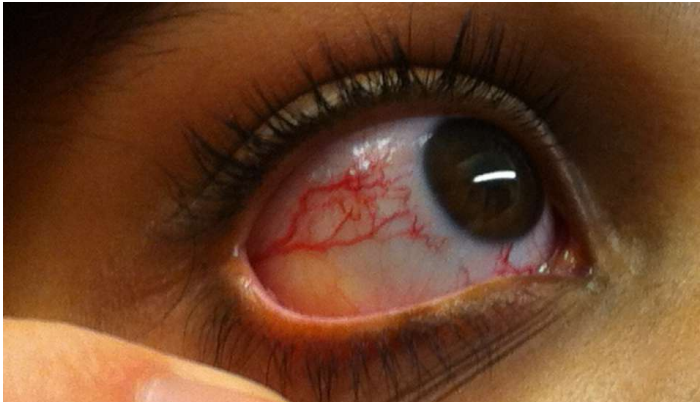


Explanation Why

Loss of [neurons](#) in the frontal and [temporal lobes](#) is the defining histological feature of [frontotemporal dementia \(FTD\)](#). Although [FTD](#) can manifest with early changes in personality and behavior (e.g., inappropriate social behavior), which are seen in this patient, [memory](#) is typically unaffected. Furthermore, the [mean](#) survival of patients with [FTD](#) is 6 years after symptom onset, much longer than the 4 months seen in this case. In addition, elevated levels of 14-3-3 protein in [CSF](#) would not be expected in [FTD](#).

Question # 29

A 13-year-old girl is brought to the physician by her mother because of a 1-year history of worsening clumsiness. Initially, she swayed while walking; over the past 3 months, she has fallen 4 times. Ophthalmic examination shows a horizontal nystagmus. Proprioception and vibratory sensation are decreased in the distal extremities. Deep tendon reflexes are 1+ bilaterally. Further evaluation of the patient shows a genetic disorder involving an iron-binding mitochondrial protein encoded on chromosome 9. Which of the following findings is most likely to also be seen in this patient?

	Answer	Image
A	Hyperpigmented skin	
B	Telangiectasias	
C	Hammer toes	
D	Myoclonic jerks	

	Answer	Image
E	Adenoma sebaceum	

Hint

An autosomal recessive GAA trinucleotide expansion mutation in the frataxin gene on chromosome 9, which encodes an iron-binding mitochondrial protein, is the underlying cause of Friedreich ataxia (FA). This condition usually manifests in the 1st or early 2nd decade of life.

Correct Answer

A - Hyperpigmented skin

Explanation But

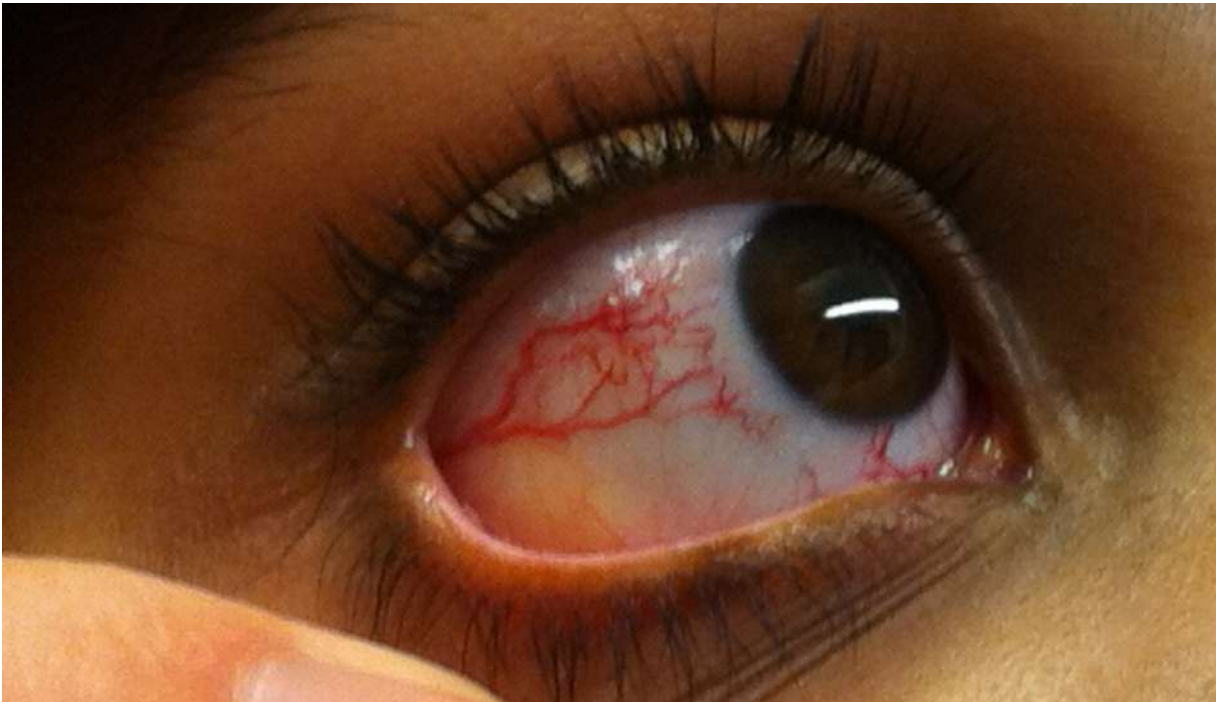
Other causes of [hyperpigmentation](#) include [niacin deficiency](#) ([pellagra](#)), [porphyria](#), excess [ACTH](#) production ([primary adrenal insufficiency](#), [congenital adrenal hyperplasia](#), [secondary hypercortisolism](#)) and certain drugs (e.g., [bleomycin](#), [busulfan](#), [oral contraceptives](#)).

Explanation Why

[Hyperpigmentation](#) of the [skin](#) is characteristic of hereditary [hemochromatosis](#) (HH), which is caused by abnormal [iron](#) deposition in specific organs. HH is asymptomatic in the first few decades of life, usually manifesting in the 3rd–5th decade with [hepatomegaly](#), arthralgias, [diabetes mellitus](#), and [cardiomyopathy](#). The [pituitary](#) is the only [CNS](#) organ that is affected in HH, resulting in [hypopituitarism](#). The [ataxia](#), nystagmus, [dorsal column](#) dysfunction, and [hyporeflexia](#) seen in this patient are not features of HH. Genetic testing would also show a mutation in the [HFE gene](#) on [chromosome](#) 6.

B - Telangiectasias

Image



Explanation But

Other causes of [telangiectasias](#) include [liver cirrhosis](#) and [Osler-Weber-Rendu syndrome](#).

Explanation Why

[Telangiectasias](#) on the face and [conjunctivae](#) are typical findings in [ataxia telangiectasia](#) (AT), which can present with [ataxia](#), nystagmus, and [hyporeflexia](#), as seen here. However, AT typically manifests in [infancy](#) or early childhood and a history of frequent sinopulmonary infections would be expected. [Dorsal column](#) dysfunction (loss of vibratory sensation and [proprioception](#)) is not usually seen, and genetic testing would show a mutation in the *ATM* [gene](#), which is located on [chromosome](#) 11 and is responsible for double-stranded [DNA](#) repair.

C - Hammer toes

Image



Explanation Why

[Friedreich ataxia](#) (FA) is characterized by the progressive degeneration of the [spinocerebellar tract](#), [lateral corticospinal tract](#), [dorsal column](#), and [dorsal root ganglia](#) due to intramitochondrial accumulation of [iron](#). Degeneration of the [spinocerebellar tract](#) can result in [cerebellar signs](#) such as [ataxia](#), nystagmus, and [dysarthria](#). Degeneration of the [lateral corticospinal tract](#) causes [spasticity](#), which can result in deformities such as [hammer toe](#), [pes cavus](#), and kyphoscoliosis. Despite the presence of [spasticity](#), patients often have decreased [deep tendon reflexes](#) due to the damage to [dorsal root ganglia](#) and the [dorsal column](#). [Dorsal column](#) damage also causes impaired [proprioception](#) (which contributes to [ataxia](#)) as well as [impaired vibration sense](#). Patients with FA will eventually develop [diabetes mellitus](#) and [hypertrophic cardiomyopathy](#), which is the most common cause of death in FA.

D - Myoclonic jerks

Explanation But

Some other causes of myoclonic jerks include [juvenile myoclonic epilepsy](#) and spongiform encephalopathies (e.g. [Creutzfeld-Jakob disease](#)).

Explanation Why

Myoclonic jerks and [ataxia](#) are characteristic of [myoclonic epilepsy with ragged red fibers](#) ([MERRF](#)) and [opsoclonus-myoclonus syndrome](#) (OMS). [MERRF](#) can manifest in childhood and cause [hyporeflexia](#) due to [peripheral neuropathy](#). However, a history of [seizures](#) and muscle weakness would also be expected, and nystagmus and [dorsal column](#) dysfunction are not features of [MERRF](#). In addition, genetic testing would show a mutation in the [mitochondrial MT-TK gene](#), not the [chromosomal genome](#). OMS can cause nystagmus in addition to myoclonic jerks and [ataxia](#), but it would not cause [hyporeflexia](#). Moreover, OMS is a [paraneoplastic syndrome](#) caused in children by a [neuroblastoma](#), which presents with abdominal distention and is associated with a mutation of the [N-myc oncogene](#) on [chromosome 2](#).

E - Adenoma sebaceum

Image



Explanation Why

[Adenoma sebaceum](#) is one of the characteristic [skin](#) manifestations of [tuberous sclerosis \(TSC\)](#), which can be caused by a mutation on [chromosome 9](#) and could potentially present with [ataxia](#) and nystagmus due to a [hamartoma](#) in the [cerebellum](#) or a subependymal giant cell astrocytoma causing [hydrocephalus](#). However, the affected [gene](#) on [chromosome 9](#) would be [TSC1](#), which produces the [tumor suppressor protein hamartin](#), not an [iron](#)-binding [mitochondrial](#) protein. Also, this patient's features of [dorsal column](#) dysfunction (loss of vibratory sensation and [proprioception](#)) and [hyporeflexia](#) would not be expected.

Question # 30

A 47-year-old woman comes to the physician because of a 3-month history of recurrent episodes of nausea and feeling like the room is spinning. Each episode lasts less than a minute and usually occurs when she gets out of bed in the morning or suddenly turns her head. She has not vomited and does not have headaches. She is asymptomatic between episodes. Which of the following findings most closely correlates with this patient's symptoms?

	Answer	Image
A	Intention tremor	
B	Nystagmus	
C	Positive Romberg test	
D	Binocular diplopia	
E	Abnormal Rinne test	
F	Orthostatic hypotension	
G	Expressive aphasia	

Hint

This patient presents with vertigo and nausea, which are common symptoms of a vestibular disorder.

Correct Answer

A - Intention tremor

Explanation Why

[Intention tremor](#) is a sign of [cerebellar dysfunction](#) that can result from a variety of neurological conditions. While some patients with [intention tremor](#) experience [dizziness](#), this is due to disequilibrium secondary to [cerebellar dysfunction](#) rather than vestibular dysfunction. [Dizziness](#) due to a balance disorder is triggered by walking instead of head rotation, as seen in this patient.

B - Nystagmus

Explanation But

Patients with a positive [Dix Hallpike test](#) for right-sided [BPPV](#) (with the head rotated to the right) will have rotational nystagmus with a counterclockwise rapid phase. Clockwise rapid phase nystagmus on rotation to the left is positive for left-sided [BPPV](#).

Explanation Why

[Vertigo](#) and nausea are common symptoms of dysfunctions of the [vestibular system](#), which often also present with pronounced nystagmus. This patient's episodic [vertigo](#) triggered by specific types of head movement suggests [benign paroxysmal positional vertigo](#) ([BPPV](#)), which is confirmed by observing nystagmus during a provoked maneuver such as the [Dix Hallpike test](#).

C - Positive Romberg test

Explanation Why

A positive [Romberg test](#) is indicative of dysfunction of the [dorsal columns](#), which can result from conditions such as longstanding uncontrolled [diabetes mellitus](#) or [syphilis](#). [Dorsal column](#) dysfunction leads to [sensory ataxia](#), which may manifest with [vertigo](#). However, [vertigo](#) due to a

[sensory ataxia](#) is triggered by movement of the extremities instead of head rotation as the symptoms in this patient.

D - Binocular diplopia

Explanation Why

Binocular diplopia, commonly known as [double vision](#), is a sign of dysfunction of the [extraocular muscles](#). While visual impairment can induce [vertigo](#), it is not triggered by head rotation as in this patient.

E - Abnormal Rinne test

Explanation Why

An abnormal [Rinne test](#) is a sign of [conductive hearing loss](#), which can be caused by a variety of conditions, including [cerumen impaction](#), [otosclerosis](#), and [otitis media](#). Although these conditions can cause [dizziness](#), this patient's pattern of episodic [vertigo](#) triggered by specific types of head movement indicates a different cause for her symptoms.

F - Orthostatic hypotension

Explanation Why

[Orthostatic hypotension](#) is an episodic phenomenon that causes [dizziness](#) or faintness upon standing and may indicate cardiac or neurologic disease if it becomes recurrent. Although [orthostatic hypotension](#) is episodic, it does not present with [vertigo](#) and nausea as experienced by this patient. Furthermore, while [orthostatic hypotension](#) has positional triggers such as standing up, turning of the head does not trigger symptoms.

G - Expressive aphasia

Explanation Why

[Expressive aphasia](#), also known as [Broca aphasia](#), is a sign of dysfunction of the [frontal lobe](#) at the inferior frontal [gyrus](#). Brain lesions can cause central vertigo, but this is usually due to lesions of the [brain stem](#) or [cerebellum](#), not the [frontal lobe](#). This patient's [vertigo](#) is episodic rather than chronic, as would be expected in a patient with lesions of the [CNS](#).

Question # 31

A 23-year-old man comes to the physician because of severe daytime sleepiness and random episodes of falling asleep during the day for short periods of time. When he wakes up from these episodes, he feels refreshed. He sleeps 6–7 hours at night. He reports that sometimes he is unable to move for a few minutes when he first wakes up in the morning. Last week, he suddenly “lost control” of his legs and neck for about 30 seconds after his classmate had told him a joke. An analysis of this patient's cerebral spinal fluid is most likely to show which of the following findings?

	Answer	Image
A	Oligoclonal bands	
B	Decreased orexin-A	
C	Increased neuron-specific enolase	
D	Increased 14-3-3 protein	
E	Anti-ganglioside antibodies	
F	Decreased beta-amyloid 1-42	

Hint

This patient's excessive daytime sleepiness, sleep attacks, sleep paralysis, and episode of cataplexy indicate narcolepsy.

Correct Answer

A - Oligoclonal bands

Explanation Why

[Oligoclonal bands](#) are characteristic [serum electrophoretic](#) bands found in the [CSF](#) of [multiple sclerosis](#) patients. In rare cases, MS may cause sleep disturbances, [cataplexy](#), daytime [somnolence](#), and hypnopompic paralysis. However, this patient has not exhibited any of the symptoms associated with MS, including impaired vision, sensory deficits, abnormal reflexes, [cranial nerve palsies](#), or [autonomic dysfunction](#), making the diagnosis unlikely.

B - Decreased orexin-A

Explanation Why

[Orexin](#) ([hypocretin](#)) is a neuropeptide that is released to increase the activity of brain regions involved in wakefulness, including the raphe nuclei and tuberomammillary nucleus and [locus coeruleus](#). [Orexin](#) is decreased in the [CSF](#) levels of patients with [narcolepsy](#) due to a loss of orexigenic [neurons](#) in the [lateral hypothalamus](#) (type-1 [narcolepsy](#)).

C - Increased neuron-specific enolase

Explanation Why

[Neuron-specific enolase](#) is a [CSF](#) biomarker that reflects neuronal damage and brain injury. A [transient ischemic attack](#) can present with a temporary loss of motor function and muscle weakness. However, a [TIA](#) would not explain the daytime sleepiness, hypnopompic paralysis, and [cataplexy](#) in this patient.

D - Increased 14-3-3 protein

Explanation Why

14-3-3 is a protein that increases in [CSF](#) levels in [Creutzfeldt Jakob disease](#). While [CJD](#) causes nonspecific neurological manifestations, which may include sleep disturbances, [excessive daytime sleepiness](#), and [sleep paralysis](#), it would not explain the patient's [cataplexy](#).

E - Anti-ganglioside antibodies

Explanation Why

Anti-ganglioside antibodies detection is a method by which autoimmune neuropathies are diagnosed, primarily Guillain-Barré Syndrome. GBS paralysis occurs in both upper and lower limbs and follows a pattern of muscle weakness in a stocking-glove distribution, which is not present in this patient. GBS would also not cause this patient's sleeping problems or [cataplexy](#).

F - Decreased beta-amyloid 1-42

Explanation Why

[Beta-amyloid](#) 1-42 is a 42 [amino acid](#) residue of [amyloid](#) beta and is used as a [CSF](#) indicator of [Alzheimer's disease](#). Patients with Alzheimer's experience shorter sleep duration, decreased sleep efficiency, and daytime sleepiness. However, AD would not cause this patient's [cataplexy](#). In addition, this patient has no signs of cognitive impairment.

Question # 32

A 60-year-old man is brought to the emergency department because of a 1-hour history of disorientation and slurred speech. He has a 10-year history of hypertension and hypercholesterolemia. His blood pressure is 210/110 mm Hg, and pulse is 90/min. Once the patient is stabilized, an MRI of the brain is performed, which shows an infarct of the left precentral gyrus involving the region that supplies the facial nerve. Given the MRI findings, which of the following neurological findings would most be expected?

	Answer	Image
A	Loss of taste in the posterior third of the right half of the tongue	
B	Flattening of the right nasolabial fold	
C	Decreased lacrimation of the left eye	
D	Drooping of the left eyelid	
E	Hyperacusis of the left ear	
F	Inability to raise the right eyebrow	

Hint

A lesion of the corticobulbar tract between the precentral gyrus and the brainstem nuclei of the facial nerve causes central facial nerve palsy.

Correct Answer

A - Loss of taste in the posterior third of the right half of the tongue

Explanation Why

[Taste](#) to the [posterior](#) third of the [tongue](#) is supplied by the [glossopharyngeal nerve](#) and would therefore not be impaired in [central facial nerve palsy](#). [Facial nerve palsy](#) may affect [taste](#) sensation in the [anterior](#) two-thirds of the [tongue](#), since this region is innervated by the [parasympathetic](#) fibers supplied by the [chorda tympani](#). However, [central facial nerve palsy](#) causes contralateral deficits, and a lesion to the precentral [gyrus](#), the location of the [primary motor cortex](#), does not affect [taste](#).

B - Flattening of the right nasolabial fold

Explanation Why

Flattening of the right [nasolabial fold](#) would be expected in [central facial nerve palsy](#). The facial motor nucleus has two regions: one that supplies the muscles of the forehead and a second that supplies the rest of the face. The branches of the [facial nerve](#) that innervate the forehead are activated by both cerebral hemispheres, whereas the branches innervating the lower portion of the face are only activated by the contralateral cerebral hemisphere. As a result, the forehead is spared with unilateral [infarction](#) of the precentral [gyrus](#), while the contralateral lower face becomes paralyzed.

C - Decreased lacrimation of the left eye

Explanation Why

Lacrimation of the [eye](#) is modulated by the greater petrosal nerve, a branch of the [facial nerve](#) that carries [parasympathetic](#) fibers, and could therefore be impaired by [peripheral facial nerve palsy](#). Decreased lacrimation of the left [eye](#) would be expected in left-sided [peripheral facial palsy](#). However, [central facial nerve palsy](#) causes contralateral deficits, and a lesion to the precentral [gyrus](#), the location of the [primary motor cortex](#), does not affect lacrimation.

D - Drooping of the left eyelid

Explanation Why

Drooping of the ipsilateral [eyelid](#) is seen in third nerve palsy, which may be caused by trauma, [ischemia](#), [migraine](#) ([cranial](#) neuralgia), [intracranial aneurysm](#) or is idiopathic ([Bell palsy](#)). In [central facial nerve palsy](#), drooping of the [eyelid](#) would not be expected, since the forehead is innervated by fibers from both cerebral hemispheres.

E - Hyperacusis of the left ear

Explanation Why

[Hyperacusis](#) of the left ear would be a result of paralysis of the [stapedius muscle](#). The [stapedius muscle](#) is supplied by the [nerve to stapedius](#), a branch of the [facial nerve](#), and could therefore be impaired in [facial nerve palsy](#). [Hyperacusis](#) of the left ear would be expected in left-sided [peripheral facial palsy](#). However, since [central facial nerve palsy](#) causes contralateral lesions, in this patient [hyperacusis](#) of the right ear would be expected.

F - Inability to raise the right eyebrow

Explanation Why

Inability to raise the right eyebrow is seen in ipsilateral [peripheral facial nerve palsy](#), which is commonly caused by trauma (e.g., zygomatic [fractures](#), lacerations), infection (e.g., herpes simplex virus, [varicella-zoster virus](#)), tumors (e.g., [neuromas](#), [parotid gland](#) tumors), or is idiopathic ([Bell palsy](#)). In [central facial nerve palsy](#), drooping of the eyebrow would not be expected, since the forehead is innervated by fibers from both cerebral hemispheres.

Question # 33

A 54-year-old man with hypertension and congenital blindness comes to the physician because he is unable to recognize objects by touch with his right hand. The symptoms started about 2 hours ago. When given a house key, he can feel the object in his right hand but is not able to identify what it is. This patient's condition is most likely caused by a lesion in which of the following locations?

	Answer	Image
A	Ipsilateral inferior frontal gyrus	
B	Ipsilateral superior temporal gyrus	
C	Contralateral superior parietal lobule	
D	Contralateral precentral gyrus	
E	Ipsilateral cingulate gyrus	

Hint

The ability to recognize objects by touch is called stereognosis. Tactile information is processed by the secondary somatosensory cortex (somatosensory association cortex).

Correct Answer

A - Ipsilateral inferior frontal gyrus

Explanation Why

The inferior frontal [gyrus](#) of the dominant hemisphere encompasses the [Broca area](#), which is involved in [speech](#) production. A lesion in the [Broca area](#) causes [expressive aphasia](#), not [astereognosis](#).

B - Ipsilateral superior temporal gyrus

Explanation Why

The [superior temporal gyrus](#) consists of the [primary auditory cortex](#) and auditory association cortex, which is part of [Wernicke area](#) in the dominant hemisphere. A lesion in this area causes slight loss of hearing, difficulty of sound localization, and [Wernicke aphasia](#) if the dominant hemisphere is involved.

C - Contralateral superior parietal lobule

Explanation Why

The [somatosensory association cortex](#) is located in the superior parietal lobule and is involved in tactile information processing and spatial orientation. A lesion in the left superior parietal lobule can cause right-sided [astereognosis](#), as seen in this patient. [Hemispatial neglect](#) can also result from [parietal lobe](#) damage; however, it is more characteristic of right [parietal lobe](#) lesions, rather than the left [parietal lobe](#) lesion seen here.

D - Contralateral precentral gyrus

Explanation Why

The precentral [gyrus](#) is the location of the [primary motor cortex](#), which controls the motor function of the contralateral body. A lesion in this area leads to contralateral [spastic paralysis](#), not [astereognosis](#).

E - Ipsilateral cingulate gyrus

Explanation Why

The [cingulate gyrus](#) is part of the [limbic system](#), which is involved in emotion, feeding, mating, learning, and [memory](#) formation. Decreased volume of the [anterior cingulate gyrus](#) has been associated with a lowered level of social functioning in patients with [schizophrenia](#). A [cingulate gyrus](#) lesion does not cause [astereognosis](#).

Question # 34

An otherwise healthy 43-year-old woman comes to the physician because of several episodes of involuntary movements of her head over the past few months. They are sometimes associated with neck pain and last minutes to hours. Neurologic examination shows no abnormalities. During examination of the neck, the patient's head turns horizontally to the left. She states this movement is involuntary, and that she is unable to unturn her head. After 5 minutes, her head re-straightens. Which of the following best describes this patient's disorder?

	Answer	Image
A	Akathisia	
B	Hemiballismus	
C	Myoclonus	
D	Dystonia	
E	Chorea	
F	Athetosis	

Hint

Other common examples of this disorder include blepharospasm and writer's cramp.

Correct Answer

A - Akathisia

Explanation Why

[Akathisia](#) is a movement disorder characterized by an intense urge to move. Affected individuals have difficulty in sitting still and typically exhibit a fidgety behavior (e.g., pacing, rocking). Movements are characteristically voluntary, repetitive, and driven by a subjective sense of restlessness, unlike this patient's involuntary, non-repetitive head movement. [Akathisia](#) is most commonly seen as a side-effect of [antipsychotic](#) medications and [antiparkinson medications](#), which this patient is not taking.

B - Hemiballismus

Explanation Why

[Hemiballismus](#) is an involuntary movement disorder characterized by large amplitude movements of one side of the body (e.g., flinging of an arm or leg), and may indicate a lesion of the contralateral [subthalamic nucleus](#). Sustained contraction of a single muscle, as observed here, is not a feature of [hemiballismus](#).

C - Myoclonus

Explanation Why

Myoclonus is an involuntary movement disorder characterized by multiple, brief, [shock](#)-like twitches caused by sudden muscular contraction or inhibition. Sustained contraction of a muscle, as seen in this patient, is not a feature of myoclonus.

D - Dystonia

Explanation But

Focal [dystonia](#) responds well to [botulinum toxin](#) injections.

Explanation Why

[Dystonia](#) is a movement disorder characterized by episodic, prolonged, involuntary muscular contractions. The patient presents with involuntary contractions of the right [sternocleidomastoid muscle](#) (head turns to the left) in the absence of other neurological signs. This is typical of [spasmodic torticollis](#), the most common focal [dystonia](#) that is often idiopathic and typically manifests for the first time after the age of 30, as in this patient.

E - Chorea

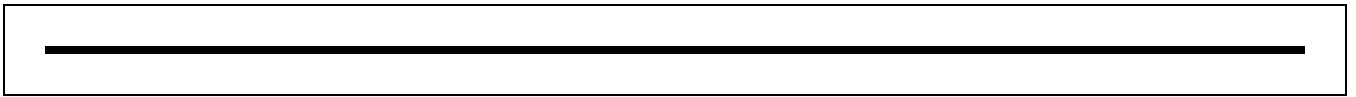
Explanation Why

[Chorea](#) is an involuntary movement disorder characterized by continuous, jerky, purposeless movements that cannot be suppressed. It is a sign of a lesion in the [basal ganglia](#) and is typically seen in [Huntington disease](#) or [acute rheumatic fever](#) ([Sydenham chorea](#)). [Chorea](#) typically affects the limbs and/or face. Sustained contraction of a muscle, as seen in this patient, is not a feature of [chorea](#).

F - Athetosis

Explanation Why

[Athetosis](#) is an involuntary movement disorder characterized by continuous, nonrhythmic, low-amplitude, slow, writhing movements. It can develop secondary to [basal ganglia](#) and/or thalamic damage (e.g., [Huntington disease](#) in adults; [cerebral palsy](#) and [kernicterus](#) in children). Sustained contraction of a muscle, as seen in this patient, is not a feature of [athetosis](#). Furthermore, [athetosis](#) typically affects the hands and feet, and only rarely the face and neck.



Question # 35

A 56-year-old male comes to the physician because of a 2-month history of excessive sleepiness. He reports that he has been sleeping for an average of 10 to 12 hours at night and needs to take multiple naps during the day. Six months ago, he was diagnosed with small cell lung carcinoma and underwent prophylactic cranial irradiation. This patient's symptoms are most likely caused by damage to which of the following structures?

	Answer	Image
A	Preoptic nucleus	
B	Ventromedial nucleus	
C	Suprachiasmatic nucleus	
D	Supraoptic nucleus	
E	Caudate nucleus	
F	Subthalamic nucleus	

Hint

This structure is responsible for the central regulation of the circadian rhythm.

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Correct Answer

A - Preoptic nucleus

Explanation Why

The [preoptic nucleus](#) is located in the [anterior hypothalamus](#) and is responsible for thermoregulation and the release of [GnRH](#). Dysregulation of [GnRH](#) in males would cause changes in sexual behavior and [erectile dysfunction](#) but would not cause sleep disturbances.

B - Ventromedial nucleus

Explanation Why

The [ventromedial nucleus](#) located in the [hypothalamus](#) is responsible for satiety and is stimulated by [leptin](#). Damage or lesions to this region can cause [hyperphagia](#) and [obesity](#) but would not cause sleep disturbances.

C - Suprachiasmatic nucleus

Explanation Why

The [suprachiasmatic nucleus](#) lies in the [hypothalamus](#) and plays an important role in the [circadian rhythm](#) pathway. It receives input (light) from the [retina](#). When there is decreased input, the [suprachiasmatic nucleus](#) releases [norepinephrine](#), which stimulates the release of sleep-inducing [melatonin](#) from the [pineal gland](#). Damage to this pathway (e.g., due to [metastasis](#) or radiation) can cause hypersomnolence or sleep-wake disturbances.

D - Supraoptic nucleus

Explanation Why

The [supraoptic nucleus](#) in the [hypothalamus](#) primarily synthesizes [ADH](#) (released by the [posterior pituitary](#)). Disruption or damage to the [supraoptic nucleus](#) would, therefore, decrease levels of [ADH](#) and lead to diuresis (i.e., [central diabetes insipidus](#)), but it would not cause [hypersomnia](#).

E - Caudate nucleus

Explanation Why

The [caudate nucleus](#) in the [basal ganglia](#) is primarily associated with motor function. Damage to this region is associated with psychomotor disease, e.g., [Huntington disease](#). Although the [caudate nucleus](#) contributes to the [sleep cycle](#), the absence of motor dysfunction in this patient suggests damage to another neurological structure.

F - Subthalamic nucleus

Explanation Why

The [subthalamic nucleus](#) is involved in both the direct and indirect motor pathways within the [basal ganglia](#). Lesions in this region are associated with motor dysregulations such as contralateral [hemiballismus](#), or [tremor](#) in [Parkinson disease](#). Damage to the [subthalamic nucleus](#) is not associated with sleep disturbances.

Question # 36

A male newborn is evaluated 24 hours after delivery for high-pitched crying, poor feeding, rhinorrhea, and low-grade fever. He was born at 40 weeks' gestation at 2514 g (5.54 lb) to a 28-year-old woman, gravida 3, para 2, by an uncomplicated cesarean section. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. The mother did not receive prenatal care. The infant's temperature is 38.0°C (100.4°F), pulse is 170/min, and blood pressure is 71/39 mm Hg. Examination shows hyperreflexia, tremors, and an excessive startle response. These symptoms are mostly likely due to maternal use of which of the following?

	Answer	Image
A	GABA _A receptor agonist	
B	Mu receptor agonist	
C	Nicotinic acetylcholine receptor agonist	
D	Monoamine reuptake antagonist	
E	Thyroperoxidase inhibitor	

Hint

The irritability, poor feeding, evidence of autonomic dysfunction (diaphoresis, hyperthermia, tremors), and hyperreflexia in this neonate is consistent with neonatal abstinence syndrome.

Correct Answer

A - GABA_A receptor agonist

Explanation But

[Benzodiazepines](#) are also [GABA_A receptor agonists](#) that have an unclear [teratogenicity](#) during [pregnancy](#).

Explanation Why

[GABA_A receptor agonists](#) (e.g., alcohol and [phenobarbital](#)) are [teratogens](#). [Neonates](#) exposed to alcohol during [pregnancy](#) may develop [fetal alcohol syndrome](#), which manifests with cardiac and facial [malformations](#) not seen in this patient. Similarly, exposure to [phenobarbital](#) during [pregnancy](#) increases the risk of developing a [cleft palate](#). Neither drugs cause the high-pitched cry or autonomic instability seen in this patient.

B - Mu receptor agonist

Explanation Why

This [infant](#) presents with symptoms of [neonatal abstinence syndrome](#), which suggests maternal use of [opioids](#) ([mu receptor agonist](#)) during [pregnancy](#). In [infants](#) with mild [opiate](#) withdrawal symptoms, supportive care (e.g., swaddling, [IV fluids](#), quiet room) is preferred. For [infants](#) with more severe symptoms, as seen in this [infant](#), administration of oral [morphine](#) is recommended to treat the withdrawal.

C - Nicotinic acetylcholine receptor agonist

Explanation Why

[Nicotine](#), a [nicotinic acetylcholine receptor agonist](#), is associated with [preterm birth](#) and [intrauterine growth restriction](#), which are not present in this patient. It also does not cause the high-pitched cry or

autonomic instability seen in this patient.

D - Monoamine reuptake antagonist

Explanation Why

[Cocaine](#) (a monoamine reuptake antagonist) exposure during [pregnancy](#) is associated with a high-pitched cry and irritability in [neonates](#) within 2–3 days of [birth](#), as seen in this patient. However, it is associated with hyperactivity and milder autonomic instability, and it does not cause the [fever](#) and poor feeding seen in this patient.

E - Thyroperoxidase inhibitor

Explanation But

[Propylthiouracil](#) is used to treat maternal [hyperthyroidism](#) during the [first trimester](#) because it is less likely to cross the [placenta](#), but the risk of maternal hepatotoxicity increases over time. [Methimazole](#) is used in place of [PTU](#) after 10–12 weeks' [gestation](#) when the fetus produces its own [thyroid hormone](#) and is no longer dependent on maternal [thyroxine](#).

Explanation Why

[Thyroperoxidase](#) inhibitors (e.g., [propylthiouracil](#) [[PTU](#)] and [methimazole](#)) treat [hyperthyroidism](#). [Methimazole](#) crosses the [placenta](#) more readily than [PTU](#) and causes [aplasia cutis congenita](#), while [PTU](#) has unclear [teratogenicity](#). Neither cause irritability, poor feeding, high-pitched cry, or autonomic instability ([diaphoresis](#), hyperthermia, [tremors](#)) in [neonates](#).

Question # 37

A 7-year-old boy is brought to the physician for recurrent 3–4 minutes episodes of facial grimacing and staring over the past month. He is nonresponsive during these episodes and does not remember them afterward. He recalls a muddy taste in his mouth before the onset of symptoms. One week ago, his brother witnessed an episode where he woke up, stared, and made hand gestures. After the incident, he felt lethargic and confused. Examination shows no abnormalities. Which of the following is the most likely diagnosis?

	Answer	Image
A	Absence seizures	
B	Atonic seizures	
C	Narcolepsy	
D	Myoclonic seizure	
E	Simple partial seizures	
F	Generalized tonic-clonic seizures	
G	Breath-holding spell	
H	Complex partial seizure	

Hint

The presence of a muddy taste preceding the onset of motor symptoms suggests that the pathology arises within the mesial temporal lobe.

Correct Answer

A - Absence seizures

Explanation But

[Absence seizure](#) is an important differential diagnosis in this patient. They can occur several hundred times a day and may be accompanied by automatisms such as lip smacking, [eye](#) fluttering, or head nodding.

Explanation Why

[Absence seizures](#) can present with periods of brief unresponsiveness, interrupted motion or activity, and [anterograde amnesia](#) while postural tone and staring are maintained. However, [absence seizures](#) usually last less than 20 seconds and are not accompanied by any [prodromal](#) symptoms, postictal [lethargy](#), or confusion.

B - Atonic seizures

Explanation Why

[Atonic seizures](#) are characterized by a sudden transient loss of muscle tone (typically lasting less than 2 seconds), resulting in head nodding or [drop attacks](#). However, muscle tone is retained in this patient during his episodes. Additionally, [atonic seizures](#) do not produce an [aura](#) (i.e., muddy [taste](#)) or involve postictal confusion and [lethargy](#), as seen in this patient.

C - Narcolepsy

Explanation Why

[Narcolepsy](#) presents with [excessive daytime sleepiness](#), [hallucinations](#) upon waking up and falling asleep, [sleep paralysis](#), and [cataplexy](#), which are not seen here. Although some patients with [narcolepsy](#) may involuntarily perform activities during sleep (e.g., talking, walking), episodes of

[gustatory hallucinations](#) (muddy [taste](#) in the mouth), facial grimacing, and staring followed by confusion are more consistent with a different condition.

D - Myoclonic seizure

Explanation Why

[Myoclonic seizures](#) sometimes cause alterations in consciousness and can be associated with [epilepsy](#) syndromes that present in childhood, such as [juvenile myoclonic epilepsy](#). However, [myoclonic seizures](#) involve brief jerking movements, which this patient lacks, and they do not cause an [aura](#) (e.g., muddy [taste](#)) or postictal confusion.

E - Simple partial seizures

Explanation Why

Simple [partial seizures](#) (focal aware [seizures](#)) can present with an [aura](#) (e.g., muddy [taste](#)) and abnormal motor movements, as seen in this patient. However, he experiences impaired awareness during each episode, which by definition excludes simple [partial seizures](#).

F - Generalized tonic-clonic seizures

Explanation Why

[Generalized tonic-clonic seizures](#) result in loss of consciousness (ictal phase) followed by postictal confusion and [lethargy](#), as seen here. However, patients characteristically have generalized stiffness (tonic phase) followed by rhythmic jerking movements in all limbs (clonic phase). Moreover, [auras](#) (i.e., muddy [taste](#)) and automatisms (i.e., facial grimacing, hand gesturing) are not features of [generalized tonic-clonic seizures](#), unless preceded by a [focal seizure](#) that later generalized into a [tonic-clonic seizure](#).

G - Breath-holding spell

Explanation Why

[Breath-holding spells](#) can cause unresponsiveness due to [syncope](#). However, these episodes would result in a loss of postural tone such that the patient would not remain seated, and most children would be [cyanotic](#) during such spells. Breath-holding spells, which are typically seen in crying preschool children, are an unlikely diagnosis in this 7-year-old child who was not distressed before the onset of the episode.

H - Complex partial seizure

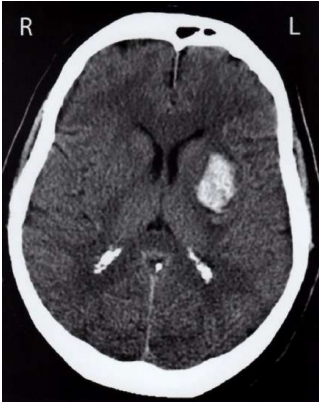
Explanation Why

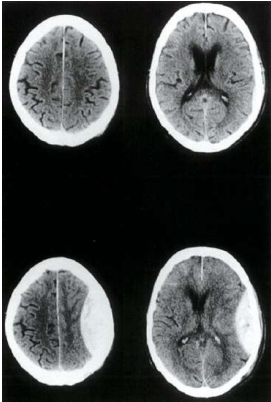
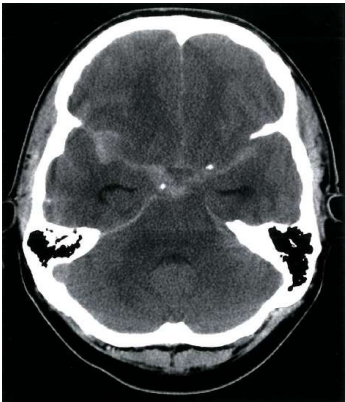
This patient's presentation is most consistent with recurring [complex partial seizures](#) ([focal seizures with impaired awareness](#)), which result from abnormal electrical activity arising from the [temporal lobe](#). The gustatory [aura](#) (muddy [taste](#)) marks the onset of the [seizure](#). The ictal phase consists of his unresponsive staring and automatisms (e.g., facial grimacing and hand gestures). The postictal phase is characterized by [lethargy](#), temporary confusion, and [amnesia](#).

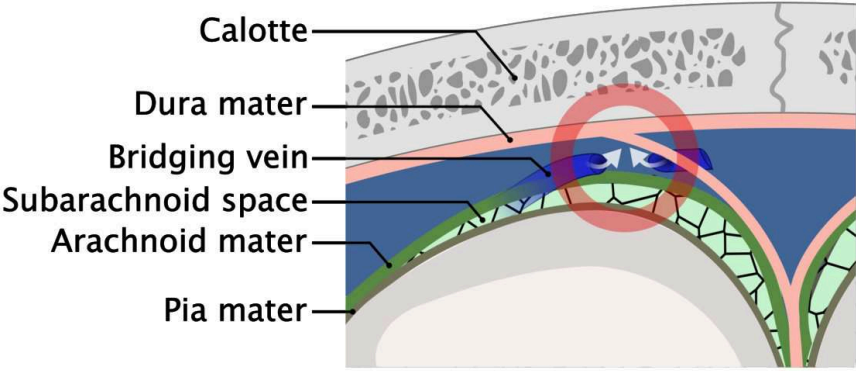
Question # 38

A 68-year-old man is brought to the emergency department by his wife because of a 2-week history of progressive disorientation and a 1-day history of left-sided weakness and difficulty speaking. The wife reports that the patient had a minor fall 4 months ago, during which he may have hit his head. He has hypertension and hyperlipidemia. He drinks 3–4 bottles of beer daily. He is only oriented to person. Neurological examination shows moderate spastic weakness, decreased sensation, and increased deep tendon reflexes in the left upper and lower extremities. A CT scan of the head is shown. Which of the following is the most likely cause of this patient's condition?



	Answer	Image
A	Damage to lenticulostriate arteries	

	Answer	Image
B	Injury to middle meningeal artery	
C	Rupture of saccular aneurysm	
D	Embolus to middle cerebral artery	

	Answer	Image
E	Tearing of bridging veins	 Calotte Dura mater Bridging vein Subarachnoid space Arachnoid mater Pia mater
F	Bleeding from intraventricular vascular malformation	

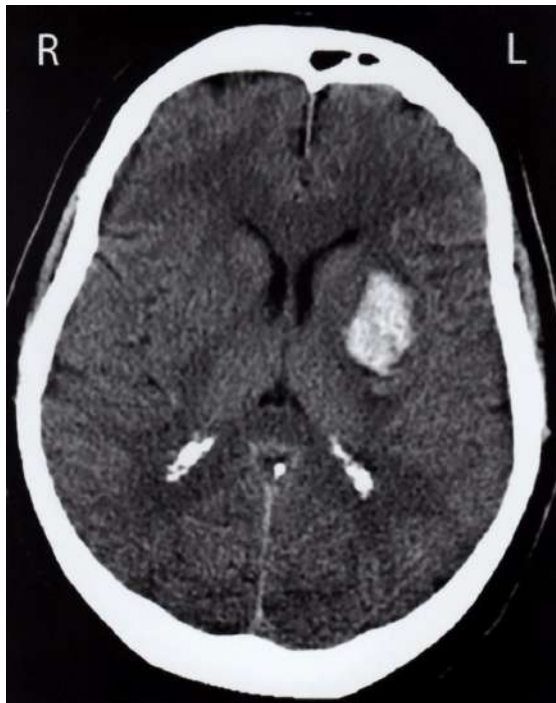
Hint

The CT scan shows a crescent-shaped, concave hemorrhage that crosses suture lines but not the midline. This is characteristic of a subdural hematoma.

Correct Answer

A - Damage to lenticulostriate arteries

Image

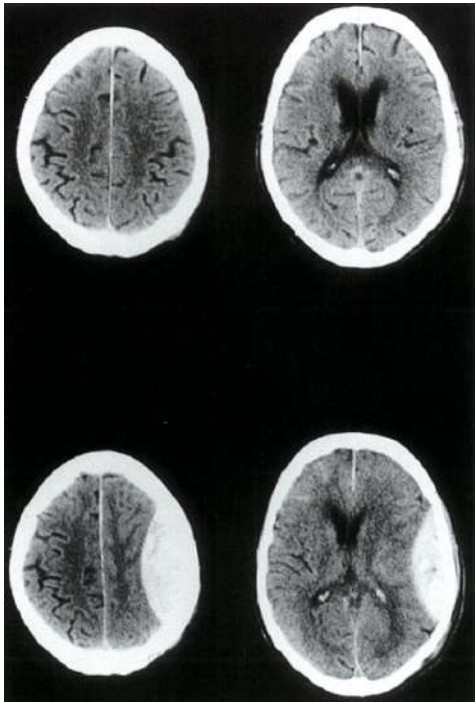


Explanation Why

Damage to the [lenticulostriate arteries](#) is most often a consequence of [hypertension](#) ([Charcot-Bouchard](#) microaneurysm), [cerebral amyloid angiopathy](#), or [vasculitis](#). Patients typically present with severe [headache](#), focal neurologic deficits, and loss of consciousness. The onset is acute and progresses rapidly. CT imaging would show a solitary [hyperdense](#) lesion, surrounded by [hypodense edema](#) within the cerebral parenchyma.

B - Injury to middle meningeal artery

Image

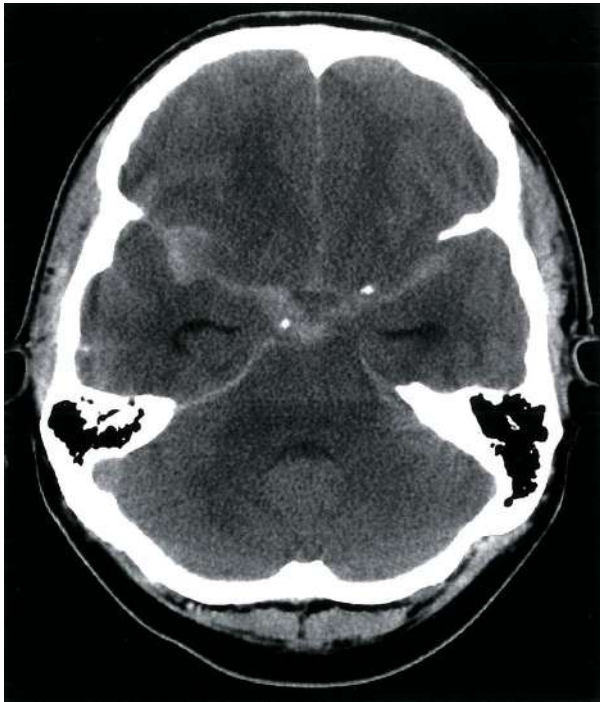


Explanation Why

Injury to the [middle meningeal artery](#) can lead to an [epidural hemorrhage](#). The typical presentation of this injury is [head trauma](#) followed by normal sensorium ([lucid interval](#)) before onset of [symptoms of increased intracranial pressure](#). [CT scan](#) would show a characteristic lentiform hemorrhagic collection (hemorrhage limited by suture lines).

C - Rupture of saccular aneurysm

Image

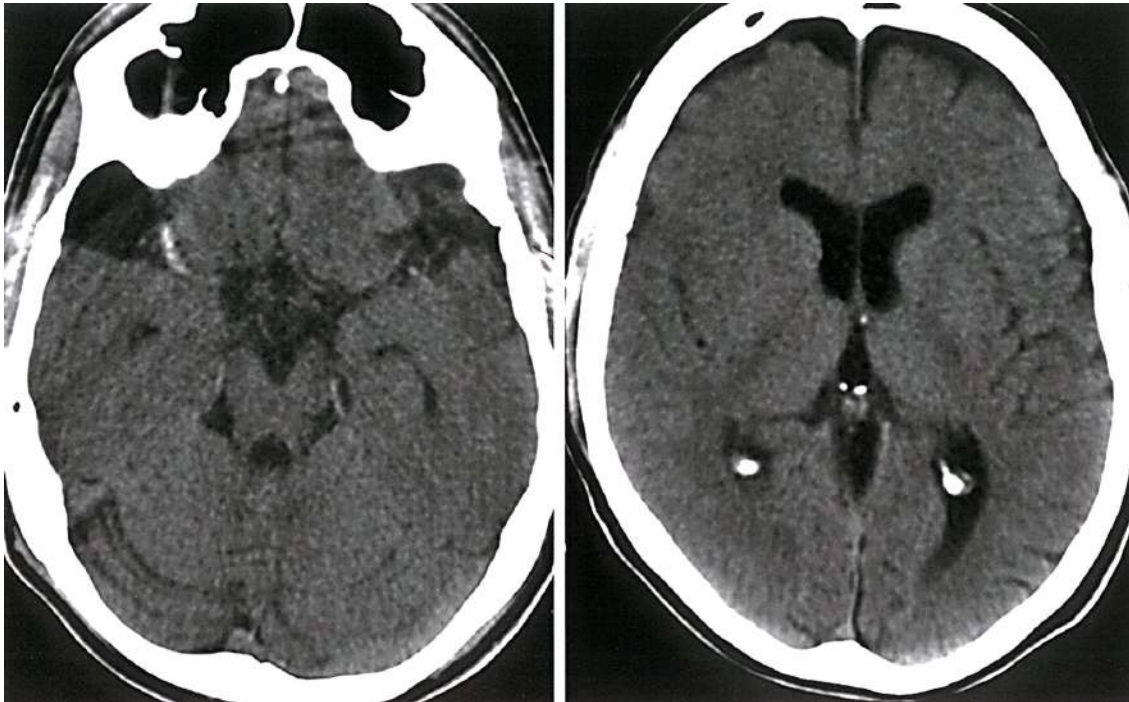


Explanation Why

[Saccular aneurysm](#) rupture leads to [subarachnoid hemorrhage](#), which characteristically causes severe, abrupt-onset [headaches](#) (thunderclap [headaches](#)) that may be associated with vomiting, neck [pain](#), and decreased [levels of consciousness](#). While this patient has decreased [levels of consciousness](#), he does not have any of the other characteristic symptoms, nor does his [CT scan](#) show blood in the [subarachnoid space](#), as would be expected.

D - Embolus to middle cerebral artery

Image

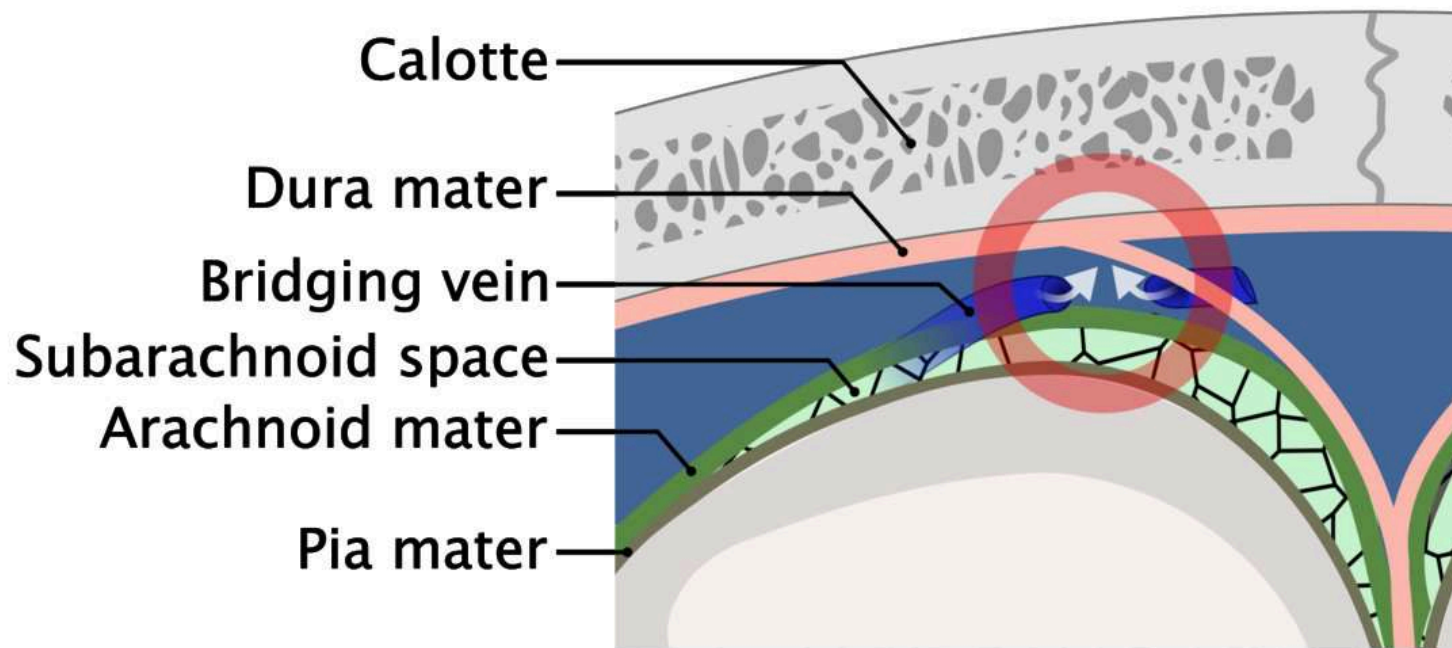


Explanation Why

Embolus to the [middle cerebral artery](#) would cause an [ischemic stroke](#). Most commonly, embolism results in acute-onset neurological defects as opposed to the subacute progression of this patient's symptoms. [CT scans](#) can present with [hyperdense MCA sign](#) but are usually unremarkable for up to 24 hours after an [ischemic stroke](#). [MRI](#) is the preferred modality for imaging acute [ischemic stroke](#).

E - Tearing of bridging veins

Image



Explanation But

The main [risk factor](#) for the development of this condition is diffuse cerebral atrophy associated with [aging](#) and chronic alcohol use.

Explanation Why

This [CT scan](#) shows a classic [subdural hematoma](#). The history of minor [head trauma](#) followed by the insidious onset of unilateral neurological symptoms ([spastic paresis](#), [hyperreflexia](#), decreased sensation) is consistent with a [chronic subdural hematoma](#). This type of bleeding results from tears in the [bridging veins](#) that cross the [subdural space](#).

F - Bleeding from intraventricular vascular malformation

Explanation Why

Intraventricular vascular [malformations](#) are a common cause of [intraventricular hemorrhage](#). Like other [intracranial bleeding](#) events, the characteristic presentation includes sudden onset of [headache](#), vomiting, and altered [level of consciousness](#). [Seizures](#) are common but focal neurological findings are not. CT imaging would show blood within the [ventricular system](#).

Question # 39

A 61-year-old woman comes to the physician because of a 1-week history of dizziness, nausea, vomiting, and repeated falls. Neurologic examination shows past-pointing on a finger-nose test. She has a broad-based gait. Ophthalmologic exam shows rhythmic leftward movement of the globes. A serum antibody assay is positive for anti-Yo antibodies directed at proteins expressed by Purkinje cells. This patient's condition is most likely associated with which of the following tumors?

	Answer	Image
A	Ovarian teratoma	
B	Neuroblastoma	
C	Breast cancer	
D	Thymoma	
E	Small cell lung cancer	
F	Hodgkin lymphoma	

Hint

The anti-Yo antibody, or Purkinje cell cytoplasmic antibody type 1, is an autoantigen that causes paraneoplastic cerebellar degeneration (PCD). These antibodies are associated with a tumor that may be caused by amplification or overexpression of the gene that encodes human epidermal growth factor receptor 2.

Correct Answer

A - Ovarian teratoma

Explanation Why

Ovarian [teratomas](#) can present with anti-[NMDA receptor encephalitis](#), which is associated with [antibodies](#) to the GluN1 (NR1) subunit of the NMDA receptor, not the [anti-Yo antibodies](#) detected here. In addition, this patient is 61 years and ovarian [teratomas](#) primarily occur in women between 10 and 30 years of age. [Ovarian carcinomas](#), on the other hand, are a cause of [anti-Yo antibody](#)-associated PCD.

B - Neuroblastoma

Explanation Why

[Neuroblastomas](#) are associated with [opsoclonus-myoclonus](#) syndrome. While this disorder is thought to be immune-mediated, there is currently no known association with an [antibody](#). This patient has [ataxia](#) and jerking [eye](#) movements but she does not have myoclonus. In addition, this patient is 61 years and [neuroblastomas](#) occur almost exclusively in children.

C - Breast cancer

Explanation Why

[Breast cancer](#) is the most common cause of [anti-Yo antibody](#)-associated PCD in women. PCD is a rare syndrome that usually occurs as the first manifestation of the [malignancy](#) and presents with symptoms of [cerebellar dysfunction](#) (e.g., [dizziness](#), [ataxia](#), nystagmus, [dysmetria](#)). Other causes of [anti-Yo antibody](#)-associated PCD are [malignant tumors](#) of the [ovary](#), [endometrium](#), and [fallopian tubes](#).

D - Thymoma

Explanation Why

[Thymomas](#) are associated with [antibodies](#) against the postsynaptic acetylcholine receptors at the [neuromuscular junction \(AChR-Ab\)](#), not [anti-Yo antibodies](#). AChR-Abs are involved in the pathogenesis of [myasthenia gravis](#), not PCD.

E - Small cell lung cancer

Explanation Why

[Small cell lung cancers](#) can cause PCD, but they are associated with anti-Hu [antibodies](#), not [anti-Yo antibodies](#).

F - Hodgkin lymphoma

Explanation Why

[Hodgkin lymphomas](#) can cause PCD, but they are associated with anti-Tr [antibodies](#), not [anti-Yo antibodies](#).

Question # 40

A 76-year-old woman with hypertension and coronary artery disease is brought to the emergency department after the sudden onset of right-sided weakness. Her pulse is 83/min and blood pressure is 156/90 mm Hg. Neurological examination shows right-sided facial drooping and complete paralysis of the right upper and lower extremities. Tongue position is normal and she is able to swallow liquids without difficulty. Knee and ankle deep tendon reflexes are exaggerated on the right. Sensation to vibration, position, and light touch is normal bilaterally. She is oriented to person, place, and time, and is able to speak normally. Occlusion of which of the following vessels is the most likely cause of this patient's current symptoms?

	Answer	Image
A	Ipsilateral anterior cerebral artery	
B	Anterior spinal artery	

	Answer	Image
C	Contralateral middle cerebral artery	
D	Ipsilateral posterior inferior cerebellar artery	
E	Contralateral lenticulostriate artery	

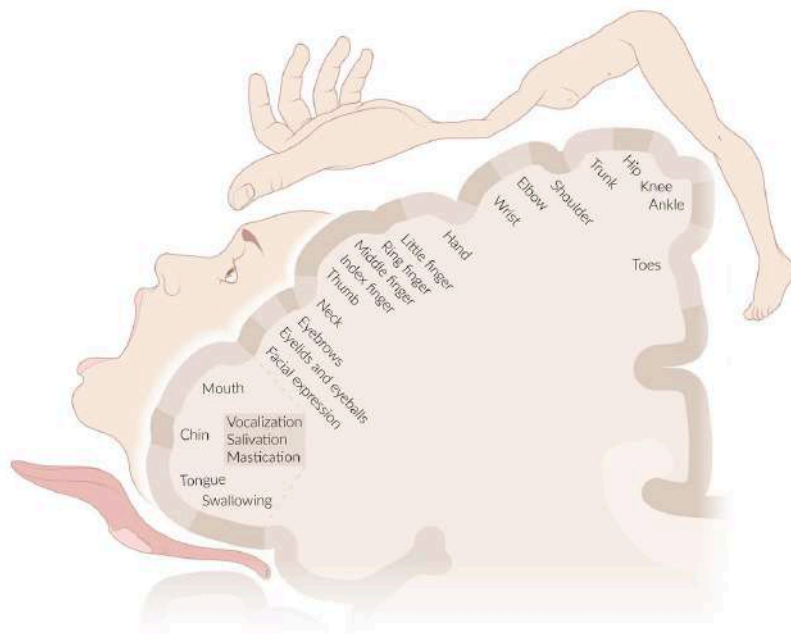
Hint

This patient has features of a pure motor stroke without any sensory deficits or cortical signs (e.g., aphasia, agnosia, apraxia). The lesion is most likely located at the posterior limb of the internal capsule.

Correct Answer

A - Ipsilateral anterior cerebral artery

Image

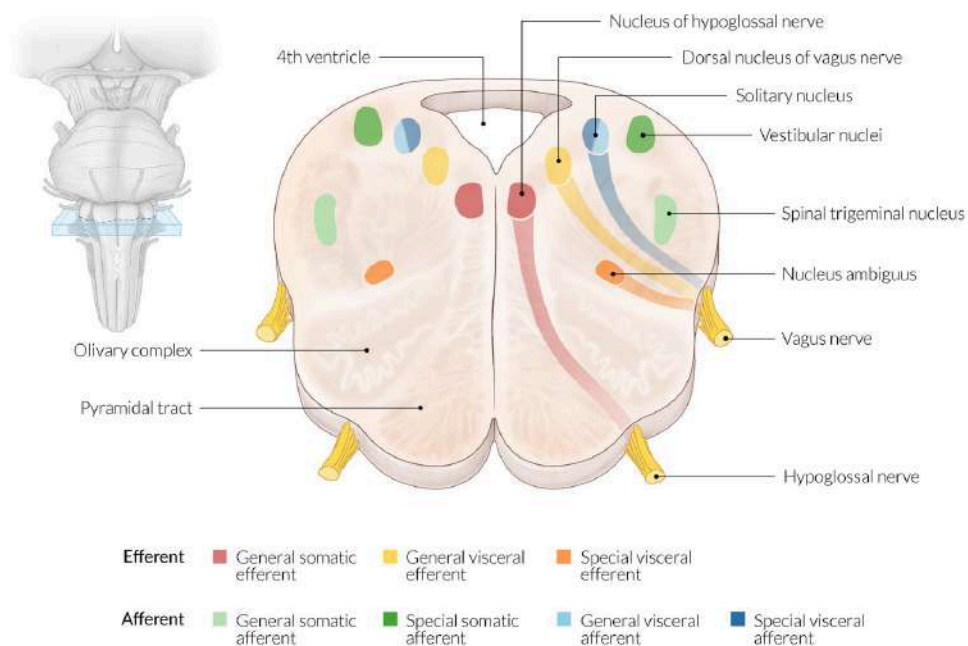


Explanation Why

Occlusion of the [anterior cerebral artery](#) would cause motor deficits. However, the motor deficit would predominantly affect the lower extremity and sensory deficits in the lower extremity would also be expected. The upper extremity is usually spared or only mildly affected and the face would be spared. Moreover, an ipsilateral (right) [anterior cerebral artery infarct](#) would produce deficits on the contralateral (left) side.

B - Anterior spinal artery

Image



Explanation But

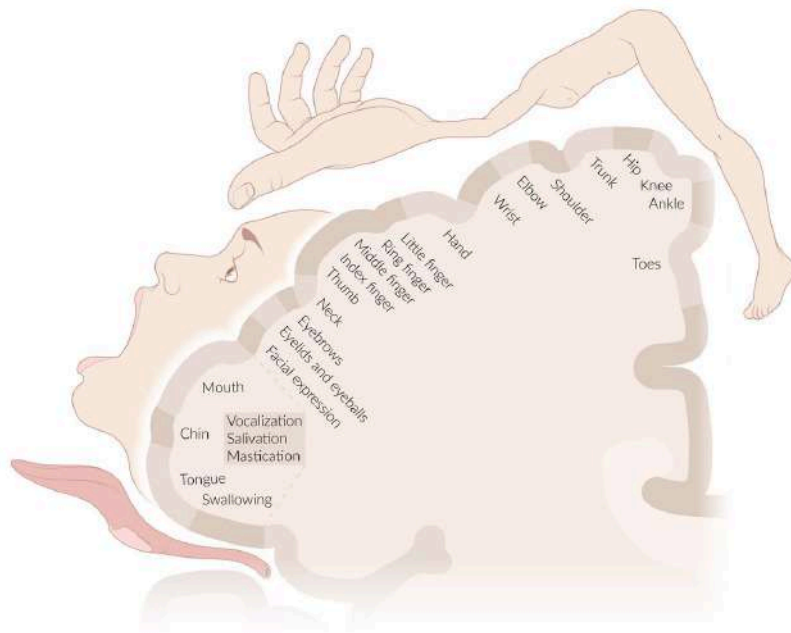
Occlusion of the [anterior spinal artery](#) at the level of the [spinal cord](#) would cause [anterior spinal artery syndrome](#) characterized by motor deficits and loss of temperature and [pain](#) sensation below the level of the lesion.

Explanation Why

The [anterior spinal artery](#) and [vertebral artery](#) supply the [medial](#) regions of the lower medulla. Occlusion of the [anterior spinal artery](#) at the level of the [brainstem](#) can therefore damage the [corticospinal tract](#) and cause motor deficits. However, facial palsy would not be expected since this [facial nerve](#) nucleus arises in the [lateral](#) region of the upper medulla. Moreover, patients would also have impaired [pain](#) and [proprioception](#) (due to damage to the [medial lemniscus](#)) and features of [hypoglossal nerve palsy](#) (e.g., inability to protrude the [tongue](#), [tongue](#) deviation).

C - Contralateral middle cerebral artery

Image

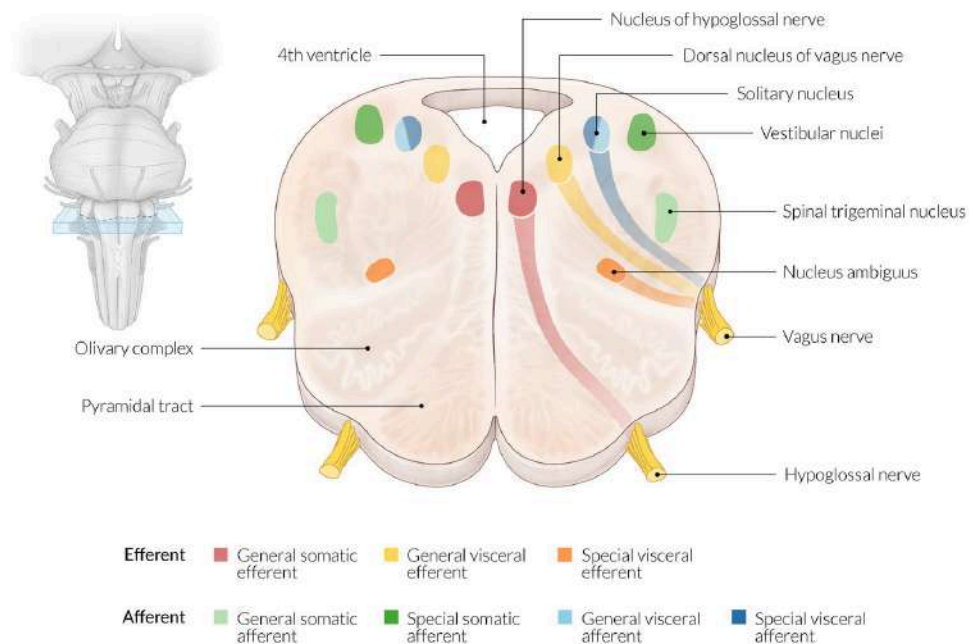


Explanation Why

Occlusion of the [middle cerebral artery](#) causes contralateral motor deficits, which are seen in this patient. However, it also causes sensory changes, gaze deviation, and [aphasia](#) (dominant hemisphere) or [hemineglect](#) (non-dominant hemisphere).

D - Ipsilateral posterior inferior cerebellar artery

Image

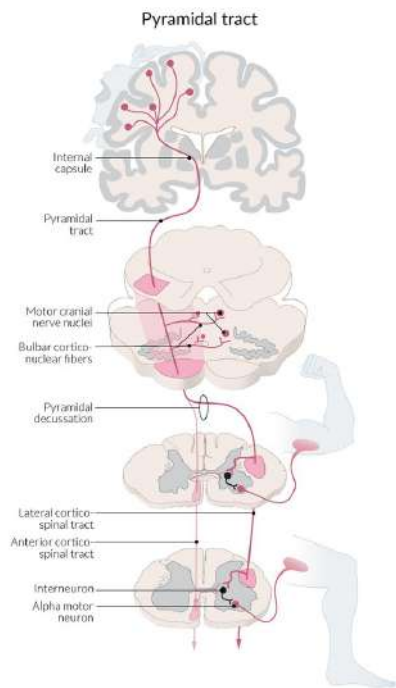


Explanation Why

Occlusion of the [posterior inferior cerebellar artery](#) causes [Wallenberg syndrome](#) ([lateral medullary syndrome](#)), which is characterized by ipsilateral [Horner syndrome](#), ipsilateral [cerebellar signs](#) (e.g., [hemiataxia](#)), impaired [pain](#) and temperature sensation in the contralateral body and ipsilateral face, and features of ipsilateral [cranial nerve IX](#), X, and XI palsy (e.g., [dysphagia](#), [dysphonia](#)). This patient with pure motor deficits in one half of the body would not have [Wallenberg syndrome](#).

E - Contralateral lenticulostriate artery

Image



Explanation Why

A [pure motor stroke](#) is caused by [infarction](#) in the [posterior](#) limb of the [internal capsule](#), which contains the corticospinal and corticobulbar fibers that innervate the motor nuclei on the contralateral side. Therefore, a lesion at this site can cause contralateral [hemiplegia](#) as well as weakness in the lower half of the face because the region of the [facial nerve](#) nucleus that supplies the lower half of the face only receives unilateral corticobulbar innervation. Other [cranial nerve](#) nuclei as well as the region of the [facial nerve](#) nucleus that innervates the forehead receive bilateral corticobulbar innervation and are therefore spared. The most common cause of [stroke](#) in this region is a [lacunar stroke](#) of the contralateral [lenticulostriate artery](#) (a branch of the [MCA](#)).

Question # 1

An 84-year-old woman is brought by her caretaker to the physician because of a 2-day history of fever, severe headache, neck pain, and aversion to bright light. She appears uncomfortable. Her temperature is 38.5°C (101.3°F), pulse is 110/min, and blood pressure is 145/75 mm Hg. Physical examination shows involuntary flexion of the bilateral hips and knees with passive flexion of the neck. Cerebrospinal fluid analysis shows a leukocyte count of 1200/mm³ (76% segmented neutrophils, 24% lymphocytes), a protein concentration of 113 mg/dL, and a glucose concentration of 21 mg/dL. A CT scan of the brain shows leptomeningeal enhancement. Which of the following is the most appropriate initial pharmacotherapy?

	Answer	Image
A	Vancomycin, gentamicin, and cephalexin	
B	Vancomycin, metronidazole, and cefotaxime	
C	Vancomycin and cefepime	
D	Ampicillin and gentamicin	
E	Ceftriaxone, vancomycin, and ampicillin	

Hint

This patient has classic findings of bacterial meningitis: fever, confusion, Brudzinski sign, and CSF analysis showing ↑ cell count, ↑ protein, and ↓ glucose. The most common causes of community-acquired bacterial meningitis in patients older than 60 years are the gram-positive bacteria *S. pneumoniae* and *L. monocytogenes*, and the gram-negative bacteria *H. influenzae* and *E. coli*.

Correct Answer

A - Vancomycin, gentamicin, and cephalexin

Explanation Why

[1st generation cephalosporins](#) (e.g., [cephalexin](#)) are ineffective against [Listeria](#), [Haemophilus](#), and [Neisseria](#). [Vancomycin](#) is ineffective against gram-negative organisms and is not very effective against [CNS Listeria](#) infections. [Aminoglycosides](#) (e.g., [gentamicin](#)) are effective against [H. influenzae](#) but are ineffective against [N. meningitidis](#) and [L. monocytogenes](#). Therefore, a combination of [vancomycin](#), [gentamicin](#), and [cephalexin](#) would be ineffective against [L. monocytogenes](#) and [N. meningitidis](#). Since [L. monocytogenes](#) is an important cause of community-acquired bacterial [meningitis](#) in patients older than 60 years, a different regimen would be indicated for this patient.

B - Vancomycin, metronidazole, and cefotaxime

Explanation Why

[Metronidazole](#) is effective against [anaerobic bacteria](#). [Metronidazole](#) is used in combination with other [antibiotics](#) (e.g., [cefotaxime](#), [vancomycin](#)) for [empirical therapy](#) of a [brain abscess](#), which is commonly associated with [anaerobic](#) organisms such as [Peptostreptococcus](#) and [Bacteroides](#). [Brain abscesses](#) can cause [headache](#) and [fever](#), as seen here but this patient does not have a space-occupying lesion on imaging to suggest a [brain abscess](#). [Metronidazole](#) would not be indicated for this patient because [anaerobic](#) organisms are not typically implicated in community-acquired bacterial [meningitis](#).

C - Vancomycin and cefepime

Explanation Why

A combination of [vancomycin](#) and an antipseudomonal [antibiotic](#) (e.g., [cefepime](#), [ceftazidime](#), [meropenem](#)) would be used in patients with hospital-acquired bacterial [meningitis](#) (e.g.,

neurosurgical patients) because [Pseudomonas aeruginosa](#) is an important cause of [meningitis](#) in this group. This patient has community-acquired bacterial [meningitis](#). A regimen of [vancomycin](#) and [cefepime](#) would not cover [CNS](#) infection by [Listeria monocytogenes](#), which is an important cause of community-acquired bacterial [meningitis](#) in elderly patients.

D - Ampicillin and gentamicin

Explanation Why

A combination of [ampicillin](#) with an [aminoglycoside](#) (e.g., [gentamicin](#)) or a 3rd generation [cephalosporin](#) (e.g., [cefotaxime](#)) would cover the most common causes of neonatal bacterial [meningitis](#) such as [Streptococcus agalactiae](#) (group B streptococci), [Listeria monocytogenes](#), [E. coli](#), and [Haemophilus influenzae](#). In adults, [Streptococcus pneumoniae](#) is an important cause of [meningitis](#). Since [gentamicin](#) does not cover [S. pneumoniae](#) and the [incidence](#) of penicillin-resistant [pneumococcal meningitis](#) has increased in recent years, a different [antibiotic](#) regimen would be indicated for this patient.

E - Ceftriaxone, vancomycin, and ampicillin

Explanation But

[Listeria](#) is also a common cause of [meningitis](#) in [immunocompromised](#) patients and [neonates](#). Therefore, an [immunocompromised](#) patient (regardless of age) or a [neonate](#) with community-acquired bacterial [meningitis](#) should also receive [ampicillin](#) as a part of the [empirical antibiotic](#) regimen. In immunocompetent patients between the age of 2 months and 50 years, [Listeria](#) is not a common cause of community-acquired bacterial [meningitis](#). Therefore, [ampicillin](#) is not necessary for this group of patients; a combination of [vancomycin](#) and a 3rd generation [cephalosporin](#) would suffice.

Classic triad of [meningitis](#): [fever](#), [headache](#), and neck stiffness; Photophobia; [Brudzinski sign](#); [Streptococcus pneumoniae](#) (most common); [Gram-negative bacilli](#); [Listeria monocytogenes](#); Age > 50 years; [Cerebrospinal fluid analysis in meningitis](#); significant [pleocytosis](#) ([leukocyte count](#) > 1000/mm³); ↑ [Granulocytes](#);

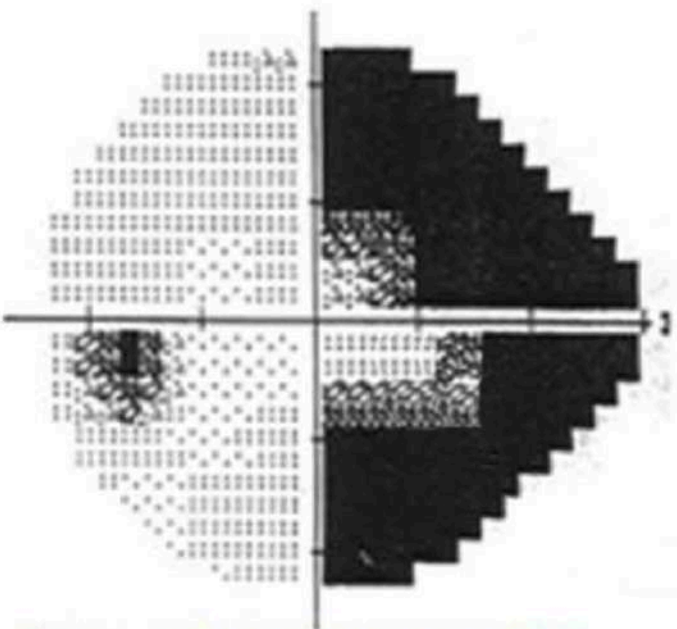
Explanation Why

[Third generation cephalosporins](#) (e.g., [cefotaxime](#), [ceftriaxone](#)) are broad-spectrum [antibiotics](#) that are effective against most gram-negative and [gram-positive bacteria](#) with the exception of

Enterococcus and *Listeria*. Since *L. monocytogenes* is an important cause of bacterial [meningitis](#) in patients > 60 years, [empiric antibiotic therapy](#) in this group should include [ampicillin](#), an anti-listerial [antibiotic](#). [Ampicillin](#) would also provide coverage against gram-positive and [gram-negative bacteria](#), but its spectrum of activity is not as broad as [3rd generation cephalosporins](#). [Vancomycin](#), which acts only against [gram-positive bacteria](#), should be included in the [antibiotic](#) regimen because the [incidence](#) of penicillin- and [cephalosporin](#)-resistant [pneumococcal](#) infection has increased in recent years. [Vancomycin](#), while effective in [Listeria bacteremia](#), is not very effective against [CNS Listeria](#) infections. Therefore, [ampicillin](#) should be used despite the addition of [vancomycin](#) to the regimen.

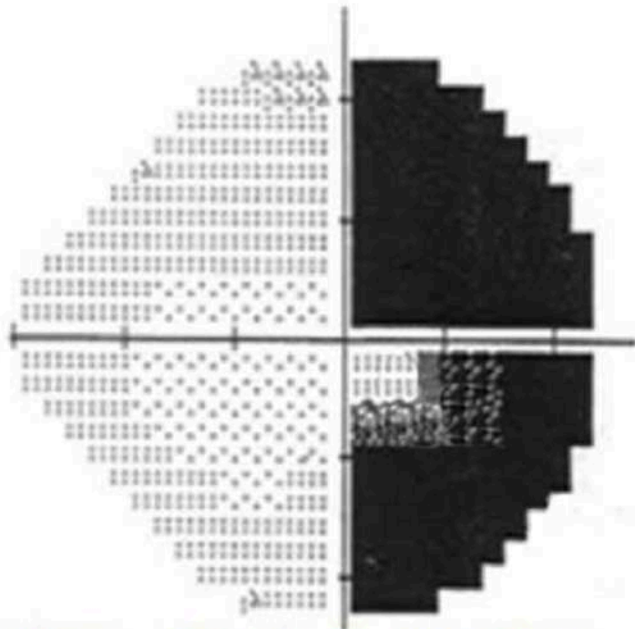
Question # 2

A 62-year-old woman comes to the physician for decreased vision and worsening headaches since this morning. She has hypertension and hypercholesterolemia. Pulse is 119/min and irregular. Current medications include ramipril and atorvastatin. Ocular and fundusoscopic examination shows no abnormalities. The findings of visual field testing are shown. Which of the following is the most likely cause of this patient's symptoms?



MD : -16.57 dB ;P<0.5%

Left eye



MD : -12.12 dB ;P<0.5%

Right eye

	Answer	Image
A	Degeneration of the macula	
B	Impaired perfusion of the retina	
C	Occlusion of the posterior cerebral artery	

	Answer	Image
D	Occlusion of the anterior inferior cerebellar artery	
E	Embolism to middle cerebral artery	
F	Occlusion of anterior cerebral artery	

Hint

Visual field testing shows the inability to see the right visual field in either eye (right homonymous hemianopia) with macular sparing, which most commonly results from decreased blood flow to the left occipital lobe.

Correct Answer

A - Degeneration of the macula

Explanation Why

Degeneration of the [macula](#) can be observed in [age-related macular degeneration \(AMD\)](#), which is subdivided into dry and wet [AMD](#) types and causes a gradual loss of central vision and [metamorphopsia](#) in the affected eyes, unlike what is seen in this patient.

B - Impaired perfusion of the retina

Explanation Why

Impaired perfusion of the [retina](#) has been observed in [central retinal artery occlusion](#), which is caused by [cardiac emboli](#) in young patients and carotid [atherosclerosis](#) in old patients. It presents with an acute painless visual loss in the affected [eye](#); it is usually unilateral and does not spare the [macula](#), unlike in this patient.

C - Occlusion of the posterior cerebral artery

Explanation Why

Occlusion of the [posterior cerebral artery](#), usually due to emboli from the [vertebral](#) vessels, aorta, or [heart](#), results in contralateral [homonymous hemianopia](#) with [macular sparing](#). The [macula](#) is spared because the [macular](#) tracts have additional blood supply from the [middle cerebral arteries](#).

D - Occlusion of the anterior inferior cerebellar artery

Explanation Why

Occlusion of the [anterior inferior cerebellar artery](#) causes [lateral pontine syndrome](#). It manifests with vomiting, [vertigo](#), nystagmus, ipsilateral [cerebellar ataxia](#), [Horner syndrome](#), facial muscle paralysis ([lower motor neuron lesion](#) type), and [sensorineural hearing loss](#) as well as contralateral hemisensory loss, none of which is seen in this patient.

E - Embolism to middle cerebral artery

Explanation But

The contralateral [homonymous hemianopia](#) in [MCA](#) occlusion rarely exhibits [macular sparing](#). This is because the [MCA](#) supplies an extensive area of the brain and, thus, occlusion of the [MCA](#) affects not only the occipital visual cortex but also the [visual pathways](#).

Explanation Why

The [middle cerebral artery](#) ([MCA](#)) is the most commonly occluded [artery](#) in [ischemic strokes](#). Embolic occlusion of the [MCA](#) can occasionally lead to the development of contralateral [homonymous hemianopia](#). However, owing to the extensive area of the brain that the [MCA](#) supplies, the other signs of [stroke](#), such as contralateral limb weakness and sensory loss, would also be present. Isolated [visual field](#) defects are highly unlikely to occur in [MCA](#) embolism.

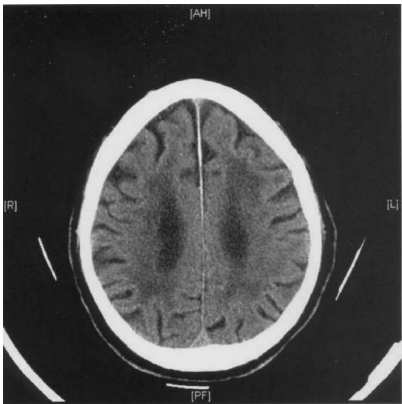
F - Occlusion of anterior cerebral artery

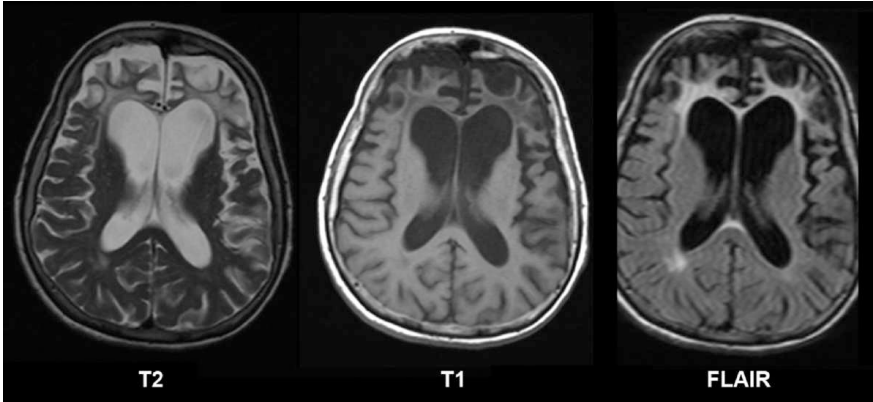
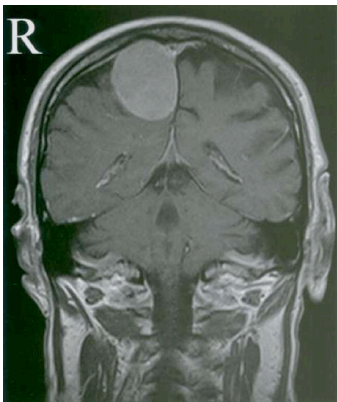
Explanation Why

Occlusion of the [anterior cerebral artery](#) does not affect the visual cortex but causes contralateral limb weakness and sensory loss affecting the lower limb more prominently than the upper limb. [Primitive reflexes](#), like [grasp reflexes](#) and [rooting reflexes](#), are also likely to re-emerge. This patient has none of these symptoms.

Question # 3

A 39-year-old man is brought to the physician by his wife because of personality changes over the past year. He has become increasingly irritable, loud, aggressive, and impulsive. His wife also reports jerky movements of his limbs and trunk for the past few months. His father had dementia in his mid-40s, but the details of his condition are unclear. The patient appears restless. Examination shows irregular movements of the extremities and twitching of the face and tongue. Mental status examination shows impaired memory. This patient's condition is most likely associated with which of the following changes on MRI?

	Answer	Image
A	Reduced hippocampal volume	
B	Multiple cortical and subcortical infarctions	

	Answer	Image
C	Degeneration of the frontal and temporal lobes	 T2 T1 FLAIR
D	Periventricular plaques	 AS PI PI
E	Extra-axial tumor with dural attachments	 R
F	Atrophy of the striatum	

Hint

This patient most likely has Huntington disease (HD) based on the presence of chorea (e.g., involuntary limb and trunk movements), behavioral changes (aggression, impulsivity), and cognitive impairments (impaired memory). His father's dementia may have also been associated with HD, which would be consistent with the autosomal dominant inheritance pattern of the condition.

Correct Answer

A - Reduced hippocampal volume

Image

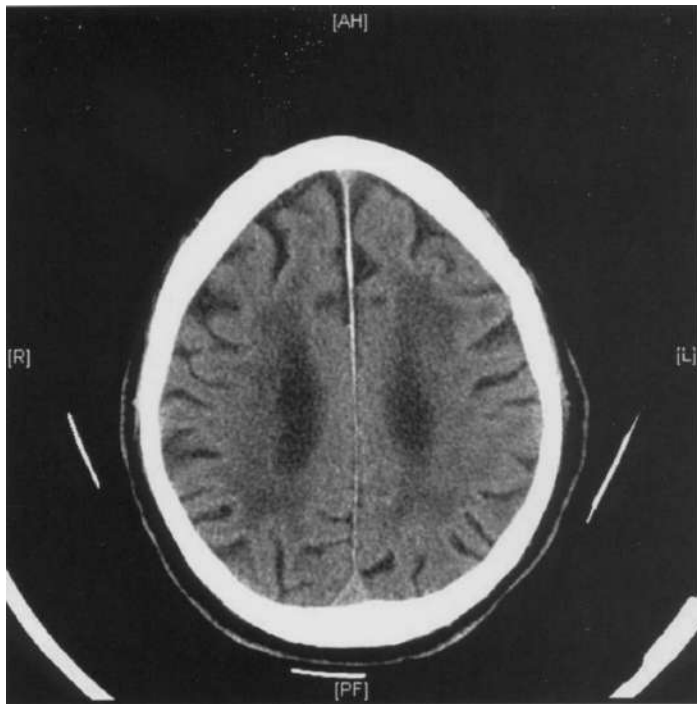


Explanation Why

Reduced volume of the [hippocampus](#) can be seen on brain [MRI](#) in patients with [Alzheimer dementia](#) (AD). Even though familial forms of AD (e.g., with [presenilin-1](#) mutation) can manifest in middle-aged patients such as this man, early symptoms would include impaired short-term [memory](#) and depressed mood, not impulsive behavior. Furthermore, AD would not account for the presence of [chorea](#) in this patient.

B - Multiple cortical and subcortical infarctions

Image

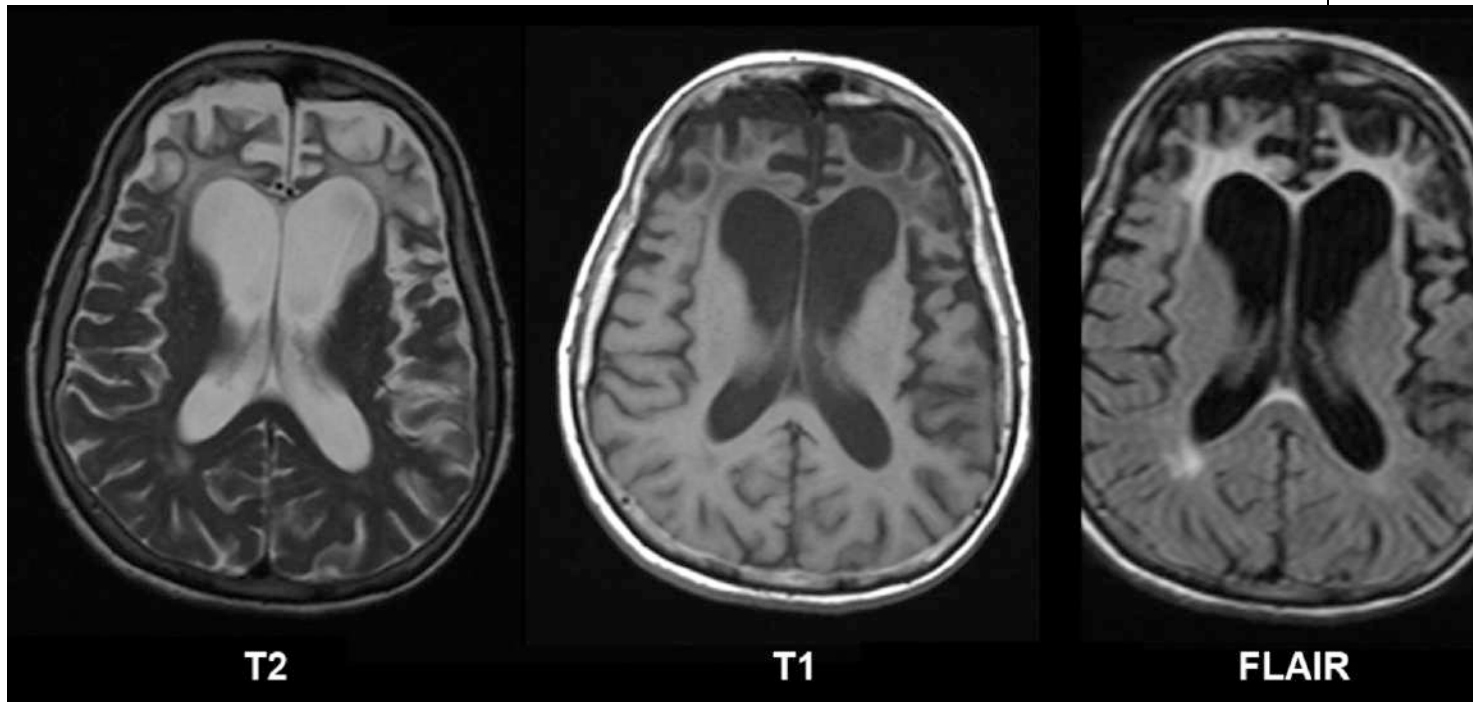


Explanation Why

Multiple cortical and subcortical infarctions on brain imaging are characteristic of [vascular dementia](#), which would present with a stepwise deterioration of mental capacity, similar to what this patient is experiencing in that it would be progressive. It could also explain his abnormal behavior; however, it would not present with [chorea](#), and he does not have any significant [atherosclerotic risk factors](#) to predispose him to cerebral [ischemia](#).

C - Degeneration of the frontal and temporal lobes

Image

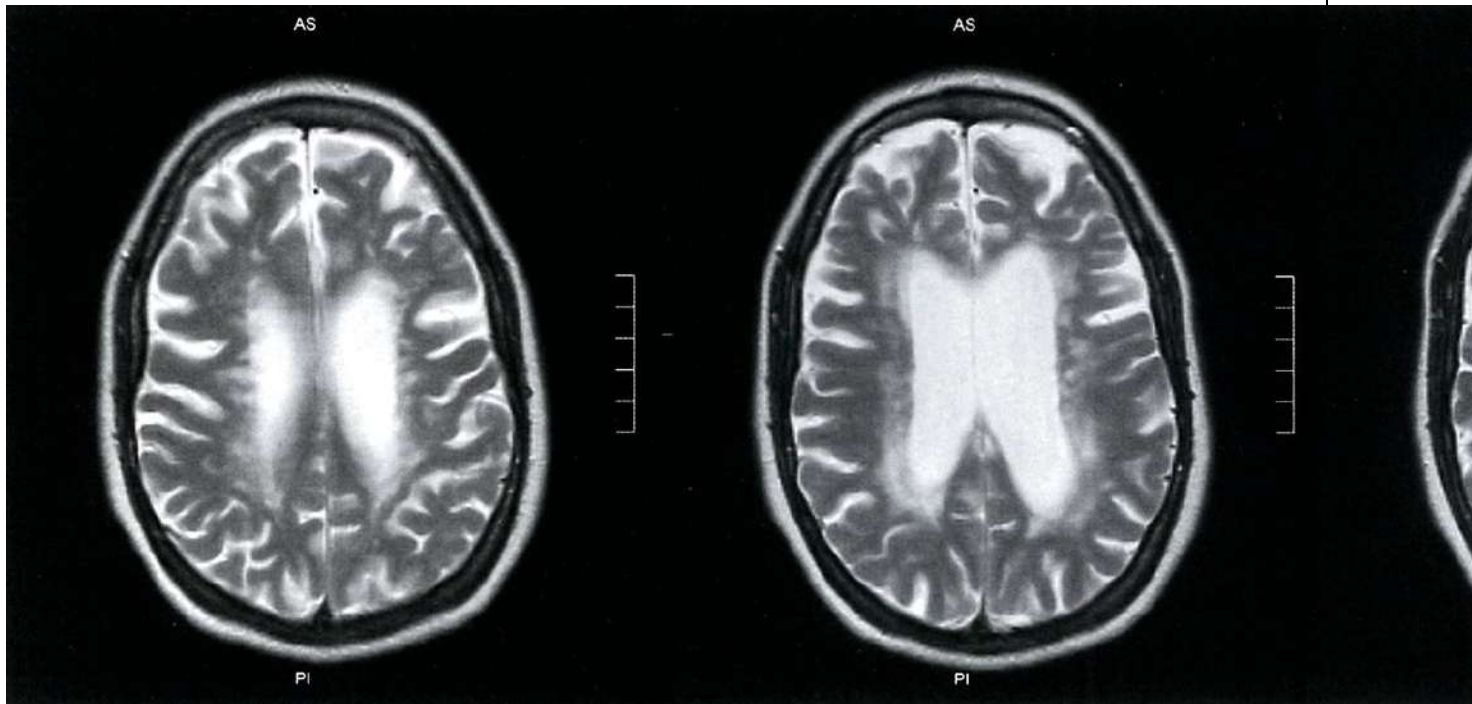


Explanation Why

Degeneration of the frontal and [temporal lobes](#) occurs in [frontotemporal dementia \(FTD\)](#). This patient's [memory](#) impairment, personality changes (particularly his disinhibited and impulsive behavior), and the hereditary component could likely all be attributed to [FTD](#). However, the presence of [chorea](#) suggests a different diagnosis.

D - Periventricular plaques

Image

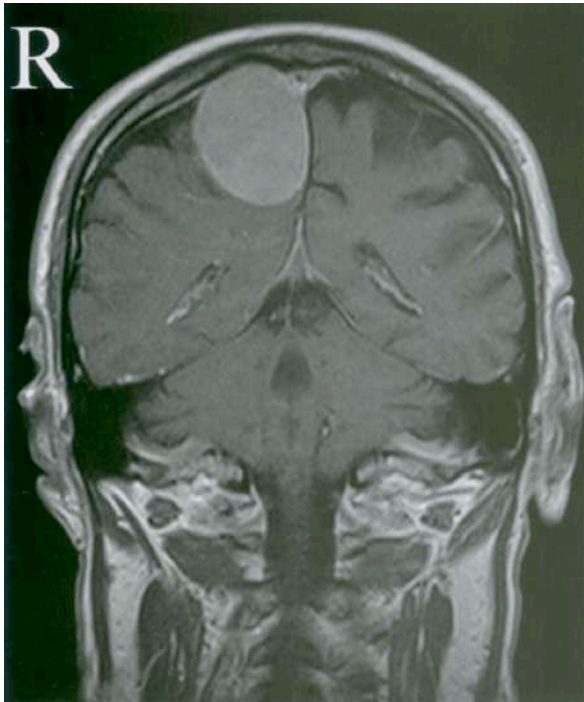


Explanation Why

Periventricular plaques on brain [MRI](#) in combination with neurologic dysfunction are diagnostic of [multiple sclerosis](#) (MS), which, as a very late feature, is associated with cognitive impairment, including [memory](#) deficits and depression. The majority of affected individuals have [relapsing-remitting MS](#) and experience alternating flare-ups with near complete remission of symptoms, rather than the continuous, progressive pattern seen in this patient. This patient has no history of symptoms that would suggest MS (e.g., impaired vision, [diplopia](#), or sensory disturbances). Furthermore, MS is not associated with [chorea](#).

E - Extra-axial tumor with dural attachments

Image



Explanation Why

An extra-axial [tumor](#) with dural attachments is consistent with a [meningioma](#). Though [meningiomas](#) are initially asymptomatic in most patients due to their slow growth, a symptomatic [meningioma](#) could manifest with a variety of neurological symptoms, including mental status change, due to [mass effect](#) of the [tumor](#) on the surrounding structures. However, [memory](#) impairment and [chorea](#) would not be expected in [meningioma](#).

F - Atrophy of the striatum

Explanation But

The father, in this case, became ill later and possibly less severely than the son, a fact that can be attributed to the phenomenon of [anticipation \(genetics\)](#), a characteristic of [trinucleotide repeat](#)

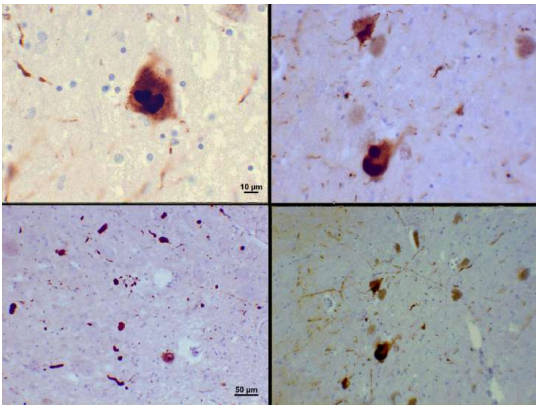
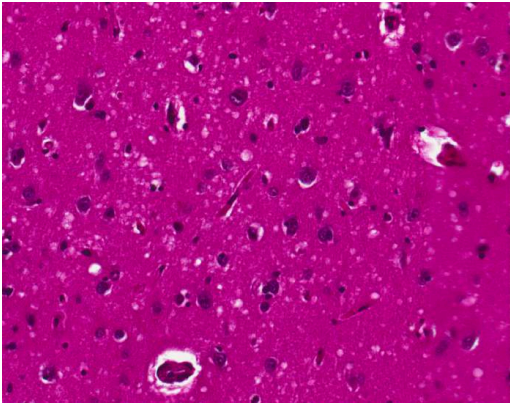
disorders.

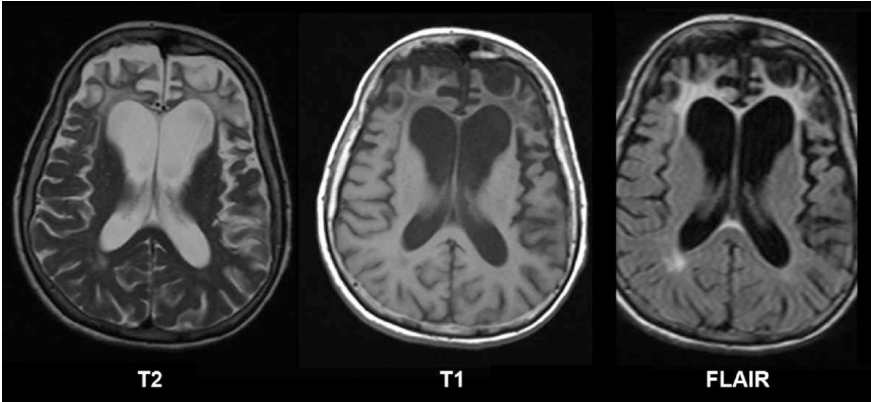
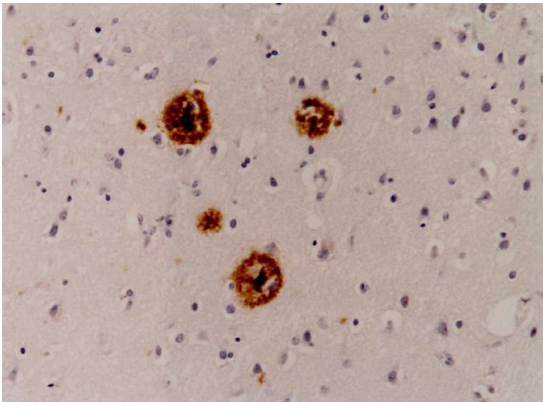
Explanation Why

[Atrophy](#) of the [striatum](#), specifically the [caudate nucleus](#) and [putamen](#), is a classic finding on brain imaging in patients with [Huntington disease](#) (HD). HD is caused by CAG [trinucleotide repeats](#) in the [huntingtin gene](#), which cause aggregates of abnormal huntingtin protein to accumulate, resulting in neuronal death and [gliosis](#) in the [striatum](#). The disorder is diagnosed via genetic testing, with neuroimaging used to rule out other intracranial pathologies.

Question # 4

A 44-year-old male is brought to the physician by his father. Over the past year, the patient has become progressively forgetful and withdrawn. He frequently has trouble remembering names of acquaintances, and has been requiring increasing amounts of assistance with getting dressed, cooking, and personal hygiene. He was diagnosed with a genetic disorder during infancy. Physical examination shows prominent epicanthal folds, low-set small ears, and a protruding tongue. Mental examination shows significant deficits in short- and long-term memory. This patient's cognitive symptoms are most likely the result of which of the following neuropathologic changes?

	Answer	Image
A	Intracellular aggregations of alpha-synuclein	
B	Multifocal deposition of excess copper	
C	Synaptic build-up of abnormal prion protein	

	Answer	Image
D	Cytoplasmic inclusions of ubiquitinated TDP-43	 T2 T1 FLAIR
E	Extracellular accumulation of amyloid plaques	

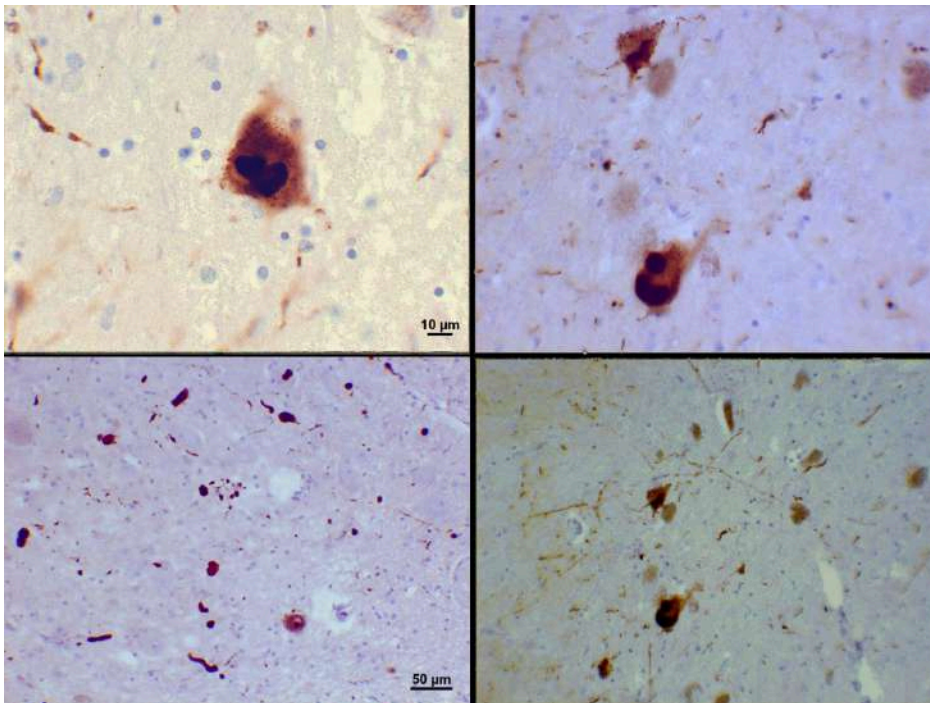
Hint

Prominent epicanthal folds, low-set small ears, and a protruding tongue are signs of trisomy 21. This patient's presentation of cognitive and memory impairments are consistent with a condition that manifests early in patients with this genetic disorder.

Correct Answer

A - Intracellular aggregations of alpha-synuclein

Image



Explanation Why

Intracellular aggregations of alpha-synuclein ([Lewy bodies](#)) is observed in [Lewy body dementia](#) and [Parkinson disease](#); neither condition is associated with [trisomy 21](#). Unlike this patient, who presents with early [memory](#) impairment, patients with [Lewy body dementia](#) show early impairment of attention, visuospatial, and executive functions. Moreover, [Lewy body dementia](#) is usually associated with other findings, such as visual [hallucinations](#), movement disorders, [dysautonomia](#), and [sleep disorders](#).

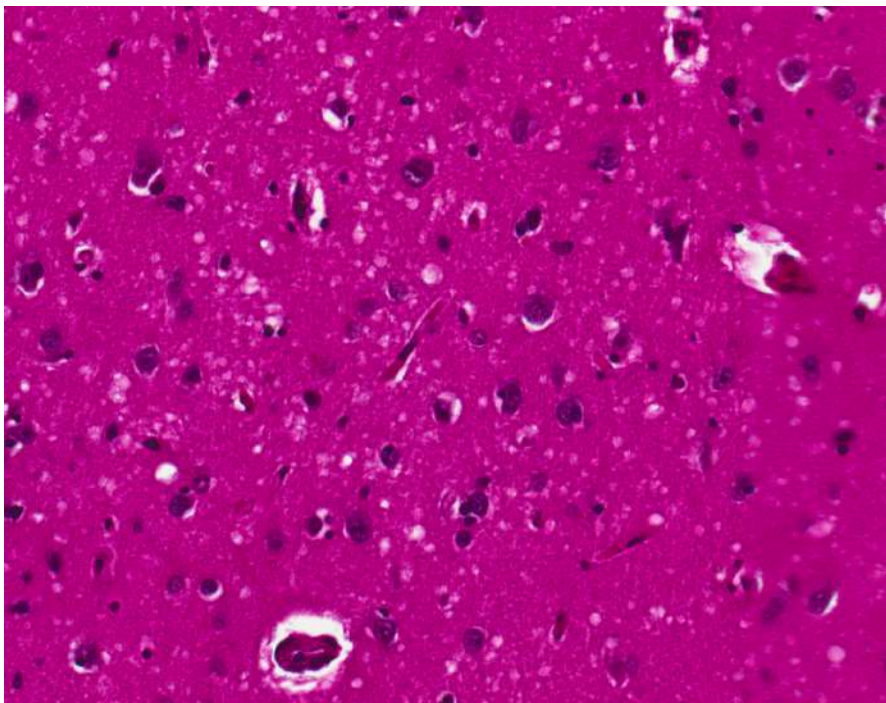
B - Multifocal deposition of excess copper

Explanation Why

Multifocal deposition of excess [copper](#) in the [lentiform nucleus](#), [liver](#), and other organs has been observed in [Wilson disease](#), which is caused by impaired hepatocellular [copper](#) transport due to ATPB7 [gene](#) mutation. [Wilson disease](#) typically presents with [liver](#) disease, movement disorder, and psychiatric manifestations before the age of 35. None of these features are present in this patient.

C - Synaptic build-up of abnormal prion protein

Image



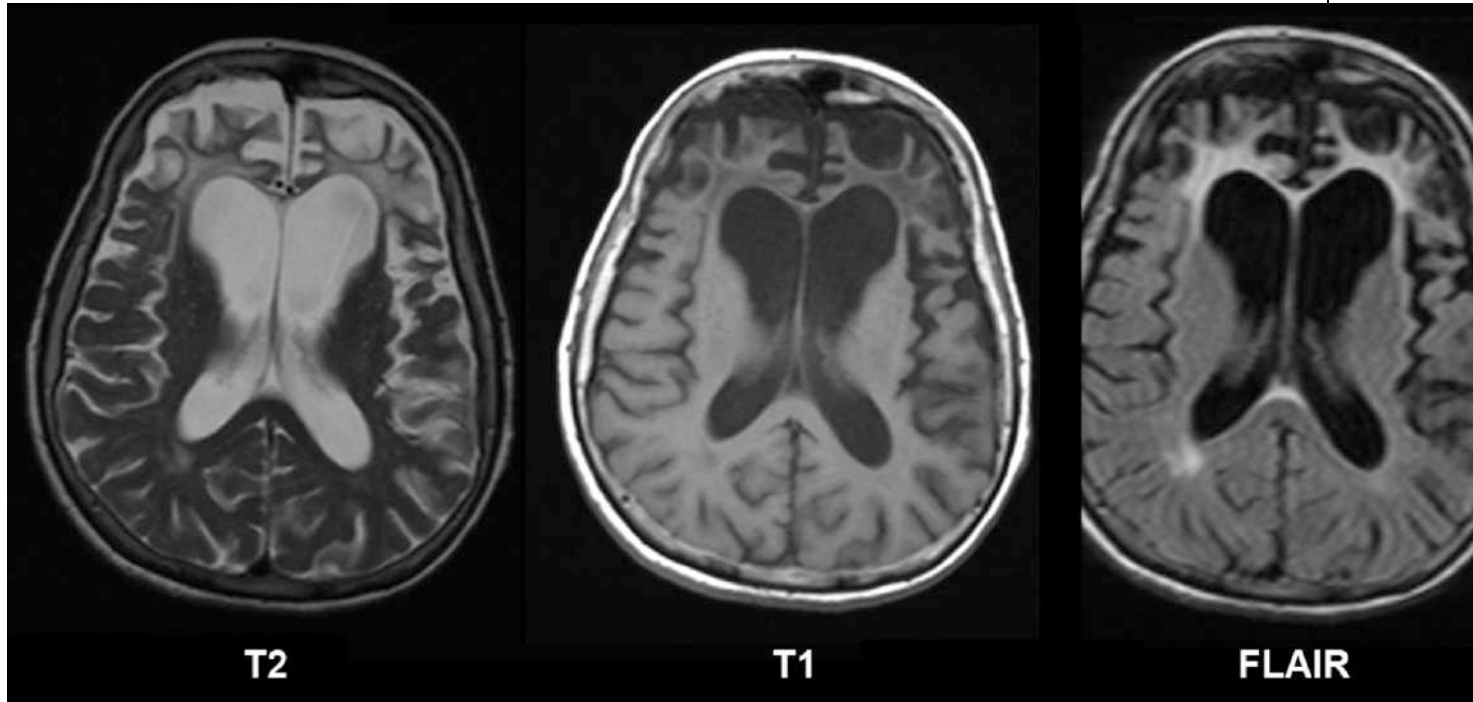
Explanation Why

Synaptic build-up of abnormal [prion](#) protein causes [prion diseases](#), such as [Creutzfeldt-Jakob disease](#), which is characterized by rapidly deteriorating cognitive function and myoclonus provoked by startle. Even though this patient has [dementia](#), the protracted course of his illness favors another

diagnosis. Moreover, [trisomy 21](#) is not a [risk factor](#) for [prion diseases](#).

D - Cytoplasmic inclusions of ubiquitinated TDP-43

Image

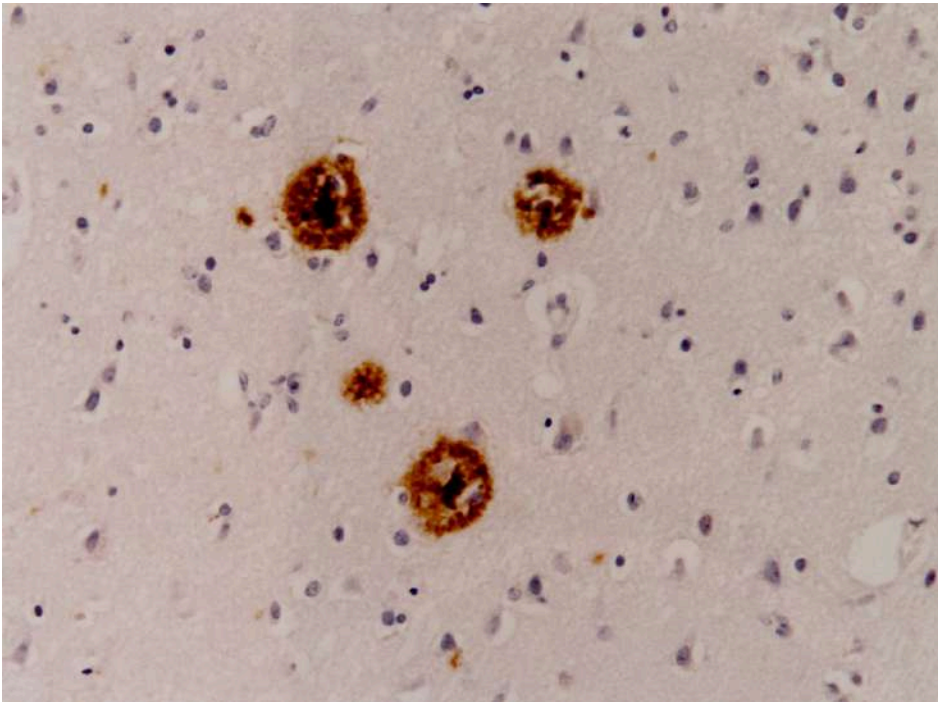


Explanation Why

[Cytoplasmic](#) inclusions of ubiquitinated [TDP-43](#) are observed in one of the pathologic variants of the frontotemporal [dementia](#) ([FTD](#)) clinical spectrum, FTLD-TDP. [FTD](#) manifests in middle-aged individuals; however, unlike with this patient, [memory](#) and orientation are initially preserved and early symptoms include changes to personality and social behavior. Moreover, [trisomy 21](#) is not a [risk factor](#) for [FTD](#).

E - Extracellular accumulation of amyloid plaques

Image



Explanation Why

Accumulation of extracellular [amyloid plaques](#) and intracellular [neurofibrillary tangles](#) are observed in [Alzheimer disease](#) (AD). A majority of patients with [trisomy 21](#) ([Down syndrome](#)) develop early-onset AD since an extra copy of the [amyloid precursor protein \(APP\) gene](#) (located on [chromosome 21](#)) leads to higher absolute levels of [APP](#) expression and deposition of the encoded [amyloid-beta peptide](#) in the brain as well as the [cerebral vasculature](#). Mutations in the [APP gene](#) are associated with early-onset familial AD.

Question # 5

A 38-year-old woman comes to the physician because of a 3-week history of involuntary movements of her extremities. One year ago, she was fired from her position as an elementary school teacher because she had stopped preparing lessons and was frequently absent without notice. She now lives with her mother. She appears emaciated and malodorous. Examination shows rapid, nonrepetitive jerks of her limbs and face that frequently end with the patient covering her face and yawning. She has an unsteady gait. Genetic testing shows a mutation on chromosome 4. This patient's condition is most likely associated with increased levels of which of the following substances?

	Answer	Image
A	Glutamate	
B	Gamma-aminobutyric acid	
C	Acetylcholine	
D	Dopamine	
E	N-acetyl aspartate	

Hint

The patient's apparent changes in personality, mood, and/or cognitive function (recent termination of her job, lack of personal hygiene) and the finding of chorea on examination are consistent with Huntington disease (HD). HD is an autosomal dominant progressive neurodegenerative disorder caused by a trinucleotide expansion of CAG in the Huntington gene on chromosome 4p.

Correct Answer

A - Glutamate

Explanation Why

A reduced level of [glutamate](#) has been observed in the cingulate cortex of patients with [Huntington disease](#).

B - Gamma-aminobutyric acid

Explanation Why

Patients with [Huntington disease](#) have a profoundly decreased (not increased) [GABA](#) level in the [striatum](#) (caudate and [putamen](#)), [globus pallidus](#), and [substantia nigra](#). Decreased [GABA](#) levels have also been observed in [anxiety disorder](#).

C - Acetylcholine

Explanation Why

Reduced levels of [acetylcholine](#) have been observed in the [striatum](#) of patients with [Huntington disease](#). Likewise, cholinergic transmission is reduced in [Alzheimer disease](#).

D - Dopamine

Explanation Why

Increased [dopaminergic](#) transmission has been observed in the early phases of [Huntington disease](#)

leading to hyperkinetic movements, as seen in this patient. [Huntington disease](#) involves selective degeneration of medium spiny neurons in the caudate and [putamen](#), preferentially affecting the [indirect pathway of the basal ganglia](#) in the early stages of the disease. In the late phase of HD, there is [dopamine](#) depletion, which leads to the development of [bradykinesia](#) and [rigidity](#).

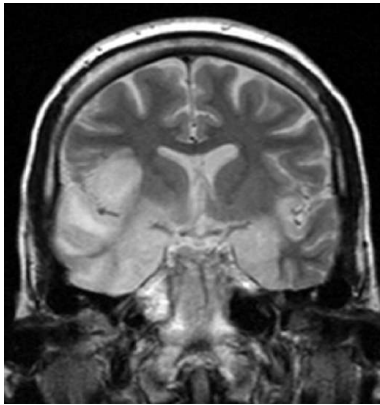
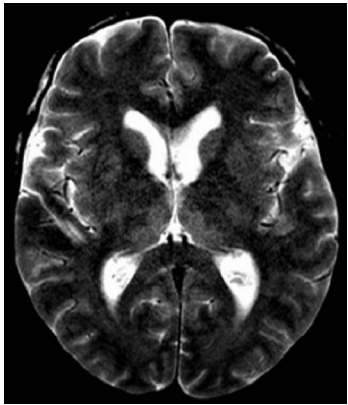
E - N-acetyl aspartate

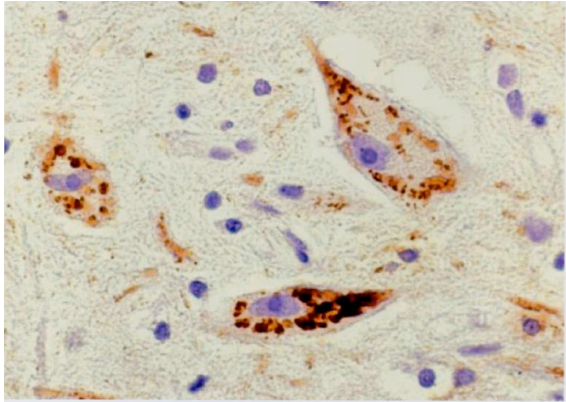
Explanation Why

Levels of N-acetyl [aspartate](#) are reduced in patients with early [Huntington disease](#), [mild cognitive impairment](#), and [Alzheimer disease](#).

Question # 6

A 68-year-old man is brought to the emergency department 30 minutes after the onset of uncontrollable jerking movements of his arms and legs followed by loss of consciousness. His wife says that he seemed confused this morning and had a headache. Immediately before the shaking episode, he said that he smelled rotten eggs. He is unresponsive. Cerebrospinal fluid (CSF) analysis shows a leukocyte count of 700/ μ L (70% lymphocytes), a glucose concentration of 60 mg/dL, and a protein concentration of 80 mg/dL. Despite appropriate lifesaving measures, the man dies. Which of the following is most likely to be found on postmortem examination of this patient?

	Answer	Image
A	Hemorrhage into the adrenal glands	
B	Necrosis of the temporal lobes	
C	Atrophy of the mammillary bodies	
D	Spore-forming, obligate anaerobic rods	

	Answer	Image
E	Cytoplasmic inclusions in cerebellar Purkinje cells	 A light micrograph of a cerebellar section stained with hematoxylin and eosin (H&E). The image shows several large, triangular or polygonal cells with prominent, dark purple nuclei and pale, foamy cytoplasm, characteristic of Purkinje cells. Some of these cells contain dark brown, granular inclusions within their cytoplasm, which are likely lipid accumulations or inclusions associated with a specific pathology. The background consists of a lighter, more cellular area representing the granular layer of the cerebellum.

Hint

This man had viral encephalitis, which manifests with altered mental status, seizures and lymphocytic pleocytosis with normal glucose concentration and mildly elevated protein concentration on CSF analysis.

Correct Answer

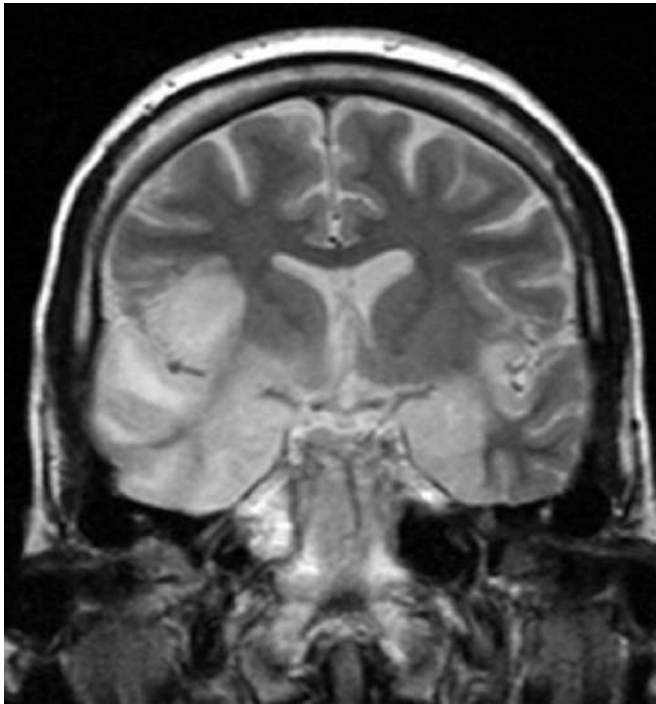
A - Hemorrhage into the adrenal glands

Explanation Why

Hemorrhage into the [adrenal glands](#) is observed in [Waterhouse-Friderichsen syndrome](#). This condition is commonly associated with [meningococcal meningitis](#), which typically manifests with [headache](#), altered mental status, and [seizures](#), as seen here. However, this patient lacks other manifestations of [Waterhouse-Friderichsen syndrome](#) such as high [fever](#), myalgia, [petechial](#) rash, signs of [disseminated intravascular coagulation](#), and [adrenal insufficiency](#). Moreover, [CSF analysis](#) in patients with bacterial [meningitis](#) usually shows granulocytic (not [lymphocytic](#)) [pleocytosis](#).

B - Necrosis of the temporal lobes

Image

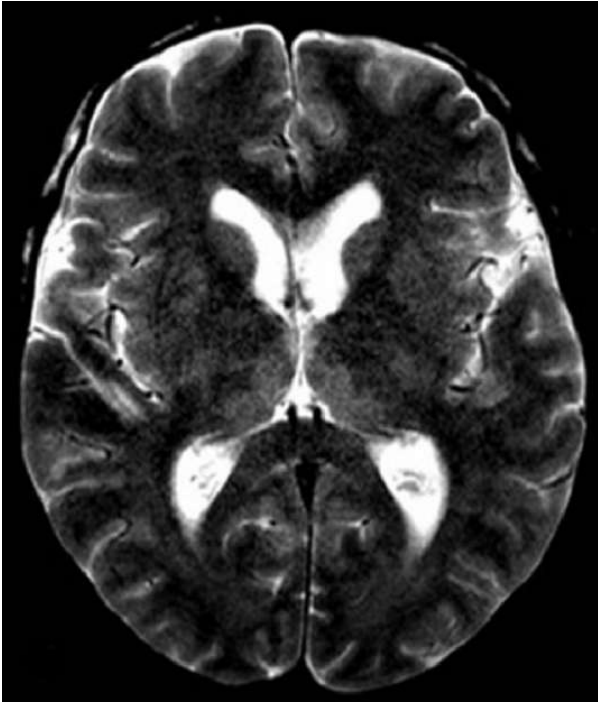


Explanation Why

[Necrosis](#) of the [temporal lobes](#) is a relatively specific finding in [herpes simplex encephalitis](#), which is most commonly caused by [HSV-1](#). Damage to the [temporal lobe](#) can cause clinical features such as [olfactory hallucinations](#) and [aphasia](#). Biopsy of the lesion would show intranuclear eosinophilic inclusions, which is characteristic of [herpes virus infections](#). [HSV encephalitis](#) is fatal in up to 70% of cases if left untreated; intravenous [acyclovir](#) is the first-line therapy.

C - Atrophy of the mammillary bodies

Image



Explanation Why

[Atrophy](#) of the [mammillary bodies](#) and [medial](#) thalamic nuclei is observed in patients with [Wernicke encephalopathy](#), which is caused by [vitamin B1](#) deficiency. Although [Wernicke encephalopathy](#) commonly causes confusion, [olfactory hallucinations](#) would not be expected and [CSF analysis](#) is usually within normal limits. Moreover, other typical manifestations of [Wernicke encephalopathy](#) such as [ataxia](#), nystagmus, and [ophthalmoplegia](#) have not been reported in this patient.

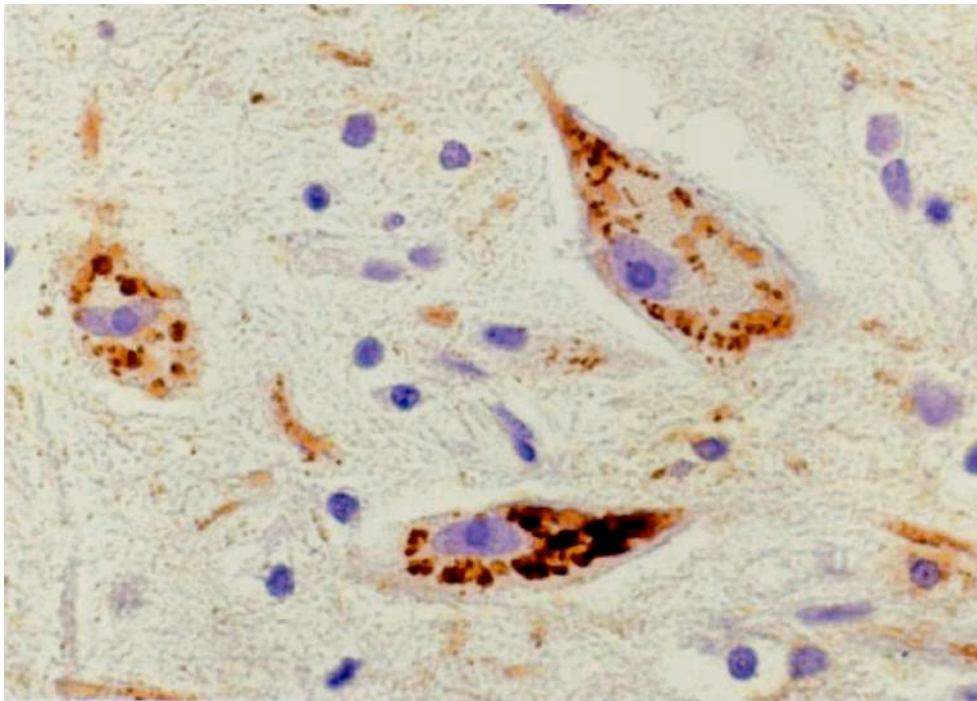
D - Spore-forming, obligate anaerobic rods

Explanation Why

Clostridium tetani is a [spore-forming](#), obligate [anaerobic](#) rod that causes [tetanus](#). Patients with [tetanus](#) typically develop spasms, [risus sardonicus](#), [opisthotonus](#), and [trismus](#) with intact sensorium. [Headache](#), altered mental status, focal neurologic deficits, and [seizures](#) would not be expected. Moreover, [CSF analysis](#) in patients with [tetanus](#) is usually within normal limits.

E - Cytoplasmic inclusions in cerebellar Purkinje cells

Image



Explanation Why

Eosinophilic [cytoplasmic](#) inclusions ([Negri bodies](#)) in the [cerebellum](#) or [hippocampus](#) are typically seen in patients with [rabies](#). This condition can cause confusion and [seizures](#); however, this patient lacks other typical manifestations such as [flu-like symptoms](#), [hydrophobia](#), photophobia, agitation,

and progressive paralysis. [CSF analysis](#) of patients with [rabies](#) usually shows a milder [lymphocytic pleocytosis](#) (~ 60 cells/ μ L). Moreover, there is no evidence that this patient had an exposure to a potentially rabid animal. The inclusions found on postmortem examination of this patient would be intranuclear and typically occur at a different site.

Question # 7

A 62-year-old man is brought to the emergency department by his wife because she thinks he has had a stroke. He has hypertension and type 2 diabetes mellitus. Current medications include enalapril and metformin. He has smoked 1 pack of cigarettes per day for the past 35 years. His blood pressure is 162/95 mm Hg. A CT scan of the brain shows a lacunar stroke involving the left subthalamic nucleus. The patient most likely presented with which of the following findings on physical examination?

	Answer	Image
A	Cogwheel rigidity	
B	Dystonia	
C	Hemiballismus	
D	Truncal ataxia	
E	Vertical gaze palsy	
F	Hemispatial agnosia	

Hint

The patient's wife could have been injured if she had been standing nearby when the patient was having the stroke.

Correct Answer

A - Cogwheel rigidity

Explanation Why

[Cogwheel rigidity](#) is typically seen in [Parkinson disease](#), which is caused by progressive loss of [dopaminergic neurons](#) in the [substantia nigra](#). A [lacunar stroke](#) of the [subthalamic nucleus](#) is unlikely to present with [cogwheel rigidity](#).

B - Dystonia

Explanation Why

[Dystonia](#) can be seen secondary to lesions of the [thalamus](#), the [putamen](#), or the [globus pallidus](#). A [lacunar stroke](#) of the [subthalamic nucleus](#) is unlikely to present with [dystonia](#).

C - Hemiballismus

Explanation Why

Contralateral [hemiballismus](#) and [choreiform movements](#) are common symptoms of a [lacunar infarct](#) of the [subthalamic nucleus](#). They are caused by a reduction in the activity of the [indirect pathway of the basal ganglia](#). [Lacunar infarcts](#) are noncortical [infarcts](#), characterized by the absence of cortical signs. [Subthalamic strokes](#) are usually [ischemic](#) in etiology, and uncontrolled [hypertension](#), [diabetes mellitus](#), and a significant smoking history are known [risk factors](#).

D - Truncal ataxia

Explanation Why

[Truncal ataxia](#) is usually seen in lesions of the [cerebellar vermis](#). Other signs that can be seen in a [cerebellar stroke](#) include [dysarthria](#), [dysmetria](#), and oculomotor disorders (nystagmus). A [lacunar stroke](#) of the [subthalamic nucleus](#) is unlikely to present with [truncal ataxia](#).

E - Vertical gaze palsy

Explanation Why

[Vertical gaze palsy](#) is usually caused by [midbrain](#) lesions, e.g., [dorsal midbrain syndrome](#), and can present with [vertical gaze palsy](#), dissociation of pupillary response to light and [accommodation](#), and/or [convergence-retraction](#) nystagmus. Lesions of the [subthalamic nucleus](#), on the other hand, are unlikely to cause [vertical gaze palsy](#).

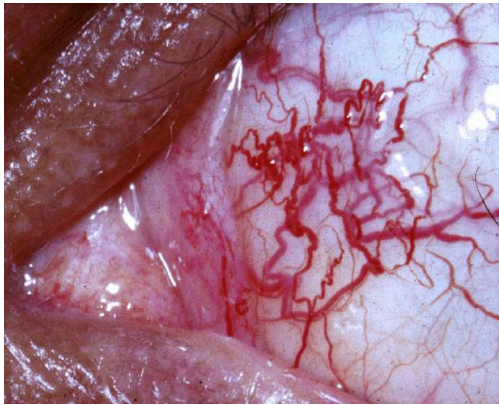
F - Hemispatial agnosia

Explanation Why

[Hemispatial agnosia](#) is unlikely to be seen in this patient, as it is caused by lesions of the non-dominant parietal cortex, not the [subthalamic nucleus](#). Also, this patient's lesion is on the left side, whereas [hemispatial agnosia](#) usually affects the nondominant (typically the right) parietal cortex.

Question # 8

A 2-year-old girl is brought to the physician by her parents because of clumsiness and difficulty walking. She began to walk at 12 months and continues to have difficulty standing still without support. She also appears to have difficulty grabbing objects in front of her. Over the past year, she has had 5 episodes of sinusitis requiring antibiotic treatment and was hospitalized twice for bacterial pneumonia. Physical examination shows an unstable, narrow-based gait and several hyperpigmented skin patches. Serum studies show decreased levels of IgA and IgG and an increased level of alpha-fetoprotein. Over the next 5 years, which of the following complications is this patient most likely to develop?

	Answer	Image
A	Chronic eczema	
B	Conjunctival telangiectasias	
C	Pes cavus	
D	Cardiac rhabdomyoma	
E	Celiac disease	
F	Chronic lymphocytic leukemia	

Hint

This young patient presents with cerebellar ataxia and recurrent sinopulmonary infection along with laboratory evidence of decreased immune competency and elevated alpha-fetoprotein (AFP). This constellation of findings strongly suggests an underlying mutation in the *ATM* gene.

Correct Answer

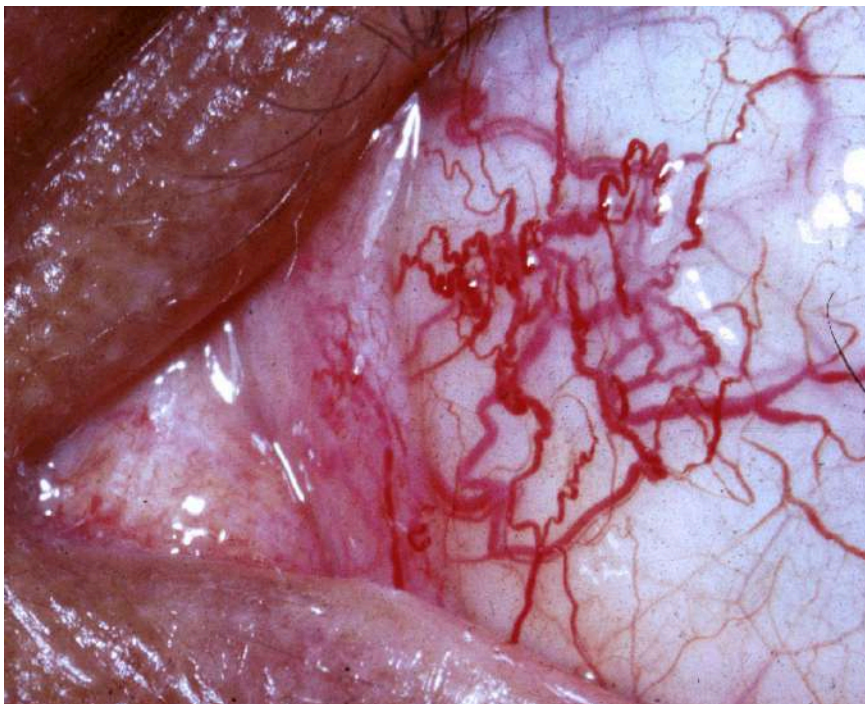
A - Chronic eczema

Explanation Why

Chronic [eczema](#) is expected to develop in patients with [Wiskott-Aldrich syndrome](#) (WAS). While this condition could account for this patient's history of repeated infections, [laboratory studies](#) usually show increased (not decreased) [IgA](#) levels. Moreover, WAS does not cause neurological symptoms such as [ataxia](#). Finally, because the condition is [x-linked recessive](#), it would be very unlikely to affect a female patient.

B - Conjunctival telangiectasias

Image



Explanation But

This patient also presents with café-au-lait spots ([hyperpigmented skin patches](#)). These are common in AT as well as other neurocutaneous conditions, e.g., [neurofibromatosis type I](#).

Explanation Why

[Conjunctival telangiectasias](#) are a hallmark of the inherited syndrome [ataxia telangiectasia](#) (AT) and typically develop before the age of 5. [Telangiectasias](#) may also appear on other areas of exposed [skin](#), particularly the face. The decreased serum levels of [immunoglobulins](#) predispose to infections, particularly of the respiratory tract. AT is due to an [autosomal recessive](#) mutation in the [ATM gene](#), which assists in [DNA](#) break repair ([nonhomologous end joining](#)).

C - Pes cavus

Explanation Why

[Pes cavus](#) and other musculoskeletal abnormalities (e.g., kyphoscoliosis) are commonly observed early on in patients with [Friedreich ataxia](#) (FA). In contrast to the [ataxia](#) seen here, FA usually manifests as a staggering wide-based gait with onset in [adolescence](#). Further symptoms include [spastic paralysis](#) and decreased vibration sensation, [proprioception](#), and reflexes. [Hypertrophic cardiomyopathy](#) and [diabetes](#) are also strongly associated with FA, whereas [immunodeficiency](#) would not be expected.

D - Cardiac rhabdomyoma

Explanation Why

Cardiac [rhabdomyoma](#) rarely develops sporadically but can be seen in patients with [tuberous sclerosis](#) (TS). While patients with TS may have an impaired gait as a result of [central nervous system hamartomas](#), [immunodeficiency](#) (as evidenced by this patient's repeated infections and low [immunoglobulins](#)) would not be expected. Moreover, this patient's [hyperpigmented skin patches](#) are not consistent with the [skin](#) findings seen in TS (i.e., [adenoma sebaceum](#), [ash leaf spots](#), and [Shagreen patches](#)).

E - Celiac disease

Explanation Why

[Celiac disease](#) is associated with [selective IgA deficiency](#). As a result, affected patients may present with recurrent sinopulmonary infections in conjunction with or instead of the classic [diarrhea](#) and [malabsorption](#). However, this patient has both [IgA](#) and [IgG](#) deficiency, which is not associated with [celiac disease](#). This diagnosis also fails to explain the neurological symptoms and increased serum [alpha-fetoprotein](#) seen in this patient.

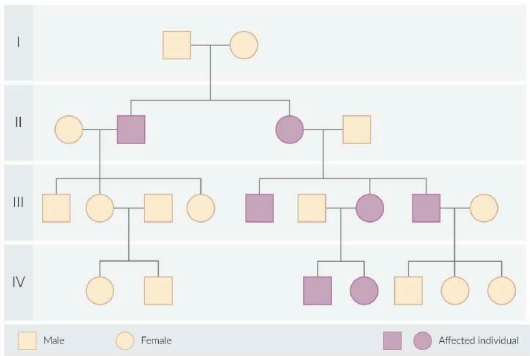
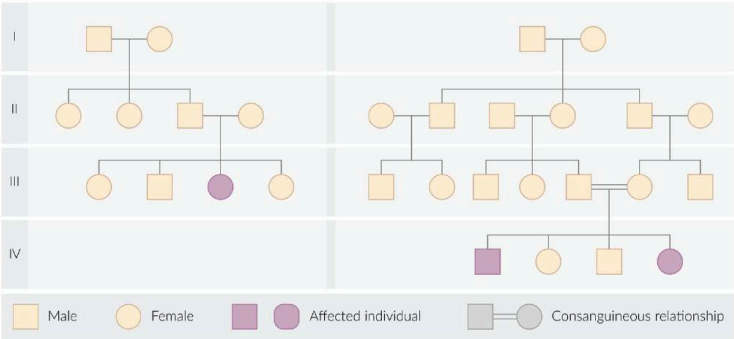
F - Chronic lymphocytic leukemia

Explanation Why

[Chronic lymphocytic leukemia \(CLL\)](#) is typically seen in older patients (usually > 60 years of age). Because many cases remain asymptomatic for a long period, it is often diagnosed late or incidentally. This patient has a hereditary condition that predisposes her to malignancies (especially acute leukemias and [lymphomas](#)), but that risk is not significantly increased in the next 5 years. Moreover, [CLL](#) is not one of the cancers typically associated with this patient's condition.

Question # 9

A 24-year-old man comes to the physician because his vision has worsened rapidly over the last 2 months. His maternal uncle lost his vision suddenly over a period of 3 months at 26 years of age. The patient's wife and 1-year-old son have normal vision. Fundusoscopic examination of the patient shows bilateral circumpapillary telangiectasia. Genetic testing shows a missense mutation in one of the genes of the electron transport chain complexes. The probability that this patient's son will be affected by the same disease is closest to which of the following?

	Answer	Image
A	0%	
B	25%	
C	33%	

	Answer	Image
D	50%	The pedigree chart illustrates three generations (I, II, III) of a family. Generation I consists of an unaffected male (I-1) and an affected female (I-2). They have four children in Generation II: an affected female (II-1), an unaffected male (II-2), an affected female (II-3), and an unaffected male (II-4). Generation II-1 and II-2 have two children in Generation III: an affected female (III-1) and an affected male (III-2). Generation II-3 and II-4 have three children in Generation III: an unaffected male (III-3), an affected female (III-4), and an affected female (III-5). The legend indicates that yellow squares represent males, yellow circles represent females, and purple squares/circles represent affected individuals.
E	100%	

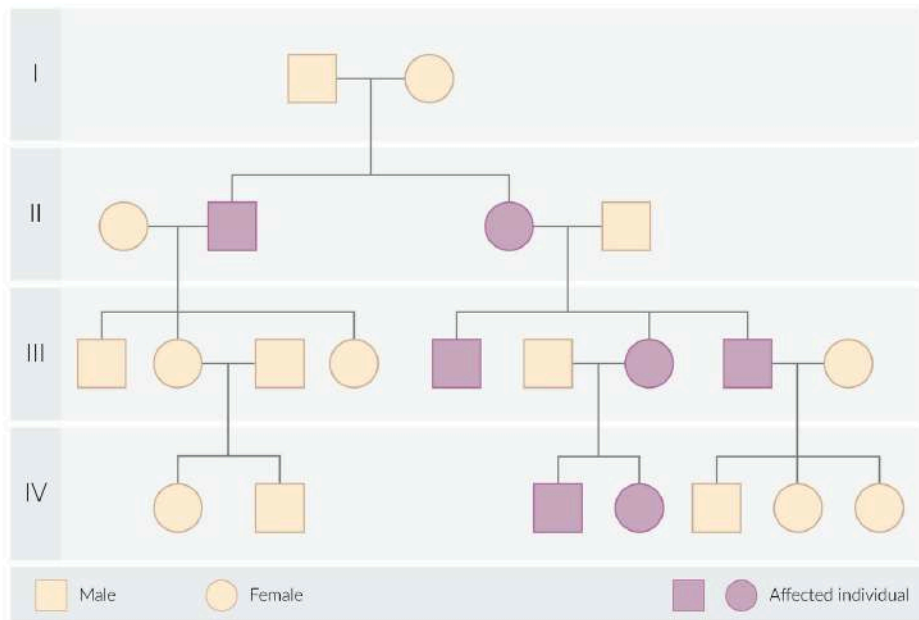
Hint

Rapidly worsening vision, circumpapillary telangiectasia on fundoscopy, and a mutation affecting the mitochondrial electron transport chain are diagnostic of Leber hereditary optic neuropathy.

Correct Answer

A - 0%

Image

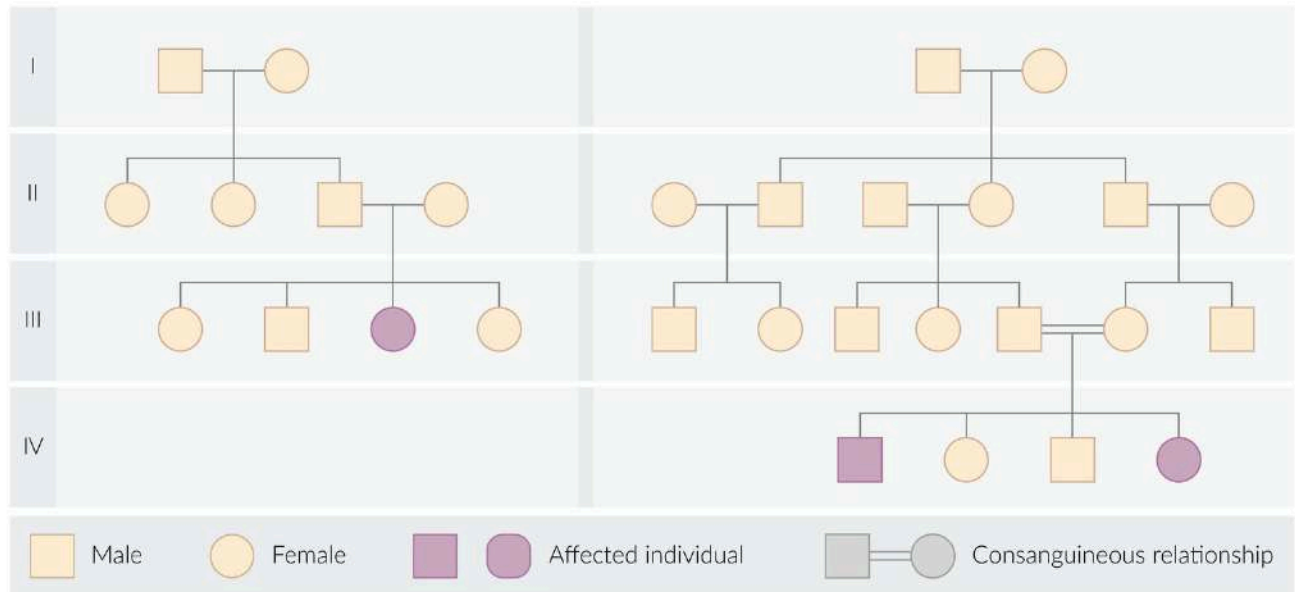


Explanation Why

[Leber hereditary optic neuropathy](#) typically presents with acute monocular vision loss in a young adult followed by contralateral vision loss in the following weeks or months. A [family history](#) of similar ocular disease is common. The condition is passed exclusively from mother to child (as are all diseases inherited via [mitochondrial DNA](#)) since [mitochondria](#) from [sperm](#) cells are not transmitted during [fertilization](#). Offspring of affected males, therefore, are at the same risk as the general population (about 1 in 50,000). Other conditions that demonstrate [mitochondrial inheritance](#) include [mitochondrial myopathies](#) (e.g., [MERRF](#) or [MELAS syndrome](#)).

B - 25%

Image



Explanation Why

This is the [probability](#) that would be observed in [autosomal recessive](#) disorders, with both parents being [heterozygous](#) (silent carriers) for the recessive [allele](#). This patient's vision loss is due to an inherited [mitochondrial](#) disorder, which follows a different inheritance pattern than [autosomal recessive](#) diseases.

C - 33%

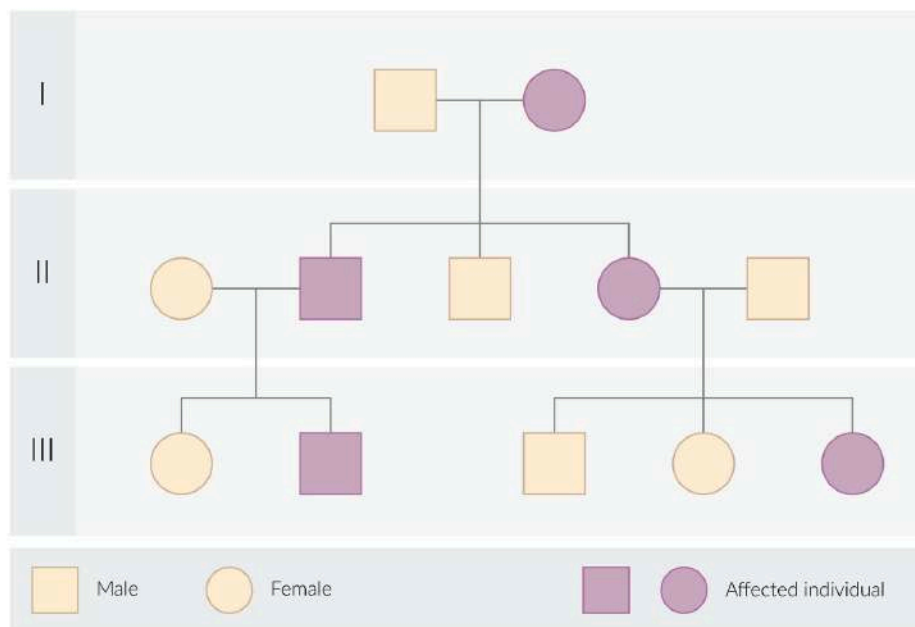
Explanation Why

The simplest scenario in which multiples of $\frac{1}{3}$ factor into genetics calculations are those involving carriers. For example, given two parents who are [heterozygous](#) for an [autosomal recessive allele](#) and their unaffected offspring with unknown [genotype](#), the [odds](#) of their offspring not being a carrier are

33% (the [homozygous](#) recessive [phenotype](#) is eliminated in an unaffected individual, leaving a 33% chance of [homozygous](#) dominant and a 66% chance of [heterozygous](#)). This patient's condition is governed by the rules of [mitochondrial inheritance](#) and does not follow such a pattern.

D - 50%

Image



Explanation Why

This is the [probability](#) that would be observed if the patient's vision loss was attributable to an [autosomal dominant](#) disorder. In such a scenario, the affected parent has one copy of the mutated [allele](#) and the unaffected parent has two normal [alleles](#). In contrast, this patient's vision loss is due to an inherited [mitochondrial](#) disorder, so a different inheritance pattern is expected.

E - 100%

Explanation Why

This would be the [probability](#) of passing a disease to an offspring where both parents each had the same [autosomal dominant](#) mutated [allele](#) (e.g. both parents have [autosomal dominant polycystic kidney disease](#)) or both parents had two [autosomal recessive alleles](#) (e.g. both parents have the same mutation causing [cystic fibrosis](#)). Such scenarios are exceptionally uncommon. Moreover, this patient's vision loss is due to an inherited [mitochondrial](#) disorder, which follows a different inheritance pattern.

Question # 10

A 57-year-old man comes to the physician because of a 3-month history of fatigue, difficulty swallowing, and weight loss. He has smoked 1 pack of cigarettes daily for 30 years. He is 173 cm (5 ft 8 in) tall, and weighs 54 kg (120 lb); BMI is 18 kg/m². Upper gastrointestinal endoscopy shows an exophytic tumor at the gastroesophageal junction. The patient is diagnosed with advanced esophageal adenocarcinoma. Palliative treatment is begun. Two months later, he complains of difficulty sleeping. His husband says that the patient does not get out of bed most days and has lost interest in seeing his friends. Mental status examination shows a blunted affect, slowed speech, and poor concentration. This patient is at increased risk of developing which of the following findings on polysomnography?

	Answer	Image
A	Decreased REM sleep duration	
B	Increased spike-and-wave discharge	
C	Increased slow-wave sleep-cycle duration	
D	Increased periodic sharp-wave discharge	
E	Decreased REM sleep density	
F	Decreased REM sleep latency	

Hint

A cancer diagnosis is a life-changing event that can significantly increase a patient's stress levels. Stress that exceeds a patient's coping mechanisms may result in major depressive episodes.

Correct Answer

A - Decreased REM sleep duration

Explanation Why

[Rapid eye movement sleep](#) (REM) represents ~ 20% of a healthy person's total sleep. The disruptive sleep patterns caused by [obstructive sleep apnea](#) decrease the duration of [REM sleep](#). Depression, however, is associated with an increase in the duration of the [REM sleep](#) state.

B - Increased spike-and-wave discharge

Explanation Why

Increased spike-and-wave discharge during [stage N3](#) sleep points to [epileptic](#) encephalopathy. These EEG spike-and-wave patterns project over both hemispheres in a diffuse, synchronous manner, and may be caused by anoxic brain injury, toxic encephalopathies, and [neurosyphilis](#). However, such waveforms are not seen in depressed patients.

C - Increased slow-wave sleep-cycle duration

Explanation Why

In healthy adults, 10–20% of sleep time occurs during [slow-wave sleep \(stage N3\)](#). An increase in [slow-wave sleep](#) represents a deeper, more restful sleep, and can be the effect of [antidepressants](#) such as [trazodone](#). In depression, however, the duration of [stage N3](#) is decreased.

D - Increased periodic sharp-wave discharge

Explanation Why

Periodic sharp-wave discharges are EEG waveforms that fire with frequencies of 1–2 Hz. These discharges are indicative of nonspecific brain dysfunctions or unilateral brain lesions, including fast-growing [brain tumors](#), [brain abscesses](#), viral encephalitis, and [Creutzfeldt-Jakob disease](#). These waveforms, however, are not associated with depression.

E - Decreased REM sleep density

Explanation Why

REM density is the frequency of rapid [eye](#) movements recorded during [REM sleep](#). It negatively correlates with the restfulness of the brain during sleep. Patients with depression show an increased REM density, which contributes to their poor sleep.

F - Decreased REM sleep latency

Explanation Why

[REM sleep latency](#) is the period between the onset of sleep and the first [REM sleep](#). In a healthy patient, this period lasts 90–120 minutes. The shorter [REM sleep latency](#) in depressed patients leads to a decrease in the amount of time in [non-REM sleep](#), thus lowering the quality of sleep. Prolonged periods of damaged sleep architecture exacerbate [mood](#) dysfunction, decrease concentration, and impair [memory](#), all of which worsen the patient's depression.

Question # 11

A 73-year-old woman is brought to the physician by her son because of a 2-year history of increasing forgetfulness. She does not remember her children's names; she cannot go outside the house unaccompanied because she forgets where she is and what she is supposed to do. Her son reports that over the past year, she has withdrawn herself from social gatherings and avoids making conversation. Mental status examination shows both impaired short- and long-term memory. She is oriented only to person. Her abstract reasoning is impaired. She appears indifferent about her memory lapses and says this is normal for someone her age. This patient's condition is most likely associated with decreased production of which of the following substances?

	Answer	Image
A	Gamma-aminobutyric acid	
B	Glutamate	
C	Acetylcholine	
D	Norepinephrine	
E	Serotonin	
F	Dopamine	

Hint

The patient's memory impairment, disorientation, and executive dysfunction suggest a diagnosis of Alzheimer disease (AD), the most common cause of dementia.

Correct Answer

A - Gamma-aminobutyric acid

Explanation Why

[Gamma-aminobutyric acid \(GABA\)](#) is an inhibitory [neurotransmitter](#) that is targeted by sedatives (e.g., [benzodiazepines](#), [barbiturates](#)). [GABA](#) is typically synthesized in the nucleus accumbens and [GABA](#) levels are decreased in [Huntington disease](#) and anxiety. [GABA](#) levels should not be decreased in this patient.

B - Glutamate

Explanation But

[Memantine](#) acts as an [N-methyl-D-aspartate](#) (NMDA) receptor antagonist and is thought to block the action of [glutamate](#) on those receptors. [Memantine](#) is used in patients with moderate-to-severe AD and suboptimal response to the preferred first-line pharmacologic agent, [donepezil](#).

Explanation Why

[Glutamate](#) is the most abundant excitatory [neurotransmitter](#) in the [central nervous system \(CNS\)](#) and is involved in the pathophysiology of [Alzheimer disease](#) (AD). [Glutamate](#)'s excitotoxicity and promotion of [cell death](#) underlie a potential mechanism of the neurodegeneration occurring in AD. [Glutamate](#) levels will not be decreased in this patient.

C - Acetylcholine

Explanation Why

[Alzheimer disease](#) is characterized by a degeneration of cholinergic [neurons](#) in the [temporal lobe](#) cortex, [hippocampus](#), and [nucleus basalis of Meynert](#), leading to impaired cholinergic transmission to the cortex and reduced levels of choline acetyltransferase. [Acetylcholine \(ACh\)](#) is generally

synthesized in the [nucleus basalis of Meynert](#). [ACh](#) levels would be increased in [Parkinson disease](#) and decreased in [Alzheimer disease](#) and [Huntington disease](#).

D - Norepinephrine

Explanation Why

[Norepinephrine](#) levels are commonly decreased in patients with [major depressive disorder \(MDD\)](#). While depression may cause [dementia](#) symptoms (i.e., [pseudodementia](#)) and this patient presents with some symptoms that might suggest depression (disturbed sleep, social withdrawal), she does not meet diagnostic criteria for major depression (i.e., [SIGECAPS](#)).

E - Serotonin

Explanation Why

[Serotonin](#) is commonly decreased in patients with anxiety and in those with [major depressive disorder \(MDD\)](#). While depression may cause [dementia](#) symptoms (i.e., [pseudodementia](#)) and this patient presents with some symptoms that might suggest depression (disturbed sleep, social withdrawal), she does not meet [diagnostic criteria for MDD](#) (i.e., [SIGECAPS](#)). [Serotonin](#) is synthesized in the Raphe nucleus of the [pons](#), medulla, and [midbrain](#).

F - Dopamine

Explanation Why

Loss of [dopaminergic neurons](#) in the [substantia nigra](#) is associated with [Parkinson disease \(PD\)](#). While advanced PD can cause [dementia](#), as seen in this patient, PD is unlikely in the absence of the typical motor features (e.g., [resting tremor](#), mask-like facies, [bradykinesia](#), [rigidity](#), shuffling gait). [Dopamine](#) levels are also decreased in [major depressive disorder](#) but will be elevated in [Huntington disease](#).

Question # 12

A 47-year-old woman comes to the physician because of a 5-month history of insomnia. She frequently experiences leg discomfort when trying to fall asleep that is relieved temporarily by movement. Her husband tells her that she frequently flexes her ankles upward when she sleeps. She appears fatigued and anxious. Physical examination shows no abnormalities. Laboratory studies including a complete blood count and iron studies are within the reference range. Which of the following is the most appropriate pharmacotherapy?

	Answer	Image
A	Ropinirole	
B	Zolpidem	
C	Nortriptyline	
D	Atenolol	
E	Sertraline	
F	Clonazepam	

Hint

This patient has leg discomfort that is relieved by movement, which is disrupting her sleep. She also displays involuntary, forceful dorsiflexion of her feet during sleep, a phenomenon known as periodic leg movements of sleep. These symptoms are consistent with restless leg syndrome (RLS).

Correct Answer

A - Ropinirole

Explanation But

Alpha-2-delta calcium channel [ligands](#) like [gabapentin](#) or [pregabalin](#) are acceptable first-line alternatives and may also be combined with [dopamine agonists](#) in patients who do not respond to treatment with a single first-line agent.

Explanation Why

[Ropinirole](#) and other [dopamine agonists](#) are considered first-line pharmacological agents for [restless leg syndrome](#). Pharmacologic therapy is reserved for cases of RLS in which symptoms result in functional impairment and sleep disturbance, or when symptoms persist despite behavioral interventions (e.g., [sleep hygiene](#), leg massage) and/or correction of any [iron deficiency](#).

B - Zolpidem

Explanation Why

[Benzodiazepine-like](#) substances such as [zolpidem](#) can be used to treat [sleep disorders](#). Because they have been associated with an increased frequency of [sleepwalking](#), however, they are generally not recommended for the treatment of RLS.

C - Nortriptyline

Explanation Why

[Tricyclic antidepressants](#) such as [nortriptyline](#) can be used to treat [neuropathic pain](#), which is usually worse at night and when resting. However, although the patient has leg discomfort, it is relieved by movement, and this is not typically the case with [neuropathic pain](#).

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D - Atenolol

Explanation Why

[Beta-blockers](#) such as [atenolol](#) can be used to treat performance anxiety. Although this patient appears anxious, her anxiety is most likely secondary to lack of sleep, which in turn is related to her leg discomfort. There is no indication that she has performance anxiety.

E - Sertraline

Explanation Why

[SSRIs](#) such as [sertraline](#) can be used to treat depression and [anxiety disorders](#). While this patient's difficulty sleeping and anxious appearance could potentially be features of depression or an [anxiety disorder](#), her leg discomfort is not explained by either diagnosis.

F - Clonazepam

Explanation Why

[Benzodiazepines](#) such as [clonazepam](#) are used in cases of [restless leg syndrome](#) that have not responded to other forms of pharmacotherapy. Long-term maintenance therapy with [benzodiazepines](#) leads to tolerance and dependence, which limits their use over an extended period of time.

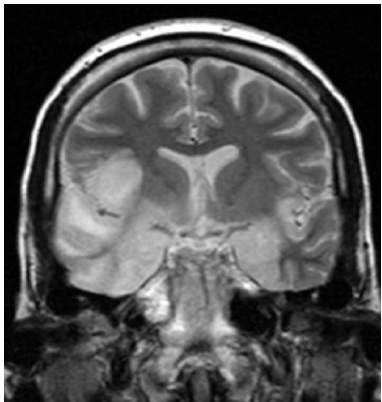
Question # 13

A previously healthy 53-year-old man is brought to the emergency department 45 minutes after the onset of a severe headache. He returned from a vacation in the mountains 2 weeks ago, where he camped near a lake. On arrival, he is confused. His temperature is 39°C (102.2°F) and blood pressure is 105/68 mm Hg. Neurologic examination shows diffuse hyperreflexia. An MRI of the brain shows asymmetrical, bitemporal hyperintensities. A lumbar puncture is performed. Cerebrospinal fluid analysis shows:

Leukocyte count	120/mm ³
Segmented neutrophils	10%
Lymphocytes	90%
Erythrocyte count	15/mm ³
Glucose	58 mg/dL
Opening pressure	130 mm Hg
Protein	75 mg/dL

Which of the following is the most likely causal pathogen?

	Answer	Image
A	Naegleria fowleri	
B	Tick-borne encephalitis virus	
C	Neisseria meningitidis	

	Answer	Image
D	West Nile virus	
E	Cytomegalovirus	
F	Herpes simplex virus	
G	La Crosse virus	
H	Enterovirus	
I	Rabies virus	
J	Rickettsia rickettsii	

Hint

Acute illness associated with headache, fever, altered mental status, and CSF showing lymphocytic pleocytosis with normal glucose levels and elevated protein levels is indicative of acute viral encephalitis. The localized temporal abnormalities seen on MRI are virtually pathognomonic of this pathogen.

Correct Answer

A - *Naegleria fowleri*

Explanation Why

Naegleria fowleri is a rare and extremely lethal pathogen capable of causing [meningoencephalitis](#) that is usually transmitted via inhalation of infested warm, stagnant freshwater. Individuals exposed to this organism remain asymptomatic for a period of about one week, after which time they rapidly develop [headache](#), [fever](#), meningismus, [seizures](#), confusion, and [hallucinations](#). This patient's history of camping near a freshwater lake raises suspicion of *Naegleria* infection, but, given the exceptional rarity of this disease (33 cases over 10 years in the US), the [CSF](#) findings that indicate a viral etiology, and the characteristic [MRI](#) findings, another causal pathogen is much more likely.

B - Tick-borne encephalitis virus

Explanation Why

[Tick-borne encephalitis virus](#) causes encephalitis and is [endemic](#) to eastern Europe and Asia. The presentation is highly variable; [CNS](#) involvement most commonly takes the form of meningismus, altered mental status, and transient paralysis. While there is evidence of an acute viral [CNS](#) infection in this patient's [cerebrospinal fluid](#), it is highly unlikely that this pathogen is the cause, since he has not traveled to an [endemic](#) area.

C - *Neisseria meningitidis*

Explanation Why

Neisseria meningitidis causes rapidly progressive [meningitis](#), especially in children and young adults. [Meningococcal meningitis](#) classically manifests with intense [headache](#), high [fever](#), neck stiffness, vomiting, photophobia, and, in some cases, encephalitis. Disease progression can cause large [petechial](#) hemorrhages, [adrenal](#) hemorrhage ([Waterhouse-Friderichsen syndrome](#)), and [coma](#). While this patient has a [headache](#) and [fever](#), the localized bitemporal hyperintensities seen on [MRI](#) would not be typical of meningococcal infection.

D - West Nile virus

Explanation Why

[West Nile virus](#) infection is usually asymptomatic but can cause a nonspecific [flu-like](#) syndrome involving mild [fever](#), fatigue, and myalgia. In a very limited number of patients, [CNS](#) invasion (encephalitis) is possible, which manifests primarily with motor abnormalities (e.g., [extrapyramidal symptoms](#), myoclonus, or [tremor](#)); [cognition](#) can also be affected. In such cases, results of [CSF analysis](#) may be similar to this patient's. While this patient has [fever](#) and signs of encephalitis, he does not have any [extrapyramidal symptoms](#). Moreover, his [MRI](#) findings are strongly suggestive of a different diagnosis.

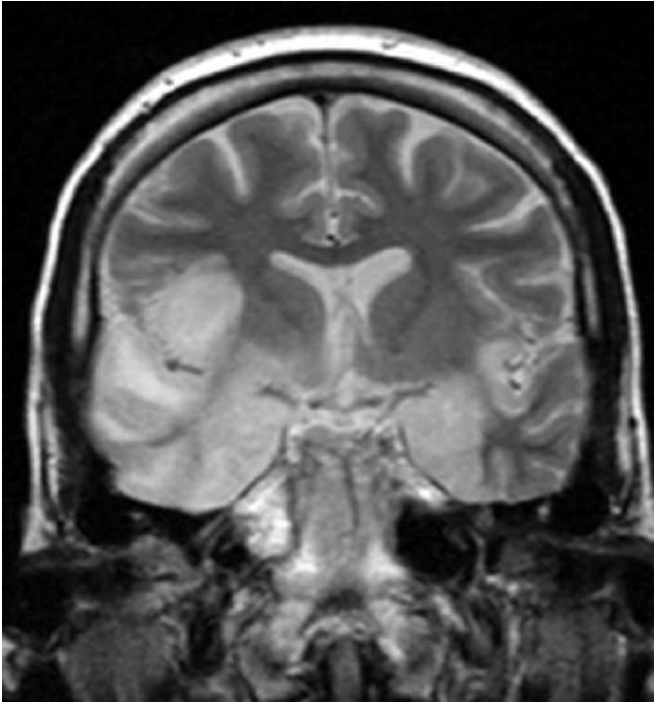
E - Cytomegalovirus

Explanation Why

[Cytomegalovirus](#) virtually never causes encephalitis, except in cases of marked [immunosuppression](#). This patient has no history of [HIV](#) infection or pharmacological [immunosuppression](#) (e.g., chronic [steroid](#) use or history of an organ transplant) that would make him susceptible to [cytomegalovirus encephalitis](#).

F - Herpes simplex virus

Image



Explanation But

Patients should receive empiric IV [acyclovir](#) therapy as soon as the diagnosis is suspected because neurologic complications of the disease are devastating. Even with prompt treatment, $\frac{2}{3}$ of patients are left with significant neurologic deficits.

Explanation Why

Herpes simplex virus is the most common cause of viral encephalitis. [MRI](#) of the brain classically shows [temporal lobe](#) involvement, possibly including hemorrhagic changes. Damage to the [temporal lobe](#) is also responsible for some of the other clinical features that may be seen in [herpes simplex encephalitis](#) such as [olfactory hallucinations](#), [aphasia](#), and [focal seizures](#).

G - La Crosse virus

Explanation Why

Infection with [La Crosse virus](#) is usually asymptomatic but may cause [California encephalitis](#), which is characterized by [seizures](#), [coma](#), focal neurologic findings, and paralysis. [MRI](#) findings may show [temporal lobe](#) abnormalities, which are seen on this patient's imaging. Although the clinical and radiographic features of [La Crosse virus](#) infection are consistent with this patient's presentation, another diagnosis is statistically much more likely.

H - Enterovirus

Explanation Why

[Enteroviruses](#) are a common cause of viral [meningitis](#) but an uncommon cause of encephalitis. In cases of [enterovirus](#) infection of the [central nervous system](#), leptomeningeal enhancement on [MRI](#) is the most typical finding. Asymmetrical, bitemporal hyperintensities are not characteristic.

I - Rabies virus

Explanation Why

Infection with the [rabies virus](#) causes [rabies](#). The infection first manifests with a nonspecific [prodrome](#) of fatigue, weakness, malaise, and low-grade [fever](#). In some instances, the patient may recall being bitten by an animal (e.g., a bat, raccoon, or coyote) and report [paresthesias](#) or anesthesia at the site of the bite (a finding pathognomonic for [rabies](#)). [CNS](#) invasion can cause acute agitation, hyperactivity, and [hydrophobia](#), or relative [somnolence](#) and paralysis. [Rabies](#) is extremely rare in the United States and this patient has no history of an animal bite, making [rabies](#) highly unlikely.

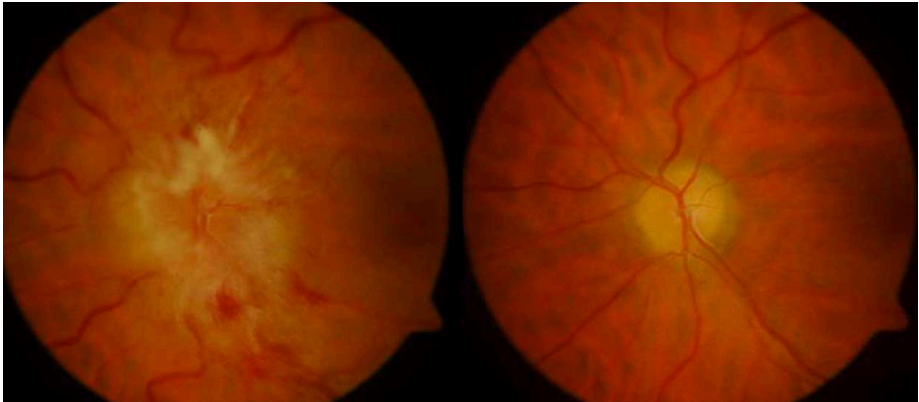
J - *Rickettsia rickettsii*

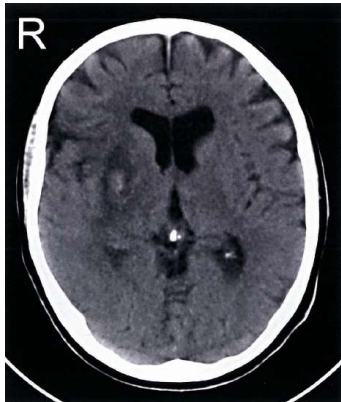
Explanation Why

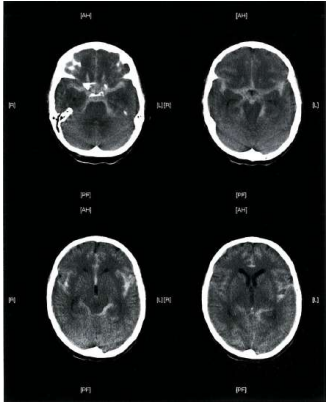
Rickettsia rickettsii causes [Rocky Mountain spotted fever \(RMSF\)](#), which classically manifests with a [maculopapular rash](#) that first affects the palms and soles, then spreads to the trunk. Other common findings include [fever](#), [headache](#), myalgia, and, in rare cases, encephalitis. Infected patients often have a history of [tick bites](#) and travel to an [endemic](#) region in spring or summer. The patient does not exhibit the classic [RMSF](#) rash, however, and his [MRI](#) findings point to a different diagnosis.

Question # 14

A 68-year-old man is brought to the emergency department because of a severe headache, nausea, and vomiting for 30 minutes. Forty-five minutes ago, he fell and struck his head, resulting in loss of consciousness for 1 minute. After regaining consciousness, he felt well for 15 minutes before the headache began. On arrival, the patient becomes rigid and his eyes deviate to the right; he is incontinent of urine. Intravenous lorazepam is administered and the rigidity resolves. Which of the following is the most likely cause of the patient's condition?

	Answer	Image
A	Intracerebral hemorrhage	
B	Cerebrospinal fluid production/absorption mismatch	

	Answer	Image
C	Rupture of bridging veins	
D	Acute insufficiency of cerebral blood flow	
E	Bleeding between dura mater and skull	

	Answer	Image
F	Aneurysm rupture	

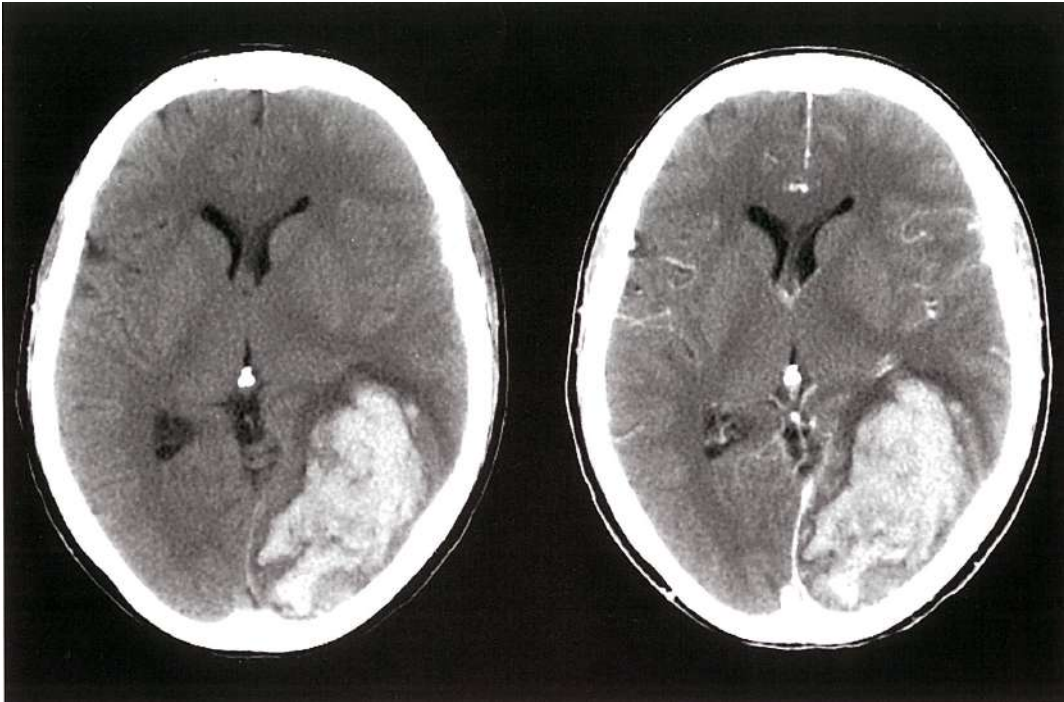
Hint

After sustaining a head injury and briefly losing consciousness, the patient experienced a brief asymptomatic period (a lucid interval), followed by signs and symptoms of elevated intracranial pressure (headache, nausea, vomiting, and seizure).

Correct Answer

A - Intracerebral hemorrhage

Image

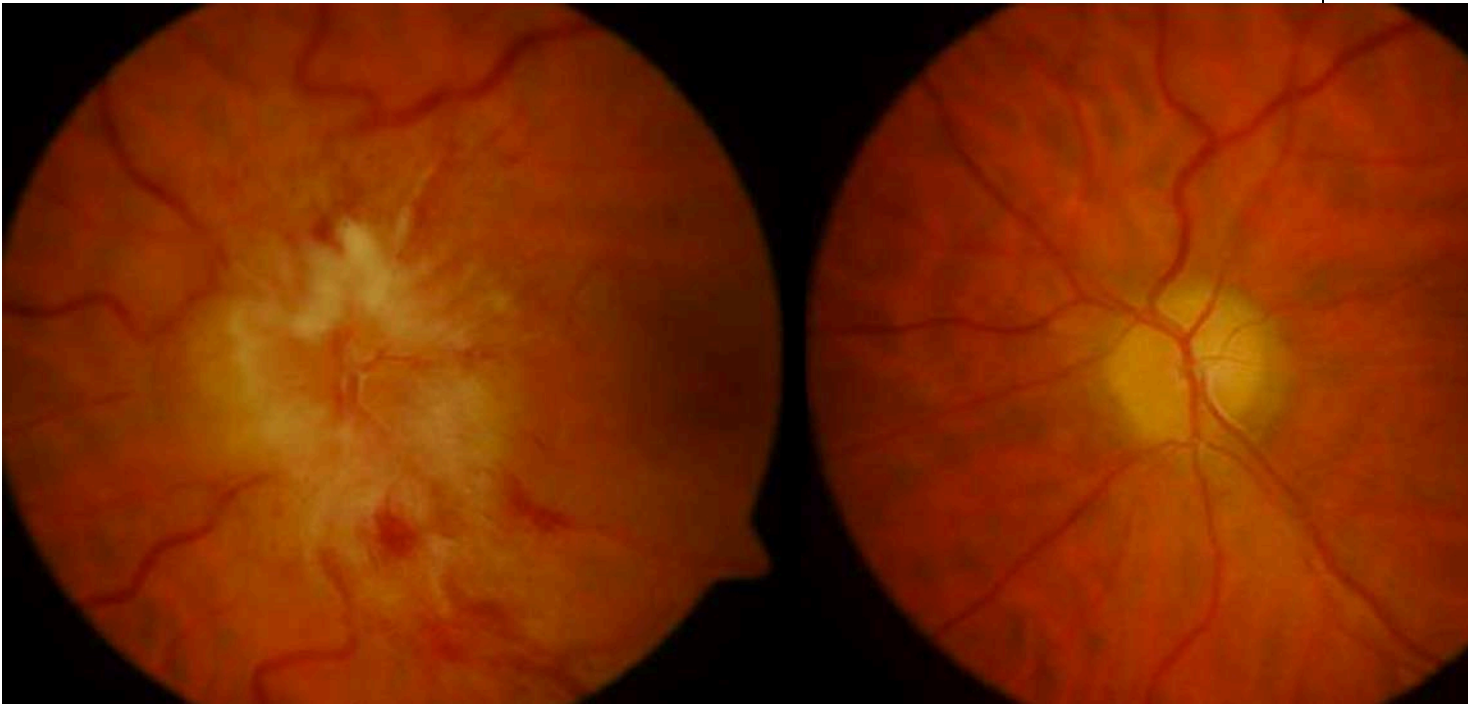


Explanation Why

[Intracerebral hemorrhage](#) typically results from a spontaneous (i.e., nontraumatic) rupture of vessels secondary to structural changes of the vessel walls, e.g., in chronic [hypertension](#) or [cerebral amyloid angiopathy](#). Patients present with [headache](#) and focal neurologic deficits such as [hemiparesis](#). Rarely, it is caused by a [head trauma](#) with direct damage of the vessel. [Signs of increased ICP](#) and a [lucid interval](#) are more suggestive of another diagnosis.

B - Cerebrospinal fluid production/absorption mismatch

Image



Explanation Why

A mismatch between production and absorption of [CSF](#) is the cause of [idiopathic intracranial hypertension](#), which usually presents with chronic [headaches](#) and visual symptoms (e.g., transient loss of vision) that worsen over months to years. It is not associated with [head trauma](#).

C - Rupture of bridging veins

Image

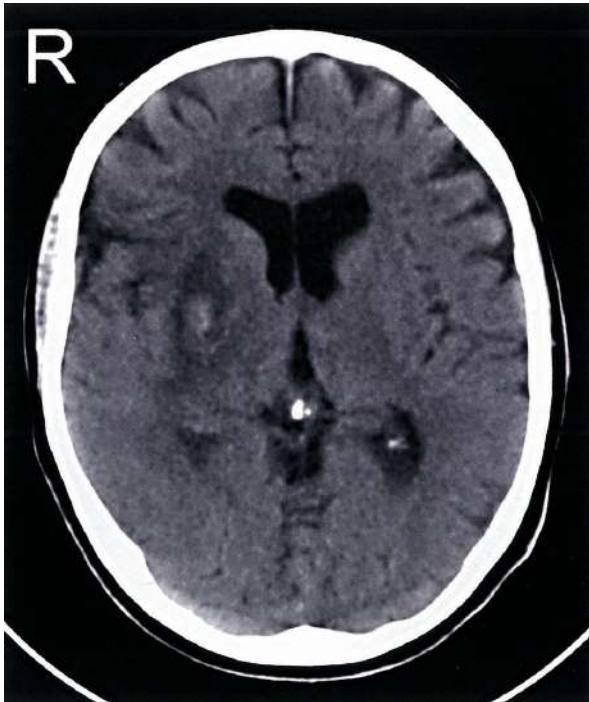


Explanation Why

Rupture of [bridging veins](#) causes [subdural hematoma \(SDH\)](#). The onset of symptoms in patients with [subdural hematoma](#) depends on the size, location, and rate of growth of the [SDH](#). In acute-onset [SDH](#), the patient can also present with [headache](#) and [signs of increased ICP](#) immediately following [head trauma](#). In rare cases, patients may also experience a [lucid interval](#). However, the temporary recovery of consciousness is more commonly associated with a different diagnosis.

D - Acute insufficiency of cerebral blood flow

Image



Explanation But

In malignant [middle cerebral artery \(MCA\) infarction](#), the most devastating form of acute [stroke](#), complete occlusion leads to acute [brain edema](#) and [elevated ICP](#), which may cause herniation of the brain, usually over a course of 1–5 days. Although this condition cannot be entirely ruled out in this patient, the absence of [risk factors](#) for [ischemic stroke](#), the acute deterioration of symptoms, and the presence of a [lucid interval](#) make this scenario unlikely.

Explanation Why

Acute insufficiency of cerebral blood flow causes an [ischemic stroke](#), the symptoms of which depend on the affected area of the brain. Patients typically have [risk factors](#) such as [diabetes](#) or [hypercholesterolemia](#) and present with focal neurological deficits like [hemiparesis](#), none of which applies to this patient. In addition, [seizures](#), [elevated ICP](#), and traumatic etiology are all unusual findings for [ischemic stroke](#).

E - Bleeding between dura mater and skull

Image



Explanation But

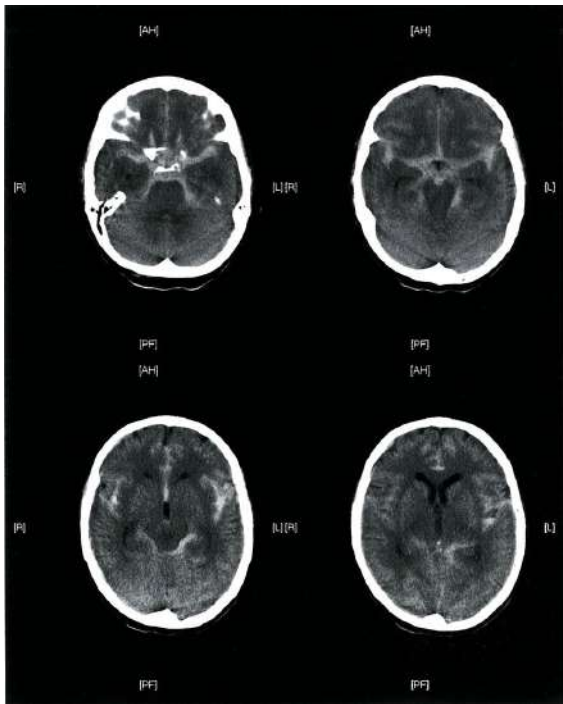
The diagnosis is confirmed by noncontrast [cranial](#) CT which shows a biconvex, [hyperdense](#), sharply demarcated lesion located between the brain and the [calvarium](#), limited by suture lines. Emergency treatment is necessary and involves surgical opening of the [skull](#) and evacuation of the [hematoma](#).

Explanation Why

Bleeding between the [dura mater](#) and the [skull](#) causes [epidural hematoma](#). This diagnosis should be suspected in any patient with [head trauma](#) causing loss of consciousness followed by a [lucid interval](#) and subsequently renewed deterioration and [signs of elevated ICP](#). The [lucid interval](#) represents the time required for the blood to accumulate in the [epidural space](#) to [proportions](#) great enough to compress the brain.

F - Aneurysm rupture

Image



Explanation Why

Rupture of a [cerebral aneurysm](#) is a potential cause of a [subarachnoid hemorrhage](#) that can also occur after [head trauma](#). Patients typically present with sudden, excruciating [headaches](#) ([thunderclap headache](#)), meningism, and loss of consciousness. While this patient experienced [headache](#) and a loss of consciousness, the [signs of elevated ICP](#) and his momentary recovery of consciousness suggest another diagnosis.

Question # 15

A previously healthy 42-year-old woman comes to the physician because of a 7-month history of diffuse weakness. There is no cervical or axillary lymphadenopathy. Cardiopulmonary and abdominal examination shows no abnormalities. A lateral x-ray of the chest shows an anterior mediastinal mass. Further evaluation of this patient is most likely to show which of the following?

	Answer	Image
A	Acetylcholine receptor antibodies	
B	Smoking history of 30 pack years	
C	Elevated serum alpha-fetoprotein level	
D	History of fever, night sweats, and weight loss	
E	Increased urinary catecholamines	
F	Elevated TSH and a nodular anterior cervical mass	

Hint

Thymoma is the most common type of anterior mediastinal mass.

Correct Answer

A - Acetylcholine receptor antibodies

Explanation Why

Acetylcholine receptor [antibody](#) detection is used to diagnose [myasthenia gravis](#), which is present in about 30% of patients with [thymoma](#) and may present with diffuse weakness. [Thymic](#) lesions, including [thymoma](#), are the most common underlying cause of [anterior mediastinal masses](#), accounting for ~ 50% of cases. The peak [incidence](#) of [thymomas](#) is between 40–60 years of age. Patients with [thymoma](#) may be asymptomatic, or they may present with [chest pain](#), [dyspnea](#), and [cough](#).

B - Smoking history of 30 pack years

Explanation Why

[Small cell lung cancer \(SCLC\)](#), which typically develops in smokers, can cause [proximal](#) muscle weakness ([Lambert-Eaton myasthenic syndrome](#)). However, the [mediastinal](#) manifestations of [SCLC](#) are typically due to hilar [lymphadenopathy](#), which occurs in the [middle mediastinum](#), not the [anterior mediastinum](#), making this diagnosis unlikely.

C - Elevated serum alpha-fetoprotein level

Explanation Why

[Alpha-fetoprotein](#) is a [tumor marker](#) that can be elevated in some germ cell tumors, especially [nonseminomatous germ cell tumors \(NSGCT\)](#). [NSGCT](#) typically occurs in young men (20–30 years of age) and is, therefore, less likely in this patient. Although germ cell tumors can cause [anterior mediastinal masses](#), they are not the most likely cause.

D - History of fever, night sweats, and weight loss

Explanation Why

[B symptoms](#) are classically associated with [lymphoma](#). Although [lymphoma](#) can cause an [anterior mediastinal mass](#) due to [anterior mediastinal lymphadenopathy](#), it is not the most common cause.

E - Increased urinary catecholamines

Explanation Why

Urinary [catecholamines](#) are elevated in some neural tumors such as [neuroblastoma](#). [Neuroblastoma](#) is rare in adults and would present as a [posterior mediastinal mass](#) rather than an [anterior mediastinal mass](#).

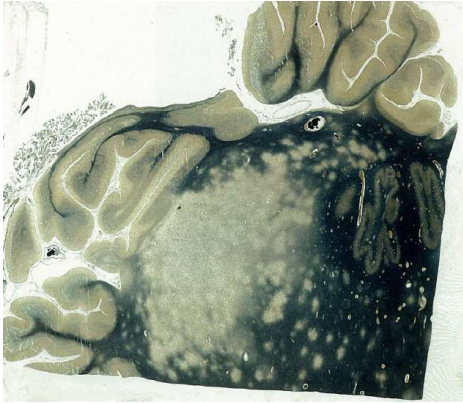
F - Elevated TSH and a nodular anterior cervical mass

Explanation Why

A nodular [anterior](#) cervical mass in association with elevated [TSH](#) is consistent with [goiter](#). Chronic, untreated [goiter](#) can grow into the substernal space, causing an [anterior mediastinal mass](#). However, [goiter](#) is not the most likely cause of an [anterior mediastinal mass](#). In addition, substernal [goiter](#) typically causes compressive symptoms (e.g., [dysphagia](#)), which are not present in this patient.

Question # 16

A 68-year-old man is brought to the emergency department 25 minutes after he was found shaking violently on the bathroom floor. His wife reports that he has become increasingly confused over the past 2 days and that he has been sleeping more than usual. He was started on chemotherapy 4 months ago for chronic lymphocytic leukemia. He is confused and oriented to person only. Neurological examination shows right-sided ptosis and diffuse hyperreflexia. An MRI of the brain shows disseminated, nonenhancing white matter lesions with no mass effect. A polymerase chain reaction assay of the cerebrospinal fluid confirms infection with a virus that has double-stranded, circular DNA. An antineoplastic drug with which of the following mechanisms of action is most likely responsible for this patient's current condition?

	Answer	Image
A	Free radical formation	
B	Tyrosine kinase inhibitor	
C	Topoisomerase II inhibitor	
D	Monoclonal antibody against EGFR	
E	Monoclonal antibody against CD20+	

Hint

Common therapeutic agents for CLL include rituximab, fludarabine, cyclophosphamide, chlorambucil, and alemtuzumab. However, only one of these drugs is known to increase the risk of progressive multifocal leukoencephalopathy (PML), a condition that manifests in MRI with nonenhancing lesions disseminated throughout the white matter.

Correct Answer

A - Free radical formation

Explanation Why

[Bleomycin](#) induces the formation of [free radicals](#), leading to breaks in [DNA](#) and halting cell replication. This agent is used to treat [testicular cancer](#) and [Hodgkin lymphomas](#), not [CLL](#). Side effects of [bleomycin](#) include pulmonary [fibrosis](#) and [hyperpigmented skin](#), not [PML](#).

B - Tyrosine kinase inhibitor

Explanation Why

[Tyrosine kinase inhibitors](#) such as [imatinib](#), [nilotinib](#), and [dasatinib](#) are used in the treatment of [CML](#), not [CLL](#). Side effects of these agents include fluid retention, [pulmonary edema](#), [QT prolongation](#), nausea, vomiting, [diarrhea](#), and [pancytopenia](#). No association with [PML](#) has been found.

C - Topoisomerase II inhibitor

Explanation Why

[Etoposide](#) and [teniposide](#) are [topoisomerase II inhibitors](#) that increase the degradation of [DNA](#) and decrease its replication. [Topoisomerase II inhibitors](#) are used in the treatment of [testicular cancer](#), [small cell lung cancer](#), [ovarian cancer](#), [lymphomas](#), and [acute myeloid leukemia](#), but they are not commonly used to treat [CLL](#). Furthermore, side effects of treatment with [etoposide](#) or [teniposide](#) include [alopecia](#) and myelotoxicity, not [PML](#).

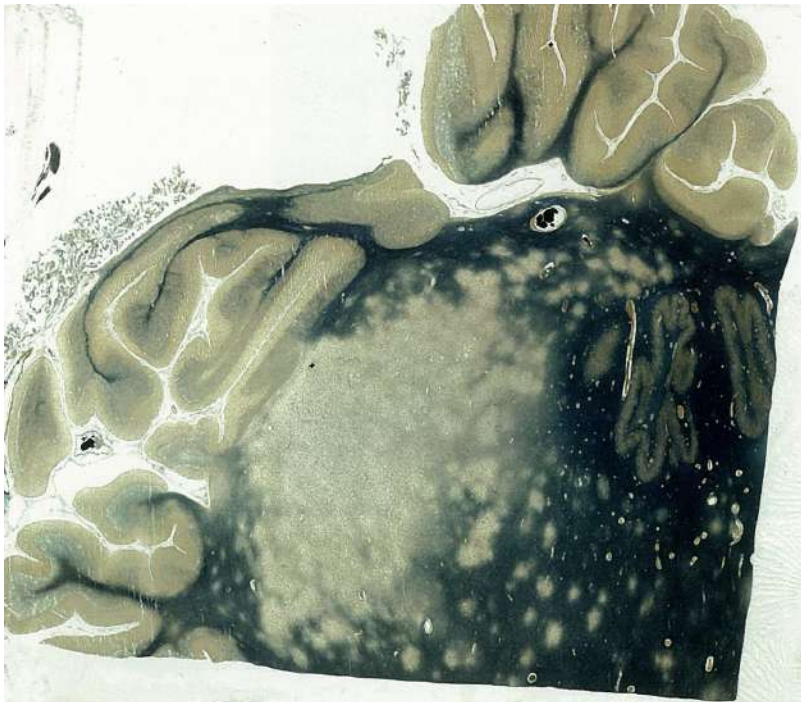
D - Monoclonal antibody against EGFR

Explanation Why

[Cetuximab](#) is a monoclonal [EGFR inhibitor](#) used in the treatment of stage IV [colorectal cancer](#) (without [KRAS](#) mutation), as well as head and neck cancer. This agent is not used in the treatment of [CLL](#). Side effects of [cetuximab](#) include [diarrhea](#), [skin](#) rash, and elevated [liver](#) enzymes, not [PML](#).

E - Monoclonal antibody against CD20+

Image



Explanation Why

[Rituximab](#) is a chimeric [monoclonal antibody](#) against the [B-cell](#) marker [CD20](#) that is used in the treatment of [CLL](#). This drug is associated with an increased risk of [PML](#), a [demyelinating](#) disease of the [CNS](#) caused by the destruction of [oligodendrocytes](#) secondary to reactivation of [JC virus](#). Other drugs associated with an increased risk of [PML](#) include [natalizumab](#), which is used to treat [multiple](#)

[sclerosis](#) and [Crohn disease](#). [PML](#) predominantly develops in patients with severe [immunosuppression](#) (e.g., patients with [AIDS](#) or those undergoing certain [immunosuppressive therapy](#)) and may present with decreased cognitive function, focal neurological deficits, and [seizures](#), as seen here.

Question # 17

A 52-year-old woman is brought to the emergency department for a severe, sudden-onset headache, light-sensitivity, and neck stiffness that began 30 minutes ago. A CT scan of the head shows hyperdensity between the arachnoid mater and the pia mater. The patient undergoes an endovascular procedure. One week later, she falls as she is returning from the bathroom. Neurologic examination shows 3/5 strength in the right lower extremity and 5/5 in the left lower extremity. Treatment with which of the following drugs is most likely to have prevented the patient's current condition?

	Answer	Image
A	Enalapril	
B	Nimodipine	
C	Fresh frozen plasma	
D	Aspirin	
E	Fosphenytoin	
F	Nitroglycerin	

Hint

This patient has signs of acute cerebral ischemia (new-onset unilateral lower extremity weakness) 7 days after a subarachnoid hemorrhage. Blood in the subarachnoid space leads to the release of vasoactive substances; this can bring about vasospasm in nonbleeding vessels that manifests with focal neurologic deficits.

Correct Answer

A - Enalapril

Explanation Why

Intravenous [enalapril](#) is used in the initial management of [hypertension](#) in [subarachnoid hemorrhage](#) because of its rapid onset of action. Five days after initial presentation, this patient's hemorrhage is no longer acute. [Enalapril](#) may also be indicated in cases of rebleeding with a [systolic](#) blood pressure > 160 mm Hg, but it is not used for prophylaxis of vasospasm.

B - Nimodipine

Explanation But

This patient should be evaluated with CT and angiography in order to distinguish a potential vasospasm from rebleeding and should receive prompt treatment to prevent [ischemic stroke](#).

Explanation Why

Oral [nimodipine](#) should be given after [subarachnoid hemorrhage](#) to prevent vasospasm, which can lead to [ischemic stroke](#). This patient's sudden-onset neurologic deficit 7 days after [SAH](#) is a common presentation of vasospasm, which is a complication in ~ 30% of [SAH](#) cases and is more common with [aneurysms](#). [Nimodipine](#) has been shown to reduce [morbidity](#) and [mortality](#) associated with [SAH](#), but the exact mechanism of benefit of [nimodipine](#) is unknown.

C - Fresh frozen plasma

Explanation Why

[Fresh frozen plasma](#) (FFP) is used for the treatment of severe [coagulopathy](#) (e.g., caused by [warfarin](#) overdose complicated by [intracranial hemorrhage](#)). This patient has no underlying conditions that would cause [coagulopathy](#) (such as [liver](#) failure) and does not take [warfarin](#). [FFP](#) is not used for

prophylaxis of vasospasm after [SAH](#).

D - Aspirin

Explanation Why

[Antiplatelet therapy](#) is for [secondary prevention](#) of [ischemic stroke](#). Given the onset of this patient's [ischemic](#) symptoms (7 days after [SAH](#)), they are more likely to be due to vasospasm than to a recurrent [ischemic](#) event caused by thrombosis. [Antiplatelet therapy](#) is not used for prophylaxis of vasospasm after [SAH](#).

E - Fosphenytoin

Explanation Why

[Fosphenytoin](#) is used to treat and prevent [seizures](#). While focal weakness may manifest after a [seizure](#) ([Todd palsy](#)), this patient has not had jerking movements or mental status changes that are characteristic of [seizure](#) activity. [Seizure](#) prophylaxis is not typically indicated for [subarachnoid hemorrhage](#) because it may be associated with worse neurologic outcomes. It may be appropriate in select cases when there is associated [intracerebral bleeding](#), unsecured [aneurysm](#), or concurrent intracranial pathology.

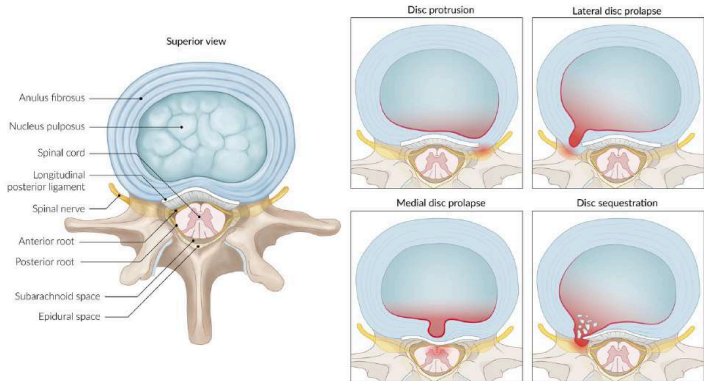
F - Nitroglycerin

Explanation Why

Blood pressure control is an important component of initial therapy for [subarachnoid hemorrhage](#) and rebleeding. However, [nitrates](#) such as [nitroglycerin](#) should be avoided because of their potential to raise [intracranial pressure](#). Moreover, [nitrates](#) are not used for prophylaxis of vasospasm after [SAH](#).

Question # 18

A 65-year-old woman with osteoarthritis comes to the physician because of severe lower back and left leg pain. She has chronic lower back pain that is usually well-controlled with ibuprofen, but 3 hours ago her back pain acutely worsened after she picked up her 3-year-old granddaughter. The pain radiates from her lower back over her left outer thigh and knee towards the top of her big toe. Physical examination shows a diminished posterior tibial reflex on the left side. Muscle strength is 5/5 in all extremities and there are no sensory deficits. Steroid injection into which of the following anatomical locations is most likely to relieve her symptoms?

	Answer	Image
A	Inferior facet joint	
B	Intervertebral disc	
C	Subdural space	
D	Subarachnoid space	
E	Intervertebral foramen	 The image contains five anatomical diagrams of a lumbar vertebra and its disc. The main diagram is a 'Superior view' showing the vertebra and disc with labels: Anulus fibrosus, Nucleus pulposus, Spinal cord, Longitudinal posterior ligament, Spinal nerve, Anterior root, Posterior root, Subarachnoid space, and Epidural space. To the right are four smaller diagrams showing different disc pathologies: 'Disc protrusion' (nucleus pushed back), 'Lateral disc prolapse' (nucleus pushed to the side), 'Medial disc prolapse' (nucleus pushed forward), and 'Disc sequestration' (nucleus broken into pieces).

Hint

Acute worsening of back pain in a 65-year-old woman after lifting something should raise suspicion for lateral disc herniation. The radiation of her pain to the lateral left leg suggests compression of the L5 nerve root.

Correct Answer

A - Inferior facet joint

Explanation Why

Facet joint osteoarthritis is a common cause of lower back [pain](#) in the elderly. While this patient does have chronic lower back [pain](#) that is well controlled with [NSAIDs](#), [pain](#) that radiates down the lower extremity suggests a [disc herniation](#) rather than facet joint osteoarthritis as the acute cause of her symptoms. Injection of [steroids](#) around the [facet joints](#) may temporarily alleviate her chronic [pain](#), but it would not address the cause of her acute symptoms.

B - Intervertebral disc

Explanation Why

[Disc herniation](#) occurs when a tear in the tough outer part of the disc ([annulus fibrosus](#)) allows the gelatinous inner substance of the disc ([nucleus pulposus](#)) to protrude and compress nearby [nerve roots](#). Surgical removal of the [intervertebral disc](#) may be considered in severe cases; however, a [steroid](#) injection into the disc would not improve her current symptoms of [nerve root](#) compression.

C - Subdural space

Explanation But

Unlike in the [spine](#), [cranial arachnoid mater](#) does not closely adhere to the [dura mater](#), which is why the formation of a [subdural space](#) can occur in the brain (e.g., due to hemorrhage from ruptured [bridging veins](#)).

Explanation Why

The [subdural space](#) is a potential cavity located between the [arachnoid mater](#) and the [dura mater](#). This space does not exist under physiological circumstances because the [arachnoid mater](#) and [dura](#)

[mater](#) of the [spine](#) are attached to each other.

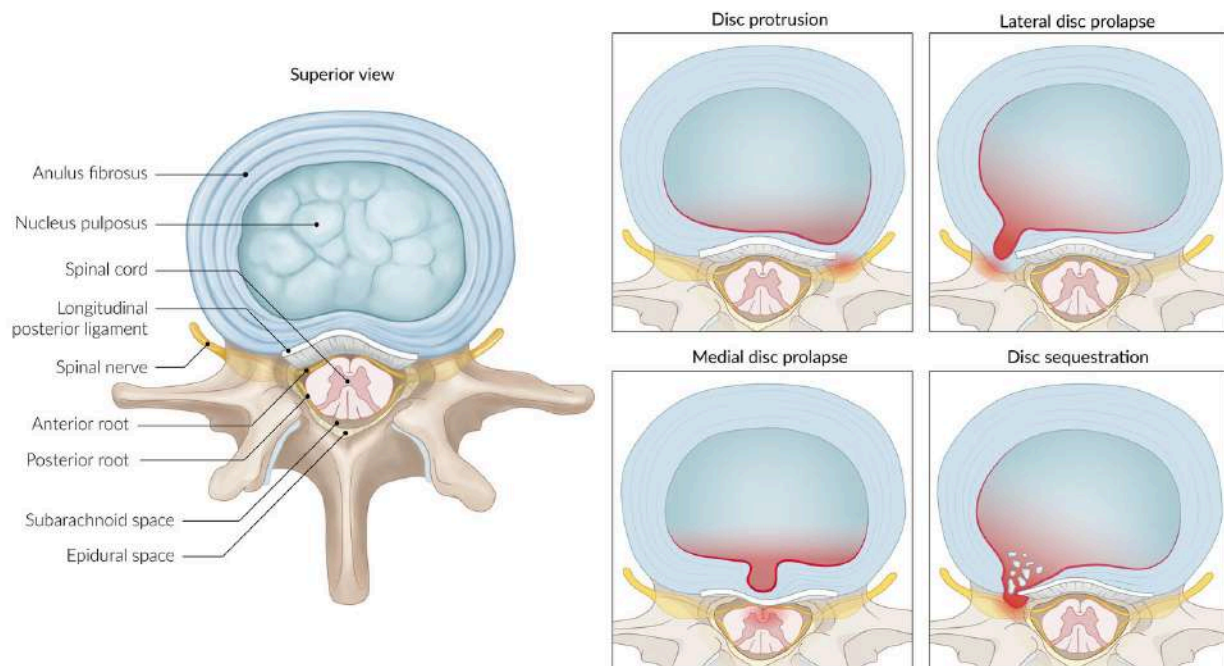
D - Subarachnoid space

Explanation Why

The [subarachnoid space](#) between [lumbar vertebrae](#) L3 and L5 is the target for [analgesic](#) medications in [spinal anesthesia](#). It is commonly used in surgical settings in which general anesthesia is not necessary and causes complete loss of motor and sensory function below the level of injection. [Steroid](#) injection into the [subarachnoid space](#) would not be an appropriate treatment for this patient with [disc herniation](#).

E - Intervertebral foramen

Image



Explanation Why

[Disc herniation](#) can cause [nerve root](#) compression, as the root exits the [central nervous system](#) through the [intervertebral foramen](#). [Steroid](#) injection at the [intervertebral foramen](#) helps reduce [inflammation](#) and [edema](#) around the [nerve root](#) and [spinal cord](#) and can relieve [nerve root](#) compression and alleviate symptoms of [disc herniation](#).

Question # 19

A 23-year-old man comes to the emergency department for 2 days of episodic headaches. The pain is most intense on his left forehead and eye. He had similar symptoms last summer. He has been taking indomethacin every 6 hours for the last 24 hours but has not had any relief. He has smoked 1 pack of cigarettes daily for the past 5 years. He works as an accountant and describes his work as very stressful. He appears restless. Physical examination shows drooping of the left eyelid, tearing of the eye, and rhinorrhea. The left pupil is 2 mm and the right pupil is 4 mm. There is localized tenderness along the right supraspinatus muscle. The remainder of the examination shows no abnormalities. Which of the following is the most likely diagnosis?

	Answer	Image
A	Giant cell arteritis	
B	Subarachnoid hemorrhage	
C	Medication overuse headache	
D	Cluster headache	

	Answer	Image
E	Trigeminal neuralgia	
F	Migraine headache	
G	Tension headache	

Hint

This headache can be aborted by administering 100% oxygen.

Correct Answer

A - Giant cell arteritis

Explanation Why

[Giant cell arteritis](#) ([GCA](#)) is a rheumatic disorder that can present with a unilateral [headache](#), [jaw claudication](#), and [amaurosis fugax](#). This patient's age, lacrimation, [miosi](#)s, and [rhinorrhea](#) are more consistent with a different diagnosis.

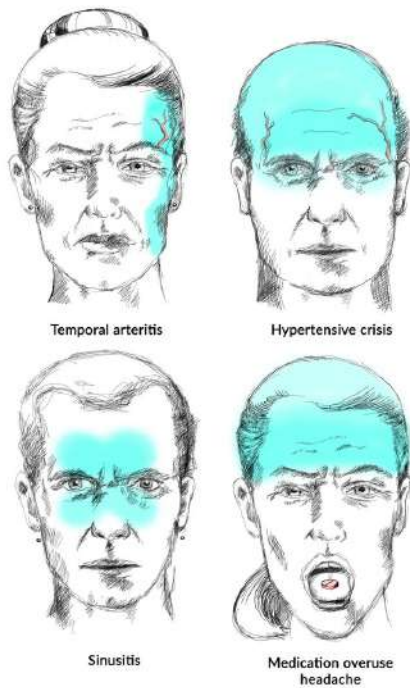
B - Subarachnoid hemorrhage

Explanation Why

[Subarachnoid hemorrhage](#) ([SAH](#)) classically manifests with an acute, holocephalic, excruciating [headache](#) ("[thunderclap headache](#)") and is most commonly caused by the rupture of intracranial [aneurysms](#). Although smoking is a known [risk factor](#) for [SAH](#) and patients can present with various neurological findings (including [miosi](#)s), this patient lacks other important clinical signs of [SAH](#) (e.g., meningism, altered consciousness) and has had symptoms for 2 days. Moreover, neither [conjunctival](#) symptoms nor [rhinorrhea](#) is consistent with [SAH](#).

C - Medication overuse headache

Image

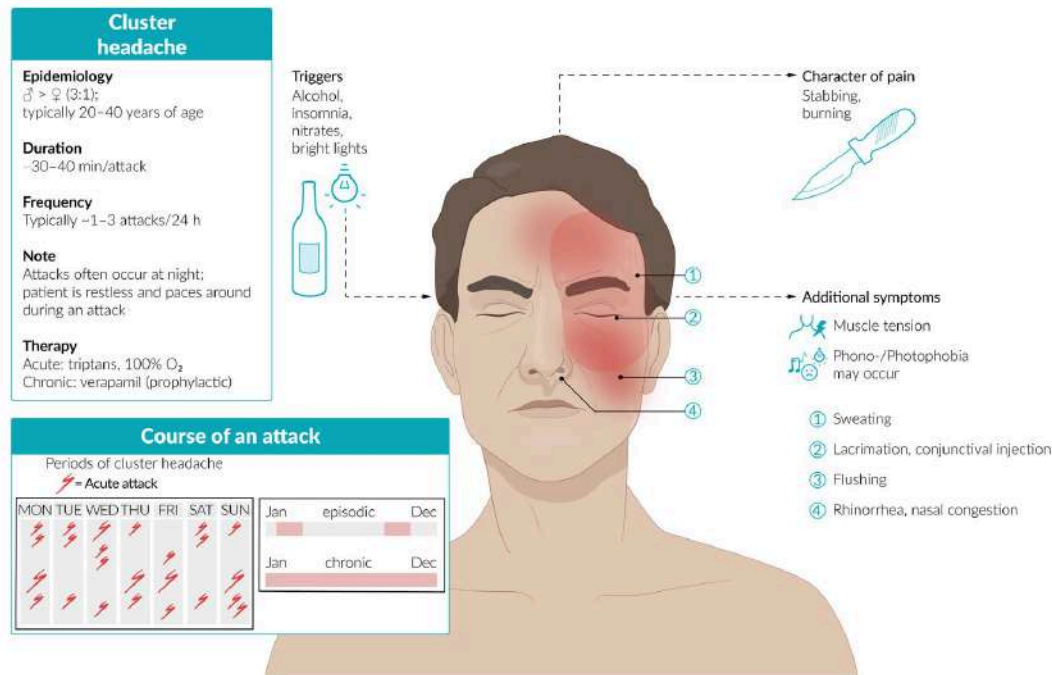


Explanation Why

[Medication overuse headache \(MOH\)](#) typically manifests as a dull, long-lasting [headache](#) in the setting of regular use of [headache](#) medication (defined as ≥ 10 days per month for ≥ 3 months). The patient's acute [indomethacin](#) use is not long enough to induce [MOH](#). Furthermore, [MOH](#) is associated with nausea but would not explain the lacrimation or [rhinorrhea](#) seen in this patient.

D - Cluster headache

Image



Explanation Why

[Cluster headache](#) is characterized by agonizing, unilateral periorbital or temporal [pain](#). It is more common in men and attacks are commonly accompanied by lacrimation and [rhinorrhea](#). Pupillary changes can be seen as part of partial [Horner syndrome](#) (no decreased vision). [Cluster headache](#) does not respond to [NSAIDs](#) but is treated with oxygen and [triptans](#).

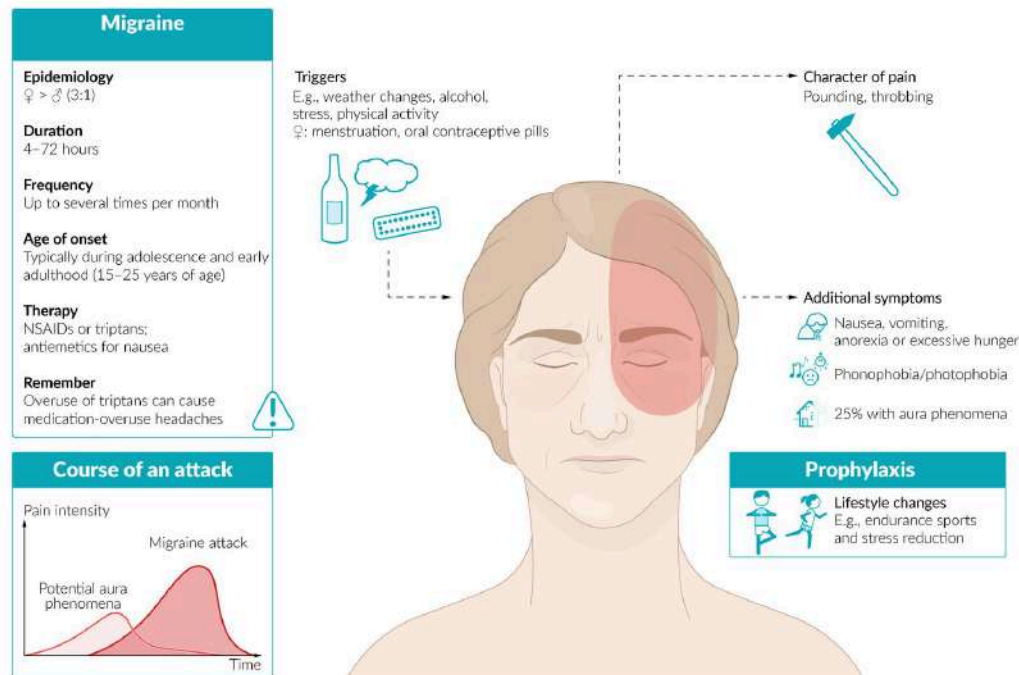
E - Trigeminal neuralgia

Explanation Why

[Trigeminal neuralgia](#) is characterized by a paroxysmal, severe shooting [headache](#) affecting the distribution of the [trigeminal nerve](#) that may be triggered by certain movements (e.g., talking). [Trigeminal neuralgia](#) is typically unilateral but is not associated with lacrimation or [rhinorrhea](#).

F - Migraine headache

Image

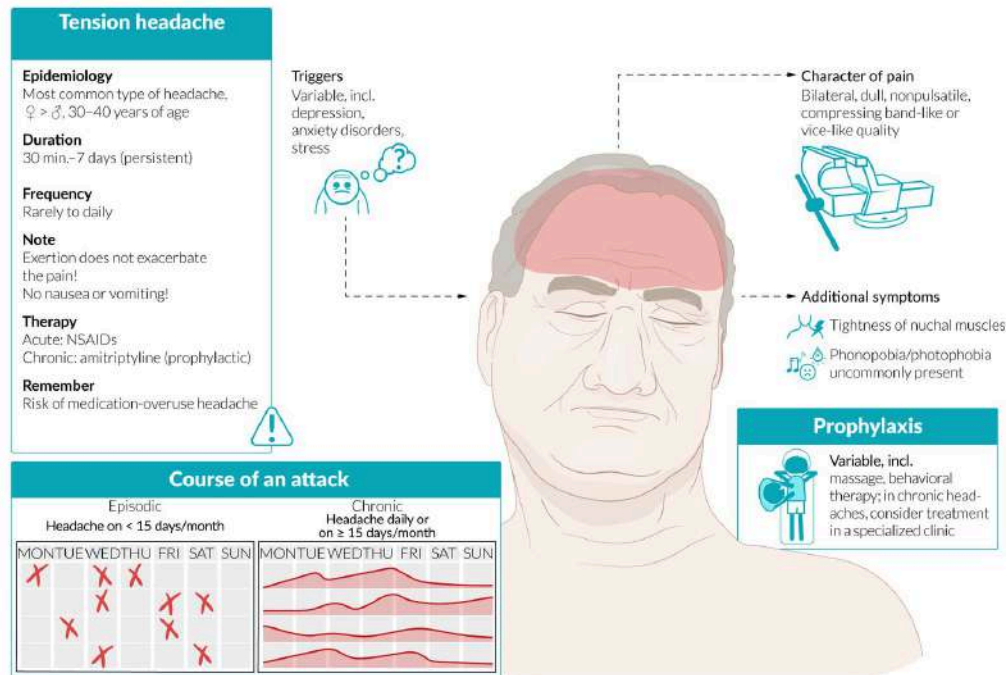


Explanation Why

A [migraine](#) is characterized as recurrent pulsating and throbbing [headache](#) that lasts multiple hours or days and is usually unilateral. [Migraine](#) is typically associated with nausea, photophobia, on hypersensitivity to sound, and is exacerbated by exercise, none of which is seen in this patient. Furthermore, [migraine headaches](#) do not manifest with [rhinorrhea](#), lacrimation, or [miosis](#).

G - Tension headache

Image



Explanation Why

[Tension headaches](#) are characterized by episodic, mild to moderate, non-pulsating, dull, holocranial or bifrontal [headaches](#). Although [risk factors](#) include stress, [tension headaches](#) are not usually unilateral and do not present with lacrimation or [rhinorrhea](#). Moreover, [tension headaches](#) are relieved with [NSAIDs](#).

Question # 20

A 63-year-old man comes to the physician for blurry vision and increased difficulty walking over the past month. He feels very fatigued after watering his garden but feels better after taking a nap. He has not had any recent illness. He has smoked one pack of cigarettes daily for 35 years. Examination shows drooping of the upper eyelids bilaterally and diminished motor strength in the upper extremities. Sensation to light touch and deep tendon reflexes are intact. An x-ray of the chest shows low lung volumes bilaterally. A drug with which of the following mechanisms of action is most appropriate for this patient?

	Answer	Image
A	Inhibition of muscarinic ACh receptor	
B	Regeneration of acetylcholinesterase	
C	Stimulation of D2 receptors	
D	Stimulation of β_2 adrenergic receptors	
E	Inhibition of acetylcholinesterase	

Hint

This patient has ptosis as well as weakness that is worse with activity and improves with rest. These clinical features suggest a diagnosis of myasthenia gravis (MG).

Correct Answer

A - Inhibition of muscarinic ACh receptor

Explanation Why

[Muscarinic ACh receptor](#) antagonists (e.g., [atropine](#)) can be used to treat patients with excess [ACh](#) due to [organophosphate poisoning](#) or cholinesterase inhibitor overdose. However, clinical features indicating excess [ACh](#), such as [diarrhea](#), increased secretions, and muscle [tremors](#), are absent in this patient.

B - Regeneration of acetylcholinesterase

Explanation Why

Choline-reactivating [oximes](#), such as [pralidoxime](#), are effective [antidotes](#) in [organophosphate \(insecticide\) poisoning](#). Patients with [organophosphate poisoning](#) present with increased salivation, lacrimation, [diarrhea](#), bronchospasm, [tremor](#), and paralysis, which this patient does not have.

C - Stimulation of D2 receptors

Explanation But

[D2 receptor agonists](#) can also be used to treat [restless leg syndrome](#) and [prolactinomas](#).

Explanation Why

[D2 receptors agonists](#) (e.g., [bromocriptine](#) and [pramipexole](#)) can be used to treat [Parkinson disease](#) but are not used in the management of MG. While [Parkinson disease](#) manifests with weakness, it also presents with other symptoms such as [tremor](#), [rigidity](#), [bradykinesia](#), [masked face](#), not the bilateral [eyelid](#) droop and decreased [lung volumes](#) seen in this patient.

D - Stimulation of β 2 adrenergic receptors

Explanation Why

[\$\beta\$ 2 adrenergic receptor agonists](#) (e.g., [albuterol](#), [salmeterol](#), and [formoterol](#)) may be used to treat [COPD](#). Although this patient's smoking history puts him at increased risk of developing [COPD](#), he lacks all of the typical symptoms, such as chronic [cough](#) with [sputum](#) and [dyspnea](#). β 2 adrenergic [agonists](#) are not effective in [myasthenia gravis](#) (MG).

E - Inhibition of acetylcholinesterase

Explanation But

Some [cholinesterase inhibitors](#) can also cross the [blood-brain barrier](#) (e.g., [physostigmine](#)) and can be used to treat [glaucoma](#) or [atropine](#) overdose.

Explanation Why

[Cholinesterase inhibitors](#) are used to manage the symptoms of [myasthenia gravis](#) (MG) because they increase the availability of endogenous [acetylcholine](#) ([ACh](#)) in the [neuromuscular junction](#), which competes with the [ACh](#) receptor [antibodies](#) that would otherwise block [ACh](#) receptors. [Pyridostigmine](#) or alternatively neostigmine are the preferred drugs, since they only act on peripheral [ACh](#) receptors and do not cross the [blood-brain barrier](#), which limits their adverse effects.

Question # 21

A 27-year-old man comes to the physician because of a 1-day history of right-sided facial weakness and sound intolerance. Three days ago, he hit the right side of his head in a motor vehicle collision. He neither lost consciousness nor sought medical attention. Physical examination shows drooping of the mouth and ptosis on the right side. Sensation over the face is not impaired. Impedance audiometry shows an absence of the acoustic reflex in the right ear. Which of the following muscles is most likely paralyzed in this patient?

	Answer	Image
A	Tensor tympani	
B	Posterior cricoarytenoid	
C	Stylopharyngeus	
D	Cricothyroid	
E	Anterior belly of the digastric	
F	Stylohyoid	

Hint

Asymmetric facial weakness and hyperacusis with an absent acoustic reflex indicate palsy of the facial nerve, which innervates structures derived from the 2nd branchial arch. An undisplaced temporal bone fracture can result in delayed-onset facial nerve palsy due to edema that leads to nerve compression.

Correct Answer

A - Tensor tympani

Explanation But

The [mandibular branch of the trigeminal nerve](#) passes through the foramen ovale in the [temporal bone](#). Infrequently, [temporal bone fractures](#) can cause [mandibular nerve](#) palsies, resulting in paralysis of the [muscles of mastication](#) and decreased/absent sensation of the ipsilateral lower half of the face.

Explanation Why

The [tensor tympani muscle](#), which dampens loud sounds such as chewing or thunder, is innervated by the [mandibular branch of the trigeminal nerve](#). Therefore, a [facial nerve palsy](#) would not cause paralysis of this muscle.

B - Posterior cricoarytenoid

Explanation Why

The [posterior cricoarytenoid muscle](#), which opens the [vocal cords](#), is derived from the [6th branchial arch](#) and is innervated by the [recurrent laryngeal nerve](#). A [facial nerve palsy](#) would not cause paralysis of this muscle.

C - Stylopharyngeus

Explanation Why

The [stylopharyngeus muscle](#), which elevates the [larynx](#) and pharynx during [swallowing](#), is derived from the [3rd branchial arch](#) and innervated by the [glossopharyngeal nerve](#). A [facial nerve palsy](#) would not cause paralysis of this muscle.

D - Cricothyroid

Explanation Why

The [cricothyroid muscle](#), which tenses and elongates the [vocal cords](#), is derived from the [4th branchial arch](#) and is innervated by the external portion of the [superior laryngeal nerve](#). A [facial nerve palsy](#) would not cause paralysis of this muscle.

E - Anterior belly of the digastric

Explanation Why

The [anterior](#) belly of the [digastric muscle](#), which assists the [posterior](#) belly of the [digastric muscle](#) in [jaw](#) opening, is derived from the [1st branchial arch](#) and is innervated by the mylohyoid nerve. A [facial nerve palsy](#) would not cause paralysis of this muscle.

F - Stylohyoid

Explanation Why

The [stylohyoid muscle](#), which elevates the [tongue](#) and moves the [hyoid bone](#) backward during [swallowing](#), develops from the [2nd branchial arch](#). Therefore, [facial nerve palsy](#) causes paralysis of this muscle. Other muscles that are derived from the [2nd branchial arch](#) and thus innervated by the [facial nerve](#) include the facial muscles, [platysma](#), [posterior](#) belly of the [digastric](#), and [stapedius](#). [Stapedius](#) involvement is demonstrated in this case by [hyperacusis](#) with absent [acoustic reflex](#).

Question # 22

A 26-year-old woman comes to the physician because of painful paresthesia in her right foot. Examination shows decreased sensation in the first interdigital space and a hallux valgus deformity. This patient's paresthesia is most likely caused by compression of which of the following nerves?

	Answer	Image
A	Superficial peroneal nerve	
B	Tibial nerve	
C	Deep peroneal nerve	
D	Sural nerve	
E	Saphenous nerve	

	Answer	Image
F	Medial plantar nerve	

Hint

Weakness of toe dorsiflexion may also be seen in this patient.

Correct Answer

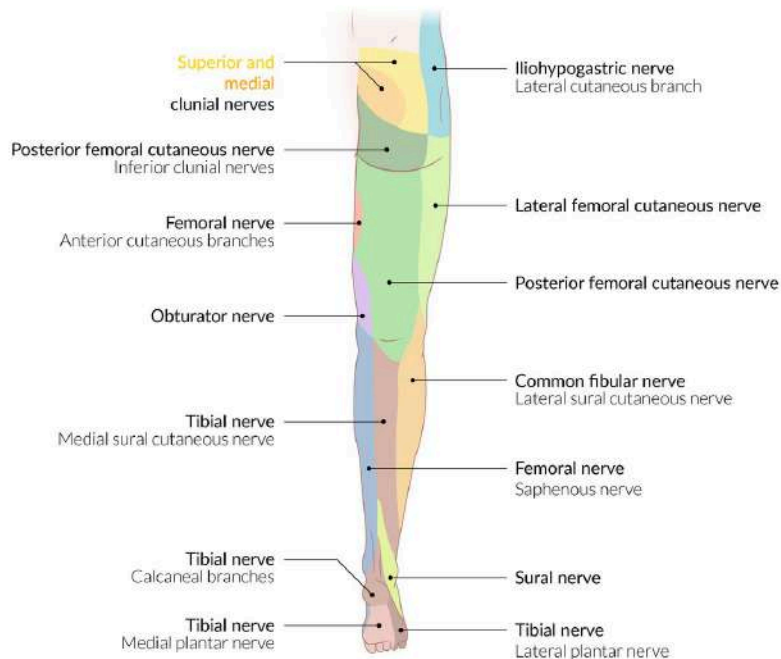
A - Superficial peroneal nerve

Explanation Why

The [superficial peroneal nerve](#) provides sensory innervation to the [anterior](#) and [lateral](#) leg and [dorsal](#) foot, with the important exception of the first web space, which is the area of decreased sensation in this patient. This nerve also plays an important role in ankle [eversion](#) by providing motor innervation to the [peroneus longus](#) and [peroneus brevis](#) (i.e., the [lateral](#) compartment of the lower leg).

B - Tibial nerve

Image



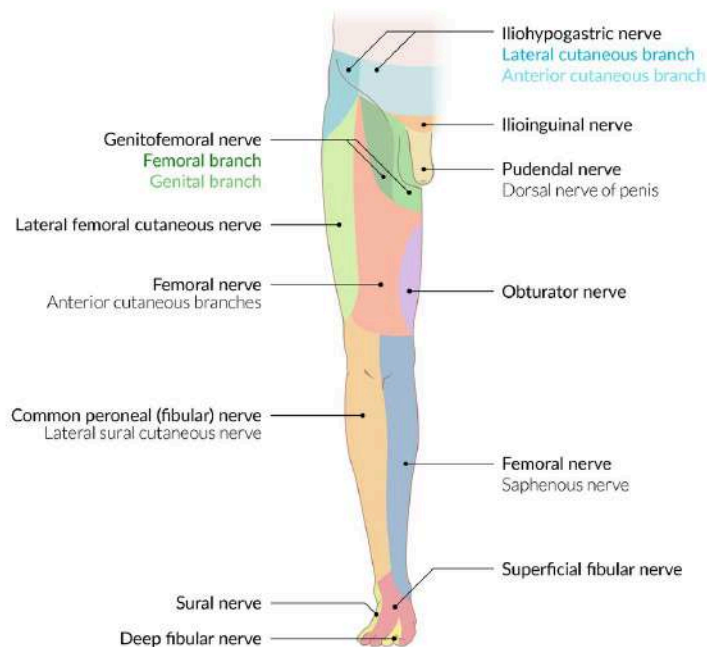
Explanation Why

The [tibial nerve](#), a mixed motor and sensory nerve, carries sensory input from the [plantar](#) surface of

the foot and the area innervated by its branch, the [sural nerve](#). It also innervates the muscles of the [posterior compartment of the leg](#) (e.g., [gastrocnemius](#), [soleus](#), [plantaris](#), and the deep toe flexors). The [tibial nerve](#) does not provide sensory innervation to the first web space, the area of decreased sensation in this patient.

C - Deep peroneal nerve

Image



Explanation Why

The [deep peroneal nerve](#) provides sensory innervation to the [skin](#) between the first two toes. It also provides motor innervation to the muscles of the [anterior compartment of the leg](#) (e.g., [tibialis anterior](#), [extensor hallucis longus](#), [extensor digitorum longus](#)), which [dorsiflex](#) the toes and [ankle joint](#); thus, injury to the nerve can result in a [high-stepping gait](#). [Deep peroneal nerve](#) compression can be caused by tight-fitting shoes, which are suggested by this patient's [hallux valgus](#) deformity ([bunion](#)). It may also occur following trauma, especially [navicular fracture](#).

D - Sural nerve

Explanation Why

The [sural nerve](#) is a pure sensory nerve that supplies the [skin](#) over the posterolateral aspect of the [distal](#) third of the leg and the [lateral](#) border of the foot. The [sural nerve](#) does not provide sensation to the first web space, which is the area of decreased sensation in this patient.

E - Saphenous nerve

Explanation Why

The [saphenous nerve](#) is a pure sensory nerve that innervates the [medial](#) aspect of the calf and ankle. This nerve does not provide sensation to the first web space, which is the area of decreased sensation in this patient.

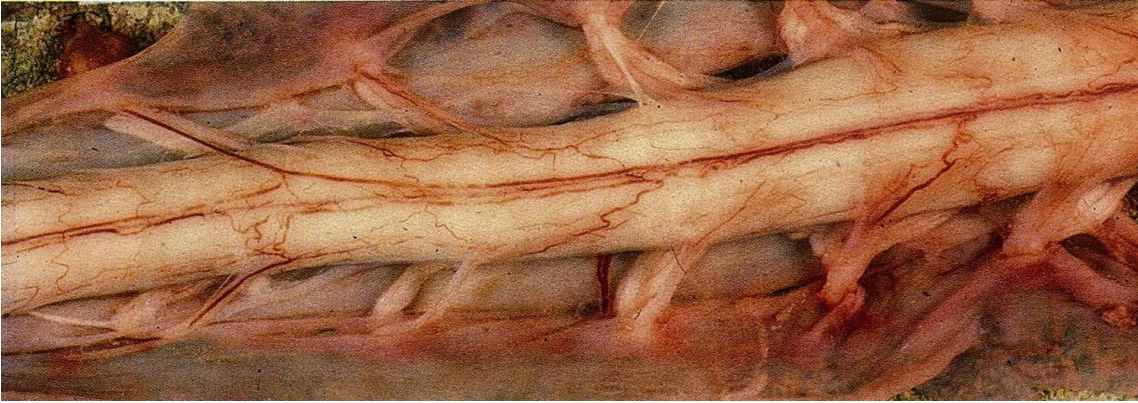
F - Medial plantar nerve

Explanation Why

The [medial plantar](#) nerve is a [distal](#) branch of the [tibial nerve](#) and provides sensory innervation to the [medial](#) aspect of the [plantar](#) foot, including the [medial](#) three and a half toes. It also provides motor innervation to the intrinsic toe flexors and abductor hallucis. The [medial plantar](#) nerve does not provide sensation to the first web space, which is the area of decreased sensation in this patient.

Question # 23

A 62-year-old woman is brought to the physician because of 6 months of progressive weakness in her arms and legs. During this time, she has also had difficulty swallowing and holding her head up. Examination shows pooling of oral secretions. Muscle strength and tone are decreased in the upper extremities. Deep tendon reflexes are 1+ in the right upper and lower extremities, 3+ in the left upper extremity, and 4+ in the left lower extremity. Sensation to light touch, pinprick, and vibration are intact. Which of the following is the most likely diagnosis?

	Answer	Image
A	Amyotrophic lateral sclerosis	
B	Guillain-Barré syndrome	
C	Syringomyelia	
D	Myasthenia gravis	
E	Spinal muscular atrophy	

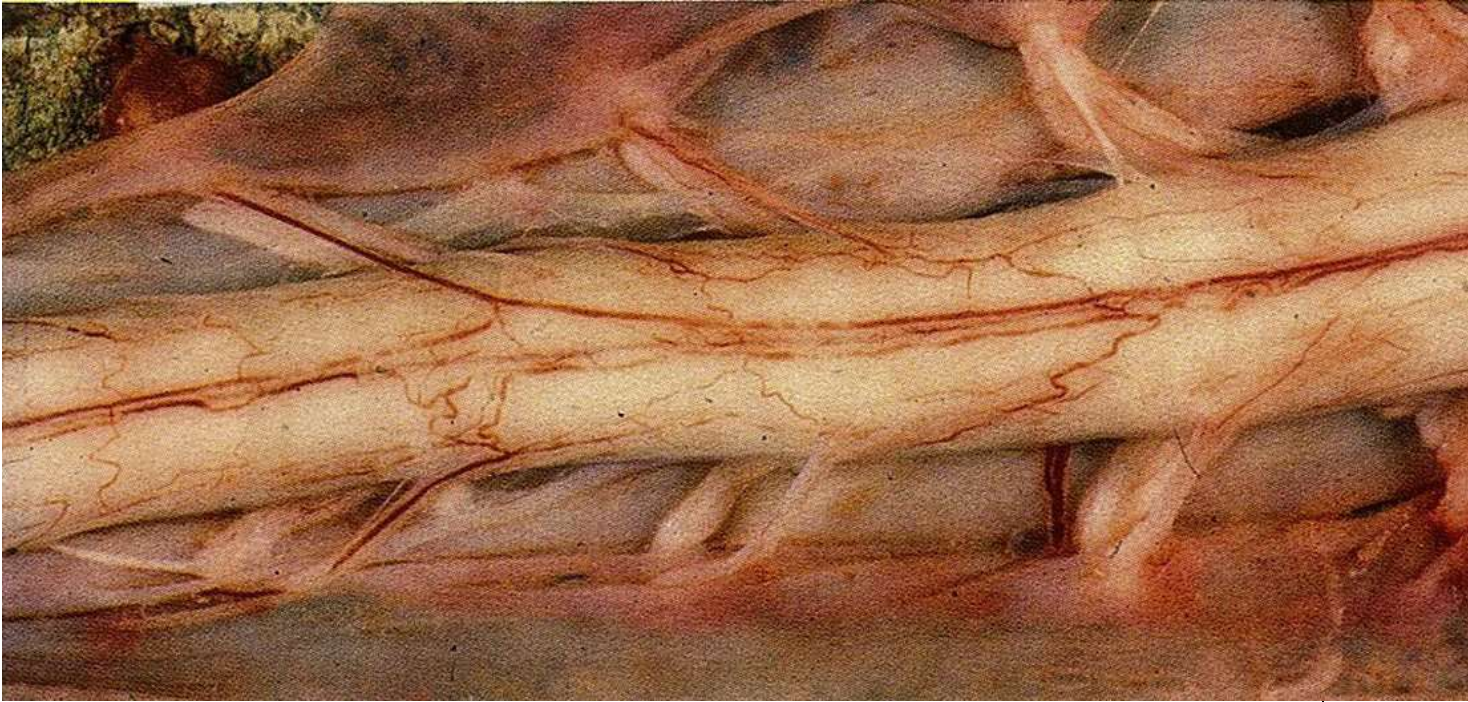
Hint

This patient's progressive weakness, upper motor neuron signs (e.g., hyperreflexia), and lower motor neuron signs (e.g., muscle weakness and decreased muscle tone), and intact sensation is consistent with a condition caused by selective degeneration of motor fibers.

Correct Answer

A - Amyotrophic lateral sclerosis

Image



Explanation Why

[Amyotrophic lateral sclerosis](#) (ALS) typically presents between 50–70 years of age with progressively worsening features of both [upper motor neuron](#) degeneration ([hyperreflexia](#), increased muscle tone, [Babinski sign](#)) and [lower motor neuron](#) degeneration ([hyporeflexia](#), decreased muscle tone, [atrophy](#)), as seen in this patient. While [dysphagia](#) from bulbar [atrophy](#) is present in approximately 20% of patients at disease onset, it is most often a late clinical feature and suggests a poor prognosis.

B - Guillain-Barré syndrome

Explanation Why

Guillain-Barré Syndrome (GBS) can manifest with weakness in the upper and lower extremities, as seen in this patient. However, it usually begins with back [pain](#) (due to [nerve root inflammation](#)) and rapidly progressive symmetric ascending paresis in the legs after a recent infection (e.g. [Campylobacter jejuni](#) and [CMV](#)). Moreover, GBS is associated with symmetric [hyporeflexia](#) (not [hyperreflexia](#)) due to damage of [Schwann cells](#), which impairs [signal transduction](#) in peripheral nerves. Additionally, it usually manifests with peripheral symmetric [paresthesias](#), in contrast to this patient's normal sensory exam.

C - Syringomyelia

Explanation Why

[Syringomyelia](#) can result from an inborn defect or be caused by trauma (e.g. motor vehicle collision). It most commonly presents with loss of [pain](#) and temperature sensation, unlike in this patient, and [flaccid paralysis](#) in a typical cape-like distribution involving the neck, shoulders, and arms. The presence of bulbar symptoms ([dysphagia](#)), [hyperreflexia](#), and the lack of sensory symptoms suggest another diagnosis.

D - Myasthenia gravis

Explanation Why

[Myasthenia gravis](#) (MG) can present with generalized muscle weakness most commonly involving the extraocular or [eyelid](#) muscles that becomes worse with prolonged muscle activity. This patient's weakness is unrelated to activity and the presence of upper/[lower motor neuron signs](#) is inconsistent with this diagnosis. Also, [deep tendon reflexes](#) are usually normal in patients with MG.

E - Spinal muscular atrophy

Explanation Why

[Spinal muscular atrophy](#) (SMA) can manifest with weakness in the upper and lower extremities, as seen in this patient, due to degeneration of [anterior horn cells](#). It also causes bulbar symptoms, while sensations are preserved. In contrast to this patient's asymmetric neurological findings, patients with SMA usually present with symmetric diffuse [proximal](#) muscle weakness that is more pronounced in the lower extremities, and [hyporeflexia](#), not [hyperreflexia](#). Moreover, SMA rarely manifests in late adulthood.

Question # 24

A 61-year-old man with a history of type 1 diabetes mellitus and depression is brought to the emergency department because of increasing confusion and fever over the past 14 hours. Four days ago, he was prescribed metoclopramide by his physician for the treatment of diabetic gastroparesis. His other medications include insulin and paroxetine. His temperature is 39.9°C (103.8°F), pulse is 118/min, and blood pressure is 165/95 mm Hg. Physical examination shows profuse diaphoresis and flushed skin. There is generalized muscle rigidity and decreased deep tendon reflexes. His serum creatine kinase is 1250 U/L. Which of the following drugs is most likely to also cause this patient's current condition?

	Answer	Image
A	Nortriptyline	
B	Desflurane	
C	Fluphenazine	
D	Methamphetamine	
E	Scopolamine	
F	Tranlycypromine	

Hint

This patient's clinical features of hyperthermia, generalized muscle rigidity, altered mental status, autonomic instability (tachycardia, hypertension) in combination with elevated creatine kinase (indicating muscle breakdown) suggest neuroleptic malignant syndrome (NMS).

Correct Answer

A - Nortriptyline

Explanation Why

[Nortriptyline](#), a [tricyclic antidepressant](#), is not associated with [NMS](#). It can, however, cause [serotonin syndrome](#) (SS), which shares many of the same features of [NMS](#), including [fever](#), [diaphoresis](#), psychomotor agitation, and altered mental status. While this patient is taking [paroxetine](#), which puts him at risk of developing SS, the condition usually also presents with gastrointestinal symptoms (e.g., [diarrhea](#)), and neurological findings of [tremor](#), [hyperreflexia](#), myoclonus, and/or [ataxia](#), none of which he has.

B - Desflurane

Explanation Why

[Desflurane](#), a [volatile anesthetic](#), is not a cause of [NMS](#). However, an important complication of inhalation of [desflurane](#) is [malignant hyperthermia](#) (MH). Clinically, MH can present similarly to [NMS](#) with hyperthermia, severe muscle [rigidity](#), and autonomic instability, but the progression is typically hyperacute over minutes to hours, which is not the case in this patient. In addition, MH is usually triggered by [volatile anesthetics](#) or [succinylcholine](#) during anesthesia, which this patient has not recently undergone.

C - Fluphenazine

Explanation But

The most important therapeutic measure is the discontinuation of the triggering substance. This patient should be transferred to the ICU for supportive treatment including [fluid resuscitation](#), cardiorespiratory management, and measures to lower body temperature. Administration of [dopamine agonists](#) (e.g., [bromocriptine](#)) and/or [dantrolene](#) can be considered.

Explanation Why

High-potency antipsychotics such as fluphenazine are the most common cause of neuroleptic malignant syndrome (NMS), but low-potency or atypical antipsychotics, as well as antiemetics like metoclopramide (which was likely the triggering substance in this patient), have also been associated with NMS. While symptoms usually develop during the first 2 weeks of therapy, as seen in this patient, NMS may also develop after years of continuous therapy and without any associated increase of dose. Nonetheless, higher doses or switching antipsychotics are risk factors for the development of NMS.

D - Methamphetamine

Explanation Why

Methamphetamine and other amphetamines do not cause NMS, but intoxication with these substances can present with similar symptoms of psychomotor agitation, diaphoresis, hyperthermia, altered mental status, and autonomic instability. However, generalized muscle rigidity would not be expected and the relatively slow progression of this patient's symptoms over the course of 14 hours would not be typical of intoxication with amphetamines.

E - Scopolamine

Explanation Why

Scopolamine, a muscarinic antagonist, does not cause NMS, but it may induce anticholinergic syndrome, which can, like NMS, cause tachycardia, hyperthermia with flushed skin, and confusion. However, muscle rigidity and an associated increase in CK levels are not seen in anticholinergic syndrome. Furthermore, anticholinergic syndrome does not cause diaphoresis, as seen in this patient. Instead, one of its hallmark features is dry skin due to anhidrosis.

F - Tranylcypromine

Explanation Why

[Tranylcypromine](#), a [monoamine oxidase inhibitor](#), is not associated with [NMS](#). However, if combined with foods rich in [tyramine](#) (e.g., cheese or red wine), it can result in [hypertensive crisis](#). While this patient has [elevated blood pressure](#), it is not in the range of [hypertensive crisis](#) (i.e., > 180/120 mmHg).

Question # 25

A 31-year-old man comes to the physician because of a 4-week history of a painless lump near the left wrist and tingling pain over his left hand. Physical examination shows a transilluminating, rubbery, fixed, non-tender mass over the lateral volar aspect of the left wrist. There is decreased sensation to pinprick on the thumb, index finger, middle finger, and radial half of the ring finger of the left hand. The tingling pain is aggravated by tapping over the swelling. Which of the following adjacent structures is at risk of entrapment if this mass persists?

	Answer	Image
A	Ulnar artery	
B	Extensor pollicis brevis tendon	
C	Flexor pollicis longus tendon	
D	Flexor carpi radialis tendon	
E	Ulnar nerve	

Hint

This patient has a transilluminating, firm mass over the wrist, which is most likely a ganglion cyst. Decreased sensation and paresthesia in the median nerve distribution along with a positive Tinel's sign indicate that the cyst is in a location where it is causing compression of the carpal tunnel (e.g., carpal tunnel syndrome).

Correct Answer

A - Ulnar artery

Explanation But

The ulnar artery passes through the [Guyon canal](#), together with the ulnar nerve.

Explanation Why

The ulnar artery lies [superficial](#) and ulnar to the [carpal tunnel](#). [Arteries](#) are relatively resistant to [mass effect](#) (e.g., stenosis or obstruction) from local soft tissue masses because of their robust, muscular arterial walls. Moreover, the ulnar artery is not contained within the [carpal tunnel](#), so the increased pressure from this patient's [ganglion cyst](#) would be unlikely to exert an effect here.

B - Extensor pollicis brevis tendon

Explanation Why

The [extensor pollicis brevis](#) tendon runs along the radial aspect of the wrist, midway between the [volar](#) and [dorsal](#) surfaces. It is neither contained within nor adjacent to the [carpal tunnel](#). In this case of [carpal tunnel syndrome](#) caused by a [ganglion cyst](#), structures within the [carpal tunnel](#) are more likely to be affected by the increasing tunnel pressure than structures lying outside the [carpal tunnel](#).

C - Flexor pollicis longus tendon

Explanation Why

The [flexor pollicis longus](#) tendon travels through the [carpal tunnel](#) with the median nerve. The other structures that traverse the [carpal tunnel](#) are the four tendons of the [flexor digitorum profundus](#) and the four tendons of the [flexor digitorum superficialis](#). Further growth of this patient's [ganglion cyst](#) could endanger any of the structures within the [carpal tunnel](#).

D - Flexor carpi radialis tendon

Explanation Why

The [flexor carpi radialis](#) tendon runs radial to and outside the [carpal tunnel](#). It is not contained within the [carpal tunnel](#). In this case of [carpal tunnel syndrome](#) caused by a [ganglion cyst](#), structures within the [carpal tunnel](#) are more likely to be affected by the increasing tunnel pressure than structures lying outside the [carpal tunnel](#).

E - Ulnar nerve

Explanation But

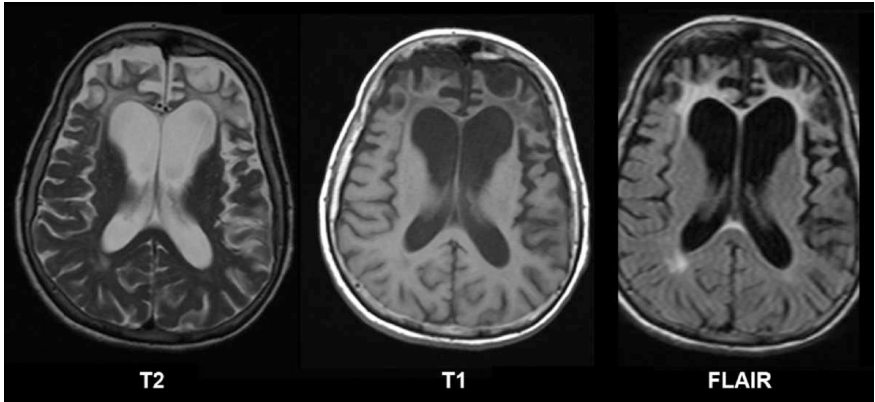
The ulnar nerve is affected in [Guyon canal syndrome](#).

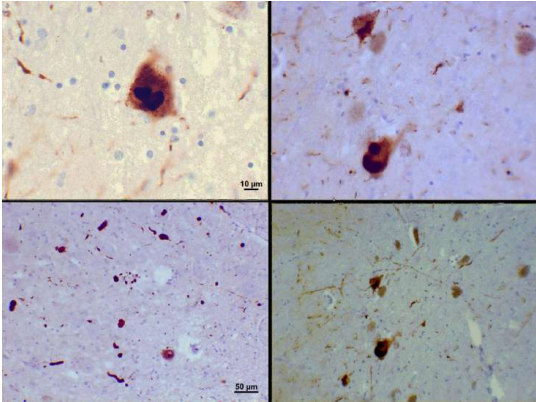
Explanation Why

The ulnar nerve lies [superficial](#) and ulnar to the [carpal tunnel](#). In this case of [carpal tunnel syndrome](#) caused by a [ganglion cyst](#), structures within the [carpal tunnel](#) are more likely to be affected by the increasing tunnel pressure than structures lying outside the [carpal tunnel](#).

Question # 26

A 62-year-old man is brought to the physician by his wife for increased forgetfulness and unsteady gait over the past 3 months. He is a journalist and has had difficulty concentrating on his writing. He also complains of urinary urgency recently. His temperature is 36.8°C (98.2°F) and blood pressure is 139/83 mm Hg. He is oriented only to person and place. He is able to recall 2 out of 3 words immediately and 1 out of 3 after five minutes. He has a slow, broad-based gait and takes short steps. Neurological examination is otherwise normal. Urinalysis is normal. Which of the following is the most likely diagnosis?

	Answer	Image
A	Alzheimer disease	
B	Normal pressure hydrocephalus	
C	Vascular dementia	
D	Frontotemporal dementia	

	Answer	Image
E	Lewy body dementia	
F	Vitamin B12 deficiency	

Hint

This patient's confusion, ataxic gait, and urinary symptoms suggest a cause of reversible dementia in older adults.

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Correct Answer

A - Alzheimer disease

Explanation Why

[Alzheimer disease](#) is the most common cause of [dementia](#), with increasing [prevalence](#) after 60 years of age. [Memory](#) impairment is the cardinal and most common initial symptom, while behavioral symptoms, [primitive reflexes](#), and [urinary incontinence](#) may manifest late in the disease course. The early development of gait disturbances in this patient is not typical of [Alzheimer disease](#).

B - Normal pressure hydrocephalus

Image



Explanation Why

[Normal pressure hydrocephalus](#) (NPH) manifests with gait instability, cognitive disturbance, and

[urinary incontinence](#) – the classic “wet, wacky, and wobbly” triad. Gait changes are typically symmetrical, while cognitive impairment primarily takes the form of decreased attention span and concentration. NPH is an important diagnosis to consider in a patient with [dementia](#), as it may be reversible if the [hydrocephalus](#) is addressed (e.g., with a [lumbar puncture](#) to remove [CSF](#)). In most patients > 60 years of age, the accumulation of [CSF](#) is idiopathic, but it may also occur due to secondary causes (e.g., [inflammation](#), hemorrhage) that lead to obstruction of the subarachnoid villi that normally resorb [CSF](#) in the [ventricular system](#).

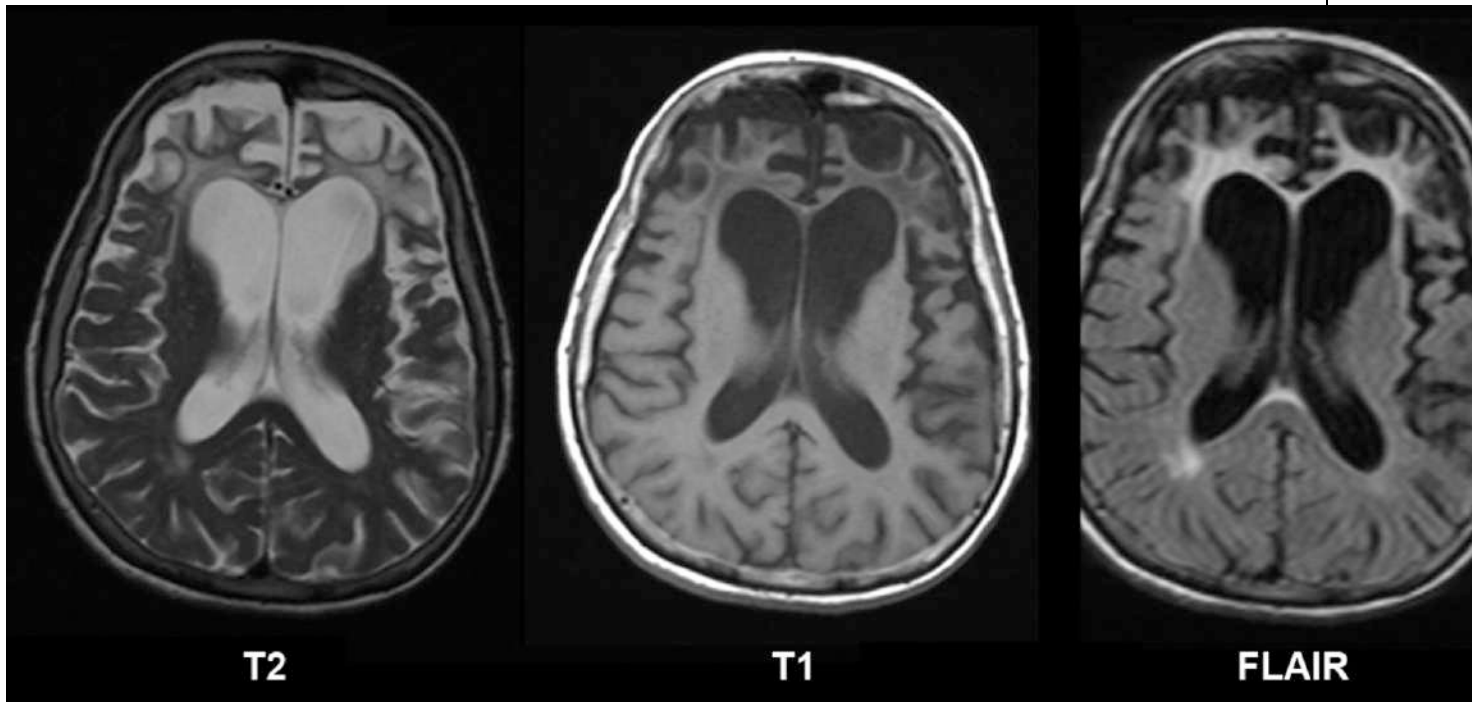
C - Vascular dementia

Explanation Why

[Risk factors](#) for [vascular dementia](#) include [hypertension](#) and [dyslipidemia](#). Its clinical presentation is highly variable, as different regions of the brain may be involved in the vascular insults that lead to cognitive deterioration. Symptoms can include gait disturbances, personality and [mood](#) changes, and cognitive deficits, as well as cortical symptoms such as [aphasia](#) or [amnesia](#). However, the development of deficits in [vascular dementia](#) usually occurs in a stepwise manner, while this patient's deficits developed in a short time period.

D - Frontotemporal dementia

Image

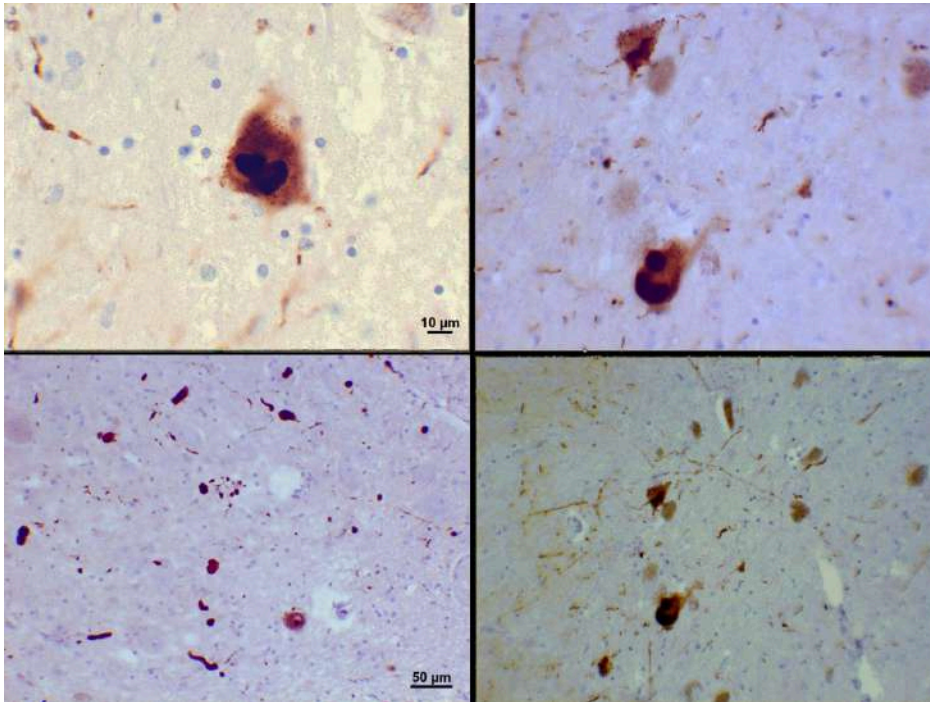


Explanation Why

The hallmarks of [frontotemporal dementia \(FTD\)](#) are early, progressive [aphasia](#) or behavior and personality changes (e.g., disinhibition, [apathy](#), [hyperorality](#), and compulsive behaviors), which occur alongside degeneration of the frontal and/or [temporal lobes](#). While this patient's performance on the five-minute recall test should raise suspicion for [dementia](#), the lack of language dysfunction or personality changes and the presence of gait abnormalities make [FTD](#) an unlikely diagnosis in this case.

E - Lewy body dementia

Image



Explanation Why

[Lewy body dementia](#) is characterized by early impairment in attention and [executive function](#), with [memory](#) impairment developing later in the disease course. Diagnosis requires two of the following: cognitive fluctuations, [visual hallucinations](#), and [parkinsonism](#). While this patient demonstrates cognitive impairment, he does not have any [hallucinations](#) or features of [parkinsonism](#), e.g., [tremor](#) or [rigidity](#).

F - Vitamin B12 deficiency

Explanation Why

[Vitamin B12 deficiency](#) develops after years of inadequate intake, [malabsorption](#), or increased demand. The condition can manifest with symptoms such as [memory](#) impairment, personality

changes, and [paresthesias](#), which could lead to gait abnormalities. However, [vitamin B₁₂ deficiency](#) typically results in loss of [distal vibratory sense](#) in the extremities (lower > upper), which is not present in this patient. Furthermore, [urinary urgency](#) would not be explained by [B12 deficiency](#).

Question # 27

A 73-year-old woman recently diagnosed with colonic adenocarcinoma comes to the physician because of a 1-week history of nausea and multiple episodes of vomiting. These symptoms started shortly after her first infusion of oxaliplatin and fluorouracil. The patient is started on an appropriate medication. Three weeks later, at a follow-up appointment, she states that she has developed headaches and constipation. The patient was most likely treated with a drug with which of the following mechanisms of action?

	Answer	Image
A	H1 receptor antagonist	
B	GABA _A receptor agonist	
C	M1 receptor antagonist	
D	D2 receptor antagonists	
E	NK1 receptor antagonist	
F	5-HT ₃ receptor antagonist	
G	Cannabinoid receptor agonist	

Hint

Ondansetron is a common antiemetic drug, with adverse effects that include headache and constipation.

Correct Answer

A - H1 receptor antagonist

Explanation Why

[H1 antagonists](#) ([antihistamines](#)), such as [dimenhydrinate](#), have an antiemetic effect in the [CNS](#) and may be used for vestibular nausea. They may also be used in women with [hyperemesis gravidarum](#). However, this group of drugs is currently not part of first-line treatment in patients with [chemotherapy](#)-induced [nausea and vomiting](#). Typical side effects of [H1 antagonists](#) include sedation and confusion, as well as symptoms related to their [anticholinergic](#) properties ([mydriasis](#), blurred vision, and [urinary retention](#)).

B - GABA_A receptor agonist

Explanation Why

GABA_A [agonists](#) ([benzodiazepines](#)), such as [lorazepam](#), have antiemetic effects mainly because they cause sedation and anxiety reduction. They can be useful in the treatment of patients who have anticipatory emesis in conjunction with [chemotherapy](#)-induced [nausea and vomiting](#) ([CINV](#)) or in patients with refractory nausea with contraindications to other medications. However, this patient presents with new-onset [CINV](#), which should be treated with a different antiemetic drug. Typical side effects of [benzodiazepines](#) include confusion, impaired motor coordination, and respiratory depression, none of which are seen in this patient.

C - M1 receptor antagonist

Explanation Why

M1 antagonists ([muscarinic antagonists](#)), such as [scopolamine](#), have an antiemetic effect in the [area postrema](#) of the medulla and cause peripheral inhibition of the intestinal tract's [vagal nerve](#) signals. They are mainly used to treat motion sickness or vestibular-induced [nausea and vomiting](#) and are not part of first-line treatment in patients with [chemotherapy](#)-induced [nausea and vomiting](#). Adverse

effects of M1 antagonists are related to their [anticholinergic](#) properties and include [mydriasis](#), [tachycardia](#), and [urinary retention](#), none of which are seen in this patient.

D - D2 receptor antagonists

Explanation Why

D2 antagonists ([dopamine receptor antagonists](#)), such as [prochlorperazine](#), have an antiemetic effect because they target the [area postrema](#) in the medulla. They are mainly used in women with severe [hyperemesis gravidarum](#) or in patients with refractory nausea. However, this group of drugs is currently not part of first-line treatment in patients with [chemotherapy](#)-induced [nausea and vomiting](#). Typical side effects include depression, fatigue, [diarrhea](#), and [hyperprolactinemia](#), none of which are seen in this patient.

E - NK1 receptor antagonist

Explanation Why

NK1 antagonists ([neurokinin receptor antagonists](#)), such as [aprepitant](#), have strong central and peripheral antiemetic effects. This group of drugs is useful in the treatment of patients with acute and delayed phases of [chemotherapy](#)-induced [nausea and vomiting](#). Typical side effects include fatigue and hiccups. This patient, however, presents with [headaches](#) and [constipation](#), which makes it more likely she received a different medication.

F - 5-HT₃ receptor antagonist

Explanation Why

[5-HT₃ antagonists](#), such as [ondansetron](#), have a central-acting antiemetic effect and cause peripheral inhibition of the intestinal tract's [vagal nerve](#) signals. They are especially effective in relieving [chemotherapy](#)-induced and [postoperative nausea and vomiting](#) and are commonly used as first-line [antiemetics](#). Possible side effects include [headaches](#), [constipation](#) or [diarrhea](#), and elevated [liver](#) enzymes. In severe cases, they may also cause [QT interval prolongation](#) (which may lead to [torsades de pointes](#)) and [serotonin syndrome](#); caution should therefore be exercised in patients receiving

frequent doses.

G - Cannabinoid receptor agonist

Explanation Why

Cannabinoid receptor agonists (synthetic cannabinoids), such as [dronabinol](#), have peripheral antiemetic effects mainly due to the fact that they decrease intestinal motility. They can be used in the treatment of refractory emesis in patients with [chemotherapy](#)-induced [nausea and vomiting \(CINV\)](#). However, this patient presents with new-onset [CINV](#), which should be treated with a different antiemetic drug. Moreover, synthetic cannabinoids have only moderate antiemetic effects compared to other antiemetic drugs and can cause a variety of unfavorable side effects, including sedation, [vertigo](#), and [dizziness](#), none of which are seen in this patient.

Question # 28

A 6-year-old boy is brought to the physician because of a 2-week history of frequent episodes of unresponsiveness. During these episodes, he stares blankly, rhythmically nods his head, and does not respond to verbal stimulation for several seconds. Hyperventilation for 30 seconds precipitates an episode of unresponsiveness and head nodding that lasts for 7 seconds. He regains consciousness immediately afterward. An electroencephalogram shows 3-Hz spikes and waves. Which of the following best describes the mechanism of action of the most appropriate pharmacotherapy for this patient's condition?

	Answer	Image
A	Increased frequency of GABA _A channel opening	
B	Blockade of thalamic T-type calcium channels	The diagram illustrates the mechanisms of action for various antiepileptic drugs at excitatory and inhibitory synapses. Excitatory synapse (neurotransmitter: glutamate): Presynaptic: Inhibition of voltage-gated Na⁺ channels (Carbamazepine) and inhibition of voltage-gated Ca²⁺ channels (Gabapentin) reduce glutamate release. Postsynaptic: Activation of GABA-synthesis (Valproate) and inhibition of glutamate release via voltage-gated Na⁺ and Ca²⁺ channel inhibition (Topiramate) are shown. Inhibitory synapse (neurotransmitter: GABA): Presynaptic: Inhibition of GABA-transmission (Vigabatrin) and activation of GABA-synthesis (Valproate) are shown. Postsynaptic: Inhibition of GABA reuptake (Tigabalin) and GABA-A receptor agonists (Diazepam, phenobarbital) are shown.
C	Inhibition of presynaptic voltage-activated Ca ²⁺ channels	

	Answer	Image
D	Irreversible inhibition of GABA transaminase	
E	Increased duration of GABA _A channel opening	
F	Blockade of voltage-gated Na ⁺ channels	
G	Inhibition of GABA reuptake into presynaptic neurons	

Hint

This boy has childhood absence epilepsy. Absence seizures typically manifest with episodes of staring, inattentiveness, and head nodding and can be triggered by hyperventilation. Patients typically maintain muscle tone during seizures and do not experience a postictal phase. The diagnosis is confirmed with EEG findings of a 3-Hz spike and wave pattern. First-line therapy is ethosuximide.

Correct Answer

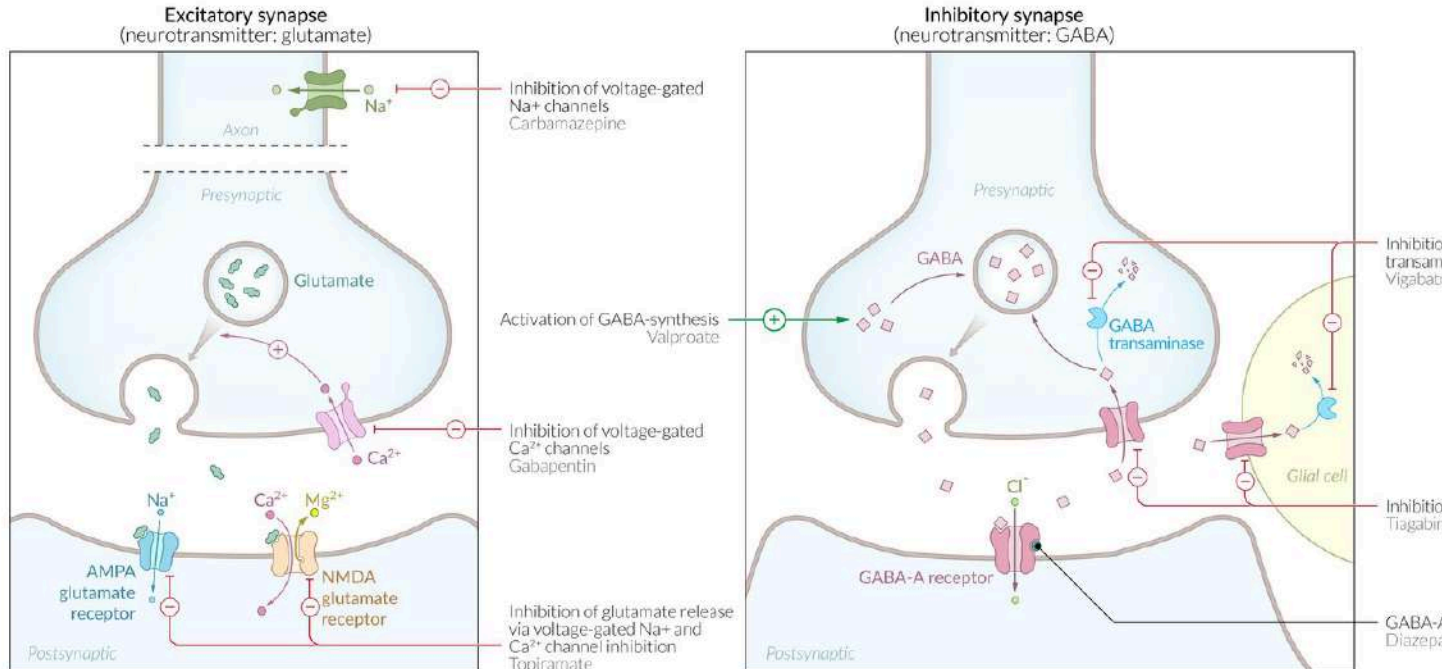
A - Increased frequency of GABA_A channel opening

Explanation Why

Increased frequency of GABA_A channel opening is the mechanism of action of [benzodiazepines](#). [Benzodiazepines](#) are the treatment of choice for [status epilepticus](#). These drugs are also used for refractory cases of [childhood absence epilepsy](#) but are not used as first-line therapy.

B - Blockade of thalamic T-type calcium channels

Image



Explanation But

[Ethosuximide](#) halves the [incidence](#) of [absence seizures](#) in at least 90% of patients and decreases the [incidence](#) by more than 90% in half of all patients.

Explanation Why

Blockade of [T-type calcium channels](#) in the [thalamus](#) is the mechanism of action of [ethosuximide](#), which is the first-line therapy for [seizure](#) prophylaxis in patients with [childhood absence epilepsy](#). T-type calcium channels are thought to be responsible for the rhythmic 3-Hz discharge seen on EEG during [absence seizures](#).

C - Inhibition of presynaptic voltage-activated Ca^{2+} channels

Explanation Why

Inhibition of presynaptic voltage-activated [Ca²⁺](#) channels is the mechanism of action of [gabapentin](#). This drug is contraindicated in patients with [childhood absence epilepsy](#) because it can precipitate [absence seizures](#). [Gabapentin](#) is often used to treat [focal seizures](#).

D - Irreversible inhibition of GABA transaminase

Explanation Why

Irreversible inhibition of [GABA transaminase](#) is the mechanism of action of [vigabatrin](#). This drug is contraindicated in patients with [childhood absence epilepsy](#) because it can precipitate [absence seizures](#). [Vigabatrin](#) is used to treat refractory [focal seizures](#). The agent is also the first-line therapy for [West syndrome](#), especially if the underlying cause is [tuberous sclerosis](#).

E - Increased duration of GABA_A channel opening

Explanation Why

Increased duration of GABA_A channel opening is the mechanism of action of [barbiturates](#) (e.g., [phenobarbital](#)). [Phenobarbital](#) is often used to treat [seizures](#) in [neonates](#) but is ineffective for [absence seizures](#).

F - Blockade of voltage-gated Na⁺ channels

Explanation Why

Blockade of voltage-gated Na⁺ channels is the mechanism of action of [lamotrigine](#). This drug is a third-line therapy for [seizure](#) prophylaxis in patients with [childhood absence epilepsy](#); another drug is more appropriate as first-line therapy. Several other [anticonvulsant drugs](#) also act on Na⁺ channels, including [valproic acid](#) (a second-line therapy that increases channel inactivation), [carbamazepine](#) (which blocks the channels but is not used because it can precipitate [absence seizures](#)), and [phenytoin](#) (which block the channels but is ineffective in treating [absence seizures](#)).

G - Inhibition of GABA reuptake into presynaptic neurons

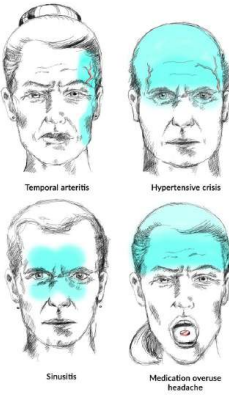
Explanation Why

Inhibition of [GABA](#) reuptake into presynaptic [neurons](#) is the mechanism of action of [tiagabine](#). This drug is contraindicated in patients with [childhood absence epilepsy](#) because it can precipitate [absence seizures](#). [Tiagabine](#) is often used to treat [focal seizures](#).

Question # 29

A 28-year-old man comes to the emergency department because of an excruciating headache that started 30 minutes ago. The pain is located around the right eye and it awoke him from sleep. Over the past two weeks, he has had similar headaches around the same time of the day, and he reports pacing around restlessly during these episodes. Physical examination shows conjunctival injection and tearing of the right eye. In addition to supplemental oxygen therapy, administration of which of the following drugs is most likely to provide acute relief in this patient?

	Answer	Image
A	Indomethacin	
B	Sumatriptan	Cluster headache Epidemiology $\bar{M}$ ~ $\bar{F}$ (3:1) typically 20–40 years of age Duration ~30–60 min/attack Frequency Typically ~1–3 attacks/24 h Note Attacks often occur at night; patient is restless and paces around during an attack Therapy Acute: triptans, 100% O₂ Chronic: verapamil (prophylactic) Triggers Alcohol, insomnia, nitrates, bright lights Character of pain Stabbing, burning Additional symptoms Muscle tension Phono-/Photophobia may occur Course of an attack Periods of cluster headache Acute attack Jan episodic Dec Jan chronic Dec ① Sweating ② Lacrimation, conjunctival injection ③ Flushing ④ Rhinorrhea, nasal congestion
C	Ibuprofen	
D	Carbamazepine	Ophthalmic nerve (V1) Maxillary nerve (V2) Mandibular nerve (V3) Shooting pain Trigeminal neuralgia

	Answer	Image
E	Amitriptyline	
F	Prednisone	 The image contains four line drawings of human faces, each with a specific area highlighted in red to indicate a headache location. The top-left drawing shows red shading on the temples, labeled 'Temporal arteritis'. The top-right drawing shows red shading across the forehead and temples, labeled 'Hypertensive crisis'. The bottom-left drawing shows red shading over the bridge of the nose and cheeks, labeled 'Sinusitis'. The bottom-right drawing shows red shading across the forehead, labeled 'Medication overuse headache'.
G	Oxycodone	

Hint

This young man has recurrent attacks of severe unilateral headache that are associated with ipsilateral cranial autonomic symptoms (conjunctival injection, lacrimation), which is indicative of cluster headache.

Correct Answer

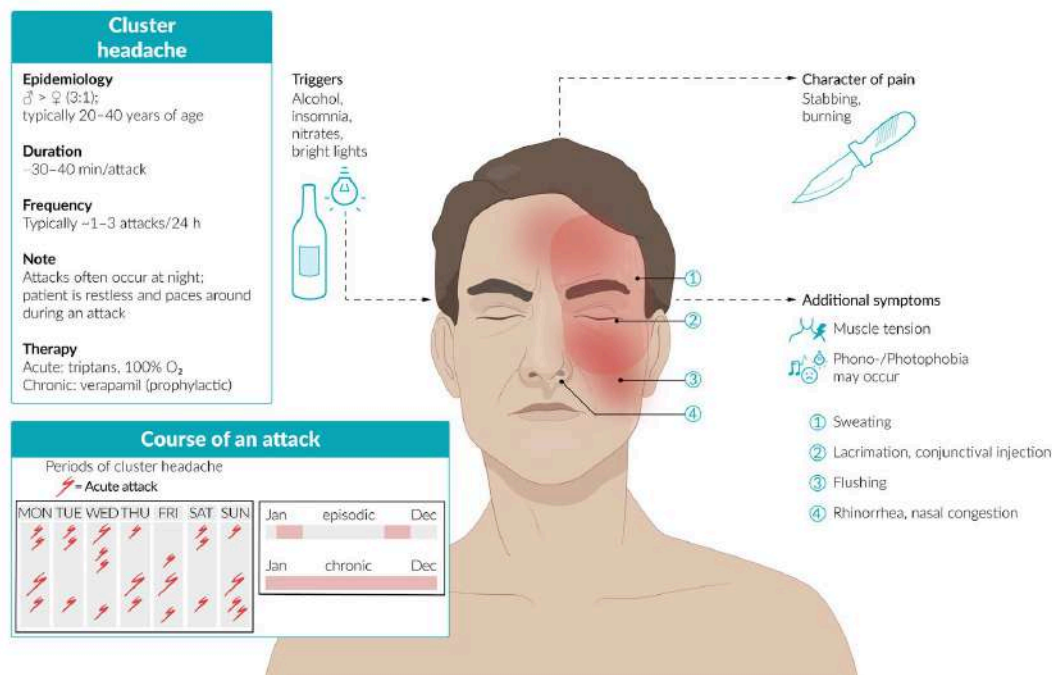
A - Indomethacin

Explanation Why

[Indomethacin](#) is highly effective in preventing attacks of [paroxysmal hemicrania](#) (PH), a rare form of [trigeminal](#) autonomic [cephalalgia](#), but not very effective as an abortive therapy in acute cases. While PH may present very similarly, the attacks are usually more frequent (≥ 5 per day) and often shorter. In [cluster headache](#), [NSAIDs](#) like [indomethacin](#) are generally not recommended because their onset of action is too slow.

B - Sumatriptan

Image



Explanation But

[Tryptans](#) are also the treatment of choice for severe [migraine](#) attacks.

Explanation Why

[Tryptans](#) like [sumatriptan](#) are the first-line pharmacological treatment for acute attacks of [cluster headache](#). They abort the [headache](#) and provide resolution of the [conjunctival injection](#) associated with these attacks. The exact mechanism is unclear, but it is thought to involve the vasoconstriction of [cranial](#) blood vessels in response to stimulation of [5-hydroxytryptamine \(5-HT\)](#) receptors. Inhalation of 100% oxygen is also effective in terminating acute episodes of [cluster headache](#) and has a rapid onset of action.

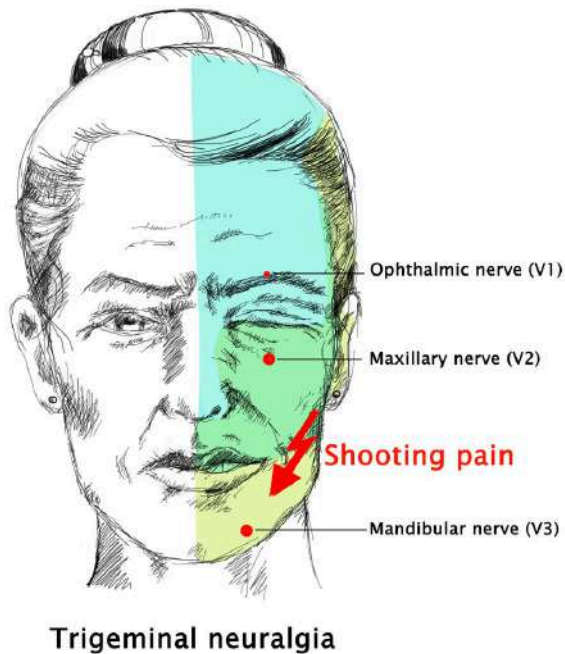
C - Ibuprofen

Explanation Why

[NSAIDs](#) like [ibuprofen](#) can be used for [pain](#) relief in, e.g. mild to moderate [migraine](#) attacks or acute tension-type [headaches](#) ([TTH](#)). While the [pain](#) associated with [TTH](#) is usually holocephalic or bifrontal, and [cranial](#) autonomic symptoms, as seen in this patient, do not occur; [migraine](#) is characterized by episodes of typically unilateral [headache](#) lasting 4–72 hours accompanied or preceded by nausea, phono- and photophobia, and/or [aura](#), which are absent in this patient. Furthermore, while patients with [migraine](#) tend to rest motionlessly in a quiet, dark room, this patient prefers to pace around during the episodes of [pain](#).

D - Carbamazepine

Image



Explanation Why

[Carbamazepine](#) is the drug of choice for the treatment of [trigeminal neuralgia](#). While [trigeminal neuralgia](#) can present with unilateral facial [pain](#) that occurs in repetitive attacks, unlike in this patient, these attacks usually only last a few seconds and are characterized by shooting or stabbing [pain](#) (like an [electric shock](#)) from mouth to the angle of the [jaw](#) on the affected side. Frontal [headache](#), [conjunctival injection](#), [rhinorrhea](#), and lacrimation are not features of [trigeminal neuralgia](#).

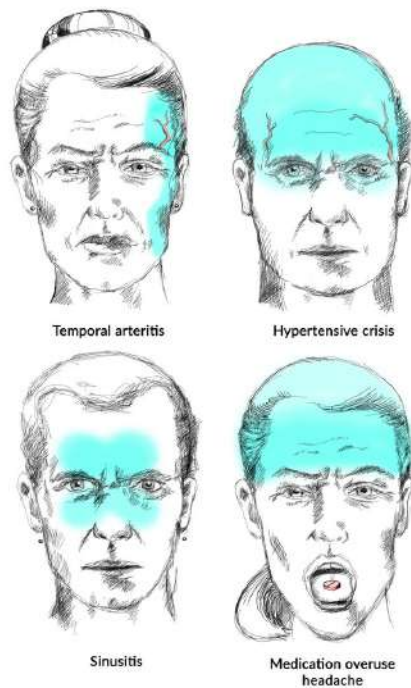
E - Amitriptyline

Explanation Why

[Amitriptyline](#) is used to prevent chronic tension-type [headaches](#) and [migraine](#) attacks. [Amitriptyline](#) is not used, however, to acutely treat any type of [headache](#).

F - Prednisone

Image



Explanation But

[Prednisone](#) can be used as a preventive treatment for [cluster headache](#); however, this patient with an acute presentation needs an abortive therapy.

Explanation Why

High-dose [steroid](#) therapy is the treatment of choice for [giant cell arteritis \(GCA\)](#), which can present with severe unilateral [headache](#), as seen in this patient. However, autonomic symptoms do not occur, and symptoms such as [jaw claudication](#) and scalp tenderness, which are not seen in this patient, are usually present. More importantly, [GCA](#) usually occurs in elderly individuals (peak [incidence](#): 70–79 years) and is rare in patients younger than 50.

G - Oxycodone

Explanation Why

Oxycodone is an orally administered [opiate analgesic](#) that is used to treat chronic and/or severe [pain](#) that cannot be managed with [NSAIDs](#). [Opiate analgesics](#) should not, however, be used in the management of [primary headache disorders](#) because of the risk of [opiate](#) dependence.

Question # 30

An 8-year-old boy is brought to the emergency department because of a 4-day history of severe, left-sided ear pain and purulent discharge from his left ear. One week ago, he returned with his family from their annual summer vacation at a lakeside cabin, where he spent most of the time outdoors hiking and swimming. Examination shows tragal tenderness and a markedly edematous and erythematous external auditory canal. Audiometry shows conductive hearing loss of the left ear. Which of the following is the most likely cause of this patient's symptoms?

	Answer	Image
A	Abnormal epithelial growth on tympanic membrane	
B	Infection with <i>Aspergillus</i> species	
C	Infection with <i>Streptococcus pneumoniae</i>	
D	Infection with varicella zoster virus	
E	Pleomorphic replacement of normal bone	
F	Infection with <i>Pseudomonas aeruginosa</i>	

Hint

The patient has ear pain and purulent discharge after returning from a vacation that involved outdoor swimming. Examination shows an inflamed external auditory canal and conductive hearing loss. These features are consistent with otitis externa.

Correct Answer

A - Abnormal epithelial growth on tympanic membrane

Explanation Why

A [cholesteatoma](#) is a growth of keratinizing [squamous epithelium](#) from the [tympanic membrane](#) or auditory canal into the [middle ear](#) mucosa. It is often asymptomatic, but it can manifest with discharge from [the ear](#), [dizziness](#), and [conductive hearing loss](#). However, it affects the [middle ear](#) and is therefore not associated with tragal tenderness or [edema](#) of the [external auditory canal](#).

B - Infection with Aspergillus species

Explanation Why

Aspergillus and *Candida* species are the most common causal pathogens of fungal [otitis externa](#), which can manifest with tragal [pain](#), [ear discharge](#), [edema](#), and [erythema](#). However, in fungal [otitis externa](#), the [pain](#) is usually not severe and the [edema](#) is usually mild. [Pruritus](#) is normally the most troubling symptom. Furthermore, fungal otitis externa accounts for < 10% of all [otitis externa](#) cases and is usually associated with concurrent [antibiotic](#) use.

C - Infection with Streptococcus pneumoniae

Explanation Why

Streptococcus pneumoniae, a common cause of [otitis media](#), rarely infects the external ear. While [otitis media](#) can manifest with ear [pain](#) and discharge as well as [conductive hearing loss](#), tragal tenderness and [edema](#) of the [external auditory canal](#) are usually absent. Furthermore, [otitis media](#) tends to occur in winter months and is often associated with a history of cold and congestion.

D - Infection with varicella zoster virus

Explanation Why

Infection of the external ear with the [varicella zoster virus](#) causes [herpes zoster oticus](#), which can manifest with tragal tenderness. However, [herpes zoster oticus](#) is usually associated with facial paralysis and [blisters](#) in or on [the ear](#) as well as [vertigo](#), [tinnitus](#), and dysgeusia. Moreover, [herpes zoster oticus](#) usually results in [sensorineural hearing loss](#) rather than [conductive hearing loss](#).

E - Pleomorphic replacement of normal bone

Explanation Why

[Otosclerosis](#) involves pleomorphic replacement of the normal bone. It causes slowly progressive [conductive hearing loss](#) in adults but is not associated with ear [pain](#), discharge, tragal tenderness, or [edema](#) of the [external auditory canal](#).

F - Infection with *Pseudomonas aeruginosa*

Explanation Why

[Pseudomonas aeruginosa](#) is the most common causal pathogen of [otitis externa](#) (commonly following swimming activities). Other common causal pathogens of [otitis externa](#) include [Staphylococcus epidermidis](#) and [Staphylococcus aureus](#).

Question # 31

A 51-year-old man comes to the physician because of recurrent episodes of dizziness, tinnitus, and hearing loss on the left side for 6 weeks. These episodes last for hours at a time and are associated with the sensation that the room is spinning. He has no history of major medical illness and takes no medications. Examination shows horizontal nystagmus to the left. Weber test shows lateralization to the right ear. The Rinne test is positive bilaterally. Which of the following is the most likely cause of this patient's symptoms?

	Answer	Image
A	Dislodged otoliths	1 Anterior semicircular duct 2 Perilymphatic space 3 Utricle 4 Saccule 5 Ductus reuniens 6 Cochlear duct 7 Modiolus 8 Helicotrema Bony labyrinth Membranous labyrinth Vestibular nerve Cochlear nerve Cochlea Oval window Round window Tympanic duct Vestibular duct
B	Inflammation of the vestibular nerve	
C	Acoustic neuroma	
D	Demyelinating plaques	
E	Endolymphatic hydrops	
F	Posterior inferior cerebellar artery infarction	

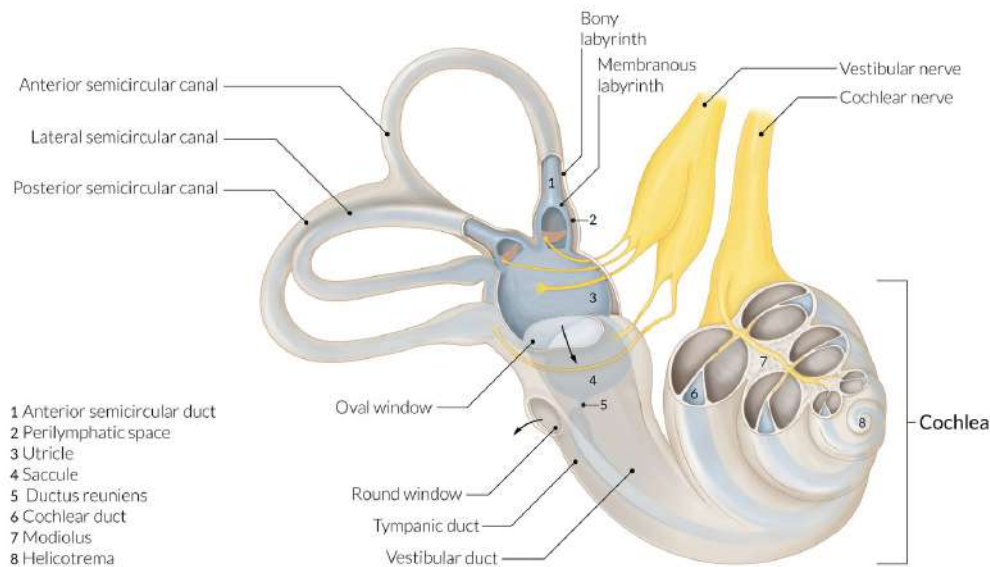
Hint

The triad of vertigo, tinnitus, and sensorineural hearing loss (normal Rinne test, lateralization to the unaffected side) is characteristic of Ménière disease.

Correct Answer

A - Dislodged otoliths

Image



Explanation Why

Dislodged [otoliths](#) can cause the severe [vertigo](#) attacks seen in [benign paroxysmal positional vertigo \(BPPV\)](#). When [otoliths](#) become displaced into one of the semicircular ducts, they can disrupt the endolymph and thus lead to stimulation of the [hair](#) cells on the cupula. This stimulation sends signals to the brain that suggest motion even if the patient is not moving, thus triggering the sensation of [vertigo](#). Although this patient has [vertigo](#), he also has cochlear symptoms ([tinnitus](#) and [hearing loss](#)), which are typically absent in patients with [BPPV](#). In addition, contrary to this patient's presentation, [vertigo](#) in [BPPV](#) lasts only for a few seconds and is triggered by movement.

B - Inflammation of the vestibular nerve

Explanation Why

[Vestibular neuritis](#), which is caused by [inflammation](#) of the vestibular portion of [cranial nerve VIII](#) and most often occurs following a recent upper respiratory infection (URI) can also manifest with [vertigo](#) and nystagmus. However, this patient has no history of URI. In addition, [vertigo](#) from [vestibular neuritis](#) is usually directed at the unaffected side and continuous (rather than intermittent). Moreover, cochlear symptoms ([sensorineural hearing loss](#), [tinnitus](#)) are not typically seen.

C - Acoustic neuroma

Explanation Why

[Acoustic neuroma](#) can manifest with [vertigo](#), [tinnitus](#), and [hearing loss](#). In addition, the results of Weber and [Rinne tests](#) are similar to those seen in this patient. However, [acoustic neuromas](#) grow slowly, and the [CNS](#) is capable of compensating the imbalances from the injured [vestibular system](#), making recurrent attacks of [vertigo](#) unlikely.

D - Demyelinating plaques

Explanation Why

Plaques of [demyelination](#) are a typical [MRI](#) finding in patients with [multiple sclerosis](#). Some patients can develop [vertigo](#) (in the case of [cerebellar](#) or [brainstem](#) involvement), but [hearing loss](#) and [tinnitus](#) are very rare symptoms. A common first manifestation of [multiple sclerosis](#) is impaired vision (due to [retrobulbar neuritis](#)), and as the disease progresses, other sensory and/or motor neurological deficits appear.

E - Endolymphatic hydrops

Explanation But

Audiometry typically shows low-frequency [hearing loss](#), which can be a helpful finding in differentiating Ménière disease from other conditions that present with [hearing loss](#) in other frequency ranges (e.g., [acoustic neuroma](#)).

Explanation Why

[Endolymphatic hydrops](#), which results in accumulation of endolymph within the [membranous labyrinth](#), is the underlying mechanism of Ménière disease. In addition to [vertigo](#), [tinnitus](#), and [sensorineural hearing loss](#), patients often have ear fullness and nystagmus that can be directed towards the affected side (irritative nystagmus) or the healthy side (reversed nystagmus).

F - Posterior inferior cerebellar artery infarction

Explanation Why

[Infarction](#) of the [posterior inferior cerebellar artery](#) causes [lateral medullary \(Wallenberg\) syndrome](#). Symptoms include [vertigo](#) and nystagmus but not typically [tinnitus](#) or [hearing loss](#). In addition, patients with [Wallenberg syndrome](#) generally develop [dysphagia](#), hoarseness, ipsilateral [Horner syndrome](#), and contralateral loss of [pain](#) and temperature sensation, none of which is seen in this patient.

Question # 32

A 58-year-old man comes to the physician for evaluation of increasing swelling in his left cheek and recurrent oral ulcers for 1 year. He has smoked a pack of cigarettes daily for 25 years. Examination shows a mild, nontender swelling above the angle of the left jaw. An ultrasound-guided biopsy of the mass confirms the diagnosis of parotid adenoid cystic carcinoma. A left-sided total parotidectomy is performed. This patient is at greatest risk for which of the following complications?

	Answer	Image
A	Hyperesthesia of the left ear lobe	
B	Impaired taste of the posterior 1/3 of the tongue	
C	Flushing of the right cheek while eating	
D	Inability to wrinkle the left side of the forehead	

	Answer	Image
E	Hyperacusis of the left ear	

Hint

The facial nerve runs through the parotid gland and is most likely to be damaged during a procedure such as total parotidectomy.

Correct Answer

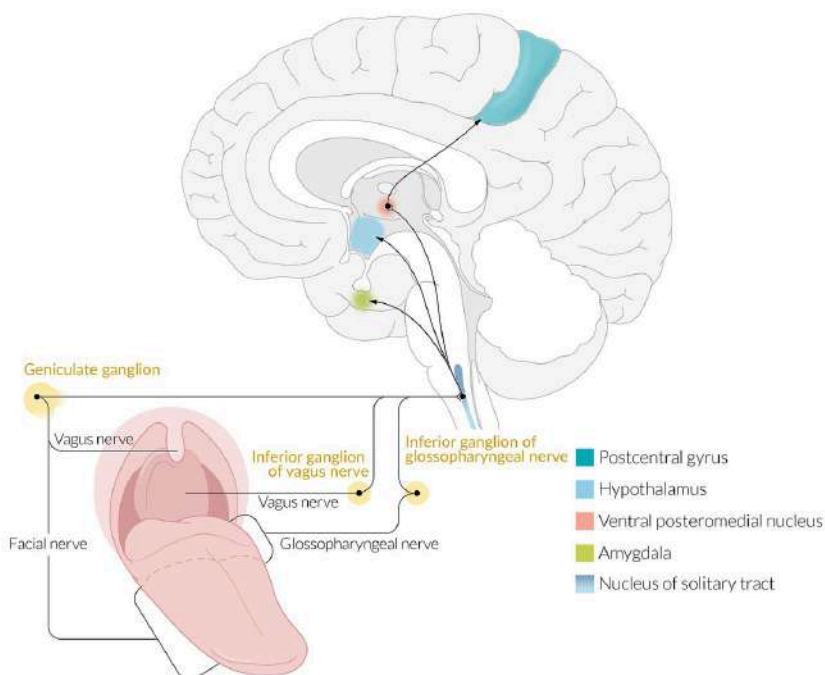
A - Hyperesthesia of the left ear lobe

Explanation Why

Sensation of the earlobe is provided by the greater auricular nerve. [Hypoesthesia](#), not [hyperesthesia](#), of the [skin](#) innervated by the greater auricular nerve is a common complication of parotidectomy due to nerve transection during surgery.

B - Impaired taste of the posterior 1/3 of the tongue

Image



Explanation But

The [chorda tympani](#) branch of the [facial nerve](#) is responsible for transmitting [taste](#) from the [anterior](#) two-thirds of the [tongue](#). However, it joins the [facial nerve](#) inside the facial canal (thus inside the

[skull](#)), which means that [chorda tympani](#) dysfunction is not a potential complication of parotidectomy.

Explanation Why

[Taste](#) and sensation in the [posterior](#) third of the [tongue](#) are provided by the [glossopharyngeal nerve](#), which does not run near the [parotid gland](#) but more dorsally, between the [internal jugular vein](#) and the [internal carotid artery](#). [Glossopharyngeal nerve damage](#) is, therefore, not an expected complication of parotidectomy.

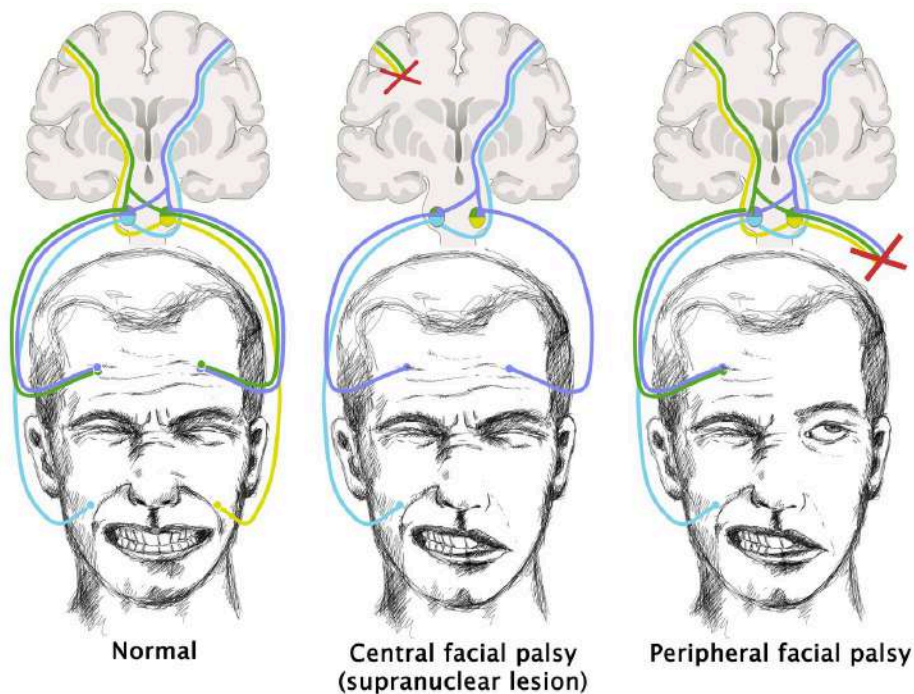
C - Flushing of the right cheek while eating

Explanation Why

Flushing and sweating of the cheek while eating is characteristic of [Frey syndrome](#), which is a late complication of parotidectomy. [Frey syndrome](#) is due to inappropriate [parasympathetic](#) nerve regrowth. However, [Frey syndrome](#) affects the ipsilateral cheek and would, therefore, affect the left cheek in a patient who underwent left parotidectomy, not the right cheek.

D - Inability to wrinkle the left side of the forehead

Image



Explanation But

Most cases of post-parotidectomy [facial nerve palsy](#) resolve within one month.

Explanation Why

Unilateral inability to [wrinkle](#) the forehead is a sign of ipsilateral [peripheral facial nerve palsy](#), the most common complication of parotidectomy. Injury to the [facial nerve](#) during parotidectomy results in an impairment of the ipsilateral muscles of facial expression, including the muscles responsible for [eyelid](#) and forehead movements.

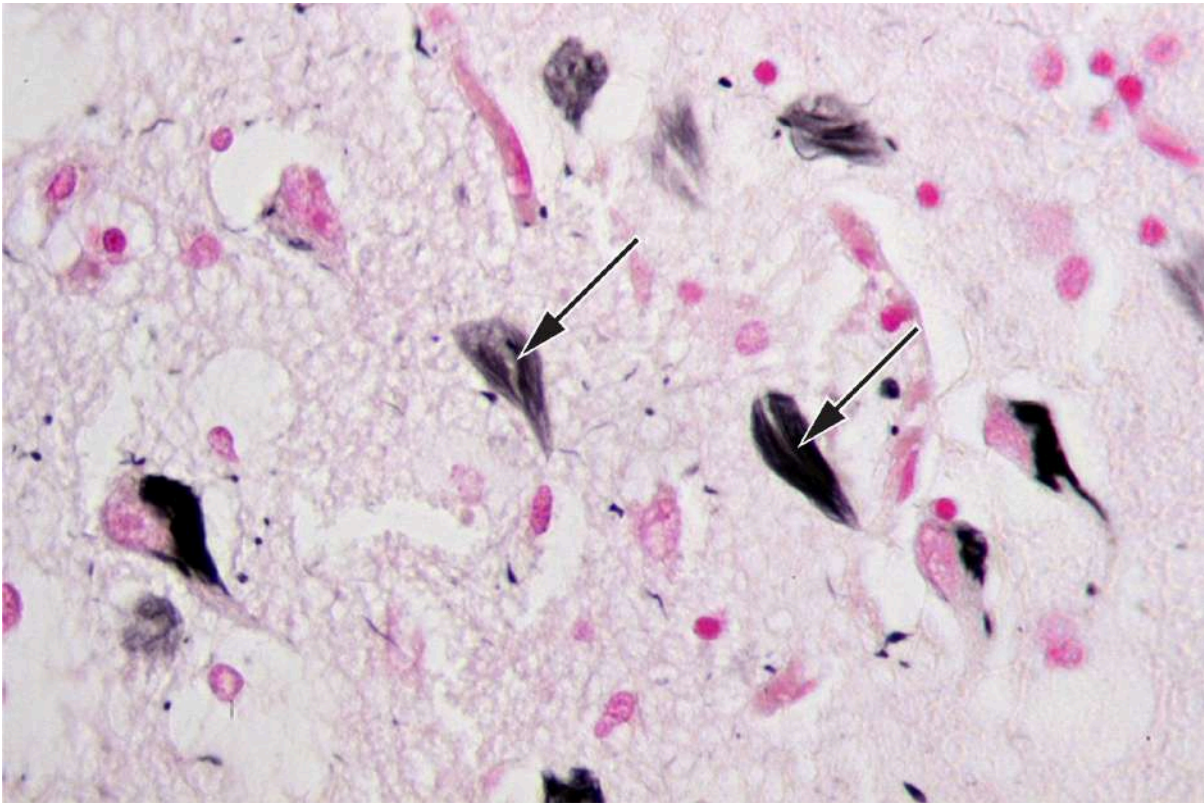
E - Hyperacusis of the left ear

Explanation Why

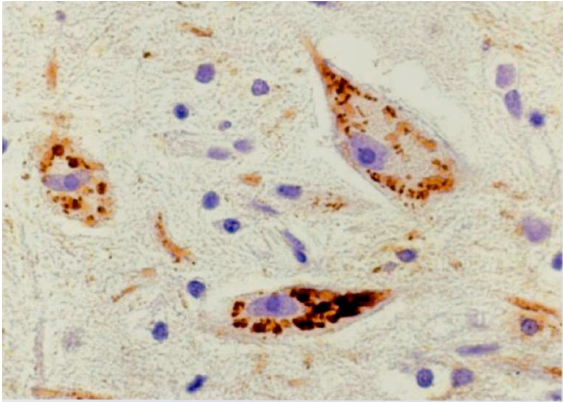
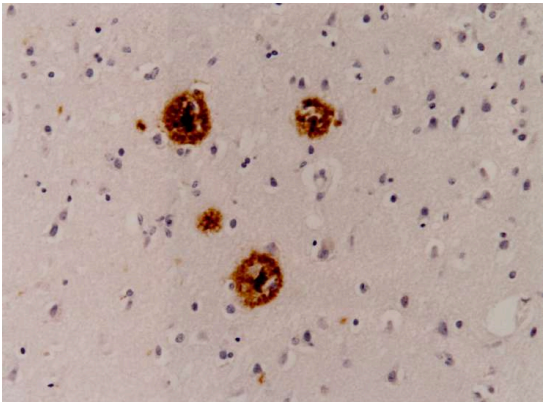
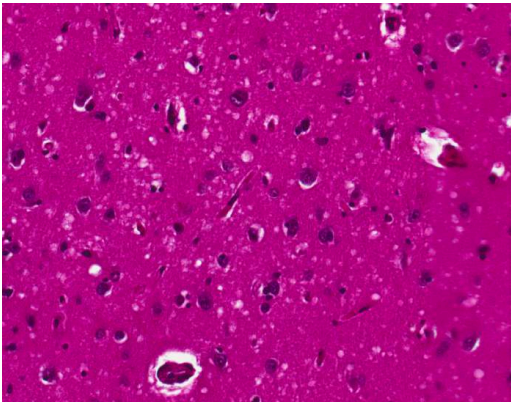
[Hyperacusis](#) may be a symptom of [facial nerve](#) dysfunction (e.g., [Bell palsy](#)) due to associated weakness of the [stapedius muscle](#). The [nerve to the stapedius](#) branches off of the [facial nerve](#) before the [facial nerve](#) exits the [skull](#), which means that [stapedius](#) dysfunction cannot be a complication of parotidectomy.

Question # 33

A 73-year-old woman is brought to the physician by her daughter for evaluation of impaired memory and word-finding difficulties for 2 years. She was recently asked to step down from her position as volunteer accountant for a local charity organization because she was no longer able to coordinate her tasks. She reports that she has become unable to taste or smell her food. Two years later, the patient dies. At autopsy, examination of the brain shows generalized cortical atrophy. A photomicrograph of a section of the brain is shown. The inclusions indicated by the arrows are predominantly composed of which of the following substances?



	Answer	Image
A	Alpha-synuclein	Four panels of immunohistochemical staining for alpha-synuclein. The top-left panel shows a single neuron with a large, dark brown, eosinophilic inclusion. The top-right panel shows a neuron with a smaller, dark brown inclusion. The bottom-left panel shows a field of neurons with scattered dark brown inclusions. The bottom-right panel shows a field of neurons with scattered dark brown inclusions. Scale bars are present in the bottom-right panels.

	Answer	Image
B	Viral ribonuclear proteins	
C	Amyloid-β	
D	Hyperphosphorylated tau	
E	Prion protein	

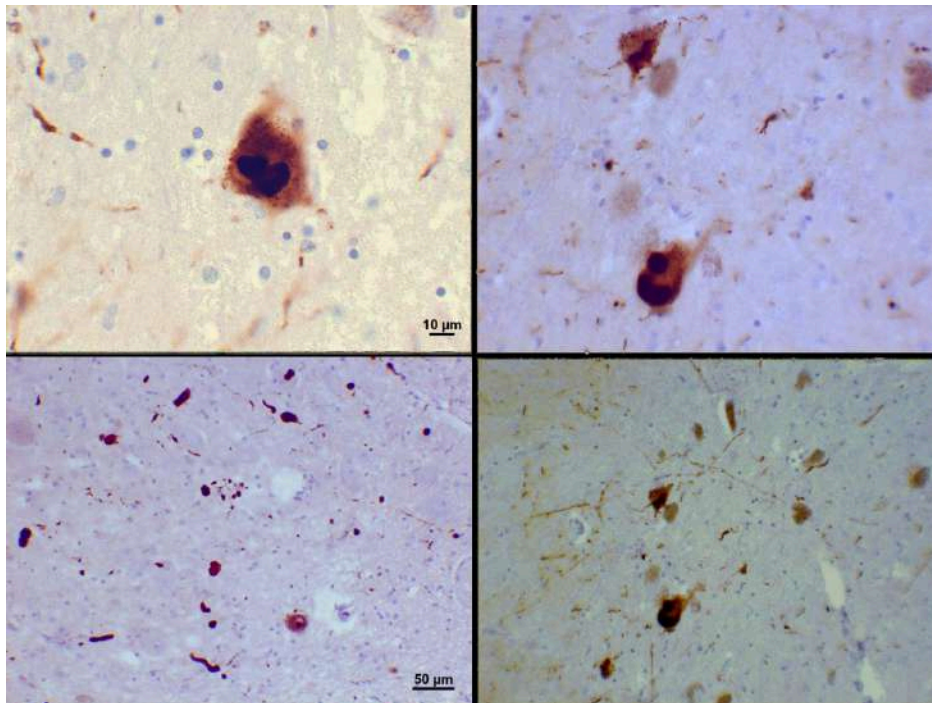
Hint

This patient's memory deficits, amnesic aphasia, hyposmia (and associated hypogeusia), and generalized cortical atrophy are suggestive of Alzheimer disease, the most common type of dementia.

Correct Answer

A - Alpha-synuclein

Image

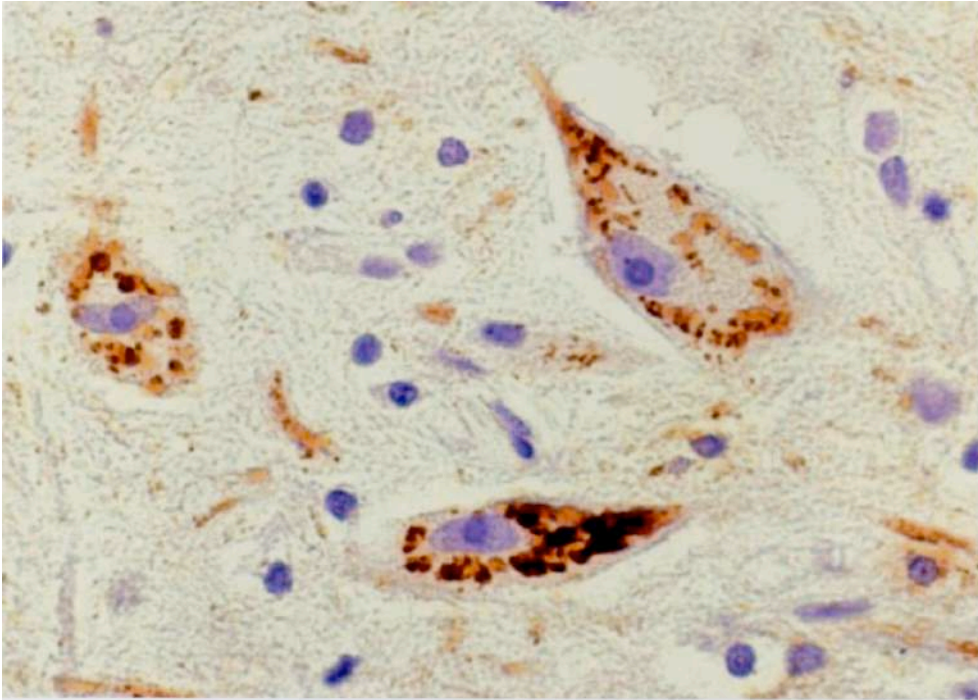


Explanation Why

Alpha-synuclein aggregates, among [ubiquitin](#) and [neurofilaments](#), can be found in [Lewy bodies](#), which constitute the underlying pathology of [Lewy body dementia](#) and [Parkinson disease](#). Although [Lewy body dementia](#) can present with cognitive impairment, distinctive clinical features such as [visual hallucinations](#) or sleep behavior dysfunction were not present in this patient. Moreover, she did not have any symptoms of [parkinsonism](#) (e.g., [tremor](#), [rigidity](#), [bradykinesia](#)).

B - Viral ribonuclear proteins

Image

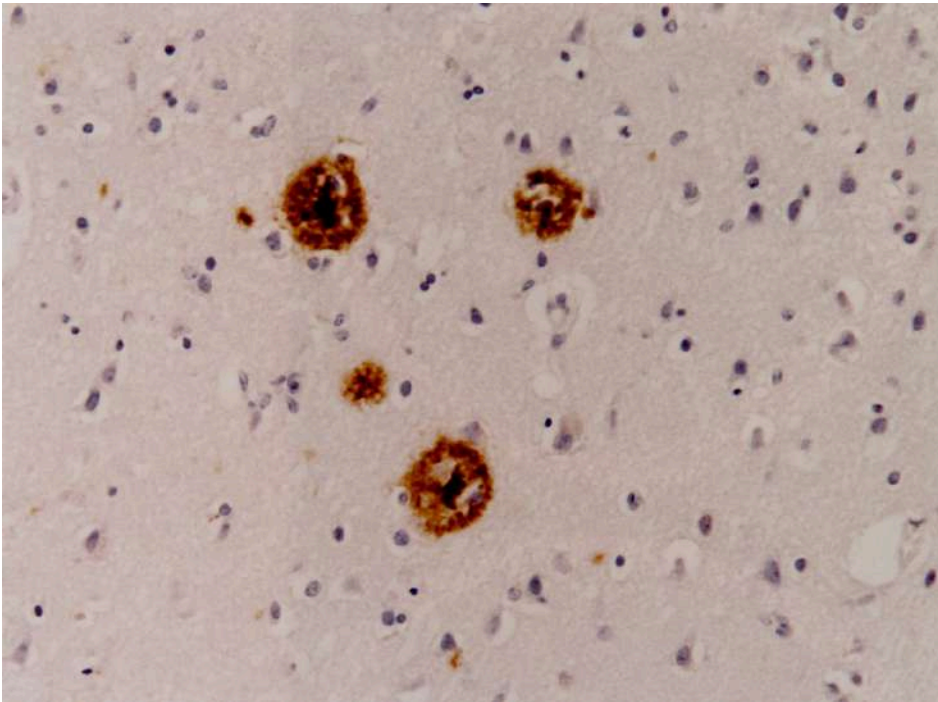


Explanation Why

Viral ribonuclear [proteins](#) ([Negri bodies](#)) can be found in the setting of [rabies](#), as the virus reaches the brain through retrograde transport. They are seen as round [cytoplasmic](#) inclusions in Purkinje cells of the [cerebellum](#) and in hippocampal [neurons](#). Even though [rabies](#) does cause [CNS](#) symptoms (confusion, [seizures](#)), [dementia](#) is not a feature. Moreover, [rabies](#) is typically lethal within days to weeks after onset of neurologic symptoms rather than gradually progressive as the [dementia](#) seen in this patient.

C - Amyloid-β

Image



Explanation Why

[Amyloid-β](#), a derivative of [amyloid precursor protein](#), accumulates in patients with [Alzheimer disease](#) and plays a major role of its underlying pathogenesis. This patient did have [Alzheimer disease](#), but [amyloid-β](#) aggregates are found extracellularly in the form of [senile plaques](#), not intracellularly as the inclusions seen in this image.

D - Hyperphosphorylated tau

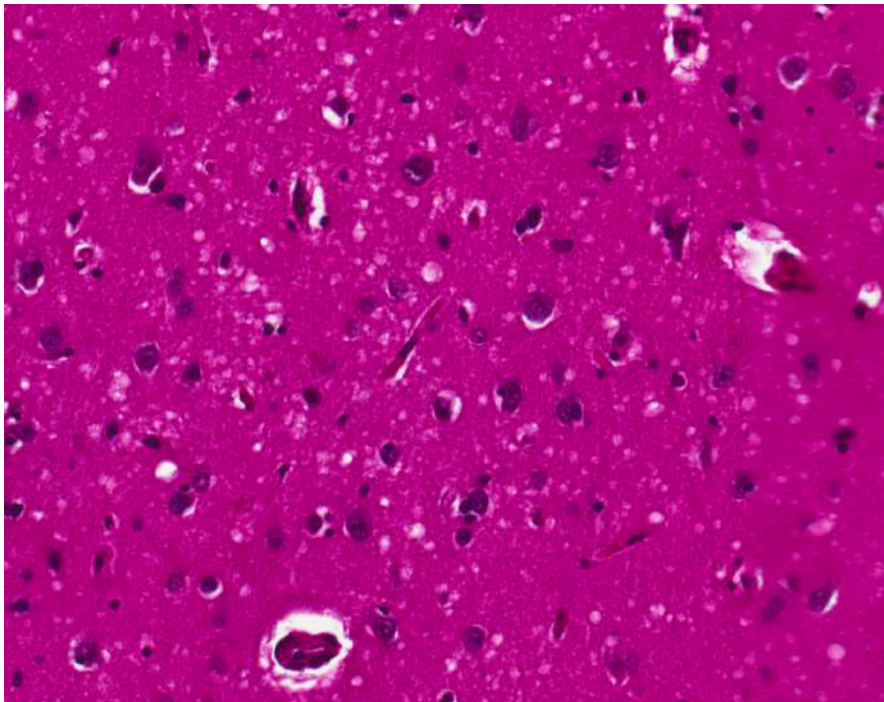
Explanation Why

Hyperphosphorylated [tau](#) constitutes the greater part of [neurofibrillary tangles](#), which are seen in the photomicrograph. [Tau proteins](#) are [microtubule-associated proteins](#) that play a central role in the preservation of cell structure. Activation of [glycogen synthase kinase-3](#) and other protein [kinases](#)

induces increased [phosphorylation](#) of [tau](#) which leads to cluster formation and development of tangles. These tangles impair neuronal function and eventually cause neuronal death, which manifests as gradual onset of [dementia](#), as was seen in this patient.

E - Prion protein

Image



Explanation Why

Abnormal [prion proteins](#) lead to deposition and formation of plaques, which promote cellular degeneration and ultimately neuronal death, as, e.g., in [Creutzfeldt Jakob disease](#). Affected individuals classically present with rapidly progressive [dementia](#) in combination with myoclonus, not with the gradually developing symptoms over several years that were seen in this patient. In addition, brain autopsy would reveal not just [atrophy](#) but rather a characteristic pattern of spongiform encephalopathy.

Question # 34

A 19-year-old girl comes to the physician for evaluation after a minor motor vehicle collision. While driving down a residential street, a young boy ran out in front of her, chasing after a ball. She applied the brakes of her vehicle and avoided hitting the boy, but then she suddenly experienced generalized weakness that rendered her unable to operate the vehicle and collided at low speed with a parked car. One minute later, she recovered her strength. She was uninjured. She has had several similar episodes of transient generalized weakness over the past month, once during an argument with her mother and another time while watching her favorite comedy movie. She has also had excessive daytime sleepiness for 18 months despite 9 hours of sleep nightly and 2 daily naps. She has fallen asleep in class several times. She often sees intensely bright colors as she is falling asleep. During this time, she is often unable to move; this inability to move is very distressing to her. Which of the following is the most appropriate nighttime pharmacotherapy for this patient?

	Answer	Image
A	Quetiapine	
B	Guanfacine	
C	Modafinil	
D	Sodium oxybate	
E	Amphetamine	
F	Duloxetine	
G	Fluoxetine	

Hint

This patient presents with cataplexy, hypnagogic hallucinations, sleep paralysis, and excessive daytime sleepiness despite good sleep hygiene. These symptoms are characteristic of narcolepsy. Pharmacotherapy should target the patient's cataplexy, which has resulted in a (minor) motor vehicle collision.

Correct Answer

A - Quetiapine

Explanation Why

[Quetiapine](#), an [atypical antipsychotic](#), is a first-line treatment option for [psychotic disorders](#), which can manifest with [hallucinations](#). However, this patient's [hypnagogic hallucinations](#) are occurring in the context of [narcolepsy](#), for which [atypical antipsychotics](#) are not an adequate treatment.

B - Guanfacine

Explanation Why

[Guanfacine](#), an α_2 adrenergic agonist, is used in the treatment of [tics](#) associated with [Tourette syndrome](#). However, this patient does not display motor or vocal [tics](#) and is therefore unlikely to have [Tourette syndrome](#). [Guanfacine](#) is not used in the treatment of [cataplexy](#).

C - Modafinil

Explanation Why

[Modafinil](#) is a recommended treatment option for patients with [narcolepsy](#) who have persistent [excessive daytime sleepiness](#) despite lifestyle modifications (e.g., > 7.5 hours of sleep per night and scheduled daytime naps). However, [modafinil](#) does not treat [cataplexy](#), which is this patient's most disabling symptom. In addition, [modafinil](#) is a stimulant and should not be taken at night.

D - Sodium oxybate

Explanation Why

[Sodium oxybate](#) is the preferred drug for severe [cataplexy](#) in [narcolepsy](#). It lowers the number of [cataplexy](#) attacks and improves nighttime sleep, thereby reducing [excessive daytime sleepiness](#). Considering it is a powerful, rapidly acting sedative, [sodium oxybate](#) is taken at night. Caution should be exercised in the prescription of [sodium oxybate](#), as it has a high potential for abuse. Overdose can cause respiratory depression, [coma](#), and death.

E - Amphetamine

Explanation Why

[Amphetamine](#) is a recommended treatment option for patients with [narcolepsy](#) who have persistent [excessive daytime sleepiness](#) despite lifestyle modifications (e.g., > 7.5 hours of sleep per night and scheduled daytime naps). However, [amphetamines](#) do not treat [cataplexy](#), which is this patient's most disabling symptom. In addition, [amphetamines](#) are stimulants and should not be taken at night.

F - Duloxetine

Explanation Why

[Duloxetine](#), an [SNRI](#), can be used to treat [cataplexy](#) as well as [sleep paralysis](#) and [hypnagogic hallucinations](#) due to [narcolepsy](#). However, it is not the most appropriate treatment for severe [cataplexy](#).

G - Fluoxetine

Explanation Why

[Fluoxetine](#), an [SSRI](#), can be used to treat [cataplexy](#), as well as [sleep paralysis](#) and [hypnagogic hallucinations](#) due to [narcolepsy](#). However, it is not the most appropriate treatment for severe [cataplexy](#).

Question # 35

A 59-year-old man is brought to the physician by his wife for a psychiatric evaluation. Over the past 12 months, his behavior has become increasingly disruptive. His wife no longer brings him along shopping because he has attempted to grope a female cashier on 2 occasions. He has begun to address the mail carrier using a racial epithet. Three years later, the patient dies. Light microscopy of sections of the frontal and temporal lobes shows intracellular inclusions of transactive response DNA binding protein (TDP-43). These proteins are bound to a regulatory molecule that usually marks them for degradation. The regulatory molecule in question is most likely which of the following?

	Answer	Image
A	Tau	
B	Kinesin	
C	Cyclin	
D	Ubiquitin	
E	Chaperone	
F	Clathrin	

Hint

This man had frontotemporal dementia, which causes changes in personality and social behavior. The postmortem histopathologic findings of intracellular inclusions of TDP-43 in the frontal and temporal lobes confirms the diagnosis. Binding of the regulatory molecule in question to proteins such as TDP-43 normally results in transport of the proteins to the proteasome.

Correct Answer

A - Tau

Explanation Why

[Tau proteins](#) stabilize [microtubules](#). Abnormal aggregates of [tau proteins](#) are seen in various [neurodegenerative brain diseases](#), including [Alzheimer disease](#) and [frontotemporal dementia](#), the diagnosis in this patient. However, [tau proteins](#) do not mark protein targets for degradation.

B - Kinesin

Explanation Why

[Kinesin](#) and [dynein](#) are motor [proteins](#) involved in transport along [microtubules](#) (e.g., movement of synaptic vesicles along [axons](#)). Mutations in [genes](#) encoding [kinesin](#) family [proteins](#) have been found in hereditary nerve disorders such as [Charcot-Marie-Tooth disease](#). However, [kinesin](#) does not mark other [proteins](#) for degradation.

C - Cyclin

Explanation Why

[Cyclins](#) control [the cell cycle](#) and transitions between [cell cycle](#) phases. [Cyclin](#) dysfunction can lead to uncontrolled cell division that causes [malignancy](#). [Cyclins](#) do not mark protein targets for degradation.

D - Ubiquitin

Explanation Why

Tagging with [ubiquitin](#) marks [proteins](#) for degradation by the [ubiquitin-proteasome system](#) (UPS). Dysfunction of the UPS is implicated in various [neurodegenerative brain diseases](#), including [frontotemporal dementia](#), as seen here, as well as [Alzheimer disease](#), [Parkinson disease](#), and [Huntington disease](#).

E - Chaperone

Explanation Why

[Chaperone proteins](#) assist in molecular assembly and folding of other [proteins](#). Defects or losses of [chaperone proteins](#) can lead to [protein misfolding](#) and contribute to neurodegeneration as seen in this patient. However, [chaperone proteins](#) do not mark other [proteins](#) for degradation.

F - Clathrin

Explanation Why

[Clathrin](#) is a protein that coats vesicles and assists in vesicular [endocytosis](#) and trafficking. Although dysfunction of [clathrin](#)-mediated [endocytosis](#) is hypothesized to be involved in the development of some [neurodegenerative brain diseases](#), [clathrin](#) does not mark protein targets for degradation.

Question # 36

A 68-year-old man is brought to the emergency department because of a 1-day history of fever and cloudy urine. He lives in a group home and has a chronic indwelling urinary catheter for benign prostatic hyperplasia. He has depression, for which he takes vilazodone. His temperature is 38.3°C (100.9°F), pulse is 89/min, and blood pressure is 110/74 mm Hg. Urine cultures grow *Enterococcus faecium* resistant to vancomycin, and therapy with intravenous linezolid is initiated. Eight hours later, he becomes agitated and starts to sweat profusely. His temperature is 39.6°C (103.3°F), pulse is 120/min, and blood pressure is 184/105 mm Hg. Neurologic examination shows increased deep tendon reflexes and clonus of the arms and legs. In addition to discontinuation of his current medication, administration of which of the following drugs is most appropriate in this patient?

	Answer	Image
A	Fluphenazine	
B	Flumazenil	
C	Dantrolene	
D	Octreotide	
E	Cyproheptadine	
F	Benztropine	

Hint

Agitation, hyperthermia, tachycardia, hypertension, diaphoresis, and evidence of neuromuscular hyperactivity (hyperreflexia, clonus) in a patient taking vilazodone (a serotonergic drug) suggest serotonin syndrome. The administration of linezolid, an antibiotic that has mild monoamine oxidase inhibitor activity, was likely the trigger.

Correct Answer

A - Fluphenazine

Explanation Why

[Fluphenazine](#) is a typical high-[potency antipsychotic](#) that is used for the treatment of acute agitation in the setting of [psychotic episodes](#). The anti-[dopaminergic](#) effects of this drug would not be helpful in the management of [serotonin syndrome](#).

B - Flumazenil

Explanation Why

[Flumazenil](#) is a selective antagonist of the GABA_A-receptor and that is used in the treatment of [benzodiazepine overdose](#). This patient does not exhibit any findings indicative of [benzodiazepine overdose](#), which manifests as sedation and respiratory depression. Administration of [flumazenil](#) is not indicated in a patient with [serotonin syndrome](#).

C - Dantrolene

Explanation Why

[Dantrolene](#) is a [ryanodine receptor](#) antagonist that is used as the first-line treatment for [malignant hyperthermia](#), which could explain this patient's [fever](#) and signs of autonomic hyperactivity ([hypertension](#), [tachycardia](#)). However, [malignant hyperthermia](#) almost exclusively occurs after exposure to certain drugs, such as [succinylcholine](#) and anesthetic inhalants, and is not associated with administration of [antidepressants](#) or serotonergic agents.

D - Octreotide

Explanation Why

[Octreotide](#) is a [somatostatin](#) analog that is used for symptomatic relief in patients with [carcinoid syndrome](#). It decreases [serotonin](#) secretion and impairs peripheral conversion of [serotonin](#) to [5-HIAA](#). Despite these antiserotonergic properties, [octreotide](#) is not used for the treatment of [serotonin syndrome](#), as it does not block binding of [serotonin](#) to [serotonin](#) receptors.

E - Cyproheptadine

Explanation Why

[Cyproheptadine](#) is a H_1 -, $5-HT_{1A}$ -, and $5-HT_{2A}$ -receptor antagonist and is used as first-line [antidote](#) in patients with [serotonin syndrome](#) who do not respond to supportive measures and discontinuation of the offending drug. This drug competes with the excess [serotonin](#) for receptor binding, reducing pathological overstimulation. [Cyproheptadine](#) should be used in conjunction with cooling measures (e.g., application of ice packs, cold compresses) and [benzodiazepines](#) for sedation.

F - Benztropine

Explanation Why

[Benztropine](#) is a [muscarinic antagonist](#) that is commonly used in the treatment of parkinsonian and [extrapyramidal symptoms](#). [Benztropine](#) can also be used in the setting of mild [neuroleptic malignant syndrome](#), a condition that manifests with findings very similar to those seen in this patient (e.g., autonomic hyperactivity) but without myoclonus or [hyperreflexia](#). Because [benztropine](#) does not exhibit antiserotonergic activity, it would not be indicated in a patient with [serotonin syndrome](#).

Question # 37

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

Opening pressure	120 mm H ₂ O
Appearance	Clear
Protein	47 mg/dL
Glucose	68 mg/dL
White cell count	280/mm ³
Segmented neutrophils	15%
Lymphocytes	85%

Which of the following is the most likely causal organism?

	Answer	Image
A	Mumps virus	
B	Echovirus	
C	Listeria monocytogenes	

	Answer	Image
D	Herpes simplex virus	
E	Streptococcus pneumoniae	
F	Neisseria meningitidis	

Hint

Involuntary flexion of the knees and hips in response to forced flexion of the neck is referred to as a positive Brudzinski sign. Together with fever, headaches, photophobia, and neck stiffness, this suggests acute meningitis. CSF findings of normal opening pressure, clear appearance, slightly elevated protein, normal glucose, and lymphocytic pleocytosis are consistent with aseptic meningitis.

Correct Answer

A - Mumps virus

Explanation Why

The [mumps virus](#) may cause aseptic [meningitis](#) in rare cases, in which case patients present with [fever](#), [headache](#), photophobia, [nuchal rigidity](#), and signs of meningeal irritation. However, other classic symptoms of [mumps](#), e.g., [inflammation](#) of the salivary glands (particularly [parotitis](#)), would also be expected. [Mumps](#) is also unlikely in a patient who has received all age-appropriate [vaccinations](#).

B - Echovirus

Explanation But

Other organisms that cause [meningitis](#) in teenagers include [N. meningitidis](#), [S. pneumoniae](#), and [HSV-2](#).

Explanation Why

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

C - Listeria monocytogenes

Explanation Why

[Listeria monocytogenes](#) is a common cause of bacterial [meningitis](#), especially in [immunocompromised](#) patients, [neonates](#), and the elderly. Patients present with [fever](#), [headache](#), [nuchal rigidity](#), and signs of meningeal irritation. However, bacterial [meningitis](#) would manifest

more acutely and with more severe features, e.g., altered mental status or [seizures](#). Furthermore, [CSF](#) would have a cloudy appearance, elevated opening pressure, neutrophilic-predominant [leukocytosis](#), elevated protein, low glucose, and elevated [lactate](#).

D - Herpes simplex virus

Explanation Why

Herpes simplex virus (HSV) is a common cause of encephalitis and [meningitis](#) in children and teenagers. [HSV encephalitis](#) is mainly caused by [HSV-1](#), whereas HSV [meningitis](#) is typically caused by [HSV-2](#). Either can manifest with [fever](#), [headache](#), photophobia, [nuchal rigidity](#), and [lymphocytic pleocytosis](#) with slightly elevated [proteins](#) in [CSF](#). However, another virus is statistically more common than [HSV-2](#) as a cause of aseptic [meningitis](#). Furthermore, since [HSV-1](#) mainly affects the [temporal lobe](#), focal neurological deficits such as altered [sense of smell](#), [aphasia](#), [memory](#) loss, or [ataxia](#) would be expected. Other typical symptoms include [seizures](#), altered mental status, and behavioral changes.

E - Streptococcus pneumoniae

Explanation Why

[Streptococcus pneumoniae](#) is the most common cause of bacterial [meningitis](#) in [infants](#), adults, and the elderly. Patients present with [fever](#), [headache](#), [nuchal rigidity](#), and signs of meningeal irritation. However, bacterial [meningitis](#) would manifest more acutely and with more severe features, e.g., altered mental status or [seizures](#). Furthermore, [CSF](#) would have a cloudy appearance, elevated opening pressure, neutrophilic-predominant [leukocytosis](#), elevated protein, low glucose, and elevated [lactate](#).

F - Neisseria meningitidis

Explanation Why

[Neisseria meningitidis](#) is the most common cause of [meningitis](#) in children and teenagers, as well as the main cause of [meningitis](#) on college campuses. It usually manifests with [fever](#), [headache](#), [nuchal](#)

[rigidity](#), and signs of meningeal irritation. A rash is present in some cases. However, bacterial [meningitis](#) would manifest more acutely and with more severe features, e.g., altered mental status or [seizures](#). [CSF](#) would have a cloudy appearance, elevated opening pressure, neutrophilic [pleocytosis](#), elevated protein, low glucose, and elevated [lactate](#).

Question # 38

A 58-year-old woman with HIV infection is brought to the emergency department because of a 2-week history of headaches, blurred vision, and confusion. Her current medications include antiretroviral therapy and trimethoprim-sulfamethoxazole. Neurological examination shows ataxia and memory impairment. Her CD4+ T-lymphocyte count is $90/\text{mm}^3$. Analysis of her cerebrospinal fluid analysis shows lymphocytic predominant pleocytosis, and PCR is positive for Epstein-Barr virus DNA. An MRI of the brain with contrast shows a solitary, weakly ring-enhancing lesion with well-defined borders involving the corpus callosum. Which of the following is the most likely diagnosis?

	Answer	Image
A	AIDS dementia	
B	Cerebral toxoplasmosis	
C	Primary cerebral lymphoma	
D	Progressive multifocal leukoencephalopathy	
E	Bacterial brain abscess	
F	Glioblastoma multiforme	

Hint

This patient with HIV and a low CD4 count presents with neurological impairment (ataxia, confusion, memory dysfunction). The likely diagnosis can be inferred from her MRI findings (a solitary ring-enhancing lesion) and CSF analysis result (EBV DNA in the CSF).

Correct Answer

A - AIDS dementia

Explanation Why

[AIDS dementia](#) refers to the clinical syndrome of cognitive deficits that frequently affects [AIDS](#) patients, which ranges from minor [memory](#) impairment to severe neurologic deficits. Although this patient's symptoms could potentially correspond to [AIDS dementia](#), her [MRI](#) does not show the cerebral atrophy that would confirm such a diagnosis but rather shows a solitary [ring-enhancing](#) lesion consistent with another condition.

B - Cerebral toxoplasmosis

Explanation Why

[Cerebral toxoplasmosis](#) is often asymptomatic in immunocompetent individuals. Reactivation of [T. gondii](#) usually occurs in the [CNS](#) of [immunocompromised](#) patients, resulting in [toxoplasmic encephalitis](#) (which presents with [fever](#), [headache](#), impaired vigilance, [seizures](#), and focal neurological deficits) and multiple [ring-enhancing](#) cerebral lesions on imaging. For this reason, [HIV](#) patients with a [CD4](#) count $< 100/\text{mm}^3$ are typically started on [toxoplasmosis](#) prophylaxis with [TMP-SMX](#) to reduce the chance of reactivation, as is the case in this patient. This patient's solitary cerebral lesion, the [CSF analysis](#) result (positive for [EBV DNA](#)), and prophylaxis history make [toxoplasmosis](#) less likely.

C - Primary cerebral lymphoma

Explanation Why

Primary cerebral [lymphoma](#) is a [non-Hodgkin lymphoma](#) with a much higher [incidence](#) in [HIV/AIDS](#) patients than in the general population. It has a strong association with [EBV infection](#) and is derived from [B cells](#). The condition can present with focal neurological deficits, neuropsychiatric symptoms, [signs of elevated intracranial pressure](#), and/or [seizures](#). It also results in solitary [ring-](#)

[enhancing](#) cerebral lesions on imaging. If findings on [CSF](#) are inconclusive, pathologic examination of a brain biopsy specimen is indicated to confirm the diagnosis prior to starting treatment with [chemotherapy](#) and/or radiation.

D - Progressive multifocal leukoencephalopathy

Explanation Why

[PML](#) is a [demyelinating](#) disease of the [CNS](#). It is an [AIDS-defining](#) condition and is caused by reactivation of the [JC virus](#). It does not cause [ring-enhancing](#) cerebral lesions on imaging, as seen in this patient, but rather disseminated non-enhancing lesions. Furthermore, [CSF analysis](#) in [PML](#) shows [JC virus DNA](#) on [PCR](#), but the [CSF](#) findings in this patient only include [EBV DNA](#).

E - Bacterial brain abscess

Explanation Why

Although bacterial [abscesses](#) can cause [ring-enhancing](#) lesions in patients with [HIV/AIDS](#), they are not the most common cause of [ring-enhancing](#) lesions and are not associated with [EBV](#) in the [CSF](#). Furthermore, bacterial [brain abscess](#) would present with neutrophilic [pleocytosis](#) on [CSF](#) rather than the [lymphocytic pleocytosis](#) seen here.

F - Glioblastoma multiforme

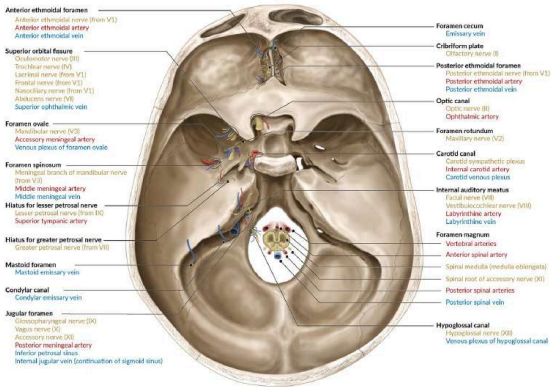
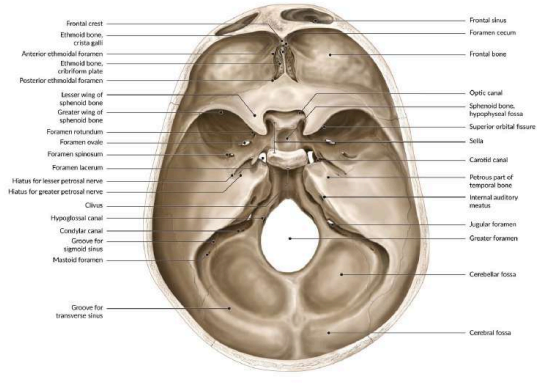
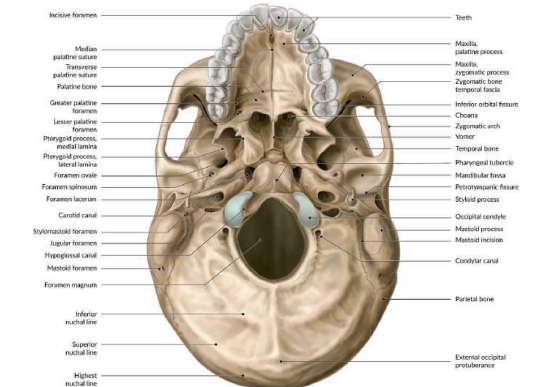
Explanation Why

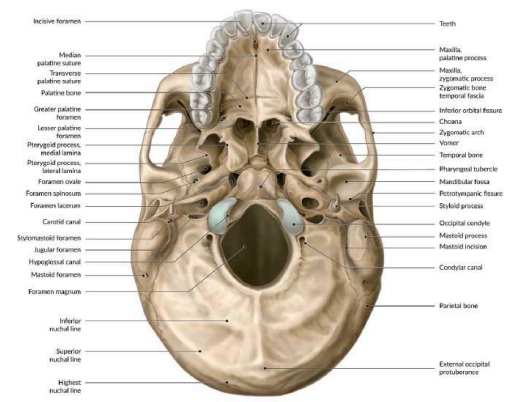
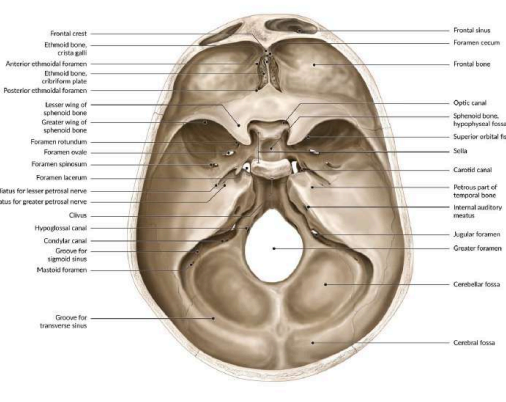
[Glioblastoma multiforme](#) is the most common primary malignant [brain tumor](#) in adults and often involves the corpus callosum. It presents with [headaches](#), personality changes, [seizures](#), and/or other neurological deficits. While [glioblastomas](#) may appear as a [ring-enhancing](#) lesion on imaging, they are poorly-defined tumors that often have a central clearing reflecting [necrosis](#), unlike this patient's well-defined lesion. A different cause of [ring-enhancing lesion](#) in this patient with [AIDS](#) is more likely.

Question # 39

A 28-year-old man comes to the physician because of a persistent tingling sensation in the right side of his face. The sensation began after he underwent an extraction of an impacted molar 2 weeks ago. Examination shows decreased sensation of the skin over the right side of the mandible, chin, and the anterior portion of the tongue. Taste sensation is preserved. The affected nerve exits the skull through which of the following openings?

	Answer	Image
A	Foramen magnum	
B	Hypoglossal canal	

	Answer	Image
C	Foramen ovale	 Anterior ethmoidal foramen Anterior ethmoidal nerve (branch V1) Anterior ethmoidal artery Anterior ethmoidal vein Superior orbital fissure Oculomotor nerve (III) Trochlear nerve (IV) Lacrimal nerve (branch V1) Frontal nerve (branch V1) Nasociliary nerve (branch V1) Abducens nerve (VI) Superior ophthalmic vein Foramen ovale Mandibular nerve (V3) Accessory meningeal artery Venous plexus of foramen ovale Foramen spinosum Meningeal branch of mandibular nerve (branch V3) Middle meningeal artery Middle meningeal vein Hiatus for lesser petrosal nerve Lesser petrosal nerve (branch G) Superior tympanic artery Hiatus for greater petrosal nerve Greater petrosal nerve (branch G) Mastoid foramen Mastoid emissary vein Condylar canal Condylar emissary vein Jugular foramen Vagus nerve (X) Vagus nerve (X) Accessory nerve (XI) Posterior meningeal artery Inferior petrosal sinus Internal jugular vein (continuation of sigmoid sinus) Foramen occiput Emissary vein Cubiform plate Occipital nerve (II) Posterior ethmoidal foramen Posterior ethmoidal artery Posterior ethmoidal vein Optic canal Optic nerve (II) Ophthalmic artery Foramen rotundum Maxillary nerve (V2) Carotid canal Carotid intropetrous plexus Internal carotid artery Carotid venous plexus Internal auditory meatus Facial nerve (VII) Vestibulocochlear nerve (VIII) Labyrinthine artery Labyrinthine vein Foramen magnum Vertebral arteries Anterior spinal artery Spinal medulla (medulla oblongata) Spinal root of accessory nerve (XI) Posterior spinal arteries Posterior spinal vein Hypoglossal canal Hypoglossal nerve (XII) Venous plexus of hypoglossal canal
D	Foramen rotundum	 Frontal crest Ethmoidal bone, cribriform Anterior ethmoidal foramen Ethmoidal bone, cribriform plate Posterior ethmoidal foramen Lesser wing of sphenoid bone Greater wing of sphenoid bone Foramen rotundum Foramen ovale Foramen spinosum Foramen lacerum Hiatus for lesser petrosal nerve Hiatus for greater petrosal nerve Olivus Hypoglossal canal Condylar canal Groove for sigmoid sinus Mastoid foramen Groove for transverse sinus Frontal sinus Foramen occiput Frontal bone Optic canal Sphenoid bone Hypophyseal fossa Superior orbital fissure Sella Carotid canal Petrous part of temporal bone Internal auditory meatus Jugular foramen Greater foramen Cerebellar tonsil Cerebellar fossa
E	Jugular foramen	 Incisive foramen Mandibular foramen Transverse palatine suture Palatine bone Greater palatine foramen Lesser palatine foramen Pharyngeal process, medial lamina Pharyngeal process, lateral lamina Foramen ovale Foramen spinosum Foramen lacerum Carotid canal Stylomastoid foramen Jugular foramen Hypoglossal canal Mastoid foramen Foramen magnum Inferior nuchal line Superior nuchal line Highest nuchal line Teeth Mandible, palatine process Mandible, zygomatic process Zygomatic bone Temporal bone Inferior orbital fissure Choana Zygomatic arch Vomer Temporal bone Pharyngeal tubercle Mandibular fossa Pharyngeal process Styloid process Occipital condyle Mastoid process Mastoid incision Condylar canal Parietal bone External occipital protuberance

	Answer	Image
F	Stylomastoid foramen	 This anatomical illustration shows the inferior view of the base of the human skull. The central feature is the foramen magnum, with the occipital condyles on either side. The petrous parts of the temporal bones are visible, with the stylomastoid foramen clearly marked. Numerous other foramina and bony landmarks are labeled, including the internal acoustic meatus, jugular foramen, and various cranial nerve exits. The labels are organized in two columns flanking the central skull image.
G	Superior orbital fissure	 This anatomical illustration shows the superior view of the base of the human skull, focusing on the cranial base. The superior orbital fissures are prominently displayed on either side of the sella turcica. The image highlights the foramina through which the optic nerves and other cranial nerves pass. Labels identify structures such as the optic canals, sphenoid bone, and the various foramina of the anterior and middle cranial fossae. The labels are organized in two columns flanking the central skull image.

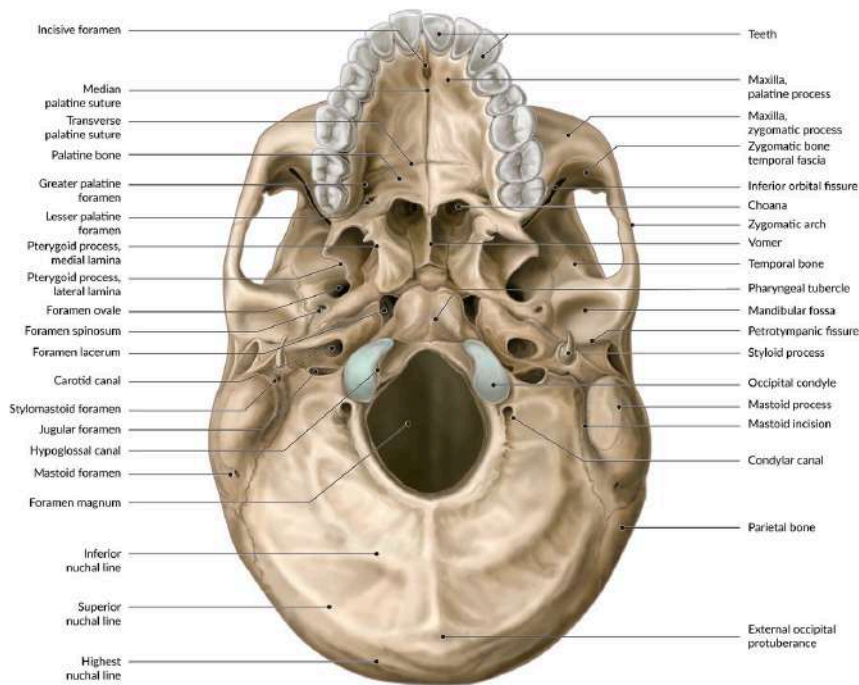
Hint

The patient's symptoms suggest a lesion of the mandibular branch of the trigeminal nerve (CN V₃).

Correct Answer

A - Foramen magnum

Image

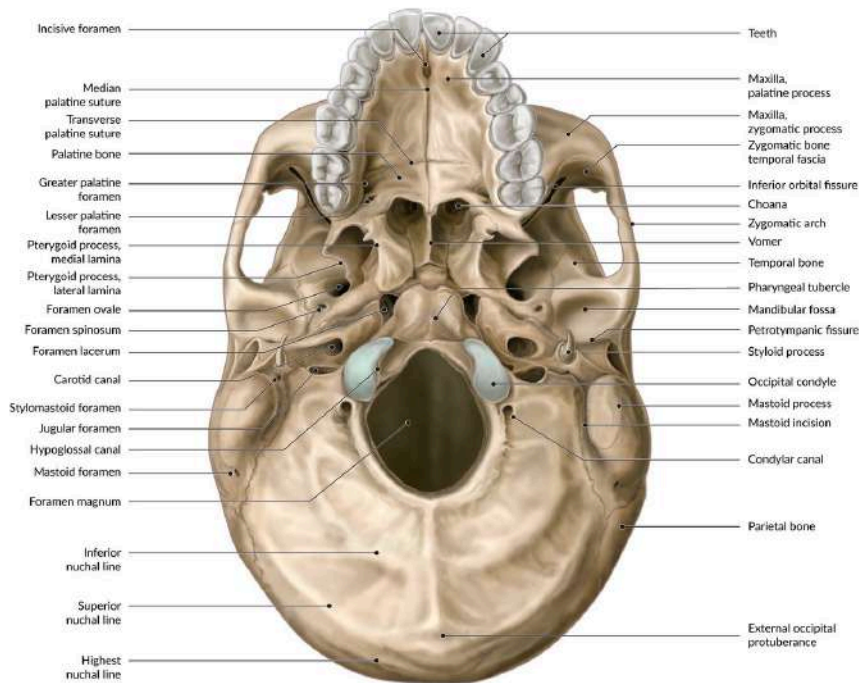


Explanation Why

The [foramen magnum](#) serves as the passage for the [medulla oblongata](#), [accessory nerve \(XI\)](#), [vertebral arteries](#), [spinal arteries](#), and [spinal veins](#). The mandibular branch of the [trigeminal nerve](#) does not exit the [skull](#) through the [foramen magnum](#).

B - Hypoglossal canal

Image



Explanation Why

The [hypoglossal canal](#) serves as the passage for the [hypoglossal nerve](#), not the mandibular branch of the [trigeminal nerve](#). Lesions of this nerve would result in [atrophy](#) and [fasciculations](#) of the [tongue](#) on the side of the lesion and deviation of the [tongue](#) to the ipsilateral side.

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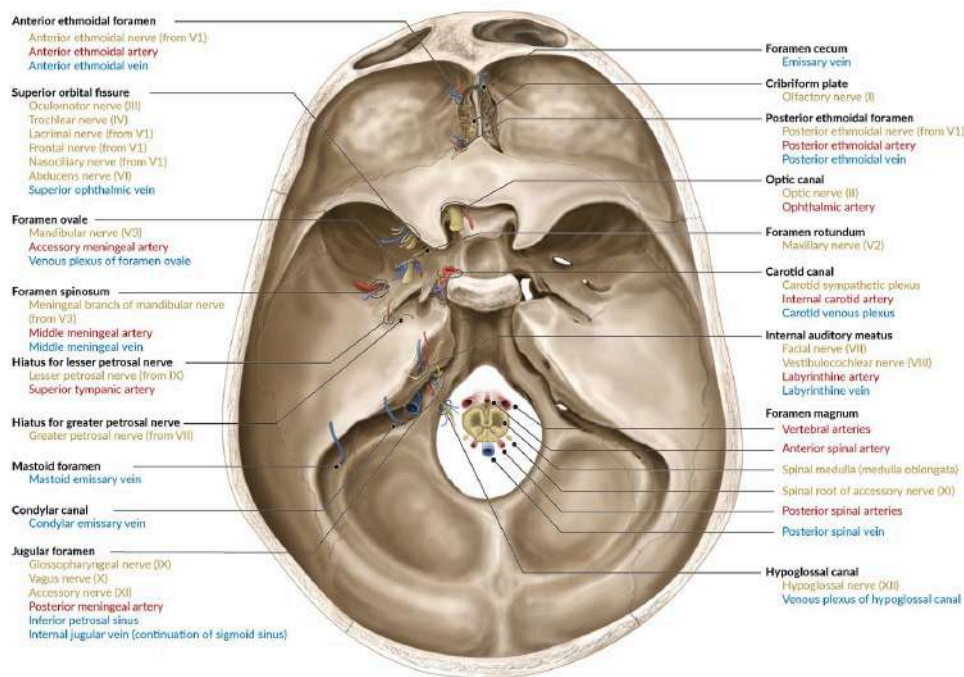
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C - Foramen ovale

Image

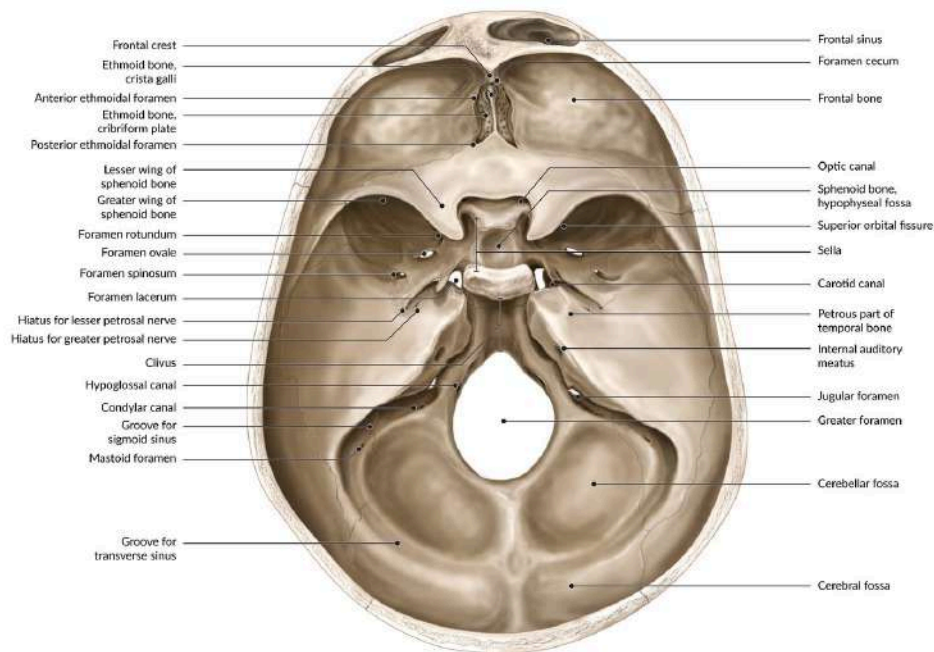


Explanation Why

The mandibular branch of the [trigeminal nerve](#) exits the [skull](#) through the foramen ovale. A lesion of this nerve, as is most likely present in this patient, results in ipsilateral decreased sensation of the [skin](#) over the [mandible](#), chin, parts of the [auricle](#) and the temple, the buccal mucosa, and the [anterior](#) $\frac{2}{3}$ of the [tongue](#). The mandibular branch also provides motor innervation to the [muscles of mastication](#). The other structures that pass through the foramen ovale are the accessory meningeal artery, the lesser petrosal nerve, and the emissary veins connecting the [cavernous sinus](#) with the pterygoid plexus.

D - Foramen rotundum

Image

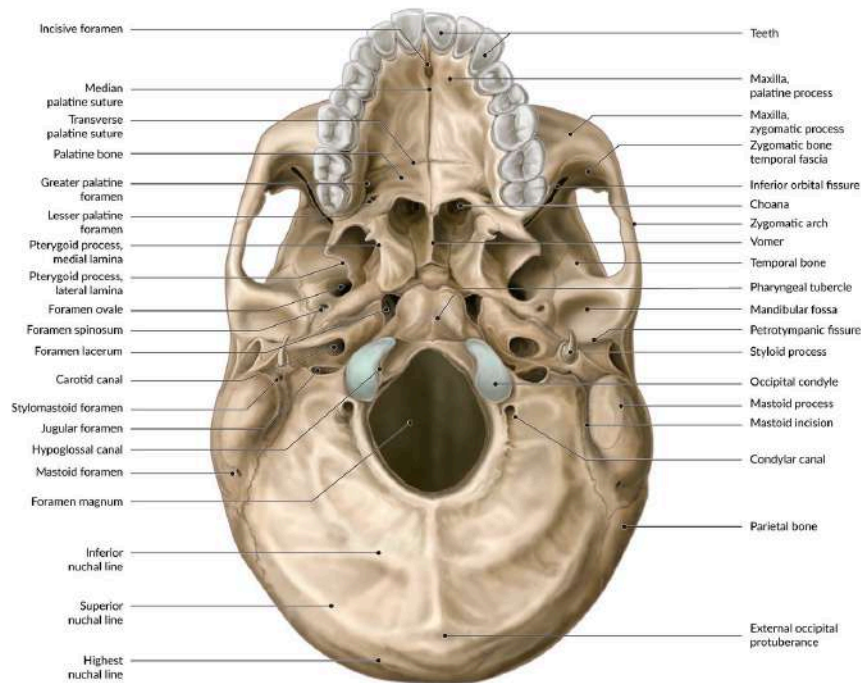


Explanation Why

The [foramen rotundum](#) serves as the passage for the [maxillary branch of the trigeminal nerve](#), not the mandibular branch. A lesion of this nerve would result in anesthesia to the mid-face, not to the lower part of the face, as seen in the patient here.

E - Jugular foramen

Image

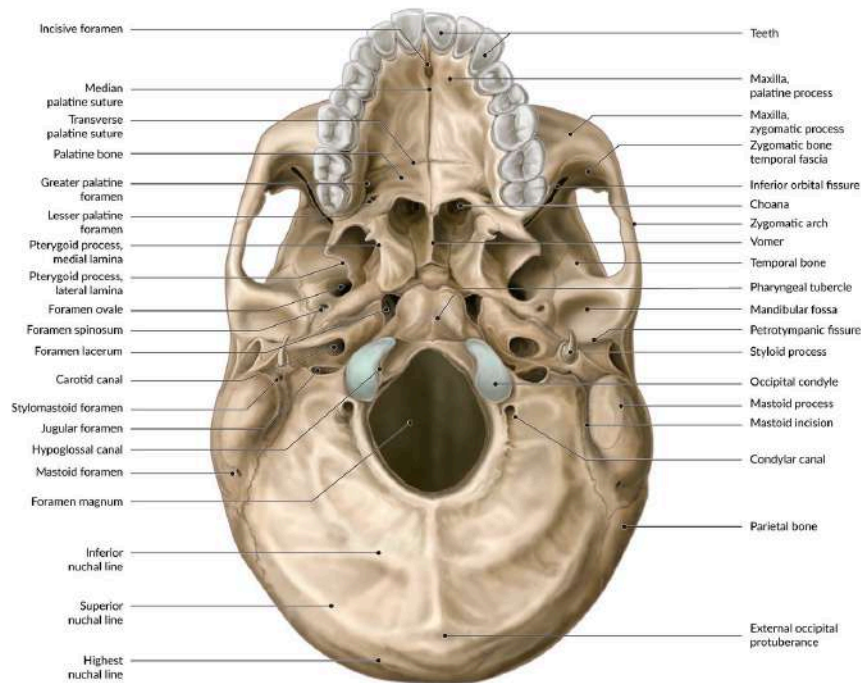


Explanation Why

The [jugular foramen](#) serves as the passage for the [glossopharyngeal nerve](#) (IX), [vagus nerve](#) (X), [accessory nerve](#) (XI), and the [internal jugular vein](#). The mandibular branch of the [trigeminal nerve](#) does not exit the [skull](#) through the [jugular foramen](#).

F - Stylomastoid foramen

Image

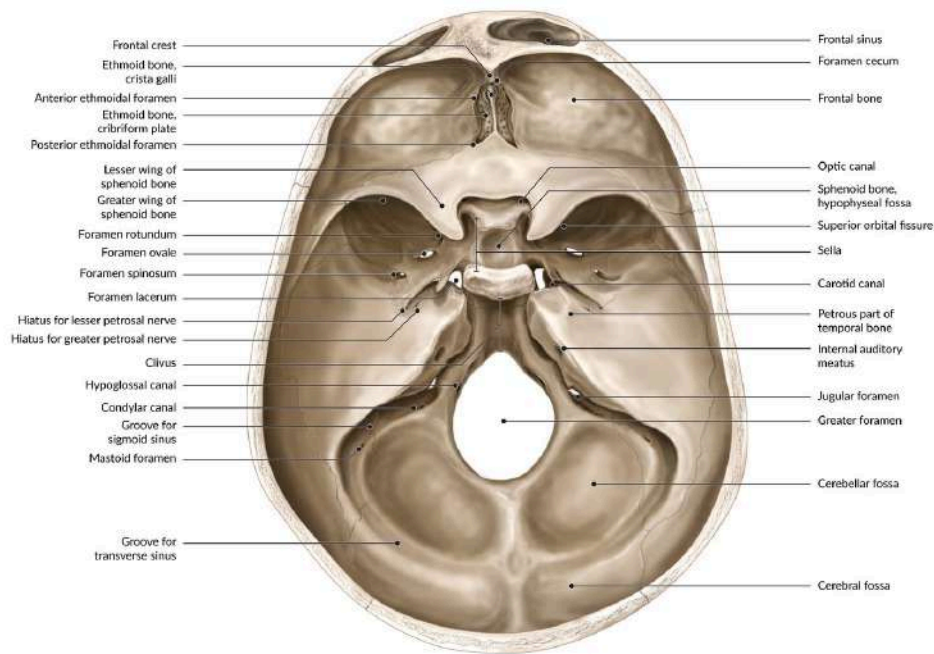


Explanation Why

The [stylomastoid foramen](#) serves as the passage for the [facial nerve](#), not the mandibular branch of the [trigeminal nerve](#). Lesions of the [facial nerve](#) at this level would cause [peripheral facial nerve palsy](#), which presents with paralysis of the ipsilateral [eyelid](#), forehead, and lower facial muscles.

G - Superior orbital fissure

Image

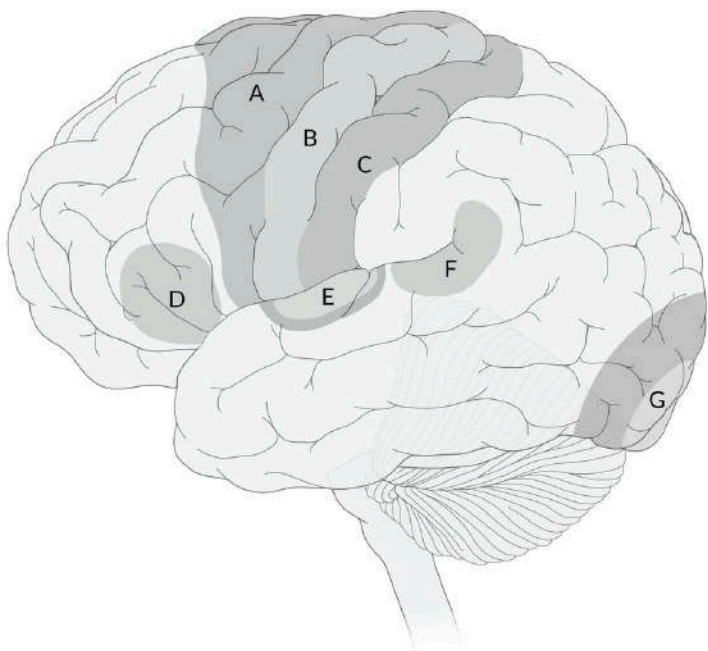


Explanation Why

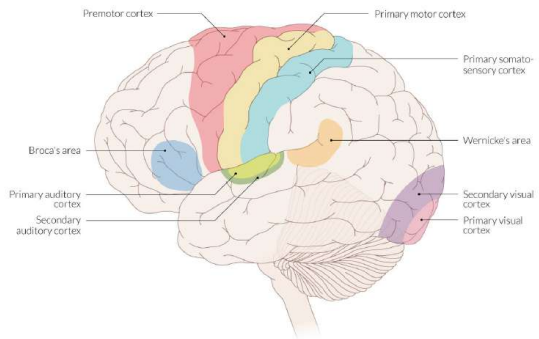
The [superior orbital fissure](#) serves as the passage for the [oculomotor nerve](#) (III), the [trochlear nerve](#) (IV), branches of the [ophthalmic nerve](#) (V₁), the [abducens nerve](#) (VI), and the superior [ophthalmic vein](#). The mandibular branch of the [trigeminal nerve](#) does not exit the [skull](#) through the [superior orbital fissure](#).

Question # 40

A 55-year-old man is brought to the emergency department because of sudden-onset of difficulty speaking for 1 hour. He has hypertension, dyslipidemia, and type 2 diabetes mellitus. Current medications include atorvastatin, lisinopril, and metformin. He is 213 cm (7 ft) tall. On examination, the patient speaks slowly in simple sentences that consist of only one word. He seems to have difficulties understanding grammatically complex sentences and appears to be frustrated at the inability to speak fluently. He is able to follow commands. When another individual tries to enter the room, the physician asks the patient to “hold the door,” and he does so immediately. Based on his symptoms, which of the following labeled areas in the schematic overview of a normal brain is most likely affected in this patient?



	Answer	Image
A	A	
B	B	

	Answer	Image
C	C	
D	D	 A lateral view of the human brain with various cortical areas highlighted in different colors and labeled. The labels include: Premotor cortex (red), Primary motor cortex (yellow), Primary somato-sensory cortex (light blue), Broca's area (dark blue), Primary auditory cortex (green), Secondary auditory cortex (light green), Wernicke's area (orange), Secondary visual cortex (purple), and Primary visual cortex (dark purple).
E	E	
F	F	
G	G	

Hint

In response to further questioning, the patient says, “Hodor Hodor Hodor Hodor Hodor Hodor Hodor Hodor Hodor.”

Correct Answer

A - A

Explanation Why

An [ischemic](#) injury to area A, the [premotor cortex](#), is associated with difficulty of planning, initiating, and maintaining muscle movements despite no presence of muscle weakness ([apraxia](#)) along with difficulties using sensory feedback for the control of movement. Hence, patients with [premotor cortex](#) lesions may be unable to execute motor movements needed to produce [speech](#) (verbal apraxia). Verbal apraxia is a disorder of [speech](#) articulation, characterized by halting [speech](#) and [speech](#) sound distortions and errors. This patient, however, has difficulty with language expression.

B - B

Explanation Why

An [ischemic](#) injury to area B, the [primary motor cortex](#), manifests with contralateral [hemiplegia](#) or [hemiparesis](#) as well as [dysarthria](#) due to a motor dysfunction of the facial muscles and [tongue](#) muscles. This results in typical pathologic [speech](#) patterns such as slurring, mumbling, and changes in speed and pitch. However, this patient has difficulty with language expression, not with the production of [speech](#) sounds.

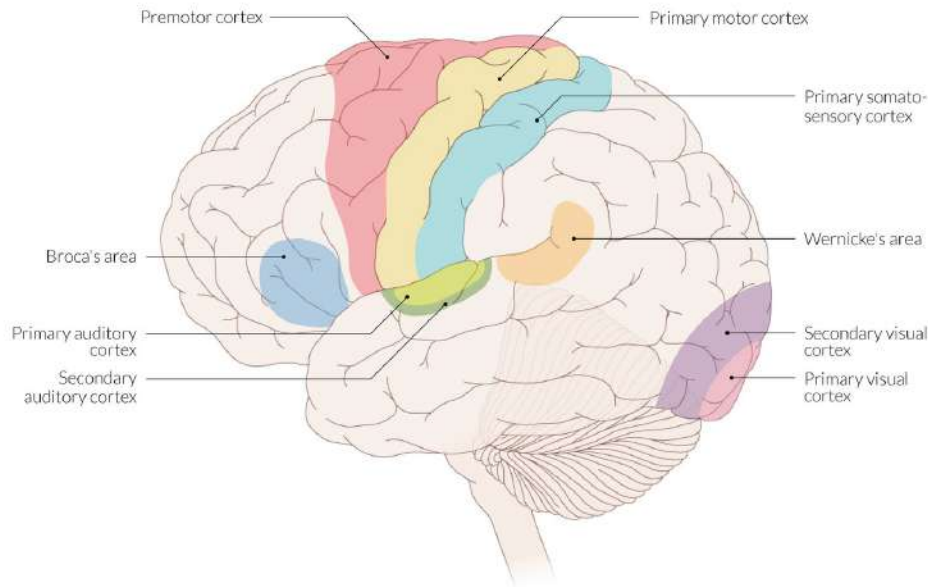
C - C

Explanation Why

An [ischemic](#) injury to area C, the [primary somatosensory cortex](#), causes contralateral numbness, tingling, and partial sensory loss, which this patient does not have. Moreover, [primary somatosensory cortex](#) lesions would not affect [speech](#) production.

D - D

Image



Explanation But

Taking into account this patient's cardiovascular [risk factors](#) ([hypertension](#), [hyperlipidemia](#), and [type 2 diabetes mellitus](#)), his symptoms are likely the result of an acute [ischemic stroke](#). This patient's tall stature could result from underlying [homocystinuria](#), which predisposes to thromboses and [atherosclerosis](#), and subsequent [stroke](#). However, he lacks other features of [homocystinuria](#), which include [osteoporosis](#), [lens dislocation](#), and a [Marfanoid habitus](#) with long, thin extremities.

Explanation Why

This patient's nonfluent, telegraphic [speech](#) pattern with constant repetition of one word, in combination with preserved comprehension of simple sentences and commands, is characteristic of [Broca aphasia](#) ([expressive aphasia](#)). An [ischemic stroke](#) involving area D, the [Broca area](#), in the dominant (usually left) hemisphere results in [expressive aphasia](#). Affected individuals typically appear frustrated by their [speech](#) deficits. Language comprehension is relatively intact as long as the [Wernicke area](#) in the [temporal lobe](#) is unaffected, although there may be difficulties understanding grammatically complex [speech](#). [Broca aphasia](#) due to cerebral [infarction](#) may occur as an isolated finding or can be accompanied by contralateral, brachiofacial sensorimotor [hemiparesis](#).

E - E

Explanation Why

An [ischemic](#) injury to area E, the [primary auditory cortex](#), can cause difficulty in sound localization and subtle hearing dysfunction if the injury is unilateral or it can cause cortical deafness with complete loss of comprehension if the injury is severe and bilateral. However, this patient's hearing is intact.

F - F

Explanation Why

An [ischemic](#) injury to area F, the [Wernicke area](#), causes [Wernicke aphasia](#), which is characterized by markedly impaired comprehension, [neologisms](#), long and grammatically correct but nonsensical sentences, and a lack of [insight](#) regarding the condition. This patient, however, expresses frustration at his [speech](#) impairment, showing [insight](#) and can understand simple sentences.

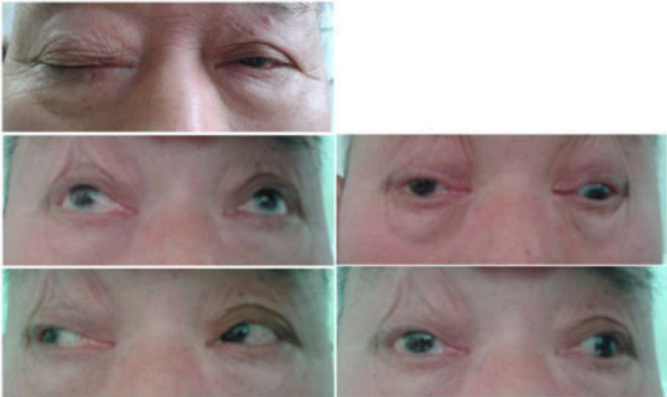
G - G

Explanation Why

An [ischemic](#) injury to area G, the [primary visual cortex](#), causes cortical blindness with [macular sparing](#), not [aphasia](#).

Question # 1

A 56-year-old man comes to the physician because of worsening double vision and drooping of the right eyelid for 2 days. He has also had frequent headaches over the past month. Physical examination shows right eye deviation laterally and inferiorly at rest. The right pupil is dilated and does not react to light or with accommodation. The patient's diplopia improves slightly on looking to the right. Which of the following is the most likely cause of this patient's findings?

	Answer	Image
A	Thrombosis of the cavernous sinus	
B	Ischemic damage to intraneural arterioles	
C	Aneurysm of the posterior communicating artery	
D	Demyelination of the medial longitudinal fasciculus	
E	Enlarging pituitary adenoma	
F	Infarction of the midbrain	

Hint

Double vision, eyelid droop, lateral and inferior eye deviation at rest, and a dilated pupil that does not react to light point to oculomotor nerve (CN III) palsy, with both somatic and parasympathetic involvement.

Correct Answer

A - Thrombosis of the cavernous sinus

Explanation Why

Thrombosis of the [cavernous sinus](#) has a highly variable clinical presentation because of the number of [cranial nerves](#) passing through the region ([CN III](#), IV, V1, V2 VI). Patients with [cavernous sinus thrombosis](#) can present with [headaches](#) and unilateral [CN III](#) palsy. However, this patient does not have the typical signs of [fever](#), unilateral [periorbital edema](#), photophobia, and [chemosis](#) seen in [cavernous sinus thrombosis](#). Moreover, isolated involvement of [CN III](#) without damage to any of the other [cranial nerves](#) that pass through the [cavernous sinus](#) would be uncommon.

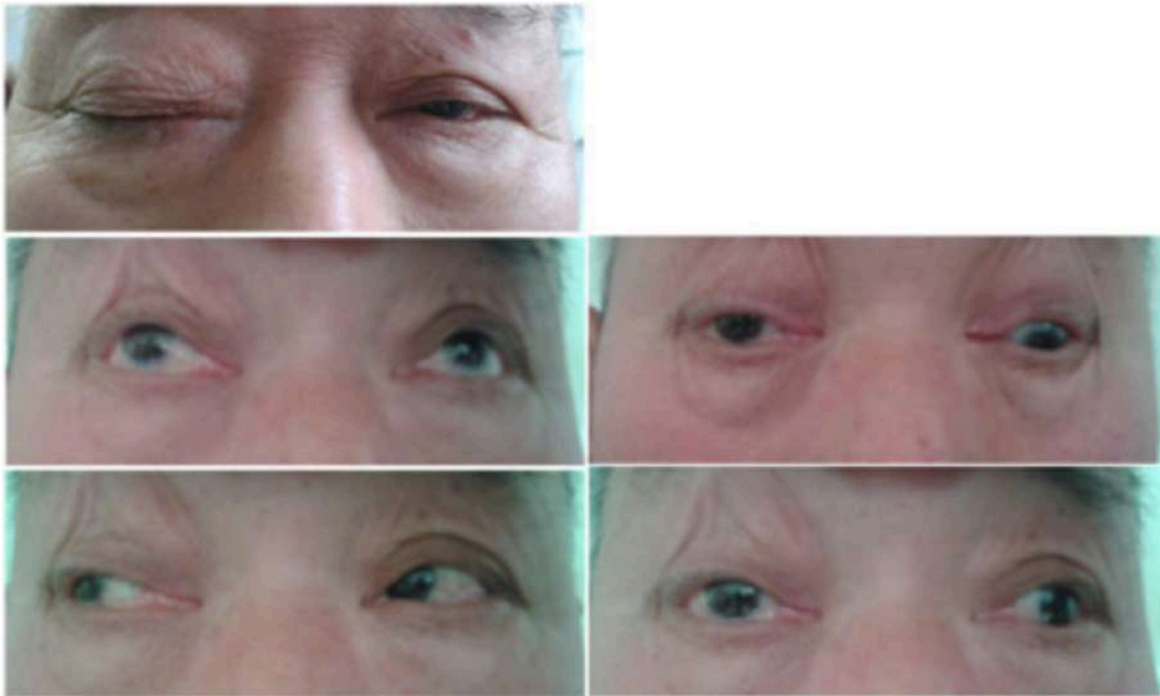
B - Ischemic damage to intraneural arterioles

Explanation Why

[Ischemia](#) of the intraneural [arterioles](#) of [CN III](#) is commonly caused by [nonenzymatic glycosylation](#) of vasculature, in which prolonged periods of [hyperglycemia](#) (due to [diabetes mellitus](#)) lead to irreversible damage to small vessels. The inner part of [CN III](#) provides motor output to the [extraocular muscles](#) and is most sensitive to [ischemia](#) because of its reliance on diffusion for oxygen and nutrients. However, [ischemic](#) damage to [CN III](#) typically manifests with a pupil-sparing palsy.

C - Aneurysm of the posterior communicating artery

Image



Explanation But

Acute [CN III palsy](#) due to a [cerebral aneurysm](#) is very concerning for imminent rupture. A patient presenting with dilated pupils and a history of recent [headaches](#) should, therefore, be tested with an urgent [MRI](#) with MR angiography.

Explanation Why

An [aneurysm](#) of the [posterior communicating artery](#) can cause compression of the nearby [oculomotor nerve](#) ([CN III](#)). Compressive lesions are characterized by pupillary involvement due to injury to the outer [parasympathetic](#) layer of [CN III](#) (which controls pupil dilation, light reactivity, and [accommodation](#)). Additional injury to the deeper somatic fibers of the nerve (which control [extraocular muscles](#)) is responsible for this patient's [ptosis](#) and “down and out” gaze.

D - Demyelination of the medial longitudinal fasciculus

Explanation Why

[Demyelination](#) of the [medial longitudinal fasciculus](#) ([MLF](#)) causes [internuclear ophthalmoplegia](#) ([INO](#)). When present bilaterally, [INO](#) is often a sign of [multiple sclerosis](#). Lesions in the [MLF](#) cause horizontal [diplopia](#) and impaired [adduction](#) on [lateral](#) gaze in one [eye](#), with nystagmus in the contralateral [abducting eye](#). However, this patient does not have nystagmus and the [diplopia](#) in [INO](#) is only present when the patient's gaze moves towards the contralateral side of the lesion, in contrast to this patient's resting [diplopia](#). Moreover, [INO](#) would not explain this patient's [eyelid](#) droop, [lateral](#) and inferior [eye](#) deviation at rest, or the dilated pupil.

E - Enlarging pituitary adenoma

Explanation Why

Enlarging [pituitary adenomas](#) typically present with [bitemporal hemianopsia](#) due to compression of the [optic chiasm](#). Sufficiently large [adenomas](#) can cause [headaches](#) and [CN III](#) palsy due to compression resulting from [lateral](#) extension of the [tumor](#). However, a [tumor](#) at the [optic chiasm](#) is unlikely to cause an isolated [CN III](#) palsy.

F - Infarction of the midbrain

Explanation Why

Infarctions of the [posterior cerebral artery](#) cause damage to the third nerve nucleus in the [midbrain](#). Patients present with ipsilateral [CN III](#) palsy and [diplopia](#), which are seen in this case. However, such an [infarct](#) would usually also damage other parts of the [midbrain](#), causing further neurologic features based on the structures involved (e.g., contralateral hemiataxia or [cerebellar tremor](#)). Furthermore, because the innervation of the levator palpebrae superioris muscles is supplied by a single subnucleus in the [midbrain](#), [ptosis](#) would be expected to be bilateral, not unilateral as seen here.

Question # 2

A 28-year-old woman comes to the physician because of a 4-day history of lower extremity numbness, weakness, and urinary incontinence. She has not had any trauma. Neurologic examination shows bilateral lower extremity weakness. Stroking the lateral side of the sole of the foot from the heel to the base of the small toe and medially to the base of the big toe elicits dorsiflexion of the big toe and fanning of the other toes. Further examination of this patient is most likely to show which of the following additional findings?

	Answer	Image
A	Spasticity	
B	Palmar grasp reflex	
C	Hyporeflexia	
D	Fasciculation	
E	Atrophy	

Hint

This patient has a positive Babinski sign (extension of the hallux with abduction of all toes), which indicates damage to the corticospinal tract (i.e., upper motor neurons).

Correct Answer

A - Spasticity

Explanation But

In combination with [urinary incontinence](#), signs of [upper motor neuron damage](#) in an otherwise healthy young woman raise suspicion of [multiple sclerosis](#).

Explanation Why

Muscle [spasticity](#) is due to hyperexcitable tonic reflexes and occurs when [upper motor neuron \(UMN\)](#) regulation of [alpha motor neurons](#) is lost, which leads to net disinhibition of the spinal reflexes. The [Babinski reflex](#) is a [primitive reflex](#) mediated by the [extrapyramidal tracts](#). It is lost progressively as the [pyramidal tracts](#) gain functionality through increasing myelination. As such, a positive [Babinski reflex](#) is normal in children up to 1 year of age, after which time it is usually suppressed by the [pyramidal tracts](#).

B - Palmar grasp reflex

Explanation Why

The [palmar grasp reflex](#) is a [primitive reflex](#) elicited in [infants](#) that persists until 3–6 months of age. A positive [palmar grasp reflex](#) in an adult may be a sign of [frontal lobe](#) damage ([frontal release sign](#)). It does not indicate [upper motor neuron damage](#).

C - Hyporeflexia

Explanation Why

A decrease in the activity of a reflex arc points to injuries in the efferent arm of the loop (i.e., [lower motor neuron damage](#)). In contrast, the presence of [upper motor neuron damage](#) will lead to an increase in reflex strength (i.e., [hyperreflexia](#)).

D - Fasciculation

Explanation Why

Isolated [fasciculations](#) without further medical signs are benign but indicate [lower motor neuron damage](#) if they are accompanied by muscle weakness. [Muscle fasciculations](#) would be unlikely in this patient, given that her examination indicates [upper motor neuron damage](#) (positive [Babinski reflex](#)).

E - Atrophy

Explanation Why

In combination with muscle weakness, [atrophy](#) of muscles isolated to a specific root or peripheral nerve suggests damage to the [lower motor neurons](#). However, a positive [Babinski sign](#) points to [upper motor neuron damage](#).

Question # 3

A 58-year-old man is brought to the emergency department because of sudden-onset right-sided body numbness for 1 hour. He reports that he has a 15-year history of hypertension treated with hydrochlorothiazide. He is alert and oriented to time, place, and person. Neurological examination shows decreased sensation to light pinprick and temperature on the right side of the face and body. Motor strength is 5/5 and deep tendon reflexes are 2+ bilaterally. Perfusion of which of the following structures of the brain is most likely impaired in this patient?

	Answer	Image
A	Parietal lobe	
B	Posterior limb of the internal capsule	
C	Lateral medulla	
D	Basal pons	
E	Ventral thalamus	
F	Subthalamic nucleus	

Hint

This patient's symptoms and risk factor (hypertension) suggest that he has a pure sensory stroke.

Correct Answer

A - Parietal lobe

Explanation Why

Diminished perfusion of the [parietal lobe](#) results from occlusion of one of its blood supplying vessels (predominantly the ACA, and [MCA](#)). Occlusion of the ACA or [MCA](#) may result in numbness, as seen in this patient. However, a [stroke](#) on the nondominant side would manifest with symptoms of contralateral neglect, while [infarction](#) of the dominant side would manifest with [aphasia](#), finger [agnosia](#), [agraphia](#), or [dyscalculia](#), none of which are present in this patient.

B - Posterior limb of the internal capsule

Explanation Why

[Infarction](#) of the [posterior](#) limb of the [internal capsule](#) occurs due to hemorrhage or occlusion of the [lenticulostriate arteries](#), which supply blood to the greater part of the [internal capsule](#). As fibers of the [corticospinal tract](#) pass downward through the [posterior](#) limb of the [internal capsule](#), [infarction](#) of the [posterior](#) limb usually leads to a [pure motor stroke](#) with [hemiparesis](#) of the leg, arm, and face contralateral to the site of the lesion. Rarely, [ischemia](#) of the [posterior](#) limb of the [internal capsule](#) manifests as isolated contralateral sensory loss, but this is not the most likely etiology of this patient's [pure sensory stroke](#).

C - Lateral medulla

Explanation Why

Diminished perfusion of the [lateral](#) medulla occurs due to occlusion of either the [posterior inferior cerebellar artery](#) or branches of the [vertebral artery](#). [Infarction](#) of the [lateral](#) medulla causes [Wallenberg syndrome](#), which manifests as numbness of the leg and arm contralateral to the lesion. However, affected individuals would also have [vestibulocerebellar](#) symptoms, bulbar muscle weakness, and facial [paresthesias](#) ipsilateral to the lesion.

D - Basal pons

Explanation Why

Hypoperfusion of the basal [pons](#) results from occlusion of the penetrating [arteries](#), eventually leading to the development of [dysarthria-clumsy](#) hand syndrome. Affected individuals present with facial weakness, [dysphagia](#), [dysarthria](#), and weakness of the hand ipsilateral to the site of the lesion; sensory deficits are absent.

E - Ventral thalamus

Explanation Why

A [pure sensory stroke](#) is caused by diminished perfusion of the [ventral](#) posterolateral and [ventral posteromedial nucleus](#) of the [thalamus](#), which relays sensory information of [proprioception](#), [pain](#), pressure, and temperature to the [primary somatosensory cortex](#). Affected individuals generally present with one-sided numbness of the face and body (contralateral to the affected side of the [thalamus](#)), as observed in this patient. Chronic [hypertension](#) and the resulting [lipohyalinosis](#) of small vessels are major [risk factors](#) for lacunar infarctions which include thalamic [strokes](#).

F - Subthalamic nucleus

Explanation Why

Hypoperfusion of the [subthalamic nucleus](#) leads to contralateral [hemiballismus](#), not sensory deficits.

Question # 4

An otherwise healthy 58-year-old man comes to the physician because of a 1-year history of episodic coughing whenever he cleans his left ear. There is no history of hearing loss, tinnitus, or vertigo. Stimulating his left ear canal with a cotton swab triggers a bout of coughing. The physician informs him that these symptoms are caused by hypersensitivity of a cranial nerve. A peripheral lesion of this nerve is most likely to manifest with which of the following findings on physical examination?

	Answer	Image
A	Inability to raise ipsilateral eyebrow	
B	Ipsilateral deviation of the tongue	
C	Decreased secretion from ipsilateral sublingual gland	
D	Ipsilateral vocal cord palsy	
E	Ipsilateral deviation of the uvula	
F	Ipsilateral sensorineural hearing loss	

Hint

The posterior external auditory canal is innervated by the auricular branch of the vagus nerve (CN X). In some individuals, this nerve can trigger an oto-respiratory reflex, causing coughing.

Correct Answer

A - Inability to raise ipsilateral eyebrow

Explanation Why

Inability to raise the ipsilateral eyebrow is a sign of a peripheral [facial nerve palsy](#) ([CN VII](#)), which could also lead to [ptosis](#), mouth drooping, and further symptoms depending on the height of the lesion (e.g., sensory disturbances, dry mouth, ocular features). A lesion of [CN X](#) does not affect the muscles of facial expression.

B - Ipsilateral deviation of the tongue

Explanation Why

Ipsilateral deviation of the [tongue](#) would be a sign of a lesion to the [hypoglossal nerve](#) ([CN XII](#)). Damage to this [cranial nerve](#) could also lead to [atrophy](#) and [fasciculations](#) of the [tongue](#). A lesion of [CN X](#) would not affect the motor function of the [tongue](#).

C - Decreased secretion from ipsilateral sublingual gland

Explanation Why

Decreased secretion from the ipsilateral [sublingual gland](#) is a sign of a lesion to the [chorda tympani](#) branch of the [facial nerve](#) ([CN VII](#)). It would also cause a loss of [taste](#) to the [anterior](#) two-thirds of the [tongue](#). Damage to [CN X](#) would not affect secretion of salivary glands.

D - Ipsilateral vocal cord palsy

Explanation But

Irritation of the auricular branch of the [vagus nerve](#) by [cerumen](#) or a foreign body is a rare cause of chronic [cough](#). Stimulation of the auricular branch of the [vagus nerve](#) (e.g., during [otoscopic examination](#)) can result in [vasovagal syncope](#).

Explanation Why

Ipsilateral [vocal cord](#) palsy would occur in a lesion of the [recurrent laryngeal nerve](#), which is a branch off the [vagus nerve](#) (CN X). Paralysis of the [vagus nerve](#) could also lead to loss of the [gag reflex](#), [dysphagia](#), decreased [taste](#) from the supraglottic region, as well as ipsilateral paralysis of the [soft palate](#), leading to deviation of the uvula away from the side of the lesion.

E - Ipsilateral deviation of the uvula

Explanation Why

Contralateral (not ipsilateral) deviation of the uvula would be caused by a lesion of the [glossopharyngeal nerve](#) (CN IX) or the [vagus nerve](#) (CN X) due to paralysis of the [soft palate](#). CN IX palsy could also lead to [dysphagia](#), loss of the [gag reflex](#), and sensory loss over the [soft palate](#), upper pharynx, and [posterior](#) third of the [tongue](#).

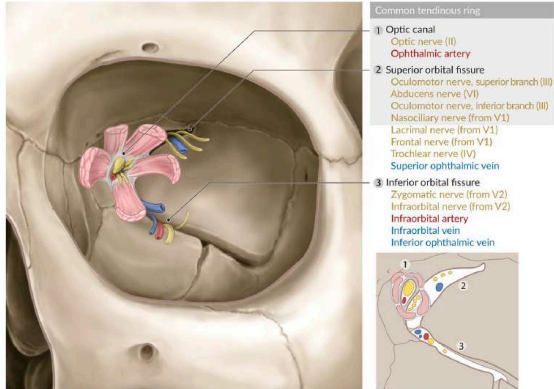
F - Ipsilateral sensorineural hearing loss

Explanation Why

Ipsilateral [sensorineural hearing loss](#) would occur from a lesion of the [vestibulocochlear nerve](#) (CN VIII). Such a lesion could also lead to [vertigo](#) and horizontal nystagmus. Damage to CN X would not be associated with hearing or vestibular changes.

Question # 5

A 25-year-old man is brought to the emergency department 30 minutes after he was involved in a motorcycle collision. He was not wearing a helmet. Physical examination shows left periorbital ecchymosis. A CT scan of the head shows a fracture of the greater wing of the left sphenoid bone with compression of the left superior orbital fissure. Physical examination of this patient is most likely to show which of the following findings?

	Answer	Image
A	Decreased sense of smell	
B	Numbness of the left cheek	
C	Fixed miotic left pupil	
D	Preserved left lateral gaze	
E	Absent left corneal reflex	 Common tendinous ring 1 Optic canal - Optic nerve (II) - Ophthalmic artery 2 Superior orbital fissure - Oculomotor nerve, superior branch (III) - Abducens nerve (VI) - Oculomotor nerve, inferior branch (IV) - Nasociliary nerve (from V1) - Lacrimal nerve (from V1) - Frontal nerve (from V1) - Trochlear nerve (IV) - Superior ophthalmic vein 3 Inferior orbital fissure - Zygomatic nerve (from V2) - Infraorbital nerve (from V2) - Infraorbital artery - Infraorbital vein - Inferior ophthalmic vein
F	Complete loss of vision of the left eye	

Hint

The superior orbital fissure contains cranial nerves III, IV, V₁, and VI.

Correct Answer

A - Decreased sense of smell

Explanation Why

Decreased [sense of smell](#) would be an indication that there is an injury to the [olfactory nerve](#) ([cranial nerve I](#)). This nerve passes through the cribriform plate so it is vulnerable with [fractures](#) of this bone. Pathologies of the [superior orbital fissure](#) would not be expected to affect this nerve.

B - Numbness of the left cheek

Explanation Why

The sensory innervation of the left cheek is carried out by the [maxillary nerve](#) ([cranial nerve V2](#)), which exits the [cranium](#) via the [foramen rotundum](#). Injury to this nerve would not be expected with a [sphenoid bone fracture](#) with compression of the left [superior orbital fissure](#), but rather as a result of an inferior orbital rim or maxillary [fracture](#).

C - Fixed miotic left pupil

Explanation Why

A fixed, [miotic](#) pupil would not be an expected finding in this patient. [Fractures](#) impinging on the [superior orbital fissure](#) can lead to [fixed, dilated pupils](#) as a result of damage to the [parasympathetic](#) fibers of the [oculomotor nerve](#) ([cranial nerve III](#)). [Miosis](#) is seen in other nervous system conditions such as [Horner syndrome](#) and [lateral pontine strokes](#).

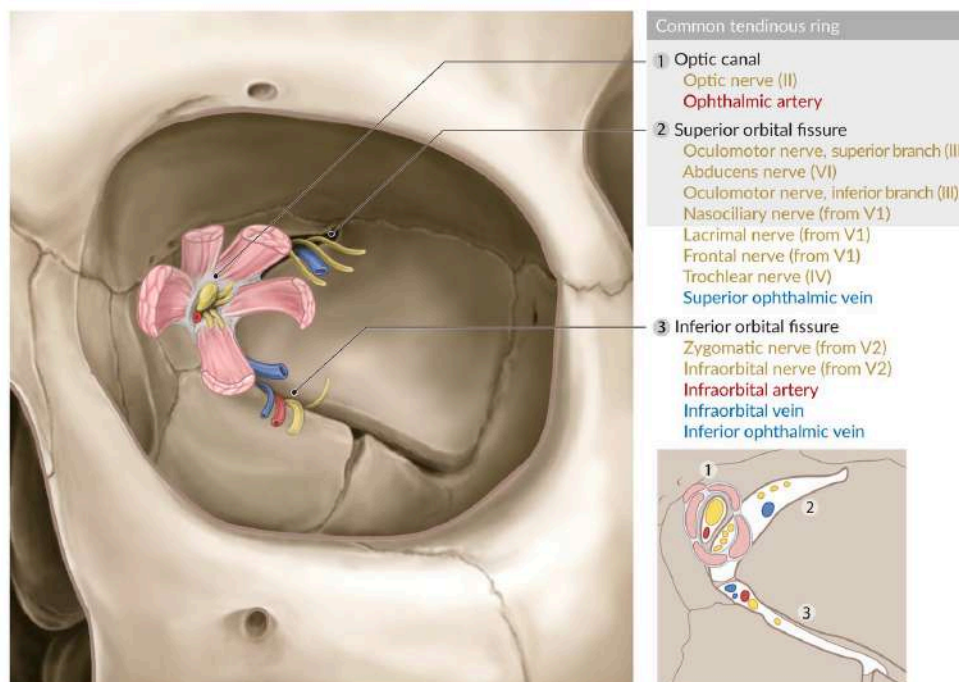
D - Preserved left lateral gaze

Explanation Why

Lateral gaze is achieved via contraction of the lateral rectus muscle. This muscle is innervated by the abducens nerve (cranial nerve VI), which passes through the superior orbital fissure. Fractures that impinge on this bony cleft, as in this patient, are likely to interfere with the function of the nerves that pass through. Thus, the expected finding would be abducens nerve palsy and loss of lateral gaze on the left.

E - Absent left corneal reflex

Image



Explanation Why

The corneal reflex requires uninterrupted signal transmission via the ophthalmic nerve (cranial nerve V1). Since this structure passes through the superior orbital fissure, it is likely to be disrupted in this

patient with a compressive [fracture](#) through the [superior orbital fissure](#). Without the afferent limb of the reflex pathway ([cranial nerve V1](#)), there is no motor response ([cranial nerve VII](#)).

F - Complete loss of vision of the left eye

Explanation Why

Complete loss of vision in the left [eye](#) would be a result of injury to the [optic nerve](#) ([cranial nerve II](#)). This nerve does not pass through the [superior orbital fissure](#), but rather it enters the [orbit](#) via the [optic canal](#).

Question # 6

A 34-year-old woman comes to the physician because of a 6-week history of depressed mood, loss of interest, and difficulty sleeping. She also has had a 4.5-kg (10-lb) weight loss during this period. She has not been as productive as before at work due to difficulty concentrating. There is no evidence of suicidal ideation. Laboratory studies including thyroid-stimulating hormone are within the reference range. The physician prescribes treatment with escitalopram. This drug targets a neurotransmitter that is produced in which of the following brain structures?

	Answer	Image
A	Caudate nucleus	
B	Locus coeruleus	
C	Basal nucleus of Meynert	
D	Nucleus accumbens	
E	Raphe nucleus	
F	Substantia nigra	

Hint

Escitalopram is a selective serotonin reuptake inhibitor (SSRI) used in the treatment of major depressive disorder.

Correct Answer

A - Caudate nucleus

Explanation Why

The [caudate nuclei](#) are part of the [basal ganglia](#) associated with motor processes, learning, and inhibitory control of actions. The [caudate nuclei](#) are highly innervated by [dopaminergic neurons](#) from the [substantia nigra](#) pars compacta and would be affected by [antidepressants](#) with [dopaminergic](#) effects (e.g., [bupropion](#)). However, [escitalopram](#) does not target [dopamine](#).

B - Locus coeruleus

Explanation Why

The [locus coeruleus](#) in the [pons](#) is the major site of [norepinephrine](#) production in the brain. Decreased levels of [norepinephrine](#) in the brain are associated with depression. Therefore, inhibiting [norepinephrine](#) reuptake can be an effective treatment for depression. This is the mechanism of action of [serotonin-norepinephrine](#) reuptake inhibitors ([SNRI](#)), not [escitalopram](#).

C - Basal nucleus of Meynert

Explanation Why

The [basal nucleus of Meynert](#) is the major site of [acetylcholine](#) production in the brain. Increased levels of [acetylcholine](#) are associated with [Parkinson disease](#), while decreased levels are associated with Alzheimer and [Huntington disease](#). However, [acetylcholine](#) does not appear to play a role in depression. Furthermore, [escitalopram](#) does not target [acetylcholine](#).

D - Nucleus accumbens

Explanation Why

The nucleus accumbens is located in the basal forebrain, between the caudate and [putamen](#) and is the major site of [GABA](#) synthesis. A decreased [GABA](#) concentration is associated with [anxiety disorders](#) and [Huntington disease](#) but rarely with depression. Furthermore, [escitalopram](#) does not target [GABA](#).

E - Raphe nucleus

Explanation Why

The raphe nucleus in the [midbrain](#) is the primary site of [serotonin](#) production in the [central nervous system](#). A decreased [serotonin](#) concentration is associated with depression. Therefore, increasing its concentration in the [synaptic cleft](#) by inhibiting its reuptake, as mediated by drugs of the [SSRI](#) class (e.g. [escitalopram](#)), is an effective treatment for depression. Other conditions associated with low [serotonin](#) concentrations are [anxiety disorders](#) and [Parkinson disease](#).

F - Substantia nigra

Explanation Why

The [substantia nigra](#) pars compacta is the major site of [dopamine](#) production in the brain. Decreased levels of [dopamine](#) are associated with [Parkinson disease](#) and depression. Therefore, inhibiting [dopamine](#) reuptake can be an effective treatment against depression. This is the mechanism of action of the [atypical antidepressant bupropion](#), not [escitalopram](#).

Question # 7

A 25-year-old man comes to the physician because of a 2-week history of numbness in his left lower extremity. One month ago, he sustained a fracture of the neck of the left fibula during soccer practice that was treated with immobilization in a plaster cast. Physical examination of the left lower extremity is most likely to show which of the following findings?

	Answer	Image
A	Impaired dorsiflexion of the foot	
B	Loss of sensation over the medial calf	
C	Inability to stand on tiptoes	
D	Decreased ankle reflex	
E	Loss of sensation on the sole of the foot	
F	Inability to invert the foot	

Hint

The common peroneal nerve runs in close proximity to the lateral aspect of the fibular head, which makes it susceptible to damage or compression due to fracture of the fibular neck, tight casts, crossing of the legs, or protracted squatting.

Correct Answer

A - Impaired dorsiflexion of the foot

Explanation But

The [common peroneal nerve](#) gives rise to the [superficial peroneal nerve](#), which innervates the dorsum of the foot, and the [deep peroneal nerve](#), which innervates the web space between the first two toes.

Explanation Why

[Dorsiflexion](#) of the foot is accomplished through contraction of muscles in the [anterior compartment of the leg](#), including the [tibialis anterior](#) (main dorsiflexor), [extensor hallucis longus](#), [extensor digitorum longus](#), and [peroneus tertius](#). These muscles are innervated by the [deep peroneal nerve](#), which branches from the [common peroneal nerve](#). Injury to the [common peroneal nerve](#), either from the initial [fibula fracture](#) or, more likely, compression from the [plaster cast](#), explains this patient's numbness and would result in impaired [dorsiflexion](#) and [eversion](#) on motor examination. Patients with injury to the [common peroneal nerve](#) typically present with [steppage gait](#).

B - Loss of sensation over the medial calf

Explanation Why

Loss of sensation over the [medial](#) calf occurs in cases of injury to the [saphenous nerve](#). These injuries typically arise following saphenous [vein](#) harvest for cardiac surgery or trauma to the [posterior](#) leg, not from fibular [fracture](#).

C - Inability to stand on tiptoes

Explanation Why

Standing on one's tiptoes requires contraction of the muscles in the [superficial posterior compartment](#)

of the leg, [gastrocnemius](#), and [soleus](#). Direct injury to these muscles or damage to the [tibial nerve](#), which innervates these muscles, would make it impossible to stand on one's tiptoes, but this patient's history of isolated [fracture](#) of the fibular neck does not suggest these pathologies.

D - Decreased ankle reflex

Explanation Why

The [ankle reflex](#) is diminished in patients with [spinal cord](#), [spinal](#) root, and peripheral nerve conditions. Specifically, processes affecting the sacral [spinal cord](#), S1/S2 roots, or [tibial nerve](#) would be expected to manifest with reduced ankle reflexes. This patient does not have a history to suggest injury or damage to any of these structures.

E - Loss of sensation on the sole of the foot

Explanation Why

The sole of the foot is innervated by the [tibial nerve](#). [Tibial nerve injury](#) is typically a result of deep lacerations to the [posterior](#) leg or severely posteriorly displaced [tibia fracture](#). Fibular [fractures](#) do not commonly affect this nerve.

F - Inability to invert the foot

Explanation Why

An inability to [invert the foot](#) would be the result of an injury affecting the [tibialis posterior](#) muscle, which is innervated by the [tibial nerve](#). This patient has no history to suggest injury to this nerve (e.g., deep laceration to the [posterior](#) leg).

Question # 8

A 62-year-old man comes to the physician because of tremors in both hands for the past few months. He has had difficulty buttoning his shirts and holding a cup of coffee without spilling its content. He has noticed that his symptoms improve after a glass of whiskey. His maternal uncle began to develop similar symptoms around the same age. He has bronchial asthma controlled with albuterol and fluticasone. Examination shows a low-amplitude tremor bilaterally when the arms are outstretched that worsens during the finger-to-nose test. Which of the following is the most appropriate pharmacotherapy in this patient?

	Answer	Image
A	Alprazolam	
B	Levodopa	
C	Primidone	
D	Propranolol	
E	Valproic acid	

Hint

This patient has a bilateral low-amplitude tremor that worsens with purposeful voluntary movement (e.g., finger-to-nose test). Improvement with alcohol and a family history of similar symptoms makes essential tremor the most likely diagnosis.

Correct Answer

A - Alprazolam

Explanation Why

[Alprazolam](#) and other [benzodiazepines](#) are a second-line treatment for [essential tremor](#) due to their addictive potential and severity of withdrawal symptoms, particularly with sudden cessation of their use. This patient's treatment should be initiated with a first-line medication.

B - Levodopa

Explanation Why

[Levodopa](#) is used for the treatment of [resting tremor](#) due to [Parkinson disease](#), not [essential tremor](#). Although [Parkinson disease](#) also manifests with a low-amplitude [tremor](#), the [tremor](#) is typically asymmetrical and improves rather than worsens with purposeful voluntary movement.

C - Primidone

Explanation Why

[Primidone](#) is the first-line pharmacotherapy for patients with [essential tremor](#). Treatment should be offered to patients in whom the condition causes intermittent or persistent impairment. Although the severity of [essential tremor](#) typically remains stable over time, some patients experience disability from [tremor](#) progression. [Primidone](#) is also used as an [anticonvulsant](#) in the treatment of [grand mal](#), psychomotor, and [focal seizures](#). Its primary active metabolite is [phenobarbital](#), which is responsible for its sedative effects as well as strong [cytochrome P450](#) induction.

D - Propranolol

Explanation Why

[Propranolol](#) is a first-line drug for the treatment of [essential tremor](#). However, it is relatively contraindicated in this patient because of his [bronchial asthma](#), as nonselective [beta blockers](#) are known to worsen [asthma](#) symptoms due to their bronchoconstrictive effects. Therefore, another drug would be more appropriate for this patient.

E - Valproic acid

Explanation Why

[Valproic acid](#) is a second-line drug for the treatment of [essential tremor](#). This patient's treatment should be initiated with a first-line medication.

Question # 9

A 55-year-old man with a history of repeated hospitalization for chronic pancreatitis comes to the physician because of difficulty walking and standing steadily. Neurological examination shows an unsteady, broad-based gait, distal muscle weakness, decreased deep tendon reflexes, and an abnormal Romberg test. His hemoglobin concentration is 11.9 g/dL, mean corpuscular volume is $89\mu\text{m}^3$, and serum lactate dehydrogenase is 215 U/L. His serum haptoglobin is slightly decreased. A deficiency of which of the following substances is the most likely cause of this patient's findings?

	Answer	Image
A	Tocopherol	
B	Folate	
C	Riboflavin	
D	Pyridoxine	
E	Cobalamin	
F	Niacin	
G	Phytomenadione	

Hint

In infants, excess of this vitamin has been associated with necrotizing enterocolitis.

Correct Answer

A - Tocopherol

Explanation But

Treatment involves oral [vitamin E](#) supplementation.

Explanation Why

[Tocopherol](#) ([vitamin E](#)) deficiency classically presents with [hemolytic anemia](#) and symptoms of [posterior column](#) and [spinocerebellar tract](#) dysfunction ([ataxia](#), loss of [proprioception](#), and diminished reflexes). It is an uncommon condition in developed countries, but specific populations, such as patients with fat [malabsorption](#) disorders (e.g., [chronic pancreatitis](#), [abetalipoproteinemia](#), children with [cystic fibrosis](#)) are at significant risk. [Vitamin E deficiency](#) is harmful to [neurons](#) and [red blood cells](#) specifically as they are particularly sensitive to the oxidative damage that results from the loss of [vitamin E](#) antioxidative effects.

B - Folate

Explanation Why

[Folate](#) ([vitamin B9](#)) deficiency typically occurs in individuals with a history of excessive alcohol use or patients taking [folate](#) antagonists such as [sulfonamides](#) or [methotrexate](#). However, [glossitis](#) is the main clinical finding, whereas neurological symptoms, as seen in this patient, are not typically present. Also, patients with [folate deficiency](#) have [megaloblastic anemia](#), not the [hemolytic anemia](#) seen in this patient.

C - Riboflavin

Explanation Why

[Riboflavin](#) ([vitamin B2](#)) deficiency can occur due to [malnutrition](#) (e.g., from a restricted diet), and it

may present with normocytic normochromic [anemia](#), as seen in this patient. However, it is not associated with neurological dysfunction but presents with instead with dry, [scaling skin](#) of the [lips](#) and mouth ([cheilosis](#)). Affected individuals may also have vision loss due to corneal vascularization.

D - Pyridoxine

Explanation Why

[Pyridoxine](#) ([vitamin B₆](#)) deficiency can occur with prolonged [isoniazid](#) administration and chronic alcohol use. It may present with neurological compromise, most often in the form of [peripheral neuropathy](#), which could explain this patient's neurological findings. However, [anemia](#) associated with [pyridoxine deficiency](#), if present, manifests as (microcytic) [sideroblastic anemia](#), not (normocytic) [hemolytic anemia](#).

E - Cobalamin

Explanation Why

[Cobalamin](#) ([vitamin B₁₂](#)) deficiency causes [subacute combined degeneration](#), which may manifest with neurological signs and symptoms similar to the ones seen in this patient, including [ataxia](#) and muscle weakness. However, [cobalamin deficiency](#) typically also manifests with symmetrical [paresthesias](#) of the extremities and [dementia](#). In addition, it causes [megaloblastic anemia](#). Finally, common [risk factors](#) for this [vitamin deficiency](#) include restricted diets, lack of [intrinsic factor](#), or terminal [ileum](#) disease (e.g., [Crohn disease](#)), none of which are present in this patient.

F - Niacin

Explanation Why

[Niacin](#) ([vitamin B₃](#)) deficiency can be seen in severe [malnutrition](#), [carcinoid syndrome](#), or [Hartnup disease](#). Moderate deficiency may cause [glossitis](#) whereas severe cases may lead to [pellagra](#). However, neurological symptoms and [hemolytic anemia](#) that would not be present.

G - Phytomenadione

Explanation Why

[Phytomenadione](#) ([vitamin K](#)) deficiency is a concern in [neonates](#) (owing to the lack of intestinal flora capable of synthesizing it), patients on long regimens of broad-spectrum [antibiotics](#), and in patients taking [coumarin](#). Clinically, deficiency manifests with spontaneous bleeding from minimal trauma (e.g. [hematoma](#), mucosal bleeding) with elevated [prothrombin time/INR](#). However, neurological symptoms and [hemolytic anemia](#), as seen in this patient, would not be present.

Question # 10

A 70-year-old woman comes to the physician for a follow-up examination 2 months after undergoing a total hip replacement surgery. She reports that she has persistent difficulty in walking since the surgery despite regular physiotherapy. Examination of her gait shows sagging of the left pelvis when her right leg is weight-bearing. Which of the following nerves is most likely to have been injured in this patient?

	Answer	Image
A	Left superior gluteal nerve	
B	Right femoral nerve	
C	Right inferior gluteal nerve	
D	Left inferior gluteal nerve	
E	Left femoral nerve	
F	Right obturator nerve	
G	Right superior gluteal nerve	

	Answer	Image
H	Left obturator nerve	

Hint

Examination in this patient shows a positive Trendelenburg sign, which is caused by weakness of the hip abductors (i.e., the gluteus medius and minimus).

Correct Answer

A - Left superior gluteal nerve

Explanation Why

The left [superior gluteal nerve](#) innervates the left [gluteus medius](#) and minimus, which are responsible for [abducting](#) the left [hip](#). Neurological weakness of these muscles would lead to a positive [Trendelenburg sign](#) or downward tilting of the [pelvis](#) toward the right side when the patient stands on her left leg.

B - Right femoral nerve

Explanation Why

The right [femoral nerve](#) innervates the right [quadriceps](#), [sartorius](#), [pectineus](#), and iliopsoas, which control [knee](#) extension and thigh [flexion](#). [Femoral nerve injury](#) would cause [knee](#) buckling (from [quadriceps](#) weakness), difficulty lifting up the thigh (problem climbing stairs), and dragging of the leg (from iliopsoas weakness); it would not cause a positive [Trendelenburg sign](#). Sensory loss would also be seen over the [medial](#) and [anterior](#) thigh as well the [medial](#) calf, which is not present in this patient.

C - Right inferior gluteal nerve

Explanation Why

The right [inferior gluteal nerve](#) innervates the right [gluteus maximus muscle](#). As this muscle is the primary right thigh extensor, [inferior gluteal nerve](#) damage would lead to impairment of this function. Although rare, injuries to this nerve may occur due to misdirected intramuscular injections and operations (e.g., [posterior](#) approach to [hip arthroplasty](#)).

D - Left inferior gluteal nerve

Explanation Why

The left [inferior gluteal nerve](#) innervates the left [gluteus maximus muscle](#). As this muscle is the primary left thigh extensor, [inferior gluteal nerve](#) damage would lead to impairment of this function. This nerve is rarely injured, but possible reasons are misdirected intramuscular injections and operations (e.g. [posterior](#) approach to [hip arthroplasty](#)).

E - Left femoral nerve

Explanation Why

The left [femoral nerve](#) innervates the left [quadriceps](#), [sartorius](#), [pectineus](#), and iliopsoas, which control [knee](#) extension and thigh [flexion](#). [Femoral nerve injury](#) would cause [knee](#) buckling (from [quadriceps](#) weakness), difficulty lifting up the thigh (problem climbing stairs), and dragging of the leg (from iliopsoas weakness), it would not cause a positive [Trendelenburg sign](#). Sensory loss would also be seen over the [medial](#) and [anterior](#) thigh as well the [medial](#) calf, which is not present in this patient.

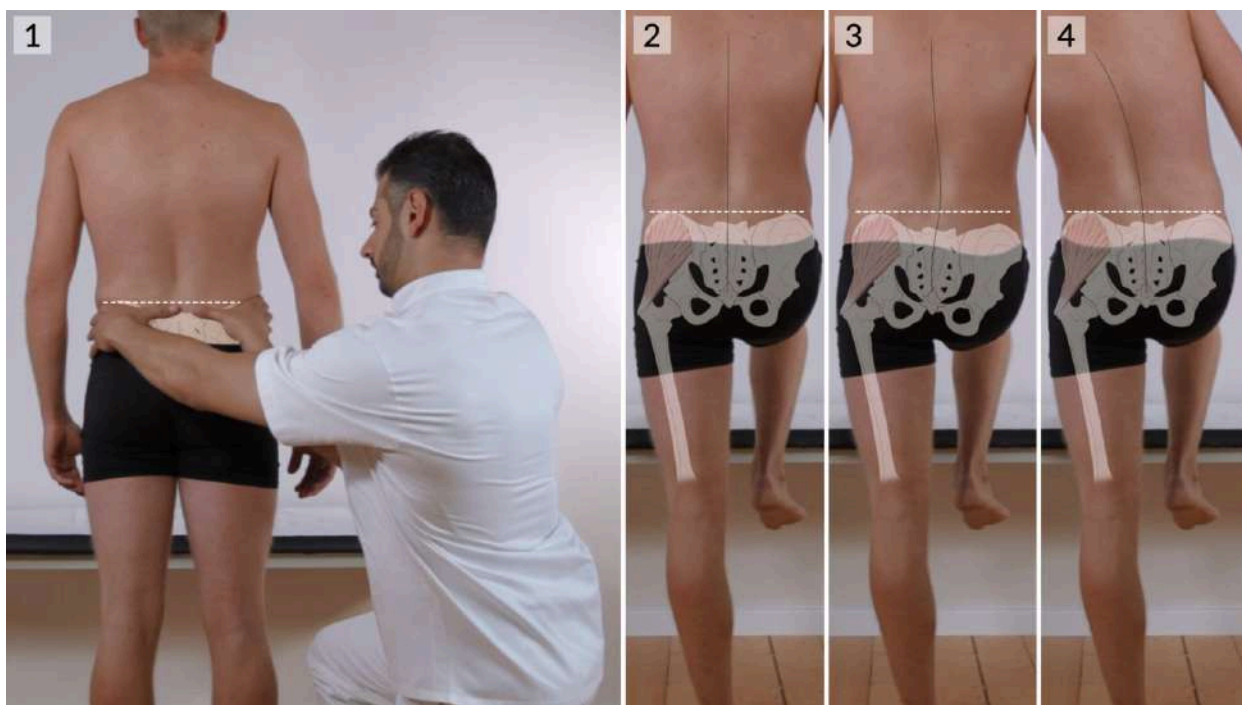
F - Right obturator nerve

Explanation Why

The right [obturator nerve](#) innervates the right [obturator externus](#), [pectineus](#), [gracilis](#), and adductors magnus, longus and brevis. Damage to the [obturator nerve](#) results in weakness of [adduction](#), [external rotation](#) of the thigh, and a tendency for the thigh to abnormally [abduct](#) while walking; it would not cause a positive [Trendelenburg sign](#). Damage to this nerve would also cause sensory loss in the mid and lower thirds of the right [medial](#) thigh, which is not present in this patient.

G - Right superior gluteal nerve

Image



Explanation Why

The right [superior gluteal nerve](#) innervates the right [gluteus medius](#) and minimus, which are responsible for [abducting](#) the right [hip](#). Damage of the right [superior gluteal nerve](#) results in lowering of the left [hip](#) while standing on the right foot (positive [Trendelenburg sign](#)). This patient's symptoms suggest that she suffered damage to the right [superior gluteal nerve](#) during [total hip replacement surgery](#).

H - Left obturator nerve

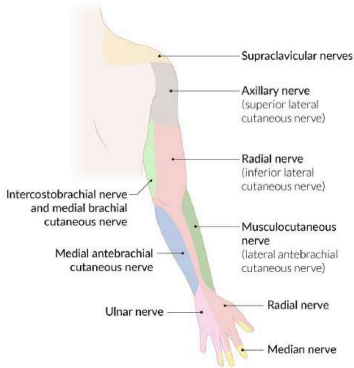
Explanation Why

The left [obturator nerve](#) innervates the left [obturator externus](#), [pectineus](#), [gracilis](#), and adductors magnus, longus, and brevis. Damage to the [obturator nerve](#) results in weakness of [adduction](#), [external](#)

[rotation](#) of the thigh, and a tendency for the thigh to abnormally [abduct](#) while walking; it would not cause a positive [Trendelenburg sign](#). Damage to this nerve would also cause sensory loss in the mid and lower thirds of the left [medial](#) thigh, which is not present in this patient.

Question # 11

A 32-year-old man comes to the physician because of a 1-month history of intermittent tingling of his hand. He is an avid cyclist and has recently started training for a cycle marathon. Physical examination shows decreased grip strength in the right hand and wasting of the hypothenar eminence. On asking the patient to grasp a piece of paper between his right thumb and right index finger in the first web space, there is hyperflexion of the right thumb interphalangeal joint. Which of the following additional findings is most likely in this patient?

	Answer	Image
A	Loss of sensation over dorsal aspect of 1 st web space	
B	Inability to flex the index finger at the interphalangeal joints	
C	Loss of sensation over the dorsum of the medial half of the hand	

	Answer	Image
D	Loss of sensation over the palmar aspect of the middle finger	
E	Inability to extend the ring finger at the metacarpophalangeal joint	
F	Inability to extend the little finger at the proximal interphalangeal joints	

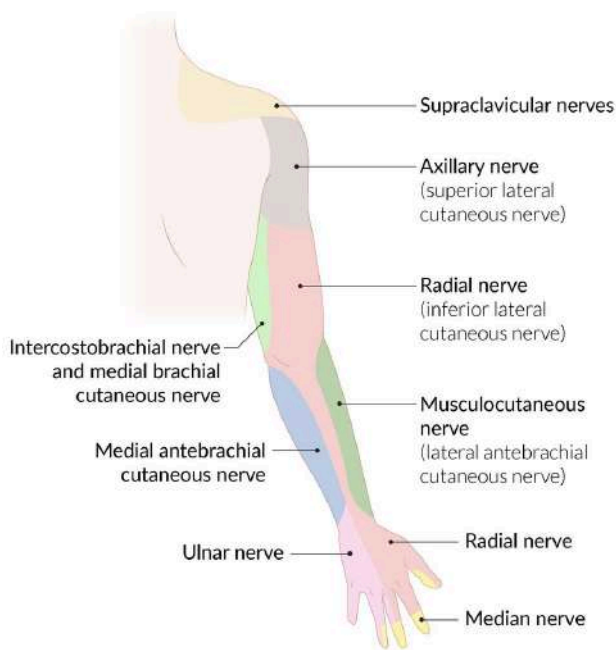
Hint

A positive Froment sign (hyperflexion of the thumb due to paralysis of the adductor pollicis and unopposed action of flexor pollicis longus) and wasting of the hypothenar eminence are suggestive of ulnar nerve entrapment.

Correct Answer

A - Loss of sensation over dorsal aspect of 1st web space

Image



Explanation Why

Sensation in the [dorsal](#) web space between the thumb and index finger is often examined to assess intact radial nerve sensation. It would not be affected by this patient's [ulnar nerve compression](#).

B - Inability to flex the index finger at the interphalangeal joints

Explanation Why

[Flexion](#) of the index finger at either the [proximal](#) or [distal interphalangeal joints](#) requires the action of the [flexor digitorum superficialis](#) ([proximal joint](#)) or [flexor digitorum profundus](#) ([proximal](#) and

[distal joints](#)). The [flexor digitorum superficialis](#) and the [lateral](#) aspect of the flexor digitorum profundus (which flexes the index and middle finger) are innervated by the median nerve and would be unaffected by this patient's [ulnar nerve compression](#).

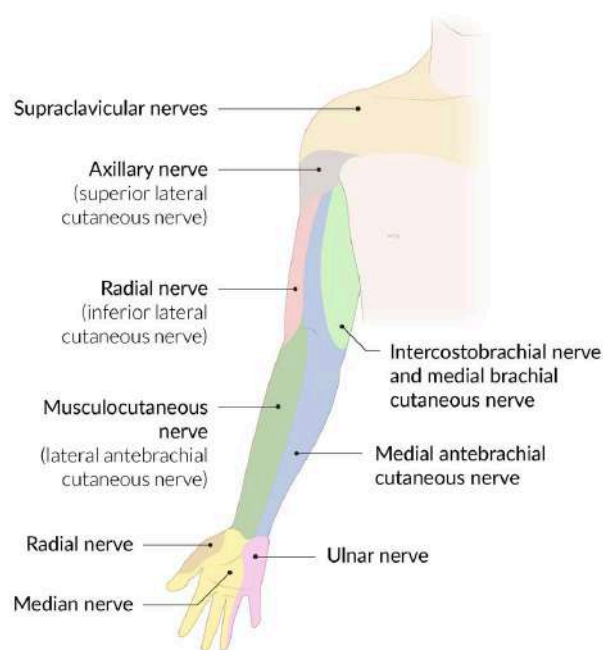
C - Loss of sensation over the dorsum of the medial half of the hand

Explanation Why

The dorsum of the [medial](#) half of the hand (ring and small fingers) is innervated by the dorsal cutaneous branch of the ulnar nerve, which arises in the forearm [proximal](#) to the passage of the ulnar nerve through [Guyon canal](#). As this patient exhibits nerve compression at the level of Guyon canal, the sensory innervation to the [medial](#) half of the dorsum of the hand will remain intact.

D - Loss of sensation over the palmar aspect of the middle finger

Image



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Explanation Why

Loss of sensation over the [palmar](#) aspect of the middle finger is seen in patients with median nerve compression, such as in [carpal tunnel syndrome](#). Sensation to this area would not be affected by this patient's [ulnar nerve compression](#).

E - Inability to extend the ring finger at the metacarpophalangeal joint

Explanation Why

Extension of the ring finger at the [metacarpophalangeal joint](#) is mediated by the action of the [extensor digitorum](#) muscle, which is innervated by the radial nerve. The function of this muscle would not be affected by [ulnar nerve compression](#).

F - Inability to extend the little finger at the proximal interphalangeal joints

Image



Explanation But

While splinting, [cortisone](#) injections, and [NSAIDs](#) may improve this patient's complaints, surgical release of the [volar carpal ligament](#) is required in refractory cases.

Explanation Why

This patient's [physical exam](#) is suggestive of long-term [ulnar nerve compression](#) at the level of [Guyon canal](#) ([Guyon canal syndrome](#)), which is common in avid cyclists due to long-term pressure of the wrist against bike handlebars. This compression disrupts innervation to the ulnar innervated intrinsic hand muscles, including the [lumbricals](#), which are responsible for little finger extension at the [proximal interphalangeal joint](#). Additional [physical exam](#) findings typically seen in this syndrome include numbness of the [palmar](#) surface of the small and ring fingers.

Question # 12

An 81-year-old woman is brought to the physician by her son because of worsening forgetfulness and disorientation over the past 2 years. She has to be reminded of her grandchildren's names and frequently forgets her current address. She lives with her son. She has occasional episodes of urinary incontinence. She appears well nourished. Neurologic examination shows no abnormalities; her gait is normal. Mental status examination shows mild memory impairment. She is oriented to self and place, but not to time. Which of the following is the most appropriate pharmacotherapy?

	Answer	Image
A	Acetazolamide	
B	Levodopa and carbidopa	
C	Thiamine	
D	Galantamine	
E	Perphenazine	
F	Benztropine	
G	Fluoxetine	

Hint

The patient's mental status examination suggests mild dementia; the predominant symptoms of memory loss and disorientation are consistent with Alzheimer disease.

Correct Answer

A - Acetazolamide

Explanation Why

[Acetazolamide](#) can be used to treat [normal pressure hydrocephalus](#) (NPH) in patients who do not respond effectively to drainage of excess [cerebrospinal fluid](#) via a [cerebral shunt](#). While NPH can manifest with [dementia](#) and [urinary incontinence](#), this patient has no gait disturbance, which is characteristic for NPH. Moreover, in NPH, pharmacotherapy would be preceded by removal of small amounts of [cerebrospinal fluid](#) by [lumbar puncture](#) to alleviate symptoms and support the diagnosis.

B - Levodopa and carbidopa

Explanation Why

[Levodopa](#) and [carbidopa](#) are used in the treatment of parkinsonian symptoms in [Lewy body dementia \(LBD\)](#). Although this patient presents with [dementia](#), she does not have other typical features consistent with [LBD](#), such as [extrapyramidal motor symptoms](#) or [visual hallucinations](#).

C - Thiamine

Explanation Why

[Thiamine](#) is used in the treatment of [Wernicke encephalopathy](#), a syndrome seen in patients with poor nutrition that is typically associated with [alcohol use disorder](#). This patient does not have a history of excessive alcohol use, and her normal appearance does not suggest [malnutrition](#) (although it cannot be ruled out entirely, especially in an elderly patient). Moreover, patients with [Wernicke encephalopathy](#) also present with gait dysfunction and oculomotor dysfunction, such as nystagmus, [lateral rectus palsy](#), or conjugate gaze palsy, none of which is seen in this patient.

D - Galantamine

Explanation But

[Observational studies](#) suggest that increased [vitamin E](#) intake may have a protective effect against [Alzheimer disease](#) and [vascular dementia](#). However, [randomized controlled trials](#) have not been able to confirm this effect.

Explanation Why

Patients with mild-to-moderate [Alzheimer disease](#) (AD) show improved [cognition](#) and ability to perform everyday activities when treated with [acetylcholinesterase inhibitors](#), such as [galantamine](#), [donepezil](#), or [rivastigmine](#). These drugs induce an increase in the [neurotransmitter acetylcholine](#), which is decreased in AD. If this patient's condition progresses to moderate-to-severe AD, [memantine](#) (an [NMDA](#)-receptor antagonist) will become indicated and may be given in combination with an [acetylcholinesterase inhibitor](#).

E - Perphenazine

Explanation Why

[Antipsychotics](#) such as [perphenazine](#) are indicated for [psychotic symptoms](#) (e.g., [hallucinations](#)) that may sometimes complicate [Alzheimer disease](#). Because this patient is not experiencing [hallucinations](#), [perphenazine](#) would not be indicated at this time.

F - Benztropine

Explanation Why

[Benztropine](#) is used to treat [extrapyramidal symptoms](#) associated with [antipsychotic](#) drugs and as an adjunct therapy in [Parkinson disease](#). [Benztropine](#) is not used in [Alzheimer disease](#) and may actually exacerbate this patient's symptoms due to its [anticholinergic effects](#).

G - Fluoxetine

Explanation Why

[SSRIs](#), such as [fluoxetine](#), may be indicated for the treatment of depression in [Alzheimer disease](#) (AD), but not for the treatment of AD itself. Although AD and other forms of [dementia](#) are often associated with neuropsychiatric symptoms, this patient does not have symptoms of depression, (e.g., loss of interest, sleep disturbance).

Question # 13

An otherwise healthy 45-year-old man comes to the physician because of a painful ulcer on his tongue for 3 days. Examination shows a shallow, tender 5-mm wide ulcer on the lateral aspect of the tongue, adjacent to his left first molar. There is no induration surrounding the ulcer or cervical lymphadenopathy. A lesion of the cranial nerve responsible for the transmission of pain from this ulcer would most likely result in which of the following?

	Answer	Image
A	Decreased sensation in the upper lip	
B	Difficulty chewing	
C	Loss of taste from the supraglottic region	
D	Diminished gag reflex	

	Answer	Image
E	Inability to wrinkle the forehead	The diagram illustrates the neural pathways for the forehead. The postcentral gyrus is highlighted in blue. The hypothalamus is highlighted in red. The ventral posteromedial nucleus is highlighted in green. The amygdala is highlighted in yellow. The nucleus of solitary tract is highlighted in blue. The geniculate ganglion is highlighted in yellow. The vagus nerve is highlighted in blue. The inferior ganglion of vagus nerve is highlighted in yellow. The inferior ganglion of glossopharyngeal nerve is highlighted in yellow. The glossopharyngeal nerve is highlighted in blue. The facial nerve is highlighted in blue.
F	Lateral deviation of the tongue	

Hint

Since this patient's lesion is located opposite the first molar, it lies anterior to the sulcus terminalis, the structure separating the anterior two-thirds of the tongue from the posterior third. Somatic sensation (e.g., pain) from the anterior two-thirds of the tongue is transmitted by the lingual nerve, which is a branch of the mandibular division of the trigeminal nerve (CN V₃).

Correct Answer

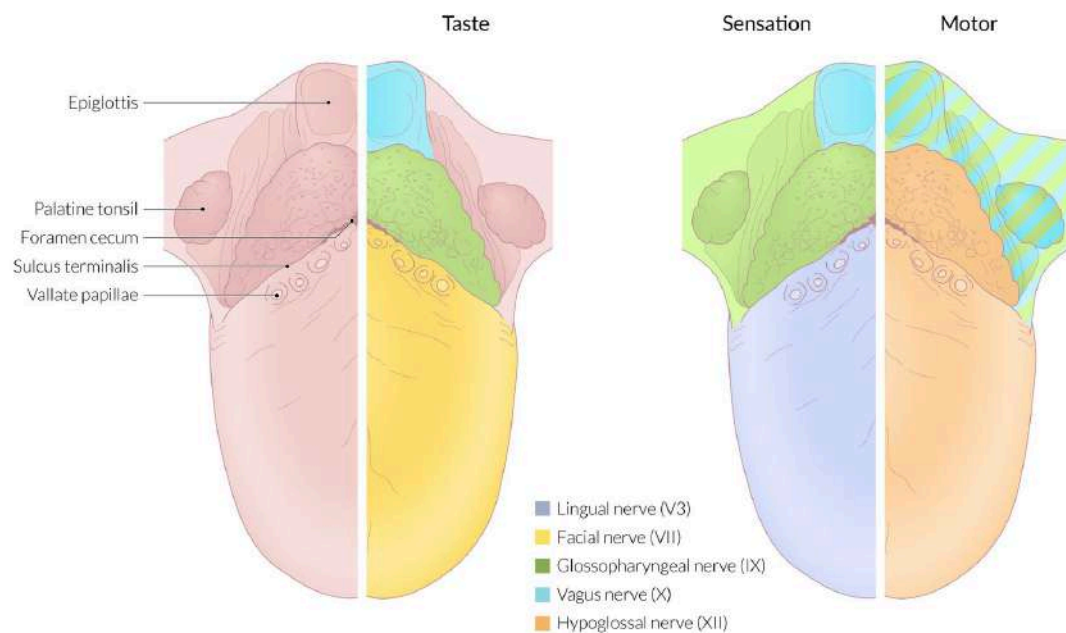
A - Decreased sensation in the upper lip

Explanation Why

Decreased sensation in the upper lip would be caused by a lesion of the [maxillary nerve \(CN V₂\)](#), not the mandibular division of the [trigeminal nerve](#).

B - Difficulty chewing

Image



Explanation Why

A lesion of the [mandibular branch of the trigeminal nerve \(CN V₃\)](#) results in difficulty chewing due to paralysis of the [muscles of mastication](#) ([medial](#) and [lateral pterygoid](#), [masseter](#), [temporalis](#)). [CN](#)

[V3](#) also innervates the mylohyoid muscle, [anterior digastric](#) belly, [tensor veli palatini](#), and tensor tympani, and transmits sensory input from the lower third of the face and [anterior](#) wall of the [external auditory canal](#). [CN V3](#) is a part of both the afferent and efferent arms of the [jaw jerk reflex](#).

C - Loss of taste from the supraglottic region

Explanation Why

Loss of [taste](#) from the supraglottic region would be caused by a lesion in the [vagal nerve](#), which does not innervate the [tongue](#).

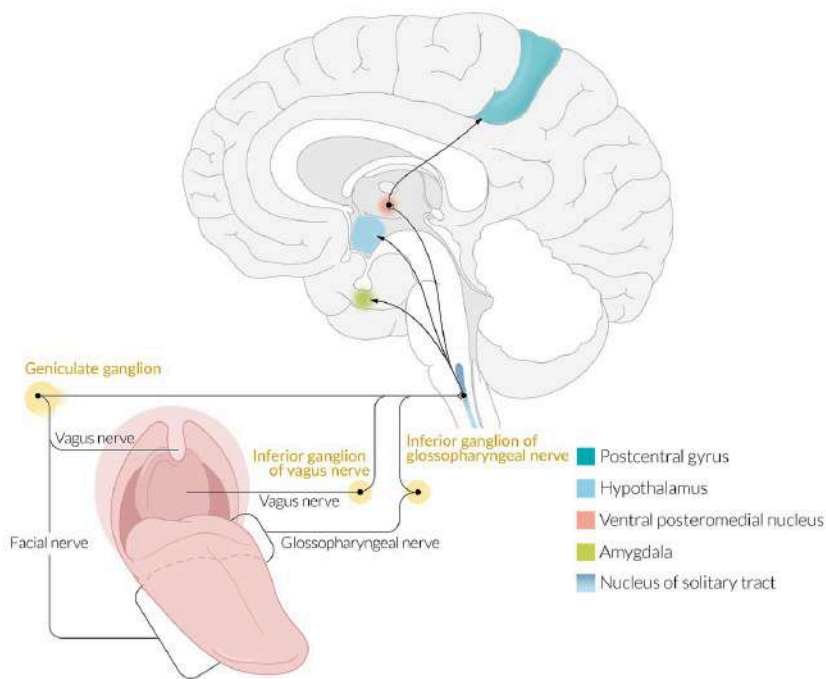
D - Diminished gag reflex

Explanation Why

A diminished [gag reflex](#) is caused by a lesion in the [vagal nerve](#) or [glossopharyngeal nerve](#). The [glossopharyngeal nerve](#) provides [taste](#) and somatic sensation to the [posterior](#) third of the [tongue](#) but not to the [anterior](#) two-thirds, where this patient's lesion is located.

E - Inability to wrinkle the forehead

Image



Explanation Why

An inability to [wrinkle](#) the forehead is seen in [facial nerve](#) palsy. The [facial nerve](#) transmits [taste](#) sensation from the [anterior](#) two-thirds of the [tongue](#) via the [chorda tympani](#) division but does not transmit somatic sensation (e.g., [pain](#)).

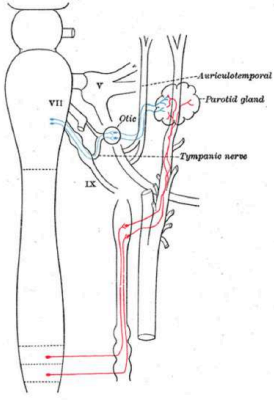
F - Lateral deviation of the tongue

Explanation Why

[Lateral](#) deviation of the [tongue](#) is caused by a lesion of the [hypoglossal nerve](#), which innervates the muscles of the [tongue](#). The [hypoglossal nerve](#) does not transmit somatic or [taste](#) sensation from the [tongue](#).

Question # 14

A 55-year-old woman with a 1-year history of left-sided tinnitus is diagnosed with a tumor of the left jugular fossa. Sialometry shows decreased production of saliva from the left parotid gland. The finding on sialometry is best explained by a lesion of the nerve that is also responsible for which of the following?

	Answer	Image
A	Protrusion of the tongue	
B	Taste sensation of tip of the tongue	
C	Closing of the jaw	
D	Afferent limb of the gag reflex	
E	Afferent limb of the cough reflex	
F	Equilibrium and balance	

Hint

The most common tumor of the jugular foramen is a paraganglioma (glomus jugulare), which typically presents with pulsatile tinnitus. The parotid gland is innervated by the tympanic branch of the glossopharyngeal nerve (CN IX), which exits the skull at the jugular foramen, posterior to the jugular fossa.

Correct Answer

A - Protrusion of the tongue

Explanation Why

Protrusion of the [tongue](#) is mediated by the [hypoglossal nerve](#) (CN XII) through the left and right [genioglossus](#) muscles. [CN XII](#) does not pass through the [jugular foramen](#), but rather through the [hypoglossal canal](#) of the [occipital bone](#).

B - Taste sensation of tip of the tongue

Explanation Why

[Taste](#) sensation of the [anterior](#) two-thirds of the [tongue](#) is supplied by the [chorda tympani](#) branch of the [facial nerve](#) (CN VII). [Parasympathetic](#) fibers from the [chorda tympani](#) also stimulate the sublingual and submandibular salivary glands, but not the [parotid](#). Furthermore, the [chorda tympani](#) exits the [skull](#) through the [petrotympanic fissure](#), not the [jugular foramen](#).

C - Closing of the jaw

Explanation Why

Closing of the [jaw](#) is mediated by the [mandibular nerve](#), a branch of the [trigeminal nerve](#) (CN V₃) that controls the [muscles of mastication](#). The [auriculotemporal nerve](#), which is a branch of the [mandibular nerve](#), carries the [parasympathetic](#) fibers of the [glossopharyngeal nerve](#) to the [parotid gland](#) but neither the [trigeminal nerve](#) nor the [mandibular nerve](#) carries any [parasympathetic](#) fibers. Therefore, an isolated [auriculotemporal nerve](#) lesion would decrease [parotid gland](#) secretion but it would not affect the [muscles of mastication](#). On the other hand, a lesion of the [trigeminal nerve](#) or the [mandibular nerve](#) would impair closing of the [jaw](#) but it would not decrease [parotid gland](#) secretion. Furthermore, the [mandibular nerve](#) exits through the foramen ovale, not the [jugular foramen](#).

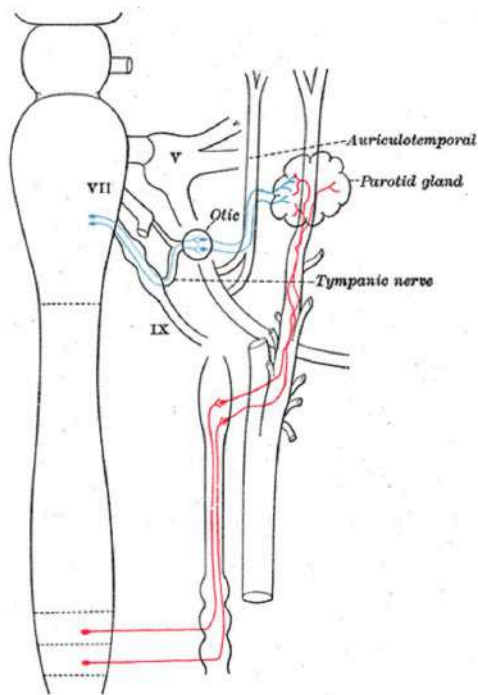
D - Afferent limb of the gag reflex

Explanation Why

The afferent sensory limb of the [gag reflex](#) is formed by the [glossopharyngeal nerve \(CN IX\)](#) and the efferent motor limb formed by the [vagus nerve \(CN X\)](#). Upon irritation of the [posterior](#) pharyngeal wall, the reflex elicits elevation of the [soft palate](#) and bilateral contraction of the pharyngeal muscles.

E - Afferent limb of the cough reflex

Image



Explanation Why

The afferent impulses of the [cough reflex](#) are carried from the [trachea](#) and pharynx along the [superior laryngeal nerve](#), which is a branch of the [vagus nerve](#). Although the [vagus nerve](#) does pass through the [jugular foramen](#), neither the vagus nor its branches innervate the [parotid gland](#). The [vagus nerve](#) is, instead, responsible for increasing secretion in the [gastrointestinal tract](#) (e.g. [gastric acid](#)

secretion).

F - Equilibrium and balance

Explanation Why

The vestibular division of the [vestibulocochlear nerve \(CN VIII\)](#) carries information from the [inner ear](#) to the [brain stem](#). A [CN VIII](#) lesion would explain this patient's [tinnitus](#). However, [CN VIII](#) travels through the [internal acoustic meatus](#) in the [temporal bone](#) rather than through the [jugular foramen](#), and a lesion of this nerve would not affect saliva production in the [parotid gland](#).

Question # 15

A 43-year-old man is brought to the emergency department by his wife because of a 1-hour history of confusion and strange behavior. She reports that he started behaving in an agitated manner shortly after eating some wild berries that they had picked during their camping trip. His temperature is 38.7°C (101.7°F). Physical examination shows warm, dry skin and dry mucous membranes. His pupils are dilated and minimally reactive to light. His bowel sounds are decreased. The patient is admitted and pharmacotherapy is initiated with a drug that eventually results in complete resolution of all of his symptoms. This patient was most likely administered which of the following drugs?

	Answer	Image
A	Scopolamine	
B	Rivastigmine	
C	Atropine	
D	Physostigmine	
E	Neostigmine	
F	Pyridostigmine	

	Answer	Image
G	Benzotropine	

Hint

This patient presents with delirium, hyperthermia, mydriasis, decreased intestinal motility, and dry skin and mucus membranes. This constellation of symptoms is suggestive of anticholinergic syndrome, likely due to intoxication from belladonna alkaloids in the wild berries.

Correct Answer

A - Scopolamine

Explanation Why

[Scopolamine](#) is primarily used to treat motion sickness. In this patient with [anticholinergic syndrome](#), administering an [anticholinergic drug](#) such as [scopolamine](#) would actually worsen his symptoms.

B - Rivastigmine

Explanation Why

[Rivastigmine](#) is used primarily to treat [Alzheimer disease](#). While it can act on the [central nervous system](#), it is not the drug of choice for [anticholinergic syndrome](#).

C - Atropine

Explanation Why

[Atropine](#) is used to treat symptomatic [bradycardia](#) and reverse [organophosphate poisoning](#). This patient's [anticholinergic syndrome](#) is likely caused by ingestion of [belladonna](#) alkaloids, which contain [atropine](#). Administering additional [atropine](#) would therefore not lead to symptom resolution.

D - Physostigmine

Image



Explanation Why

[Physostigmine](#) is a [CNS](#)-penetrating [acetylcholinesterase inhibitor](#) used to treat [anticholinergic toxicity](#), the diagnosis in this case. The berries of the [atropa belladonna](#) plant contain [atropine](#), which can cause [anticholinergic syndrome](#), as seen in this patient. The first-line treatment is to reversibly inhibit acetylcholinesterase both centrally and peripherally with [physostigmine](#).

E - Neostigmine

Explanation Why

[Neostigmine](#) is used to treat [myasthenia gravis](#). However, it does not cross the [blood-brain barrier](#) and would be inappropriate for this patient's [anticholinergic syndrome](#), which includes central symptoms (e.g., [delirium](#)) as well as peripheral ones (e.g., decreased intestinal motility). He therefore

requires an [acetylcholinesterase inhibitor](#) that functions well both peripherally and in the [central nervous system](#).

F - Pyridostigmine

Explanation Why

[Pyridostigmine](#) is used to treat [myasthenia gravis](#). However, it has a low [blood-brain barrier](#) penetration and would be inappropriate for this patient's [anticholinergic syndrome](#), which includes central symptoms (e.g., [delirium](#)) as well as peripheral ones (e.g., decreased intestinal motility). This patient therefore requires an [acetylcholinesterase inhibitor](#) that functions well both peripherally and in the [central nervous system](#).

G - Benztropine

Explanation Why

[Benztropine](#) is used to treat [Parkinson disease](#) and the [extrapyramidal symptoms](#) caused by [antipsychotics](#). In this patient with [anticholinergic syndrome](#), administering an [anticholinergic](#) drug would worsen rather than resolve his symptoms.

Question # 16

A 68-year-old man is brought to the emergency department because of right-sided weakness for 2 hours. He has hypertension, dyslipidemia, and type 2 diabetes. Current medications include hydrochlorothiazide, metoprolol, amlodipine, pravastatin, and metformin. His pulse is 87/min and blood pressure is 164/98 mm Hg. Neurological examination shows right-sided weakness, facial droop, and hyperreflexia. Sensation is intact. Which of the following is the most likely cause of these findings?

	Answer	Image
A	Rupture of an intracranial aneurysm	
B	Lipohyalinosis of penetrating vessels	
C	Dissection of the vertebral artery	
D	Stenosis of the internal carotid artery	
E	Embolism from the left atrium	

Hint

This patient presents with right-sided weakness without associated sensory dysfunction, which suggests a pure motor lacunar infarct.

Correct Answer

A - Rupture of an intracranial aneurysm

Explanation Why

The rupture of an intracranial (berry) [aneurysm](#) would typically result in [subarachnoid hemorrhage](#), manifesting with a sudden-onset severe [headache](#) (“worst [headache](#) of my life”), rapidly worsening nausea/vomiting, and clinical features of meningism (e.g., neck [rigidity](#)), which are not seen in this patient.

B - Lipohyalinosis of penetrating vessels

Explanation Why

Lipohyalinotic thickening of penetrating cerebral vessels (e.g., [lenticulostriate arteries](#)) is the most likely cause of this patient's pure motor [lacunar infarct](#); obliteration of the lumina of the poorly-collateralized [lenticulostriate arteries](#) leads to the [infarction](#) of the genu and [anterior](#) $\frac{2}{3}$ of the [posterior](#) limb of the [internal capsule](#), where motor fibers are densely packed. Chronic, uncontrolled [hypertension](#), [diabetes mellitus](#), smoking, and [hyperlipidemia](#) are [risk factors](#) for [lipohyalinosis](#).

C - Dissection of the vertebral artery

Explanation Why

A [stroke](#) due to dissection of the left [vertebral artery](#) would typically result in left [lateral medullary syndrome](#), which would manifest with right-sided weakness. However, other features such as [vertigo](#), ipsilateral [hearing loss](#), [ataxia](#), [dysarthria](#), and contralateral loss of [pain](#) and temperature sensation would also be evident. Patients with [vertebral artery dissection](#) usually typically have neck [pain](#) and/or occipital [headache](#), which are not seen here. Furthermore, they are typically younger ([mean](#) age approx. 45 years) and often report a history of trauma or [sports injury](#).

D - Stenosis of the internal carotid artery

Explanation Why

A [stroke](#) due to [carotid artery stenosis](#) is usually an [ischemic](#) cortical [infarct](#) of the [middle cerebral artery](#) (MCA) or (less commonly) [anterior cerebral artery](#) (ACA) due to [atheroembolism](#). A left-sided cortical [infarct](#) that is large enough to cause weakness in the entire right half of the body would also have [aphasia](#), [frontal lobe](#) defects, and/or deficits in sensation, none of which are seen here. Moreover, patients with CAS often have a history of [amaurosis fugax](#) or [transient ischemic attacks](#) and a [carotid bruit](#) on neck auscultation, which this patient does not have.

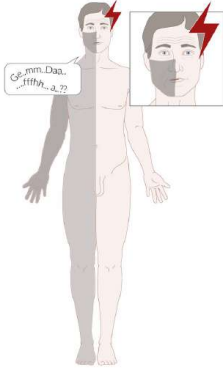
E - Embolism from the left atrium

Explanation Why

An embolus from the [left atrium](#) is the most common cause of [stroke](#) in patients with [atrial fibrillation](#) and usually causes large subcortical and/or cortical [infarcts](#). Although this patient has several [risk factors for atrial fibrillation](#), such as increased age and [hypertension](#), he does not have evidence of [atrial fibrillation](#) (e.g., an [irregularly irregular pulse](#)). Furthermore, a left-sided cortical [infarct](#) that is large enough to cause weakness in the entire right half of the body would likely also have [aphasia](#), [frontal lobe](#) defects, and/or deficits in sensation, none of which are seen here. This patient's isolated motor symptoms suggest a small subcortical [infarct](#) of the [internal capsule](#).

Question # 17

A 69-year-old right-handed man comes to the physician for a routine health maintenance examination. On questioning, he has had some difficulty speaking for 3 months. During a conversation, he often has difficulty repeating what his interlocutor has said. He has hypertension and takes hydrochlorothiazide. His vital signs are within normal limits. The patient speaks fluently in full sentences and demonstrates normal comprehension. When asked to say the word “kindergarten,” he replies with, “Sintelmarvin... no, that's wrong...kinterflargin, no that isn't it either...kantolargen...no? How about, kindergarten?” The most likely cause of the patient's symptoms is occlusion of a branch of which of the following arteries?

	Answer	Image
A	Right posterior cerebral	
B	Left middle cerebral	
C	Right middle cerebral	
D	Right penetrating	
E	Right posterior inferior cerebellar	
F	Right vertebral	

	Answer	Image
G	Left posterior inferior cerebellar	
H	Left posterior cerebral	
I	Left vertebral	
J	Left penetrating	

Hint

The patient's impaired repetition with paraphasia, together with preserved comprehension, is called conduction aphasia. Lesions in the supramarginal gyrus can cause this syndrome, which often presents without other neurologic symptoms.

Correct Answer

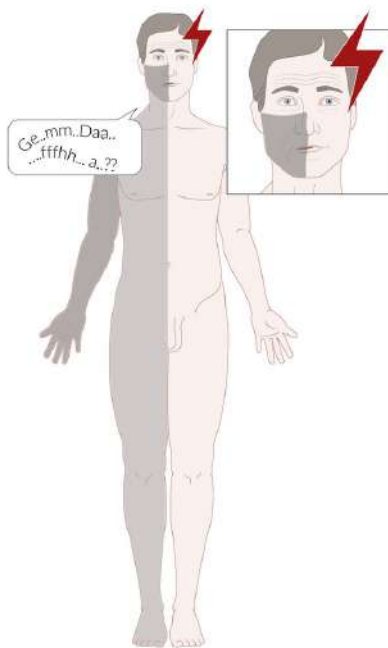
A - Right posterior cerebral

Explanation Why

Occlusion of the right [posterior cerebral artery](#) would cause left-sided weakness and left [homonymous hemianopia](#) with [macular sparing](#); it would not cause conductive [aphasia](#).

B - Left middle cerebral

Image



Explanation Why

In a right-handed person, the supramarginal [gyrus](#) is supplied by a branch of the left middle cerebral. A lesion to this area can disrupt the articulate fasciculata and result in conductive [aphasia](#).

C - Right middle cerebral

Explanation Why

In a right-handed person, occlusion of the right [middle cerebral artery](#) would cause left-sided weakness and [hemineglect](#); it would not cause conductive [aphasia](#). In some left-handed individuals, the language center is located in the right hemisphere. In these patients, a lesion to the right [middle cerebral artery](#) could cause conductive [aphasia](#).

D - Right penetrating

Explanation Why

[Ischemia](#) to the right [posterior](#) limb of the [internal capsule](#) due to occlusion of right penetrating [arteries](#) would cause left-sided weakness; it would not cause conductive [aphasia](#).

E - Right posterior inferior cerebellar

Explanation Why

Occlusion of the right [posterior inferior cerebellar artery](#) can result in [lateral medullary syndrome](#), which presents with ipsilateral face and contralateral body [pain](#)/temperature sensory deficits, [dysphagia](#), hoarseness, and ipsilateral [Horner syndrome](#). [Conduction aphasia](#) is not seen in [lateral medullary syndrome](#).

F - Right vertebral

Explanation Why

Occlusion of the right [vertebral artery](#) can cause [dizziness](#) along with other neurologic signs such as [diplopia](#), [hemiparesis](#), or numbness. It would not manifest with conductive [aphasia](#).

G - Left posterior inferior cerebellar

Explanation Why

Occlusion of the left [posterior inferior cerebellar artery](#) can result in [lateral medullary syndrome](#), which presents with ipsilateral face and contralateral body [pain](#)/temperature sensory deficits, [dysphagia](#), hoarseness, and ipsilateral [Horner syndrome](#). [Conduction aphasia](#) is not seen in [lateral medullary syndrome](#).

H - Left posterior cerebral

Explanation Why

Occlusion of the left [posterior cerebral artery](#) would cause right-sided [hemiparesis](#) and a right [homonymous hemianopia](#) with [macular sparing](#); it would not cause conductive [aphasia](#).

I - Left vertebral

Explanation Why

Occlusion of the left [vertebral artery](#) can cause [dizziness](#) along with other neurologic signs such as [diplopia](#), [hemiparesis](#), or numbness. It would not manifest with conductive [aphasia](#).

J - Left penetrating

Explanation Why

Occlusion of the left penetrating [arteries](#) that supply the left [posterior](#) limb of the [internal capsule](#) would result in right-sided weakness; it would not cause conductive [aphasia](#).

Question # 18

A 23-year-old woman comes to the physician because of an 8-month history of weakness and intermittent burning pain in her neck, shoulders, and arms. She was involved in a motor vehicle collision 1 year ago. Examination of the upper extremities shows absent reflexes, muscle weakness, and fasciculations bilaterally. Sensation to temperature and pain is absent; vibration and proprioception are preserved. The pupils are equal and reactive to light. Which of the following is the most likely diagnosis?

	Answer	Image
A	Tabes dorsalis	
B	Syringomyelia	Syringomyelia - Lesion at C4-C5 Syrinx: Symptoms (see below) depend on degree of severity Antihorn Pyramidal tract: Spastic paralysis, Central segments extend laterally, Sacral segments extend laterally Anterior horn Damaged region Disassociated sensory loss (of temperature and pain): from damage to pathways of spinothalamic sensitivity crossing at segment level Flaccid paralysis: from bilateral damage to anterior horns at segment level Spastic paralysis: from damage of the ventral portion of left pyramidal tract Note: Both the loss of sensation and the effects on motor function are depicted according to the associated dermatomes. Since most muscles are innervated by several segments, they are usually paralytic, but not atrophic. Autonomic disorders (e.g., Horner's syndrome, bladder dysfunction) can also occur if the lateral horns (C8-L2/L3) are involved.
C	Subacute combined degeneration	
D	Amyotrophic lateral sclerosis	
E	Brown-Séquard syndrome	
F	Multiple sclerosis	

	Answer	Image
G	Cervical disk prolapse	

Hint

The presence of pain along with sensory deficits to pain and temperature in a cape-like distribution over the neck and upper extremities while sparing more distal sensory levels suggests injury to decussating fibers in the cervical and upper thoracic spinal cord. A history of motor vehicle collision and progressive symptoms point to a traumatic etiology.

Correct Answer

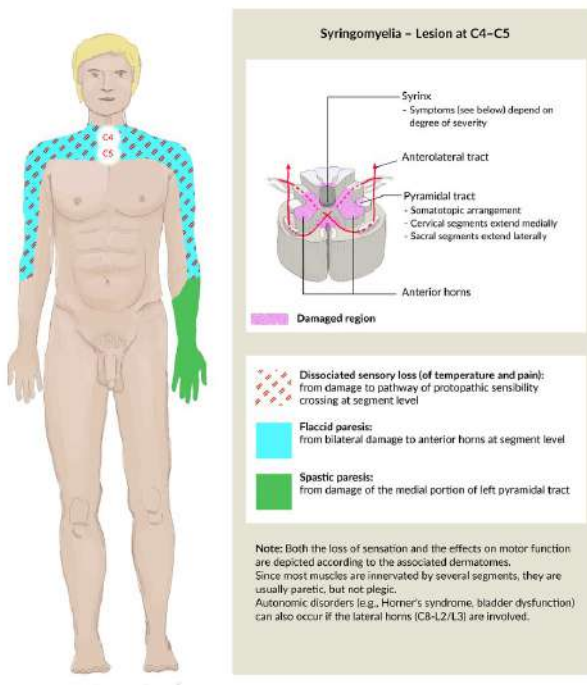
A - Tabes dorsalis

Explanation Why

Tabes dorsalis, a manifestation of tertiary syphilis, refers to degeneration of the dorsal columns of the spinal cord that causes dysesthesia, as seen in this patient. It is also characterized by proprioceptive loss leading to ataxia, whereas proprioception is preserved in this patient. Pupillary irregularities, such as Argyll-Robertson pupil, are commonly associated with tabes dorsalis but are not seen here. While tabes dorsalis can sometimes cause absent lower extremity reflexes, it would not cause areflexia or other upper motor neuron signs of the upper extremities.

B - Syringomyelia

Image



Explanation But

As the lesion expands, the patient will develop an [upper motor neuron](#) palsy of the lower extremities and lower half of the trunk (due to involvement of the [corticospinal tracts](#)), as well as complete sensory loss below the level of the lesion (including loss of vibration and position sense). However, sensations around the sacral region will usually be spared.

Explanation Why

Post-traumatic [syringomyelia](#) can occur months to years after whiplash-type injury to the neck and presents with the classical findings of a [central cord syndrome](#). Patients develop a symmetric cape-like distribution of [pain](#) and temperature sensory loss around the upper trunk, shoulders and upper limbs. Vibration and position sense are selectively spared because fibers of the [posterior columns](#) decussate higher up in the medulla. As [syringomyelia](#) progresses, [lower motor neuron](#) weakness develops symmetrically in the upper limbs (evident by areflexia and [fasciculations](#) in this patient) because the fluid-filled cavity begins to compress the [anterior horn cells](#) of the [spinal cord](#) at the level of the lesion. [Syringomyelia](#) is commonly associated with [Chiari type I malformation](#).

C - Subacute combined degeneration

Explanation Why

[Subacute combined degeneration](#) (SCD) of the [spinal cord](#) affects the [posterior](#) and posterolateral columns of the [spinal cord](#), presenting with [upper motor neuron](#) pattern weakness of the extremities and impaired fine touch and [proprioception](#). This patient has preserved fine touch and [proprioception](#) along with [lower motor neuron signs](#).

D - Amyotrophic lateral sclerosis

Explanation Why

[Amyotrophic lateral sclerosis](#) (ALS) may present with a combination of [upper motor neuron](#) and [lower motor neuron](#) weakness that progresses over time. However, [ALS](#) is more typically asymmetric and does not present with sensory deficits.

E - Brown-Séquard syndrome

Explanation Why

[Brown-Séquard syndrome](#), which results from a hemisection of the [spinal cord](#), presents with [dissociated sensory loss](#) and unilateral motor deficits below the level of the injury. This patient has deficits affecting only her arms and chest without involvement of the remaining trunk and lower extremities, as would be seen in Brown-Séquard syndrome. In addition, Brown-Séquard syndrome typically occurs immediately following [spinal cord](#) injury; it is unlikely to develop 4 months later, as this patient's deficits did.

F - Multiple sclerosis

Explanation Why

[Multiple sclerosis](#) can manifest with sensory deficits, weakness, and [dysesthesia](#), as seen in this patient. But it would more typically manifest with [upper motor neuron signs](#) instead of [lower motor neuron signs](#) (e.g., [fasciculations](#), loss of reflexes).

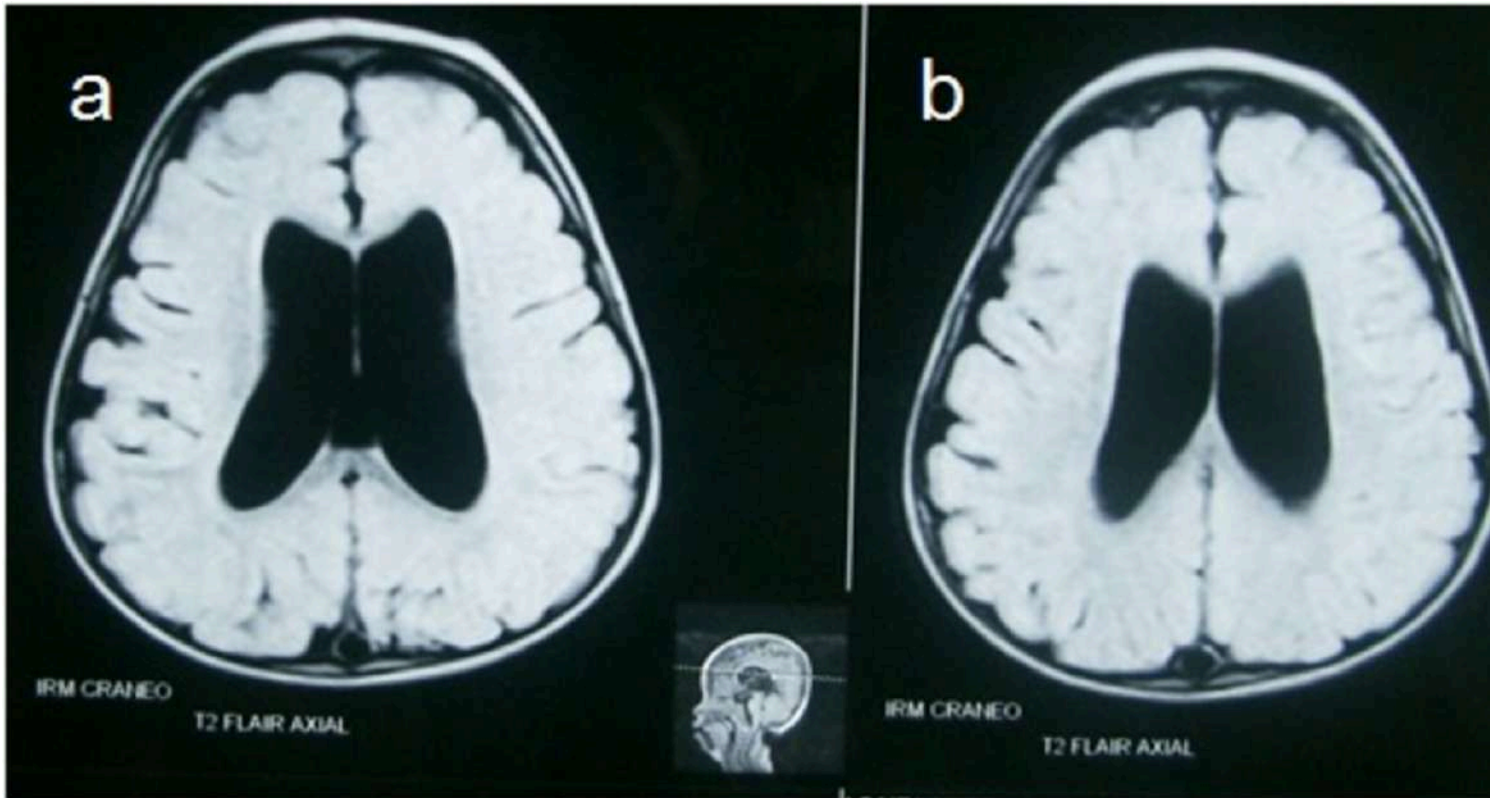
G - Cervical disk prolapse

Explanation Why

Cervical disk prolapse can lead to [nerve root](#) compression ([radiculopathy](#)), which may present with [dysesthesia](#) as well as sensory and/or motor deficits. However, neurological symptoms produced by disc prolapse are usually unilateral and localized to the distribution of the compressed [nerve root](#). It is very unlikely that [nerve root](#) compression is the cause of this patient's symmetrical distribution of deficits; many [nerve roots](#) would have to be compressed simultaneously on both sides. In addition, all sensations are usually affected by [nerve root](#) compression, and the preservation of vibration and positional sense suggests a different diagnosis.

Question # 19

A 2-year-old boy is brought to the physician by his parents several weeks after the family immigrated from Russia. The parents are worried because the child appears to have trouble seeing and has not started walking. The child was born at home and has never been evaluated by a physician. During the pregnancy, the mother had a week of fever, myalgia, diffuse rash, and bilateral nontender cervical adenopathy after the family adopted a new cat. An MRI of the head is shown. Which of the following additional findings is most likely in this patient?



	Answer	Image
A	Continuous machinery murmur	
B	Pupils do not react to light but constrict with accommodation	
C	Spasticity of bilateral lower extremities	

	Answer	Image
D	Tuft of hair over the lumbosacral area	
E	Loss of pain sensation in shawl distribution	

Hint

This patient likely developed congenital toxoplasmosis after his mother had a primary infection (fever, myalgia, and nontender cervical adenopathy after exposure to an infected cat). One of the cardinal manifestations of congenital toxoplasmosis is hydrocephalus, which manifests as dilation of the ventricles, as seen on MRI.

Correct Answer

A - Continuous machinery murmur

Explanation Why

A continuous [machinery murmur](#) arises from a [patent ductus arteriosus \(PDA\)](#). [PDA](#) is associated with [congenital rubella infection](#) but is not seen in [congenital toxoplasmosis](#) infection. While [congenital rubella](#) can also cause difficulty with vision (due to [cataracts](#)), it also presents with [sensorineural hearing loss](#), which this patient does not have.

B - Pupils do not react to light but constrict with accommodation

Explanation Why

Pupils that do not react to light but constrict with [accommodation](#) are termed [Argyll-Robertson pupils](#). This finding can be seen in [tertiary syphilis](#), which would be extremely unusual for a child to have. Furthermore, the patient has no history of findings seen in [congenital syphilis](#), [primary syphilis](#), or [secondary syphilis](#).

C - Spasticity of bilateral lower extremities

Explanation But

Other classic findings in [congenital toxoplasmosis](#) include [chorioretinitis](#) (which may explain the patient's poor eyesight) and intracranial calcifications. Pregnant women should avoid raw meats and contact with cat litter to prevent [toxoplasmosis](#).

Explanation Why

[Spasticity](#) of the lower extremities is a common finding in advanced, chronic [hydrocephalus](#) due to stretching of the motor cortices and [pyramidal tracts](#) around the dilated ventricles. [Hyperreflexia](#), another sign of [upper motor neuron damage](#), can also be seen in many cases. Other symptoms of

[hydrocephalus](#) in children include difficulty feeding, irritability, and [macrocephaly](#).

D - Tuft of hair over the lumbosacral area

Explanation Why

A tuft of [hair](#) in the lumbosacral region is associated with [spina bifida occulta](#). More severe forms of [spina bifida](#) can be associated with a [myelomeningocele](#), which itself is associated with [hydrocephalus](#). However, patients with [myelomeningoceles](#) have obvious, gross deformity of the lumbosacral area, not relatively minor findings such as a tuft of [hair](#).

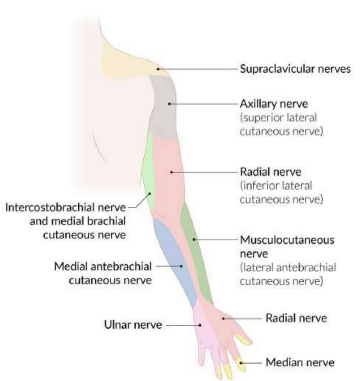
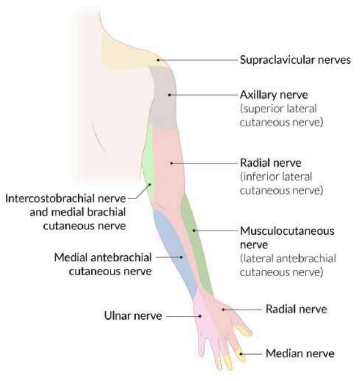
E - Loss of pain sensation in shawl distribution

Explanation Why

Loss of [pain](#) sensation in a shawl distribution is consistent with [syringomyelia](#). The development of a [syrinx](#) in the center of the cervical [spinal cord](#) progressively compresses [neurons](#) of the [spinothalamic tract](#), which explains the loss of [pain](#) (and typically temperature) sensation in the upper extremities. Later findings can include weakness or even paralysis as [alpha motor neurons](#) become compromised. [Syringomyelia](#) does not cause [hydrocephalus](#).

Question # 20

A 32-year-old man comes to the physician because of a 2-day history of a tingling sensation in his right forearm. He reports that his symptoms started after he lifted heavy weights at the gym. Physical examination shows loss of sensation on the lateral side of the right forearm. Sensation over the thumb is intact. Range of motion of the neck is normal. His symptoms do not worsen with axial compression or distraction of the neck. Further examination of this patient is most likely to show weakness of which of the following actions?

	Answer	Image
A	Shoulder abduction	
B	Elbow flexion	

	Answer	Image
C	Forearm pronation	Supraclavicular nerves Axillary nerve (superior lateral cutaneous nerve) Radial nerve (inferior lateral cutaneous nerve) Musculocutaneous nerve (lateral antebrachial cutaneous nerve) Intercostobrachial nerve and medial brachial cutaneous nerve Medial antebrachial cutaneous nerve Radial nerve Ulnar nerve Median nerve
D	Index finger flexion	Supraclavicular nerves Axillary nerve (superior lateral cutaneous nerve) Radial nerve (inferior lateral cutaneous nerve) Musculocutaneous nerve (lateral antebrachial cutaneous nerve) Intercostobrachial nerve and medial brachial cutaneous nerve Medial antebrachial cutaneous nerve Radial nerve Ulnar nerve Median nerve
E	Wrist extension	Supraclavicular nerves Axillary nerve (superior lateral cutaneous nerve) Radial nerve (inferior lateral cutaneous nerve) Intercostobrachial nerve and medial brachial cutaneous nerve Medial antebrachial cutaneous nerve Musculocutaneous nerve (lateral antebrachial cutaneous nerve) Ulnar nerve Radial nerve Median nerve

	Answer	Image
F	Pincer grip	

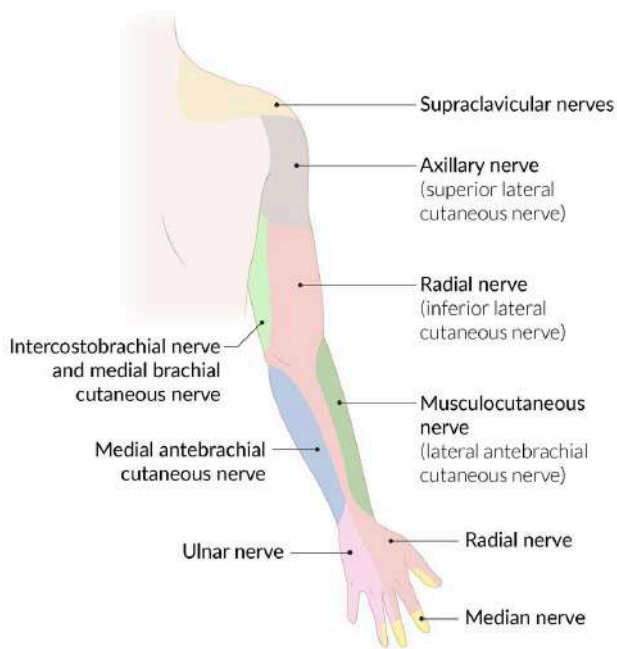
Hint

The lateral cutaneous nerve of the forearm, which innervates the lateral surface of the forearm, is a branch of the musculocutaneous nerve.

Correct Answer

A - Shoulder abduction

Image

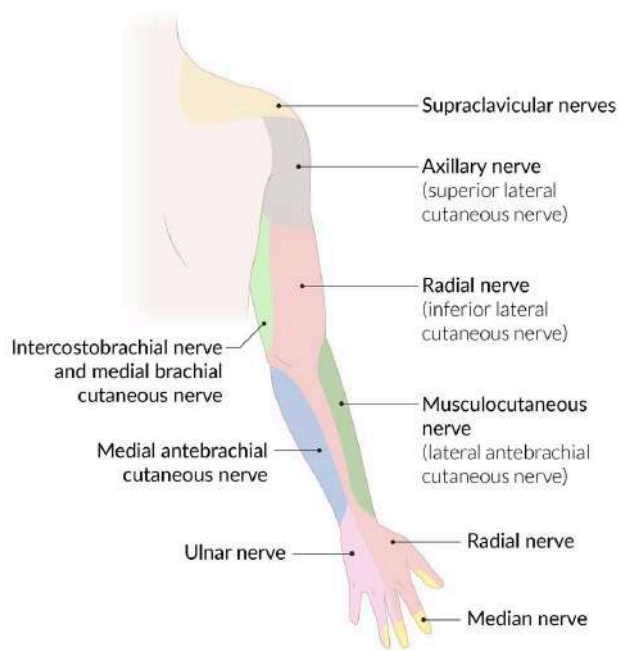


Explanation Why

Shoulder [abduction](#) is predominantly controlled by the [deltoid muscle](#), which is innervated by the [axillary nerve](#). The [axillary nerve](#) also controls sensation over the [distal](#) half of the deltoid region. Given this patient's sensory changes over the [lateral](#) forearm, it is unlikely that he has an [axillary nerve injury](#).

B - Elbow flexion

Image



Explanation But

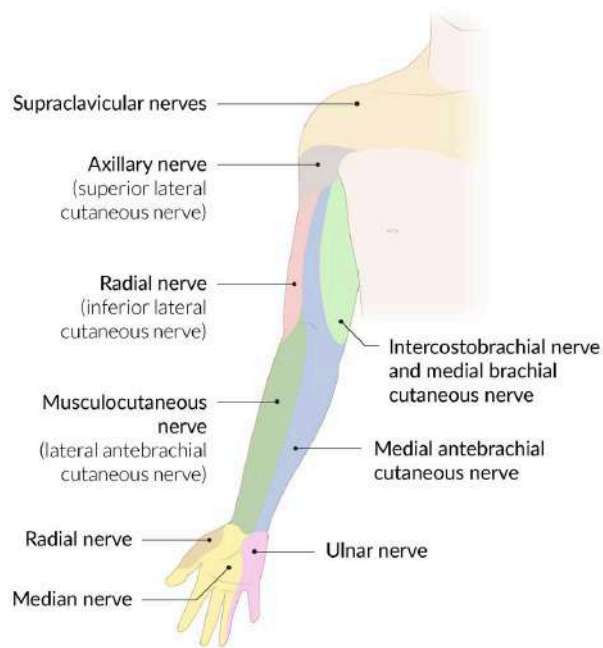
Some symptoms of [musculocutaneous nerve injury](#) may be masked by the fact that the [supinator muscle](#) (innervated by the radial nerve) can at least partially compensate for the [supination](#) deficit; in addition, the [brachioradialis muscle](#) (also innervated by the radial nerve) is an [elbow](#) flexor.

Explanation Why

[Elbow flexion](#) is controlled by the [biceps brachii](#) and [brachialis](#) muscles, which are innervated by the [musculocutaneous nerve](#). [Musculocutaneous nerve injury](#) can result from lifting heavy weights as seen in this case. This injury also impairs forearm [supination](#) and the [biceps](#) tendon reflex. The normal range of motion in the neck and negative [Spurling sign](#) indicate that this patient has a [peripheral nerve lesion](#).

C - Forearm pronation

Image

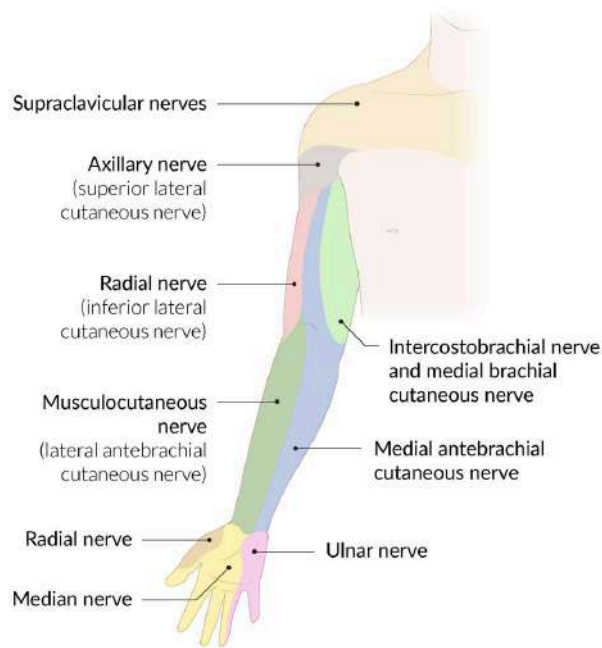


Explanation Why

Forearm [pronation](#) is controlled by the [pronator teres](#) and [pronator quadratus](#) muscles, which are innervated by the median nerve. The median nerve also controls sensation on the [lateral](#) aspect of the palm, including the thumb. Given this patient's symptoms of primarily [lateral](#) forearm sensory loss without involvement of the thumb or hand, it is unlikely that he has a [median nerve injury](#).

D - Index finger flexion

Image

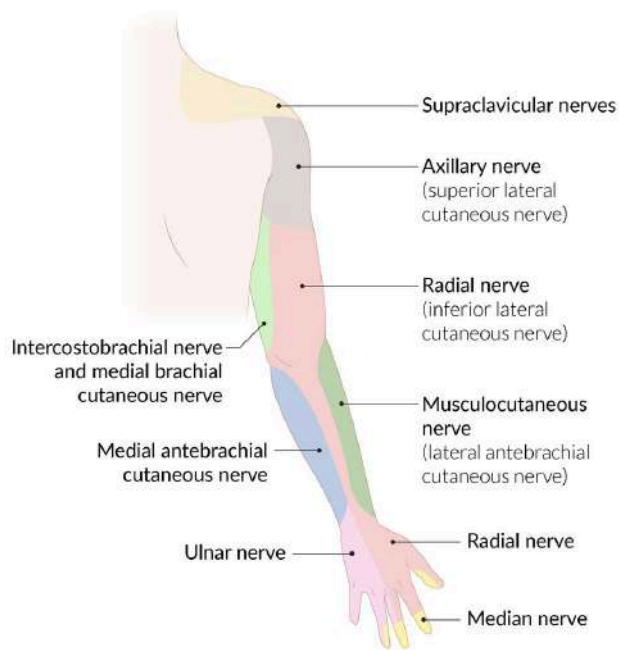


Explanation Why

Index finger [flexion](#) is controlled by the median nerve. [Median nerve injury](#) leads to sensory loss over the [lateral](#) aspect of the palm, including the thumb. Though the median nerve controls many of the [muscles of the forearm](#), it does not control sensation of the forearm. Given this patient's symptoms of primarily [lateral](#) forearm sensory loss without involvement of the thumb or hand, it is unlikely that he has a [median nerve injury](#).

E - Wrist extension

Image

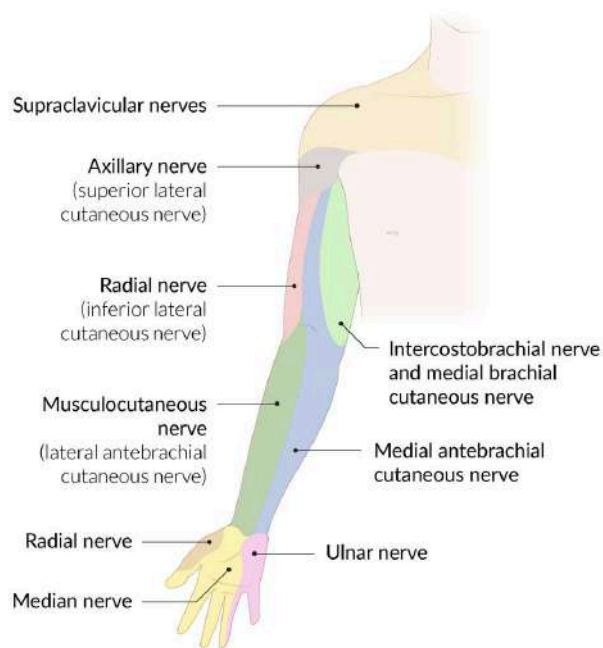


Explanation Why

Wrist extension is controlled by the radial nerve, which also controls sensation over the [posterior](#) surface of the forearm extending to the dorsolateral hand. Since this patient's sensory loss is over the [lateral](#) portion of the forearm without any hand involvement, it is unlikely that he has a [radial nerve injury](#).

F - Pincer grip

Image



Explanation Why

The pincer grip is controlled by the ulnar nerve, which controls sensation of the [medial](#) aspect of the hand. The ulnar nerve does not control sensation over the forearm and is unlikely to be the cause of this patient's sensory changes.

Question # 21

A 64-year-old man with osteoarthritis of the knee comes to the physician for evaluation of weakness in his foot. Physical examination shows a swelling in the popliteal fossa. There is marked weakness when attempting to invert his right foot. He is unable to curl his toes. Further evaluation of this patient is most likely to show decreased sensation over which of the following locations?

	Answer	Image
A	Second dorsal web space	
B	Sole of the foot	
C	First dorsal web space	
D	Medial plantar arch	
E	Lateral border of the foot	

Hint

Swelling of the popliteal fossa can lead to compression of the inlying structures, including the tibial nerve. Compression of the tibial nerve can result in neuropraxia, causing marked motor weakness of foot inversion and toe plantarflexion, as well as sensory deficits in the tibial nerve distribution.

Correct Answer

A - Second dorsal web space

Explanation Why

The second [dorsal](#) web space, the anterolateral inferior third of the leg, and most of the foot dorsum (except for the first web space) receive sensory innervation from the [superficial peroneal nerve](#). The motor portion of this nerve supplies the [lateral compartment of the leg](#), allowing for foot eversion. Injury to the [superficial peroneal nerve](#) occurs secondary to entrapment at the [lateral](#) ankle or via fibular [fracture](#), not as a result of the popliteal swelling seen in this patient. Likewise, deficits of [foot inversion](#) and toe [plantar flexion](#) do not correlate with a [superficial peroneal nerve](#) injury.

B - Sole of the foot

Explanation Why

The sole of the foot, [lateral](#) foot, and posterolateral leg are innervated by sensory branches of the [tibial nerve](#) (nerve stem from L4–[S3](#)). The [posterior compartment of the leg](#), responsible for [foot inversion](#) and [plantarflexion](#) of the toes and ankle, is innervated by motor branches of the [tibial nerve](#). This patient's [neuropraxia](#) of the [tibial nerve](#) secondary to popliteal swelling would diminish the sensory and motor functions of these regions.

C - First dorsal web space

Explanation Why

The sensory branch of the [deep peroneal nerve](#) provides sensation to the first web space, while the motor portion supplies the [anterior compartment of the leg](#), which is responsible for foot and toe [dorsiflexion](#). Injury is usually the result of [anterior](#) compartment compression or ski boot syndrome, not the popliteal swelling seen in this patient. Likewise, deficits of [foot inversion](#) and toe [plantar flexion](#) do not correlate with [deep peroneal nerve](#) injury.

D - Medial plantar arch

Explanation Why

The [medial plantar](#) arch and the [medial](#) leg and foot are innervated by the [saphenous nerve](#), which has a purely cutaneous sensory function. Therefore, this patient's motor deficits of [foot inversion](#) and toe [plantar flexion](#) do not correlate with [saphenous nerve](#) injury. The [saphenous nerve](#) would also not be injured by popliteal swelling.

E - Lateral border of the foot

Explanation Why

The [lateral](#) border of the foot is innervated by the [sural nerve](#), which provides a purely cutaneous sensory function to the inferior portion of the posterolateral leg. Injury to the [sural nerve](#) is often secondary to [calcaneal fracture](#) or trauma, not popliteal swelling as this patient has. Likewise, deficits of [foot inversion](#) and toe [plantar flexion](#) do not correlate with [sural nerve injury](#).

Question # 22

A 5-year-old boy is brought to the physician because of an irregular gait 3 days after receiving age-appropriate vaccinations. Examination of the lower extremities shows no redness or swelling. When the child stands on his right leg, his left leg drops and his pelvis tilts towards the left. Sensation to light touch is normal in both legs. This patient's symptoms are most likely due to the injection of the vaccine into which of the following locations?

	Answer	Image
A	Superomedial quadrant of the left buttock	
B	Inferolateral quadrant of the right buttock	
C	Inferomedial quadrant of the right buttock	
D	Inferomedial quadrant of the left buttock	

	Answer	Image
E	Superomedial quadrant of the right buttock	
F	Inferolateral quadrant of the left buttock	

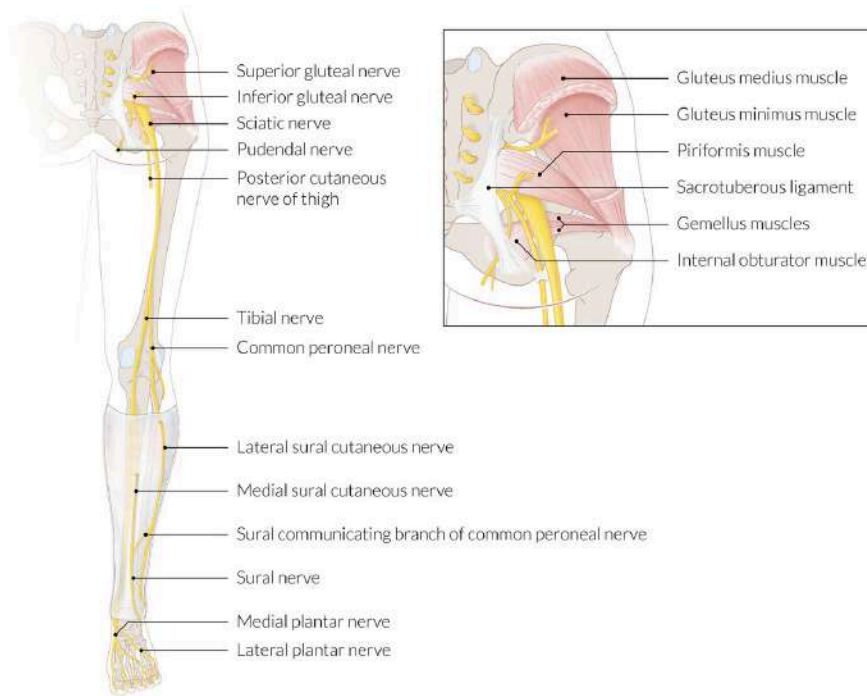
Hint

This patient's abnormal gait is most likely caused by weakness of hip abductors due to iatrogenic nerve injury.

Correct Answer

A - Superomedial quadrant of the left buttock

Image



Explanation Why

The left [superior gluteal nerve](#) lies in this region. Injury to this nerve would cause a positive [Trendelenburg sign](#) and a gait abnormality. However, with an injury to the left [superior gluteal nerve](#), a pelvic tilt would not occur when the patient stands on his right leg.

B - Inferolateral quadrant of the right buttock

Explanation Why

The right [sciatic nerve](#) courses through this region. [Sciatic nerve injury](#) can cause an abnormal gait ([high-stepping gait](#)), but features such as foot drop, weakened [knee flexion](#), and sensory loss over the

foot and [lateral](#) surface of the lower leg would also be present ipsilaterally. [Lateral](#) tilting of the [pelvis](#) would not be expected.

C - Inferomedial quadrant of the right buttock

Explanation Why

The right [sciatic nerve](#) and right [inferior gluteal nerve](#) lie in this region. While [sciatic nerve injury](#) can cause an abnormal gait ([high-stepping gait](#)), features such as foot drop, weakened [knee flexion](#), and sensory loss over the foot and [lateral](#) surface of the lower leg would also be present ipsilaterally. [Inferior gluteal nerve injury](#) can cause an abnormal gait ([backward lurching gait](#)), but the patient would also have impaired [hip](#) extension, and a [forward pelvic tilt](#) while standing on the affected side. [Lateral](#) tilting of the [pelvis](#) would not be expected with an isolated injury to either of these nerves.

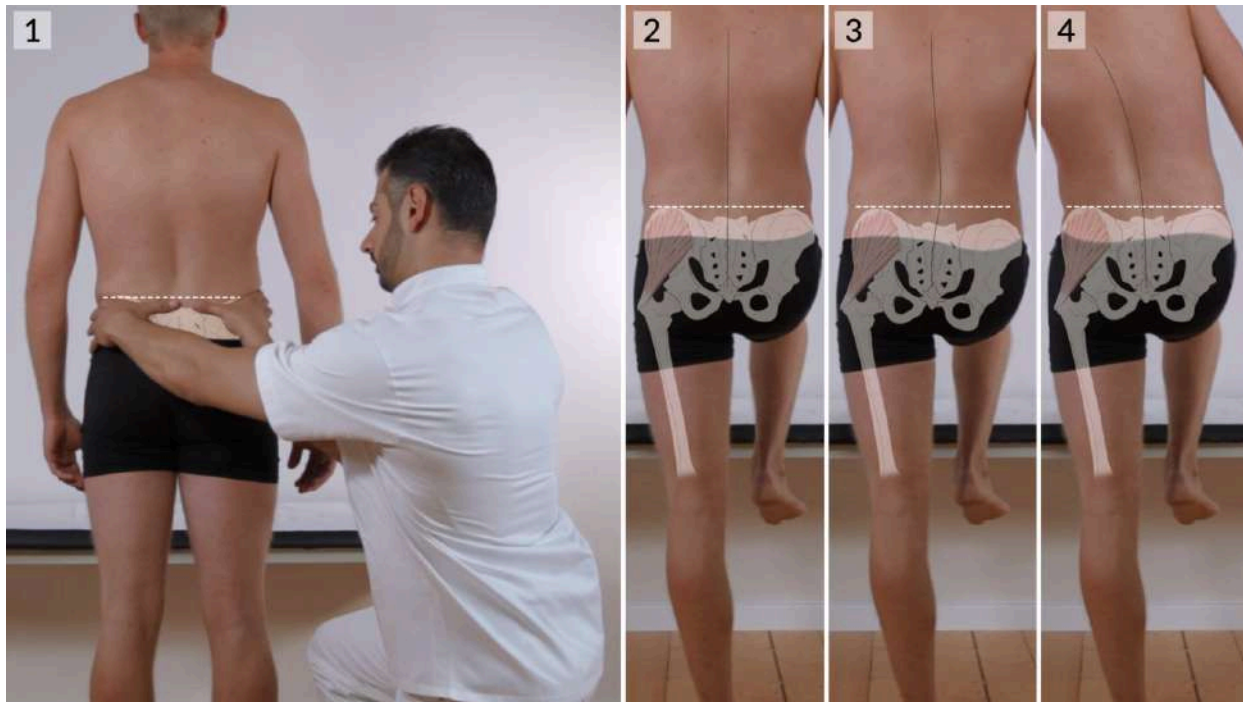
D - Inferomedial quadrant of the left buttock

Explanation Why

The left [sciatic nerve](#) and left [inferior gluteal nerve](#) lie in this region. While [sciatic nerve injury](#) can cause an abnormal gait ([high-stepping gait](#)), features such as foot drop, weakened [knee flexion](#), and sensory loss over the foot and [lateral](#) surface of the lower leg would also be present ipsilaterally. [Inferior gluteal nerve injury](#) can cause an abnormal gait ([backward lurching gait](#)), but the patient would also have impaired [hip](#) extension and a [forward pelvic tilt](#) while standing on the affected side. [Lateral](#) tilting of the [pelvis](#) would not be expected with an isolated injury to either of these nerves.

E - Superomedial quadrant of the right buttock

Image



Explanation Why

The [superior gluteal nerve](#) lies in this region and innervates the [gluteus medius](#), [gluteus minimus](#), and [tensor fasciae latae](#), which prevent the [pelvis](#) from tilting to the contralateral side. Injury to the right [superior gluteal nerve](#) would, therefore, cause the [pelvis](#) to tilt towards the left side when bearing weight on the right leg (positive [Trendelenburg sign](#)). In order to compensate for this pelvic tilt, the patient would tilt the trunk to the right. Intramuscular injections are typically given in the superolateral quadrant of the buttock to avoid nerve injury.

F - Inferolateral quadrant of the left buttock

Explanation Why

The left [sciatic nerve](#) courses through this region. [Sciatic nerve injury](#) can cause an abnormal gait

([high-stepping gait](#)), but features such as foot drop, weakened [knee flexion](#), and sensory loss over the foot and [lateral](#) surface of the lower leg would also be present ipsilaterally. [Lateral](#) tilting of the [pelvis](#) would not be expected.

Question # 23

A 23-year-old man comes to the physician for evaluation of decreased hearing, dizziness, and ringing in his right ear for the past 6 months. Physical examination shows multiple soft, yellow plaques and papules on his arms, chest, and back. There is sensorineural hearing loss and weakness of facial muscles bilaterally. His gait is unsteady. An MRI of the brain shows a 3-cm mass near the right internal auditory meatus and a 2-cm mass at the left cerebellopontine angle. The abnormal cells in these masses are most likely derived from which of the following embryological structures?

	Answer	Image
A	Neural tube	
B	Surface ectoderm	
C	Neural crest	
D	Notochord	
E	Mesoderm	

Hint

The bilateral masses in this patient causing sensorineural hearing loss, tinnitus, and vertigo are acoustic neuromas, which arise from Schwann cells of CN VIII. Compression of the adjacent CN VII causes facial weakness. The combination of multiple cutaneous neurofibromas with bilateral acoustic neuromas is pathognomic of neurofibromatosis type 2.

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Correct Answer

A - Neural tube

Explanation Why

The [neural tube](#) gives rise to [CNS glial cells](#) (e.g., [oligodendrocytes](#), [astrocytes](#), [ependymal cells](#)), which are the [glial cells](#) of [CN I](#) and [CN II](#). The [neural tube](#) does not give rise to [Schwann cells](#), which are the [glial cells](#) of [cranial nerves](#) III–XII. [Optic gliomas](#), which occur in [neurofibromatosis type 1 \(NF1\)](#), are derived from [astrocytes](#). [NF1](#) can present similarly with cutaneous [neurofibromas](#), but the absence of [cafe-au-lait spots](#) on [physical examination](#) and the presence of bilateral [acoustic neuromas](#) suggests a diagnosis of type 2 rather than [NF1](#). [NF2](#) is typically associated with [optic nerve meningiomas](#) rather than [optic nerve gliomas](#).

B - Surface ectoderm

Explanation Why

The [surface ectoderm](#) gives rise to the [anterior pituitary](#), [external auditory canal](#), and [inner ear](#) structures (e.g., [cochlea](#), vestibule, semicircular ducts) as well as glands of the [skin](#), the [parotid](#) glands, and [ameloblasts](#). It does not give rise to [neurons](#) or [glial cells](#). [Craniopharyngiomas](#) arise from the remnant of the Rathke's pouch, which is a surface ectodermal derivative. They occur in the midline above the [sella](#) turcica and present typically during childhood with [headache](#), [bitemporal hemianopsia](#), and/or symptoms of [hyperprolactinemia](#).

C - Neural crest

Explanation Why

[Schwann cells](#) are formed from [neural crest cells](#), which arise from the [lateral](#) border of the [neural plate \(neuroectoderm\)](#) and migrate along [somites](#) to different parts of the body. Other structures derived from [neural crest cells](#) are [neurons](#) of [cranial nerves](#) III to XII, peripheral nerve [neurons](#) (both somatic and autonomic), [skull](#) bones, [pia](#) and [arachnoid mater](#), [odontoblasts](#), laryngeal [cartilage](#), [adrenal medulla](#), [melanocytes](#), [aorticopulmonary septum](#), and [endocardial cushion](#). An

[immunohistochemical marker](#) of [neural crest cells](#) is [S-100](#), which is positive in [melanomas](#), [Langerhans cell histiocytosis](#), and [schwannomas](#).

D - Notochord

Explanation Why

The [notochord](#) induces the formation of the [neuroectoderm](#) from the primitive [ectoderm](#). The [lateral](#) border of the [neuroectoderm](#) will give rise to the embryological precursor of [Schwann cells](#), but the [notochord](#) itself does not give rise to any neurological structure. It only forms the [nucleus pulposus](#) of the [vertebral](#) disc.

E - Mesoderm

Explanation Why

The [mesoderm](#) gives rise to bones, muscles (smooth, skeletal, and cardiac), [connective tissue](#) (including serosal linings of body cavities, e.g., [peritoneum](#), [pericardium](#), [pleura](#)) and [dura mater](#)), [lymphatics](#), blood vessels, [spleen](#), [kidneys](#), [adrenal cortex](#), and [gonads](#). It does not form [neurons](#) or [glial cells](#).

Question # 24

A 73-year-old man is brought to the emergency department because of fever, headaches, and confusion for the past 24 hours. Three years ago, he underwent heart transplantation because of congestive heart failure. His temperature is 38.1°C (100.5°F). He is oriented only to person. Physical examination shows nuchal rigidity. A cerebrospinal fluid culture on blood agar grows colonies of a gram-positive bacillus surrounded by a narrow transparent rim. Administration of which of the following antibiotics is most likely to be effective in the treatment of this patient's condition?

	Answer	Image
A	Chloramphenicol	
B	Doxycycline	
C	Ceftriaxone	
D	Erythromycin	
E	Ampicillin	
F	Vancomycin	

Hint

This elderly patient presents with fever, headaches, altered mental status, immunosuppression (heart transplant recipient), and CSF culture showing a gram-positive rod with a narrow zone of beta-hemolysis. These signs and symptoms are suggestive of meningitis due to *Listeria monocytogenes*.

Correct Answer

A - Chloramphenicol

Explanation Why

[Chloramphenicol](#) is sometimes used for bacterial [meningitis](#) from [Chlamydiae](#), [Haemophilus influenzae](#), [Rickettsia](#), or [Salmonella](#). Due to its severe side effects, including [aplastic anemia](#) and [gray baby syndrome](#), it is only used when first-line treatments are ineffective or contraindicated. More importantly, [chloramphenicol](#) is not effective against [Listeria](#) and thus would not be indicated in the treatment of this patient's [meningitis](#).

B - Doxycycline

Explanation Why

[Doxycycline](#) is a [tetracycline antibiotic](#) effective against many gram-positive bacteria and atypical pathogens (e.g., [Chlamydia](#), [Rickettsia](#), [Mycoplasma](#)). However, it is not recommended for treatment of [Listeria](#) due to poor efficacy and [antibiotic](#) resistance.

C - Ceftriaxone

Explanation Why

[Ceftriaxone](#) is a [third-generation cephalosporin](#) used in [empiric therapy](#) for patients with suspected [meningitis](#). However, this patient's [CSF](#) culture grows [Listeria](#) against which [cephalosporins](#) are not effective.

D - Erythromycin

Explanation Why

[Erythromycin](#) is a [macrolide antibiotic](#) that is effective against many gram-positive bacteria. However, it is not recommended for treatment of [Listeria](#) due to poor efficacy and [antibiotic](#) resistance.

E - Ampicillin

Explanation But

Beside [Listeria](#), common bacterial pathogens of [meningitis](#) in [immunocompromised](#) individuals include [S. pneumoniae](#), *N. meningitidis*, and aerobic gram-negative rods. The recommended [empiric antibiotic treatment](#) is [vancomycin](#) and [ampicillin](#) in combination with either [cefepime](#) or [meropenem](#).

Explanation Why

[Ampicillin](#) is the most effective drugs for listerial [CNS](#) infection and, therefore, the treatment of choice for affected patients. In [immunocompromised](#) patients, [neonates](#), and patients with [Listeria](#) infection affecting the [endocardium](#) or the [central nervous system](#), [gentamicin](#) is added in [empiric therapy](#) for its synergistic effect.

F - Vancomycin

Explanation Why

[Vancomycin](#) is part of a multidrug [empiric therapy](#) for [meningitis](#) without a known causative pathogen. However, this patient's [CSF](#) culture grows [Listeria](#), which is not fully sensitive to treatment with [vancomycin](#).

Question # 25

A 60-year-old man is brought to the emergency department because of a 30-minute history of dizziness and shortness of breath. After establishing the diagnosis, treatment with a drug is administered. Shortly after administration, the patient develops severe left eye pain and decreased vision of the left eye, along with nausea and vomiting. Ophthalmologic examination shows a fixed, mid-dilated pupil and a narrowed anterior chamber of the left eye. The patient was most likely treated for which of the following conditions?

	Answer	Image
A	Atrioventricular block	
B	Hypertensive crisis	
C	Atrial fibrillation	
D	Mitral regurgitation	
E	Pulmonary embolism	
F	Viral pleuritis	

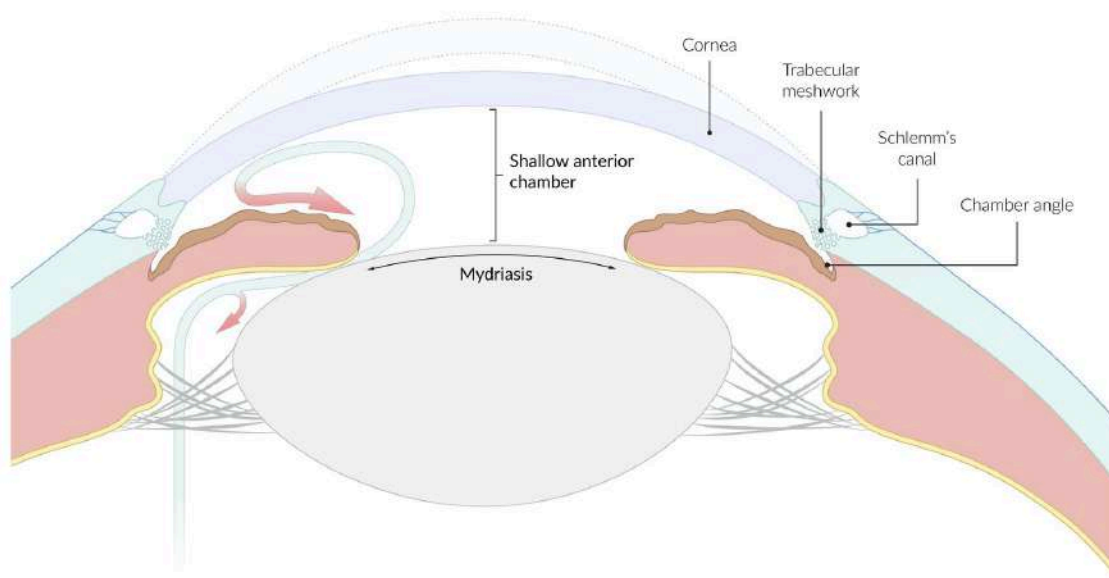
Hint

The patient's severe eye pain, fixed, mid-dilated pupil, and narrowed anterior chamber on examination are suggestive of acute angle closure glaucoma, which can be precipitated by muscarinic antagonists.

Correct Answer

A - Atrioventricular block

Image



Explanation Why

The patient was most likely treated for [atrioventricular block](#) ([AV block](#)), which can present with [shortness of breath](#) and [dizziness](#). [Atropine](#) (a [muscarinic antagonist](#)) is used to increase the [heart rate](#) in [AV block](#) due to its ability to reduce the effects of the [parasympathetic nervous system](#) on the [SA node](#) and the [AV node](#). In the [eye](#), [atropine](#) causes pupillary dilatation, which can result in narrowing of the anterior chamber angle and obstructed flow of [aqueous humor](#) between the [posterior](#) and [anterior](#) chamber, potentially leading to [acute angle-closure glaucoma](#).

B - Hypertensive crisis

Explanation Why

[Hypertensive crisis](#) may present with [dizziness](#) and [shortness of breath](#). However, the drugs used in its management (mainly [nitrates](#), [calcium channel blockers](#)) are not associated with [angle-closure glaucoma](#).

C - Atrial fibrillation

Explanation Why

[Atrial fibrillation](#) could explain this patient's symptoms of [shortness of breath](#) and [dizziness](#). However, drugs used in the management of [atrial fibrillation](#) such as [beta blockers](#), [calcium channel blockers](#), [digoxin](#), and [anticoagulants](#) are not associated with [acute angle-closure glaucoma](#).

D - Mitral regurgitation

Explanation Why

Chronic [mitral regurgitation](#) could explain this patient's symptoms of [dizziness](#) and [shortness of breath](#). Depending on the degree of [LV dysfunction](#) it is either treated conservatively or surgically ([valve repair](#) or replacement). Acute [mitral regurgitation](#) is an emergency in which [diuretics](#), [nitrates](#), and antihypertensive drugs are used to stabilize the patient. None of these drugs are commonly associated with [angle-closure glaucoma](#).

E - Pulmonary embolism

Explanation Why

While a [pulmonary embolism](#) could explain the patient's initial presenting symptoms of [dizziness](#) and [shortness of breath](#), non-invasive treatment usually consists of O₂, [analgesics](#) (e.g. [NSAIDs](#)), and [heparin](#), none of which is commonly associated with [angle-closure glaucoma](#).

F - Viral pleuritis

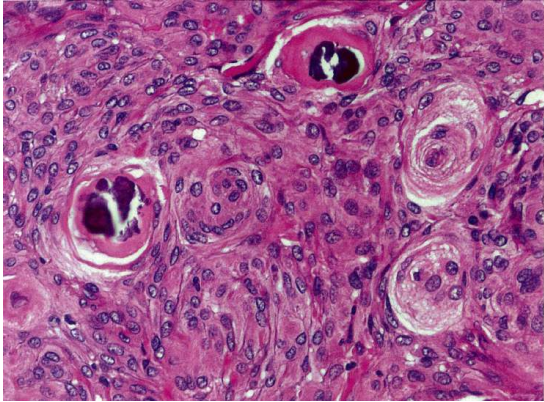
Explanation Why

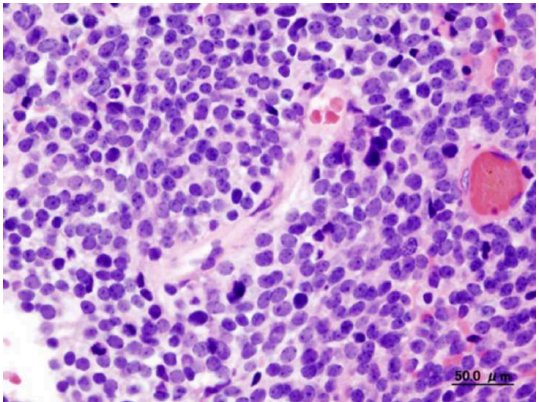
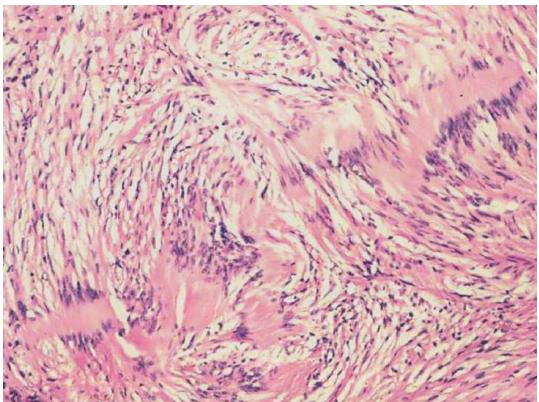
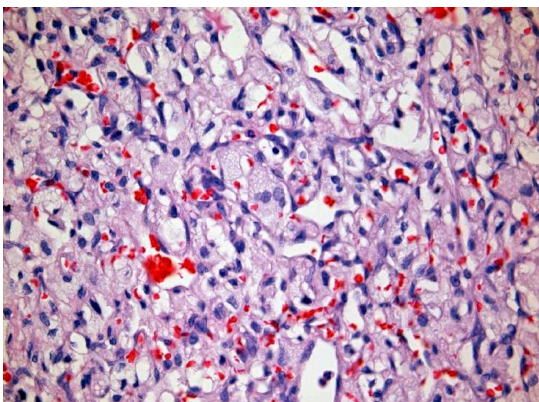
[Pleuritis](#) is an [inflammation](#) of the [pleura](#) that lines the [lungs](#) and is commonly caused by viral infection. It usually presents with a sharp [chest pain](#) that worsens with inhalation, but [shortness of breath](#) and [dizziness](#) are rare. Viral [pleuritis](#) is usually managed with [analgesic](#) drugs, e.g. [NSAIDs](#), which do not precipitate [angle-closure glaucoma](#).

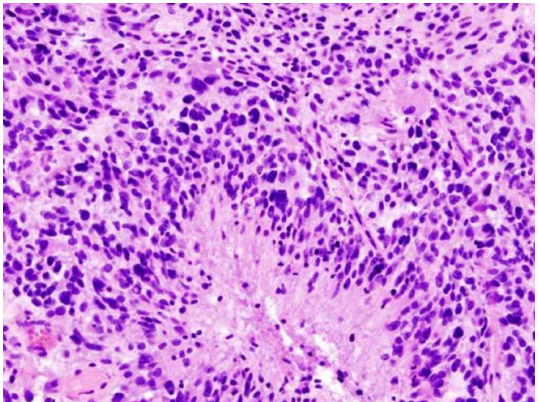
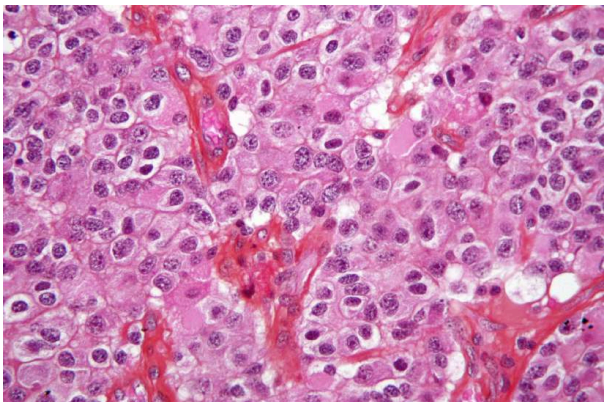
Question # 26

A 40-year-old woman comes to the physician because of a 2-month history of increasingly frequent episodes of vertigo and feeling unsteady while walking. She reports that she has had episodic tinnitus in her right ear for the past 3 years. Neurologic examination shows hearing loss in the right ear. An MRI of the brain is shown. Pathologic examination of this patient's lesion is most likely to show which of the following?



	Answer	Image
A	Whorls of densely packed cells with areas of lamellated calcification	

	Answer	Image
B	Small blue cells arranged in rosettes around a central neuropil	 A histological micrograph showing a dense population of small, round, blue-stained cells (neuroblasts) arranged in a circular pattern (rosette) around a central, lighter-stained area (neuropil). A scale bar in the bottom right corner indicates 50.0 μm.
C	Hypercellular areas of spindle cells and hypocellular areas of myxoid stroma	 A histological micrograph showing a tissue section with alternating areas of high cellularity (hypercellular) and low cellularity (hypocellular). The hypercellular areas contain spindle-shaped cells, while the hypocellular areas are filled with a myxoid (mucoid) stroma.
D	Closely packed capillaries and stromal cells filled with lipid vacuoles	 A histological micrograph showing a tissue section with numerous small, round, red-stained structures (capillaries) and stromal cells containing large, clear, vacuolated spaces (lipid vacuoles).

	Answer	Image
E	Pleomorphic cells clustered around necrotic areas forming pseudopalisades	
F	Cells with clear cytoplasm and central round nucleus resembling a fried egg	

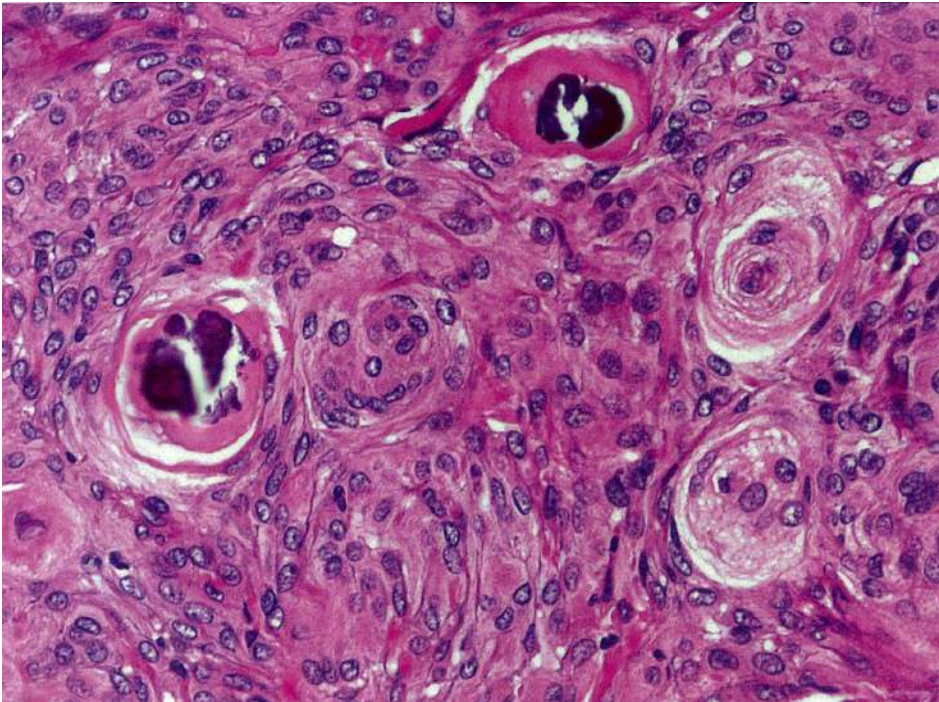
Hint

This patient presents with symptoms of vestibulocochlear nerve dysfunction (imbalance, vertigo, tinnitus, hearing loss). The MRI shows a hyperintense lesion in the right cerebellopontine angle, which is consistent with a vestibular schwannoma.

Correct Answer

A - Whorls of densely packed cells with areas of lamellated calcification

Image

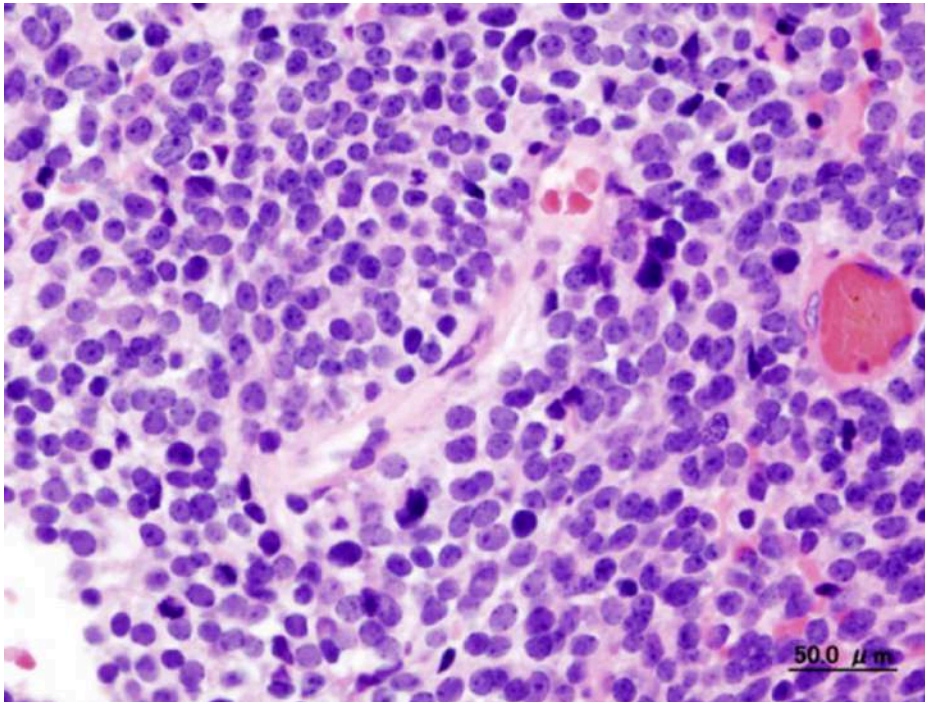


Explanation Why

Whorls of densely packed cells with areas of lamellated calcification ([psammoma bodies](#)) suggest a [meningioma](#), which arises from arachnoid cap cells. Symptoms depend on the location of the [meningioma](#), and patients are often asymptomatic if the [tumor](#) is small. On [MRI](#), [meningiomas](#) appear as round, sharply demarcated, space-occupying lesions, which is similar to this patient's [tumor](#). In rare cases, [meningiomas](#) arise at the [cerebellopontine angle](#). This can manifest with [hearing loss](#) and [ataxia](#), but usually does not cause [tinnitus](#). Furthermore, because [vestibular schwannomas](#) account for > 80% of tumors of the [cerebellopontine angle](#), this diagnosis is much more likely.

B - Small blue cells arranged in rosettes around a central neuropil

Image



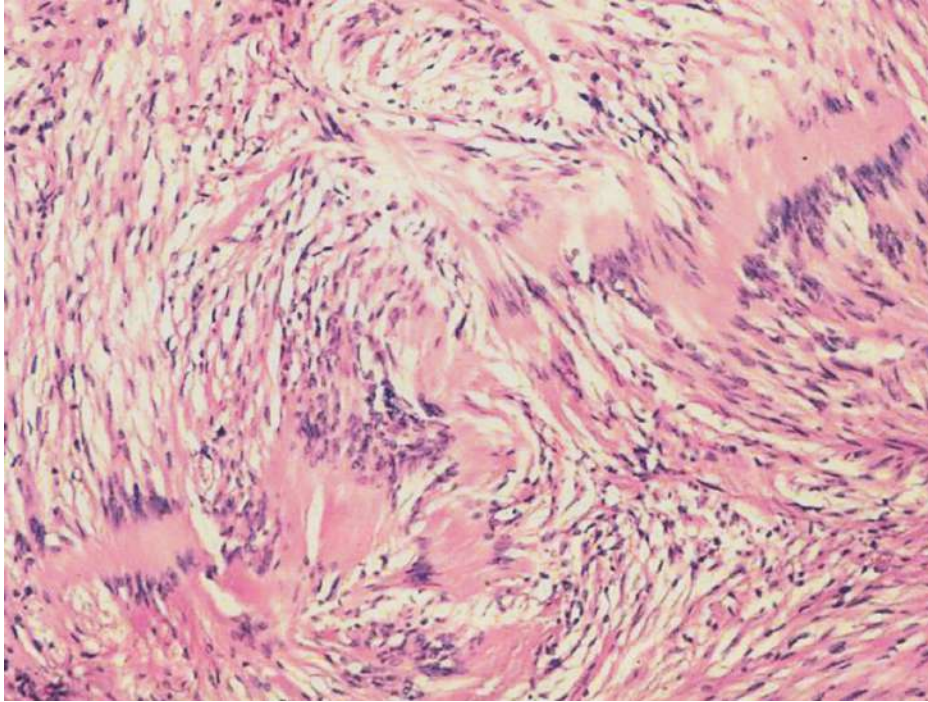
Explanation Why

Small blue cells arranged in rosettes around a central neuropil, known as [Homer-Wright rosettes](#), suggest [medulloblastoma](#). [Medulloblastomas](#) can cause gait abnormalities and manifest as unsteadiness while walking, but [tinnitus](#) and [hearing loss](#) would be uncommon. Furthermore, these tumors are the most common neurological [malignancy](#) in childhood and would, therefore, be unlikely in a 40-year-old patient. Moreover, they typically arise in the [cerebellum](#), not the [cerebellopontine angle](#).

C -

Hypercellular areas of spindle cells and hypocellular areas of myxoid stroma

Image

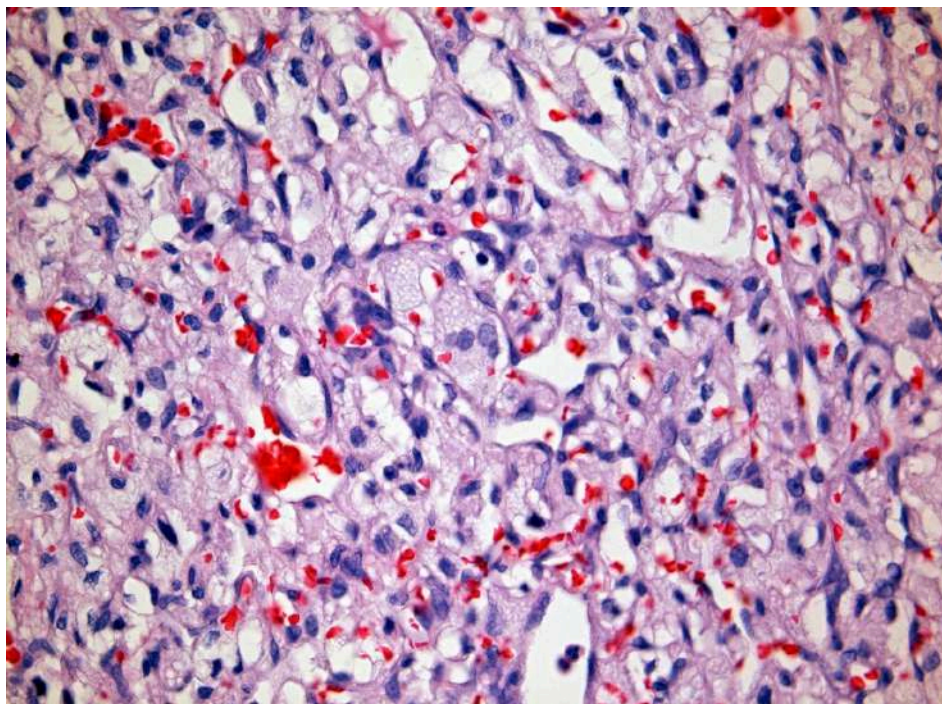


Explanation Why

Hypercellular areas of spindle cells and hypocellular areas of myxoid stroma are characteristic findings of [vestibular schwannoma](#), a [tumor](#) arising from the [Schwann cells](#) of the [vestibulocochlear nerve](#) (CN VIII). [Schwann cells](#) are of [neural crest](#) origin, which explains why [vestibular schwannomas](#) stain positive for [S100](#).

D - Closely packed capillaries and stromal cells filled with lipid vacuoles

Image

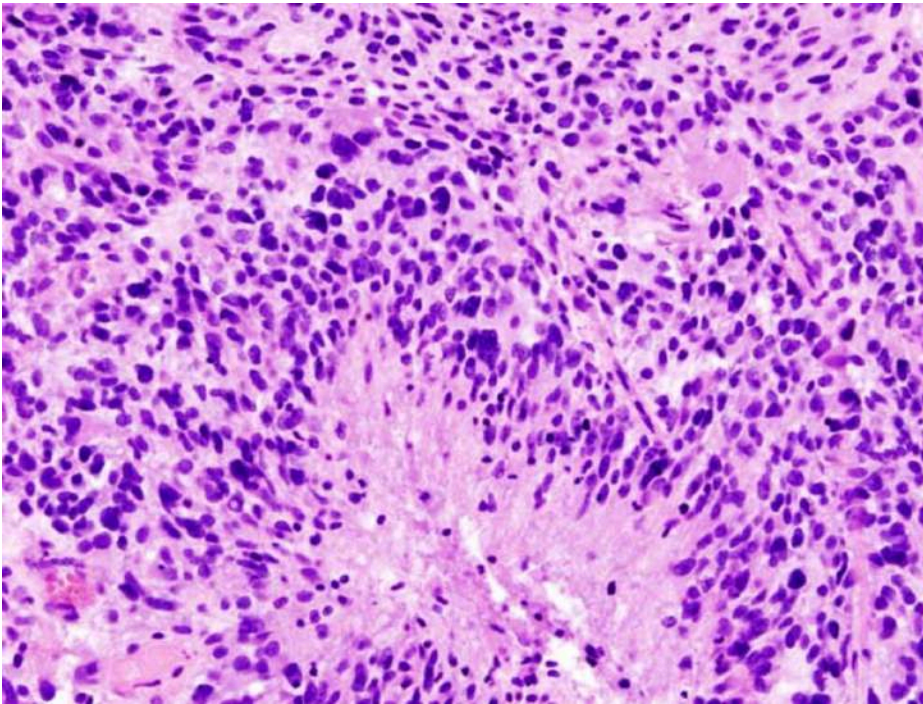


Explanation Why

Closely packed [capillaries](#) and stromal cells filled with lipid vacuoles suggest [hemangioblastoma](#), a [tumor](#) of blood vessels that is often associated with [von Hippel-Lindau disease](#). Patients with [hemangioblastoma](#) can have [cerebellar signs](#) such as [ataxia](#), which can manifest as unsteadiness while walking, but [tinnitus](#) and [hearing loss](#) would be uncommon. Moreover, [hemangioblastomas](#) typically occur in the [cerebellum](#), [brainstem](#), or [spinal cord](#) and are unlikely to be found in the [cerebellopontine angle](#).

E - Pleomorphic cells clustered around necrotic areas forming pseudopalisades

Image



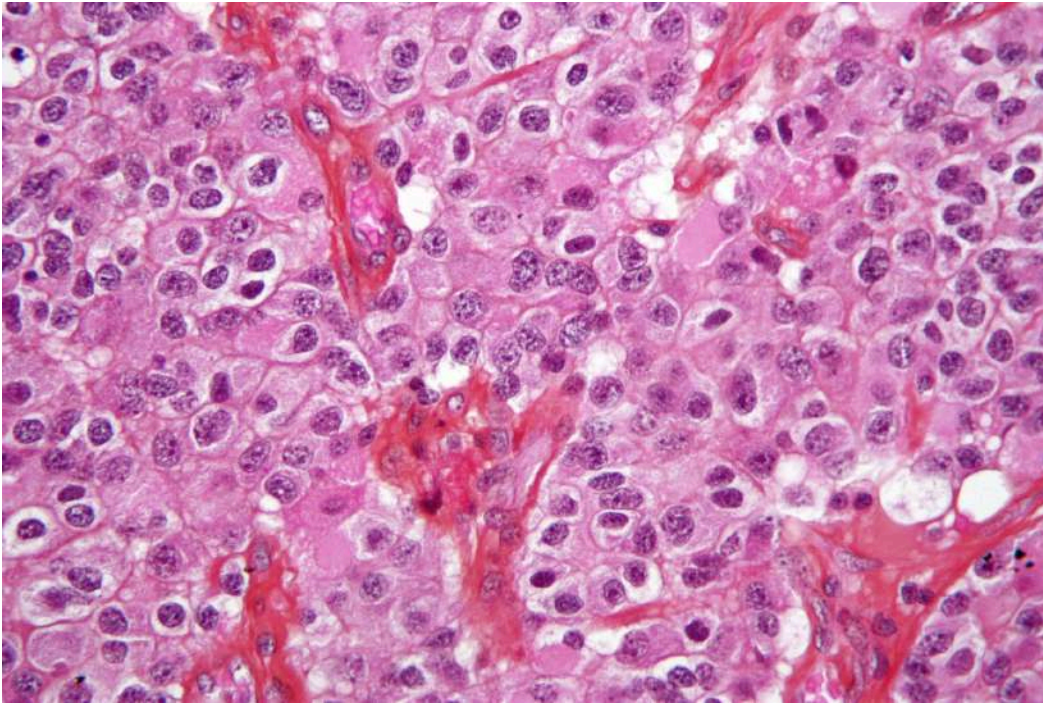
Explanation Why

Pleomorphic cells clustered around [necrotic](#) areas to form pseudopalisades suggest [glioblastoma multiforme](#) (GM), a [malignant tumor](#) of [astrocytes](#). Depending on the location, GM can manifest with focal neurologic deficits and [seizures](#). [Tinnitus](#) and [hearing loss](#) would be uncommon. However, GM typically involves the cerebral hemispheres, sometimes crossing the midline to form a “[butterfly glioma](#).” Furthermore, [MRI](#) typically shows an irregular lesion with central heterogeneity that corresponds to the central [necrosis](#), which is not consistent with this patient's imaging.

F -

Cells with clear cytoplasm and central round nucleus resembling a fried egg

Image

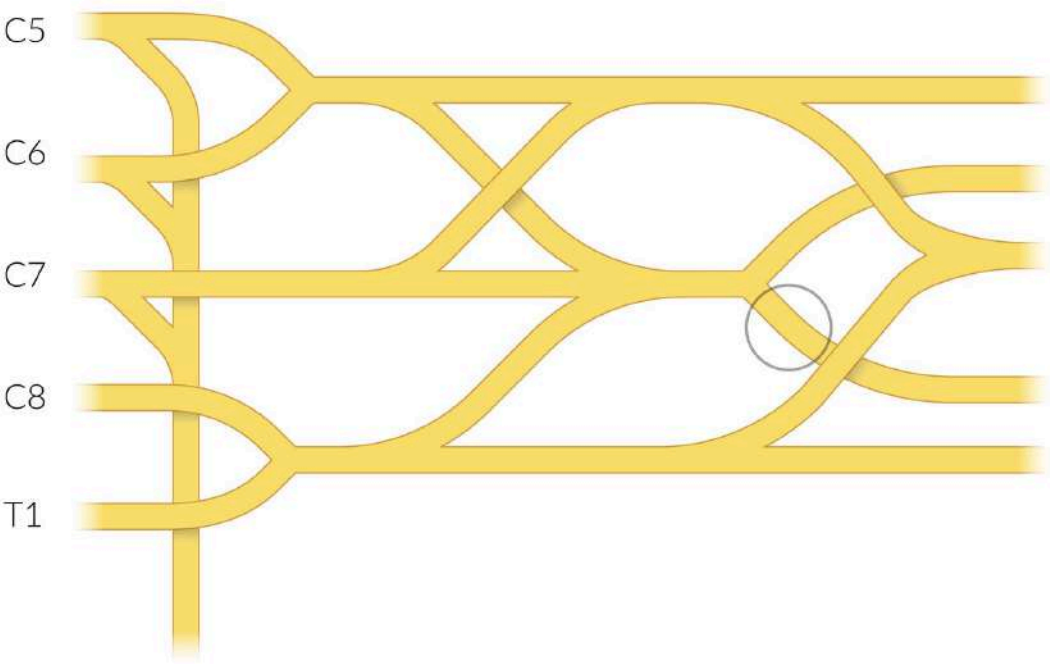


Explanation Why

Cells with clear [cytoplasm](#) and a central round nucleus resembling a fried egg suggest [oligodendroglioma](#). Patients can present with sensory deficits and [epileptic seizures](#). [Vertigo](#), [tinnitus](#), and [hearing loss](#), however, would not be expected. While oligodendrogliomas most commonly occur in the frontal and [temporal lobes](#), this patient's [tumor](#) is located in the [cerebellopontine angle](#), which is more suggestive of [vestibular schwannoma](#).

Question # 27

A 43-year-old woman comes to the physician because of tingling and weakness in her left arm for the past 2 days. An image of the brachial plexus is shown. Nerve conduction study shows decreased transmission of electrical impulses in the labeled structure. Physical examination is most likely to show impairment of which of the following movements?



	Answer	Image
A	Extension of the wrist and fingers	
B	Opposition of the thumb	

	Answer	Image
C	Flexion of the metacarpophalangeal joints	① Flexion of PIP and DIP at the 4th and 5th digits ② Hypothenar atrophy ③ Hyperextension of the 4th and 5th digits at the MCP joints ④ Atrophy of the interosseous muscles ✗ Inability to adduct thumb Frontal view Ulnar lateral view Dorsal view
D	Flexion of the forearm	
E	Abduction of the shoulder above 100 degrees	

Hint

The structure marked in the image is the radial nerve.

Correct Answer

A - Extension of the wrist and fingers

Explanation Why

The radial nerve originates from the [posterior cord of the brachial plexus](#) (comprises cervical roots C5–T1) and provides motor innervation to the [triceps](#) and muscles in the [posterior compartment of the forearm](#), including all of the wrist and hand extensors. Injury to the radial nerve, as seen in this diagram, would result in [wrist drop](#) as well as loss of sensation over the [posterior](#) forearm and [dorsal](#) hand.

B - Opposition of the thumb

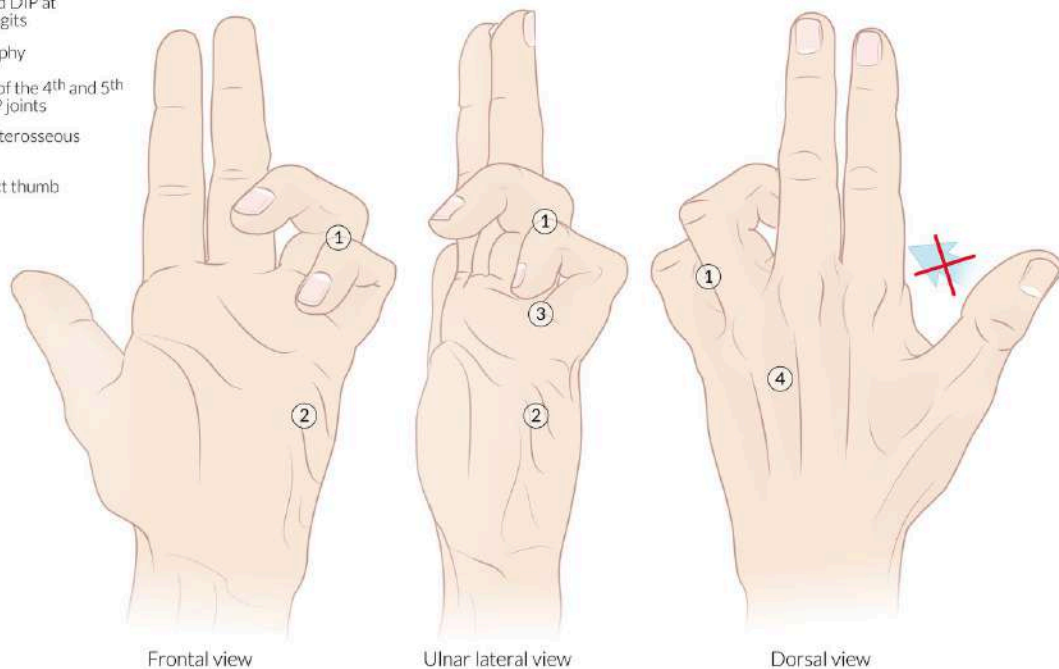
Explanation Why

Impaired opposition of the thumb would be consistent with an injury to the median nerve, which innervates the forearm flexors, [thenar muscles](#) (necessary for thumb opposition), and the radial [lumbrical](#) muscles of the hand. The median nerve originates from the [medial](#) and [lateral](#) cords of the [brachial plexus](#) and carries fibers from the [spinal nerve](#) roots C5–T1. Impaired thumb opposition is not consistent with a [radial nerve injury](#).

C - Flexion of the metacarpophalangeal joints

Image

- ① Flexion of PIP and DIP at the 4th and 5th digits
- ② Hypothenar atrophy
- ③ Hyperextension of the 4th and 5th digits at the MCP joints
- ④ Atrophy of the interosseous muscles
- ✗ Inability to adduct thumb



Explanation Why

Impaired [flexion](#) of the [metacarpophalangeal joints](#) would be seen in ulnar nerve palsy, which also typically causes impaired extension at the [proximal interphalangeal joint](#) of the little and ring fingers ([ulnar claw](#)). The ulnar nerve descends from the [medial](#) cord of the [brachial plexus](#) and carries fibers from the [spinal nerve](#) roots C8 and T1. Impaired [flexion](#) of the [MCP joints](#) is not consistent with a [radial nerve injury](#).

D - Flexion of the forearm

Explanation Why

Impaired [flexion](#) (and [supination](#)) of the forearm would be consistent with damage to the [musculocutaneous nerve](#), which innervates the [biceps brachii muscle](#) (main flexor and supinator of

the forearm), [brachialis muscle](#), and [coracobrachialis muscle](#). The [musculocutaneous nerve](#) originates from the [lateral cord](#) of the [brachial plexus](#) and carries fibers from the [spinal nerve](#) roots C5–C7. Impaired [flexion](#) of the forearm is not consistent with a [radial nerve injury](#).

E - Abduction of the shoulder above 100 degrees

Explanation Why

Impaired [abduction](#) of the shoulder above 100 degrees would be consistent with damage to the [long thoracic nerve](#), which carries fibers from the [spinal nerve](#) roots C5–C7 and innervates the [serratus anterior muscle](#). Coordinated shoulder [abduction](#) also relies on the axillary ([deltoid muscle](#)), suprascapular ([supraspinatus muscle](#)), and accessory nerves ([trapezius muscle](#)). Impaired shoulder [abduction](#) above 100 degrees is not consistent with a [radial nerve injury](#).

Question # 28

A 35-year-old woman comes to the physician because of a 1-month history of double vision, difficulty climbing stairs, and weakness when trying to brush her hair. She reports that these symptoms are worse after she exercises and disappear after she rests for a few hours. Physical examination shows drooping of her right upper eyelid that worsens when the patient is asked to gaze at the ceiling for 2 minutes. There is diminished motor strength in the upper extremities. The remainder of the examination shows no abnormalities. Which of the following is the most likely diagnosis?

	Answer	Image
A	Myasthenia gravis	
B	Lambert-Eaton syndrome	
C	Polymyositis	
D	Amyotrophic lateral sclerosis	
E	Guillain-Barré syndrome	

	Answer	Image
F	Multiple sclerosis	

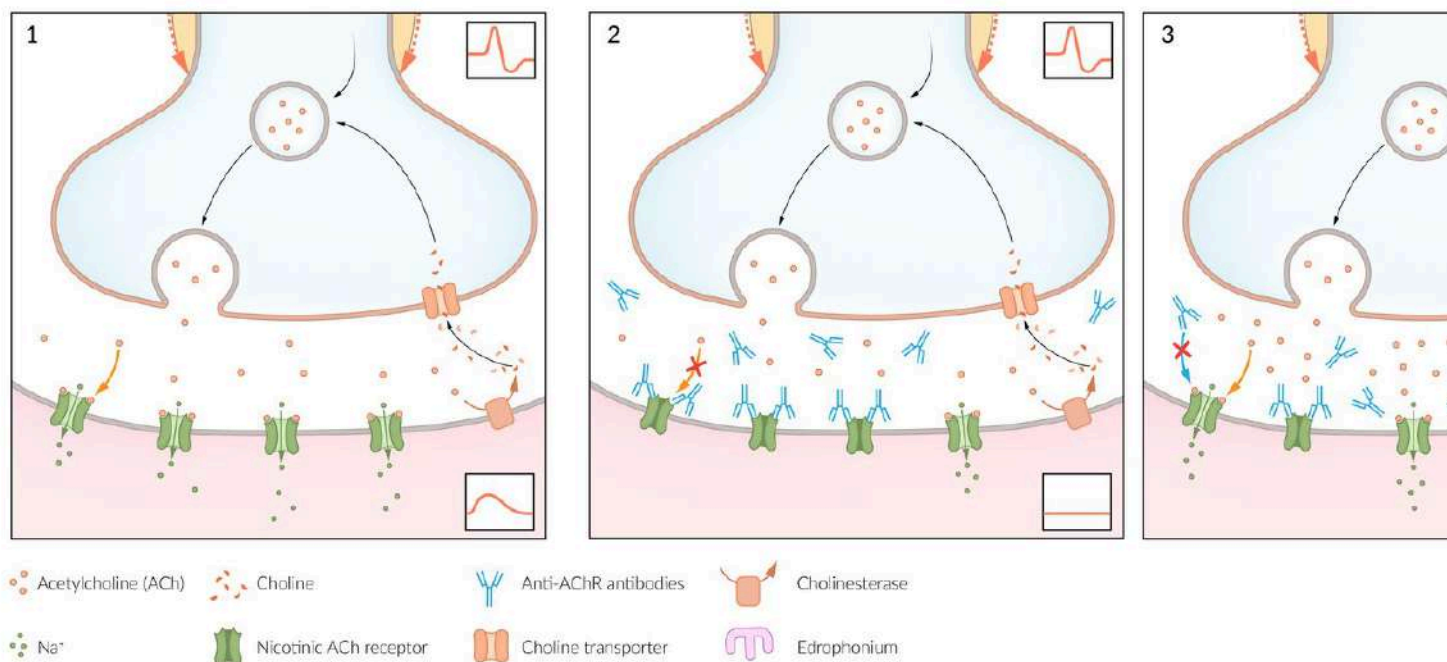
Hint

This patient's condition is caused by autoimmune-mediated destruction of postsynaptic acetylcholine receptors (AChR), which results in impaired neurotransmission and diminished skeletal muscle contraction.

Correct Answer

A - Myasthenia gravis

Image



Explanation But

CT of the chest should be obtained in patients with MG to screen for [thymoma](#).

Explanation Why

[Myasthenia gravis](#) (MG) is the most likely diagnosis in a patient with [diplopia](#), worsening [proximal](#) muscle weakness on exertion, and [ptosis](#). While [skeletal muscle](#) is affected, [deep tendon reflexes](#) and the [pupillary reflex](#) are normal. In MG, [autoantibodies](#) against the post-synaptic [acetylcholine \(ACh\)](#) receptors compete competitively with [ACh](#) in the [synaptic cleft](#). After a period of rest, the [ACh](#) levels build up, allowing for stimulation of the [motor end plate](#). As a result, symptoms worsen with exercise or constant use and improve with rest. The diagnosis of MG is based on these clinical findings, detection of [antibodies](#) ([acetylcholine receptor antibodies](#) in 90% of patients), and electrodiagnostic tests (such as repetitive nerve stimulation).

B - Lambert-Eaton syndrome

Explanation Why

While [Lambert-Eaton myasthenic syndrome \(LEMS\)](#) also manifests with muscle weakness, symptoms are worst in the morning and improve throughout the day and with repeated activity. In patients with [LEMS](#), levels of [acetylcholine](#) in the [neuromuscular junction](#) are decreased because the [autoantibodies](#) impair the release of [acetylcholine](#) from the presynaptic terminal of the [motor end plate](#). Repetitive nerve stimulation increases the amount of [acetylcholine](#) in the [synaptic cleft](#), which improves muscle strength. Moreover, this patient lacks other features of [LEMS](#) such as autonomic symptoms (e.g., dry mouth and [constipation](#)).

C - Polymyositis

Explanation Why

The hallmark of [polymyositis](#) is slowly progressive, symmetric [proximal](#) muscle weakness that affects the axial musculature (e.g., the deltoids and the [hip](#) flexors), with upper extremity involvement being more prominent. However, ocular muscles are almost never affected and the weakness would not improve with rest.

D - Amyotrophic lateral sclerosis

Explanation Why

[Amyotrophic lateral sclerosis \(ALS\)](#) typically presents in older individuals (50–70 years of age) with progressively worsening features of both [upper motor neuron](#) degeneration ([hyperreflexia](#), increased muscle tone, [Babinski sign](#)) and [lower motor neuron](#) degeneration ([hyporeflexia](#), decreased muscle tone, [atrophy](#)). Improvement of motor symptoms with rest would not be seen.

E - Guillain-Barré syndrome

Explanation Why

[Guillain-Barré syndrome](#) (GBS) usually occurs 1–4 weeks after an upper respiratory or [gastrointestinal tract](#) infection and is characterized by symmetric [flaccid paralysis](#). Although this patient does have motor weakness, she has no history of recent infection and paralysis in GBS is typically ascending, progressive, and does not improve with rest. Moreover, this patient lacks other features of GBS such as symmetric [paresthesias](#) in the hands and feet.

F - Multiple sclerosis

Explanation Why

[Multiple sclerosis](#) (MS) can present with muscle weakness and gait impairment; the presentation can be highly variable and depends on the precise location of the lesion in the [central nervous system](#). Ocular symptoms may also arise in the setting of [optic neuritis](#), which is commonly seen in MS. The timing of this patient's deterioration and improvement in muscle function is crucial, as the characteristic course of MS involves intermittent waxing and waning of symptoms over weeks to months. This patient's symptoms, however, improve with a few hours of rest, making MS unlikely.

Question # 29

A 53-year-old man comes to the physician because of a 3-month history of cough and progressively worsening difficulty walking up the stairs in his apartment. He has noticed that it is easier for him to climb the stairs after he has exercised. He has also had a 4.6-kg (10.1-lb) weight loss over the past 6 months. He has smoked one pack of cigarettes daily for 35 years. Examination shows dry mucous membranes. The pupils are equal and react sluggishly to light. Muscle strength in the proximal lower extremity is initially 3/5 but increases to 5/5 after repeated muscle tapping. His achilles reflex is 1+.

Which of the following is the most likely diagnosis?

	Answer	Image
A	Amyotrophic lateral sclerosis	
B	Polymyalgia rheumatica	
C	Myasthenia gravis	
D	Dermatomyositis	
E	Hypothyroidism	
F	Lambert-Eaton syndrome	Lambert-Eaton myasthenic syndrome (LEMS) Associated with small cell lung carcinoma Myasthenia gravis (MG) Associated with thymoma, thymic hyperplasia Symptoms: Dry mouth, Constipation, Proximal muscle weakness (initially improves with exercise), Reduced or absent reflexes. MG Symptoms: Eye muscle weakness: ptosis, diplopia, blurred vision; Bulbar muscle weakness: slurred speech, difficulty chewing and/or swallowing. Pathophysiology: LEMS: ① VGCC-Abs → ② No Ca^{2+} influx → ③ No ACh release MG: ① Anti-AChR-Ab → ② No ACh binding → ③ No muscle activation

Hint

This patient's combination of a smoking history, chronic cough, and weight loss are concerning for a lung malignancy. Proximal muscle weakness that improves on repeated stimulation, combined with decreased deep tendon reflexes are suggestive of a paraneoplastic syndrome associated with lung cancer.

Correct Answer

A - Amyotrophic lateral sclerosis

Explanation Why

[Amyotrophic lateral sclerosis \(ALS\)](#) presents with muscle weakness and may rarely be associated with [dysautonomia](#). However, muscle weakness typically is asymmetric and would not improve with exercise as in this patient, but show a progressive course. Since both upper and [lower motor neurons](#) are affected in [ALS](#), additional symptoms such as [hyperreflexia](#), [fasciculations](#), cramps, and muscle stiffness would be expected.

B - Polymyalgia rheumatica

Explanation Why

[Polymyalgia rheumatica](#) presents with [proximal myopathy](#); but the main symptoms are myalgia and muscle stiffness, not weakness as in this patient. Systemic symptoms, such as weight loss, may be seen in [polymyalgia rheumatica](#), but [autonomic dysfunction](#) and [hyporeflexia](#) would not be expected. [Polymyalgia rheumatica](#) is not associated with [lung cancer](#).

C - Myasthenia gravis

Explanation Why

[Myasthenia gravis \(MG\)](#) may cause lower limb muscle weakness. However, symptoms typically worsen throughout the day and with exercise as opposed to the improvement seen upon repetitive stimulation in this patient. MG classically presents with weakness of the [extraocular muscles](#) causing [ptosis](#) and/or [diplopia](#), whereas [deep tendon reflexes](#) and autonomic functions are unaffected. Moreover, MG is not associated with [lung cancer](#) but with [thymoma](#) and other autoimmune diseases.

D - Dermatomyositis

Explanation Why

[Dermatomyositis](#) presents with [proximal](#) muscle weakness. However, symptoms are typically progressive and would not improve with exercise as in this patient. Although [dermatomyositis](#) is a [paraneoplastic syndrome](#) associated with [lung cancer](#), cutaneous manifestations such as [Gottron papules](#) and a [heliotrope rash](#) would also be expected. Moreover, [dermatomyositis](#) is not associated with [hyporeflexia](#) and [autonomic dysfunction](#).

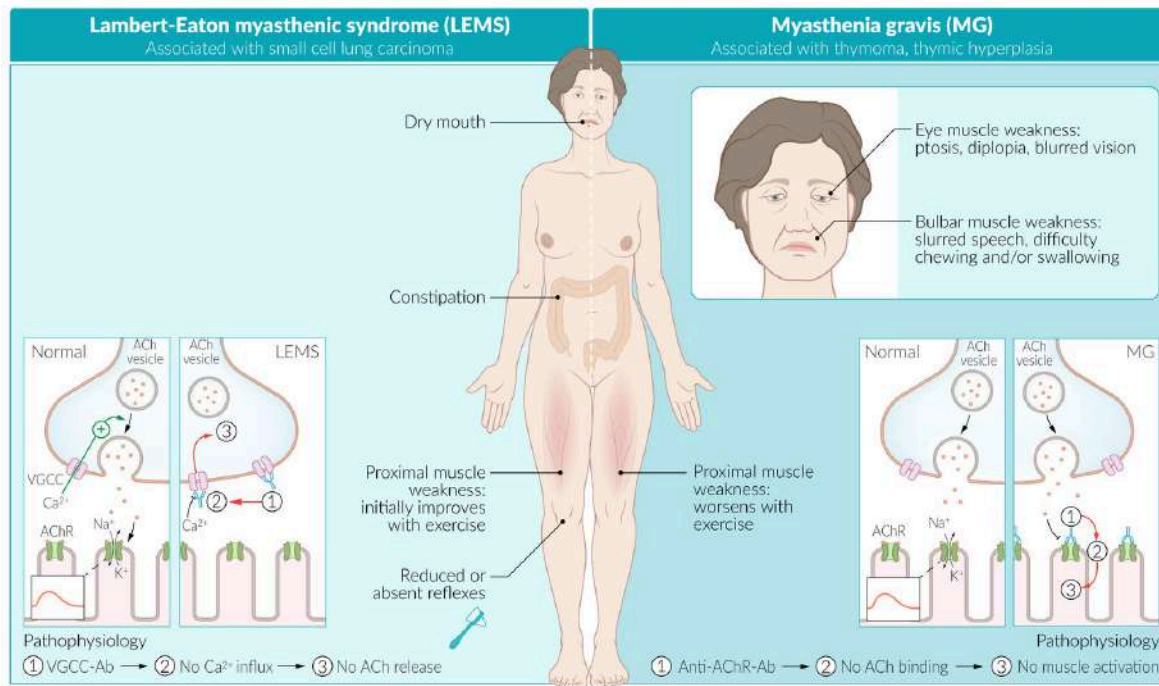
E - Hypothyroidism

Explanation Why

[Hypothyroidism](#) may cause [proximal](#) muscle weakness and [hyporeflexia](#). However, it would usually be associated with other symptoms such as weight gain, fatigue, cold intolerance, and dry [skin](#). Weight loss as seen in this patient would be unusual. [Hypothyroidism](#) is not associated with [lung cancer](#).

F - Lambert-Eaton syndrome

Image

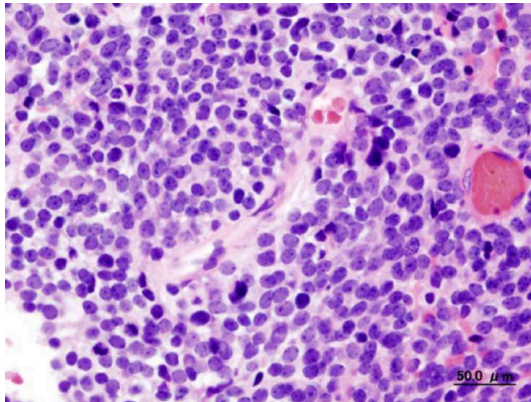
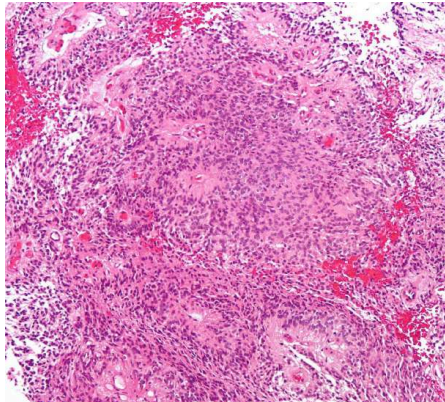


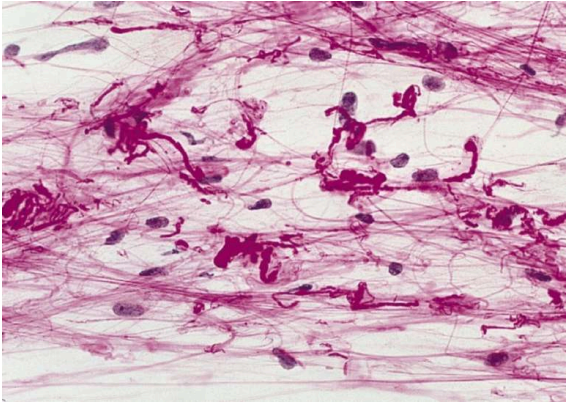
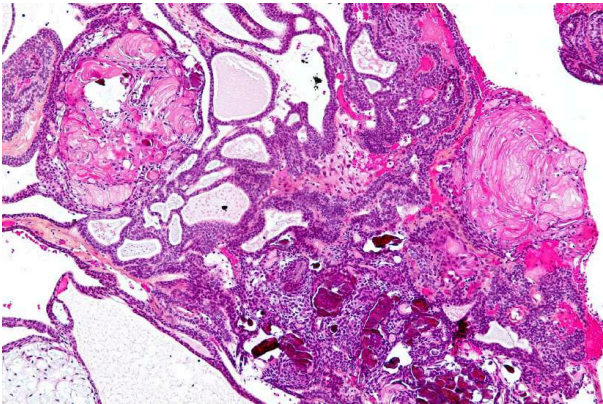
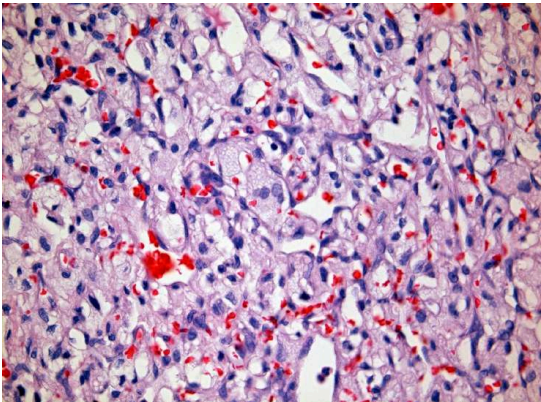
Explanation Why

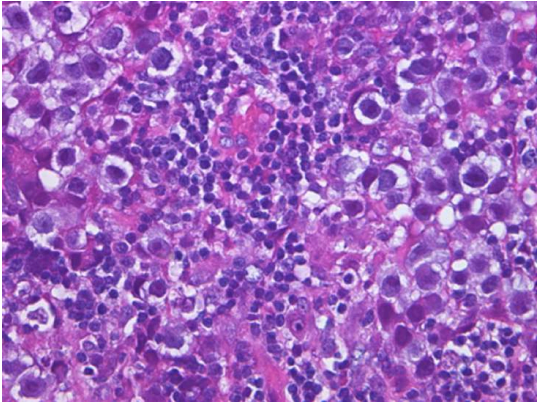
Lambert-Eaton myasthenic syndrome (LEMS), which is associated with [small-cell lung cancer](#) in two-thirds of cases, is caused by circulating [autoantibodies](#) that block presynaptic voltage-gated calcium channels at the [neuromuscular junction](#). This blockage impairs [acetylcholine](#) release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

Question # 30

A 13-year-old boy is brought to the physician because of a 4-month history of worsening dizziness, nausea, and feeling clumsy. An MRI of the brain shows a well-demarcated, 4-cm cystic mass in the posterior fossa. The patient undergoes complete surgical resection of the mass. Pathologic examination of the surgical specimen shows parallel bundles of cells with eosinophilic, corkscrew-like processes. Which of the following is the most likely diagnosis?

	Answer	Image
A	Medulloblastoma	
B	Ependymoma	

	Answer	Image
C	Pilocytic astrocytoma	
D	Craniopharyngioma	
E	Hemangioblastoma	

	Answer	Image
F	Pinealoma	

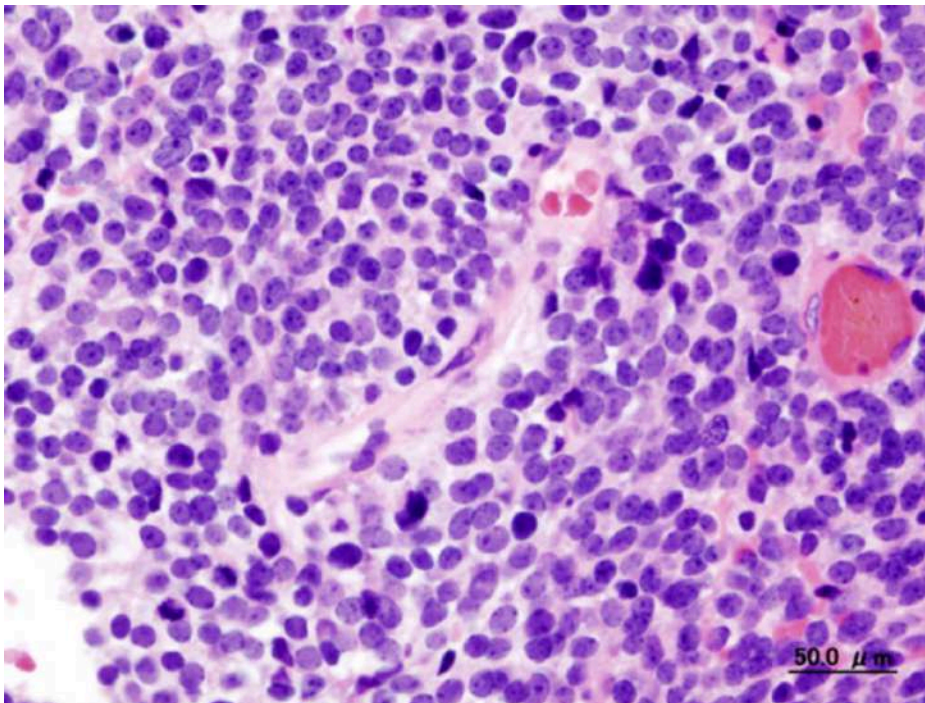
Hint

The eosinophilic, corkscrew-like processes seen in this patient's biopsy are Rosenthal fibers. The cells from this brain tumor are glial in origin and will stain positive for glial fibrillary acidic protein (GFAP).

Correct Answer

A - Medulloblastoma

Image

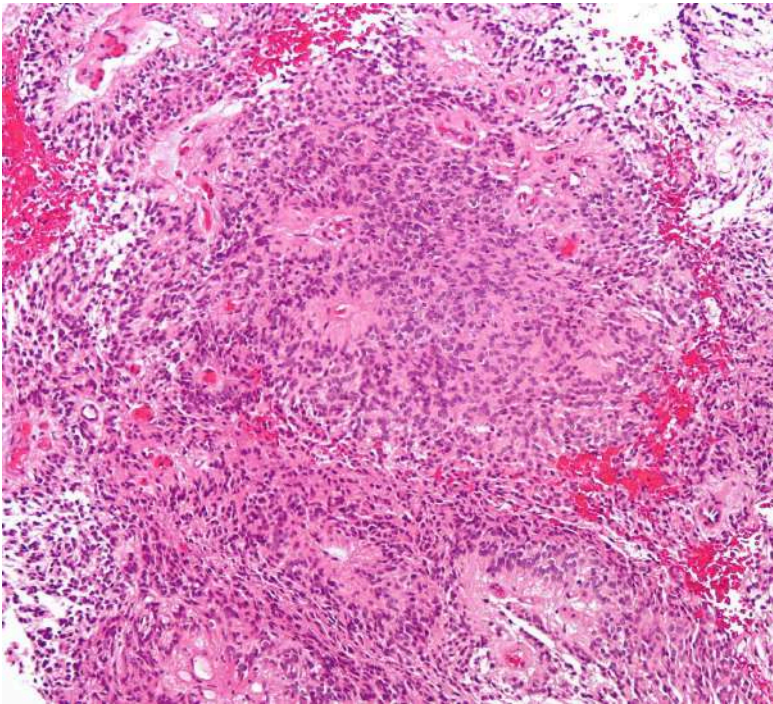


Explanation Why

[Medulloblastoma](#), the most common malignant primary [brain tumor](#) of childhood, can also cause [dizziness](#), nausea, and clumsiness (due to [hydrocephalus](#) and/or [cerebellar](#) damage) and appear as a well-defined [cerebellar](#) mass with cysts on imaging, as well. However, it is characterized histologically by the presence of small, round, undifferentiated [basophilic cells](#) (primitive [neuroectoderm](#) cells) and [Homer-Wright rosettes](#).

B - Ependymoma

Image

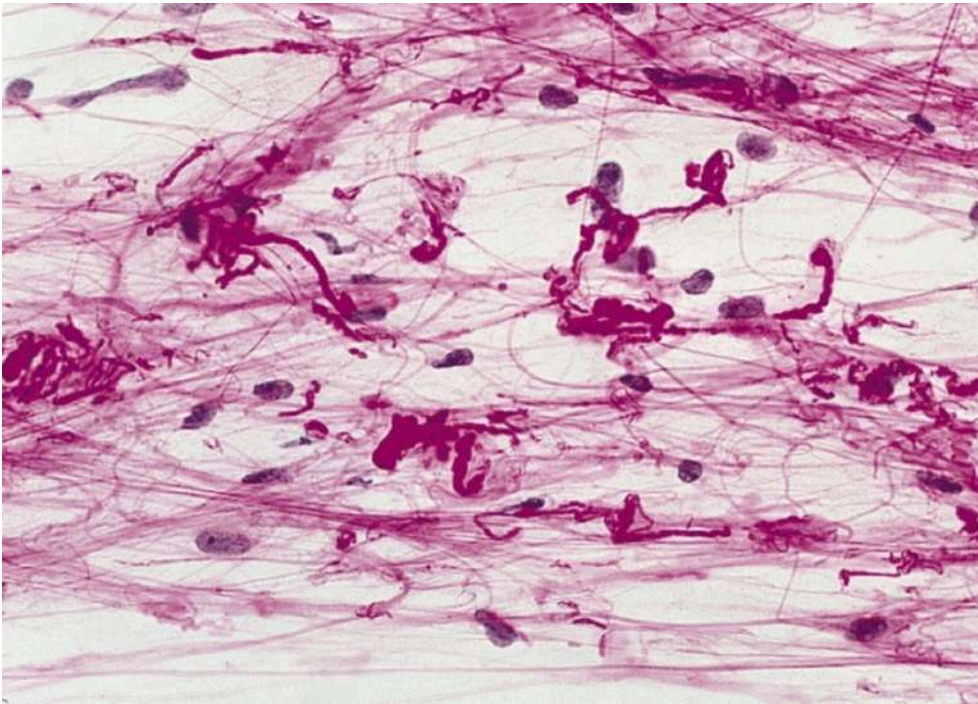


Explanation Why

Ependymomas typically occur in the posterior fossa (floor of the fourth ventricle) and can also present with dizziness, nausea, and clumsiness, due to obstructive hydrocephalus. However, they are characterized histologically by the presence of perivascular pseudorosettes and basal ciliary bodies (blepharoplasts) and are more common in early childhood.

C - Pilocytic astrocytoma

Image



Explanation But

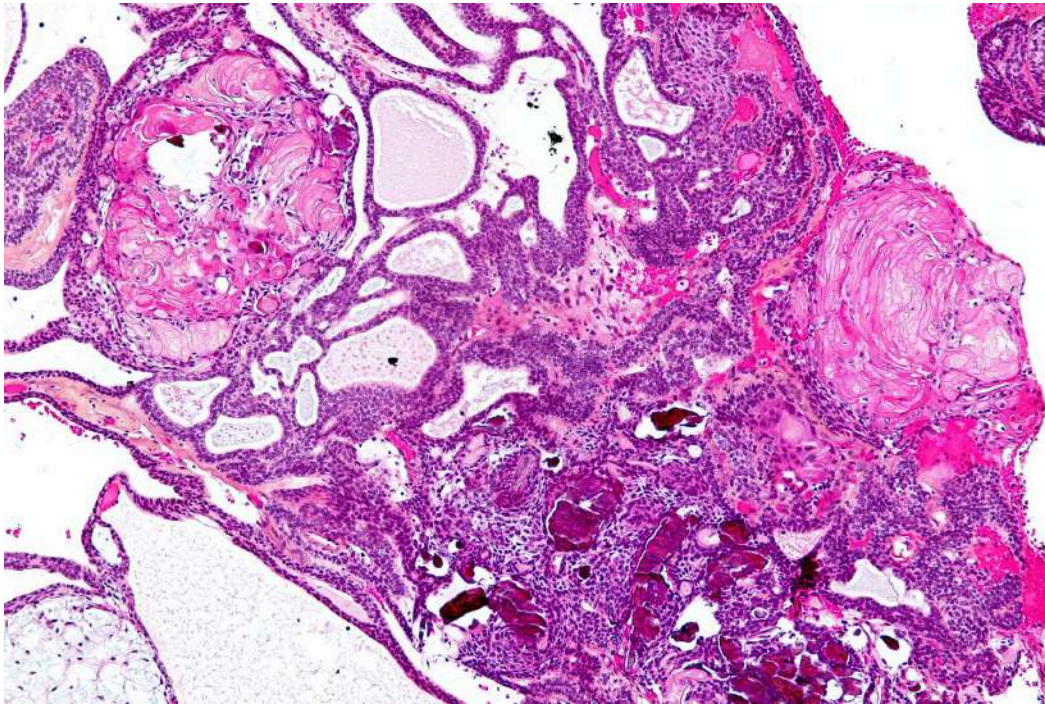
[Optic gliomas](#), a type of [pilocytic astrocytoma](#) in the optic pathway, are strongly associated with [neurofibromatosis type 1](#). A subependymal giant cell astrocytoma, another low-grade [astrocytoma](#) that occurs within ventricles, is associated with [tuberous sclerosis](#).

Explanation Why

[Pilocytic astrocytoma](#) is the most common pediatric primary [brain tumor](#). It typically occurs in the [cerebellum](#) (posterior cranial fossa), but can also occur in [supratentorial](#) regions such as the [optic nerve](#) ([optic glioma](#)) and the cerebral hemispheres. Tumors in the posterior cranial fossa can present with [dizziness](#), nausea, and clumsiness due to [obstructive hydrocephalus](#) and/or [cerebellar](#) damage. On imaging, a [pilocytic astrocytoma](#) typically appears as a well-demarcated cystic mass with a brightly enhancing nodule in the wall of the cyst.

D - Craniopharyngioma

Image

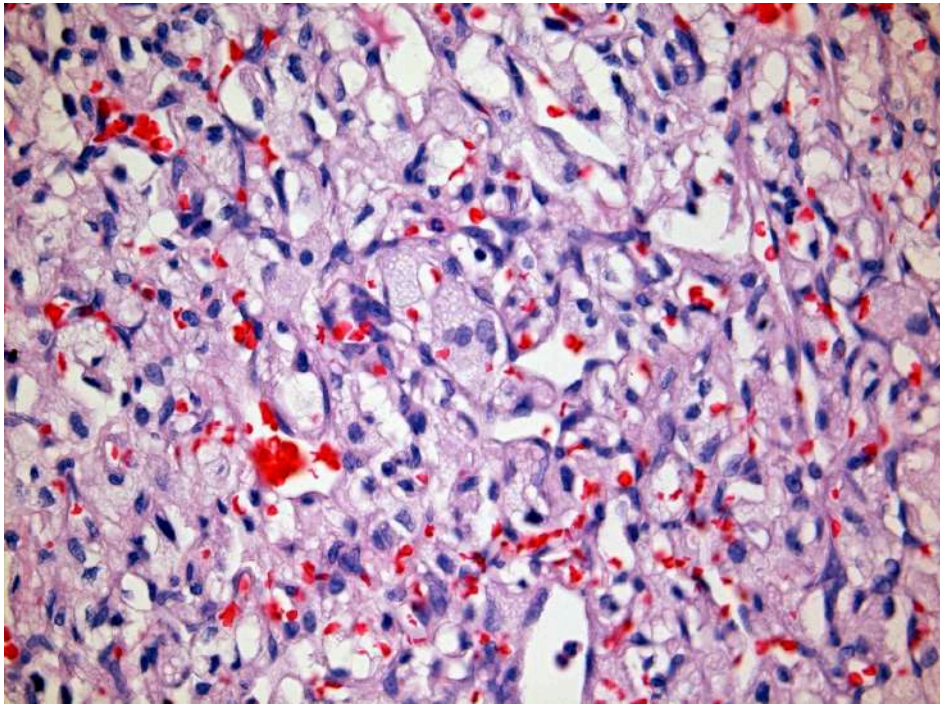


Explanation Why

[Craniopharyngiomas](#) are the most common [supratentorial](#) tumors in pediatric patients; they are typically in the suprasellar region and cause [bitemporal hemianopsia](#) or endocrine abnormalities (e.g., [hyperprolactinemia](#), [hypopituitarism](#)). [Dizziness](#), nausea, and clumsiness would not be expected. The adamantinomatous variant of this [tumor](#) is characterized histologically by the presence of [cholesterol](#) crystals, calcification, and nests of “wet [keratin](#)” (desquamated cells) surrounded by [stratified](#) odontogenic [epithelium](#), while the papillary variant is characterized by [metaplastic](#) squamous cells with very few or absent calcifications and cysts.

E - Hemangioblastoma

Image

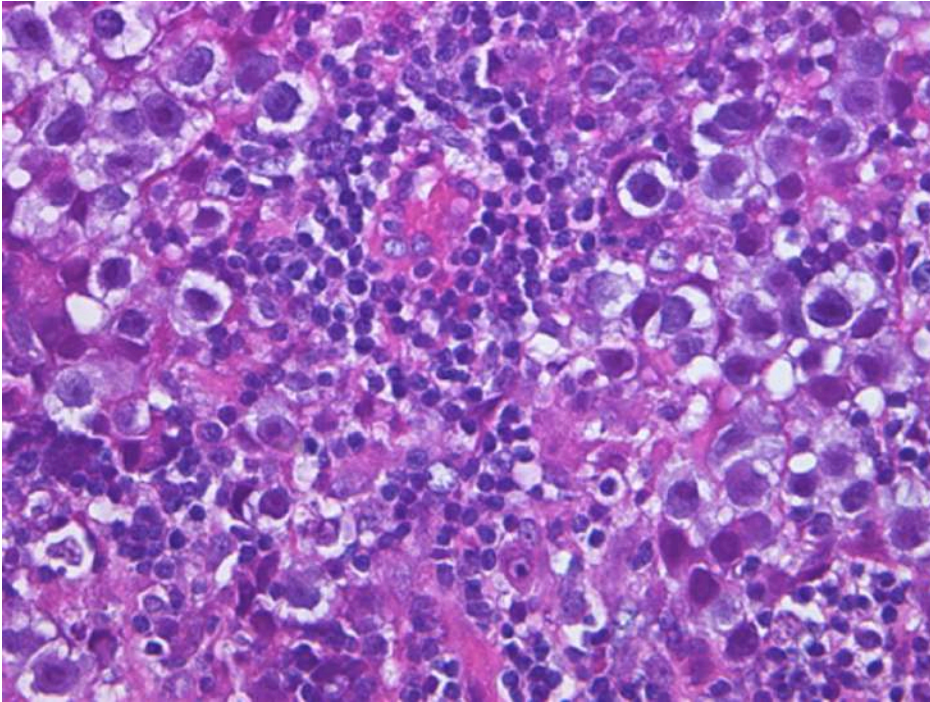


Explanation Why

A [hemangioblastoma](#) typically occurs in the posterior cranial fossa ([cerebellum](#))- It manifests with [dizziness](#), nausea, and clumsiness (due to [hydrocephalus](#) and/or [cerebellar](#) damage) and appears as a well-demarcated cystic mass on imaging. However, [hemangioblastomas](#) are vascular tumors characterized histologically by closely packed, thin-walled vessels with minimal intervening brain parenchyma, and they are extremely rare among children. They typically occur among middle-aged adults.

F - Pinealoma

Image



Explanation Why

A [pinealoma](#) typically occurs in the [posterior](#) fossa ([dorsal midbrain](#)) and can present with features of [hydrocephalus](#) (e.g., [dizziness](#), nausea, and clumsiness) during childhood. However, most childhood [pinealomas](#) are germinomas characterized histologically by a lymphoid stroma and large vacuolated cells with enlarged oval nuclei. Moreover, other features associated with [pinealomas](#), such as [Parinaud syndrome](#) ([vertical gaze palsy](#), lid [retraction](#), nystagmus, [light-near dissociation](#)) and [precocious puberty](#), are absent in this patient.

Question # 31

A 61-year-old man with Alzheimer disease is brought to the emergency department 20 minutes after ingesting an unknown amount of his medications in a suicide attempt. He reports abdominal cramps, diarrhea, diaphoresis, and muscular weakness and spasms in his extremities. His temperature is 38.4°C (101.1°F), pulse is 51/min, respirations are 12/min and labored, and blood pressure is 88/56 mm Hg. Physical examination shows excessive salivation and tearing, and small pupils bilaterally. Treatment with atropine is initiated. Shortly after, most of his symptoms have resolved, but he continues to have muscular spasms. Administration of which of the following is the most appropriate next step in treatment of this patient?

	Answer	Image
A	Carbachol	
B	Physostigmine	
C	Pancuronium	
D	Benztropine	
E	Pralidoxime	

Hint

This patient presents with symptoms of muscarinic acetylcholine excess (e.g., diarrhea, diaphoresis, bradycardia, bronchospasm, salivation, lacrimation, miosis) and nicotinic acetylcholine excess (e.g., muscle weakness). Atropine can only reverse the muscarinic effects.

Correct Answer

A - Carbachol

Explanation Why

[Carbachol](#) directly binds to acetylcholine receptors of both muscarinic and nicotinic type and is used in the treatment of [glaucoma](#). It would further exacerbate this patient's symptoms of [acetylcholine](#) excess and must be avoided in this patient.

B - Physostigmine

Explanation Why

[Physostigmine](#) can be used as an [antidote](#) in [atropine](#) overdose or as a treatment for [myasthenia gravis](#). However, in this patient with symptoms of [acetylcholine](#) excess, it would lead to exacerbation of this patient's symptoms by further increasing cholinergic stimulation.

C - Pancuronium

Explanation Why

[Pancuronium](#) belongs to the class of [nondepolarizing muscle relaxants](#) that bind to acetylcholine receptors at the [neuromuscular junction](#), which blocks nicotinic stimulation by [acetylcholine](#). Even though administration of [pancuronium](#) would lead to a reversal of neuromuscular symptoms in this patient, muscular paralysis and possibly even respiratory impairment would result. The risks of [pancuronium](#) therefore outweigh its potential benefits, especially considering that safer alternatives are available.

D - Benztropine

Explanation Why

[Benztropine](#) is a selective antagonist of [muscarinic receptors](#) that particularly decreases cholinergic overactivity in the [CNS](#). It is typically used to treat [tremor](#) in [Parkinson disease](#) and [extrapyramidal symptoms](#) caused by [antipsychotics](#). However, since this patient's muscarinic symptoms have mostly resolved following the administration of [atropine](#), an additional muscarinic inhibitor would not be particularly useful.

E - Pralidoxime

Explanation But

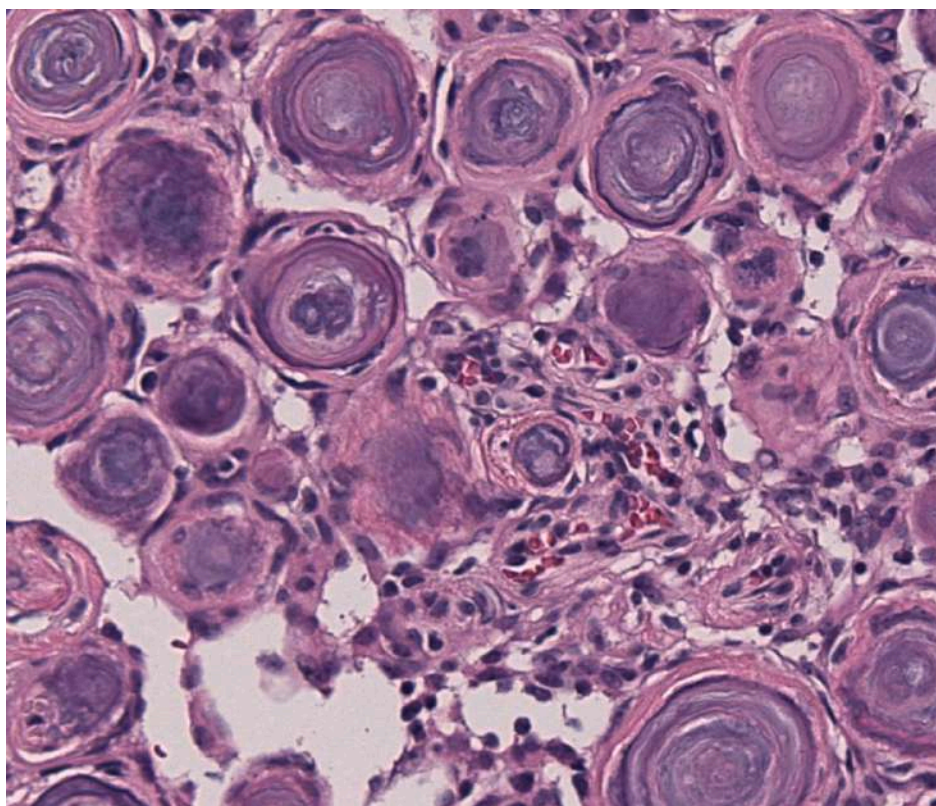
The mnemonic DUMBBELSS ([Diarrhea](#), Urination, [Miosis](#), Bronchospasm and [Bradycardia](#), neuromuscular Excitation, Lacrimation, Sweating and Salivation) is helpful for remembering symptoms of [acetylcholine](#) excess.

Explanation Why

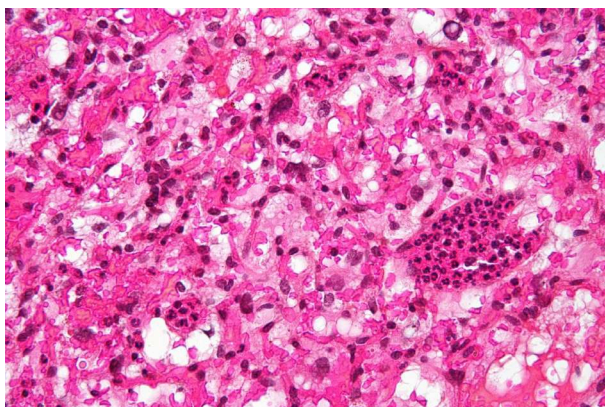
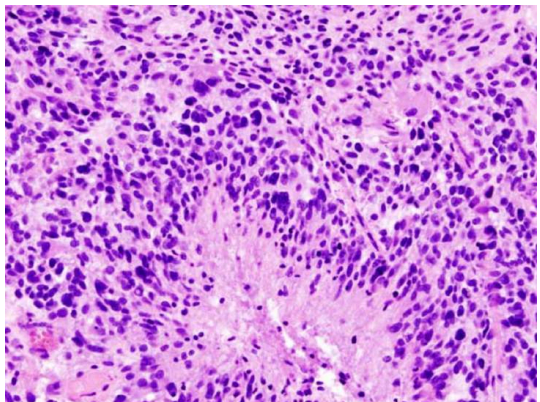
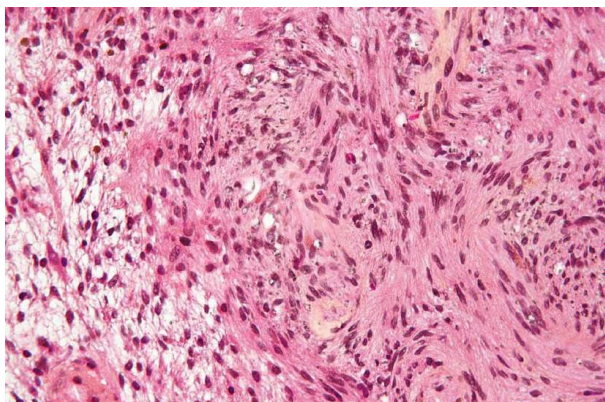
When taken in excess, medications for [Alzheimer disease](#) such as [donepezil](#) can result in symptoms similar to that of [organophosphate poisoning](#). In such cases, [pralidoxime](#) is given to restore activity of acetylcholinesterase, which then catalyzes the breakdown of excessive [acetylcholine](#) to reverse symptoms. [Atropine](#) does not act on [nicotinic cholinergic receptors](#) and thus cannot treat symptoms of neuromuscular dysfunction, for which [pralidoxime](#) is still necessary. [Pralidoxime](#) has poor [blood-brain barrier](#) penetration and can lead to a transient worsening of acetylcholinesterase inhibition following administration, which is why [atropine](#) is typically administered first to treat [CNS](#) symptoms and prevent further acetylcholinesterase inhibition.

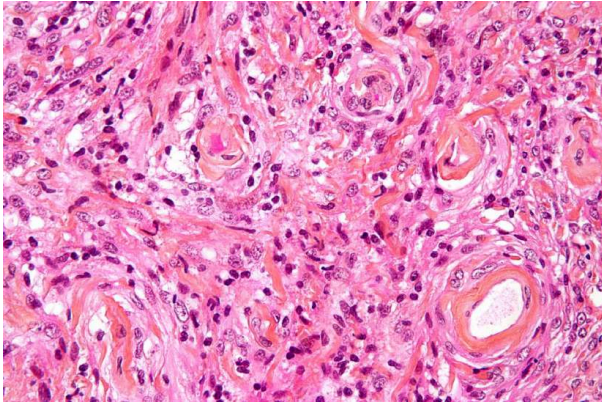
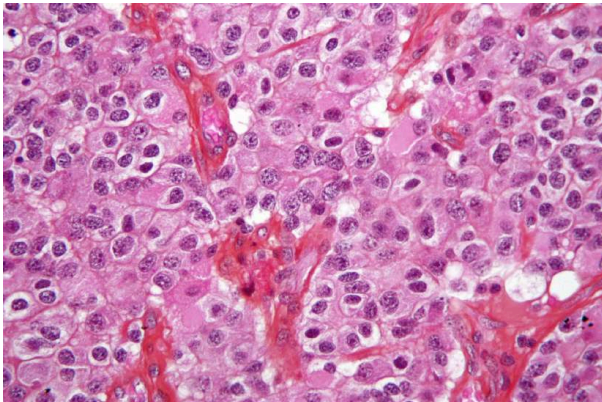
Question # 32

A previously healthy 50-year-old woman is brought to the emergency department 30 minutes after she was observed having a seizure. On arrival, she is conscious and reports that she feels drowsy. An MRI of the brain shows a 4-cm, round, sharply demarcated mass. She undergoes resection of the mass. A photomicrograph of a section of the resected specimen is shown. This patient's mass is most likely derived from which of the following?



	Answer	Image
A	Neurons	

	Answer	Image
B	Blood vessel	 A high-magnification histological image of brain tissue stained with hematoxylin and eosin (H&E). The image shows a dense population of cells with pink cytoplasm and extracellular matrix, and dark purple nuclei. A prominent blood vessel is visible on the right side, characterized by a thick, dark-stained wall and a lumen containing red blood cells.
C	Astrocytes	 A high-magnification histological image of brain tissue stained with hematoxylin and eosin (H&E). The image shows a dense population of cells with pink cytoplasm and extracellular matrix, and dark purple nuclei. The cells are arranged in a somewhat organized pattern, with some cells showing a more elongated, spindle-shaped morphology, characteristic of astrocytes.
D	Schwann cells	 A high-magnification histological image of brain tissue stained with hematoxylin and eosin (H&E). The image shows a dense population of cells with pink cytoplasm and extracellular matrix, and dark purple nuclei. The cells are arranged in a somewhat organized pattern, with some cells showing a more elongated, spindle-shaped morphology, characteristic of Schwann cells.

	Answer	Image
E	Arachnoid cells	
F	Oligodendrocytes	

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Hint

The photomicrograph shows whorls of densely packed cells with multiple areas of lamellated calcification that are known as psammoma bodies. This is the typical histopathological appearance of a meningioma.

Correct Answer

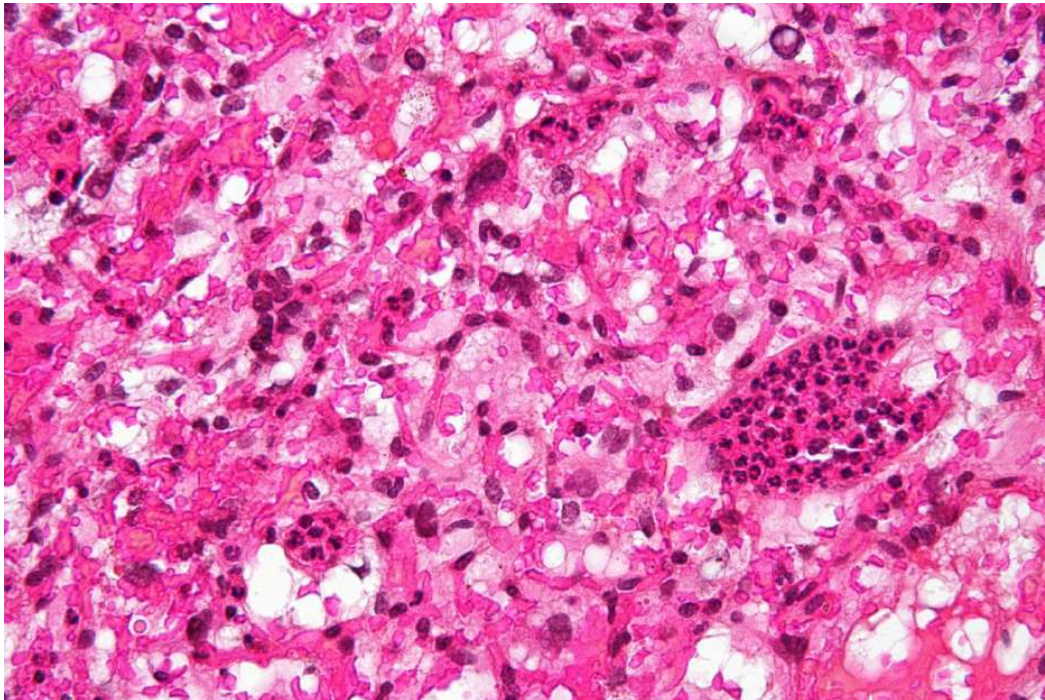
A - Neurons

Explanation Why

[Neurons](#) very rarely give rise to [brain tumors](#). The vast majority of [brain tumors](#) arise from [glial cells](#).

B - Blood vessel

Image

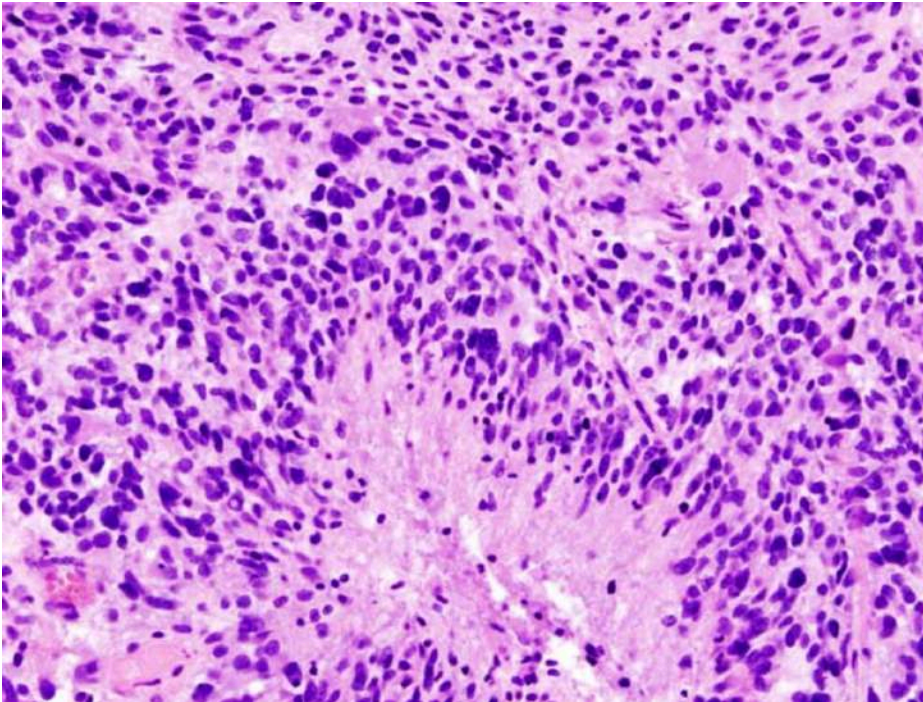


Explanation Why

[Hemangioblastomas](#) arise from blood vessels, which are usually located in the [infratentorial](#) region. Microscopic examination would show closely arranged, thin-walled [capillaries](#) with minimal intervening parenchyma.

C - Astrocytes

Image

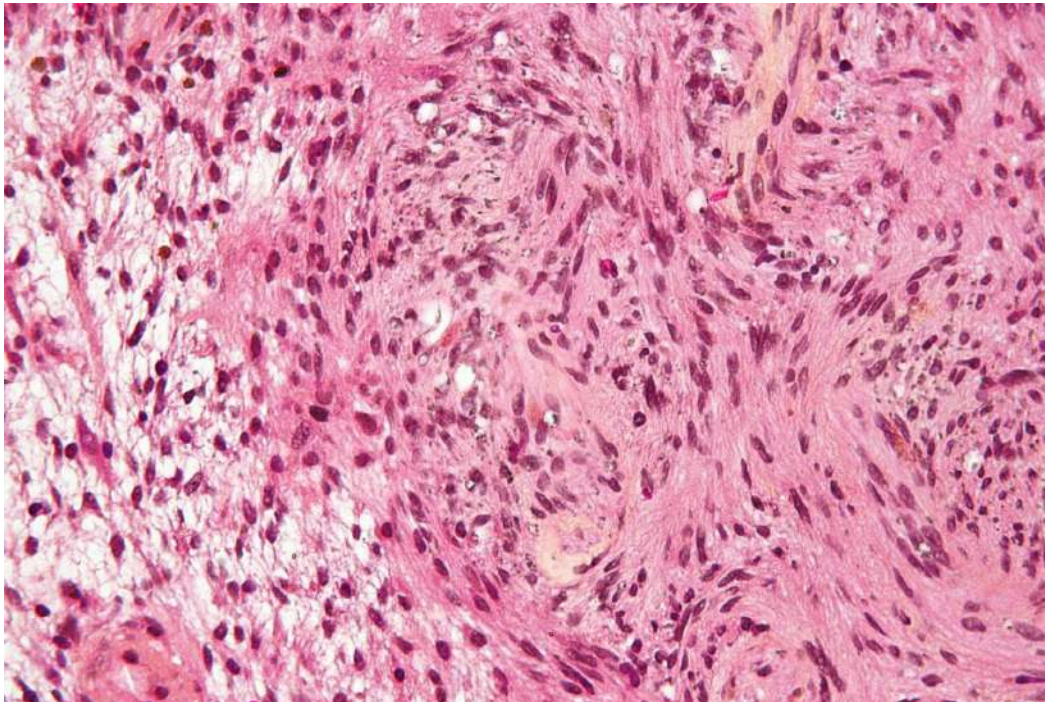


Explanation Why

[Astrocytes](#) give rise to [astrocytomas](#). [Glioblastoma multiforme](#) (high-grade [astrocytoma](#)) is the most common malignant primary [brain tumor](#) in adults and usually occurs after the age of 40. Children are more often affected by low-grade pilocytic [astrocytomas](#). [Histopathology](#) would show pleomorphic cells clustered around [necrotic](#) areas, forming pseudopalisades.

D - Schwann cells

Image

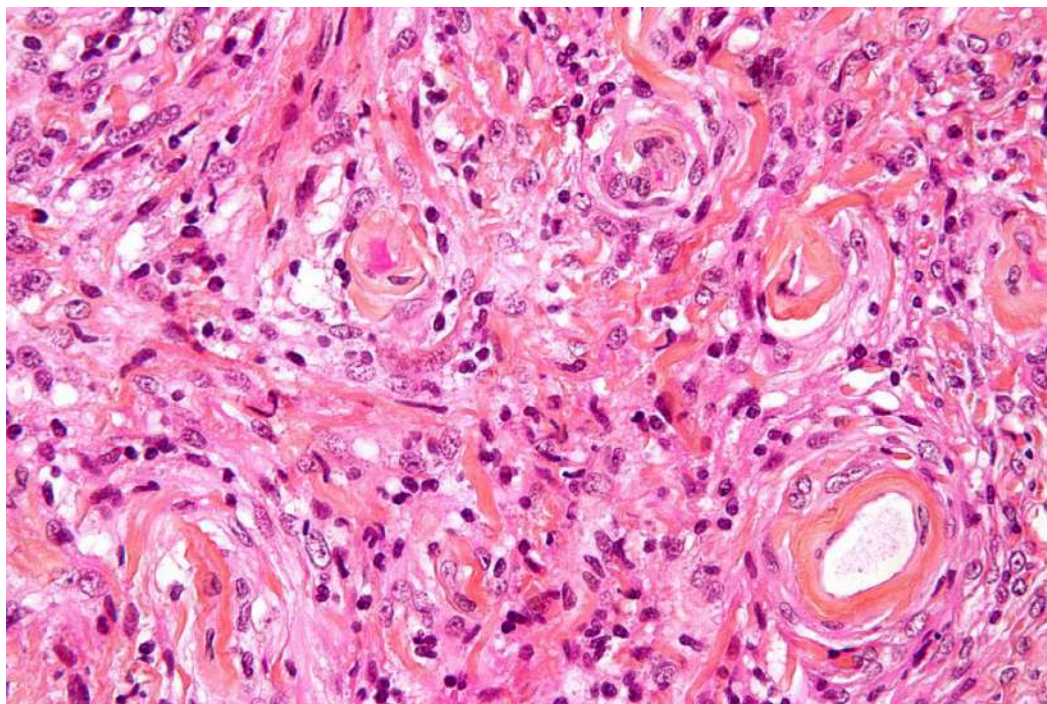


Explanation Why

[Schwann cells](#) give rise to [schwannomas](#), which occur mostly near the [cerebellopontine angle](#). The most common type is an [acoustic neuroma](#), which arises from the [vestibulocochlear nerve](#). Spindle-shaped cells with mixed hypercellular and hypocellular regions are seen on [histopathology](#).

E - Arachnoid cells

Image



Explanation But

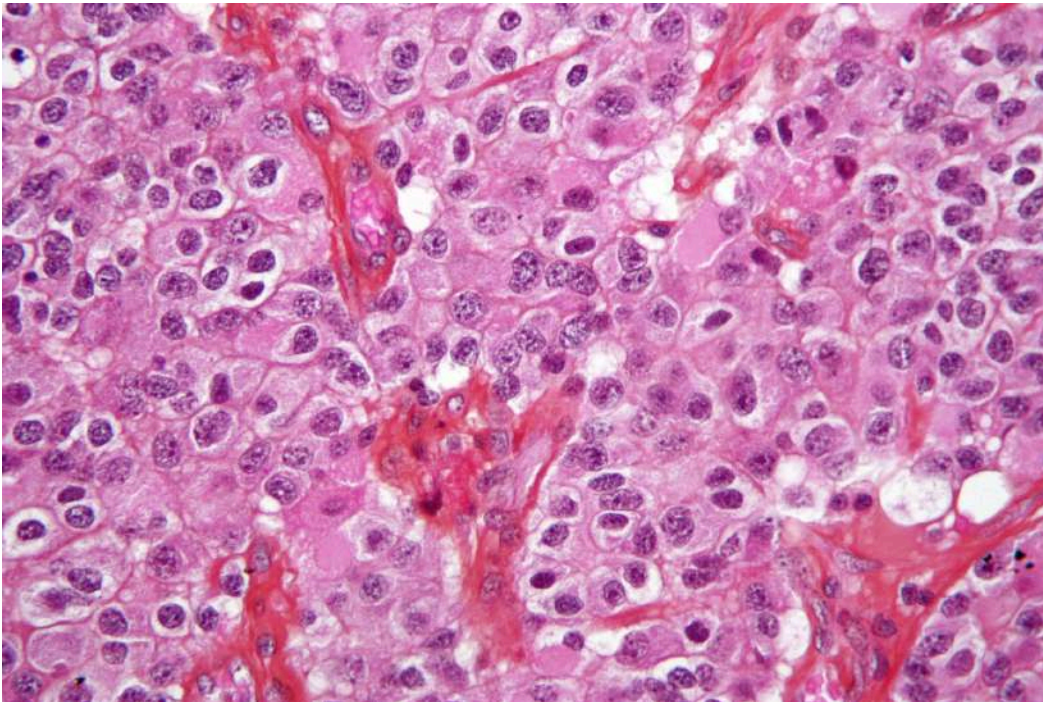
The number of [psammoma bodies](#) seen in [meningiomas](#) depends on the subtype. The psammomatous subtype seen in this patient is characterized by abundant [psammoma bodies](#). Outside of the [CNS](#), [psammoma bodies](#) are seen in papillary [carcinoma](#) of [thyroid](#), [mesothelioma](#), and serous papillary [cystadenocarcinoma](#) of [ovary](#) and [endometrium](#).

Explanation Why

[Meningiomas](#) arise from arachnoid cells of the [arachnoid villi](#). They are usually [benign tumors](#) that manifest as a slow-growing sharply demarcated mass that is composed of spindle-shaped cells arranged in a whorled pattern. The symptoms they cause are due to compression of adjacent structures, e.g., contralateral [spastic paresis](#) due to compression of the motor cortex, personality changes due to compression of the [frontal lobe](#), or [focal seizures](#).

F - Oligodendrocytes

Image



Explanation Why

[Oligodendrocytes](#) give rise to [oligodendrogliomas](#), which have cells with clear [cytoplasm](#) and a central round nucleus ('fried egg' appearance). They typically arise in the [frontal lobe](#).

Question # 33

A previously healthy 2-year-old boy is brought to the physician because of a 10-day history of unsteady gait, frequent falls, and twitching of the extremities. Physical examination shows bilateral saccadic eye movement in all directions and brief, involuntary muscle contractions of the trunk and limbs. There is an ill-defined, nontender mass in the upper right abdomen. He undergoes surgical resection of the tumor. Histopathologic examination of this mass is most likely to show which of the following?

	Answer	Image
A	Blastic skeletal muscle cells arranged in nests and sheets	
B	Numerous immature lymphocytes in a starry sky pattern	
C	Abortive glomeruli and tubules in a spindle cell stroma	
D	Small blue cells arranged in rosettes around a central neuropil	
E	Hepatocytes in fetal and embryonic stages of differentiation	

Hint

This patient presents with gait ataxia and twitching of the eyes (opsoclonus) and extremities (myoclonus). Opsoclonus-myoclonus syndrome in a patient with an abdominal mass is highly suggestive of a diagnosis of neuroblastoma, the most common extracranial solid malignancy of childhood.

Correct Answer

A - Blastic skeletal muscle cells arranged in nests and sheets

Explanation Why

Blastic [skeletal muscle](#) cells arranged in nests and sheets are histopathologic characteristics of [rhabdomyosarcoma](#). [Rhabdomyosarcoma](#) can arise from any part of the body, but the head and neck are more commonly affected than the upper abdomen, where this patient's mass was found. Moreover, this condition is not associated with [opsoclonus-myoclonus syndrome](#).

B - Numerous immature lymphocytes in a starry sky pattern

Explanation Why

Numerous immature [lymphocytes](#) in a [starry sky pattern](#) are histological characteristics of Burkitt lymphoma. The sporadic form of Burkitt lymphoma can manifest with an abdominal mass. However, this is a rare [malignancy](#) that typically occurs in older children. It commonly manifests with symptoms not seen in this patient, such as [ascites](#), [bowel obstruction](#), and [gastrointestinal bleeding](#). Moreover, this condition is not associated with [opsoclonus-myoclonus syndrome](#).

C - Abortive glomeruli and tubules in a spindle cell stroma

Explanation Why

Abortive [renal glomeruli](#) and tubules in a spindle cell stroma are histopathologic characteristics of [Wilms tumor](#), the most common renal [malignancy](#) in children. [Wilms tumor](#) typically manifests with a smooth, firm, nontender abdominal mass that does not cross the midline. This condition is not associated with [opsoclonus-myoclonus syndrome](#).

D - Small blue cells arranged in rosettes around a central neuropil

Explanation But

[Homer-Wright rosettes](#) are also a histopathologic feature of [medulloblastomas](#), a primary [brain tumor](#) that most commonly develops in children. [Medulloblastomas](#) are exclusively found in the [cerebellum](#), manifesting with [cerebellar dysfunction](#) and [elevated intracranial pressure](#).

Explanation Why

Small, blue cells arranged in rosettes around a central neuropil ([Homer-Wright rosettes](#)) are a histopathologic feature of [neuroblastomas](#). To diagnose and monitor disease activity, [urine](#) can be tested for [homovanillic acid](#) and [vanillylmandelic acid](#), which are produced when [neuroblastoma](#) cells metabolize [catecholamines](#). In some cases, genetic analysis shows a deletion in [chromosome 1p](#) that amplifies the [N-myc oncogene](#). [Neuroblastomas](#) can occur anywhere along the [sympathetic chain](#), the majority being located in the abdomen, as seen in this patient. They become symptomatic due to the [mass effect](#) of the [tumor](#) or due to [metastases](#) (e.g., [orbits](#), bones). This patient's [opsoclonus-myoclonus ataxia](#) is a [paraneoplastic syndrome](#) associated with [neuroblastoma](#).

E - Hepatocytes in fetal and embryonic stages of differentiation

Explanation Why

[Hepatocytes](#) in fetal and embryonic stages of differentiation are histopathologic characteristics of [hepatoblastoma](#), the most common primary hepatic [malignancy](#) in children. This [malignancy](#) typically manifests with an asymptomatic, upper right abdominal mass. However, this condition is not associated with [opsoclonus-myoclonus syndrome](#).

Question # 34

A 34-year-old woman comes to the physician because she has not had her period for 4 months. Menses had previously occurred at regular 28-day intervals with moderate flow. A home pregnancy test was negative. She also reports recurrent headaches and has noticed that when she goes to the movies she cannot see the outer edges of the screen without turning her head to each side. This patient's symptoms are most likely caused by abnormal growth of which of the following?

	Answer	Image
A	Astrocytes	
B	Adenohypophysis	
C	Arachnoid cap cells	
D	Ependymal cells	
E	Schwann cells	
F	Pineal gland	

Hint

A cranial contrast MRI would reveal an intrasellar mass.

Correct Answer

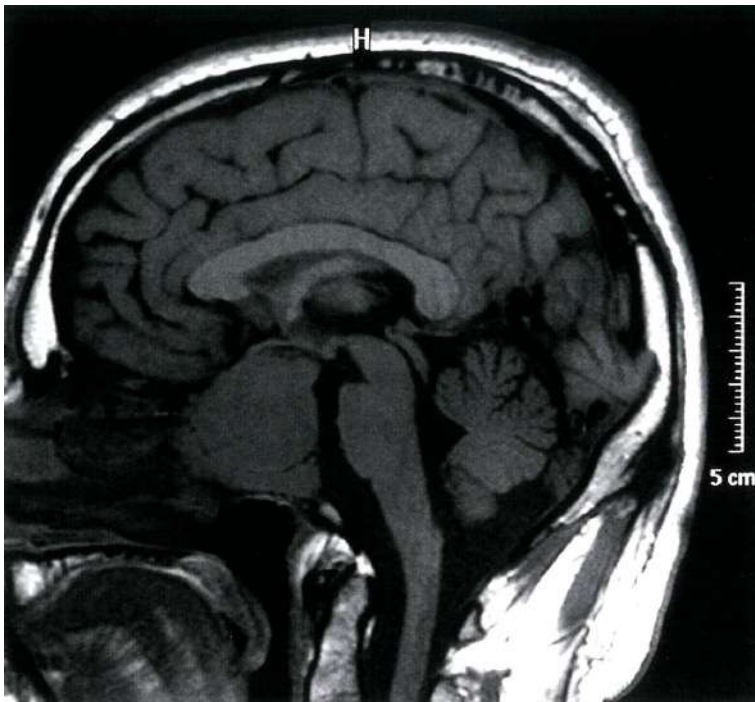
A - Astrocytes

Explanation Why

Abnormal growth of [astrocytes](#) is the underlying pathology of [astrocytomas](#). While low-grade [astrocytomas](#) commonly manifest during childhood with a benign course, high-grade [astrocytomas](#) (e.g., [glioblastoma](#) multiforme) occurs in older individuals and manifests in rapidly progressive symptoms that depend upon the location of the lesion but may include [headaches](#). This patient's prolonged course of symptoms and [secondary amenorrhea](#) is not suggestive of [glioblastoma multiforme](#).

B - Adenohypophysis

Image



Explanation But

Her symptoms could also be explained by a large nonsecreting [pituitary adenoma](#) compressing the [optic chiasm](#) ([bitemporal hemianopsia](#)) and the [pituitary stalk](#) or the gonadotropic cells ([secondary amenorrhea](#)), but the absence of other symptoms of [hypopituitarism](#) makes [prolactinoma](#) more likely.

Explanation Why

Abnormal growth of the [adenohypophysis](#) is the most likely underlying cause of this patient's symptoms, which are consistent with a [pituitary adenoma](#). [Adenomas](#) of the [pituitary gland](#) are most commonly due to aberrant [proliferation](#) of [prolactin](#)-producing cells in the [adenohypophysis](#). The resulting [hyperprolactinemia](#) eventually causes suppression of [gonadotropins](#) and subsequent [secondary amenorrhea](#), as seen in this patient. [Bitemporal hemianopsia](#) (due to compression of the [optic chiasm](#)) and [headaches](#) may develop as the [adenoma](#) grows.

C - Arachnoid cap cells

Explanation Why

Abnormal growth of arachnoid cap cells is the underlying pathology of [meningiomas](#). Even though this patient's recurrent [headaches](#) could be attributed to a [meningioma](#), this [tumor](#) would not explain this patient's [secondary amenorrhea](#) or her visual disturbances.

D - Ependymal cells

Explanation Why

Abnormal growth of [ependymal cells](#) is the underlying pathology of [ependymomas](#), most of which arise close to the [fourth ventricle](#). [Ependymomas](#) commonly cause [obstructive hydrocephalus](#), which may manifest as recurrent [headaches](#). However, [ependymomas](#) typically develop during childhood and are not associated with menstrual irregularities or visual disturbances.

E - Schwann cells

Explanation Why

Abnormal growth of [Schwann cells](#) leads to the development of a [schwannoma](#), which typically arises near the [cerebellopontine angle](#). Large tumors may lead to [symptoms of increased intracranial pressure](#), e.g., recurrent [headache](#). However, in the case of a [schwannoma](#), other features would likely be present, including [tinnitus](#), [vertigo](#), and [hearing loss](#). Moreover, menstrual irregularities or [bitemporal hemianopia](#) would not be expected in the case of a [Schwannoma](#).

F - Pineal gland

Explanation Why

Abnormal growth of the [pineal gland](#) leads to the development of a [pinealoma](#), which generally manifests during childhood. Symptoms of [pinealomas](#) include visual disturbances and [dizziness](#) or recurrent [headaches](#) (due to [hydrocephalus](#)). However, [pinealomas](#) are associated with [vertical gaze palsy](#) rather than the [bitemporal hemianopsia](#) observed in this patient. Moreover, menstrual disturbances would not be expected, as [pinealomas](#) are hormonally inactive.

Question # 35

A 72-year-old woman is brought to the physician by her daughter because of a 6-month history of worsening short-term memory deficits and social withdrawal. Treatment with galantamine is initiated. Two weeks later, the patient develops vomiting, mild crampy abdominal pain, and watery, nonbloody diarrhea. Which of the following would most likely reverse this patient's gastrointestinal symptoms?

	Answer	Image
A	Bethanechol	
B	Metoclopramide	
C	Loperamide	
D	Atropine	
E	Oxybutynin	

Hint

Galantamine is an acetylcholinesterase inhibitor (AChEI) used to treat Alzheimer disease. The most common adverse effects of AChEIs involve peristalsis and include nausea, vomiting, diarrhea, and muscle cramps, as seen in this patient. These symptoms are caused by repeated muscarinic receptor activation due to accumulation of ACh in the synaptic cleft. If this effect is not reversed, additional symptoms can develop, such as excessive lacrimation and bronchial secretion, as well as increased bowel and bladder activity, bronchospasm, and bradycardia.

Correct Answer

A - Bethanechol

Explanation Why

[Bethanechol](#) is a [cholinomimetic drug](#) that acts on [muscarinic receptors](#). Activation of these receptors will induce [smooth muscle](#) contraction and increase [exocrine gland](#) secretions (e.g., lacrimal, sweat, salivary, [gastric acid](#)) as well as bowel and [bladder](#) movement, which would worsen the patient's gastrointestinal symptoms.

B - Metoclopramide

Explanation Why

[Metoclopramide](#) exerts its anti-emetic effect by blocking [dopamine 2 receptors](#) in the [CNS](#) and [area postrema](#). Additionally, it enhances the response to [ACh](#) in the upper [GI tract](#), thereby increasing bowel motility and gastric emptying, which would worsen this patient's symptoms.

C - Loperamide

Explanation Why

[Loperamide](#) acts on [μ-opioid receptors](#), which are expressed in the [myenteric plexus](#) of the [large intestine](#). Activation of these receptors decreases bowel motility providing more time for water and food absorption. Even though [loperamide](#) is used to treat [chronic diarrhea](#), it is not appropriate for the treatment of this patient's cholinergic side effects.

D - Atropine

Explanation Why

[Atropine](#) is an [antimuscarinic agent](#), which can reverse the effects of cholinergic toxicity by blocking [ACh](#) action in [smooth muscle](#), secretory glands, and the [CNS](#). [Atropine](#) is also used to treat acute symptomatic [bradycardia](#) or [AV block](#), decrease salivation (e.g., in surgery), and reverse [organophosphate poisoning](#) (in combination with [pralidoxime](#)).

E - Oxybutynin

Explanation Why

[Oxybutynin](#) is an [antimuscarinic agent](#) used for the treatment of [urge incontinence](#). It exhibits a strong antispasmodic activity on the [bladder smooth muscle](#) but has a less potent [anticholinergic effect](#), so it would not provide relief for this patient's gastrointestinal symptoms.

Question # 36

A 63-year-old man with inoperable esophageal carcinoma undergoes palliative chemoradiotherapy. Four hours after his first infusion of carboplatin and paclitaxel, he develops nausea and 3 episodes of vomiting and dry heaving. This adverse reaction is caused by stimulation of a brain region on the floor of the fourth ventricle. Chemotherapeutic drugs are able to stimulate this region because of the absence of a cell junction that is composed of which of the following proteins?

	Answer	Image
A	Integrins	
B	Claudins and occludins	
C	Cadherins and catenins	
D	Connexins	
E	Desmogleins and desmocollins	

Hint

The brain region on the floor of the fourth ventricle is the chemoreceptor trigger zone, which is located within the area postrema. The lack of tight junctions in this zone, which normally form the blood-brain barrier, makes it vulnerable to emetic stimuli (e.g., chemotherapeutic drugs).

Correct Answer

A - Integrins

Explanation Why

[Integrins](#) are transmembrane receptor [proteins](#) that mediate cell adhesion to [basement membranes](#) and establish intercellular junctions in the [immune system](#) (e.g., for leukocyte extravasation). These [proteins](#) are not components of [tight junctions](#).

B - Claudins and occludins

Explanation But

The chemoreceptor trigger zone of the [area postrema](#) responds to signaling from muscarinic (M1), [dopaminergic](#) (D2), histaminic (H1), serotonergic (5-HT₃), and neurokininergic (NK-1) receptors. Therefore, [5-HT₃ antagonists](#) (e.g., [ondansetron](#)), D2 antagonists (e.g., [metoclopramide](#)), and NK-1 antagonists (e.g., [aprepitant](#)) are commonly used to prevent [chemotherapy-induced nausea](#).

Explanation Why

[Claudins](#) and [occludins](#) are key components of the [tight junctions](#) that form the [blood-brain barrier](#). The [tight junctions](#) seal adjacent [epithelial](#) cells together, which prevents [paracellular transport](#) of ions and molecules. The chemoreceptor trigger zone lacks [tight junctions](#) and is thus highly permeable. As a result, several [chemotherapeutic drugs](#) can freely cross the [blood-brain](#) barrier and cause nausea.

C - Cadherins and catenins

Explanation Why

[Cadherins](#) and [catenins](#) are key components of [adherens junctions](#), which connect adjacent cells together in a continuous, belt-like manner (e.g., in [epithelial](#) and [endothelial](#) tissues). These [proteins](#)

are not components of [tight junctions](#).

D - Connexins

Explanation Why

[Connexins](#) are [transmembrane proteins](#) that assemble to form [connexons](#), which then form [gap junctions](#). These channels permit the passage of electrical or chemical signals between neighboring cells (e.g., to propagate the [cardiac action potential](#)). These [proteins](#) are not components of [tight junctions](#).

E - Desmogleins and desmocollins

Explanation Why

[Desmogleins](#) and [desmocollins](#) are structural [proteins](#) within [desmosomes](#) that promote cell-to-cell adhesion. These [proteins](#) are not components of [tight junctions](#).

Question # 37

A 19-year-old man with a history of generalized tonic-clonic seizures comes to the physician for a routine health maintenance examination. He is a known user of intravenous cocaine. His vital signs are within normal limits. Physical examination shows multiple hyperpigmented lines along the forearms. Oral examination shows marked overgrowth of friable, ulcerated gingival mucosa. Which of the following is the most likely cause of this patient's oral examination findings?

	Answer	Image
A	Phenytoin	
B	Alprazolam	
C	Valproic acid	
D	Lamotrigine	
E	Cocaine	
F	Lacosamide	
G	Cyclosporine	
H	Carbamazepine	

Hint

Overgrowth of the gingival tissue is also known as gingival hyperplasia.

Correct Answer

A - Phenytoin

Explanation Why

[Phenytoin](#) is used in the prophylaxis of generalized [tonic-clonic seizures](#), as seen in this patient. The agent has many side effects, including gingival hyperplasia (drug-induced gingival overgrowth), [hirsutism](#), [Stevens-Johnson syndrome](#), [megaloblastic anemia](#), nystagmus, [ataxia](#), and [peripheral neuropathy](#). If possible, the drug should be discontinued and the patient should be advised to adhere to strict oral hygiene. If the gingival overgrowth does not improve or infection occurs, excision of excessive gingival tissue should be considered.

B - Alprazolam

Explanation But

[Benzodiazepines](#) are the first-line treatment for convulsive [status epilepticus](#), but [diazepam](#), [lorazepam](#), or [midazolam](#) are usually chosen instead of [alprazolam](#).

Explanation Why

[Alprazolam](#) is a [benzodiazepine](#) used to treat [panic disorder](#) and anxiety and is a common drug of abuse. It does not cause gingival hyperplasia. Common side effects include drowsiness, sedation, [ataxia](#), [memory](#) impairment, and cognitive dysfunction.

C - Valproic acid

Explanation Why

[Valproic acid](#) can be used to treat [tonic-clonic seizures](#). However, the agent is associated with side effects such as hepatotoxicity, [pancreatitis](#), weight gain, and [tremor](#) rather than gingival hyperplasia.

D - Lamotrigine

Explanation Why

[Lamotrigine](#) can be used to treat [tonic-clonic seizures](#) and can very rarely cause gingival hyperplasia. However, it is more typically associated with side effects such as nausea, [skin](#) rashes, and [Stevens-Johnson syndrome](#). A different agent would be more likely to cause gingival hyperplasia.

E - Cocaine

Explanation Why

This patient has a history of [cocaine](#) use. However, chronic abuse of [cocaine](#) is associated with gingival recession rather than gingival hyperplasia.

F - Lacosamide

Explanation Why

Lacosamide is used in the treatment of [focal seizures](#) but not [generalized seizures](#). It does not cause gingival hyperplasia. Common side effects of lacosamide include [dizziness](#), [ataxia](#), nausea, vomiting, [diplopia](#), and blurred vision.

G - Cyclosporine

Explanation Why

[Cyclosporine](#) can cause gingival hyperplasia, but it is used for [transplant rejection](#) prophylaxis and in the treatment of [rheumatoid arthritis](#) and [psoriasis](#), none of which apply to this patient. [Cyclosporine](#)

can cause renal and hepatic toxicity; other common side effects are [hypertension](#), [headaches](#), [hyperglycemia](#), and [hirsutism](#).

H - Carbamazepine

Explanation But

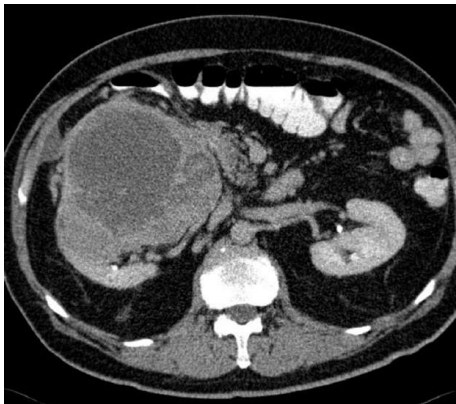
If severe [thrombocytopenia](#) occurs in conjunction with [aplastic anemia](#), patients can also present with bleeding [gums](#).

Explanation Why

[Carbamazepine](#) can be used to treat [tonic-clonic seizures](#). However, the agent is associated with side effects such as [diplopia](#), [ataxia](#), hepatotoxicity, [agranulocytosis](#), and [aplastic anemia](#) rather than gingival hyperplasia.

Question # 38

A 20-year-old man comes to the physician because of worsening gait unsteadiness and bilateral hearing loss for 1 month. He has had intermittent tingling sensations on both cheeks over this time period. He has no history of serious medical illness and takes no medications. Audiometry shows bilateral sensorineural hearing loss. Genetic evaluation shows a mutation of a tumor suppressor gene on chromosome 22 that encodes merlin. This patient is at increased risk for which of the following conditions?

	Answer	Image
A	Optic glioma	
B	Renal cell carcinoma	

	Answer	Image
C	Meningioma	
D	Astrocytoma	
E	Vascular malformations	
F	Telangiectasias	

Hint

The patient's unsteadiness, bilateral sensorineural hearing loss, and midface paresthesia are consistent with bilateral compression of CN V and CN VIII. This is usually caused by bilateral vestibular schwannomas, a hallmark feature of neurofibromatosis type 2 (NF-2). NF-2 is an autosomal dominant syndrome that it is caused by a mutation in the NF-2 gene on chromosome 22, which produces merlin, a tumor suppressor.

Correct Answer

A - Optic glioma

Image

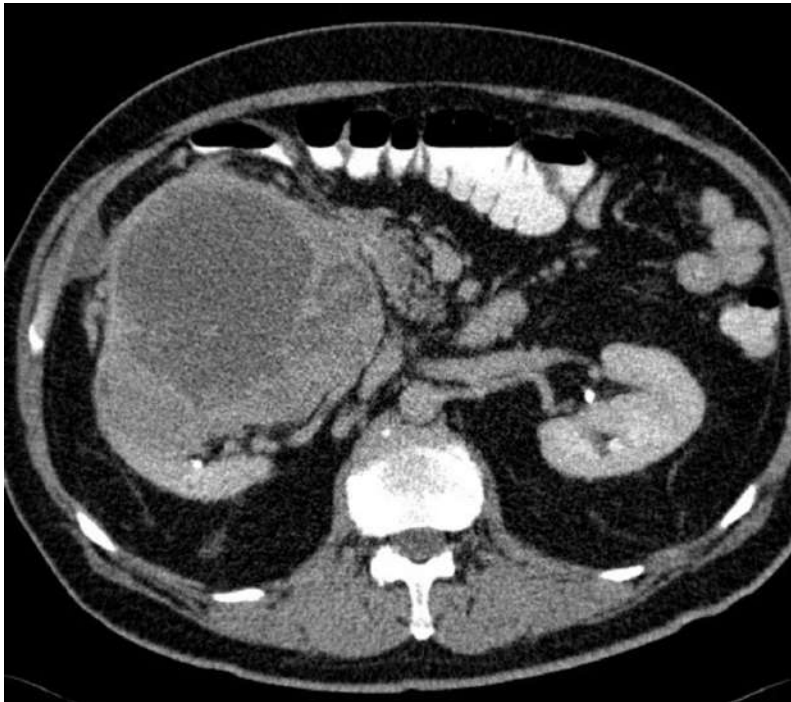


Explanation Why

[Optic gliomas](#) are often associated with [neurofibromatosis type 1 \(NF1\)](#), an [autosomal dominant](#) syndrome caused by mutation of the [NF1 tumor suppressor gene](#) on [chromosome 17](#). Other tumors that may occur in patients with [NF1](#) include benign peripheral nerve sheath tumors originating from [neural crest cells](#) ([neurofibromas](#)), [pheochromocytomas](#), and [Wilms tumors](#). However, bilateral [schwannomas](#) are not associated with [NF1](#). Moreover, patients with [NF1](#) usually present with typical [skin](#) findings (due to [melanocyte](#) dysfunction) such as [café au lait spots](#) and axillary/inguinal freckling, as well as musculoskeletal findings (e.g., [scoliosis](#), tall stature, and bone involvement) and [Lisch nodules](#) of the [iris](#), none of which is seen in this patient.

B - Renal cell carcinoma

Image



Explanation Why

The occurrence of (bilateral) [renal cell carcinoma](#) is associated with von Hippel-Lindau disease ([VHL](#)), an [autosomal dominant](#) syndrome caused by a mutation to the [tumor-suppressing](#) Hippel-Lindau [gene](#). This neurocutaneous syndrome is characterized by the development of numerous benign and [malignant tumors](#), including [hemangioblastomas](#) (highly vascularized in the [retina](#), [cerebellum](#), [brain stem](#), and [spine](#)), [pheochromocytomas](#), and renal and [pancreatic](#) cysts. Bilateral [schwannomas](#), however, are not a typical feature.

C - Meningioma

Image



Explanation Why

Beside bilateral [schwannomas](#), [neurofibromatosis](#) type 2 (NF2) often manifests with multiple cerebral and [spinal](#) tumors, as well as [meningiomas](#). Most [meningiomas](#) are slow-growing and patients may therefore be asymptomatic for a prolonged period of time. If symptoms are present, they usually include general symptoms of [CNS](#) tumors (e.g., [seizures](#)), or more specific symptoms that depend on the [tumor](#) location (e.g., paraparesis and/or uncontrolled micturition if [tumor](#) arises from the [falx cerebri](#)).

D - Astrocytoma

Explanation Why

Giant cell astrocytomas are frequently associated with [tuberous sclerosis](#), an [autosomal dominant](#)

syndrome that is caused by mutation of the [TSC1](#) or [TSC2 gene](#), which encode for [hamartin](#) or [tuberin protein](#) (both [tumor suppressors](#)), respectively. Other benign growths associated with [tuberous sclerosis](#) include [hamartomas](#) of the brain, cardiac [rhabdomyomas](#), [renal cysts](#), renal [angiomyolipomas](#), and [ungual fibromas](#). The brain lesions typically result in [infantile spasms](#) (head bobbing, flexor or extensor spasms in children < 3 years of age), [seizures](#), and [intellectual disability](#). Furthermore, [skin](#) manifestations, such as [adenoma sebaceum](#), [ash-leaf spots](#), and a [Shagreen patch](#) are commonly seen. However, [schwannomas](#) are not a feature of [tuberous sclerosis](#) and the condition is usually diagnosed before the age of 10 years.

E - Vascular malformations

Explanation Why

Vascular [malformations](#) of the [choroid](#) and the [CNS](#) such as ipsilateral [leptomeningeal angiomas](#) are a typical feature of [Sturge-Weber syndrome](#), a condition caused by somatic [mosaic](#) mutations in the [GNAQ gene](#). The vascular [malformations](#) may result in [seizures](#), early-onset [glaucoma](#) (due to increased intraorbital pressure), and [intellectual disability](#). Patients also often present with a facial [nevus flammeus](#) ([port-wine stain](#)). However, [schwannomas](#) are not associated with [Sturge-Weber syndrome](#).

F - Telangiectasias

Explanation Why

[Telangiectasias](#) on the face and [conjunctivae](#) are typical findings in patients with [ataxia telangiectasia](#), an [autosomal recessive](#) disorder caused by mutations in the [DNA-repair ATM gene](#). Other manifestations include progressive [cerebellar ataxia](#) (due to [atrophy](#) of the [cerebellar vermis](#)), [athetosis](#), [immunodeficiency](#) (e.g., increased susceptibility to ear infections, [sinusitis](#), and [pneumonia](#)), and increased sensitivity to radiation resulting in a higher risk of malignancies (e.g. [non-Hodgkin lymphoma](#), leukemia). However, the finding of bilateral [schwannomas](#) is not typical in patients with [ataxia telangiectasia](#). Furthermore, symptoms typically present during early childhood.

Question # 39

A 78-year-old man comes to the physician because of difficulty swallowing and regurgitation of undigested food for the past several months. The patient reports that his symptoms have gotten progressively worse. Physical examination shows severe halitosis and a gurgling sound after he swallows a small amount of water. Results of fluoroscopic barium esophagography are shown. The nerve responsible for motor innervation of the affected muscle is also responsible for which of the following functions?



	Answer	Image
A	Parasympathetic innervation of the AV node	
B	Sensory innervation of the posterior tongue	
C	Visceral sensory innervation of the carotid sinus	

	Answer	Image
D	Motor innervation of the ventral tongue	
E	Somatosensory innervation of the semi-circular canals	

Hint

This patient's presentation is consistent with a Zenker diverticulum, which is an outpouching of the esophagus between two parts of the inferior pharyngeal constrictor (Killian triangle). The inferior pharyngeal constrictor is innervated by branches from the pharyngeal plexus of the vagus nerve.

Correct Answer

A - Parasympathetic innervation of the AV node

Explanation Why

The [vagus nerve](#) innervates the inferior pharyngeal constrictor, which is the muscle affected in [Zenker diverticulum](#). [Parasympathetic](#) fibers that innervate both the [SA node](#) (right [vagus nerve](#)) and the [AV node](#) (left [vagus nerve](#)) also originate from the [vagus nerve](#). Additional functions of the [vagus nerve](#) include initiation of the [cough reflex](#), innervation of [taste](#) receptors of the [supraglottis](#), and innervation of chemo and [baroreceptors](#) in the [aortic arch](#).

B - Sensory innervation of the posterior tongue

Explanation Why

The [glossopharyngeal nerve](#) is responsible for sensory innervation of the [posterior tongue](#). It is also part of the pharyngeal plexus and provides motor innervation to the [stylopharyngeus muscle](#). However, it is not involved in the innervation of the inferior pharyngeal constrictor.

C - Visceral sensory innervation of the carotid sinus

Explanation Why

Branching fibers of the [glossopharyngeal nerve](#), which is located [anterior](#) to the [internal carotid artery](#), are responsible for the visceral sensory innervation of the [carotid sinus baroreceptors](#) and carotid body [chemoreceptors](#). The [glossopharyngeal nerve](#) is part of the pharyngeal plexus and provides motor innervation to the [stylopharyngeus muscle](#) but does not innervate the inferior pharyngeal constrictor.

D - Motor innervation of the ventral tongue

Explanation Why

The [hypoglossal nerve](#) is responsible for motor innervation of the [tongue](#) and its [intrinsic muscles](#). The [hypoglossal nerve](#) is not involved in the innervation of the inferior pharyngeal constrictor.

E - Somatosensory innervation of the semi-circular canals

Explanation Why

The [vestibulocochlear nerve](#) is responsible for somatosensory innervation of the semi-circular canals and transmission of equilibrium information from the [inner ear](#) to the brain. It does not provide motor innervation to the inferior pharyngeal constrictor.

Question # 40

A 59-year-old woman comes to the physician because of upper extremity weakness and fatigue for the past 4 months. She has had difficulty combing her hair and lifting objects. She has also had difficulty rising from her bed in the mornings for 2 months. Over the past month, she started using over-the-counter mouth rinses for dry mouth. She has smoked 1 pack of cigarettes daily for 40 years. Examination shows decreased deep tendon reflexes. Repetitive muscle tapping shows increased reflex activity. There are no fasciculations or muscle atrophy. A low-dose CT scan of the chest shows a 3-cm mass with heterogeneous calcifications in the center of the right lung. Which of the following is the most likely underlying mechanism responsible for this patient's current symptoms?

	Answer	Image
A	Metastasis	
B	Inflammation	
C	Autoimmunity	
D	Heredity	
E	Invasion	
F	Infection	

Hint

A CT scan showing a 3-cm pulmonary mass with irregular calcifications in a patient with a 40 pack-year history of cigarette smoking is suspicious for lung malignancy.

Correct Answer

A - Metastasis

Explanation Why

The [CNS](#) is one of the most common locations for [lung cancer metastasis](#), which can present with focal neurological deficits. Patients with [brain metastasis](#) may exhibit muscle weakness, as seen here. However, [upper motor neuron](#) symptoms (e.g., [hyperreflexia](#), [spasticity](#)) would also be expected, rather than the decreased [deep tendon reflexes](#) observed in this patient. In addition, [brain metastasis](#) commonly presents with [headaches](#), cognitive deficits, and [seizures](#), none of which are present here. Moreover, her autonomic symptom (dry mouth) and the increased reflex activity noted after repeated stimulation are inconsistent with this diagnosis.

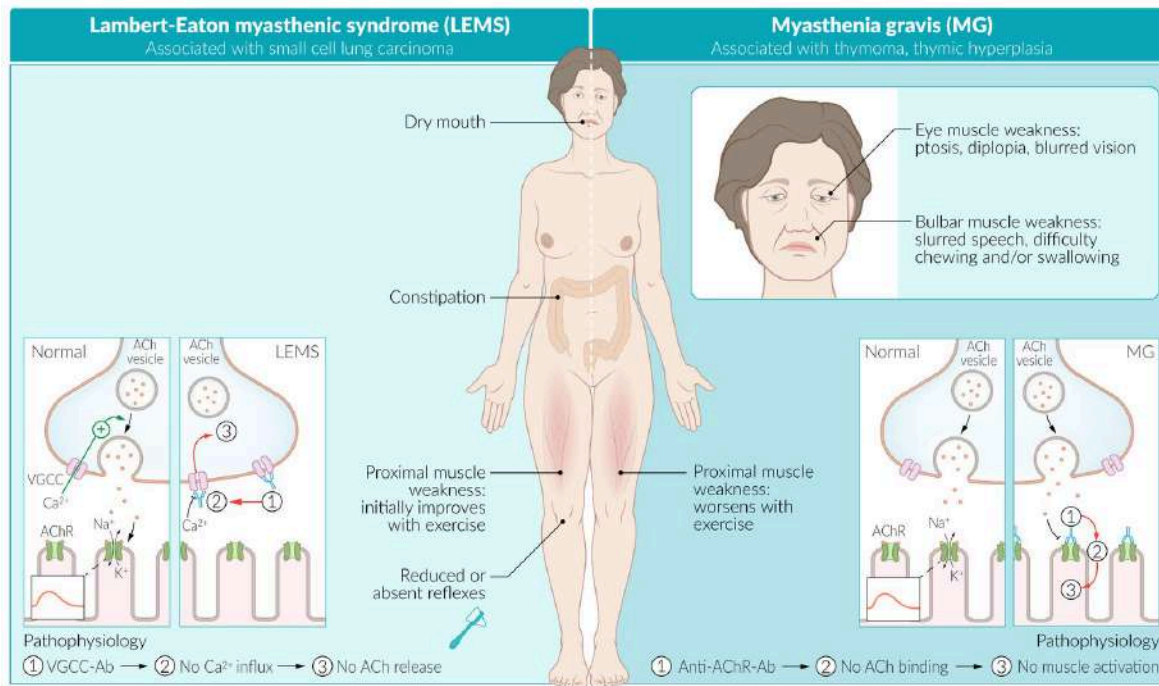
B - Inflammation

Explanation Why

[Inflammatory myopathies](#) (IM), such as [polymyositis](#) and [dermatomyositis](#), typically manifest with [proximal](#) muscle weakness, as seen in this patient. However, her autonomic symptom (dry mouth) and the decreased [deep tendon reflexes](#) with improvement after repeated stimulation are inconsistent with IM. Although a strong association exists between [dermatomyositis](#) and [malignancy](#), this patient lacks the typical cutaneous manifestations of this disease (i.e., [Gottron papules](#), [heliotrope rash](#)), which excludes [dermatomyositis](#) as the underlying mechanism responsible for her presentation.

C - Autoimmunity

Image



Explanation Why

Lambert-Eaton myasthenic syndrome (LEMS) is a **paraneoplastic** autoimmune disease, most commonly associated with **small cell lung cancer**. In **LEMS**, **antibodies** against presynaptic voltage-gated calcium channels impair **acetylcholine (ACh)** release in the **neuromuscular junction**. This leads to **proximal** muscle weakness, **autonomic dysfunction** (e.g., dry mouth, **constipation**), and decreased **deep tendon reflexes**, as seen in this patient. A unique feature of **LEMS** is an improvement in strength and reflex activity with repeated use/stimulation. Since postsynaptic **ACh** receptors remain intact in **LEMS**, once enough **ACh** has built up in the postsynaptic cleft from repeated stimulation, muscle contraction can return.

D - Heredity

Explanation Why

Hereditary causes of muscle weakness include [muscular dystrophies](#) (e.g., [Duchenne muscular dystrophy](#)), [hereditary motor sensory neuropathies](#) ([HMSN](#)) (e.g., [Charcot-Marie-Tooth disease](#)), and congenital myopathies. Although decreased [deep tendon reflexes](#), as seen here, may be found in all of these conditions, increased reflex activity after repeated stimulation would not be present. Moreover, further symptoms such as muscle [atrophy](#) and, in the case of [HMSN](#), sensory deficits would be expected. Finally, these hereditary conditions almost exclusively manifest in childhood or early adulthood.

E - Invasion

Explanation Why

Invasion of a [lung carcinoma](#) into the cervical [sympathetic chain](#) can lead to [Pancoast syndrome](#), presenting with upper extremity weakness and loss of [deep tendon reflexes](#), as seen in this patient. However, muscle weakness in [Pancoast syndrome](#) is typically unilateral. In addition, further symptoms caused by the compression or infiltration of local structures by the [tumor](#) would be expected (e.g., shoulder [pain](#), muscle [atrophy](#), sensory deficits, [Horner syndrome](#), hoarseness, and [superior vena cava syndrome](#)). An increase in reflex activity noted after repeated stimulation is inconsistent with this diagnosis. Moreover, the patient's CT revealed a mass in the center of the right [lung](#), whereas [Pancoast tumors](#) are always located in the superior sulcus.

F - Infection

Explanation Why

Some viral infections that affect the [anterior horn cells](#) can cause muscle weakness, resulting in [flaccid paralysis](#) or invasion of the muscle itself (i.e., [myositis](#)). Viruses that cause [flaccid paralysis](#) include [poliovirus](#), nonpolio [enteroviruses](#), and [West Nile virus](#), all of which are extremely unlikely in a patient without a travel history to [endemic](#) areas. Moreover, further symptoms such as [muscle fasciculations](#), [atrophy](#), and signs of infection (e.g., [fever](#), malaise, [headache](#)) would be expected.

Viral [myositis](#) is commonly caused by [influenza viruses](#) and [enteroviruses](#); patients typically present with [fever](#), myalgia, and a history of an upper respiratory tract infection, none of which are seen in this patient. Additionally, her slowly progressive symptoms, autonomic symptom (dry mouth), and the increased reflex activity noted after repeated stimulation are inconsistent with an infectious cause.

Question # 1

A 33-year-old man comes to the emergency department because of a dry mouth and blurred vision for the past 30 minutes. Prior to this, he was on a road trip and started to feel nauseous, dizzy, and fatigued, so his friend gave him a drug that had helped in the past. Physical examination shows dry mucous membranes and dilated pupils. The remainder of the examination shows no abnormalities. Administration of which of the following drugs is most likely to cause a similar adverse reaction in this patient?

	Answer	Image
A	Oxycodone	
B	Oxybutynin	
C	Metoclopramide	
D	Pilocarpine	
E	Phenylephrine	
F	Loratadine	

Hint

This patient likely received a scopolamine patch for treatment of his motion sickness and now experiences dry mouth and blurred vision as a result of its anticholinergic effects.

Correct Answer

A - Oxycodone

Explanation Why

Oxycodone is an [opioid analgesic](#) that, like other agents in its class, causes [miosis](#). It does not cause [anticholinergic toxicity](#).

B - Oxybutynin

Explanation Why

[Oxybutynin](#) is a [muscarinic antagonist](#) that treats [overactive bladder incontinence](#). Like other [muscarinic antagonists](#), such as [scopolamine](#), it has adverse [anticholinergic effects](#) including this patient's dry mucous membranes and [mydriasis](#) resulting from a lack of specificity to its target tissue. Toxicity with [anticholinergic agents](#) (causing [anticholinergic syndrome](#)) is treated with [physostigmine](#).

C - Metoclopramide

Explanation Why

[Metoclopramide](#) is an antiemetic that also functions as a promotility agent and acts as both a [dopamine receptor antagonist](#) and a [serotonin receptor antagonist](#). Adverse effects include [parkinsonism](#) and [diarrhea](#), but it does not cause symptoms of [anticholinergic toxicity](#).

D - Pilocarpine

Explanation Why

[Pilocarpine](#) is a [direct parasympathomimetic](#) that treats [glaucoma](#) and Sjögren syndrome. This drug would cause cholinergic symptoms (e.g., [diarrhea](#), urination, [miosis](#), bronchospasm, [bradycardia](#), neuromuscular excitation, lacrimation, sweating, and salivation (“DUMBBELSS” mnemonic)), not the [mydriasis](#) and dry mouth experienced by this patient.

E - Phenylephrine

Explanation Why

[Phenylephrine](#) is a [sympathomimetic drug](#) that can cause [mydriasis](#), as seen in this patient. However, it does not cause [anticholinergic toxicity](#).

F - Loratadine

Explanation Why

[Loratadine](#) is a second-generation [H1 antihistamine](#) that, unlike its first-generation counterparts, does not cause significant [anticholinergic toxicity](#).

Question # 2

A 47-year-old woman comes to the physician because of repetitive tongue twisting and abnormal movements of the hands and legs that started several days ago. She has a 2-year history of schizophrenia that has been controlled with fluphenazine. Two weeks ago, she was switched to risperidone. Examination shows protrusion of the tongue and smacking of the lips. She makes twisting movements of the arms and frequently taps her right foot. Which of the following is the most likely diagnosis?

	Answer	Image
A	Tourette syndrome	
B	Cerebellar stroke	
C	Neuroleptic malignant syndrome	
D	Akathisia	
E	Acute dystonia	
F	Tardive dyskinesia	
G	Pseudoparkinsonism	

Hint

It is common for this condition to first appear after a reduction in antipsychotic medication dose, or, as in this case, changing to a less potent antipsychotic medication due to an unmasking effect. Switching to clozapine should be considered, but this patient's condition may be irreversible.

Correct Answer

A - Tourette syndrome

Explanation Why

[Tourette syndrome](#) is a [tic disorder](#) characterized by rapid, involuntary motor and vocal [tics](#) that occur several times daily on most days. It is not associated with [antipsychotic drug](#) treatment, but with [attention deficit hyperactivity disorder](#) and obsessive-compulsive disorder. Onset is typically before the age of 18.

B - Cerebellar stroke

Explanation Why

A [cerebellar stroke](#) typically presents with acute onset [headache](#), nausea, vomiting, and [cerebellar signs](#). Repetitive involuntary movements as seen in this patient would not be present. Moreover, this patient has no [risk factors](#) associated with acute [stroke](#) (e.g., [hypertension](#), [hyperlipidemia](#), smoking history).

C - Neuroleptic malignant syndrome

Explanation Why

[Neuroleptic malignant syndrome](#) ([NMS](#)) is a life-threatening condition that usually appears within the first 2 weeks of treatment with [antipsychotic](#) medications (most often typical [antipsychotics](#), e.g., [haloperidol](#)). Repetitive involuntary movements as seen in this patient would not be present. Instead, [NMS](#) is characterized by hyperthermia, muscular [rigidity](#), autonomic instability, and mental status change. Cessation of the offending drug is the single most important treatment.

D - Akathisia

Explanation Why

[Akathisia](#) is the most common form of [antipsychotic](#)-induced [extrapyramidal symptoms](#), usually presenting within a week to a few months of treatment and manifesting with restlessness and a compelling urge to move. While constant movements, as seen in this patient, may occur, they are not entirely involuntary, repetitive, or purposeless and are more a result of an inability to sit still.

E - Acute dystonia

Explanation Why

[Acute dystonia](#) typically presents within hours to days after the intake of [antipsychotics](#) and manifests with painful and lasting muscle spasms that predominantly affect the head, neck ([torticollis](#)), and [tongue](#). Unlike in this patient, movements are nonrepetitive and affect a single muscle group.

F - Tardive dyskinesia

Explanation Why

[Tardive dyskinesia](#) (TD) is a drug-induced hyperkinetic movement disorder that usually presents within months to years of [antipsychotic](#) use with repetitive involuntary movements (e.g., lip smacking), as seen in this patient. TD may persist even after discontinuation of the offending drug and can be irreversible. [Extrapyramidal symptoms](#) generally occur more frequently in conjunction with [typical antipsychotics](#) (e.g., [fluphenazine](#)), which this patient has received for 2 years, and to a lesser extent with [atypical antipsychotics](#) (e.g., [risperidone](#)).

G - Pseudoparkinsonism

Explanation Why

[Pseudoparkinsonism](#) may develop days to weeks after initiating therapy with an [antipsychotic drug](#) and manifests with the classic symptoms of [parkinsonism](#) (e.g., [cogwheel rigidity](#), stiff gait, and [tremor](#)). Repetitive involuntary movements as seen in this patient would not be present. Medications associated with [pseudoparkinsonism](#) include [typical antipsychotics](#) (e.g., [haloperidol](#)), some [antiemetics](#) (e.g., [metoclopramide](#)), [valproate](#), and [lithium](#).

Question # 3

A 13-year-old girl is brought to the physician by her father because of a worsening pruritic rash for 2 days. Five weeks ago, she was diagnosed with juvenile myoclonic epilepsy and treatment with lamotrigine was begun. Her immunizations are up-to-date. Her temperature is 38.8°C (101.8°F). Physical examination shows facial edema and a partially confluent morbilliform rash over the face, trunk, and extremities. There is swelling of the cervical and inguinal lymph nodes and hepatomegaly. Further evaluation is most likely to show which of the following?

	Answer	Image
A	Fragmented red blood cells	
B	Increased absolute eosinophil count	
C	Positive heterophile antibody test	
D	Anti-measles IgM antibodies	
E	Elevated antistreptolysin-O titer	

Hint

Fever, facial edema, a diffuse morbilliform rash, lymphadenopathy, and hepatomegaly within some weeks after initiating treatment with an anticonvulsant agent are suggestive of DRESS syndrome.

Correct Answer

A - Fragmented red blood cells

Explanation Why

Fragmented [red blood cells](#) ([schistocytes](#)) on [peripheral blood smear](#) are seen in [microangiopathic hemolytic anemia](#) (MAHA). In children, MAHA is usually caused by [hemolytic-uremic syndrome](#) (HUS), which, in addition, presents with [thrombocytopenia](#) and [acute renal failure](#) following dysentery due to toxin-producing bacteria. This patient's presentation is not consistent with HUS.

B - Increased absolute eosinophil count

Explanation Why

Increased absolute [eosinophil](#) count is seen in [DRESS](#) ([drug rash with eosinophilia and systemic symptoms](#)) syndrome, which is a potentially fatal drug-induced [hypersensitivity reaction](#) that can occur 1–8 weeks after exposure to a substance such as an [antiepileptic drug](#) (e.g., [lamotrigine](#), [phenytoin](#), [carbamazepine](#)), [allopurinol](#), or [antibiotics](#) (e.g., [sulfonamide](#)). As seen in this patient, DRESS is characterized by systemic [inflammation](#) with typical involvement of the [skin](#) (e.g., itching rash and facial [edema](#)), [liver](#) (e.g., elevated [liver function tests](#), [hepatomegaly](#)), lymphoid tissue (e.g., diffuse [lymphadenopathy](#)), and blood (e.g., [thrombocytopenia](#), atypical [lymphocytosis](#), [eosinophilia](#)).

C - Positive heterophile antibody test

Explanation Why

The [heterophile antibody test](#) is used for the diagnosis of infection with [EBV](#) ([infectious mononucleosis](#)), which commonly presents with [fever](#), [hepatomegaly](#), and [lymphadenopathy](#), as seen in this patient. However, further symptoms would include [splenomegaly](#) and [pharyngitis](#). Furthermore, a rash would usually only develop after [antibiotic](#) treatment and facial [edema](#) would not be expected.

D - Anti-measles IgM antibodies

Explanation Why

Anti-[measles IgM antibodies](#) are found in acute [measles](#) infection, which could present with [fever](#), [lymphadenopathy](#), and a diffuse morbilliform rash of the head, trunk, and extremities. However, other symptoms, such as [conjunctivitis](#), [cough](#), [coryza](#), and pathognomic [Koplik spots](#) on oral mucosa would be expected, but not facial [edema](#) and [hepatomegaly](#). Furthermore, this patient's immunizations are up-to-date, making the diagnosis of acute [measles virus](#) infection unlikely.

E - Elevated antistreptolysin-O titer

Explanation Why

[Antistreptolysin O \(ASO\)](#) levels are primarily measured to assess for recent infections in patients presenting with complications of [streptococcal tonsillitis](#) (e.g., [scarlet fever](#), [rheumatic fever](#)), but not for acute infections. While [scarlet fever](#) also involves the [skin](#), a sandpaper-like rash would be expected, not the partially confluent morbilliform rash seen in this patient. Furthermore, this girl lacks other features of [scarlet fever](#) such as [pharyngitis](#), flushed cheeks with perioral pallor and a white-coated or strawberry-red [tongue](#) and instead shows facial [edema](#) and [hepatomegaly](#), which would not be expected.

Question # 4

An investigator is studying the function of the lateral nucleus of the hypothalamus in an experimental animal. Using a viral vector, the genes encoding chloride-conducting channelrhodopsins are injected into this nucleus. Photostimulation of the channels causes complete inhibition of action potential generation. Persistent photostimulation is most likely to result in which of the following abnormalities in these animals?

	Answer	Image
A	Hypothermia	
B	Hyperthermia	
C	Polydipsia	
D	Nocturnal hyperactivity	
E	Hyperphagia	
F	Anorexia	

Hint

The lateral nucleus of the hypothalamus is stimulated by ghrelin and inhibited by leptin.

Correct Answer

A - Hypothermia

Explanation Why

Inhibition of the [lateral nucleus](#) of the [hypothalamus](#) would not cause [hypothermia](#) since this region does not play a role in regulating temperature. Instead, [hypothermia](#) is caused by inhibition or destruction of the [posterior nucleus](#), which regulates the conservation of heat via the [sympathetic nervous system](#).

B - Hyperthermia

Explanation Why

Inhibition of the [lateral nucleus](#) of the [hypothalamus](#) would not cause hyperthermia since this region does not play a role in regulating temperature. Instead, hyperthermia is caused by inhibition or destruction of the [anterior nucleus](#), which regulates the dissipation of heat via the [parasympathetic nervous system](#).

C - Polydipsia

Explanation Why

Inhibition of the [lateral nucleus](#) of the [hypothalamus](#) would not cause [polydipsia](#) since this region does not play a role in water balance. Instead, both the [paraventricular nucleus](#) and [supraoptic nucleus](#) regulate water balance via [ADH](#). Dysfunction of these regions can result in [diabetes insipidus](#), which causes [polydipsia](#), [polyuria](#), and [nocturia](#).

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D - Nocturnal hyperactivity

Explanation Why

Inhibition of the [lateral nucleus](#) of the [hypothalamus](#) would not cause nocturnal hyperactivity since this region does not play a role in [circadian rhythm](#). Instead, the [suprachiasmatic nucleus](#) regulates [circadian rhythm](#). Dysfunction of this region can result in [sleep disorders](#) (e.g., [insomnia](#), nighttime hyperactivity).

E - Hyperphagia

Explanation Why

Inhibition of the [lateral nucleus](#) of the [hypothalamus](#) would not cause [hyperphagia](#) since this region does not play a role in regulating satiety. Instead, the [ventromedial nucleus](#) regulates satiety and is stimulated by [leptin](#). Inhibition of [action potential](#) generation or destruction of this region can result in [hyperphagia](#) and [obesity](#).

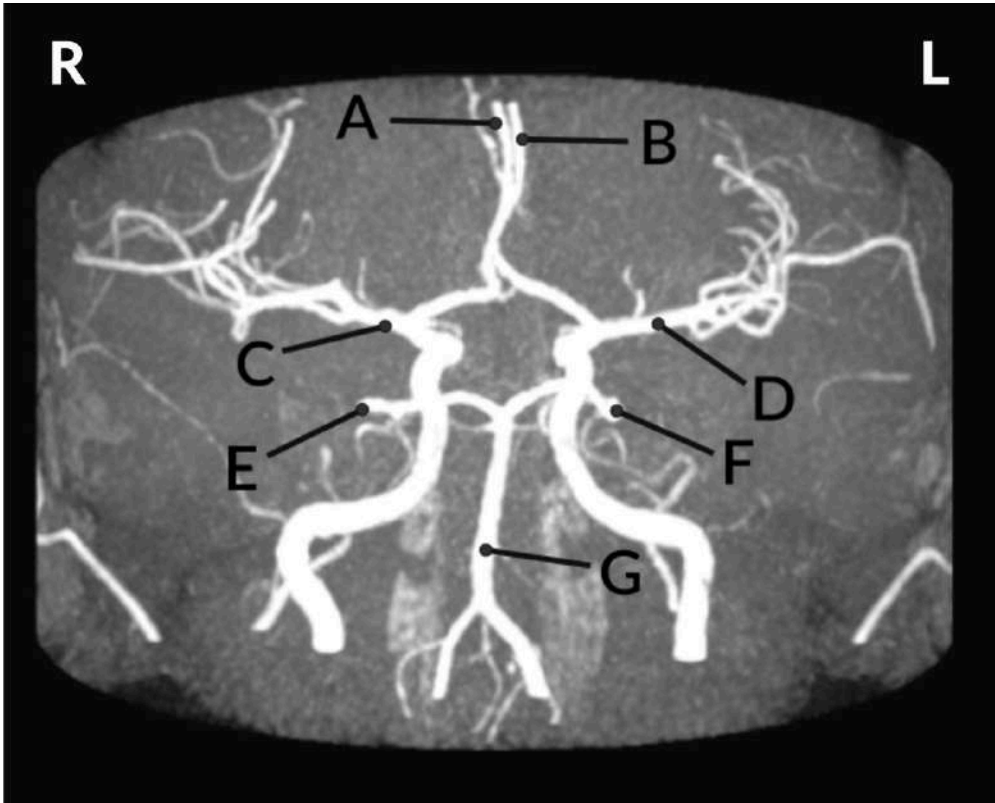
F - Anorexia

Explanation Why

The [lateral nucleus](#) of the [hypothalamus](#) regulates hunger. Inhibition of [action potential](#) generation or destruction of this region can result in anorexia, starvation, and [failure to thrive](#). [Hypothalamic](#) dysfunction plays a role in many conditions, including [Prader-Willi syndrome](#) (which manifests with [hyperphagia](#)) and [anorexia nervosa](#) (which manifests with reduced caloric intake).

Question # 5

A 62-year-old man is brought to the emergency department because of a 2-hour history of left-sided body weakness and involuntary urinary leakage. He has a 15-year history of type 2 diabetes mellitus and hyperlipidemia treated with metformin and atorvastatin. He reports having experienced a similar episode two years ago. Neurologic examination shows left-sided hemiparesis and decreased sensation. The neurologic abnormalities are more prominent in the left lower than in the left upper extremity. He is oriented to time, place, and person. Which of the following labeled vessels in the MR angiography image of a normal brain is most likely occluded in this patient?



	Answer	Image
A	A	

	Answer	Image
B	B	
C	C	
D	D	
E	E	
F	F	
G	G	

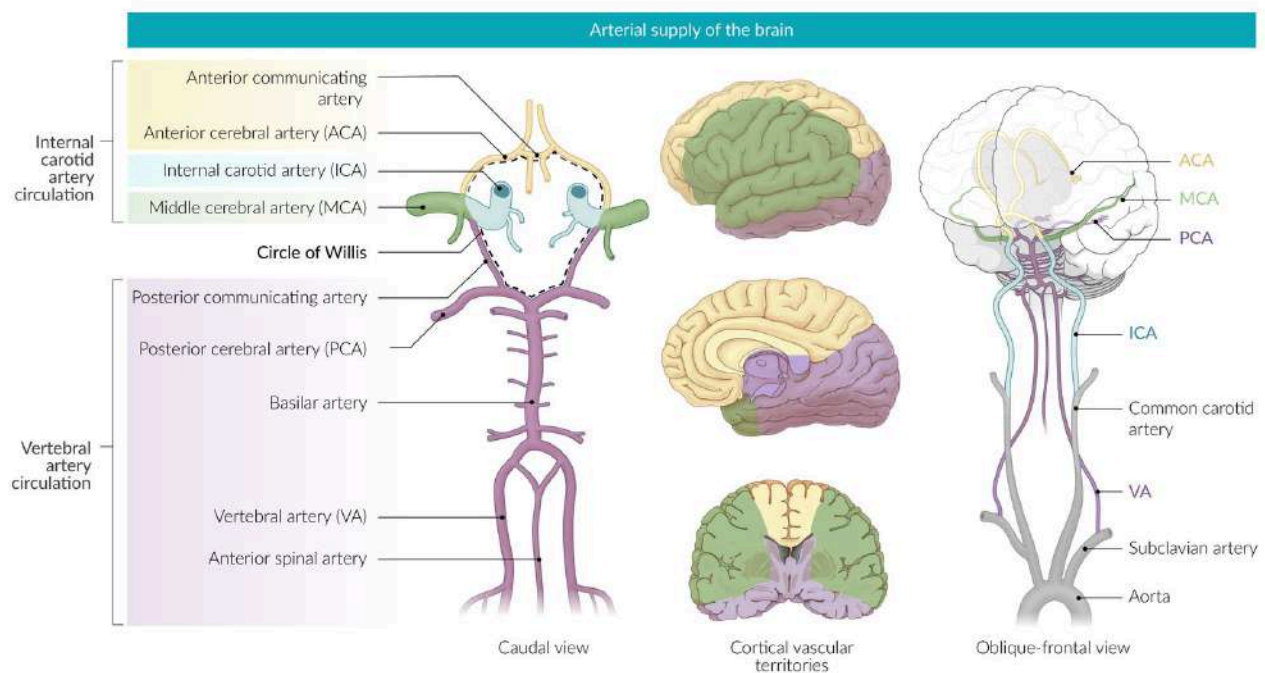
Hint

Sudden onset of urinary incontinence in conjunction with sensory and motor loss predominantly affecting the left lower extremity should raise concern for cortical injury in the region of the anterior cerebral artery.

Correct Answer

A - A

Image



Explanation Why

The right [anterior cerebral artery](#) (structure A) supplies the right anteromedial cortex including the [medial](#) portion of the frontal and [parietal lobes](#). ACA occlusion causes loss of contralateral motor function, particularly of the lower extremities, and contralateral sensory loss. The ACA also supplies the medial frontal micturition center, the part of the brain responsible for [bladder](#) control.

B - B

Explanation Why

The left [anterior cerebral artery](#) (structure B) supplies the left anteromedial cortex including the

[medial](#) portion of the frontal and [parietal lobes](#). Occlusion would cause the symptoms of motor and sensory loss of the lower extremity seen in this patient, albeit on the right (i.e., contralateral) rather than the left side.

C - C

Explanation Why

The right [middle cerebral artery](#) (structure C) supplies the right [lateral](#) cortex including the [temporal lobe](#) and the [lateral](#) portion of the frontal and [parietal lobe](#). Although occlusion of the right [middle cerebral artery](#) can manifest with left-sided sensorimotor deficits, the face and upper extremities are typically affected rather than the lower extremities. Moreover, it also causes gaze deviation and [aphasia](#) (dominant hemisphere) or [hemineglect](#) (non-dominant hemisphere), which are absent in this patient.

D - D

Explanation Why

The left [middle cerebral artery](#) (structure D) supplies the left [lateral](#) cortex including the [temporal lobe](#) and the [lateral](#) portion of the frontal and [parietal lobe](#). Although occlusion of the left [middle cerebral artery](#) can manifest with sensorimotor deficits, symptoms would be expected on the right (i.e., contralateral) rather than the left side. Moreover, unlike this patient, the face and upper extremities are typically affected rather than the lower extremities. Moreover, this patient lacks other features of [MCA](#) occlusion such as gaze deviation and [aphasia](#) (dominant hemisphere) or [hemineglect](#) (non-dominant hemisphere).

E - E

Explanation Why

The right [posterior cerebral artery](#) (structure E) supplies most parts of the right occipital cortex, the posteromedial aspects of the [temporal lobe](#), and the [thalamus](#). Occlusion of the [posterior cerebral artery](#) (PCA) typically manifests with [visual field](#) defects, contralateral hemisensory loss, and

[vertigo](#). Occlusion of the right PCA may also cause visual recognition deficits ([prosopagnosia](#)). Although this patient has left-sided sensory deficits, PCA occlusion would not explain his [hemiparesis](#) or incontinence. He also lacks the visual deficits and [vertigo](#) typically seen in PCA strokes.

F - F

Explanation Why

The left [posterior cerebral artery](#) (structure F) supplies most parts of the left occipital cortex, the posteromedial aspects of the [temporal lobe](#), and the [thalamus](#). Occlusion of the [posterior cerebral artery](#) (PCA) typically manifests with [visual field](#) defects, contralateral hemisensory loss, and [vertigo](#). Occlusion of the PCA can also cause language deficits ([alexia](#), [anomic aphasia](#)). Although this patient does have sensory deficits, a PCA occlusion would not explain his [hemiparesis](#) and incontinence. His symptoms are also left-sided, as opposed to the right-sided deficits expected in an occlusion of the left PCA.

G - G

Explanation Why

The [basilar artery](#) (structure G) is formed by the confluence of the two [vertebral arteries](#) at the central groove of the [pons](#) and supplies the lower half of the [cerebellum](#), the lower [midbrain](#), the lower [pons](#), the medulla, and the corticobulbar and [corticospinal tracts](#). [Basilar artery](#) occlusion can present with [vertigo](#), [tinnitus](#), visual deficits, [gait ataxia](#), and ipsilateral [cranial nerve](#) deficits with [paresthesias](#) and [hemiplegia](#). Rarely, it can cause [locked-in syndrome](#). Although this patient presents with sensorimotor deficits, there is no evidence of [cranial nerve](#) or [cerebellar](#) involvement. Moreover, [basilar artery](#) occlusion would not explain the [urinary incontinence](#) seen in this patient.

Question # 6

A 16-year-old boy with a seizure disorder and cognitive delay is brought to the physician because of progressively worsening right lower extremity weakness for the past 6 months. He does not make eye contact and sits very close to his mother. Physical examination shows a grade 3/6 holosystolic murmur at the cardiac apex. Neurological examination shows decreased strength in the right lower leg with normal strength in the other extremities. Fundoscopic examination shows several multinodular, calcified lesions in the retina bilaterally. A photograph of his skin findings is shown. This patient's condition is most likely due to a mutation in which of the following?



	Answer	Image
A	NF1 gene on chromosome 17	
B	NF2 gene on chromosome 22	
C	GNAQ gene on chromosome 9	

	Answer	Image
D	TSC1 gene on chromosome 9	
E	VHL gene on chromosome 3	

Hint

This patient is presenting with focal neurologic deficits, retinal hamartomas, a murmur consistent with mitral regurgitation, and ash-leaf hypopigmented lesions, all of which are characteristic of tuberous sclerosis.

Correct Answer

A - NF1 gene on chromosome 17

Explanation Why

A mutation in the [NF1 gene](#) on [chromosome 17](#) causes [neurofibromatosis type 1](#). [NF type 1](#) is an [autosomal dominant](#) neurocutaneous syndrome that is characterized by café-au-lait spots, [Lisch nodules](#) (pigmented [iris hamartomas](#)), [neurofibromas](#) (benign peripheral nerve sheath tumors), and optic pathway [gliomas](#). Although this condition has many shared features with [tuberous sclerosis](#), café-au-lait spots are [hyperpigmented](#) whereas [ash-leaf spots](#) are characteristically hypopigmented. Moreover, this patient's abnormal [cardiac examination](#) raises concern for cardiac [rhabdomyoma](#), which is not associated with [neurofibromatosis](#).

B - NF2 gene on chromosome 22

Explanation Why

A mutation in the [NF2 gene](#) on [chromosome 22](#) causes [neurofibromatosis type 2](#). [NF type 2](#) is a hereditary neurocutaneous syndrome that manifests in multiple cerebral and [spinal](#) tumors, such as acoustic [schwannomas](#) (which may be bilateral), [gliomas](#), and [meningiomas](#). This patient has cardiac and dermatologic findings that cannot be accounted for by [neurofibromatosis type 2](#).

C - GNAQ gene on chromosome 9

Explanation Why

A mutation in the [GNAQ gene](#) on [chromosome 9](#) causes [Sturge-Weber syndrome](#). This condition causes vascular [malformations](#) that affect the face, brain, and eyes, manifesting as the characteristic [port-wine stain](#) on the forehead and upper [eyelid](#), along with [seizures](#), intellectual and behavioral problems, and visual defects (episcleral [hemangioma](#), [glaucoma](#)). This patient is lacking the characteristic [port-wine stain](#), making this diagnosis very unlikely. Moreover, this patient's abnormal [cardiac examination](#) raises concern for cardiac [rhabdomyoma](#), which is not associated with this diagnosis.

D - TSC1 gene on chromosome 9

Explanation Why

[Tuberous sclerosis](#) is caused by either a mutation in the [TSC1 gene](#) on [chromosome 9](#) or a [TSC2 gene](#) mutation on [chromosome 16](#), both of which are [tumor suppressor genes](#). This patient presents with several common features of the condition such as cognitive development delay, focal neurological signs (due to [central nervous system hamartomas](#) or [giant cell astrocytomas](#)), and cardiac anomalies (either structural or due to cardiac [rhabdomyoma](#)). Additionally, the image displays one of the classic dermatologic manifestation, [ash-leaf spots](#) (others include [angiofibromas](#), Shagreen spots, and [ungual fibromas](#)).

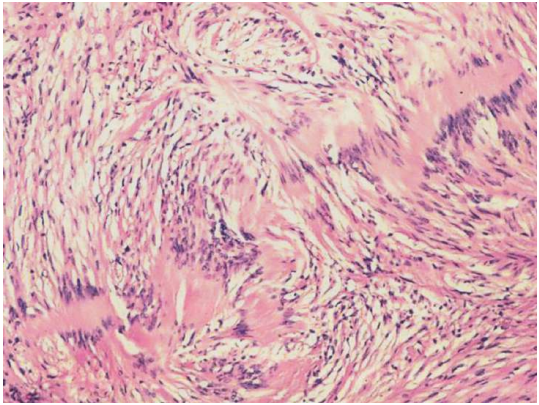
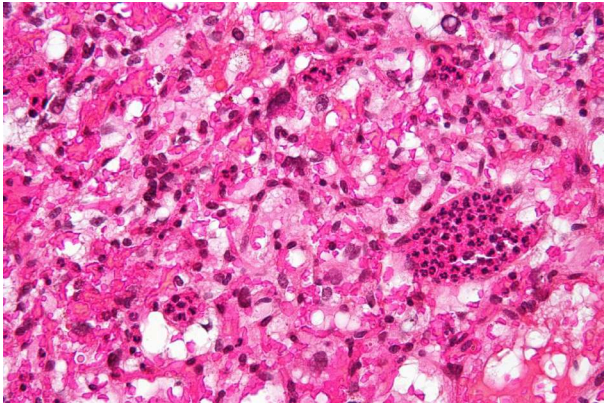
E - VHL gene on chromosome 3

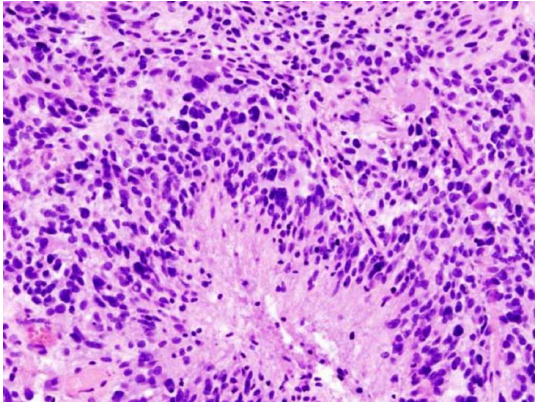
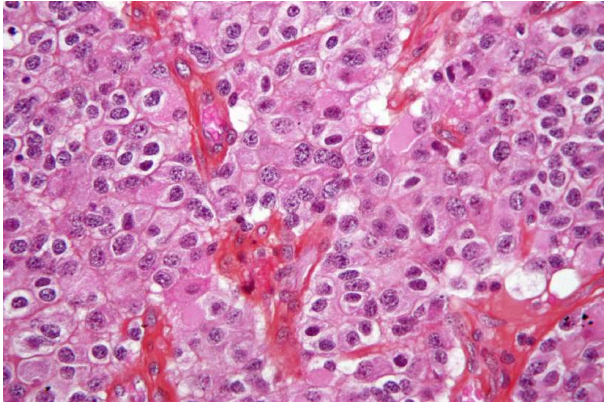
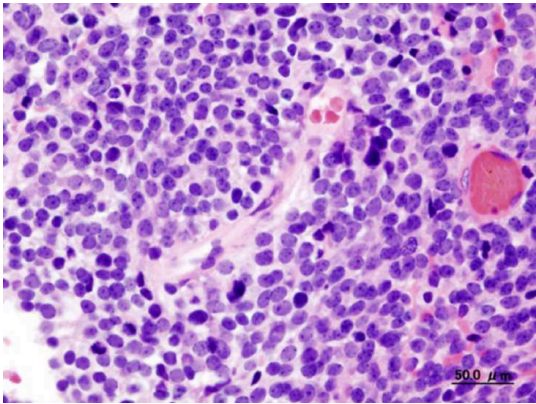
Explanation Why

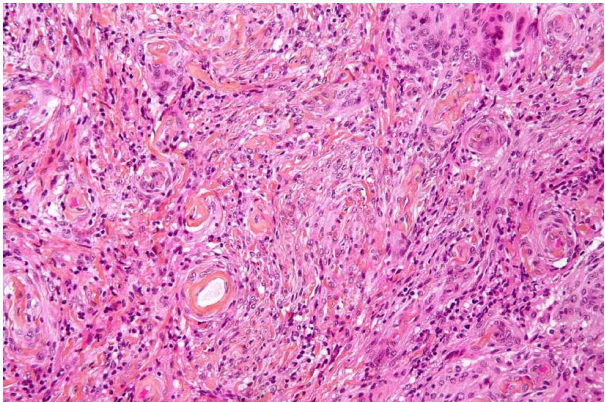
The [VHL gene](#) on [chromosome 3](#) is mutated in [von Hippel-Lindau disease \(VHL\)](#). This condition can also present with retinal growths and focal neurological defects (due to intracranial [neoplastic growths](#)) but would not account for the presence of this patient's [ash-leaf spots](#) or [heart murmur](#) (likely attributable to cardiac [rhabdomyoma](#)). Other expected findings in [VHL](#) include [hemangioblastoma](#), bilateral [renal cell carcinoma](#), and [pheochromocytoma](#).

Question # 7

An otherwise healthy 49-year-old man comes to the physician because of a 1-month history of worsening headaches and increasing irritability. Examination shows bilateral papilledema. An MRI of the brain shows a mass in the right temporal lobe with heterogeneous peripheral rim enhancement that crosses the midline. He undergoes surgical resection of the mass. Gross examination shows a poorly-demarcated mass with areas of hemorrhage and necrosis. Microscopic examination of the mass will most likely show which of the following?

	Answer	Image
A	Spindle cells with hypercellular and hypocellular regions	
B	Closely-packed capillaries and foamy stromal cells	

	Answer	Image
C	Pleomorphic cells forming pseudopalisades	 A histological micrograph showing a dense cluster of cells with varying nuclear sizes and shapes (pleomorphism). The cells are arranged in a pattern that suggests they are pushing against a central area, forming pseudopalisades. The staining is purple (hematoxylin) and pink (eosin).
D	Cells with clear cytoplasm and central round nuclei	 A histological micrograph showing a field of cells. Many cells have a distinct, clear or pale cytoplasm and a centrally located, round nucleus. The overall appearance is characteristic of certain types of epithelial cells, possibly in a glandular or solid growth pattern. The staining is pink (eosin) and purple (hematoxylin).
E	Small blue cells arranged in rosettes	 A histological micrograph showing a dense population of small, round cells with dark blue nuclei. They are arranged in a circular or rosette-like pattern, with some cells pointing towards a central point. A scale bar in the bottom right corner indicates 50.0 μm. The staining is purple (hematoxylin) and pink (eosin).

	Answer	Image
F	Areas of lamellated calcification	

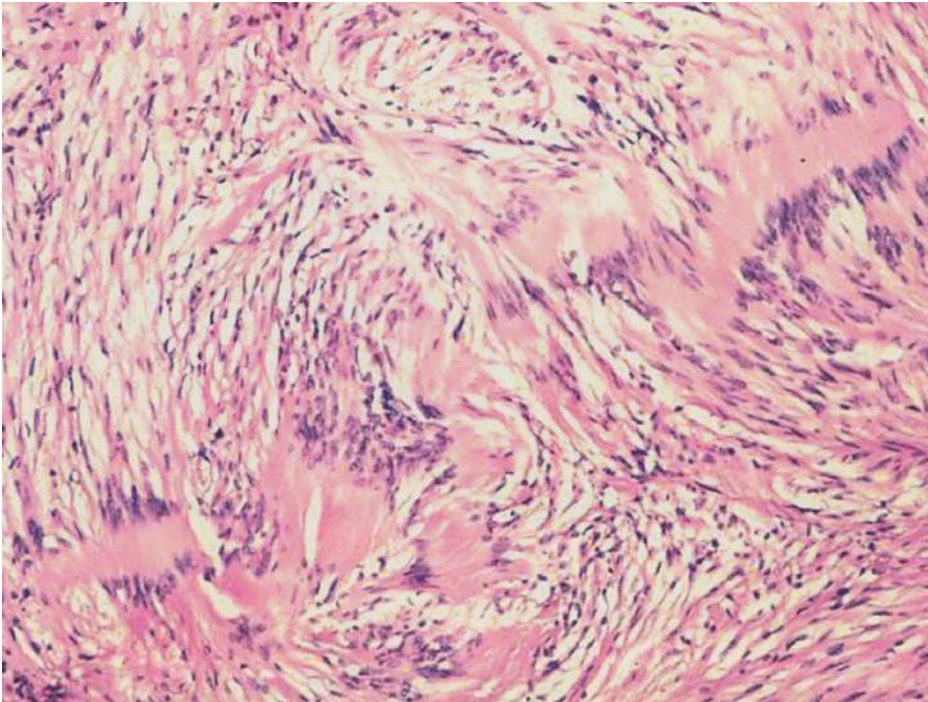
Hint

A brain tumor in the temporal lobe that crosses the midline and displays irregular rim enhancement is suggestive of glioblastoma, the most common type of malignant brain tumor in adults. The gross pathology findings of a poorly-demarcated mass with areas of hemorrhage and necrosis are consistent with this diagnosis.

Correct Answer

A - Spindle cells with hypercellular and hypocellular regions

Image

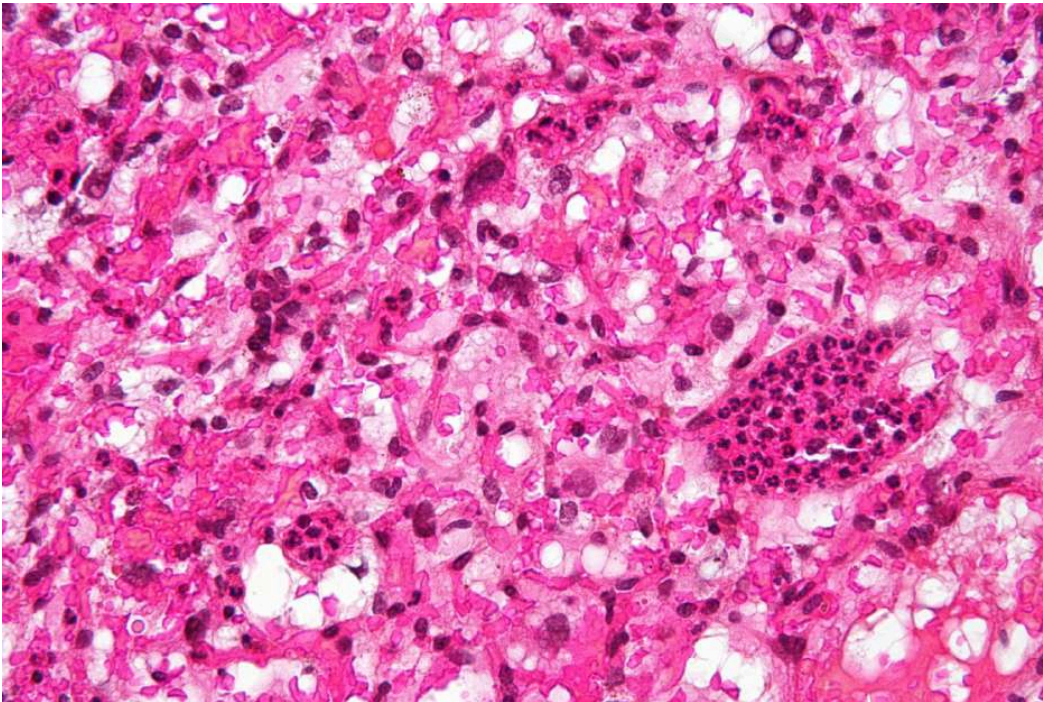


Explanation Why

Spindle cells with hypercellular and hypocellular regions are characteristic of [schwannomas](#). [Schwannomas](#) typically occur at the [cerebellopontine angle](#) and present with lateralized symptoms, especially [vestibulocochlear nerve](#) dysfunction, whereas [headache](#), irritability, and [papilledema](#) are unlikely findings. Moreover, hemorrhage or [necrosis](#) are uncommon, as [schwannomas](#) are slow-growing tumors.

B - Closely-packed capillaries and foamy stromal cells

Image

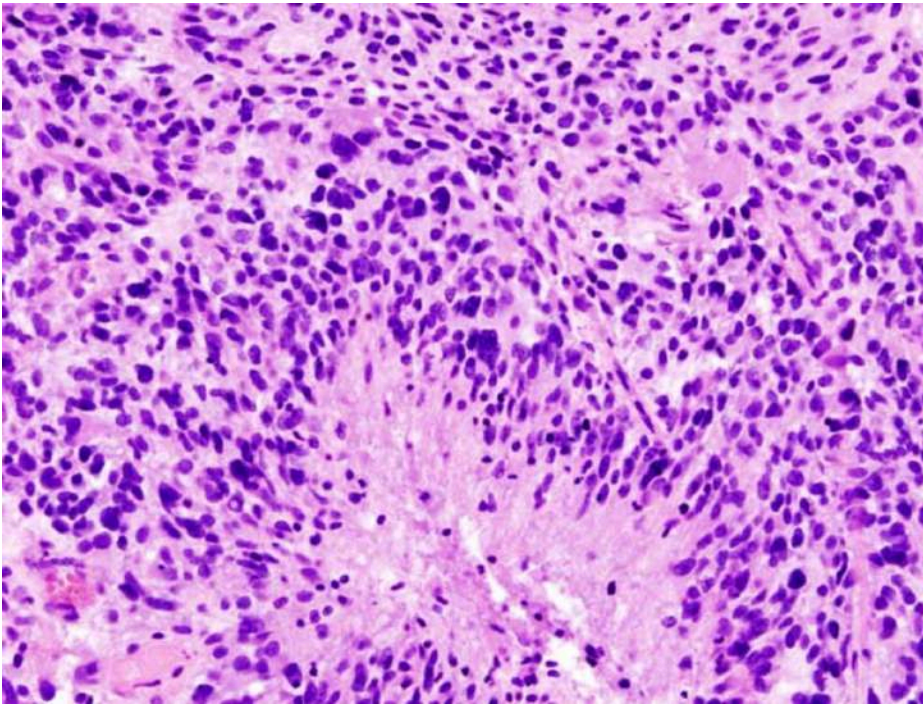


Explanation Why

Closely-packed [capillaries](#) and foamy stromal cells are characteristic of [hemangioblastomas](#), highly vascularized [benign tumors](#) most likely to be found in the [cerebellum](#). They may present in middle age with [papilledema](#), but patients would likely show [cerebellar symptoms](#) or [polycythemia](#) (due to production of erythropoietin). [Headache](#) and irritability as well as findings of hemorrhage and [necrosis](#) would be unlikely in a [hemangioblastoma](#).

C - Pleomorphic cells forming pseudopalisades

Image

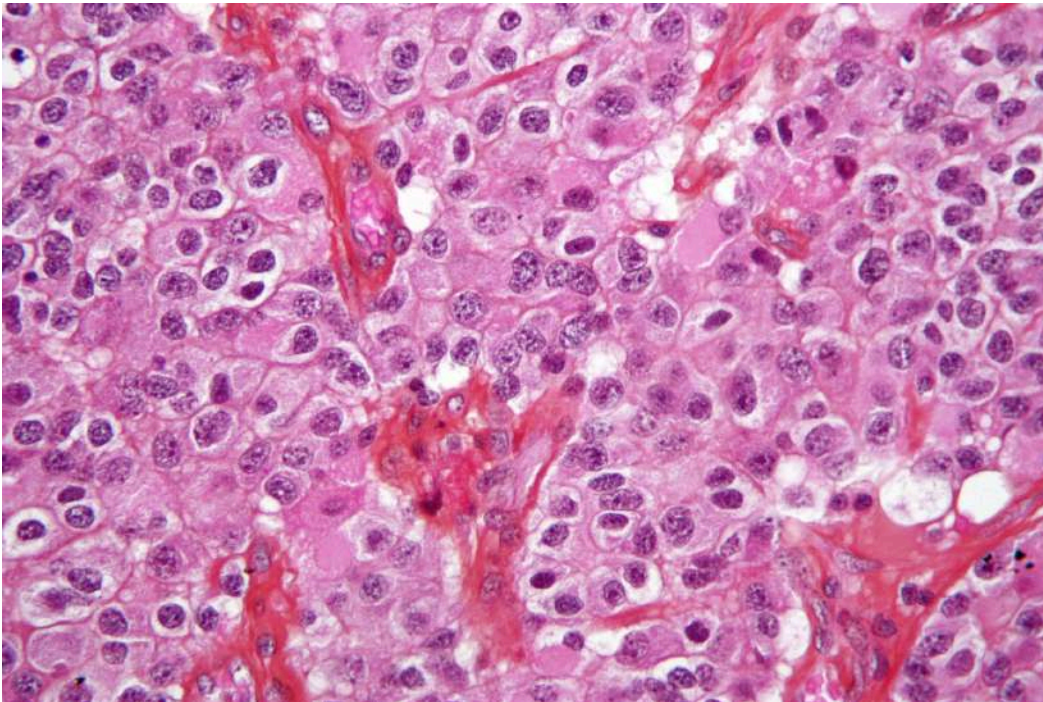


Explanation Why

Pleomorphic cells arranged in pseudopalisades are a hallmark of [glioblastoma multiforme](#), a highly malignant [brain tumor](#) that arises from [astrocytes](#). Pseudopalisades are arrays of [tumor](#) cells migrating away from an area of central [necrosis](#). Histological findings in [glioblastoma multiforme](#) vary greatly but would most likely also show [microvascular proliferation](#) as well as [necrosis](#) and hemorrhage (as already seen on gross examination).

D - Cells with clear cytoplasm and central round nuclei

Image

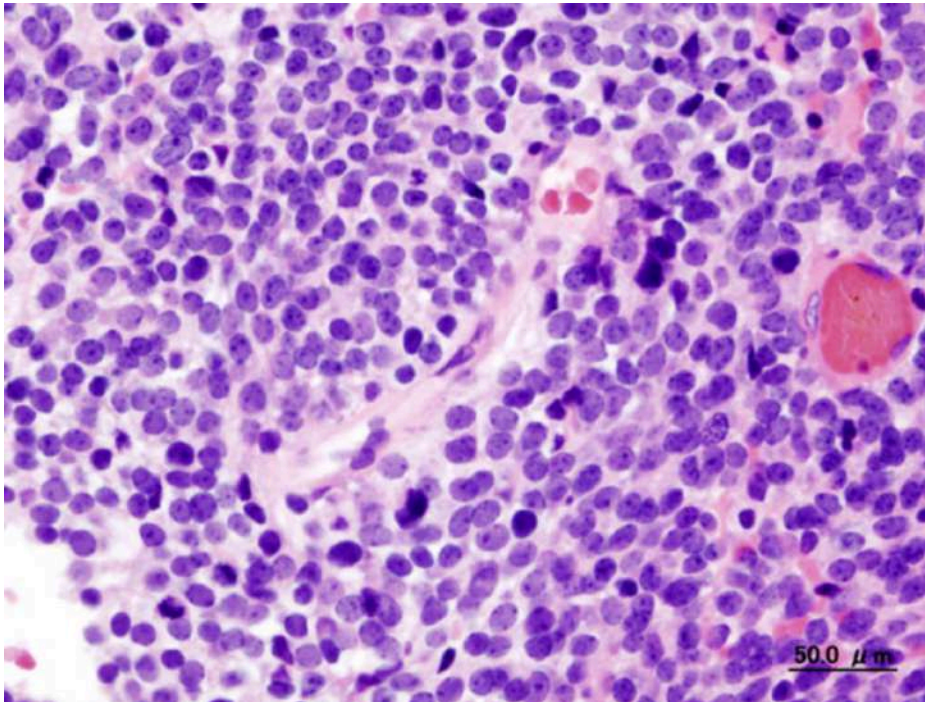


Explanation Why

Cells with clear [cytoplasm](#) and central round nuclei (fried egg appearance) are characteristics of [oligodendrogliomas](#). [Oligodendrogliomas](#) would not be expected to present with bilateral [papilledema](#) but rather with [seizures](#) and sensory deficits. They are slow-growing tumors that usually occur in the [frontal lobe](#) and manifest as well-defined gray masses with areas of calcification; [necrosis](#) would not be expected.

E - Small blue cells arranged in rosettes

Image

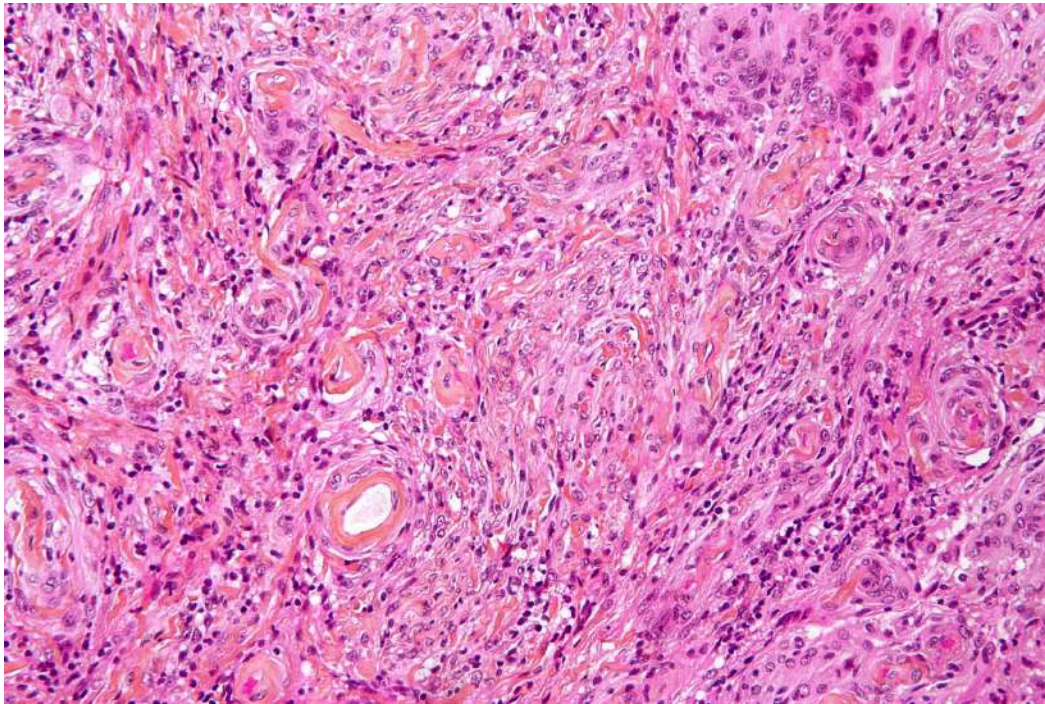


Explanation Why

Small blue cells arranged in rosettes (Homer-Wright rosettes) are characteristic of [medulloblastomas](#). [Medulloblastomas](#) originate from the primitive [neuroectoderm](#) and are the most common malignant [brain tumor](#) in children (peak [incidence](#) 3–5 years). [Medulloblastomas](#) are typically found in the [cerebellum](#), often compress the [4th ventricle](#), and manifests with [hydrocephalus](#) and posterior vermis syndrome. On [MRI](#) they show a diffuse enhancement. The location, clinical presentation, and imaging findings of this adult patient's [tumor](#) are not consistent with [medulloblastoma](#).

F - Areas of lamellated calcification

Image

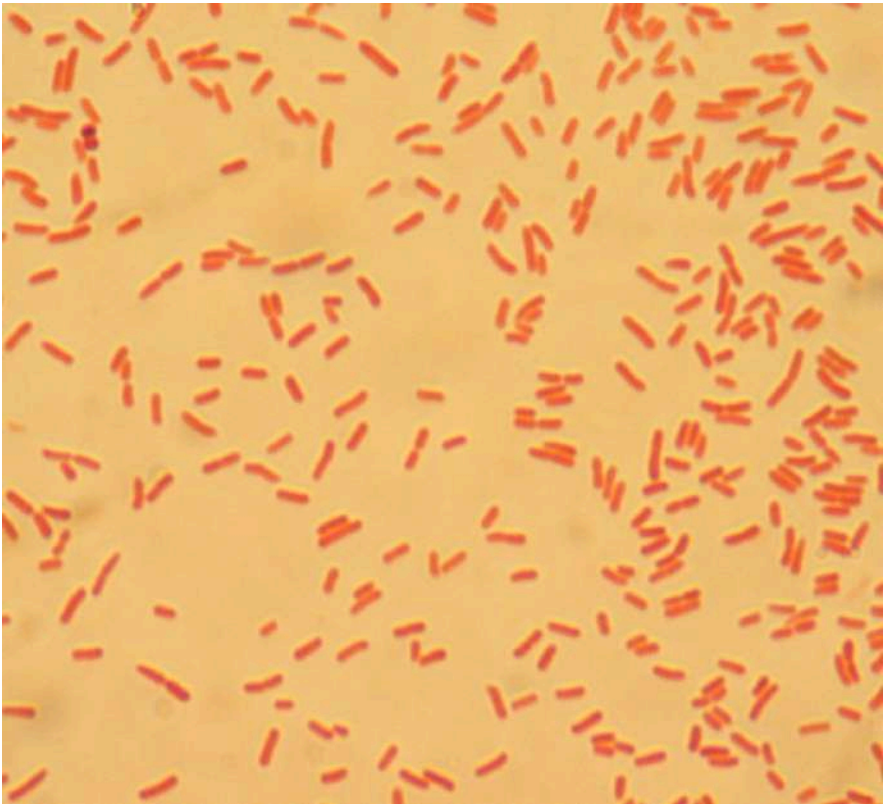


Explanation Why

Areas of lamellated calcification are consistent with [psammoma bodies](#), which are characteristic of [meningioma](#) and other noncerebral tumors. [Meningiomas](#) are composed of spindle cells arranged in a whorled pattern. While they might also show [rim enhancement](#) on [MRI](#), as seen in this patient, [meningiomas](#) usually appear as a homogeneous, well-defined lesion outside the brain without areas of hemorrhage and [necrosis](#).

Question # 8

A 3-day-old boy is brought to the physician by his mother because of irritability and feeding intolerance for 1 day. His temperature is 39.2°C (102.6°F). Physical examination shows a bulging anterior fontanelle. A photomicrograph of a Gram stain of the cerebrospinal fluid is shown. Further evaluation shows that the organism expresses the K1 capsular polysaccharide. Which of the following is the most likely causal pathogen?



	Answer	Image
A	Neisseria meningitidis	
B	Escherichia coli	
C	Listeria monocytogenes	

	Answer	Image
D	<i>Pseudomonas aeruginosa</i>	
E	<i>Salmonella typhi</i>	
F	<i>Haemophilus influenzae</i>	
G	<i>Streptococcus agalactiae</i>	

Hint

Irritability, difficulty feeding, fever, and a bulging anterior fontanelle in a newborn should raise concern for neonatal meningitis. Based on the Gram stain, the causal pathogen is a gram-negative rod.

Correct Answer

A - *Neisseria meningitidis*

Explanation Why

[*Neisseria meningitidis*](#) is one of the most common bacterial causes of [meningitis](#) in the adult and elderly population but is rare in the neonatal period. Moreover, the [Gram stain](#) of this patient's [CSF](#) is inconsistent with [Neisseria](#) species, as they are gram-negative diplococci rather than gram-negative rods. Even though [N. meningitidis](#) does have a capsule that prevents [phagocytosis](#), it does not contain K1 [polysaccharide](#).

B - *Escherichia coli*

Explanation Why

The gram-negative rod [Escherichia coli](#) is one of the most common bacterial causes of [neonatal meningitis](#). In the majority of cases, infection is caused by strains of [E. coli](#) that express the [K1 capsular polysaccharide](#). This [virulence factor](#) provides resistance to [phagocytosis](#) and antibacterial factors in the serum, facilitating the invasion of bacteria. In this patient, [antibiotic](#) treatment with [ampicillin](#) should be initiated as soon as possible.

C - *Listeria monocytogenes*

Explanation Why

[Listeria monocytogenes](#) is one of the most common bacterial causes of [neonatal meningitis](#), particularly in [premature infants](#) with [very low birth weight](#). However, [L. monocytogenes](#) is a gram-positive rod and therefore is not consistent with the organisms revealed by the [Gram stain](#) here. Moreover, important [virulence factors](#) of [L. monocytogenes](#) include [listeriolysin O](#) and actin rockets, but not [K1 capsular polysaccharide](#).

D - *Pseudomonas aeruginosa*

Explanation Why

Pseudomonas aeruginosa is a rare cause of [meningitis](#) in the neonatal period. Although the gram-negative rods found in this patient's [CSF](#) are consistent with *Pseudomonas* species, expression of [K1 capsular polysaccharide](#) would not be expected. Instead, *P. aeruginosa* produces a mucoid [polysaccharide](#) capsule that facilitates adherence to mucoid surfaces while preventing [phagocytosis](#).

E - *Salmonella typhi*

Explanation Why

Salmonella typhi is an encapsulated, gram-negative rod that is consistent with the [Gram stain](#) here. However, infection with *S. typhi* is associated with [typhoid fever](#) rather than [neonatal meningitis](#). [Typhoid fever](#) progresses from gradually rising body temperature and bowel abnormalities to persistent [fever](#) with [rose-colored](#) spots, yellow-green [diarrhea](#), the characteristic [typhoid tongue](#), and neurological symptoms. Moreover, *S. typhi* produces Vi capsular polysaccharide, not [K1 capsular polysaccharide](#).

F - *Haemophilus influenzae*

Explanation Why

Haemophilus influenzae is a rare cause of [meningitis](#) in the immediate neonatal period. While this organism is encapsulated, [Gram stain](#) would reveal gram-negative coccobacilli rather than the gram-negative rods seen in this patient.

G - Streptococcus agalactiae

Image



Explanation Why

Streptococcus agalactiae belongs to the family of [group B streptococci](#), which are the most common cause of [neonatal meningitis](#). However, *S. agalactiae* is a gram-positive coccus and therefore is not consistent with the organisms revealed by the [Gram stain](#) here. Although *S. agalactiae* does exhibit a protective capsule that functions as a [virulence factor](#), [K1 capsular polysaccharides](#) are not associated with it.

Question # 9

A 56-year-old man comes to the physician for a follow-up examination. One month ago, he was diagnosed with a focal seizure and treatment with a drug that blocks voltage-gated sodium channels was begun. Today, he reports that he has not had any abnormal body movements, but he has noticed occasional double vision. His serum sodium is 132 mEq/L, alanine aminotransferase is 49 U/L, and aspartate aminotransferase is 46 U/L. This patient has most likely been taking which of the following drugs?

	Answer	Image
A	Carbamazepine	
B	Ethosuximide	
C	Levetiracetam	
D	Gabapentin	
E	Phenytoin	
F	Lamotrigine	
G	Topiramate	

Hint

This drug is also the treatment of choice for trigeminal neuralgia.

Correct Answer

A - Carbamazepine

Explanation But

Blockage of voltage-gated sodium channels is also the mechanism of action of other [anti-epileptic](#) drugs, including [valproic acid](#), [lamotrigine](#), and [topiramate](#).

Explanation Why

[Carbamazepine](#) blocks voltage-gated sodium channels in neuronal membranes, which increases the [seizure](#) threshold and lowers neuronal excitability. [Carbamazepine](#) is commonly used as first-line treatment for [focal seizures](#) but is associated with a multitude of side effects, including [diplopia](#), hepatotoxicity, and [hyponatremia](#) (probably due to associated [SIADH](#)), all of which are seen in this patient. Other possible side effects include [Stevens-Johnson syndrome](#), [ataxia](#), [CYP-450](#) induction, and blood count abnormalities ([agranulocytosis](#), [aplastic anemia](#)).

B - Ethosuximide

Explanation Why

[Ethosuximide](#) acts by inhibiting voltage-gated calcium channels in thalamic [neurons](#) and subsequently reducing neuronal excitability. Since [ethosuximide](#) is used only to treat [absence seizures](#), administration would not be indicated in this patient. Moreover, side effects such as [diplopia](#) and [hyponatremia](#) would not be expected. [Ethosuximide](#) is rather associated with allergic [skin](#) reactions and nonspecific GI symptoms.

C - Levetiracetam

Explanation Why

[Levetiracetam](#) is a relatively new [antiepileptic drug](#) with a mechanism of action that is not yet

entirely understood. However, modulation of [GABA](#) receptors increased [glutamate](#) release, and inhibition of calcium channels have been implicated. Although [levetiracetam](#) is used as first-line treatment for [focal seizures](#), side effects such as [diplopia](#) and [hyponatremia](#) would not be expected. [Levetiracetam](#) is rather associated with neuropsychiatric disturbances.

D - Gabapentin

Explanation Why

[Gabapentin](#), most commonly administered for [neuropathic pain](#), may also be used as second-line agent for [focal seizures](#). However, it does not block voltage-gated sodium channels, instead inhibiting voltage-gated calcium channels. Moreover, the side effect profile of [gabapentin](#) does not match this patient's presentation; [gabapentin](#) is associated with [ataxia](#), dry mouth, and [somnolence](#), not [hyponatremia](#) and [diplopia](#).

E - Phenytoin

Explanation Why

[Phenytoin](#) acts by inhibiting voltage-gated sodium channels but is primarily used as first-line treatment for [tonic-clonic seizures](#) and [status epilepticus](#). Long-term administration for [focal seizures](#) is usually avoided due to its wide variety of possible side effects, including gingival hyperplasia and [hirsutism](#). [Diplopia](#), which is seen in this patient, may also occur but usually indicates toxicity and is therefore not a mere side effect. Furthermore, [hyponatremia](#) seen in this patient would not be expected.

F - Lamotrigine

Explanation Why

[Lamotrigine](#) acts by inhibiting voltage-gated sodium channels and is commonly used as a first-line treatment for [focal seizures](#). It can also cause [hyponatremia](#) and [diplopia](#). However, [diplopia](#) and [hyponatremia](#) occur extremely rarely and are, typically, associated with a rapid dose escalation, acute toxicity, or coadministration of this drug with [carbamazepine](#); all of which, are not seen here.

Moreover, [lamotrigine](#) is more often associated with dermatologic side effects (ranging from mild exanthema to [Stevens-Johnson syndrome](#)), [insomnia](#), [dyspepsia](#), and rarely, [nephrotoxicity](#) or hepatotoxicity.

G - Topiramate

Explanation Why

[Topiramate](#) can be used for [focal seizures](#) and exerts its [antiepileptic](#) properties both through blockage of voltage-gated sodium channels and increasing [GABA](#) action on neuronal cells. Even though this patient's [diplopia](#) could be a sign of new-onset [glaucoma](#), which is in fact associated with [topiramate](#) treatment, [hyponatremia](#) and elevated [transaminases](#) would not be expected.

Question # 10

A 28-year-old man is admitted to the hospital for the evaluation of symmetric, ascending weakness that started in his feet and has become progressively worse over the past 5 days. A lumbar puncture is performed to confirm the diagnosis. As the needle is advanced during the procedure, there is resistance just before entering the epidural space. This resistance is most likely due to which of the following structures?

	Answer	Image
A	Ligamentum flavum	
B	Superficial fascia	
C	Interspinous ligament	
D	Dura mater	
E	Supraspinous ligament	

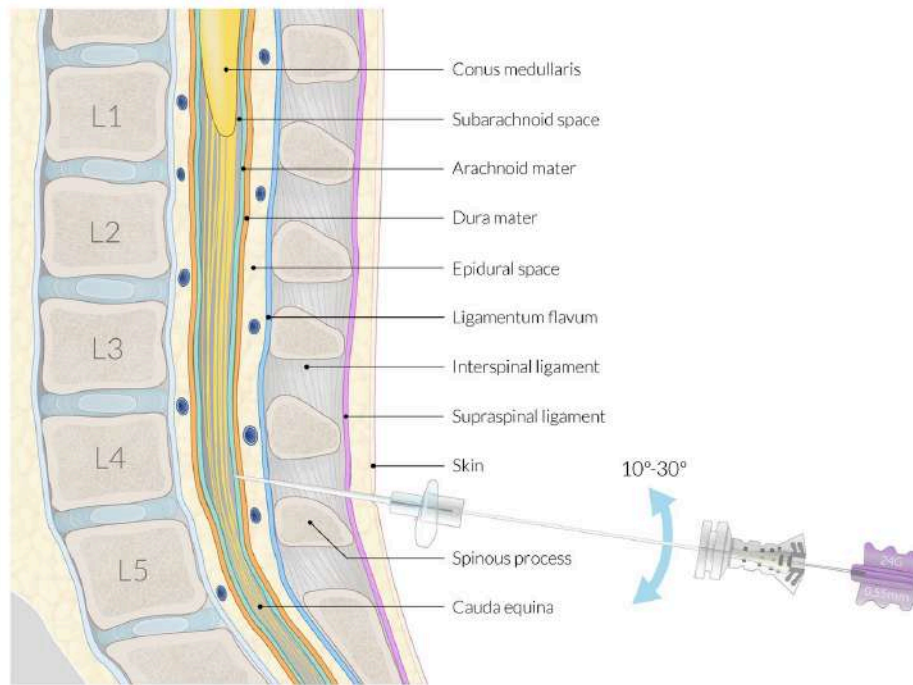
Hint

This patient's ascending flaccid paralysis suggests Guillain-Barré syndrome. The epidural space lies outside of the dura mater and contains lymphatic vessels, small arteries, spinal nerve roots, and the vertebral venous plexus, which are surrounded by connective and fatty tissue.

Correct Answer

A - Ligamentum flavum

Image



Explanation Why

The [ligamentum flavum](#) forms the [posterior](#) boundary of the [epidural space](#). As the needle is advanced during [lumbar puncture](#), there are several points of noticeable resistance. The layers encountered from [posterior](#) to [anterior](#) are the [skin](#), [fascia](#), and [subcutaneous fat](#), [supraspinous ligament](#) (first point of resistance), [interspinous ligament](#), [ligamentum flavum](#) (second point of resistance), [epidural space](#), and then the [dura](#) (third point of resistance; loss of resistance indicates entry into the [subarachnoid space](#), where the [CSF](#) is). The last point of resistance before entering the [epidural space](#) is, therefore, the [ligamentum flavum](#).

B - Superficial fascia

Explanation Why

The [superficial fascia](#) is a thin layer underneath the [dermis](#) that consists of [loose connective tissue](#) and fat. It would be the second layer after puncturing the [skin](#) in a [lumbar puncture](#). It is [posterior](#) to another structure that protects the [epidural space](#) and offers resistance during a [lumbar puncture](#).

C - Interspinous ligament

Explanation Why

The [interspinous ligaments](#) are membranous [ligaments](#) that connect adjoining [spinous processes](#) of the [vertebrae](#). In a [lumbar puncture](#), the needle hits this [ligament](#) as it passes the [spinous process](#). It is therefore [posterior](#) to another structure that directly abuts the [epidural space](#).

D - Dura mater

Explanation Why

The [dura mater](#) is a thick membrane that forms the dural sac, which contains the [spinal cord](#) and [CSF](#). In a [lumbar puncture](#), it is the last layer that is encountered by the needle after it passes through the [epidural space](#). It is therefore [anterior](#) to the structure that offers resistance before entering the [epidural space](#).

E - Supraspinous ligament

Explanation Why

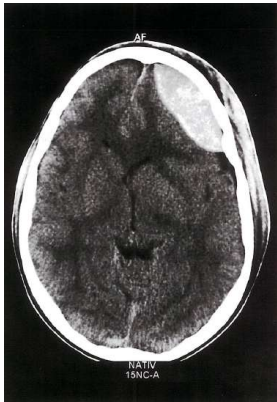
The [supraspinous ligament](#) runs [dorsal](#) to the thoracic and lumbar [vertebral column](#) and connects the [spinous processes](#) of the last [cervical vertebra](#) to the [sacrum](#). In a [lumbar puncture](#), the [supraspinous ligament](#) is the first point of resistance after the needle passes the [skin](#) and [subcutaneous tissue](#). The [supraspinous ligament](#), therefore, lies [posterior](#) to another structure that protects the [epidural space](#) and offers resistance during a [lumbar puncture](#).

Question # 11

A 54-year-old man is brought to the emergency department 30 minutes after being hit by a car while crossing the street. He had a left-sided tonic-clonic seizure and one episode of vomiting while being transported to the hospital. On arrival, he is not oriented to person, place, or time. Physical examination shows flaccid paralysis of all extremities. A CT scan of the head is shown. This patient's symptoms are most likely the result of a hemorrhage in which of the following structures?



	Answer	Image
A	Into the ventricular system	

	Answer	Image
B	Between the dura mater and the arachnoid mater	
C	Between the skull and the dura mater	
D	Into the cerebral parenchyma	

	Answer	Image
E	Between the arachnoid mater and the pia mater	Middle cerebral artery Pia mater Aneurysm Subarachnoid space Arachnoid mater Dura mater

Hint

This type of intracranial hemorrhage can also occur in the absence of trauma in individuals with ruptured saccular aneurysms.

Correct Answer

A - Into the ventricular system

Image



Explanation Why

[Intraventricular hemorrhage](#) typically occurs secondary to intracerebral or [subarachnoid hemorrhage](#) but can arise from rare vascular [malformations](#). As with other [intracranial bleeds](#), the characteristic presentation involves sudden onset of [headache](#), vomiting, and altered [level of consciousness](#). However, imaging of the head would show accumulation of blood within the [ventricular system](#), which is not seen on this patient's head CT.

B - Between the dura mater and the arachnoid mater

Image

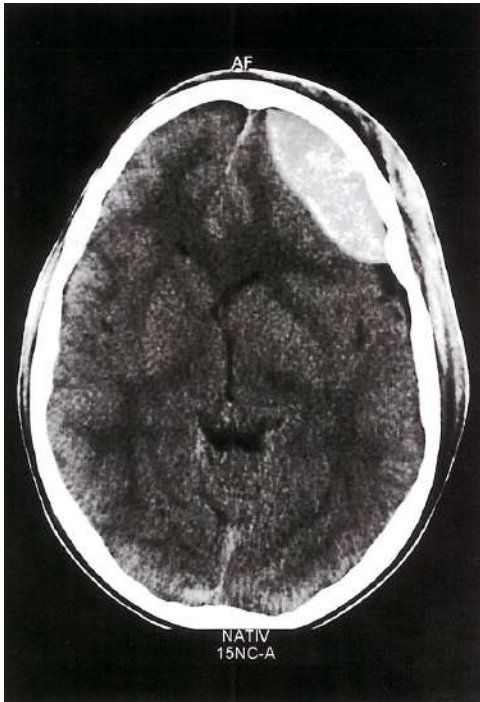


Explanation Why

Shearing of [bridging veins](#) causes [subdural hemorrhage](#), which is characterized by bleeding between the [dura mater](#) and [arachnoid mater](#). Patients may present with [headache](#) and signs of [increased ICP](#) immediately following [head trauma](#), as is the case here. However, head CT would show a high-density crescent-shaped collection (in acute cases) or a [hypodense](#) crescent-shaped collection (in chronic and subacute cases) across the hemispheric convexity, which crosses the suture lines.

C - Between the skull and the dura mater

Image



Explanation Why

Bleeding between the [dura mater](#) and the [skull](#) is known as [epidural hemorrhage](#) and is often due to traumatic injury to the [middle meningeal artery](#). [Epidural hemorrhage](#) should be suspected in any patient with [head trauma](#) that causes loss of consciousness, followed by a [lucid interval](#), and subsequent worsening with [signs of increased ICP](#). [CT scan](#) of the head would show a characteristic lentiform ([lens](#)-shaped) hemorrhagic collection that does not cross suture lines. While this patient does have [signs of increased ICP](#) following a trauma, his CT findings suggest a different diagnosis.

D - Into the cerebral parenchyma

Image

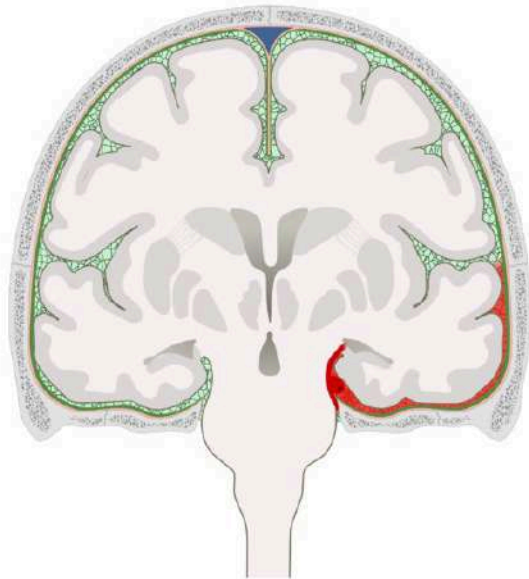


Explanation Why

Bleeding directly into the cerebral parenchyma, known as [intracerebral hemorrhage](#), is typically caused by a spontaneous rupture of vessels secondary to structural changes of the vessel walls (e.g., chronic [hypertension](#), [cerebral amyloid angiopathy](#)). Patients often present with [headache](#) and focal neurologic deficits such as [hemiparesis](#). However, [head trauma](#) rarely leads to [intracerebral hemorrhage](#), and [signs of increased ICP](#) are uncommon. Moreover, this patient's head CT is not consistent with [intracerebral hemorrhage](#).

E - Between the arachnoid mater and the pia mater

Image



Middle cerebral artery

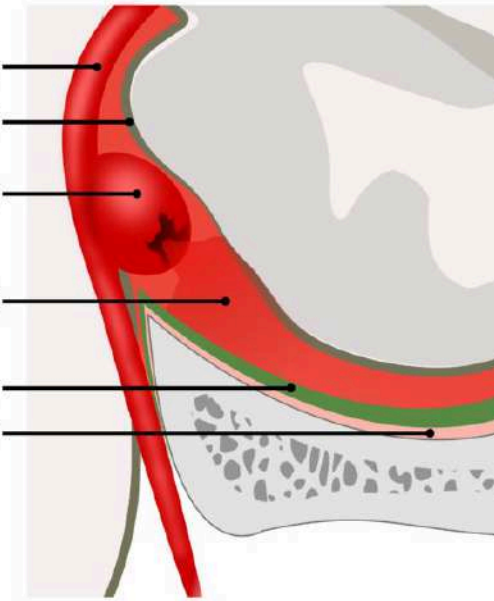
Pia mater

Aneurysm

Subarachnoid space

Arachnoid mater

Dura mater

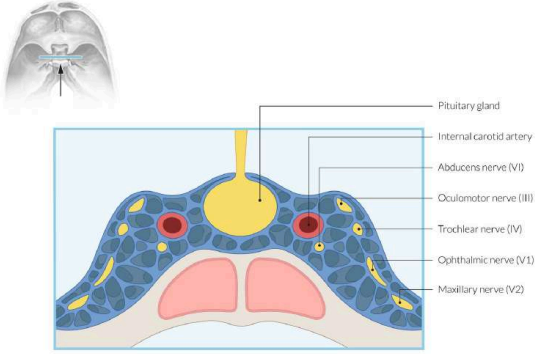


Explanation Why

[Traumatic brain injury](#) can cause [subarachnoid hemorrhage](#), which is characterized by bleeding between the [arachnoid mater](#) and [pia mater](#). Patients classically present with a sudden, severely painful [headache](#), vomiting, loss of consciousness, and, in cases of severe hemorrhage, [seizures](#). Head CT shows [hyperdense](#) signals in the area of the hemorrhage, which are seen in the [basal cistern](#) in this patient.

Question # 12

A 60-year-old man comes to the physician because his wife has noticed that his left eye looks smaller than his right. He has had worsening left shoulder and arm pain for 3 months. He has smoked two packs of cigarettes daily for 35 years. Examination shows left-sided ptosis. The pupils are unequal but reactive to light; when measured in dim light, the left pupil is 3 mm and the right pupil is 5 mm. Which of the following is the most likely cause of this patient's ophthalmologic symptoms?

	Answer	Image
A	Thrombosis of the cavernous sinus	
B	Aneurysm of the posterior cerebral artery	
C	Infarction of the hypothalamus	
D	Dissection of the carotid artery	

	Answer	Image
E	Compression of the stellate ganglion	The diagram illustrates the sympathetic innervation of the head and neck. The first neuron (central) originates in the hypothalamus and descends through the brainstem and spinal cord. The second neuron (preganglionic) exits the spinal cord and enters the superior cervical ganglion. The third neuron (postganglionic) then branches out to innervate various structures, including the sweat glands of the face, the iris dilator muscle, and the superior tarsal muscle. The internal and external carotid arteries are also shown. A legend identifies the first neuron as central, the second as preganglionic, and the third as postganglionic. An inset shows the eye with labels for the superior tarsal muscle, iris dilator muscle, and ophthalmic division of the trigeminal nerve. Another inset shows a face with symptoms of Horner Syndrome: ptosis, miosis, and anhidrosis/hyperemia.
F	Infiltration of the cervical plexus	

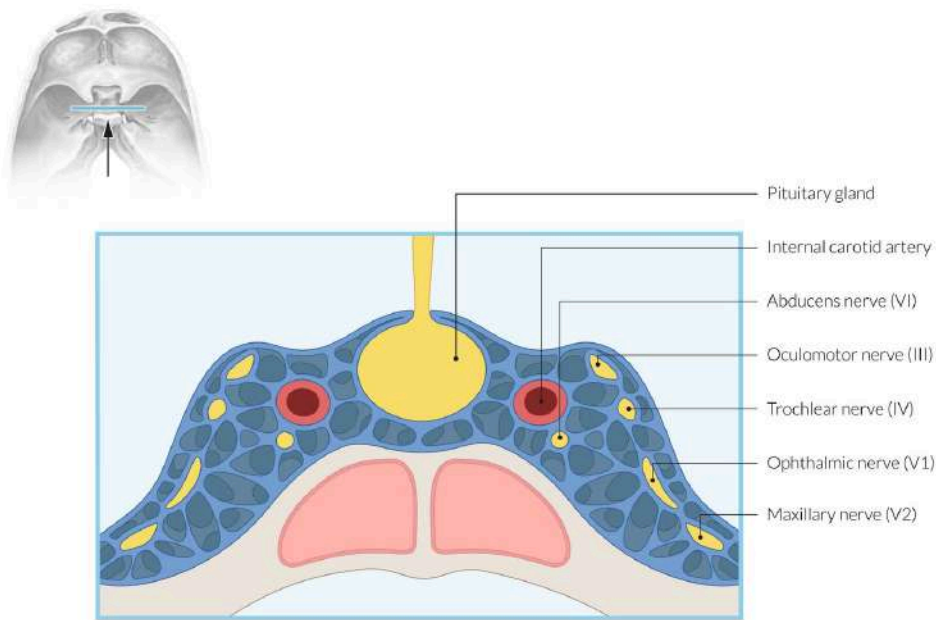
Hint

Horner syndrome (HS) is a neurological disorder characterized by a symptom triad of miosis, partial ptosis, and facial anhidrosis, of which this patient has the former two symptoms. In a heavy smoker, symptoms of Horner syndrome combined with ipsilateral shoulder and arm pain are concerning for a Pancoast tumor.

Correct Answer

A - Thrombosis of the cavernous sinus

Image



Explanation Why

[Cavernous sinus thrombosis](#) can result in [Horner syndrome](#) due to compression of [postganglionic sympathetic neurons](#). However, [cavernous sinus thrombosis](#) has additional symptoms that are not present in this case, such as [headache](#), photophobia, [proptosis](#), and other [cranial nerve palsies](#) (commonly [CN VI](#)). In addition, [cavernous sinus thrombosis](#) is most commonly caused by an ascending infection from the face or sinuses, signs of which are not present here. This patient's arm and shoulder [pain](#) would likewise not be explained by [cavernous sinus thrombosis](#).

B - Aneurysm of the posterior cerebral artery

Explanation Why

[Aneurysm](#) of the [posterior cerebral artery](#) could compress [CN III](#), which carries [parasympathetic](#) fibers to the [pupillary sphincter](#) and [ciliary muscle](#), and motor fibers to the levator palpebrae superioris and all [extraocular muscles](#) except for the [superior oblique muscle](#) and the [lateral rectus muscle](#). Such an [aneurysm](#) would result in [ptosis](#), which this patient has, as well as [diplopia](#), a fixed and dilated pupil, and a down-and-out gaze, which are not present here. Rather than [mydriasis](#), this patient has [miosis](#). Furthermore, if such an [aneurysm](#) were symptomatic, it would manifest with [headache](#) rather than the shoulder and arm [pain](#) seen here.

C - Infarction of the hypothalamus

Explanation Why

[Infarction](#) of the [hypothalamus](#) is a rare cause of [Horner syndrome](#) secondary to injury of centrally located [sympathetic neurons](#). This patient's smoking history is a [risk factor](#) for [stroke](#), including [infarction](#) of the [hypothalamus](#). However, an [infarction](#) of the [hypothalamus](#) would likely manifest with additional [stroke](#) symptoms, typically contralateral [hemiparesis](#) and [hypesthesia](#), as well as impeded homeostatic functions of the [hypothalamus](#) (e.g., thermoregulation, electrolyte balance, sleep-wake cycle). Furthermore, [infarction](#) of the [hypothalamus](#) would not explain this patient's shoulder and arm [pain](#).

D - Dissection of the carotid artery

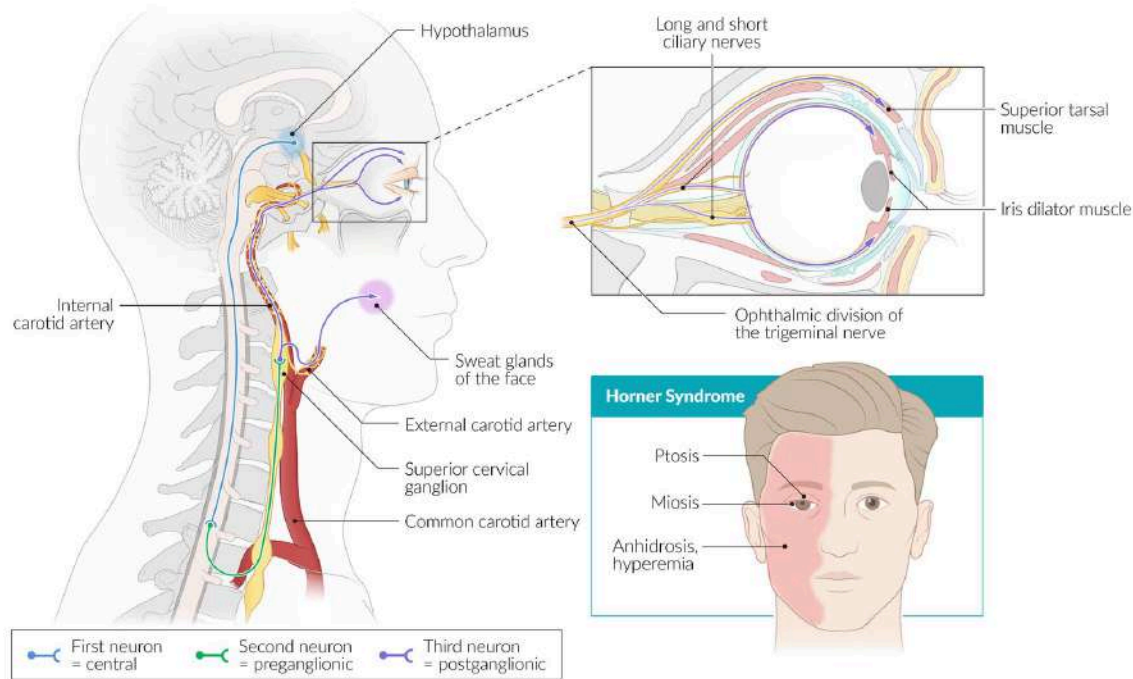
Explanation Why

[Carotid artery dissection](#) can cause [Horner syndrome](#) by compressing the [postganglionic sympathetic](#) fibers near the [internal carotid artery](#) and damaging them directly or decreasing blood flow to their vasa nervorum. This patient's smoking history is a [risk factor](#) for [carotid artery dissection](#). However, [carotid artery dissection](#) most often has an acute onset of symptoms following some types of trauma (e.g., [blunt trauma](#)), which is not the case here. Furthermore, in addition to [Horner syndrome](#), [carotid artery dissection](#) would manifest with [headache](#) and/or neck [pain](#), while this patient has shoulder and

arm [pain](#).

E - Compression of the stellate ganglion

Image



Explanation Why

Compression of the [stellate ganglion](#) by a [Pancoast tumor](#) can lead to [Horner syndrome](#) via injury of [preganglionic sympathetic](#) fibers. [Superior sulcus tumors](#) can infiltrate neighboring structures and cause additional symptoms, which is known as [Pancoast syndrome](#). This patient's shoulder and arm [pain](#) are likely symptoms of [Pancoast syndrome](#), which also includes [atrophy](#) of the arm and hand muscles, and possibly [superior vena cava syndrome](#) and hoarseness due to compression of the [recurrent laryngeal nerve](#). The most common cause of [Pancoast syndrome](#) is [NSCLC](#), for which this patient is at risk because of his history of smoking.

F - Infiltration of the cervical plexus

Explanation Why

Infiltration of the [cervical plexus](#), typically by neck soft tissue tumors or [lymph node metastases](#), manifests with [pain](#) in the neck and submandibular area, as well as sensory loss in the C2, C3, and C4 [dermatomes](#), symptoms which this patient does not have. It would not be expected to cause [Horner syndrome](#) or shoulder and arm [pain](#).

Question # 13

A 4-year-old boy is brought to the physician by his mother because of left-sided neck swelling that has slowly progressed over the past 4 weeks. He has no history of serious illness. Temperature is 38°C (100.4°F). Physical examination shows a non-tender, mobile mass in the left submandibular region with overlying erythema. A biopsy of the mass shows caseating granulomas. Pharmacotherapy with azithromycin and ethambutol is initiated. This patient is most likely to experience which of the following adverse effects related to ethambutol use?

	Answer	Image
A	Orange urine	
B	Acute kidney injury	
C	Color blindness	
D	Methemoglobinemia	
E	Peripheral neuropathy	

Hint

This patient's unilateral, non-tender submandibular lymphadenitis and fever are most likely due to an infection with nontuberculous mycobacteria (NTM), which is supported by biopsy findings of caseating granulomas. Ethambutol works by inhibiting arabinosyltransferase.

Correct Answer

A - Orange urine

Explanation Why

[Rifampin](#) is an [antibiotic](#) commonly used to treat [tuberculosis](#) that obstructs bacterial [protein synthesis](#) by preventing [transcription](#). Adverse effects include [flu-like](#) symptoms, hepatotoxicity, and a characteristic orange discoloration of body fluids (e.g., [urine](#), tears). [Ethambutol](#) does not lead to orange discoloration of [urine](#).

B - Acute kidney injury

Explanation Why

Many medications can cause [acute kidney injury](#), including, in rare cases, [ethambutol](#). However, this side effect would be more likely with [streptomycin](#), an [aminoglycoside](#) that can be used for [mycobacterial](#) infections that works by inhibiting bacterial [protein synthesis](#) and damaging the [bacterial cell wall](#). Additional adverse effects of [streptomycin](#) include ototoxicity, neuromuscular blockade ([ataxia](#)), and [nephrotoxicity](#). [Ethambutol](#) is more likely to cause another side effect.

C - Color blindness

Explanation Why

[Ethambutol](#) inhibits [arabinosyltransferase](#), an enzyme involved in the polymerization and subsequent synthesis of [mycobacterial](#) cell walls. Adverse effects include [optic neuritis](#) and [retrobulbar neuritis](#), which can manifest with blurred vision, decreased visual acuity, and red-green [color blindness](#). The mechanism of [ethambutol](#)-induced [optic neuritis](#) is not known but there is a dose-dependent [correlation](#) in risk of occurrence.

D - Methemoglobinemia

Explanation Why

[Methemoglobinemia](#) is a potential serious adverse effect of [dapson](#), an [antibiotic](#) that can be used for the treatment of [Mycobacterium leprae](#) infection (e.g. [leprosy](#)). [Ethambutol](#) is not known to cause [methemoglobinemia](#).

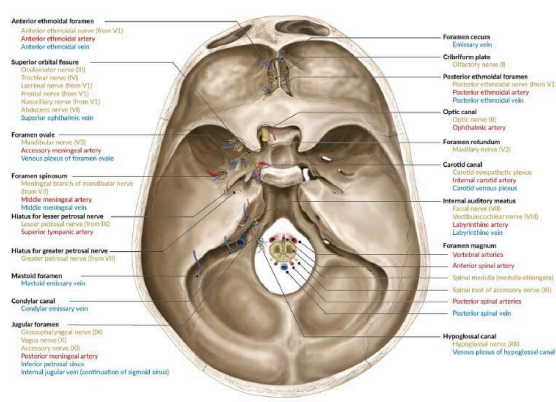
E - Peripheral neuropathy

Explanation Why

[Peripheral neuropathy](#) is commonly observed with isoniazid, a prodrug activated by bacterial [catalase-peroxidase](#) that inhibits [mycolic acid](#) synthesis, a vital component of [mycobacterial](#) cell walls ([bactericidal](#)). It is used mainly to treat [tuberculosis](#). Adverse effects include [vitamin B6](#) deficiency (a [cofactor](#) in the biosynthesis of important [neurotransmitters](#)), which can lead to [peripheral neuropathy](#). [Peripheral neuropathy](#) is not a known adverse effect of [ethambutol](#).

Question # 14

A 28-year-old man is brought to the emergency department by ambulance after being hit in the head with a baseball bat. Physical examination shows swelling and bruising around the left temple and eye. A CT scan of the head shows a transverse fracture through the sphenoid bone and blood in the sphenoid sinus. Neurological examination is most likely to show which of the following findings?

	Answer	Image
A	Left homonymous hemianopia	
B	Inward deviation of the left eye	 The diagram illustrates the base of the skull from an inferior perspective, highlighting various foramina and the structures passing through them. Labels include: Anterior ethmoidal foramen: Anterior ethmoidal nerve (from V1), Anterior ethmoidal artery, Anterior ethmoidal vein. Superior orbital foramen: Oculomotor nerve (III), Trochlear nerve (IV), Lacrimal nerve (from V1), Maxillary nerve (from V2), Abducent nerve (VI), Superior ophthalmic vein. Foramen ovale: Mandibular nerve (V3), Accessory meningeal artery, Venous plexus of foramen ovale. Foramen spinosum: Middle meningeal artery (from V3), Middle meningeal vein. Histia for lesser petrosal nerve: Lesser petrosal nerve (from IX), Superior petrosal artery. Histia for greater petrosal nerve: Greater petrosal nerve (from VII). Mastoid foramen: Mastoid emissary vein. Condylar canal: Condylar emissary vein. Jugular foramen: Glossopharyngeal nerve (IX), Vagus nerve (X), Accessory nerve (XI), Posterior meningeal artery, Inferior petrosal sinus, Internal jugular vein (continuation of sigmoid sinus). Foramen cecum: Embryonic vein. Clellery plate: Olfactory nerve (I). Posterior ethmoidal foramen: Posterior ethmoidal nerve (from V1), Posterior ethmoidal artery, Posterior ethmoidal vein. Optic canal: Optic nerve (II), Ophthalmic artery. Foramen rotundum: Maxillary nerve (V2). Carotid canal: Carotid symplophic plexus, Internal carotid artery, Carotid venous plexus. Internal auditory meatus: Facial nerve (VII), Vestibulocochlear nerve (VIII), Labyrinthine artery, Labyrinthine vein. Foramen magnum: Vertebral arteries, Anterior spinal artery, Spinal medulla (medulla oblongata), Spinal root of accessory nerve (XI), Posterior spinal arteries, Posterior spinal vein. Hypoglossal canal: Hypoglossal nerve (XII), Venous plexus of hypoglossal canal.
C	Left facial paralysis	
D	Decreased hearing in the left ear	
E	Deviation of uvula to the right	

Hint

Blood in the sphenoid sinus and a transverse fracture on imaging are indicative of an anterior fracture of the middle cranial fossa. Anterior middle cranial fossa fractures may involve the orbital apex, superior orbital fissure, and clinoid processes.

Correct Answer

A - Left homonymous hemianopia

Explanation But

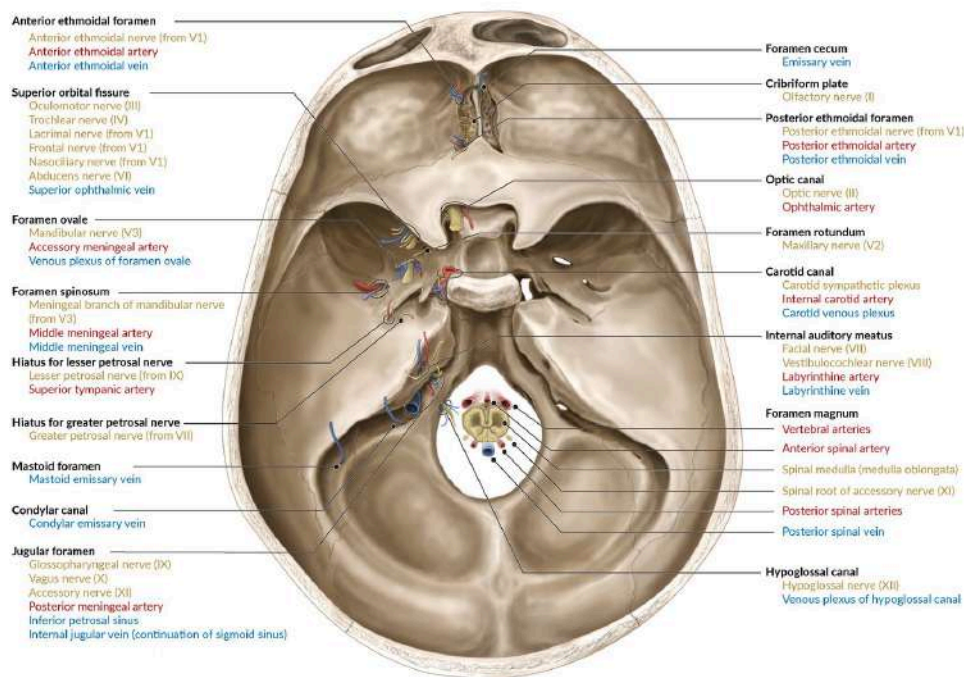
Severe [head trauma](#) can result in a [skull base fracture](#) extending through the floor of the [sella turcica](#) and [sphenoid sinus](#) to injure the crossing fibers at the [optic chiasm](#), which would cause a [bitemporal hemianopia](#).

Explanation Why

Left [homonymous hemianopia](#) would be seen with damage to the [visual pathways](#) at the level of the right [occipital lobe](#) (e.g., due to right [posterior cerebral artery stroke](#)). This young patient does not have any known [risk factors](#) for CVA and given the mechanism of injury and imaging findings, a different finding is more likely.

B - Inward deviation of the left eye

Image



Explanation Why

Inward deviation of the [eye](#) ([esotropia](#)) can result from [fractures](#) of the [sphenoid bone](#) that extend anteriorly through the [superior orbital fissure](#) to damage the [abducens nerve](#) ([CN VI](#)). Other nerves that can be injured in [skull base fractures](#) involving the [superior orbital fissure](#) are the [oculomotor nerve](#) ([ptosis](#) with a fixed and dilated pupil), [trochlear nerve](#) (ocular [extorsion](#) and vertical [diplopia](#)), and [ophthalmic nerve](#) (absent [corneal reflex](#)). [CN VI palsy](#) is the most common [cranial nerve](#) palsy because of the long and tortuous route that [CN VI](#) takes intracranially, along which the nerve is vulnerable to injury by trauma (as in this patient), neoplasms (e.g., [sphenoid ridge meningiomas](#)), increased ICP (e.g., [pseudotumor cerebri](#), [SAH](#)), neurovascular pathologies (e.g., [cavernous sinus thrombosis](#), [carotid-cavernous fistulas](#)), and infection (e.g., [syphilis](#)).

C - Left facial paralysis

Explanation Why

Left facial paralysis would indicate [facial nerve palsy](#). The [facial nerve \(CN VII\)](#) is commonly injured in [fractures](#) of the petrous part of the [temporal bone](#) (e.g., transverse [temporal bone fractures](#)) that extend from the [internal acoustic meatus](#) to the [stylomastoid foramen](#). Although this patient has [bruising](#) around his left temple, his [CT scan](#) shows a transverse [fracture](#) through the [sphenoid bone](#), for which left facial paralysis is not typical.

D - Decreased hearing in the left ear

Explanation Why

Decreased hearing in the left ear would suggest [vestibulocochlear nerve injury](#), which can result from [skull base fractures](#) extending from the petrous pyramid of the [temporal bone](#) into the [internal acoustic meatus](#). Other typical findings associated with this type of injury include signs of fluid accumulation in the [middle ear](#), [CSF otorrhea](#), [hemotympanum](#), and [mastoid ecchymosis](#). [Vertigo](#) and horizontal nystagmus may be present as well. This patient's [CT scan](#) shows a [fracture](#) through the [sphenoid bone](#) rather than the [temporal bone](#), making this finding unlikely.

E - Deviation of uvula to the right

Explanation Why

Deviation of the uvula to the right would be consistent with a left [vagus nerve palsy](#). [CN X](#) can be injured in [posterior](#) cranial fossa [fractures](#) that extend into the [jugular foramen](#), which is located between the [temporal bone](#) and [occipital bone](#). However, this patient's CT scan shows a transverse [fracture](#) through the [sphenoid bone](#).

Question # 15

A previously healthy 17-year-old female college student comes to the emergency department because of a 1-day history of fever, chills, and severe headache. Her temperature is 39.4°C (103°F). Physical examination shows nuchal rigidity and photophobia. Blood cultures are obtained and a lumbar puncture is performed. A Gram stain of cerebrospinal fluid shows gram-negative cocci in pairs. Which of the following virulence factors was most likely involved in the initial step of this patient's infection?

	Answer	Image
A	Alpha toxin	
B	Protein A	
C	Lipooligosaccharides	
D	Adhesive pili	
E	Biofilm formation	
F	Polysaccharide capsule	

Hint

This girl presents with symptoms of meningitis (i.e., fever, headache, photophobia, nuchal rigidity). The presence of gram-negative diplococci on CSF analysis indicates that the causal organism is *Neisseria meningitidis*.

Correct Answer

A - Alpha toxin

Explanation Why

The phospholipase alpha toxin is produced by [Clostridium perfringens](#), the leading mediator for myonecrosis ([gas gangrene](#)). However, it does not cause [meningitis](#). [N. meningitidis](#) does not produce [exotoxins](#).

B - Protein A

Explanation Why

[Protein A](#) is not produced by [N. meningitidis](#). Rather, it is a potent [virulence factor](#) produced by [S. aureus](#), a gram-positive coccus that arranges in clusters. [N. meningitidis](#), however, does produce [IgA protease](#). [IgA protease](#) protects the colonizing bacteria of the nasopharynx from host [IgA](#). This facilitates infection of mucosal surfaces, such as the [meninges](#).

C - Lipooligosaccharides

Explanation Why

Lipooligosaccharides (LOS; also known as [endotoxins](#)) are a component of the [outer membrane](#) in gram-negative bacteria. After cellular lysis or [endocytosis](#), LOS are released into the serum. There, they strongly stimulate [macrophages](#), [tissue factor](#), and complement. These pathways ultimately lead to the clinical signs of [shock](#) such as [fever](#), [hypotension](#), and [disseminated intravascular coagulation](#). [N. meningitidis](#) releases [endotoxin](#), but relatively late in the course of invasive infection. Lipooligosaccharides are, therefore, not a crucial part of the first step in meningeal infection.

D - Adhesive pili

Explanation But

N. meningitidis is transmitted via respiratory or oral secretions of asymptomatic nasopharyngeal carriers of the organism. Living in crowded spaces, such as college dormitories, is an important [risk factor](#) for transmission.

Explanation Why

[Pili](#) and certain [proteins](#), e.g., opacity proteins, are important [virulence factors](#) for *N. meningitidis* as they allow the bacterium to adhere to and invade [epithelial](#) and [endothelial](#) cells. [Colonization](#) of the nasal [epithelium](#) is considered the first crucial step leading to clinically apparent infection. In a small [proportion](#) of individuals colonized with *N. meningitidis*, the bacteria invade the bloodstream and gain access to the brain, presumably via the brain [postcapillary venules](#) or the [choroid plexus](#), to cause meningeal infection.

E - Biofilm formation

Explanation Why

A small number of, especially [virulent](#), strains of *N. meningitidis* strains are capable of forming a [biofilm](#). The [biofilm](#) is very effective at protecting the bacteria from [antibiotics](#). Moreover, a [biofilm](#) decreases the effectiveness of circulating [leukocytes](#) in identifying and destroying bacterial cells. Although [biofilm](#) formation is important for prolonging the presence of nasopharyngeal [colonization](#), a different [virulence factor](#) plays a more prominent role in initiating infection.

F - Polysaccharide capsule

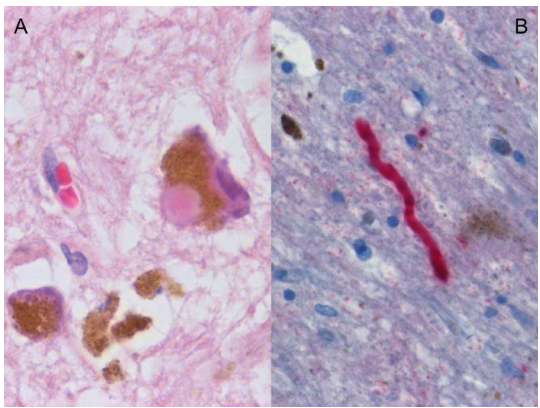
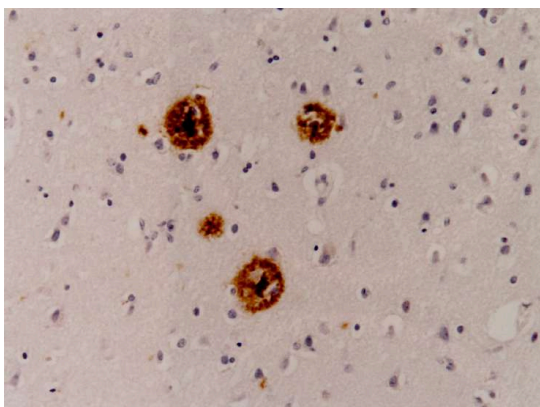
Explanation Why

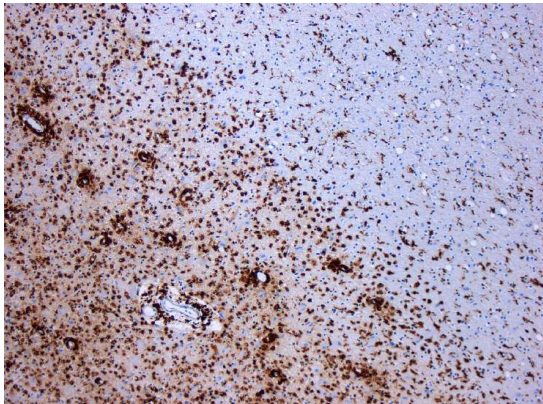
N. meningitidis has a [polysaccharide](#) capsule that plays a vital role in its pathogenicity by protecting it from [antibody](#)-/complement-mediated killing and inhibiting [phagocytosis](#). Other bacteria such as

[*Streptococcus pneumoniae*](#) and [*Haemophilus influenzae*](#) also rely on capsule formation. However, capsule formation does not play a role in the initial step of meningeal infection with [*N. meningitidis*](#).

Question # 16

A 28-year-old woman comes to the physician because of increasingly frequent episodes of double vision for 2 days. She was seen in the emergency department for an episode of imbalance and decreased sensation in her right arm 3 months ago. Examination shows impaired adduction of the right eye with left lateral gaze but normal convergence of both eyes. Deep tendon reflexes are 4+ in all extremities. The Romberg test is positive. An MRI of the brain shows hyperintense oval plaques in the periventricular region and a plaque in the midbrain on T2-weighted images. Microscopic examination of material from the midbrain plaque would most likely show which of the following?

	Answer	Image
A	Eosinophilic intracytoplasmic inclusion bodies	
B	Loss of axons and atrophy of oligodendrocytes	
C	Lymphocytic infiltration of the endoneurium	
D	Extracellular deposits of amyloid peptides	

	Answer	Image
E	Demyelination with partial preservation of axons	 A microscopic image of a tissue section, likely stained with hematoxylin and eosin (H&E). The image shows a dense population of cells with dark, granular nuclei. There are several larger, lighter-colored areas that appear to be myelin sheaths or axons, some of which are partially preserved or fragmented, consistent with the description of demyelination with partial preservation of axons.

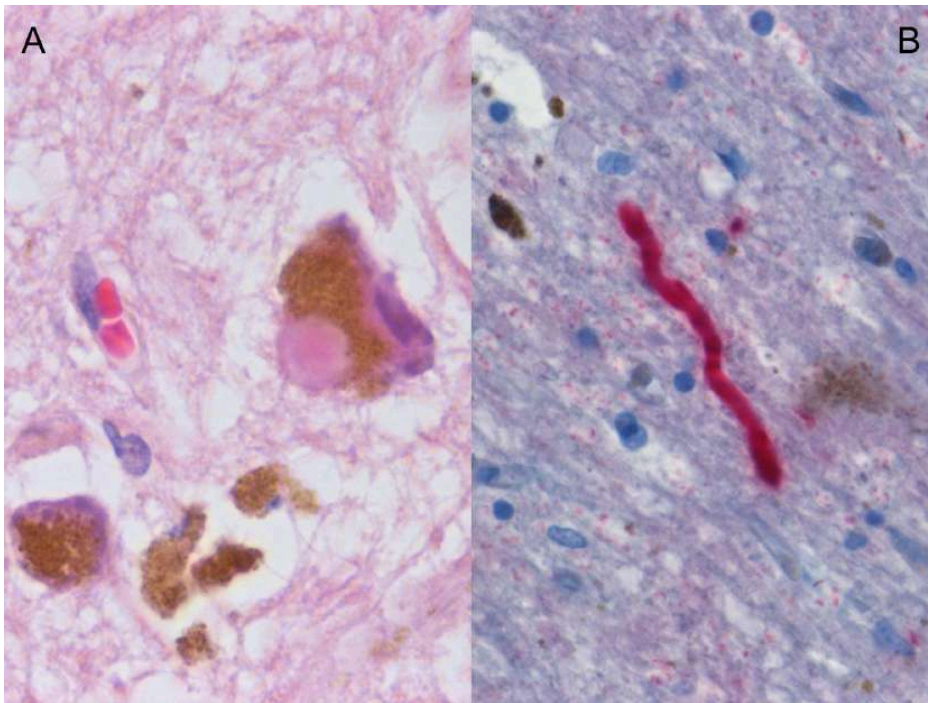
Hint

This patient presents with features of internuclear ophthalmoplegia (diplopia, impaired adduction with intact convergence), pyramidal tract involvement (generalized hyperreflexia, imbalance), and sensory disturbance (abnormal Romberg test). Together with the MRI findings, these findings are consistent with multiple sclerosis. The plaque in the midbrain most likely corresponds to a lesion of the medial longitudinal fasciculus, which is responsible for her acute symptoms.

Correct Answer

A - Eosinophilic intracytoplasmic inclusion bodies

Image



Explanation Why

Eosinophilic intracytoplasmic [inclusion bodies](#) within [neurons](#), known as [Lewy bodies](#), are typical histopathological markers of [Parkinson disease](#), [multiple system atrophy](#), and [dementia with Lewy bodies](#). These diseases can manifest with [postural instability](#). However, characteristic features of [parkinsonism](#) ([bradykinesia](#), [rigidity](#), [resting tremor](#)) would also be expected. Furthermore, it would be unusual for these diseases to manifest in a patient who is so young (typical age of onset is > 60 years).

B - Loss of axons and atrophy of oligodendrocytes

Explanation Why

Loss of [axons](#) and [atrophy](#) of [oligodendrocytes](#) is a sign of advanced neurodegeneration. It can be seen on microscopic examination of older (chronic) lesions in [multiple sclerosis](#). Here, however, in this patient, the tissue is taken from the acute [midbrain](#) plaque, where those longterm damages would not yet be evident.

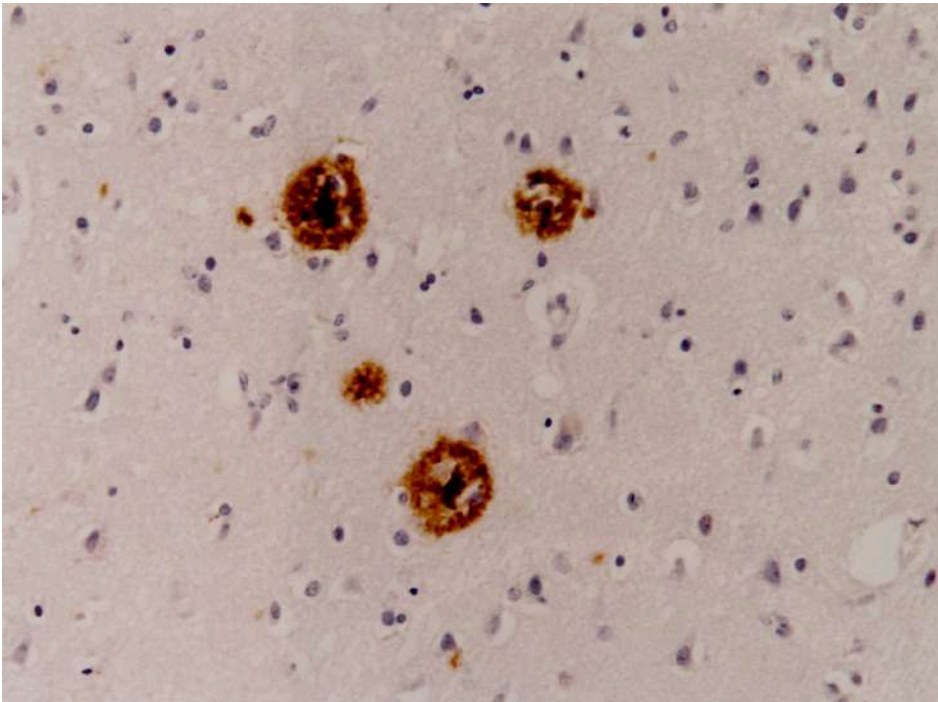
C - Lymphocytic infiltration of the endoneurium

Explanation Why

[Lymphocytic](#) infiltration of the [endoneurium](#) resulting in [myelin](#) damage is a typical finding in [Guillain-Barré syndrome](#) (GBS), which typically presents with ascending paralysis, reduced or absent muscle reflexes, peripheral, symmetric [paresthesias](#) in the hands and feet, and [neuropathic pain](#). Furthermore, GBS typically appears after a gastrointestinal or respiratory infection and would not show plaques on [MRI](#) imaging.

D - Extracellular deposits of amyloid peptides

Image

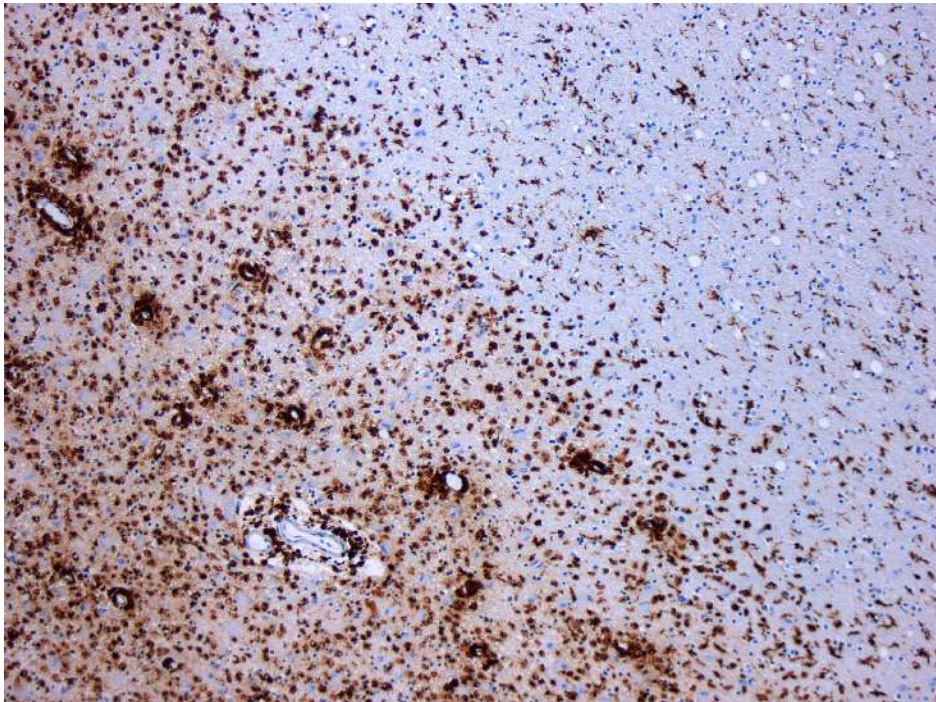


Explanation Why

Extracellular plaques composed of [amyloid beta](#) are common histopathological markers of [Alzheimer disease](#). Patients with [Alzheimer disease](#) typically present with short-term [memory](#) loss and loss of attention control/reasoning, orientation, and language, none of which is present in this patient. Furthermore, [MRI](#) would show generalized [atrophy](#) in the [CNS](#), most pronounced in the [hippocampus](#) and/or [medial temporal lobe](#). Additionally, it would be unusual for the disease to manifest in a patient who is so young (typical age of onset is > 65 years).

E - Demyelination with partial preservation of axons

Image



Explanation Why

Acute [multiple sclerosis](#) plaques are characterized by [demyelination](#) with partial preservation of [axons](#), along with infiltration of [immune cells](#), accumulation of [macrophages](#) with phagocytized [myelin](#), and parenchymal [edema](#). These changes are a result of an autoimmune reaction in which mainly [T helper cells](#) are activated against [CNS](#) antigens. This reaction can be triggered by environmental factors such as infection with [EBV](#) or [HHV 6](#), UV radiation, insufficient [vitamin D](#) consumption, and/or [cigarette smoking](#). The subsequent inflammatory process leads to focal [demyelination](#) with nerve destruction, [gliosis](#), and inadequate remyelination, which, in turn, results in impaired [saltatory conduction](#) of [action potentials](#).

Question # 17

A previously healthy 51-year-old man is brought to the emergency department because of confusion for 2 hours. His wife reports that he fell and hit his head while changing a ceiling light the previous evening. On arrival, he is unconscious. His temperature is 37.1°C (98.8°F), pulse is 54/min, respirations are 8/min and irregular, and blood pressure is 198/106 mm Hg. The right pupil is dilated and fixed; the left pupil is round and reactive to light. There is extension of the extremities to painful stimuli. He is intubated and mechanically ventilated. A mannitol infusion is begun. A noncontrast CT scan of the brain shows herniation of the right medial temporal lobe. Which of the following is the most likely additional finding in this patient?

	Answer	Image
A	Right-sided hemiplegia	
B	Left-side facial nerve palsy	
C	Bilateral spasticity	
D	Bilateral lower limb paralysis	
E	Right eye esotropia and elevation	

Hint

This man with a head injury presents with Cushing triad of bradycardia, irregular respiration, and hypertension, as well as ipsilateral oculomotor palsy. His presentation, along with his CT findings, indicates tentorial (uncal) herniation.

Correct Answer

A - Right-sided hemiplegia

Explanation But

After emergency resuscitative measures (e.g., [intubation](#), [mannitol](#), oxygen supplementation, and head of bed elevation), emergency surgical decompression is required. As the herniation progresses, the [brainstem](#) can become compressed and displaced [caudally](#), shearing the vessels, leading to [midbrain](#) and [pontine](#) hemorrhages, and subsequently resulting in [coma](#), [apnea](#), impaired circulation, and death.

Explanation Why

This patient has a large right-sided [subdural hematoma](#) that results in elevated ICP and [cerebral edema](#), causing a midline shift and herniation of the uncus. As herniation of the ipsilateral (right) uncus progresses, thereby displacing the [midbrain](#) and compressing the left cerebral peduncle (which contains the left [corticospinal tract](#)) across the tentorium, it can cause ipsilateral (right-sided) [hemiparesis](#) and [upper motor neuron \(UMN\)](#) signs (e.g., Babinski sign) as most corticospinal fibers cross over, a process called [Kernohan phenomenon](#). This can be confusing in a clinical setting because the patient's lesion is on the right side, but right-sided [hemiplegia](#) typically localizes a left-sided lesion (this is why [Kernohan syndrome](#) is also called false localizing syndrome). This patient's [extensor posturing](#) is a sign that [midbrain](#) compression has already begun.

B - Left-side facial nerve palsy

Explanation Why

Acute left-sided [facial nerve palsy](#) is commonly caused by [stroke](#) affecting the [facial nerve](#) nucleus or its tract in the [pons](#), or [inflammation](#) of the nerve peripherally (e.g., [Bell palsy](#)). This patient has suffered a severe [head injury](#), resulting in a large [subdural hematoma](#), [elevated ICP](#), and associated [uncal herniation](#). Severe, advanced [uncal herniation](#) can cause [brainstem](#) displacement leading to secondary hemorrhages and subsequent [brainstem strokes](#) and, potentially, [facial nerve palsy](#). However, other exam findings would be found earlier and are more typical of [uncal herniation](#).

C - Bilateral spasticity

Explanation Why

[Spasticity](#) indicates [upper motor neuron \(UMN\)](#) damage. Severe, advanced [uncal herniation](#) causes [brainstem](#) displacement leading to secondary hemorrhages, which, in turn, cause [brainstem strokes](#) and, potentially, concomitant bilateral [corticospinal tract](#) damage. However, [spasticity](#) is typically a late sequela of [UMN](#) injury, appearing days to weeks later. Other exam findings would be more typical and found earlier in the progression of this patient's [uncal herniation](#).

D - Bilateral lower limb paralysis

Explanation Why

Bilateral lower limb paralysis is usually caused by [spinal cord](#) trauma or [infarction](#), or bilateral upper motor damage (e.g., from a [stroke](#) affecting bilateral [corticospinal tracts](#) in the [brainstem](#)). In some cases, secondary [brainstem](#) hemorrhage could cause [brainstem strokes](#) and subsequent paraplegia (if bilateral [corticospinal tracts](#) were affected). Although [uncal herniation](#) could cause [brainstem](#) displacement that leads to secondary hemorrhages, this sequela would not occur until herniation is severe, and other exam findings would be expected earlier in the progression.

E - Right eye esotropia and elevation

Explanation But

Severe, advanced [uncal herniation](#) causes [brainstem](#) displacement, which leads to secondary hemorrhages, causing [brainstem strokes](#) and may cause concomitant [CN IV](#) and VI palsies. However, [CN III](#) would also be impaired in this case, so [eye](#) position would likely be closer to a neutral gaze.

Explanation Why

Right [eye esotropia](#) and elevation would be caused by concomitant [CN IV](#) and VI palsies, leading to unopposed [CN III](#) activity. When [CN III](#) is unopposed, the associated [extraocular muscles](#) ([medial](#)

[rectus](#), [superior rectus](#), [inferior rectus](#), and [inferior oblique muscles](#)) together produce an [adduction](#) and elevation or depression of the [eye](#). Instead, [uncal herniation](#) causes [CN III](#) palsy, resulting in pupillary dilation and absent light reflex (as seen in this patient), [abduction](#), and slight depression of the [eye](#) (“down and out” gaze).

Question # 18

A 25-year-old man comes to the physician because of an 8-hour history of painful leg cramping, runny nose, chills, diarrhea, and abdominal pain. Examination shows cool, damp skin with piloerection. The pupils are 7 mm in diameter and equal in size. Deep tendon reflexes are 3+ bilaterally. The diagnosis of opioid withdrawal is made. After the patient is stabilized, the physician initiates a withdrawal regimen with methadone. Which of the following characteristics makes this drug a suitable substance for the treatment of this patient's addiction?

	Answer	Image
A	Minimal drug interactions	
B	No CNS accumulation	
C	Low dependence risk	
D	Rapid onset of action	
E	Limited potency	
F	Long elimination half-life	
G	Low tolerance potential	

Hint

Methadone is lipophilic!

Correct Answer

A - Minimal drug interactions

Explanation Why

[Methadone](#) interacts with several drugs because it is metabolized by [CYP450](#) enzymes, most notably [CYP3A4](#) and CYP2B6. As a result, [methadone](#) can interact with HAART, [antifungal](#), and psychotropic medications, among others.

B - No CNS accumulation

Explanation Why

[Methadone](#) can accumulate in the [CNS](#). Its ability to cross the [blood-brain barrier](#) combined with its [pharmacokinetics mean](#) that a [methadone](#) overdose can cause [CNS](#) depression and respiratory compromise.

C - Low dependence risk

Explanation Why

[Methadone](#) does have dependence risk and addictive potential, much like heroin. In addition to being a [μ-opioid receptor agonist](#), [methadone](#) also has affinity for the [δ-opioid receptor](#), which can lead to tolerance and addiction.

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D - Rapid onset of action

Explanation Why

[Methadone](#) is not known for its rapid onset of action, a characteristic that better describes [opioids](#) such as [fentanyl](#), a very potent [μ-opioid receptor agonist](#). [Fentanyl](#) is a synthetic [opioid](#) commonly used as an [analgesic](#) and would not be appropriate for this patient presenting with [opioid withdrawal](#).

E - Limited potency

Explanation Why

[Methadone](#) is a potent medication with a duration of action of up to 8 hours and with high [lipophilicity](#), which results in the body retaining the drug for a longer period of time.

F - Long elimination half-life

Explanation Why

[Methadone](#) is notable for its long elimination [half-life](#), likely due to its [lipophilicity](#) and ability to distribute to [liver](#) and fat cells. This characteristic means that these cells can slowly release [methadone](#) back into the bloodstream for up to 24 hours after initial administration. [Opioid withdrawal](#) occurs when there is an acute elimination of the substance; [methadone](#)'s long elimination [half-life](#) therefore suppresses withdrawal symptoms, making it a good form of maintenance therapy for [opioid](#) withdrawal and drug users wishing to overcome their dependence.

G - Low tolerance potential

Explanation Why

[Methadone](#) has high [drug tolerance](#) potential because of its considerable affinity for the [\$\delta\$ -opioid receptor](#), which can lead to addiction.

Question # 19

A 5-year-old boy who recently emigrated from Nigeria is brought to the emergency department because of a 2-day history of lower leg weakness, swallowing difficulty, and drooling of saliva. He has not yet received any childhood vaccinations. Two days after admission, the patient develops shortness of breath. Pulse oximetry shows an oxygen saturation of 64%. Despite resuscitative efforts, the patient dies of respiratory failure. At autopsy, examination of the spinal cord shows destruction of the anterior horn cells. Neurological examination of this patient would have most likely shown which of the following findings?

	Answer	Image
A	Positive Babinski sign	
B	Clasp knife spasticity	
C	Hyporeflexia	
D	Sensory loss	
E	Myoclonus	
F	Pronator drift	

Hint

This patient's symptoms (lower leg weakness, swallowing difficulty, and drooling of saliva) and history (no vaccinations) raises suspicion for poliomyelitis, which is confirmed by the autopsy findings of destroyed anterior horn cells of the spinal cord. Lesions of axons between anterior horn cells (lower motor neurons) and the relevant muscle tissue lead to lower motor neuron signs (LMN signs).

Correct Answer

A - Positive Babinski sign

Explanation Why

The [Babinski sign](#) is a [primitive reflex](#) mediated by the [extrapyramidal tracts](#). A positive [Babinski sign](#) indicates [upper motor neuron lesion](#). It is not seen in [lower motor neuron damage](#), which this patient has.

B - Clasp knife spasticity

Explanation Why

[Clasp knife spasticity](#) is characterized by an initial resistance to passive movement due to increased muscle tone, which is followed by a sudden decrease in resistance. This is an [upper motor neuron sign](#) ([UMN sign](#)), which results from a lesion along the descending motor pathways. It is not seen in [lower motor neuron damage](#), which this patient has.

C - Hyporeflexia

Explanation Why

[Hyporeflexia](#) is a sign of [lower motor neuron lesion](#) ([LMN sign](#)) and most likely would have been seen in this patient with destruction of [anterior horn cells](#) due to [poliomyelitis](#). Other [LMN signs](#) include muscle [atrophy](#), [fasciculations](#), and decreased power and tone. The involvement of respiratory muscles can lead to respiratory failure, as seen here.

D - Sensory loss

Explanation Why

Sensory loss (e.g., fine touch, [proprioception](#), and vibration) would be expected in destruction of the [posterior horn](#) cells of the [spinal cord](#). This patient, however, has destruction of the [anterior horn cells](#) of the [spinal cord](#), which provide motor innervation to [skeletal muscles](#) in the extremities. Sensory loss is not seen in [lower motor neuron damage](#).

E - Myoclonus

Explanation Why

Myoclonus is characterized by brief, [shock](#)-like, involuntary twitches of muscles or muscle groups. Myoclonus is an [upper motor neuron sign](#) (UMN sign), which results from lesions along the descending motor pathways. It is not seen in [lower motor neuron damage](#), which this patient has.

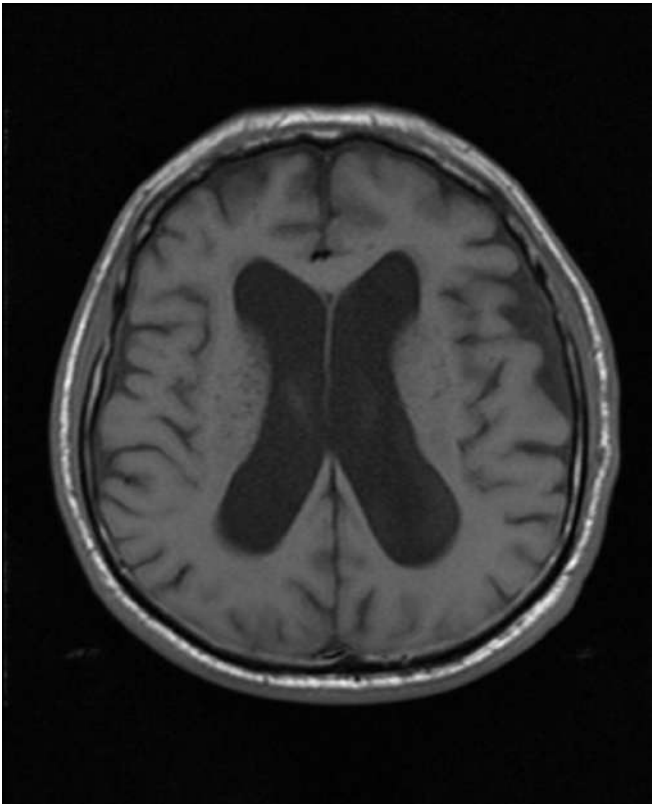
F - Pronator drift

Explanation Why

A positive [pronator drift test](#) is characterized by [pronation](#) and drift of the patient's outstretched arms. A positive test can indicate an [upper motor neuron lesion](#) but would not be seen in [lower motor neuron damage](#), which this patient has.

Question # 20

A 74-year-old man is brought to the physician by his wife for progressively worsening confusion and forgetfulness. Vital signs are within normal limits. Physical examination shows a flat affect and impaired short-term memory. An MRI of the brain is shown. Further evaluation of this patient is most likely to show which of the following findings?



	Answer	Image
A	Startle myoclonus	
B	Papilledema	
C	Broad-based gait	

	Answer	Image
D	Postural instability	
E	Pill-rolling tremor	
F	Choreiform movements	

Hint

In conjunction with the MRI findings (marked dilatation of the lateral ventricles without proportional sulcal enlargement), this patient's progressively worsening confusion and memory suggest normal pressure hydrocephalus, a condition that is most commonly seen in adults over the age of 60.

Correct Answer

A - Startle myoclonus

Explanation Why

Startle myoclonus is seen in many neurological and psychiatric syndromes. When occurring in combination with signs of rapidly progressing [dementia](#) (rapidly worsening confusion and [memory loss](#)), [Creutzfeldt-Jakob disease](#) should be considered. However, [MRI](#) of a patient with [Creutzfeldt-Jakob disease](#) would show T2 [signal amplification](#) in the [caudate nucleus](#) rather than the ventriculomegaly seen here.

B - Papilledema

Explanation Why

[Papilledema](#) can be due to either [communicating hydrocephalus](#) or [noncommunicating hydrocephalus](#). While this patient does show signs of impaired consciousness (increasing confusion and forgetfulness), he lacks characteristic [signs of elevated ICP](#) (e.g., nausea, vomiting, [headaches](#), [Cushing triad](#)), making [papilledema](#) unlikely. NPH, which this patient most likely has, is only characterized by a mild and intermittent elevation in ICP, and [papilledema](#) would not be expected.

C - Broad-based gait

Explanation Why

A broad-based gait is a clumsy, irregular pattern of walk in which small steps are taken and the legs are spread wide. Gait dysfunction, [dementia](#), and [urinary incontinence](#) make up the pathognomonic triad (“wet”, “wacky”, “wobbly”) of [normal pressure hydrocephalus](#) (NPH).

D - Postural instability

Explanation Why

[Postural instability](#) is one of the cardinal signs of [Parkinson disease](#). Patients with the disease can present with cognitive dysfunctions and [dementia](#), similar to what is seen in this patient, but only later in the course of the disease. [Parkinson disease](#) is not associated with ventriculomegaly, which is seen here.

E - Pill-rolling tremor

Explanation But

Imaging is not routinely required for the diagnosis of [Parkinson disease](#). It is reserved for atypical presentations to rule out other underlying disorders.

Explanation Why

[Pill-rolling tremors](#) are characteristic of [Parkinson disease](#). Patients with the disease can manifest with cognitive dysfunctions and [dementia](#), similar to what is seen in this patient, but only later in the course of the disease. [Parkinson disease](#) is not associated with the ventriculomegaly seen here.

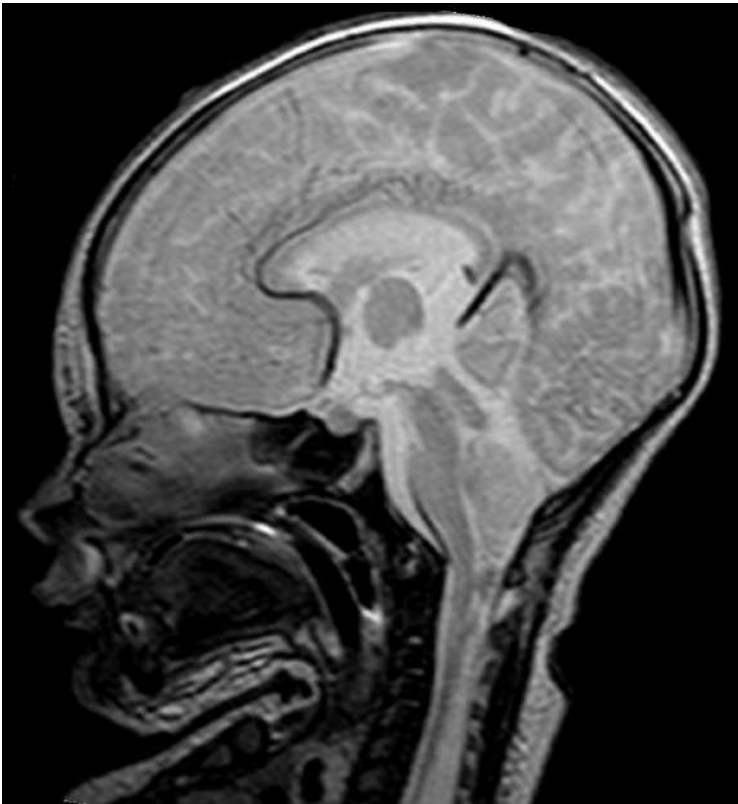
F - Choreiform movements

Explanation Why

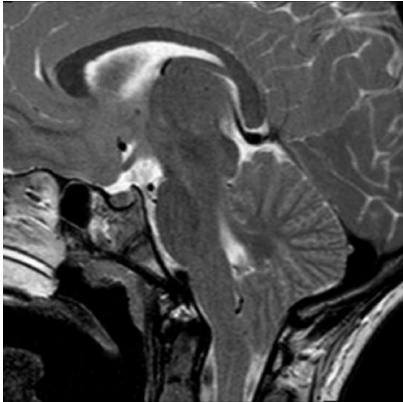
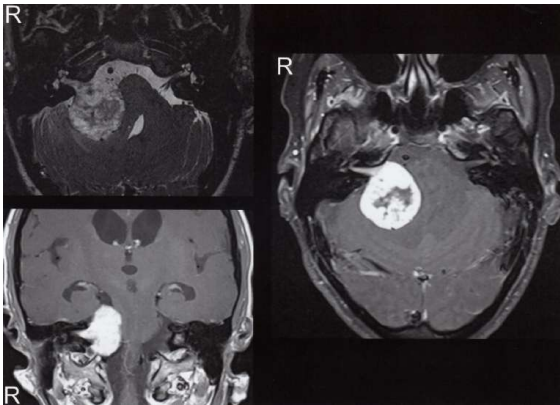
[Choreiform movements](#) are typically seen in [Huntington disease](#). [Huntington disease](#) is associated with progressive cognitive deficits in advanced stages of the disease. [MRI](#) would show brain atrophy, particularly of the [caudate nucleus](#), rather than the ventriculomegaly seen here.

Question # 21

A 2-year-old boy is brought to the physician because of progressive headaches, dizziness, and recurrent episodes of vomiting for 3 weeks. He has a history of surgical removal of a sac-like protuberance on his lower back soon after birth. Neurologic examination shows ataxia. Fundoscopy shows bilateral optic disk swelling. An MRI of the brain is shown. Which of the following is the most likely diagnosis?



	Answer	Image
A	Chiari II malformation	

	Answer	Image
B	Chiari I malformation	
C	Ependymoma	
D	Dandy-Walker malformation	
E	Vestibular schwannoma	
F	Choroid plexus carcinoma	
G	Medulloblastoma	

Hint

The MRI shows displacement of both the vermis and the cerebellar tonsils through the foramen magnum, which has likely caused an obstruction of the ventricular system. Symptoms like progressive headaches, dizziness, recurrent vomiting, abnormal gait, and papilledema suggest increased intracranial pressure (ICP). This patient's condition is almost always associated with a certain neural tube defect, which would explain the removal of the sac-like protuberance at the lower back soon after birth.

Correct Answer

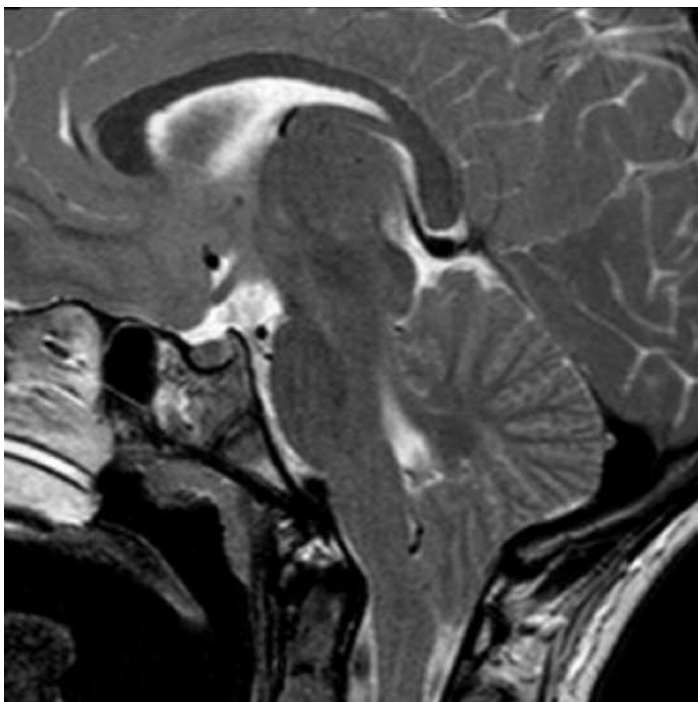
A - Chiari II malformation

Explanation Why

[Chiari II malformation](#) is characterized by a [caudal](#) displacement of the [cerebellar vermis](#) and [tonsils](#) (with or without the [medulla oblongata](#) and the [fourth ventricle](#)) into the upper cervical canal. The displacement can obstruct the flow of [cerebrospinal fluid \(CSF\)](#) and cause an accumulation of [CSF](#) within the [spinal cord](#) (producing a [syrinx](#)), or within the [cranium](#) (causing [hydrocephalus](#)). Patients often present in childhood with symptoms of [hydrocephalus](#) and resulting [increased ICP](#). This patient's history of a sac-like protuberance on his lower back suggests [spina bifida cystica](#), which is consistent with frequently associated lumbosacral [myelomeningocele](#). The patient's [MRI](#) confirms the diagnosis of [Chiari II malformation](#).

B - Chiari I malformation

Image



Explanation Why

[Chiari I malformation](#) is characterized by the [caudal](#) displacement of [cerebellar tonsils](#). While some patients may also develop symptoms of [hydrocephalus](#), as seen in this patient, it typically also manifests with occipital [headache](#), neck [pain](#), lower [cranial nerve palsies](#), a [downbeat nystagmus](#), and [radicular pain](#) in the shoulders and arms, all of which are not present here. Moreover, it usually becomes symptomatic in [adolescence](#)/young adulthood, and a history of [myelomeningocele](#) is atypical for [Chiari I malformation](#).

C - Ependymoma

Explanation Why

[Ependymoma](#) can present with [signs of increased intracranial pressure](#), as seen in this patient. However, these tumors typically arise from the floor of the [fourth ventricle](#), adapt to the shape of the ventricle, and extend through the [foramina of Luschka](#) and Magendi into the cisterns. It would be unusual for the [tumor](#) not to invade the ventricles and have cystic components on imaging, as seen in this patient. Furthermore, [ependymoma](#) would not explain this patient's history of lumbosacral [myelomeningocele](#).

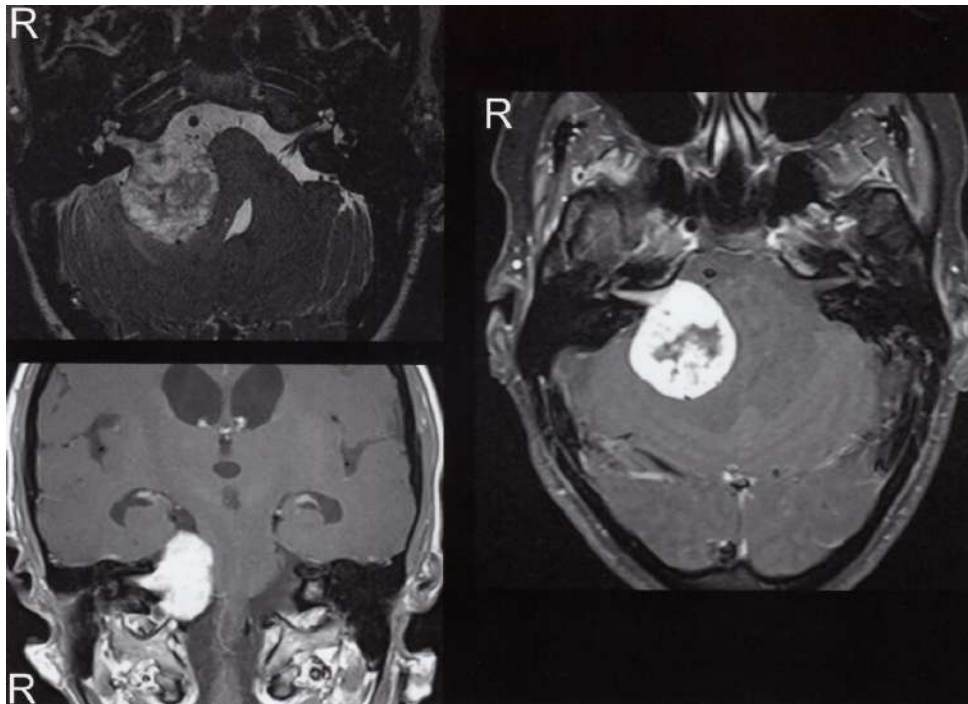
D - Dandy-Walker malformation

Explanation Why

[Dandy-Walker malformation](#) is often associated with [hydrocephalus](#), typically antenatally or early in [infancy](#), which could explain this patient's findings of [increased intracranial pressure](#). Although it is possible for [myelomeningocele](#) to occur in patients with [Dandy-Walker malformation](#), such cases are extremely rare. Much more likely associations would be orofacial and cardiac defects, as well as intellectual and motor delay (especially with crawling and walking due to lack of [cerebellar neurons](#)), none of which are present in this patient.

E - Vestibular schwannoma

Image



Explanation Why

[Vestibular schwannoma](#) presents most commonly with [sensorineural hearing loss](#) and possibly also [tinnitus](#) and balance issues. Although in very severe cases, [schwannomas](#) may grow large enough to cause [headaches](#) and [brainstem](#) compression, they do not cause [hydrocephalus](#), [intracranial hypertension](#), or [myelomeningocele](#), as observed in this patient, nor would these complications occur over the course of two weeks.

F - Choroid plexus carcinoma

Explanation Why

Choroid plexus carcinoma is a rare malignant neoplasm of the [choroid plexus](#) that typically occurs in children < 5 years and can cause [hydrocephalus](#), which would manifest with findings of [increased](#)

[intracranial pressure](#) as observed here. However, choroid plexus carcinoma is not associated with [meningomyelocele](#). Additionally, at least in the plane shown, there are no visible tumors in the [MRI](#).

G - Medulloblastoma

Explanation Why

[Medulloblastoma](#) is a common, aggressive pediatric [intracranial neoplasm](#) most commonly located in the [cerebellar vermis](#). Initially, it typically manifests with the classic triad of morning [headaches](#), vomiting, and fatigue due to [increased intracranial pressure](#). Subsequent [hydrocephalus](#) is common and would produce [symptoms of increased ICP](#) as observed in this patient. However, [medulloblastoma](#) is not associated with [myelomeningocele](#), which is suspected given the patient's history. Additionally, these [MRI](#) findings (e.g., inferiorly displaced [cerebellar tonsils](#) and [vermis](#)) suggest another diagnosis.

Question # 22

A 66-year-old man undergoes a coronary artery bypass grafting. Upon regaining consciousness, he reports that he cannot see from either eye and cannot move his arms. Physical examination shows bilaterally equal, reactive pupils. A fundoscopy shows no abnormalities. An MRI of the brain shows wedge-shaped cortical infarcts in both occipital lobes. Which of the following is the most likely cause of this patient's current symptoms?

	Answer	Image
A	Amyloid angiopathy	
B	Ruptured saccular aneurysm	
C	Lipohyalinosis	
D	Cardiac embolism	
E	Atherothrombosis	
F	Systemic hypotension	

Hint

An MRI of this patient shows symmetrical infarcts in the watershed regions of the brain. These occurred occipitally at the border of the posterior cerebral artery (PCA) and middle cerebral artery (MCA), causing his blindness.

Correct Answer

A - Amyloid angiopathy

Explanation Why

[Cerebral amyloid angiopathy](#) is a common cause of spontaneous [intracranial hemorrhage](#) in elderly patients. Affected patients may present with recurrent [TIA](#)-like symptoms and rapidly progressive [dementia](#). However, [amyloid angiopathy](#) is not a common cause of [watershed infarcts](#).

B - Ruptured saccular aneurysm

Explanation Why

A ruptured [saccular aneurysm](#) causes [subarachnoid hemorrhage \(SAH\)](#) and could lead to [hemorrhagic stroke](#) (thunderclap [headaches](#), nonreactive pupils, unconsciousness, rapidly worsening nausea, vomiting, and cardiovascular deterioration). A ruptured [aneurysm](#) is, however, not a common cause of [watershed infarcts](#), which were seen in this patient.

C - Lipohyalinosis

Explanation Why

[Lipohyalinosis](#) of the cerebral vessel walls can lead to [lacunar strokes](#) within the [basal ganglia](#). The most important predisposing factor for [lipohyalinosis](#) is chronic [hypertension](#). A common [risk factor](#) for chronic [hypertension](#) is [atherosclerosis](#), which this patient who received a bypass graft likely has. However, [lipohyalinosis](#) is not a common cause of [watershed infarcts](#), which were seen in this patient.

D - Cardiac embolism

Explanation Why

[Cardiac embolism](#) is a cause of [ischemic stroke](#) and can affect [watershed areas](#). However, although these emboli often lodge in the small leptomeningeal [arteries](#) over the [watershed areas](#), it is highly unlikely that multiple microemboli would end up concurrently blocking the same vessels bilaterally. For this reason, [watershed infarcts](#) caused by cardiac embolisms and, consequently, their associated symptoms are overwhelmingly unilateral.

E - Atherothrombosis

Explanation Why

When atherothrombosis affects an entire area supplied by a cerebral blood vessel, it can manifest with unilateral [stroke](#)-like symptoms (vision loss, weakness, numbness, slurred [speech](#)). On rare occasions, atheromatous microemboli may also cause a [watershed infarct](#). However, this would most likely be unilateral, not bilateral.

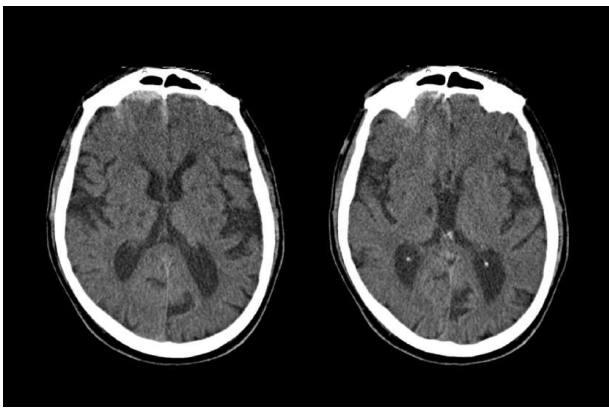
F - Systemic hypotension

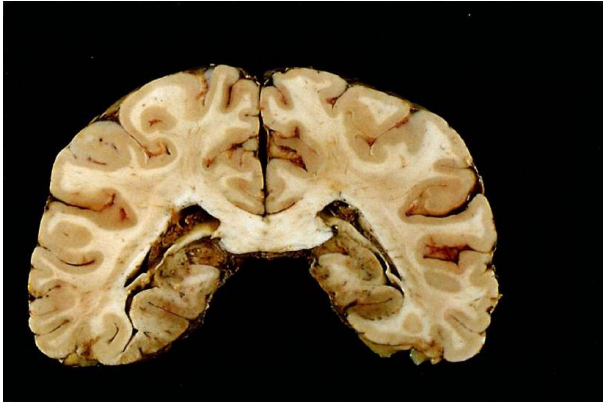
Explanation Why

Systemic [hypotension](#) leading to a decrease in perfusion to the terminal areas of the vascular fields supplied by the cerebral [arteries](#) ([watershed areas](#)) is the most common cause of a [watershed infarct](#). [Watershed](#)-distribution [strokes](#) are more prevalent in patients following cardiac surgery due to the global systemic hypoperfusion (especially, while on cardiopulmonary bypass) that occurs often during these surgeries. These [strokes](#) are associated with poor short-term outcomes.

Question # 23

An otherwise healthy 78-year-old man is brought to the emergency department by his daughter because of a 1-day history of a diffuse headache and an inability to understand speech. There is no history of head trauma. He drinks one to two beers daily and occasionally more on weekends. His vital signs are within normal limits. Mental status examination shows fluent but meaningless speech and an inability to repeat sentences. A noncontrast CT scan of the head shows an acute hemorrhage in the left temporal lobe and several small old hemorrhages in bilateral occipital lobes. Which of the following is the most likely underlying cause of this patient's neurological symptoms?

	Answer	Image
A	Vascular lipohyalinosis	
B	Ruptured vascular malformation	
C	Hypertensive encephalopathy	
D	Intracerebral malignancy	

	Answer	Image
E	Cardiac embolism	
F	Amyloid angiopathy	

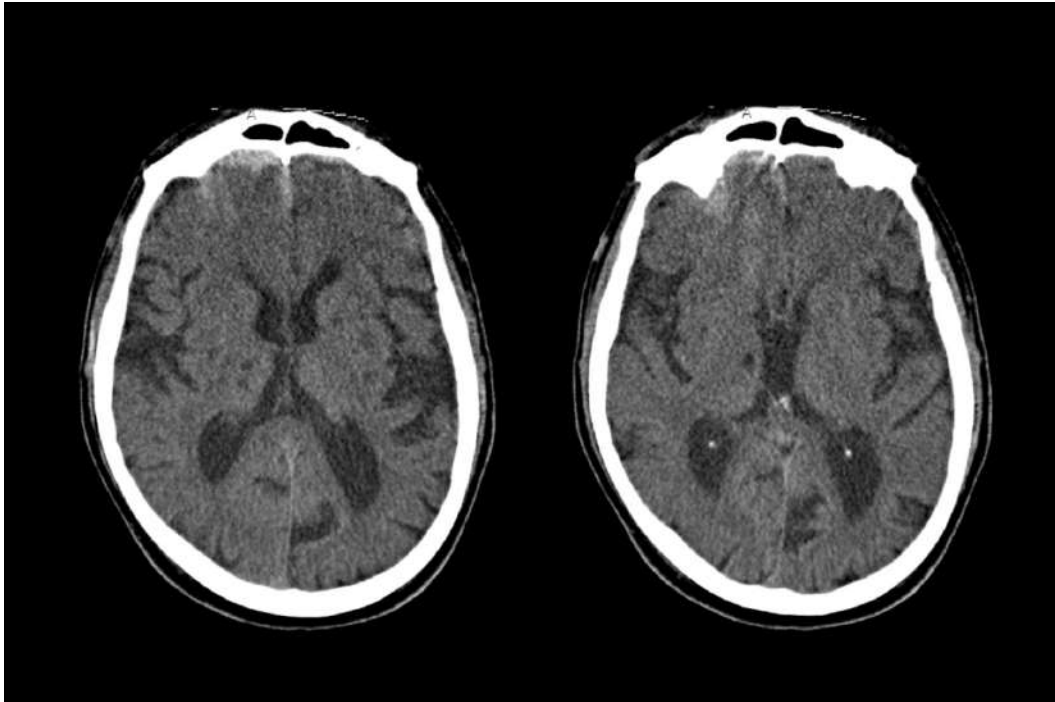
Hint

This elderly man presents with a spontaneous superficial intracerebral hemorrhage (i.e., a cortical lobar hemorrhage affecting the temporal lobe), which is most commonly caused by the deposition of a congophilic substance in the cortical blood vessels.

Correct Answer

A - Vascular lipohyalinosis

Image



Explanation Why

Vascular [lipohyalinosis](#) of the cerebral vessel walls is the most common cause of spontaneous nontraumatic [intracerebral hemorrhage](#), mostly presenting as a subcortical cerebral hemorrhage ([lacunar strokes](#)) within the [basal ganglia](#). However, the most important predisposing factor for lipohyalinosis is chronic [hypertension](#), which is absent in this patient's [medical history](#).

B - Ruptured vascular malformation

Explanation Why

A ruptured vascular [malformation](#) (e.g., [saccular aneurysms](#), [arteriovenous malformations](#)) is a

common cause of hemorrhage, which typically presents with acute neurologic symptoms such as this patient's [headache](#) or [aphasia](#). However, it is more common in younger patients, and radiological findings would show an acute [intraparenchymal hemorrhage](#), unlike the acute and old cortical hemorrhages seen in this patient.

C - Hypertensive encephalopathy

Explanation Why

[Hypertensive encephalopathy](#) occurs as a result of a sudden, sustained rise in blood pressure, which presents with diffuse [headache](#). However, findings would also include vomiting, confusion, [seizure](#), blurry vision, and [papilledema](#), but not [aphasia](#). Also, radiological findings would show [cerebral edema](#), unlike the acute and old cortical hemorrhages seen in this patient. Additionally, this patient has no history of [hypertension](#), making [hypertensive encephalopathy](#) very unlikely.

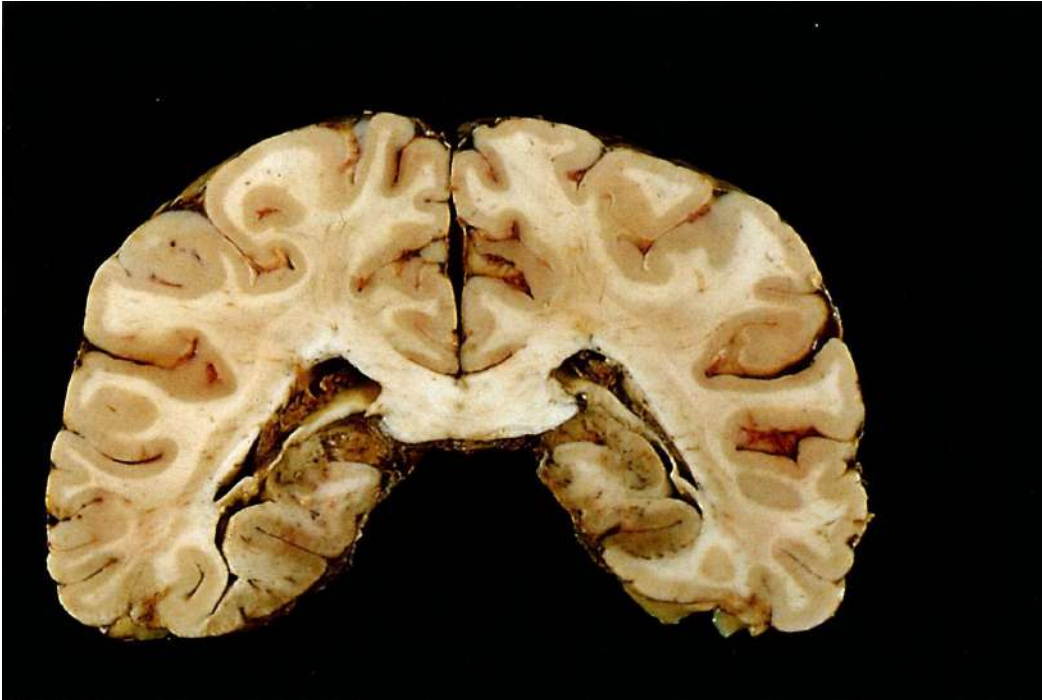
D - Intracerebral malignancy

Explanation Why

Intracerebral [malignancy](#) should be suspected in patients with primary or [metastatic brain tumors](#). Malignant and hypervascular neoplasms have the highest predilection for hemorrhage. Patients with [intracerebral hemorrhage](#) from a [malignancy](#) may present with neurological symptoms such as this patient's [headache](#) and [aphasia](#). However, [headache](#) would be due to [hydrocephalus](#) and [increased ICP](#), and radiological findings would show one or several masses in association with the hemorrhages.

E - Cardiac embolism

Image



Explanation Why

[Cardiac embolism](#) is a cause of [ischemic strokes](#), and its symptoms usually vary depending on the occluded cerebral vessel but may include [headache](#) and [aphasia](#). However, they are typically seen in patients with cardiac wall and chamber abnormalities (e.g., [patent foramen ovale](#)) as well as valve disorders (e.g., [prosthetic valves](#)) and [arrhythmias](#) (e.g., [atrial fibrillation](#)), none of which this patient has.

F - Amyloid angiopathy

Explanation Why

[Cerebral amyloid angiopathy](#) (CAA) is a common cause of spontaneous cortical [intracerebral hemorrhage](#) (ICH) in elderly patients. CAA narrows the lumen of blood vessels and causes

microaneurysms that may rupture spontaneously. In this patient's case, his age, complete [medical history](#) (no history of trauma), neurological symptoms ([TIA](#)-like symptoms), and radiological findings (both acute and subacute cortical hemorrhages) make CAA the most likely underlying cause of the hemorrhage.

Question # 24

A 58-year-old woman comes to the physician because of an itchy rash on her leg 3 days after she returned from a camping trip with her grandchildren. Examination shows a linear, erythematous, maculopapular rash on the left lower extremity. Treatment with a drug is begun that is also effective for motion sickness. One hour later, she reports dry mouth. This adverse effect is most likely mediated through which of the following?

	Answer	Image
A	Antagonism at serotonin receptors	
B	Antagonism at acetylcholine receptors	
C	Agonism at β -adrenergic receptors	
D	Antagonism at histamine receptors	
E	Antagonism at α -adrenergic receptors	

Hint

The patient's allergic rash was most likely treated with a first-generation antihistamine (e.g., diphenhydramine). These agents are also used in the treatment of motion sickness.

Correct Answer

A - Antagonism at serotonin receptors

Explanation But

Because of its [serotonin](#) receptor antagonistic action, [cyproheptadine](#) is used in the treatment of [serotonin syndrome](#).

Explanation Why

Some [antihistamines](#) (e.g., [cyproheptadine](#)) have a [serotonin](#) receptor antagonistic action in addition to [H1 receptor](#) antagonism. However, [serotonin](#) plays no role in salivary secretion, so [serotonin receptor antagonism](#) is not responsible for the dry mouth this patient experiences after consuming the drug.

B - Antagonism at acetylcholine receptors

Explanation Why

[First-generation antihistamines](#), in addition to their H1-receptor antagonist action, also have potent acetylcholine receptor blocking action. AChRs are part of the [parasympathetic](#) nerve supply of the body. As saliva is secreted secondary to [parasympathetic](#) stimulation, antagonism at AChRs results in dry mouth, as seen in this patient. Other common [anticholinergic effects](#) include decreased sweating, [tachycardia](#) (unopposed [sympathetic](#) activity on the [heart](#)), blurring of vision for near objects (loss of [accommodation reflex](#) and [mydriasis](#)), [urinary retention](#) and [constipation](#) (loss of [parasympathetic](#)-mediated sphincter relaxation and [peristalsis](#)), and drowsiness.

C - Agonism at β -adrenergic receptors

Explanation Why

[Agonism](#) at β_1 -[adrenergic receptors](#) in the salivary gland stimulates salivary protein secretion, and to

a lesser extent, also fluid secretion, and thus would not cause the dry mouth seen in this patient. β_1 -adrenergic receptors can be activated by [catecholamines](#), but [antihistamines](#) have no effect on them.

D - Antagonism at histamine receptors

Explanation Why

Drugs that antagonize [H1 histamine receptors](#) ([antihistamines](#)) are commonly used to treat [pruritic](#) rashes, since [histamine](#) release in [subcutaneous tissue](#) triggers itching and localized [vasodilation](#). Although this patient has a [pruritic](#) rash, [histamine](#) plays no role in salivary secretion, meaning [histamine](#) receptor antagonism is not responsible for this patient's dry mouth.

E - Antagonism at α -adrenergic receptors

Explanation Why

Antagonism at α_1 -adrenergic receptors in the salivary gland can lead to a decreased salivation. Some [antihistamines](#) have [\$\alpha\$ -adrenergic](#) blocking activity, which results in side effects such as [dizziness](#) and [orthostatic hypotension](#). However, this patient's dry mouth is much more likely caused by a different mechanism.

Question # 25

An 81-year-old man comes to the emergency department because of left-sided visual loss that started 1 hour ago. He describes initially seeing jagged edges, which was followed by abrupt, complete loss of central vision in the left eye. He has hypertension and type 2 diabetes mellitus. Blood pressure is 145/89 mm Hg. Neurologic examination shows no abnormalities. A photograph of the fundoscopic findings is shown. Which of the following tests is most likely to confirm this patient's underlying condition?



	Answer	Image
A	Glycated hemoglobin concentration	
B	Carotid artery duplex ultrasonography	
C	Erythrocyte sedimentation rate	

	Answer	Image
D	CD4+ T-cell count	
E	Optic tonometer	

Hint

The fundoscopy shows a pale retina with a cherry red spot at the fovea. Together with sudden, painless, transient monocular vision, this finding is concerning for central retinal artery occlusion. Causes include embolism (most common), thrombosis, vasculitis, and fibromuscular dysplasia.

Correct Answer

A - Glycated hemoglobin concentration

Explanation Why

Increased [glycated hemoglobin](#) concentrations are seen in patients with poorly controlled [diabetes mellitus](#). This patient has a history of [diabetes](#) and is therefore at risk of [diabetic retinopathy](#), a condition that can cause visual impairment and blindness. However, vision loss in [diabetic retinopathy](#) is typically bilateral and occurs over the course of many years, as opposed to the abrupt, unilateral vision loss seen in this patient. Direct fundoscopy in a patient with [diabetic retinopathy](#) shows microaneurysms, hard exudates, and [macular edema](#) (nonproliferative) or retinal [neovascularization](#) and [vitreous hemorrhage](#) (proliferative).

B - Carotid artery duplex ultrasonography

Explanation Why

Carotid [artery duplex ultrasonography](#) can be used to evaluate for carotid [atherosclerosis](#), a condition that increases the risk of [thromboembolism](#) due to rupture of [atherosclerotic plaques](#), which is the most common cause of [central retinal artery occlusion](#). This patient has several [atherosclerotic risk factors](#), including advanced age, [hypertension](#), and [diabetes mellitus](#), which make [thromboembolism](#) secondary to carotid [artery atherosclerosis](#) the most likely cause of his symptoms.

C - Erythrocyte sedimentation rate

Explanation Why

[Erythrocyte sedimentation rate \(ESR\)](#) is a nonspecific [inflammatory marker](#) that can be increased in cases of infection, [inflammation](#), or [malignancy](#). [Temporal arteritis](#) can cause significant elevation in [ESR](#) and is a rare etiology of [central retinal artery occlusion](#), the most likely diagnosis in this patient. However, he lacks other symptoms of [temporal arteritis](#) (e.g., [headache](#), [jaw claudication](#), constitutional symptoms). Moreover, a [temporal artery biopsy](#), not [ESR](#), is the gold standard for the diagnosis of [temporal arteritis](#).

D - CD4+ T-cell count

Explanation Why

A [CD4+ T cell](#) count can be used to track the prognosis in patients diagnosed with or suspected of having [HIV](#). Patients with a low [CD4](#) count are more susceptible to [cytomegalovirus](#), which can cause retinitis and vision loss. However, [CMV retinitis](#) causes progressive loss of vision over days as opposed to the abrupt onset seen in this patient's case. Direct fundoscopy in a patient with [CMV retinitis](#) shows retinal hemorrhages and [cotton wool spots](#).

E - Optic tonometer

Explanation Why

An optic tonometer is used to measure [intraocular pressure \(IOP\)](#). Increased [IOP](#) is seen in patients with [glaucoma](#) and patients with increased [intracranial pressure \(ICP\)](#). Both of these conditions can lead to visual impairment. In particular, acute, [closed-angle glaucoma](#) can cause sudden-onset visual loss. However, it is typically painful and associated with [headache](#) and vomiting, none of which is seen in this patient. Direct fundoscopy in patients with [increased ICP](#) shows [papilledema](#).

Question # 26

A 52-year-old man is brought to the physician because of a 2-week history of memory loss. Three weeks ago, he had a cardiac arrest that required cardiopulmonary resuscitation and intravenous epinephrine. On mental status examination, he cannot recall objects shown to him 20 minutes earlier but vividly recalls memories from before the incident. The remainder of the examination shows no abnormalities. Which of the following structures of the brain is most likely affected?

	Answer	Image
A	Purkinje cells of the cerebellum	
B	Microglial cells of dorsal midbrain	
C	Internal pyramidal layer of the amygdala	
D	External pyramidal layer of the parietal cortex	
E	Pyramidal cells of the hippocampus	
F	Astroglial cells of the putamen	

Hint

This patient presents with features of an ischemic stroke following a cardiac arrest. The short-term memory loss indicates selective neuronal necrosis of a structure within the limbic system.

Correct Answer

A - Purkinje cells of the cerebellum

Explanation Why

[Cerebellar Purkinje cells](#) are very vulnerable to [ischemic](#) insults. However, patients with [ischemic](#) damage to this group of cells would present with [intention tremor](#), nystagmus, and [ataxia](#).

B - Microglial cells of dorsal midbrain

Explanation Why

[Microglial cells](#) are relatively resistant to [ischemic](#) insults because they are not as metabolically active as [neurons](#). In fact, these [macrophages](#) are typically seen in the inflammatory reaction to [cellular injury](#) after [ischemia](#). [Strokes](#) affecting the [dorsal midbrain](#) present with [Parinaud syndrome](#), not [memory](#) impairment.

C - Internal pyramidal layer of the amygdala

Explanation Why

The [amygdala](#) is a complex of nuclei located in the [temporal lobe](#), it is not composed of cellular layers like the [neocortex](#) or [hippocampus](#). Moreover, [strokes](#) affecting the [amygdala](#) typically result in uninhibited, aggressive behavior ([Kluver-Bucy syndrome](#)).

D - External pyramidal layer of the parietal cortex

Explanation Why

The external pyramidal layer of the parietal cortex is very vulnerable to [ischemic](#) injury. However, neuronal [cell death](#) in the dominant parietal cortex would lead to [Gerstmann syndrome](#), not [anterograde amnesia](#) as seen here.

E - Pyramidal cells of the hippocampus

Explanation Why

Damage to the [pyramidal cells](#) of the [hippocampus](#) typically leads to [anterograde amnesia](#), as seen in this patient. The [hippocampus](#) is the brain region most vulnerable to [ischemic hypoxia](#), and only a few minutes of [ischemia](#) can lead to irreversible damage mediated by cytotoxic glutamatergic release and uptake. Other brain regions that are particularly susceptible to [ischemic](#) insults are neocortical [pyramidal cells](#), striatal [neurons](#), and Purkinje cells.

F - Astroglial cells of the putamen

Explanation Why

[Astroglial cells](#) (also known as [astrocytes](#)) of the [putamen](#) are relatively resistant to [ischemic](#) injury mainly because they can use glycogen stores for [anaerobic metabolism](#). Moreover, injury to the cells of the [putamen](#) results in impaired voluntary muscle control rather than [memory](#) loss. Following an [ischemic](#) event, [astrocytes](#) become reactive and form a [glial scar](#) ([reactive gliosis](#)).

Question # 27

A 78-year-old man is brought to the emergency department by ambulance 30 minutes after the sudden onset of speech difficulties and right-sided arm and leg weakness. Examination shows paralysis and hypoesthesia on the right side, positive Babinski sign on the right, and slurred speech. A CT scan of the head shows a hyperdensity in the left middle cerebral artery and no evidence of intracranial bleeding. The patient's symptoms improve rapidly after pharmacotherapy is initiated and his weakness completely resolves. Which of the following drugs was most likely administered?

	Answer	Image
A	Rivaroxaban	
B	Alteplase	
C	Heparin	
D	Prasugrel	
E	Warfarin	

Hint

This patient's symptoms in combination with the CT results indicate an ischemic stroke caused by an obstructive lesion in the left middle cerebral artery. The drug administered can also be used to treat patients with early myocardial infarctions or unstable patients with a pulmonary embolism.

Correct Answer

A - Rivaroxaban

Explanation Why

[Rivaroxaban](#), a direct [factor Xa](#) inhibitor, is used for the prevention of [ischemic stroke](#) in patients with [atrial fibrillation](#) and the treatment of [venous thromboembolism](#), to name a few indications. Despite its prophylactic value, it has no role in the treatment of acute [ischemic stroke](#). Hence, it is unlikely to be given to this patient with an acute [ischemic stroke](#).

B - Alteplase

Explanation Why

[Alteplase](#), a [recombinant tissue plasminogen activator](#), is the mainstay of treatment in acute [ischemic stroke](#) to salvage [ischemic](#) tissue. It converts [plasminogen](#) to [plasmin](#), which degrades [fibrin](#) and lyses formed clots. It is effective when administered within 4.5 hours of symptom onset. Several important contraindications exist such as acute [intracranial hemorrhage](#), recent surgery, severe uncontrolled [hypertension](#), [thrombocytopenia](#), and [coagulopathy](#).

C - Heparin

Explanation Why

[Heparin](#) is used for the acute treatment of several conditions such as [venous thromboembolism](#), [pulmonary embolism](#), and [STEMI](#). It activates [antithrombin III](#) in a manner that inhibits both [thrombin](#) and [factor X](#). Early use of [heparin](#) in acute [ischemic stroke](#) has been associated with higher [mortality](#) and worse outcomes as compared to other [anticoagulants](#).

D - Prasugrel

Explanation Why

[Prasugrel](#), a [platelet P2Y₁₂ receptor inhibitor](#), is given to patients with [acute coronary syndrome](#) and for those undergoing [percutaneous coronary intervention](#) (to prevent coronary [stent thrombosis](#)). The drug inhibits [platelet aggregation](#) by preventing the expression of [Gp IIb/IIIa](#) receptors on the [platelet](#) surface. [Prasugrel](#) is contraindicated in patients with a history of [stroke](#) or [TIA](#) because of the increased risk of significant or fatal bleeding.

E - Warfarin

Explanation Why

[Warfarin](#) is a [vitamin K antagonist](#) used for the prophylaxis of [ischemic stroke](#) in patients with [atrial fibrillation](#), and as treatment for patients with [venous thromboembolism](#). It inhibits hepatic [epoxide reductase](#), thereby blocking synthesis (recycling) of the active, reduced form of vit. K. Without reduced vit. K, γ -[carboxylation](#) of [glutamate](#) residues cannot occur, which reduces the production of active [coagulation factors](#) II, VII, IX, and X, as well as anticoagulatory [proteins](#) C and S. Because this drug takes days to exert and remove its clinically significant anticoagulatory effect, it is primarily used for chronic anticoagulation and has no use in the acute setting.

Question # 28

One day after undergoing surgery for a traumatic right pelvic fracture, a 73-year-old man has pain over his buttocks and scrotum and urinary incontinence. Physical examination shows right-sided perineal hypesthesia and absence of anal sphincter contraction when the skin around the anus is touched. This patient is most likely to have which of the following additional neurological deficits?

	Answer	Image
A	Paralysis of hip adductors	
B	Absent reflex erection	
C	Impaired hip flexion	
D	Impaired psychogenic erection	
E	Absent cremasteric reflex	

Hint

The history of a recent pelvic trauma, symptoms of perineal hypesthesia, and pain in the pelvis and genitals, as well as an absent sphincter reflex and urinary incontinence, indicate a pudendal nerve injury.

Correct Answer

A - Paralysis of hip adductors

Explanation Why

Paralysis of [hip](#) adductors is seen in damage to the [obturator nerve](#), which could be caused by [hip](#) or pelvic trauma. However, symptoms would include a sensory deficit on the [medial](#) surface of the [anterior](#) thigh. Right-sided perineal [hypesthesia](#), absent anal sphincter contraction, and [urinary incontinence](#) would not be expected.

B - Absent reflex erection

Explanation Why

The [pudendal nerve](#) provides sensory innervation to the [skin](#) of the perineum, external genitalia, and external urethral and anal sphincter muscles. A [reflex erection](#) occurs on tactile stimulation of the genital area, which stimulates the afferent fibers of the [pudendal nerve](#). This activates a reflex arc with the [parasympathetic nervous system](#) at the sacral roots originating at S2 to S4, forwarding the stimulus to the [inferior hypogastric plexus](#). This, in turn, leads to relaxation of the cavernous [smooth muscle](#), which causes [vasodilation](#) (mediated by [nitric oxide](#)) and [erection](#). The [pudendal nerve](#) may be injured in [pelvic fractures](#) or pelvic surgeries.

C - Impaired hip flexion

Explanation Why

Impaired [hip flexion](#) would be consistent with damage to the [femoral nerve](#) (paralysis of iliopsoas, [pectineus](#), [rectus femoris](#), and [sartorius](#) muscles). The [femoral nerve](#) can also be damaged by pelvic trauma. However, it would manifest with further motor deficits, including impaired [knee](#) extension and a decreased [patellar tendon](#) reflex (paralysis of [quadriceps femoris muscle](#)). Additionally, sensory deficits of the anteromedial thigh ([anterior](#) cutaneous branches), [medial](#) lower leg, and [medial](#) edge of the foot ([saphenous nerve](#) lesion) would be expected instead of perineal [hypesthesia](#), an absent sphincter reflex, and [urinary incontinence](#).

D - Impaired psychogenic erection

Explanation Why

[Psychogenic erection](#) is caused by cortical stimulation with visual, aural, and sensory stimuli or fantasy, which activates the thoracolumbar [erection](#) center T11–L2 via fibers from the brain to the [spine](#). These fibers can be damaged by [spinal cord](#) injury but are unlikely to be impaired by pelvic trauma or surgery. Furthermore, unilateral perineal [hypesthesia](#), an absent sphincter reflex, and [urinary incontinence](#) would not be expected.

E - Absent cremasteric reflex

Explanation Why

An absent [cremasteric reflex](#) can be seen in patients with damage to the ilioinguinal nerve, which could be caused by pelvic trauma. However, damage to the ilioinguinal nerve would result in sensory loss in the upper [medial](#) thigh (impairing the afferent limb of the [cremasteric reflex](#)), the root of the [penis](#), and the [anterior scrotum](#). Right-sided perineal [hypesthesia](#) and absent anal sphincter contraction would not be expected.

Question # 29

A 13-year-old boy is brought to the emergency department because of a 2-day history of fever, headache, and irritability. He shares a room with his 7-year-old brother, who does not have any symptoms. The patient appears weak and lethargic. His temperature is 39.1°C (102.4°F) and blood pressure is 99/60 mm Hg. Physical examination shows several purple spots over the trunk and extremities. A lumbar puncture is performed. Gram stain of the cerebrospinal fluid shows numerous gram-negative diplococci. Administration of which of the following is most likely to prevent infection of the patient's brother at this time?

	Answer	Image
A	Penicillin G	
B	Cephalexin	
C	Ciprofloxacin	
D	Conjugated vaccine	
E	Rifampin	
F	Doxycycline	

Hint

The constellation of high fever, headache, irritability, and CSF findings (gram-negative diplococci) is diagnostic of meningococcal meningitis. Post-exposure chemoprophylaxis (PEP) is important to prevent infection and disease transmission.

Correct Answer

A - Penicillin G

Explanation Why

[Penicillin G](#) is not used as prophylaxis against [N. meningitidis](#) in close contacts of infected patients. The emergence of [penicillin](#)-resistant strains of the bacteria raises concerns about this agent's ability to completely eradicate the presence of the bacteria in the nasopharynx. Additionally, [penicillin G](#) must be given intravenously several times a day, making it very inconvenient as a prophylactic agent. In cases of [penicillin](#)-sensitive [meningococcal meningitis](#), [penicillin G](#) can be used as treatment.

B - Cephalexin

Explanation Why

[Cephalexin](#), like all [first-generation cephalosporins](#), has very limited activity against [N. meningitidis](#) and is thus not indicated for treatment or prophylaxis against the pathogen.

C - Ciprofloxacin

Explanation Why

Oral [ciprofloxacin](#), although effective as a prophylactic agent against [N. meningitidis](#) in adults, is contraindicated in the patient's 7-year-old brother. This drug should not be used in patients under the age of 18 years due to the risk of drug-mediated arthropathy, [cartilage](#) toxicity, and tendinopathy.

D - Conjugated vaccine

Explanation Why

Meningococcal vaccine provides [active immunity](#) against [N. meningitidis](#) and should be administered. However, serum [antibody](#) titers do not reach a protective level until approximately 7–10 days after [vaccination](#). This time frame would leave the patient's brother vulnerable to infection for some time, necessitating a different intervention more acutely.

E - Rifampin

Explanation Why

[Rifampin](#) is a mainstay of prophylaxis against [N. meningitidis](#) for people in close contact with an infected individual. The patient's brother, as well as any other close contacts, should receive a 2-day course of this drug. In scenarios in which [rifampin](#) is contraindicated (e.g. hypersensitivity or concomitant [HIV](#) protease inhibitor administration) or unavailable, a single dose of intravenous [ceftriaxone](#) can be used for the same purpose. Oral [ciprofloxacin](#), although effective as a prophylactic agent against [N. meningitidis](#) in adults, is contraindicated in the patient's 7-year-old brother.

F - Doxycycline

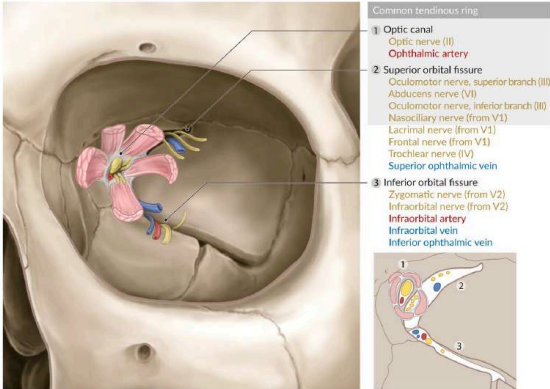
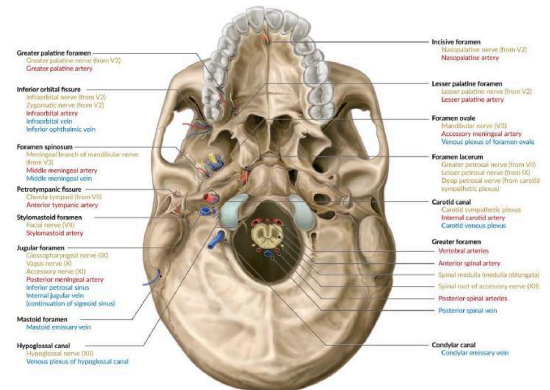
Explanation Why

[Doxycycline](#) is not used as prophylaxis against [N. meningitidis](#) because the drug does not cover this species. Moreover, [doxycycline](#) (like all [tetracyclines](#)) is contraindicated in children younger than 8 years of age due to the risk of [permanent tooth](#) staining from the drug.

Question # 30

A 44-year-old woman comes to the physician because of a 1-month history of progressively worsening headaches and fatigue. She has also had a 5-kg (11-lb) weight loss in the same time period. MRI of the head shows a hyperintense mass with extension into the right foramen rotundum. Further evaluation of this patient is most likely to show which of the following findings?

	Answer	Image
A	Decreased sensation over the cheekbone, nasolabial fold, and the upper lip	This diagram illustrates the base of the skull from an inferior perspective, highlighting various foramina and the nerves/arteries that pass through them. Labels include: Anterior ethmoidal foramen (Anterior ethmoidal nerve from V1, Anterior ethmoidal artery, Anterior ethmoidal vein), Superior orbital fissure (Oculomotor nerve (III), Trochlear nerve (IV), Trigeminal nerve (V), Lacrimal nerve from V1, Frontal nerve from V1, Maxillary nerve from V2, Abducent nerve (VI), Superior ophthalmic vein), Foramen ovale (Mandibular nerve (V3), Accessory meningeal artery, Venous plexus of foramen ovale), Foramen spinosum (Middle meningeal artery, Middle meningeal vein), Hiatus for lesser petrosal nerve (Lesser petrosal nerve from IX, Superior petrosal artery), Hiatus for greater petrosal nerve (Greater petrosal nerve from V3), Mastoid foramen (Mastoid emissary vein), Condylar canal (Condylar emissary vein), Jugular foramen (Cervicofacial nerve (XI), Vagus nerve (X), Accessory nerve (XI), Posterior meningeal artery, Inferior petrosal vein, Internal jugular vein (continuation of sigmoid sinus)), Foramen cecum (Embryonic vein), Cribriform plate (Olfactory nerve (I)), Posterior ethmoidal foramen (Posterior ethmoidal nerve from V1, Posterior ethmoidal artery, Posterior ethmoidal vein), Optic canal (Optic nerve (II), Ophthalmic artery), Foramen rotundum (Maxillary nerve (V2)), Carotid canal (Carotid sheath: internal carotid artery, Internal carotid vein), Internal auditory meatus (Facial nerve (VII), Vestibulocochlear nerve (VIII), Labyrinthine artery, Labyrinthine vein), Foramen magnum (Vertebral arteries, Anterior spinal artery, Spinal nucleus (medulla oblongata), Spinal root of accessory nerve (XI), Posterior spinal arteries, Posterior spinal vein), and Hypoglossal canal (Hypoglossal nerve (XII), Venous plexus of hypoglossal canal).
B	Hemiatrophy of the tongue with right-sided deviation when protruded	
C	Abnormal taste of the distal tongue and decreased sensation behind the ear	This diagram shows the tongue with color-coded regions for taste and sensation. The 'Taste' column shows the anterior two-thirds (blue), the circumvallate papillae (green), and the posterior one-third (yellow). The 'Sensation' column shows the anterior two-thirds (blue), the circumvallate papillae (green), and the posterior one-third (yellow). The 'Motor' column shows the anterior two-thirds (blue), the circumvallate papillae (green), and the posterior one-third (yellow). A legend identifies the nerves: Lingual nerve (V3), Facial nerve (VII), Glossopharyngeal nerve (IX), Vagus nerve (X), and Hypoglossal nerve (XII).

	Answer	Image
D	Absent corneal reflex and decreased sensation of the forehead	 Common tendinous ring 1 Optic canal Optic nerve (II) Ophthalmic artery 2 Superior orbital fissure Oculomotor nerve, superior branch (III) Abducens nerve (VI) Oculomotor nerve, inferior branch (III) Nasociliary nerve (from V1) Lacrimal nerve (from V1) Frontal nerve (from V1) Trochlear nerve (IV) Superior ophthalmic vein 3 Inferior orbital fissure Zygomatic nerve (from V2) Infraorbital nerve (from V2) Infraorbital artery Infraorbital vein Inferior ophthalmic vein
E	Masseter and temporalis muscle wasting with jaw deviation to the right	 Greater palatine foramen Greater palatine nerve (from V2) Greater palatine artery Inferior orbital fissure Inferior orbital nerve (from V2) Zygomatic nerve (from V2) Infraorbital artery Infraorbital vein Inferior ophthalmic vein Foramen spinosum Meningeal branch of maxillary nerve (from V2) Middle meningeal artery Middle meningeal vein Petrosphenic fissure Chorda tympani (from V3) Anterior tympanic artery Stylomastoid foramen Facial nerve (VII) Stylomastoid artery Jugular foramen Glossopharyngeal nerve (IX) Vagus nerve (X) Accessory nerve (XI) Posterior meningeal artery Inferior petrosal sinus Internal jugular vein (continuation of sigmoid sinus) Mastoid foramen Mastoid emissary vein Hypoglossal canal Hypoglossal nerve (XII) Venous plexus of hypoglossal canal Incisive foramen Neosensory nerve (from V2) Neosensory artery Lesser palatine foramen Lesser palatine nerve (from V2) Lesser palatine artery Foramen ovale Maxillary nerve (V2) Accessory meningeal artery Venous plexus of foramen ovale Foramen lacerum Greater petrosal nerve (from V1) Lesser petrosal nerve (from V1) Deep petrosal nerve (from carotid sympathetic plexus) Carotid canal Internal carotid artery Internal carotid vein Carotid venous sinus Greater foramen Vertebral arteries Anterior spinal artery Spinal medulla (medulla oblongata) Spinal root of accessory nerve (XI) Posterior spinal arteries Posterior spinal vein Condylar canal Condylar emissary vein

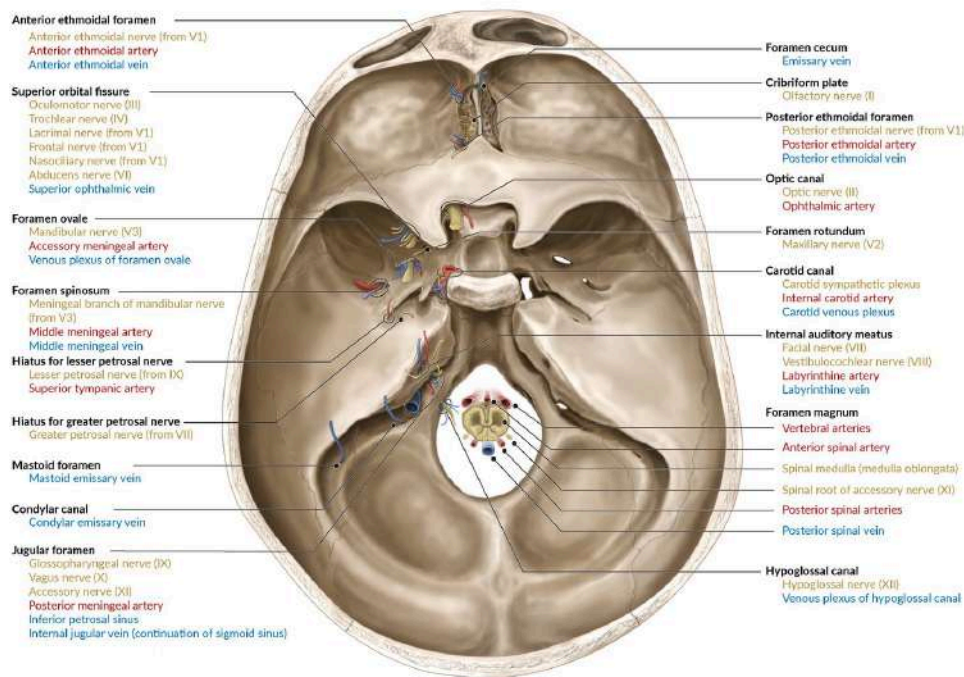
Hint

The maxillary nerve passes through the foramen rotundum.

Correct Answer

A - Decreased sensation over the cheekbone, nasolabial fold, and the upper lip

Image



Explanation Why

Sensation to the middle third of the face (i.e., cheekbone, [nasolabial fold](#), and upper lip) is supplied by the [maxillary branch of the trigeminal nerve \(CN V2\)](#). After exiting the [skull](#) through the [foramen rotundum](#), [CN V2](#) passes through the infraorbital canal to exit the [orbit](#) via the [infraorbital foramen](#) and then divides into the cutaneous branches, which supply sensation to the midface. A mass extending into the right [foramen rotundum](#), as seen in this patient's [MRI](#), could compress [CN V2](#), resulting in anesthesia of the midface.

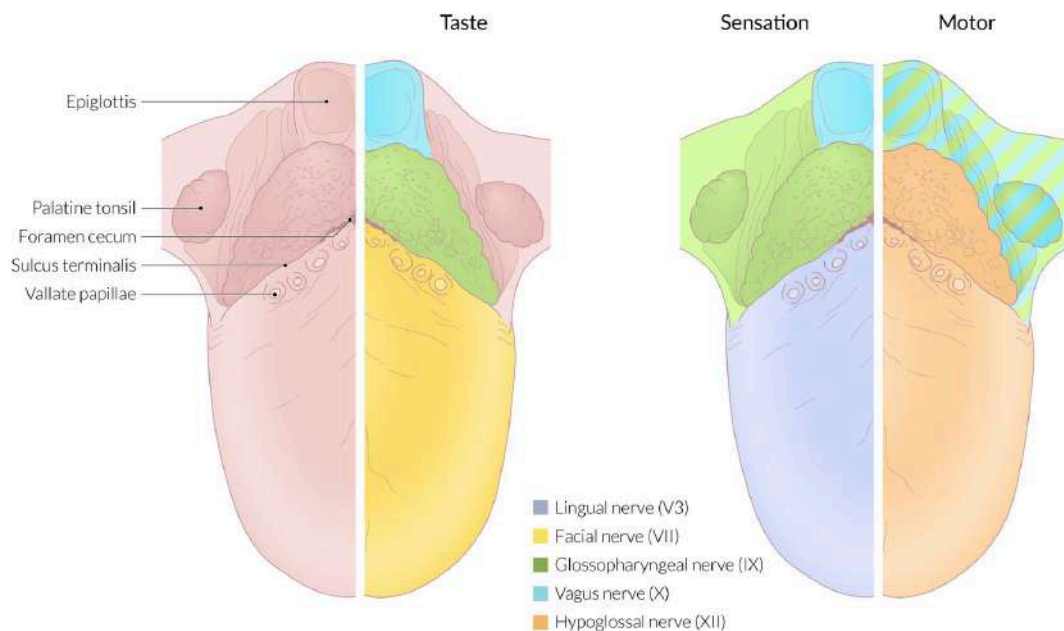
B - Hemiatrophy of the tongue with right-sided deviation when protruded

Explanation Why

Hemiatrophy of the [tongue](#) with right-sided deviation when protruded would indicate damage to the right [hypoglossal nerve](#), which supplies motor innervation to the [tongue](#). However, the [hypoglossal nerve](#) exits the [skull](#) through the hypoglossal foramen, whereas this patient's [MRI](#) shows a mass extending into the [foramen rotundum](#).

C - Abnormal taste of the distal tongue and decreased sensation behind the ear

Image



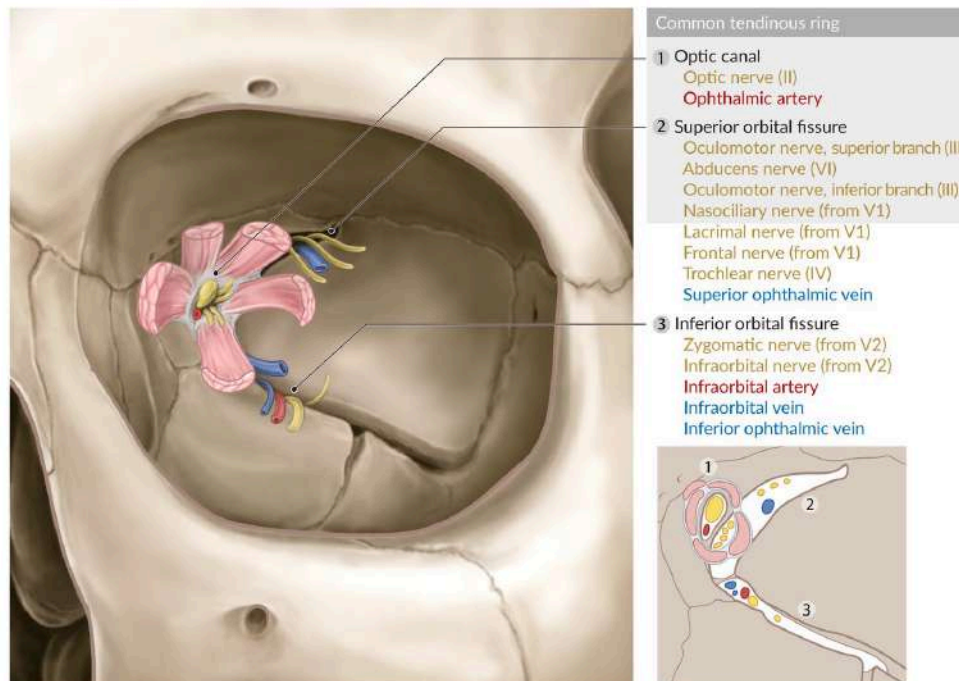
Explanation Why

Abnormal [taste](#) of the [distal tongue](#) and decreased sensation behind [the ear](#) would indicate [facial nerve palsy](#). The [facial nerve](#) (CN VII) supplies [taste](#) sensation to the [anterior](#) 2/3 of the [tongue](#) and cutaneous sensation [posterior](#) to [the ear](#). However, the [facial nerve](#) passes through the [internal](#)

[acoustic meatus](#) and partly exits the [skull](#) through the [stylomastoid foramen](#), whereas this patient's [MRI](#) shows a mass extending into the [foramen rotundum](#).

D - Absent corneal reflex and decreased sensation of the forehead

Image



Explanation But

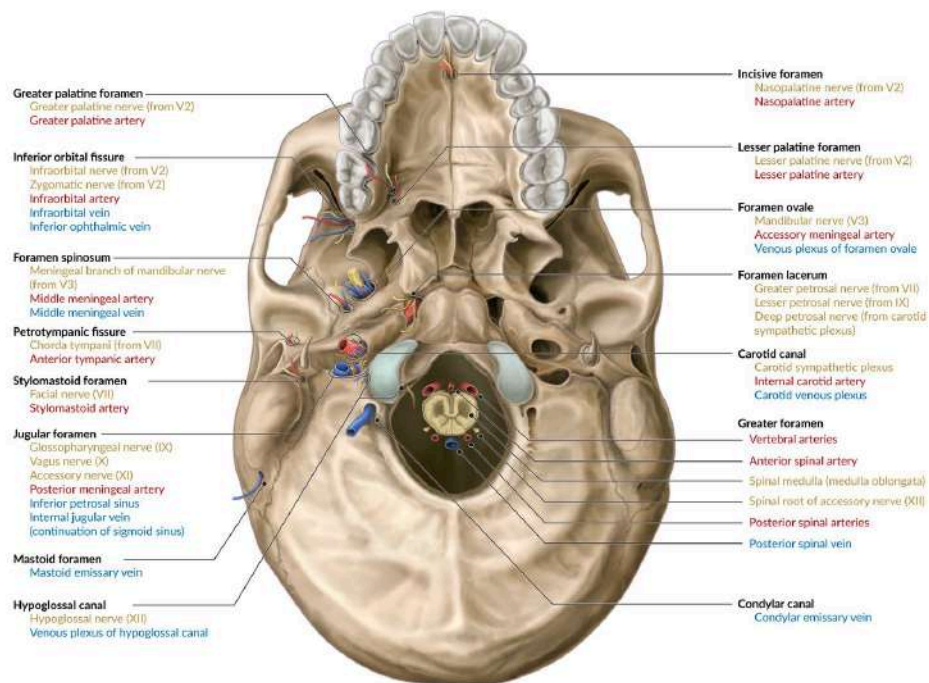
The efferent limb of the [corneal reflex](#) is mediated by the [facial nerve](#) (CN VII).

Explanation Why

An absent [corneal reflex](#) and decreased sensation of the forehead would indicate damage to the [ophthalmic branch of the trigeminal nerve](#) (CN V1), which mediates the afferent limb of the [corneal reflex](#) and supplies sensation to the superior third of the face. However, [CN V1](#) passes through the [superior orbital fissure](#), whereas this patient's [MRI](#) shows a mass extending into the [foramen rotundum](#).

E - Masseter and temporalis muscle wasting with jaw deviation to the right

Image



Explanation Why

Masseter and temporalis muscle wasting with jaw deviation to the right would indicate damage to the mandibular branch of the trigeminal nerve (CN V3), which supplies the masseter, temporalis, and other muscles of mastication. Paralysis of the CN V3 causes deviation of the jaw toward the injured side. However, CN V3 exits the skull through the foramen ovale (skull), whereas this patient's MRI shows a mass extending into the foramen rotundum.

Question # 31

A 42-year-old man is brought to the emergency department by his wife because of a 1-day history of progressive confusion. He recently lost his job. He has a history of chronic alcoholism and has been drinking 14 beers daily for the past week. Before this time, he drank 6 beers daily. He appears lethargic. His vital signs are within normal limits. Serum studies show a sodium level of 111 mEq/L and a potassium level of 3.7 mEq/L. Urgent treatment for this patient's current condition increases his risk for which of the following adverse events?

	Answer	Image
A	Wernicke encephalopathy	
B	Cerebral edema	
C	Cardiac arrhythmia	
D	Osmotic myelinolysis	
E	Hyperglycemia	
F	Respiratory depression	

Hint

This patient has acutely symptomatic hyponatremia (confusion, lethargy), for which the appropriate treatment is administration of intravenous hypertonic saline.

Correct Answer

A - Wernicke encephalopathy

Explanation Why

[Wernicke encephalopathy](#) is an acute and reversible emergency caused by severe [thiamine \(vitamin B1\)](#) deficiency. It is mainly seen in the context of [alcohol abuse](#). While this patient has a history of chronic alcohol intake and is currently confused, he lacks other classic features of [Wernicke encephalopathy](#) such as [ataxia](#) and [ophthalmoplegia](#), making this diagnosis unlikely. In patients with suspected [Wernicke encephalopathy](#), [thiamine](#) should always be administered before glucose, as glucose increases [thiamine](#) demand and can worsen encephalopathy.

B - Cerebral edema

Explanation Why

[Cerebral edema](#) can develop as a complication of overly rapid correction of [hypernatremia](#), not [hyponatremia](#), as seen in this patient. Chronic [hypernatremia](#) causes an expansion of the intravascular volume; when sodium levels are acutely decreased, fluid shifts to the extravascular space causing brain swelling and [edema](#), which can result in [seizures](#), and at times, permanent neurologic deficits and death. As such, it is recommended that sodium levels be decreased by 12 mEq/L per day.

C - Cardiac arrhythmia

Explanation Why

[Cardiac arrhythmias](#) are unlikely to develop from excess sodium correction. [Arrhythmias](#) can happen in extreme cases of [hypernatremia](#) ($\text{Na}^+ > 190 \text{ mmol/l}$), but it is a rare complication of rapid correction of [hyponatremia](#). Potassium fluctuations, on the other hand, are associated with increased risk of [arrhythmias](#). This patient's vital signs and potassium are within normal limits, making a cardiac condition unlikely to be the cause of his presentation.

D - Osmotic myelinolysis

Explanation Why

[Osmotic myelinolysis](#) develops when there is damage to the [myelin](#) sheath of nerves in the [CNS](#). It is caused by a sudden rise in the [osmolarity](#) of blood, which results in increased movement of fluid from the [interstitial](#) space of the brain to the intravascular compartment in order to maintain an osmotic balance. This patient likely has chronic [hyponatremia](#) due to his excess drinking (referred to as [beer potomania](#)), which causes chronic brain swelling. When sodium levels are increased too quickly, especially in patients with sodium levels < 120 meq/L, the fluid shifts causes the brain to shrink and [demyelinate](#). As such, it is recommended that serum sodium levels be raised by less than 6 to 8 meq/L within 24 hours, at a rate of 0.5–1 mEq/L per hour.

E - Hyperglycemia

Explanation Why

[Hyperglycemia](#) can be seen in patients given dextrose-containing [intravenous fluids](#) at a rapid rate for correction of [hypernatremia](#). This patient, however, will likely be treated with hypertonic saline given his sodium levels of 111 mmol/l.

F - Respiratory depression

Explanation Why

Respiratory depression in the setting of [alcohol abuse](#) would be seen in patients in which [benzodiazepines](#) are given to prevent [alcohol withdrawal syndrome](#). However, this patient has no features of ongoing withdrawal such as anxiety, [palpitations](#), sweating, and autonomic hyperactivity.

Question # 32

A 9-year-old boy is brought to the physician by his mother to establish care after moving to a new city. He lives at home with his mother and older brother. He was having trouble in school until he was started on ethosuximide by a previous physician; he is now performing well in school. This patient is undergoing treatment for a condition that most likely presented with which of the following symptoms?

	Answer	Image
A	Regression of verbal skills and stereotyped hand-wringing	
B	Limited attention span and poor impulse control	
C	Overwhelming daytime sleepiness and hypnagogic hallucinations	
D	Episodic jerky movements of the arm and impaired consciousness	
E	Frequent episodes of blank staring and eye fluttering	
F	Recurrent motor tics and involuntary obscene speech	

Hint

Ethosuximide is the drug of choice for childhood absence seizures.

Correct Answer

A - Regression of verbal skills and stereotyped hand-wringing

Explanation Why

Regression of skills and stereotyped hand-wringing are characteristic of [Rett syndrome](#), a rare inherited disorder associated with progressive degeneration of locomotor and fine motor skills that presents with progressive loss of cognitive (especially verbal) skills. While this could explain the patient's poor school performance, [Rett syndrome](#) almost exclusively affects females and is not treated with [ethosuximide](#).

B - Limited attention span and poor impulse control

Explanation Why

Limited attention span and poor impulse control are hallmarks of [attention deficit hyperactivity disorder](#) ([ADHD](#)). Patients present with inattention and appear hyperactive, restless and impulsive, which may lead to impaired school performance. Although this patient's trouble in school could have been mistakenly attributed to inattention, his disorder is most likely caused by episodes of unresponsiveness instead of hyperactive behavior. Moreover, [ADHD](#) is treated with stimulant medication (e.g., [amphetamines](#)) and [behavior therapy](#), not [ethosuximide](#).

C - Overwhelming daytime sleepiness and hypnagogic hallucinations

Explanation Why

[Narcolepsy](#) is characterized by [excessive daytime sleepiness](#), [cataplexy](#), [hallucinations](#) upon waking or falling asleep ([hypnagogic hallucinations](#)), and [sleep paralysis](#). [Narcolepsy](#) is treated with stimulant medications such as [modafinil](#), rather than [ethosuximide](#), making this diagnosis unlikely.

D - Episodic jerky movements of the arm and impaired consciousness

Explanation Why

Episodic jerky movements of the arm and impaired consciousness are symptoms suggestive of a [complex partial seizure](#). While most [antiepileptics](#) can be employed in its treatment, [ethosuximide](#) is not among them. This makes this diagnosis unlikely, given the patient's [medical history](#).

E - Frequent episodes of blank staring and eye fluttering

Explanation Why

[Absence seizures](#) are [generalized seizures](#) with characteristic transient periods of unresponsiveness, which may present as episodes of blank staring and [eye](#) fluttering. There is usually no preceding [aura](#), or postictal drowsiness or confusion. [Ethosuximide](#) blocks thalamic T-type calcium channels and is an effective treatment for [absence seizures](#), as indicated here by this patient's improving performance in school after therapy was started.

F - Recurrent motor tics and involuntary obscene speech

Explanation Why

Recurrent motor [tics](#) and involuntary obscene [speech](#) are characteristic of [Tourette syndrome](#), a severe neurological [tic disorder](#) that typically presents in boys and is often associated with [ADHD](#). Although it might explain this patient's poor school performance, neither [Tourette syndrome](#) nor [ADHD](#) is treated with [ethosuximide](#).

Question # 33

A 25-year-old woman is brought to the physician by her husband because she has appeared increasingly agitated over the last week. She feels restless, has not been able to sleep well, and has been pacing around her house continuously in an attempt to relieve her symptoms. Two weeks ago, she was diagnosed with schizophrenia and treatment with fluphenazine was initiated. Today, physical examination is interrupted multiple times because she is unable to sit or stand still for more than a couple minutes. Which of the following is the most likely diagnosis?

	Answer	Image
A	Restless legs syndrome	
B	Parkinsonism	
C	Athetosis	
D	Tourette syndrome	
E	Akathisia	
F	Inadequately treated schizophrenia	
G	Tardive dyskinesia	
H	Drug-induced mania	

Hint

This patient has escalating agitation, restlessness, poor sleep, continuous pacing, and the inability to remain still for more than a few minutes. She was recently started on a typical high-potency antipsychotic medication (fluphenazine). She likely has the most common subtype of extrapyramidal symptoms (EPS).

Correct Answer

A - Restless legs syndrome

Explanation Why

In [restless legs syndrome](#) (RLS), patients experience disturbed sleep caused by an urge to move, similar to this patient. However, in RLS, movement typically relieves the urge to move, whereas this patient does not find relief. This patient also has symptoms during the day as well as at night, whereas the symptoms of RLS have a [circadian rhythm](#). [Restless legs syndrome](#) is not associated with [antipsychotic](#) medications.

B - Parkinsonism

Explanation Why

[Pseudoparkinsonism](#) can be induced by [antipsychotic](#) drugs and is considered a subtype of EPS. It appears within days to months of treatment initiation, and this patient was prescribed [fluphenazine](#) 2 weeks ago. However, [pseudoparkinsonism](#) is characterized by [tremor](#), [cogwheel rigidity](#), and shuffling gait, which this patient does not have.

C - Athetosis

Explanation Why

[Athetosis](#) may occur as a feature of [tardive dyskinesia](#), which can occur as an EPS following months to years of exposure to [antipsychotic](#) drugs. However, this patient has only been taking [fluphenazine](#) for 2 weeks. Furthermore, [athetosis](#) is characterized by slow, continuous, involuntary writhing movements, which are not present here.

D - Tourette syndrome

Explanation But

[Antipsychotics](#) such as [fluphenazine](#) are sometimes used to manage [tics](#) in [Tourette syndrome](#).

Explanation Why

[Tourette syndrome](#) involves the urge to move that precedes its characteristic motor [tics](#). This patient also has an urge to move. However, Tourette [tics](#) are sudden and involuntary, which does not describe this patient's symptoms. In addition, this patient does not have any vocal [tics](#), and she is not of the typical age of onset for [Tourette syndrome](#) (i.e., before the age of 18). Lastly, [Tourette syndrome](#) is not known to be caused by [antipsychotic](#) medications and is not a known EPS.

E - Akathisia

Explanation But

If feasible, this patient should have her [fluphenazine](#) dosage reduced. Other treatment options include changing to a second-generation drug or adding a [beta blocker](#), [benztropine](#), or [benzodiazepine](#).

Explanation Why

[Akathisia](#) describes the symptoms of motor restlessness seen here. It is an [extrapyramidal side effect](#) of [antipsychotic](#) medications, especially typical high-[potency](#) drugs such as [fluphenazine](#). The onset of [akathisia](#) is typically within 1–8 weeks of treatment initiation, as seen here. Another EPS that occurs within this timeframe is [pseudoparkinsonism](#). In contrast, [acute dystonia](#) occurs more immediately (within hours to days), and [tardive dyskinesia](#) occurs later (months to years).

F - Inadequately treated schizophrenia

Explanation Why

[Schizophrenia](#) can cause agitation due to distressing [delusions](#) or [hallucinations](#). This patient does not report changes in her thoughts or perceptions but instead seems agitated by her own restlessness and inability to remain still.

G - Tardive dyskinesia

Explanation Why

[Tardive dyskinesia](#) is a potentially irreversible and disabling side effect of prolonged exposure (months to years) to [dopamine receptor antagonists](#) such as [antipsychotics](#) and certain [antiemetics](#). It is a subtype of EPS and involves motor symptoms, which are seen here. However, this patient has only been taking [fluphenazine](#) for 2 weeks. Furthermore, the most common manifestations of [tardive dyskinesia](#) are involuntary orofacial movements, whereas this patient's motor symptoms are neither involuntary nor orofacial.

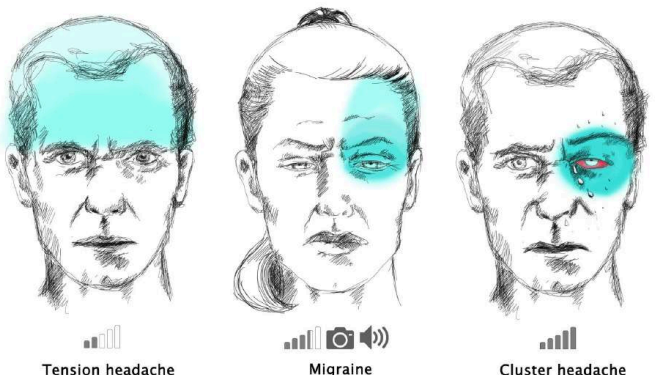
H - Drug-induced mania

Explanation Why

Drug-induced [mania](#) can be caused by medications such as stimulants and [corticosteroids](#), and [antidepressant](#) medications can induce [hypomania](#) or [mania](#) in patients with [bipolar disorder](#). This patient's restlessness, poor sleep, and anxiety would fit with the diagnosis of drug-induced [mania](#), but she is not taking [antidepressants](#), [corticosteroids](#), or stimulants. [Mania](#) is not a typical side effect of [antipsychotics](#) and is not a subtype of EPS.

Question # 34

A 32-year-old woman comes to the physician because of a 3-month history of recurrent headaches and nausea. The headaches occur a few times a month and alternately affect the right or left side. The headaches are exacerbated by loud sounds or bright light. She is in graduate school and has been under a lot of stress recently. She does not smoke or drink alcohol but does drink 2–3 cups of coffee daily. Her only medication is an oral contraceptive. Physical examination shows no abnormalities; visual acuity is 20/20. Which of the following is the most likely diagnosis?

	Answer	Image
A	Migraine headache	 Tension headache Migraine Cluster headache
B	Tension headache	
C	Trigeminal neuralgia	
D	Cluster headache	
E	Pseudotumor cerebri	

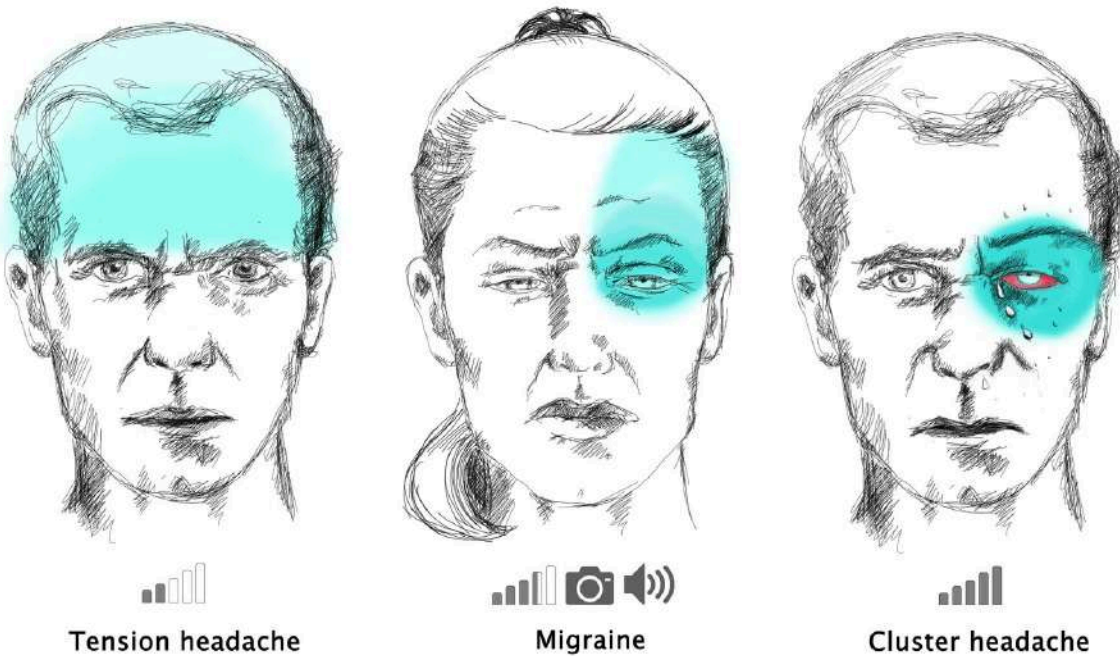
Hint

This condition is preceded by an aura in ~ 25% of affected individuals.

Correct Answer

A - Migraine headache

Image



Explanation Why

[Migraine headaches](#) are recurrent throbbing [headaches](#) that are frequently unilateral and classically accompanied by nausea, vomiting, and sensitivity to light and sound. [Migraine headaches](#) may also localize in an alternating pattern, as seen in this patient. [Risk factors](#) include stress, poor [sleep hygiene](#), and [oral contraceptive](#) use.

B - Tension headache

Explanation Why

[Tension headaches](#) are the most common type of [headache](#) and typically manifest as episodic

bilateral, band-like, dull [headaches](#). While they can be precipitated by stress and lack of sleep, autonomic symptoms such as nausea, vomiting, and photophobia would not be expected.

C - Trigeminal neuralgia

Explanation Why

[Trigeminal neuralgia](#) is a neurologic condition characterized by transient, debilitating facial [pain](#) in the distribution of the [trigeminal nerve](#). These episodes of [pain](#) typically last seconds at a time and occur up to one hundred times per day. This patient's unilateral [pain](#), nausea, and photophobia are more consistent with another condition.

D - Cluster headache

Explanation Why

[Cluster headaches](#) are an uncommon type of [headache](#) that typically manifest as severe, unilateral periorbital [pain](#). However, they are more common in males and are associated with lacrimation, [rhinorrhea](#), and partial [Horner syndrome](#), none of which is seen in this patient.

E - Pseudotumor cerebri

Explanation Why

[Pseudotumor cerebri](#) ([idiopathic intracranial hypertension](#)) is a neurologic condition caused by [increased intracranial pressure](#) that primarily affects [obese](#) women. Unlike in this patient, the [headaches](#) associated with [pseudotumor cerebri](#) are typically diffuse, positional, and associated with [tinnitus](#) and [diplopia](#). Expected [physical exam](#) findings would include [papilledema](#) and a blind spot on [visual field](#) testing, neither of which is present in this patient. This patient's history is more consistent with a different condition.

Question # 35

A 68-year-old woman comes to the physician for evaluation of diminished vision for several months. Twenty-eight years ago, she was diagnosed with systemic lupus erythematosus, which has been well controlled with hydroxychloroquine. Fundoscopic examination shows concentric rings of hypopigmentation and hyperpigmentation surrounding the fovea bilaterally. Visual field examination of this patient is most likely to show which of the following findings?

	Answer	Image
A	Bitemporal hemianopia	
B	Right monocular blindness	
C	Hemianopia with macular sparing	
D	Paracentral scotoma	
E	Homonymous hemianopia	
F	Binasal hemianopia	

Hint

The concentric rings of hypopigmentation and hyperpigmentation (“bull's eye maculopathy”) are an adverse effect of hydroxychloroquine therapy. Hydroxychloroquine maculopathy specifically targets the macular rods and cones but spares these same structures within the fovea.

Correct Answer

A - Bitemporal hemianopia

Explanation Why

[Bitemporal hemianopia](#) describes the loss of vision in the outer halves of the [visual field](#) of both eyes. It is typically caused by a compression of the central region of the [optic chiasm](#) due to midline pathologies such as [aneurysms](#), [pituitary](#) masses, or [craniopharyngioma](#). Treatment with [hydroxychloroquine](#), however, is associated with damage to the [retina](#) itself.

B - Right monocular blindness

Explanation Why

Monocular blindness describes a total visual loss in one [eye](#) that can be caused by [ischemia](#) of the vessels supplying the [retina](#), [retinal vein occlusion](#), [optic nerve](#) compression, or [optic nerve](#) neuropathy. Treatment with [hydroxychloroquine](#), however, is not associated with such a complication.

C - Hemianopia with macular sparing

Explanation Why

Hemianopia with [macular sparing](#) is a form of [homonymous hemianopia](#) in which the central [visual field](#) is spared. The visual cortex receives dual blood supply from the [posterior cerebral artery](#) (supplies the [anterior](#) visual cortex, which processes peripheral vision) and the deep branch of the [middle cerebral artery](#) (supplying the occipital pole, which processes information from the central [visual field](#)). [Infarcts](#) of the PCA would therefore lead to hemianopia with [macular sparing](#). [Hydroxychloroquine](#), in contrast, may specifically damage the [macula](#).

D - Paracentral scotoma

Explanation Why

[Paracentral scotoma](#) describes an off-center area of visual loss surrounded by normal acuity in the rest of the [visual field](#). As in this case, patients often report difficulty with tasks involving fine visual skills, such as reading, as well as visual color deficits. [Paracentral scotoma](#) represents a more advanced stage of retinopathy and is an irreversible complication of [hydroxychloroquine](#) whose [incidence](#) increases with both the dose and the duration of treatment.

E - Homonymous hemianopia

Explanation Why

[Homonymous hemianopia](#) describes the loss of vision of a unilateral [visual field](#) in both eyes. This occurs due to lesions of the [optic tract](#), such as [middle cerebral artery infarction](#), tumors or infections. Treatment with [hydroxychloroquine](#), however, is associated with damage to the [retina](#) itself.

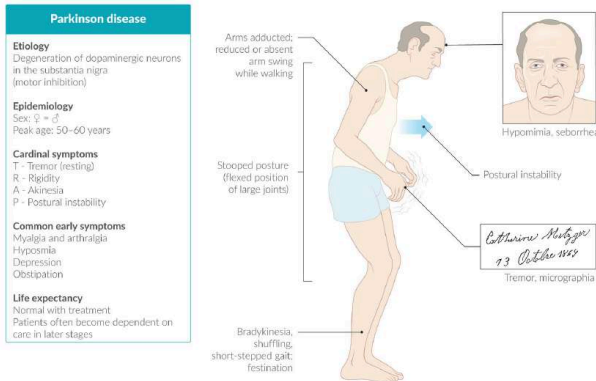
F - Binasal hemianopia

Explanation Why

[Binasal hemianopia](#) describes the loss of vision in the inner halves of the [visual field](#) of both eyes. It is a rare finding caused by bilateral lesions of the outermost fibers of the [optic chiasm](#) which hold the uncrossed fibers of the [optic nerves](#). Such lesions may result from [aneurysms](#) or tumors. Treatment with [hydroxychloroquine](#), however, is associated with damage to the [retina](#) itself.

Question # 36

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

	Answer	Image
A	Clonazepam	
B	Methimazole	
C	Propranolol	
D	Trihexyphenidyl	
E	Donepezil	
F	Pramipexole	 Parkinson disease Etiology Degeneration of dopaminergic neurons in the substantia nigra (motor inhibition) Epidemiology Sex: ♀ = ♂ Peak age: 50–60 years Cardinal symptoms T – Tremor (resting) R – Rigidity A – Akinesia P – Postural instability Common early symptoms Myalgia and arthralgia Hypomimia Depression Constipation Life expectancy Normal with treatment Patients often become dependent on care in later stages Arms adducted; reduced or absent arm swing while walking Stooped posture (flexed position of large joints) Bradykinesia, shuffling, short-stepped gait; festination Hypomimia, seborrhea Postural instability Resting tremor, micrographia

Hint

Bradykinesia and a unilateral resting tremor (“pill-rolling tremor”) that worsens with stress and improves with voluntary movement are consistent with Parkinson disease.

Correct Answer

A - Clonazepam

Explanation Why

[Clonazepam](#) can be used to treat [orthostatic tremor](#). The average age of onset of [orthostatic tremor](#) is 60 years of age, and this patient is 55. However, the typical clinical features of [orthostatic tremor](#) are triggered by longer periods of standing; they include [tremor](#) of the legs and a subjective sensation of instability. As this condition only affects the legs, it cannot be the cause of this patient's hand [tremor](#).

B - Methimazole

Explanation Why

[Methimazole](#) is used in the [treatment of hyperthyroidism](#), which can manifest with a [tremor](#) that increases with stress. However, the [tremor](#) is usually symmetric and occurs while holding positions against gravity (e.g., extending the arms in front of the body). Moreover, [hyperthyroidism](#) would not explain this patient's [bradykinesia](#). In a patient with [hyperthyroidism](#), other features (e.g., anxiety, [hyperreflexia](#), weight loss, sweating) would also be expected.

C - Propranolol

Explanation Why

[Propranolol](#) is a drug of choice in the treatment of benign [essential tremor](#). [Essential tremor](#) can be exacerbated by stress, as reported by this patient. However, unlike the asymmetric [resting tremor](#) seen here, [essential tremor](#) is symmetrical, worsens with voluntary movements, and resolves when the patient is completely at rest.

D - Trihexyphenidyl

Explanation Why

[Antimuscarinic drugs](#) such as [trihexyphenidyl](#) or [benztropine](#) can be used to treat [tremors](#) and [rigidity](#) in patients with [Parkinson disease](#). However, this type of drug would not improve [bradykinesia](#), which is seen in this patient. A different drug would therefore be preferred in a patient who has difficulty initiating movements.

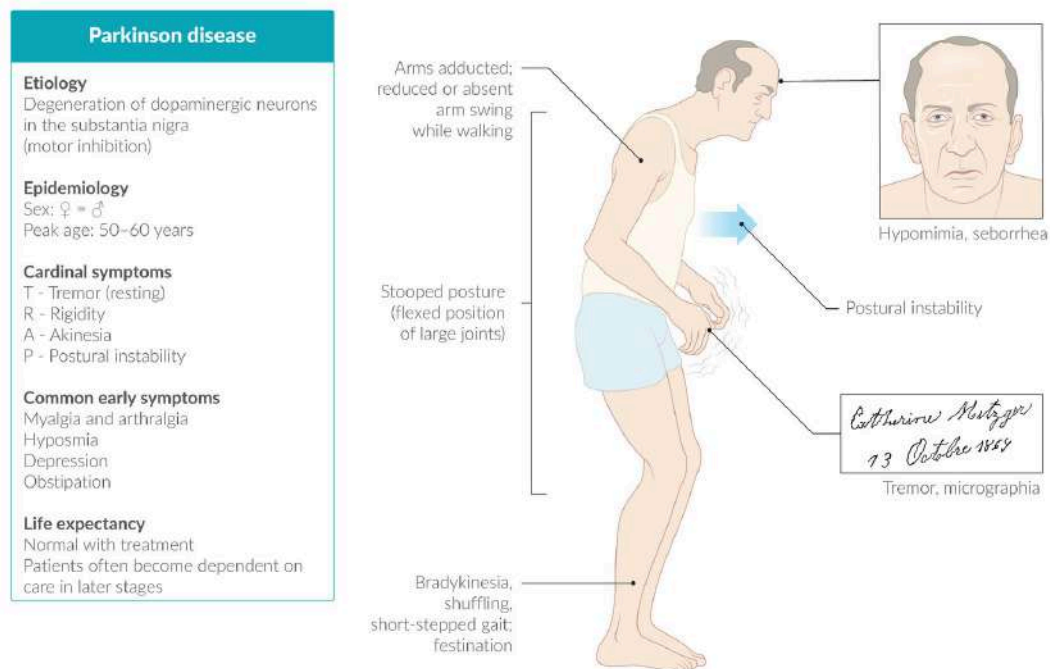
E - Donepezil

Explanation Why

[Donepezil](#) is a [cholinesterase inhibitor](#) used in the treatment of various forms of [dementia](#), such as [Alzheimer disease](#), [vascular dementia](#), [frontotemporal dementia](#), and [dementia](#) associated with late-stage [Parkinson disease](#). This patient does not yet show signs of cognitive impairment and has only recently begun noticing neurological deficits.

F - Pramipexole

Image



Explanation But

[MAO-B inhibitors](#) (e.g., [selegiline](#)) or [amantadine](#) can be used as monotherapy in patients with minimal symptoms that do not affect quality of life, or as an adjunct with [dopamine agonists](#) or [levodopa](#) in more severe cases.

Explanation Why

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

Question # 37

A 53-year-old woman is brought to the emergency department by her husband because of difficulty walking, slurred speech, and progressive drowsiness. The husband reports that his wife has appeared depressed over the past few days. She has a history of insomnia and social anxiety disorder. She appears lethargic. Her temperature is 36.2°C (97.1°F), pulse is 88/min, respirations are 12/min, and blood pressure is 110/80 mm Hg. Neurologic examination shows normal pupils. There is diffuse hypotonia and decreased deep tendon reflexes. Administration of a drug that acts as a competitive antagonist at which of the following receptors is most likely to reverse this patient's symptoms?

	Answer	Image
A	μ-opioid receptor	
B	5-hydroxytryptamine ₂ receptor	
C	Muscarinic acetylcholine receptor	
D	D ₂ dopamine receptor	
E	GABA _A receptor	
F	Ryanodine receptor	

Hint

In a patient with otherwise normal vital signs and normal pupil size, slurred speech, ataxia, altered mental status, bradypnea, hypotonia, and hyporeflexia suggest benzodiazepine overdose. This patient has a history of insomnia and anxiety disorder, both of which are commonly treated with benzodiazepines.

Correct Answer

A - μ -opioid receptor

Explanation Why

[Naloxone](#), an [opioid](#) receptor antagonist, is used to treat [opioid overdose](#). [Opioids](#) are [\$\mu\$ -opioid](#) receptors [agonists](#). They may cause altered consciousness, [lethargy](#), and respiratory depression if overdosed, all of which are seen in this patient. However, [opioid intoxication](#) would typically manifest with [bradypnea](#) that is more pronounced than what is seen in this patient, as well as with [hypotension](#), [hypothermia](#), and possibly [seizures](#). Moreover, [miosis](#) would typically be seen on [physical examination](#), rather than the normal pupils observed here.

B - 5-hydroxytryptamine₂ receptor

Explanation Why

[Cyproheptadine](#), a 5-HT₂ receptor antagonist, is used to treat [serotonin syndrome](#). This condition presents with neuromuscular hyperactivity ([clonus](#), [hyperreflexia](#)), hyperthermia, agitation, [mydriasis](#), and [diarrhea](#). In contrast, this patient presents with muscular [hypotonia](#), [hyporeflexia](#), normal body temperature, decreased [level of consciousness](#), [lethargy](#), and normal pupils.

C - Muscarinic acetylcholine receptor

Explanation Why

[Atropine](#), a [muscarinic acetylcholine receptor](#) antagonist, is used to reverse [organophosphate poisoning](#). [Organophosphates](#) are [muscarinic acetylcholine receptor agonists](#). Symptoms of [organophosphate poisoning](#) include hypersalivation, epiphora, [miosis](#), [diarrhea](#), vomiting, and confusion, all of which are not present in this patient.

D - D₂ dopamine receptor

Explanation Why

[Antipsychotics](#) act as antagonists at the D₂ [dopamine](#) receptor. They are mainly used to treat [psychosis](#) in patients with [schizophrenia](#), although they may also be used to treat [anxiety disorders](#) and depression. [Antipsychotics](#) play no role in the treatment of [benzodiazepine overdose](#).

E - GABA_A receptor

Explanation Why

[Flumazenil](#), a [GABA_A receptor](#) antagonist, is used to treat [benzodiazepine](#) overdose. [Benzodiazepines](#) are indirect GABA_A [agonists](#). They increase the affinity of [GABA](#) to bind to [GABA_A receptors](#). Increased [GABA](#) action increases the frequency with which [chloride](#) channels open, which leads to [hyperpolarization](#) of the postsynaptic neuronal membrane and thus decreased neuronal excitability. [Benzodiazepine overdose](#) typically manifests with a [sedative-hypnotic toxidrome](#), as seen in this patient. [GABA_A receptor](#) antagonists would effectively reverse the patient's symptoms.

F - Ryanodine receptor

Explanation Why

[Dantrolene](#), a [ryanodine receptor](#) antagonist, works as a [muscle relaxant](#) by inhibiting calcium release into the [sarcoplasm](#). It is administered to treat [malignant hyperthermia](#), which manifests with hyperthermia, [tachycardia](#), and [tachypnea](#). This patient, however, presents with a normal body temperature, normal [heart rate](#), muscular [hypotonia](#), and [bradypnea](#), which excludes [malignant hyperthermia](#).

Question # 38

A 27-year-old woman is brought to the emergency department by her coworker after having a generalized seizure at work. Her coworker reports that she is at 30 weeks' gestation and has mentioned headache and right upper quadrant pain earlier that day. Her temperature is 37°C (98.6°F), pulse is 91/min, and blood pressure is 170/102 mm Hg. Pulmonary examination shows bilateral rales. There is diffuse edema in the lower extremities. Deep tendon reflexes are increased bilaterally. She is not oriented to person, place, and time. Which of the following is the most appropriate initial pharmacotherapy?

	Answer	Image
A	Calcium gluconate	
B	Aspirin	
C	Phenytoin	
D	Valproic acid	
E	Lorazepam	
F	Magnesium sulfate	

Hint

This patient in her third trimester of pregnancy, presenting with generalized seizure in the context of peripheral and pulmonary edema, hyperreflexia, hypertension, and altered level of consciousness, with a history of preeclamptic symptoms (headache and right upper quadrant pain), has eclampsia.

Correct Answer

A - Calcium gluconate

Explanation Why

Calcium gluconate is indicated for the management of [magnesium](#) toxicity. But as this patient has not yet received [magnesium sulfate](#), there is no reason to administer calcium gluconate.

B - Aspirin

Explanation Why

Although [aspirin](#) is used as prophylaxis for [preeclampsia/eclampsia](#) in high-risk patients, it has no role in the acute management of [eclampsia](#).

C - Phenytoin

Explanation Why

Even though [phenytoin](#) is used in the treatment of [seizures](#) and [epilepsy](#), it is not used in the treatment of [eclampsia](#) and, as a known [teratogen](#), should be avoided during [pregnancy](#) to prevent [fetal hydantoin syndrome](#) (especially during early [pregnancy](#)).

D - Valproic acid

Explanation Why

Although [valproic acid](#) is used in the long-term management of several [seizure disorders](#), it is not

used in acute [seizure](#) management. Additionally, [valproic acid](#) use is contraindicated during [pregnancy](#), and it is excreted into [breast milk](#), which would be problematic as [seizure](#) prophylaxis must continue postpartum up to 24 hours.

E - Lorazepam

Explanation Why

[Lorazepam](#) is safe for use in [pregnancy](#) and is used as second-line treatment for [seizure](#) management in eclamptic patients. Except in cases of [myasthenia gravis](#), first-line treatment should first be initiated before considering [lorazepam](#).

F - Magnesium sulfate

Explanation Why

[Magnesium sulfate](#) is first-line [seizure](#) prophylaxis in women with [pre-eclampsia](#) or [eclampsia](#) and is administered intravenously from the time of presentation to postpartum (up to 24 hours postpartum). She should also receive [antihypertensives](#) (e.g., [hydralazine](#)) to control her blood pressure. Once the patient is stabilized, the fetus should be delivered. The patient should also be monitored for signs of [magnesium sulfate](#) toxicity, including profound [hyporeflexia](#), [oliguria](#), respiratory depression, and [cardiac arrhythmia](#) or arrest. In the event of [magnesium](#) toxicity, calcium gluconate can be given. In cases that [magnesium sulfate](#) is ineffective at controlling the [seizures](#) (~10% of eclamptic patients), the patient has [myasthenia gravis](#), or [magnesium sulfate](#) toxicity occurs, [lorazepam](#) can be given as second-line treatment to prevent [seizures](#).

Question # 39

A 21-year-old man undergoes orthopedic surgery for a leg fracture that he has sustained in a motorbike accident. After induction of anesthesia with desflurane, the patient's respiratory minute ventilation decreases notably. Which of the following additional effects is most likely to occur in response to this drug?

	Answer	Image
A	Increased glomerular filtration rate	
B	Increased cerebral metabolic rate	
C	Decreased seizure threshold	
D	Increased intracranial pressure	
E	Decreased responsiveness of area postrema	
F	Increased skeletal muscle tonus	
G	Increased myocardial contraction force	

Hint

Desflurane is a fluorinated inhalational anesthetic.

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Correct Answer

A - Increased glomerular filtration rate

Explanation Why

Increases in [glomerular filtration rate](#) would be unexpected after administration of an inhaled anesthetic such as [desflurane](#). [Desflurane](#) reduces [cardiac output](#), which in turn reduces [renal plasma flow](#) and the [glomerular filtration rate](#).

B - Increased cerebral metabolic rate

Explanation Why

An increased cerebral metabolic rate would be unexpected after administration of [desflurane](#). In fact, inhaled anesthetics cause a decrease in cerebral metabolic rate.

C - Decreased seizure threshold

Explanation Why

Decreased [seizure](#) threshold is a side effect of several medications such as [bupropion](#) and [tramadol](#). [Desflurane](#), on the other hand, acts to suppress [seizure](#) activity, especially at higher doses.

D - Increased intracranial pressure

Explanation Why

[Increased intracranial pressure](#) results from administration of inhaled anesthetics, including

[desflurane](#). Fluorinated [inhalational anesthetics](#) increase cerebral blood flow by a somewhat unknown mechanism, thereby increasing [intracranial pressure](#). This is a consequence of the Monro-Kellie theorem.

E - Decreased responsiveness of area postrema

Explanation Why

Decreased responsiveness of the [area postrema](#) is the mechanism of antiemetic medications such as [ondansetron](#). [Desflurane](#), on the other hand, stimulates the [area postrema](#) and causes [postoperative nausea and vomiting](#).

F - Increased skeletal muscle tonus

Explanation Why

A decrease in [skeletal muscle](#) tone is likely to be seen in this patient. Most anesthetic agents (with the exception of [nitrous oxide](#)) produce dose-dependent relaxation of [skeletal muscles](#) owing to inhibition of [nicotinic acetylcholine receptors](#). Among them, [desflurane](#) produces the greatest muscle relaxation. They also enhance the activity of [succinylcholine](#) and [nondepolarizing muscle relaxants](#).

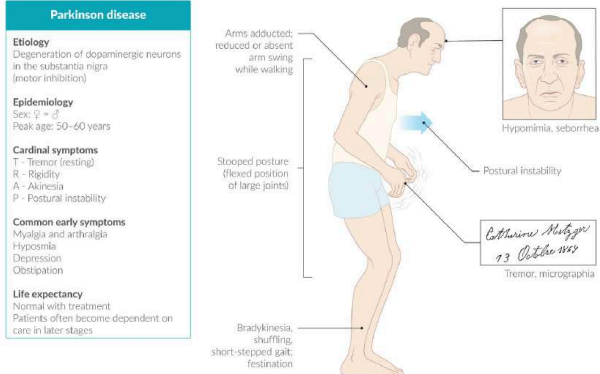
G - Increased myocardial contraction force

Explanation Why

Decreased [myocardial contractility](#) is expected after administration of [desflurane](#). This drug, like other inhaled anesthetics, acts as a direct negative [inotrope](#) in addition to stimulating the [autonomic nervous system](#) to further reduce [inotropy](#).

Question # 40

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

	Answer	Image
A	Accumulation of neurotoxic metabolites secondary to hepatocyte damage	
B	Copper accumulation due to mutations in hepatocyte copper-transporting ATPase	
C	Neuronal degeneration due to α -synuclein protein misfolding	 Parkinson disease Etiology Degeneration of dopaminergic neurons in the substantia nigra (motor inhibition) Epidemiology Sex: $\text{M} > \text{F}$ Peak age: 50–60 years Cardinal symptoms T - Tremor (resting) R - Rigidity A - Akinesia P - Postural instability Common early symptoms Myalgia and arthralgia Hyposmia Depression Obstipation Life expectancy Normal with treatment Patients often become dependent on care in later stages Arms adducted; reduced or absent arm swing while walking Scooped posture (flexed position of large joints) Postural instability Bradykinesia, shuffling, short-stepped gait, festination Hyposmia, seborrhea <i>Levodopa</i> <i>13 October 1993</i> Tremor, micrographia
D	Cerebellar ischemia due to chronic hypertension	

	Answer	Image
E	Proliferation of beta-adrenergic receptors from excessive circulating T4	

Hint

This patient's muscle rigidity, low-frequency resting tremor, shuffling gait, bradykinesia, and a change in affect are consistent with parkinsonism. Given the unilateral onset of the tremor and the patient's age, the most likely diagnosis is Parkinson disease.

Correct Answer

A - Accumulation of neurotoxic metabolites secondary to hepatocyte damage

Explanation Why

Accumulation of neurotoxic metabolites secondary to [hepatocyte](#) damage is characteristic of [hepatic encephalopathy](#) and must be ruled out in all patients with parkinsonian features, such as the low-frequency hand [tremors](#) and [mood](#) changes seen in this patient. It is important to note that [asterixis](#) is not a true [tremor](#), but rather, myoclonic jerks that typically occur bilaterally in a nonrhythmic manner when the arms and hands are extended. Absence of decompensated [liver](#) failure features (e.g., [jaundice](#), [ascites](#)) in this patient suggests that her parkinsonian features have a different pathogenesis.

B -

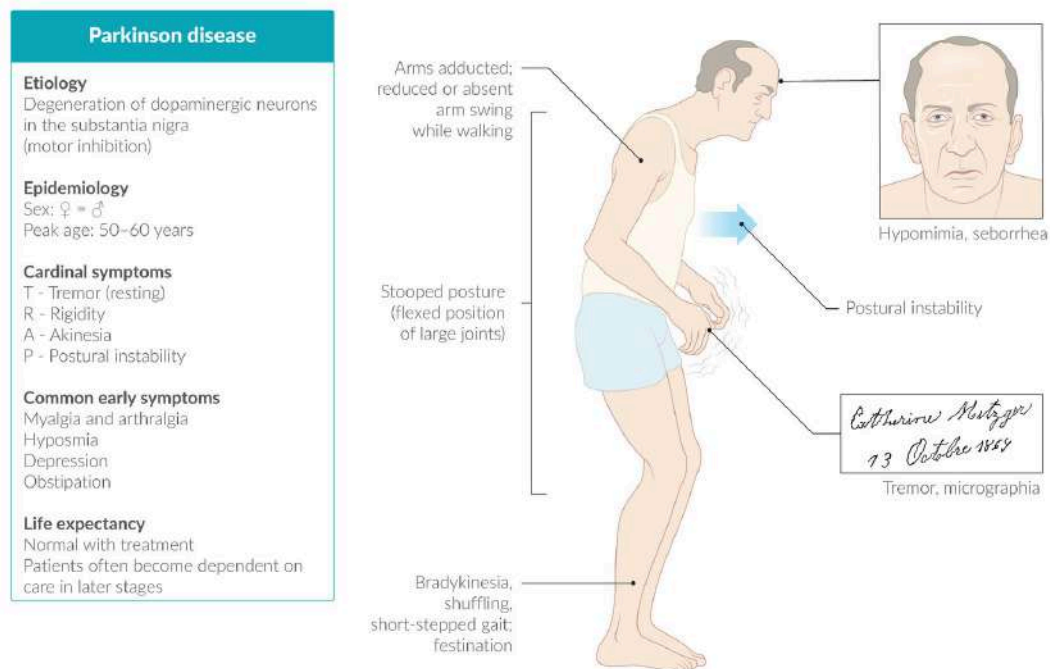
Copper accumulation due to mutations in hepatocyte copper-transporting ATPase

Explanation Why

A mutation to the [copper](#)-transporting ATPases primarily found in the [liver](#) (also sparingly seen in the [kidneys](#) and brain) is the underlying cause of [Wilson disease](#). This condition is characterized by [copper](#) accumulation in the [basal ganglia](#), which can cause parkinsonian features (e.g., [resting tremors](#), [bradykinesia](#), and [rigidity](#)). Although this patient has parkinsonian symptoms, she does not have the other characteristic findings seen in [Wilson disease](#) such as signs of [liver](#) disease, [Kayser-Fleischer rings](#), and [dysarthria](#).

C - Neuronal degeneration due to α -synuclein protein misfolding

Image



Explanation Why

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

D - Cerebellar ischemia due to chronic hypertension

Explanation But

The [blood supply of the cerebellum](#) consists of the [posterior inferior cerebellar arteries](#) (PICAs),

branches of the [vertebral artery](#), and the [anterior inferior cerebellar arteries](#) (AICAs) and the [superior cerebellar arteries](#) (SCAs), which arise from the [basilar artery](#). [Cerebellar infarcts](#) require special attention because of the danger of [cerebral edema](#) within the [posterior](#) fossa, which can compress the [brain stem](#) causing potentially fatal [transtentorial herniation](#) (of the superior [vermis](#) through the tentorial notch) or downward herniation of the [cerebellar tonsils](#) (through the [foramen magnum](#)).

Explanation Why

[Cerebellar ischemia](#) due to chronic [hypertension](#) is a major [risk factor](#) for [cerebellar infarction](#), which may result in a [tremor](#), as seen in this patient. Affected patients usually present with an acute [intention tremor](#), i.e., it worsens with goal-directed movements, which causes [dysmetria](#) while performing the finger-nose test. Other signs of [cerebellar dysfunction](#) (e.g., nystagmus, abnormal gait, [dysdiadochokinesia](#)) would also be present. This patient has none of these features and her insidious onset of symptoms suggests that her current condition is of a different pathogenesis.

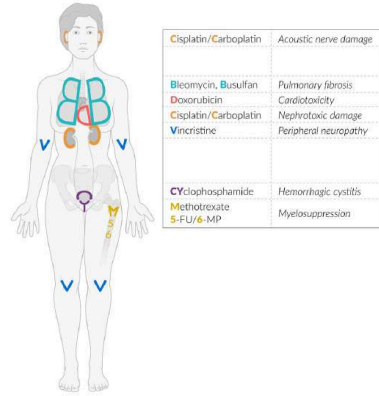
E - Proliferation of beta-adrenergic receptors from excessive circulating T4

Explanation Why

[Proliferation](#) of [β-adrenergic receptors](#) from excessive circulating T4 in patients with [hyperthyroidism](#) may result in poorly controlled [hypertension](#), anxiousness, and [tremor](#). However, the [tremor](#) seen in [hyperthyroidism](#) would be bilateral, of high frequency (10–12 Hz), and not improve with movement.

Question # 1

A 67-year-old woman with non-Hodgkin lymphoma comes to the physician because of progressively increasing numbness and tingling in her fingers and toes. Her last cycle of chemotherapy with vincristine was 1 week ago. Physical examination shows decreased sensation to light touch in all distal extremities. Knee and ankle deep tendon reflexes are decreased. Which of the following is the most likely underlying mechanism of this patient's peripheral neuropathy?

	Answer	Image																
A	Inhibition of beta-tubulin polymerization	 <table><tr><td>Cisplatin/Carboplatin</td><td>Acoustic nerve damage</td></tr><tr><td>Bleomycin, Busulfan</td><td>Pulmonary fibrosis</td></tr><tr><td>Doxorubicin</td><td>Cardiotoxicity</td></tr><tr><td>Cisplatin/Carboplatin</td><td>Nephrotoxic damage</td></tr><tr><td>Vincristine</td><td>Peripheral neuropathy</td></tr><tr><td>Cyclophosphamide</td><td>Hemorrhagic cystitis</td></tr><tr><td>Methotrexate</td><td>Myelosuppression</td></tr><tr><td>5-FU/6-MP</td><td></td></tr></table>	Cisplatin/Carboplatin	Acoustic nerve damage	Bleomycin, Busulfan	Pulmonary fibrosis	Doxorubicin	Cardiotoxicity	Cisplatin/Carboplatin	Nephrotoxic damage	Vincristine	Peripheral neuropathy	Cyclophosphamide	Hemorrhagic cystitis	Methotrexate	Myelosuppression	5-FU/6-MP	
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Vincristine	Peripheral neuropathy																	
Cyclophosphamide	Hemorrhagic cystitis																	
Methotrexate	Myelosuppression																	
5-FU/6-MP																		
B	Creation of free radicals that unwind DNA																	
C	Inhibition of dihydrofolate reductase																	
D	Inhibition of topoisomerase II																	
E	Formation of cross-links between strands of DNA																	
F	Incorporation of false pyrimidine analogues into DNA																	

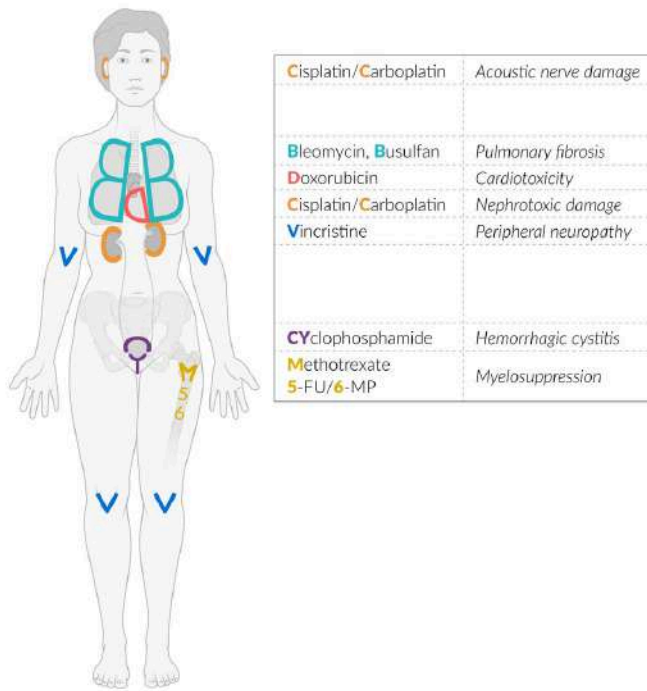
Hint

This patient with lymphoma has developed peripheral neuropathy as a side effect of her chemotherapy (vincristine).

Correct Answer

A - Inhibition of beta-tubulin polymerization

Image



Explanation Why

[Vincristine](#) inhibits beta-[tubulin](#) polymerization, which in turn inhibits the formation of the [microtubules](#) that are essential for cell division. While this mechanism is the basis of [vincristine](#)'s antineoplastic effects, it also impairs axoplasmic transport in [neurons](#). Peripheral neurotoxicity is a well-known side effect of [vincristine](#), which can manifest with areflexia and/or [distal peripheral neuropathy](#), as in this patient.

B - Creation of free radicals that unwind DNA

Explanation Why

Creation of [free radicals](#) that cause breaks in [DNA](#) is the mechanism by which [anthracyclines](#) (e.g., [doxorubicin](#), [daunorubicin](#)) target [neoplastic](#) cells. While these agents may also well-known for [lymphoma](#), [peripheral neuropathy](#) is not a common side effect. Typical side effects of [anthracyclines](#) include cardiotoxicity and myelosuppression.

C - Inhibition of dihydrofolate reductase

Explanation Why

Inhibition of [dihydrofolate reductase](#) (DHFR) is the mechanism of action of [methotrexate](#). Known side effects of [methotrexate](#) include myelosuppression (can be reversed with [leucovorin](#) supplementation), hepatotoxicity, pulmonary [fibrosis](#), and mucositis. [Vincristine](#) does not affect [folate](#) metabolism.

D - Inhibition of topoisomerase II

Explanation Why

Inhibition of [topoisomerase II](#) is the mechanism of action of several classes of [antineoplastic drugs](#), including [anthracyclines](#) (e.g., [doxorubicin](#)) and selective [topoisomerase II inhibitors](#) (e.g., [etoposide](#)). Common side effects associated with [topoisomerase inhibitors](#) include cardiotoxicity ([doxorubicin](#)) and myelosuppression ([etoposide](#), [teniposide](#)).

E - Formation of cross-links between strands of DNA

Explanation Why

Formation of cross-links between strands of [DNA](#) and subsequent inhibition of [DNA replication](#) is the mechanism of action of several [alkylating agents](#) (e.g., [busulfan](#), [cyclophosphamide](#)) and [platinum](#)-based [chemotherapeutic agents](#) (e.g., [cisplatin](#), [carboplatin](#)). These agents can also cause [peripheral neuropathy](#), but this patient is not receiving [cisplatin](#) or [carboplatin](#).

F - Incorporation of false pyrimidine analogues into DNA

Explanation Why

Incorporation of false [pyrimidine analogs](#) into [DNA](#) is the mechanism of several widely used [antineoplastic agents](#), such as 5-[fluorouracil](#). Side effects of [5-FU](#) include myelosuppression and hand-foot syndrome. However, this is not the mechanism of action of [vincristine](#).

Question # 2

A 32-year-old woman comes to the emergency department because of a 3-hour history of severe nausea, vomiting, tremor, and anxiety. She recently started a new medication but does not remember its name. She has a history of major depressive disorder treated with fluoxetine. Her temperature is 38.9 C (102.1 F), pulse is 132/min, respirations are 22/min, and blood pressure is 152/94 mm Hg. She is confused. Physical examination shows diaphoresis and an ataxic gait. Patellar reflexes are 4+ bilaterally. This patient's condition is most likely due to which of the following medications?

	Answer	Image
A	Amiodarone	
B	Sumatriptan	
C	Scopolamine	
D	Haloperidol	
E	Succinylcholine	

Hint

This woman has symptoms of serotonin syndrome such as autonomic hyperactivity (fever, tachycardia, hypertension), confusion, and hyperreflexia. This is likely the result of the combination of fluoxetine and her new medication.

Correct Answer

A - Amiodarone

Explanation Why

[Amiodarone](#) is a [class III antiarrhythmic drug](#) that acts via potassium channel blockade. Adverse effects include pulmonary [fibrosis](#), hepatic toxicity, and [QT prolongation](#), which can induce potentially fatal [torsades de pointes](#). [Amiodarone](#) is not associated with [serotonin syndrome](#).

B - Sumatriptan

Explanation But

Both [serotonin syndrome](#) and [NMS](#) can manifest with confusion and autonomic instability. Unlike [serotonin syndrome](#), in which patients demonstrate myoclonus or [hyperreflexia](#), patients with [NMS](#) develop muscle [rigidity](#) and [tremors](#).

Explanation Why

[Sumatriptan](#) is a [serotonin](#) receptor [agonist](#) used as abortive therapy in the treatment of acute [migraines](#). The use of two or more serotonergic medications (in this case, [fluoxetine](#) and [sumatriptan](#)) increases the risk of developing [serotonin syndrome](#), which causes autonomic stimulation (e.g., hyperthermia, [diaphoresis](#)) and neuromuscular hyperactivity (e.g., [tremor](#), [hyperreflexia](#), [gait ataxia](#)). Other medications associated with [serotonin syndrome](#) include [SNRIs](#), [MAOIs](#), TCAs, [buspirone](#), [ondansetron](#), [tramadol](#), [linezolid](#), [amphetamines](#), and [MDMA](#).

C - Scopolamine

Explanation Why

[Scopolamine](#) is an antiemetic medication that acts via non-selective muscarinic antagonism. It can cause [anticholinergic toxicity](#), which manifests with dry mouth, [mydriasis](#), [tachycardia](#), and [urinary](#)

[retention](#). [Scopolamine](#) is not associated with [serotonin syndrome](#).

D - Haloperidol

Explanation Why

[Haloperidol](#) is a [typical antipsychotic](#) that acts via [D2 receptor](#) antagonism. It is commonly associated with the development of [neuroleptic malignant syndrome](#), which has similar manifestations to [serotonin syndrome](#) (e.g., [fever](#), confusion) but can be differentiated by the presence of muscle [rigidity](#) (instead of the [hyperreflexia](#) seen here). [Haloperidol](#) is not associated with the development of [serotonin syndrome](#).

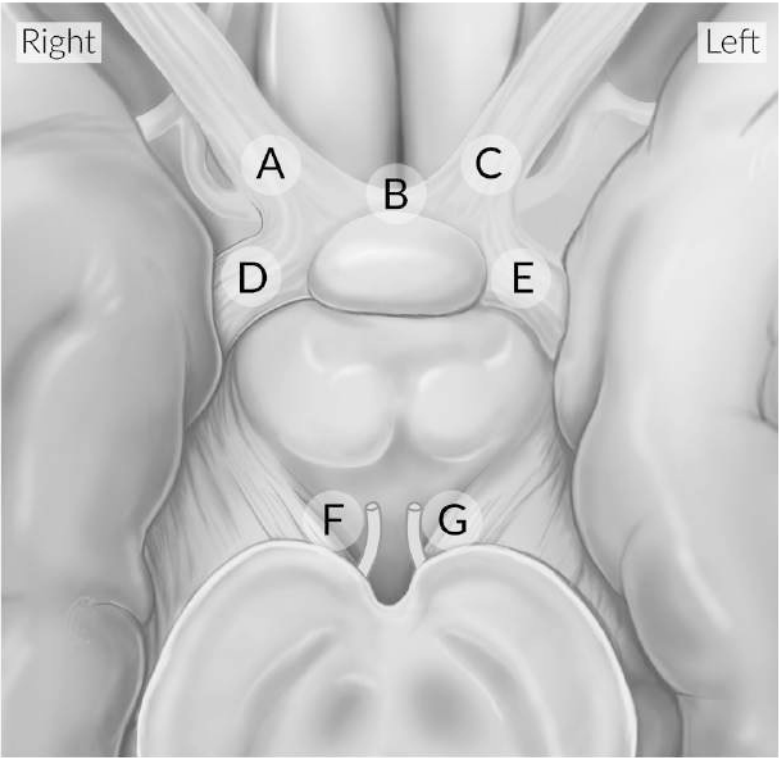
E - Succinylcholine

Explanation Why

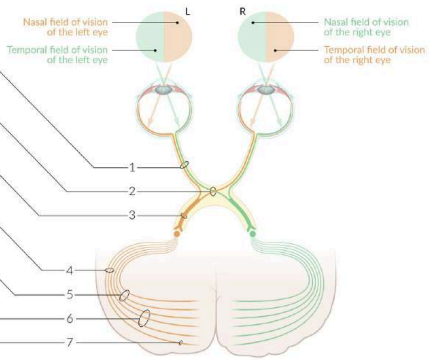
[Succinylcholine](#) is a depolarizing neuromuscular blocking agent used for [skeletal muscle](#) relaxation during the induction phase of general anesthesia. It can cause [malignant hyperthermia](#) in susceptible individuals, which manifests with high body temperature, [tachycardia](#), [tachypnea](#), muscle [rigidity](#), [arrhythmia](#), and [myoglobinuria](#); it does not cause [tremor](#) and [hyperreflexia](#) as seen in this case. [Succinylcholine](#) is not associated with [serotonin syndrome](#).

Question # 3

A 64-year-old woman comes to the physician because of a 6-month history of headache and impaired vision. She says that she frequently misses turns while driving and hurts herself by accidentally bumping into objects. Confrontational visual field testing shows decreased vision in the left side of both visual fields. The most likely cause of this patient's symptoms is a lesion in which of the following locations?



	Answer	Image
A	A	

	Answer	Image																		
B	B																			
C	C																			
D	D	<table><thead><tr><th>Site of injury</th><th>Visual field defects</th></tr><tr><th></th><th>L R</th></tr></thead><tbody><tr><td>1 Left optic nerve</td><td> </td></tr><tr><td>2 Medial portion of the optic chiasm</td><td> </td></tr><tr><td>3 Left optic tract</td><td> </td></tr><tr><td>4 Lower bundle (Meyer's loop) of the left optic radiation</td><td> </td></tr><tr><td>5 Upper bundle of the left optic radiation</td><td> </td></tr><tr><td>6 Anterior portion of the calcarine sulcus and adjacent visual cortex</td><td> </td></tr><tr><td>7 Left occipital pole</td><td> </td></tr></tbody></table> 	Site of injury	Visual field defects		L R	1 Left optic nerve	 	2 Medial portion of the optic chiasm	 	3 Left optic tract	 	4 Lower bundle (Meyer's loop) of the left optic radiation	 	5 Upper bundle of the left optic radiation	 	6 Anterior portion of the calcarine sulcus and adjacent visual cortex	 	7 Left occipital pole	 
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6 Anterior portion of the calcarine sulcus and adjacent visual cortex	 																			
7 Left occipital pole	 																			
E	E																			
F	F																			
G	G																			

Hint

A visual deficit involving homologous sides of both visual fields is known as homonymous hemianopsia.

Correct Answer

A - A

Explanation Why

The [cranial nerve II](#) ([CN II](#)) transmits visual information from the [retina](#) to the [optic chiasm](#), from where it continues on in the [optic tract](#). Damage to the right [CN II](#) can cause complete loss of vision in the ipsilateral [eye](#) (right [anopsia](#)) as well as a right [relative afferent pupillary defect](#). A lesion here would not be expected as the cause of this patient's left [homonymous hemianopsia](#).

B - B

Image



Explanation Why

The x-shaped [optic chiasm](#) is the point of partial crossing of fibers from the [optic nerve](#). Damage to

this structure would cause [bitemporal hemianopsia](#) in both [visual fields](#), as opposed to this patient's left [homonymous hemianopsia](#).

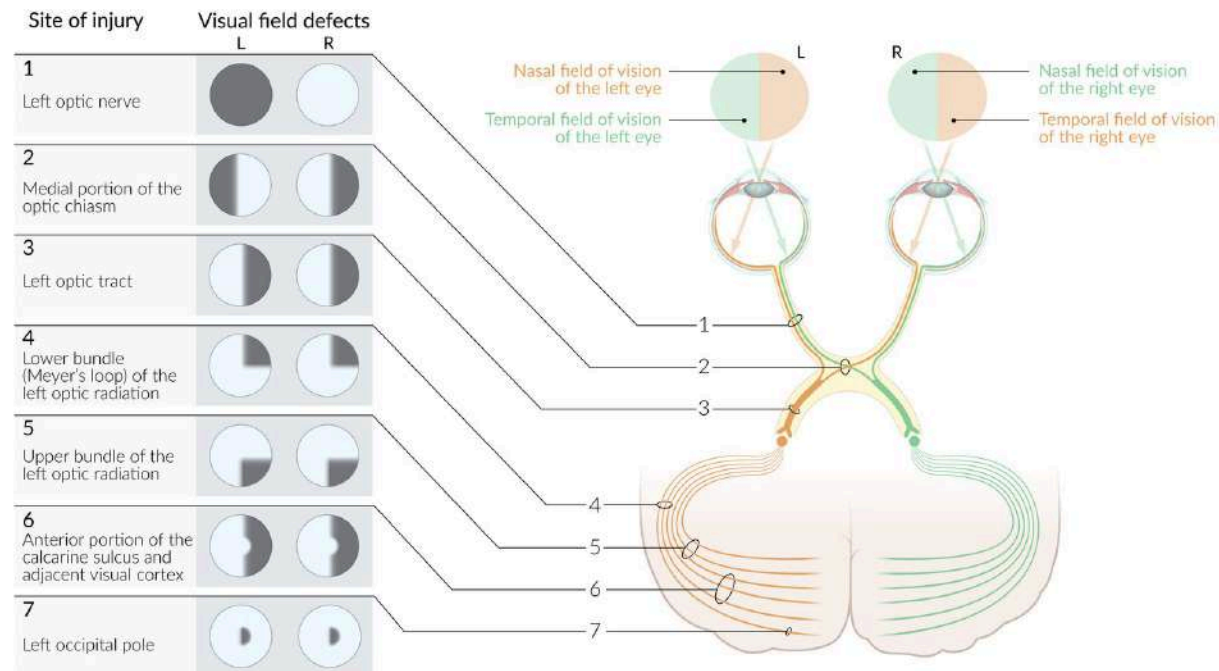
C - C

Explanation Why

The [cranial nerve II](#) (CN II) transmits visual information from the [retina](#) to the [optic chiasm](#), from where it continues on in the [optic tract](#). Damage to the left [CN II](#) can cause complete loss of vision in the ipsilateral [eye](#) (left [anopsia](#)) as well as a left [relative afferent pupillary defect](#). A lesion here would not be expected to cause this patient's left [homonymous hemianopsia](#)

D - D

Image



Explanation Why

The [optic tracts](#) relay visual information from the [optic chiasm](#) to the ipsilateral [lateral geniculate nucleus](#), from where it continues to the [occipital lobe](#) and [primary visual cortex](#). Each tract contains fibers from both the ipsilateral temporal hemiretina and the contralateral nasal hemiretina. The right [optic tract](#), therefore, transmits visual information from the left [visual field](#) and vice versa. A right [optic tract](#) lesion (e.g., due to compression by an [aneurysm](#), [multiple sclerosis](#), infection, or [stroke](#)) has likely caused this patient's left [homonymous hemianopsia](#).

E - E

Explanation Why

A left [optic tract](#) lesion would cause right [homonymous hemianopsia](#) (i.e., on the right side of both [visual fields](#)). However, this patient has left [homonymous hemianopsia](#).

F - F

Explanation Why

The [cranial nerve III \(CN III\)](#) innervates four of six [extraocular muscles](#) and provides [parasympathetic](#) stimulation to the ipsilateral [eye](#). Damage to the right [oculomotor nerve](#) would cause [monocular diplopia](#) of the right [eye](#), resulting in blurring of the [visual field](#) rather than vision loss. [CN III palsy](#) does not cause [homonymous hemianopsia](#).

G - G

Explanation Why

The [cranial nerve III \(CN III\)](#) innervates four of six [extraocular muscles](#) and provides [parasympathetic](#) stimulation to the ipsilateral [eye](#). Damage to the left [oculomotor nerve](#) would cause [monocular diplopia](#) of the left [eye](#), resulting in blurring of the [visual field](#) rather than vision loss. [CN III palsy](#) does not cause [homonymous hemianopsia](#).

Question # 4

A 27-year-old man is brought to the emergency department because of weakness, headache, and vomiting for 40 minutes. He is an amateur chef and his symptoms started 10 minutes after he ingested pufferfish that he had prepared. On arrival, he is lethargic. His temperature is 37°C (98.6°F), pulse is 120/min, respirations are 8/min, and blood pressure is 92/64 mm Hg. He is intubated and mechanical ventilation is begun. Intravenous fluid resuscitation is started. The cause of this patient's condition exerts its effect by which of the following mechanisms of action?

	Answer	Image
A	Decrease in cell membrane permeability to sodium ions	
B	Increase in cell membrane permeability to chloride ions	
C	Decrease in cell membrane permeability to calcium ions	
D	Decrease in cell membrane permeability to potassium ions	
E	Increase in cell membrane permeability to calcium ions	

Hint

Ingestion of improperly prepared pufferfish can result in intoxication with tetrodotoxin, a potentially life-threatening toxin, which is found primarily in the fish's ovaries and liver.

Correct Answer

A - Decrease in cell membrane permeability to sodium ions

Explanation Why

[Tetrodotoxin](#) blocks [voltage-gated sodium channels](#), thereby inhibiting the propagation of [action potential](#) in autonomic, motor, and sensory nerve cells. This inhibition initially causes [headache](#), vomiting, and tingling of the [tongue](#) and [lips](#); the condition can then progress to [ataxia](#), generalized weakness, paralysis, and sometimes even respiratory and cardiovascular failure. Treatment is supportive, and [mechanical ventilation](#) may be needed.

B - Increase in cell membrane permeability to chloride ions

Explanation Why

Drugs that increase the permeability of the [cell membrane](#) to [chloride](#) ions are used to treat [helminth](#) infections (e.g., [ivermectin](#)) and [constipation](#) (e.g., lubiprostone). [Tetrodotoxin](#) does not target [chloride](#) channels.

C - Decrease in cell membrane permeability to calcium ions

Explanation Why

Voltage-gated [L-type \$\text{Ca}^{2+}\$ channels](#) play an important role in the [action potential](#) of [cardiomyocytes](#) and arterial [smooth muscle cells](#). Their blocking (e.g., by [calcium channel blockers](#)) could result in [hypotension](#), as seen in this patient. However, his other symptoms ([headache](#) and altered mental status, vomiting, decreased respirations) would not be expected. Furthermore, [tetrodotoxin](#) does not target calcium channels.

D - Decrease in cell membrane permeability to potassium ions

Explanation Why

A decrease in [cell membrane](#) permeability to potassium ions is the mechanism of [dendrotoxin](#), which is released, for example, by the [mamba snake](#). Potassium channels are also targeted by some [antidiabetic drugs](#) (e.g., [sulfonylurea](#) and [repaglinide](#)) and [antiarrhythmic drugs](#) (e.g., [amiodarone](#) and [sotalol](#)). [Tetrodotoxin](#) does not target potassium channels.

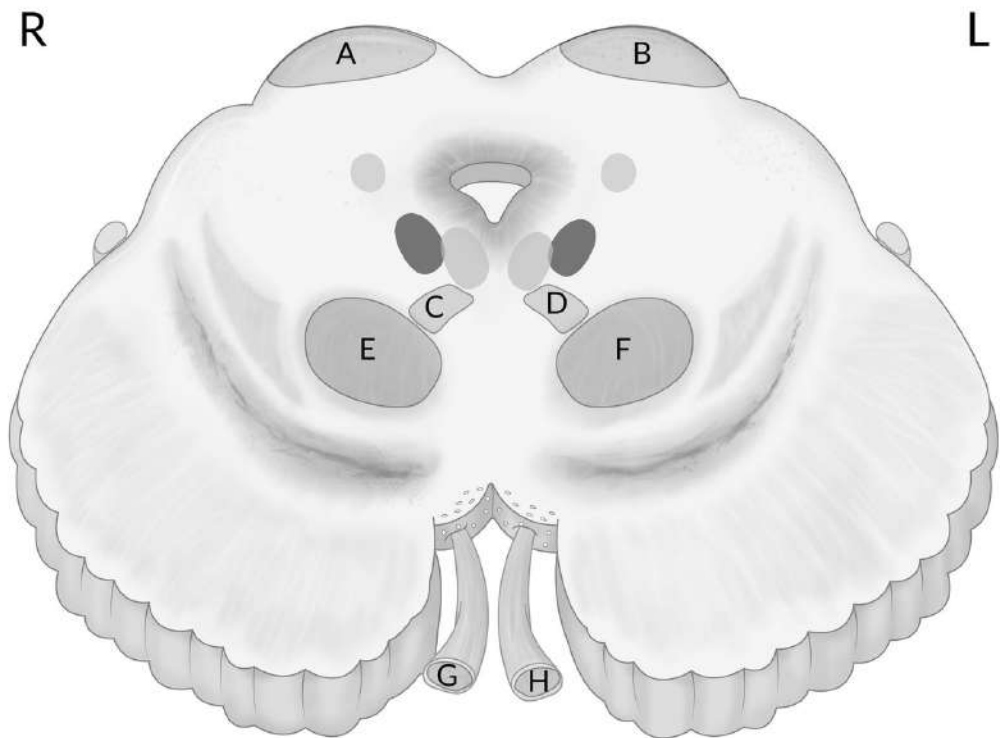
E - Increase in cell membrane permeability to calcium ions

Explanation Why

Voltage-gated [L-type \$\text{Ca}^{2+}\$ channels](#) play an important role in the [action potential](#) of [cardiomyocytes](#) and arterial [smooth muscle cells](#). They are activated by [antihelminthic drugs](#) (e.g., [praziquantel](#)), not by [tetrodotoxin](#).

Question # 5

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



	Answer	Image
A	A	
B	B	

	Answer	Image
C	C	PPRF = paramedian pontine reticular formation MLF = medial longitudinal fasciculus Frontal eye field R L PPRF Nuclei of CNVI (abducens) Nuclei of CNIII (oculomotor) MLF CNVI CNIII Medial rectus muscle Lateral rectus muscle Looking left Frontal eye field R L PPRF Nuclei of CNVI (abducens) Nuclei of CNIII (oculomotor) MLF CNVI CNIII Medial rectus muscle Lateral rectus muscle Looking right Area 19 R L PPRF Nuclei of CNVI (abducens) Nuclei of CNIII (oculomotor) MLF CNVI CNIII Medial rectus muscle Lateral rectus muscle Convergence Lesion (e.g., due to hemorrhage, multiple sclerosis) Pretectal area
D	D	
E	E	
F	F	
G	G	
H	H	

Hint

Impaired horizontal eye movements with weak adduction of one eye and abduction nystagmus of the contralateral eye are indicative of internuclear ophthalmoplegia, which results from a lesion in the medial longitudinal fasciculus. In this young woman with a previous episode of neurologic dysfunction, the most likely cause of the lesion is multiple sclerosis.

Correct Answer

A - A

Explanation Why

The right [superior colliculus](#) integrates visual, auditory, and somatosensory information with motor signals. This structure allows the orientation of the head towards stimuli. However, injury of the right [superior colliculus](#) would result in the inability to turn the head reflexively towards the left upon sensory stimulation from that side; it would not result in the impaired coordination of the eyes during [lateral](#) gaze.

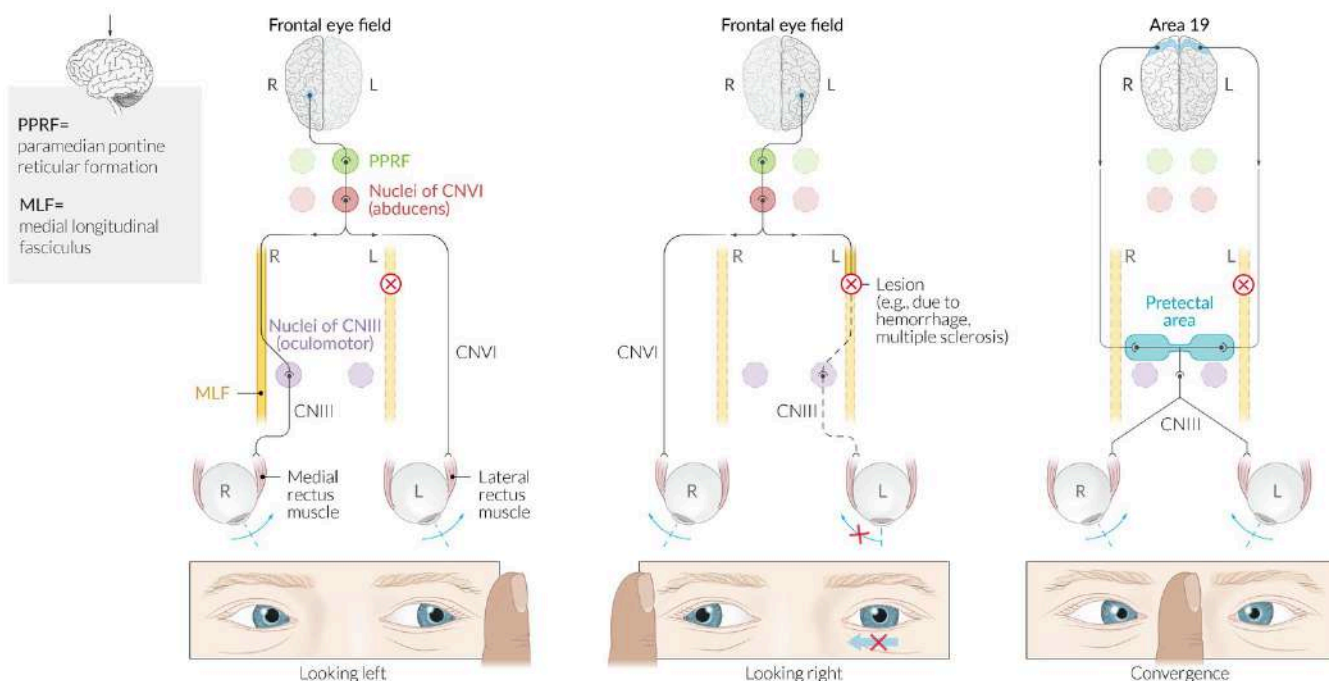
B - B

Explanation Why

The left [superior colliculus](#) integrates visual, auditory, and somatosensory information with motor signals. This structure allows the orientation of the head towards stimuli. However, injury of the left [superior colliculus](#) would result in the inability to turn the head reflexively towards the right upon sensory stimulation from that side; it would not result in the impaired coordination of the eyes during [lateral](#) gaze.

C - C

Image



Explanation Why

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

D - D

Explanation Why

Lesions in the left [medial longitudinal fasciculus](#) would cause [internuclear ophthalmoplegia](#). However, [double vision](#) would occur on right [lateral](#) gaze, not left [lateral](#) gaze as seen in this patient.

E - E

Explanation Why

The [red nucleus](#) is a large structure within the [rostral midbrain](#) that receives input from various motor areas, particularly the deep [cerebellar](#) nuclei. Lesions of the [red nucleus](#) can result in [extensor posturing](#), with extension of both upper and lower extremities. However, lesions of the [red nucleus](#) do not cause an impaired coordination of the eyes during [lateral](#) gaze.

F - F

Explanation Why

The [red nucleus](#) is a large structure within the [rostral midbrain](#) that receives input from motor areas, particularly the deep [cerebellar](#) nuclei. Lesions of the [red nucleus](#) can result in [extensor posturing](#), with the extension of both upper and lower extremities. However, lesions of the [red nucleus](#) do not cause an impaired coordination of the eyes during [lateral](#) gaze.

G - G

Explanation Why

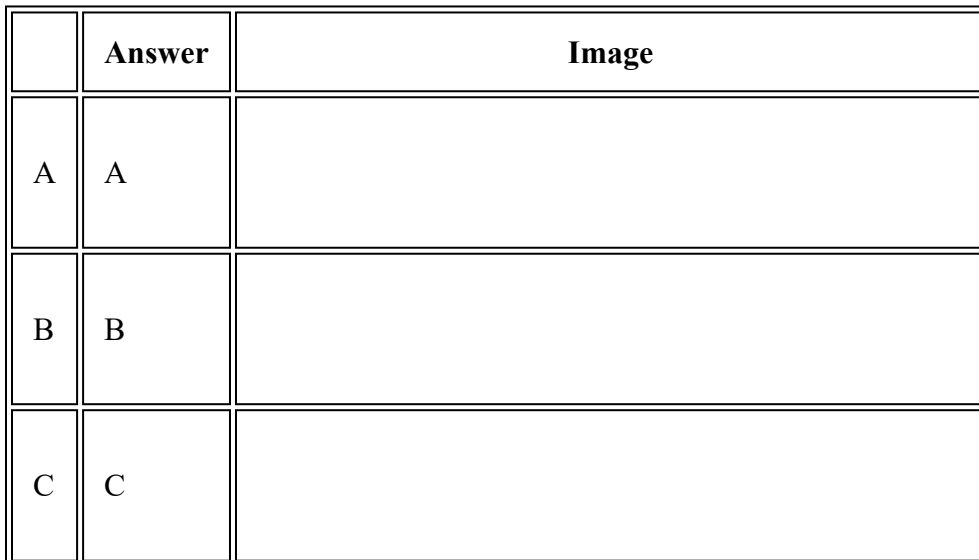
Lesions of the right [oculomotor nerve](#) would impair the function of the [medial rectus](#), which would, in turn, impair the [adduction](#) of the right [eye](#), similar to this patient. However, complete palsy of the nerve would [mean](#) that the right [eye](#) would be in a down-and-out position and would fail to converge. Thus, nystagmus would not be found.

H - H

Explanation Why

Lesions of the left [oculomotor nerve](#) would impair the function of the [medial rectus](#), impairing [adduction](#) of the ipsilateral left [eye](#). However, palsy of the left [CN III](#) would leave the left [eye](#) in a down-and-out position, without the ability to converge and with no nystagmus. [Adduction](#) of the right [eye](#) on left [lateral](#) gaze would not be impaired.

A 78-year-old man comes to the emergency department because of sudden-onset loss of vision. He has hypertension and type 2 diabetes mellitus. Current medications include hydrochlorothiazide, atenolol, metformin, and glipizide. Ophthalmologic examination shows a visual field defect in the bilateral right upper quadrants. A lesion in which of the following labeled sites in the schematic overview of the visual pathway is most likely?



	Answer	Image																		
D	D																			
E	E	<table><tr><th>Site of injury</th><th>Visual field defects</th></tr><tr><td></td><td>L R</td></tr><tr><td>1 Left optic nerve</td><td></td></tr><tr><td>2 Medial portion of the optic chiasm</td><td></td></tr><tr><td>3 Left optic tract</td><td></td></tr><tr><td>4 Lower bundle (Meyer's loop) of the left optic radiation</td><td></td></tr><tr><td>5 Upper bundle of the left optic radiation</td><td></td></tr><tr><td>6 Anterior portion of the calcarine sulcus and adjacent visual cortex</td><td></td></tr><tr><td>7 Left occipital pole</td><td></td></tr></table>	Site of injury	Visual field defects		L R	1 Left optic nerve		2 Medial portion of the optic chiasm		3 Left optic tract		4 Lower bundle (Meyer's loop) of the left optic radiation		5 Upper bundle of the left optic radiation		6 Anterior portion of the calcarine sulcus and adjacent visual cortex		7 Left occipital pole	
Site of injury	Visual field defects																			
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5 Upper bundle of the left optic radiation																				
6 Anterior portion of the calcarine sulcus and adjacent visual cortex																				
7 Left occipital pole																				
F	F																			
G	G																			

Hint

Superior homonymous quadrantanopia indicates a lesion of the Meyer loop, which carries information from the retina through the temporal lobe.

Correct Answer

A - A

Explanation Why

Damage to the left [optic nerve](#) causes ipsilateral [anopia](#) (so of the left [eye](#)). A lesion here is unlikely in this patient, who has at least some vision in both eyes.

B - B

Explanation Why

A lesion in this region would damage nerve fibers from the temporal part of the [retina](#) of the left [eye](#), which would cause contralateral (so right-sided) nasal hemianopia of the left [eye](#).

C - C

Explanation Why

Injury at the decussation of [optic nerve](#) fibers at the [optic chiasm](#) causes [bitemporal hemianopia](#). [Pituitary](#) lesions (e.g., [pituitary adenoma](#), [pituitary apoplexy](#)) and [saccular aneurysms](#) classically cause this [visual field](#) defect.

D - D

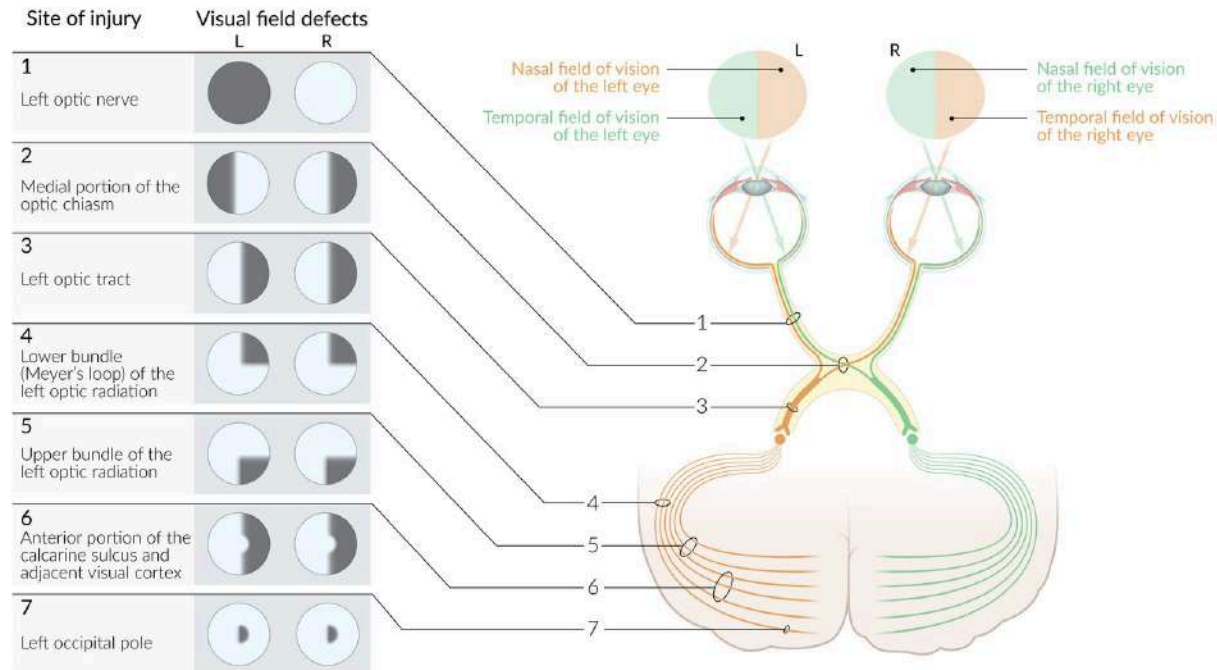
Explanation Why

Damage in this region, the left [optic tract](#), causes a contralateral (so right-sided) [homonymous](#)

[hemianopia](#). [Stroke](#), tumors, surgery, and congenital defects may cause damage to the [optic tract](#).

E - E

Image



Explanation Why

This location corresponds to the Meyer loop. Disruptions in this segment of the [visual pathway](#) classically produce contralateral superior [homonymous quadrantanopia](#). Common etiologies include [stroke](#) involving the [MCA](#), which is likely in this patient with [hypertension](#) and [diabetes](#), as well as [mass effect](#) (e.g., tumors).

F - F

Explanation Why

Injuries to the left dorsal optic radiation will classically produce contralateral (so right-sided) lower

[homonymous quadrantanopia](#). Lesions of the [parietal lobe](#), most commonly [stroke](#) involving the [MCA](#), are implicated in the development of this type of visual defect. The patient in this stem, however, has defects in the superior [visual fields](#).

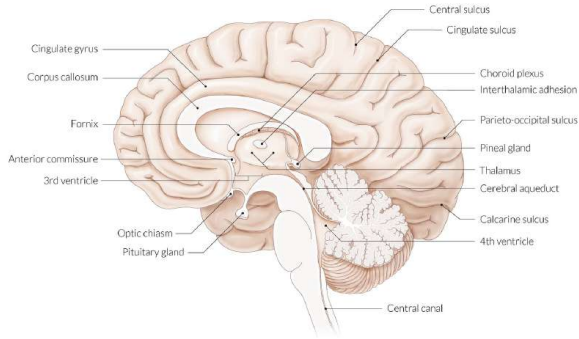
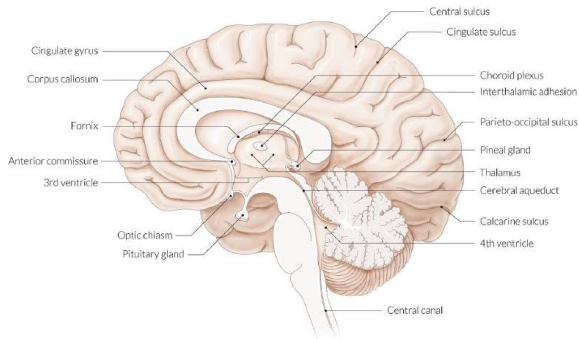
G - G

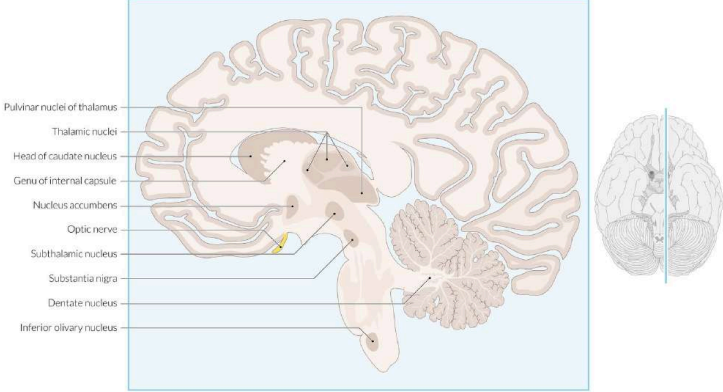
Explanation Why

An injury to the left central bundle of the [optic radiation](#) would cause either contralateral (so right-sided) hemianopia with [macular sparing](#) (typically caused by a [posterior cerebral artery infarct](#)) or complete contralateral [homonymous hemianopia](#). The patient described here has a single quadrant defect, which does not fit with either of these injury presentations.

Question # 7

A 65-year-old woman with hypertension comes to the emergency department because of sudden onset of a severe headache 2 hours ago. Her temperature is 34.7°C (94.5°F) and blood pressure is 189/115 mm Hg. Physical examination shows cold skin. A CT scan of the head shows a subarachnoid hemorrhage and she is started on appropriate pharmacotherapy. Damage to which of the following regions of the brain is most likely responsible for this patient's presentation?

	Answer	Image
A	Anterior cingulate gyrus	 Diagram of the human brain in sagittal section. Labels include: Central sulcus, Cingulate sulcus, Cingulate gyrus, Choroid plexus, Intertalamic adhesion, Parieto-occipital sulcus, Pineal gland, Thalamus, Cerebral aqueduct, Calcarine sulcus, 4th ventricle, Central canal, Optic chiasm, Pituitary gland, 3rd ventricle, Anterior commissure, Fornix, Corpus callosum.
B	Ventral lateral thalamic nucleus	
C	Pineal gland	 Diagram of the human brain in sagittal section. Labels include: Central sulcus, Cingulate sulcus, Cingulate gyrus, Choroid plexus, Intertalamic adhesion, Parieto-occipital sulcus, Pineal gland, Thalamus, Cerebral aqueduct, Calcarine sulcus, 4th ventricle, Central canal, Optic chiasm, Pituitary gland, 3rd ventricle, Anterior commissure, Fornix, Corpus callosum.
D	Preoptic nucleus	

	Answer	Image
E	Caudate nucleus	

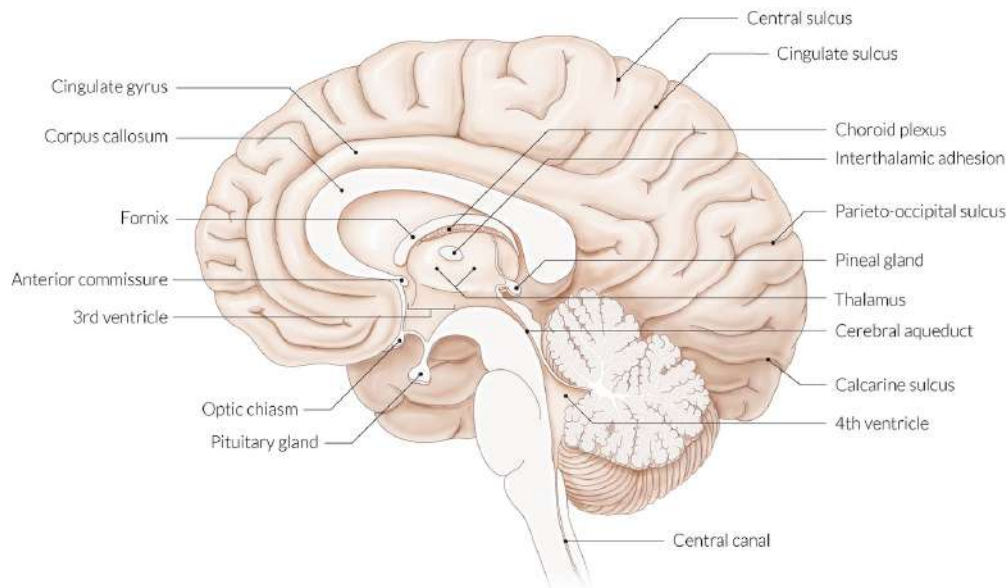
Hint

This woman has signs of hypothermia. Although primary hypothermia is caused by environmental exposure to cold, hypothermia can also occur secondary to metabolic derangements, infections, endocrine dysfunction, or lesions of the central nervous system. The latter has likely occurred in this case as a complication of subarachnoid hemorrhage.

Correct Answer

A - Anterior cingulate gyrus

Image



Explanation Why

The [anterior cingulate gyrus](#) is involved in modulation of emotional responses and autonomic activity (e.g., [heart rate](#), blood pressure). Damage to the [anterior cingulate gyrus](#) would not cause the dysfunctional thermoregulation seen in this patient.

B - Ventral lateral thalamic nucleus

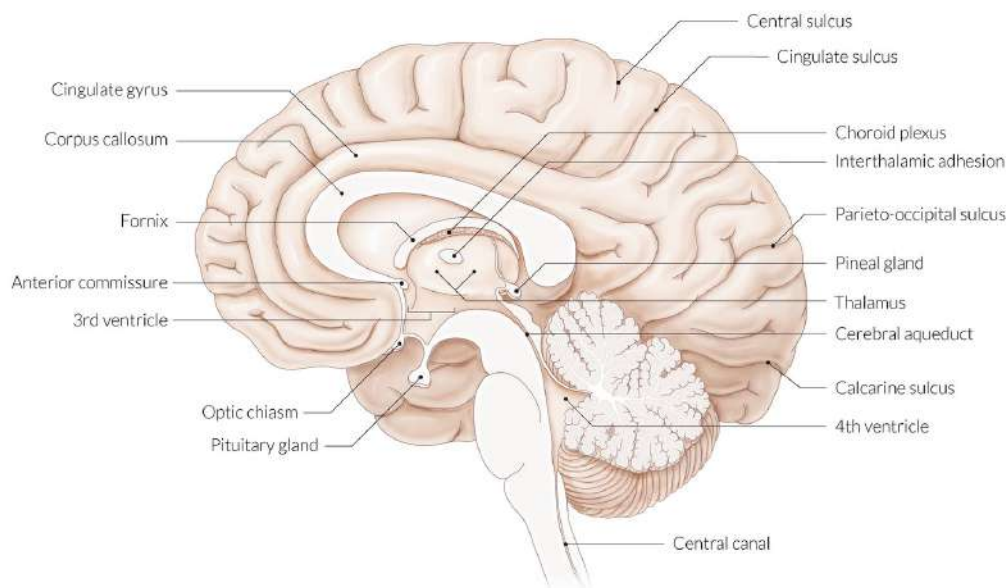
Explanation Why

The [ventral lateral nucleus](#) of the [thalamus](#) is involved in the coordination of movements. Damage to the [ventral lateral nucleus](#) of the [thalamus](#) would not cause the dysfunctional thermoregulation seen

in this patient.

C - Pineal gland

Image



Explanation Why

The [pineal gland](#) secretes [melatonin](#), which helps maintain [circadian rhythm](#), including the circadian variation in temperature (i.e., lower nocturnal core body temperatures). Damage to the [pineal gland](#) would be more likely to cause a lack of circadian variation in temperature than the more straightforward [hypothermia](#) seen in this patient.

D - Preoptic nucleus

Explanation But

In addition to temperature regulation, the [preoptic nucleus](#) secretes [GnRH](#) (dysfunctional in

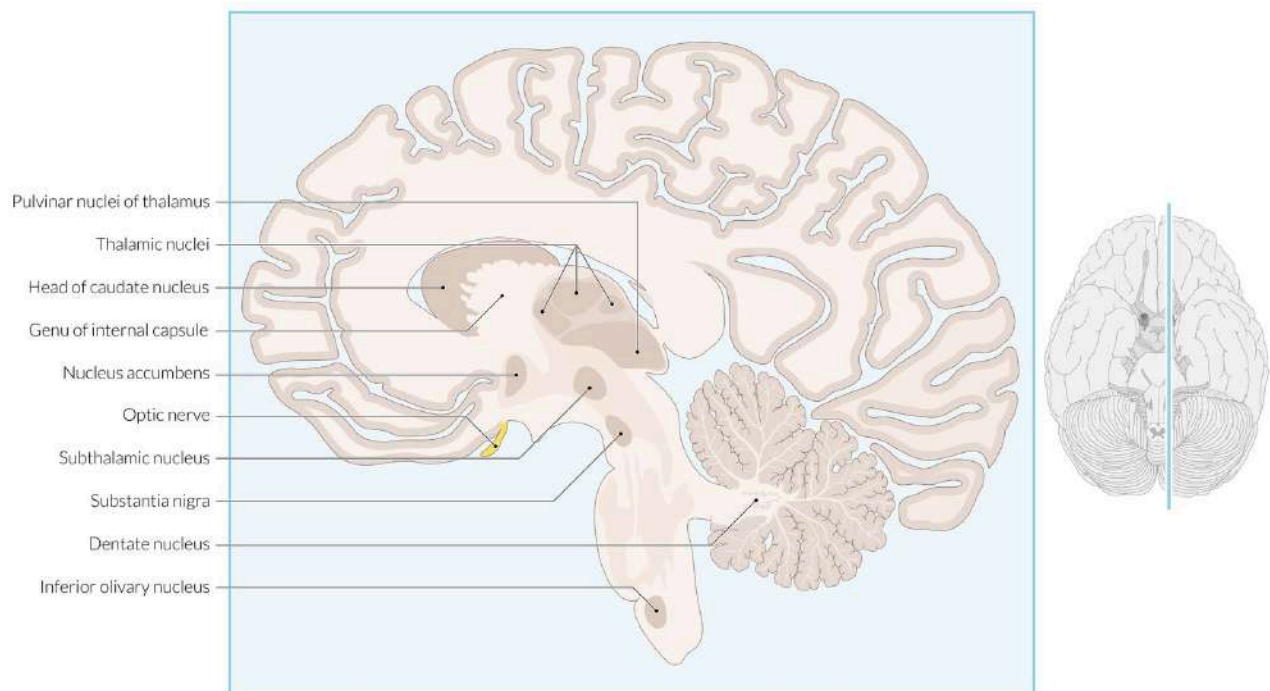
[Kallmann syndrome](#)) and is involved in the regulation of sexual behavior.

Explanation Why

The [preoptic nucleus](#) in the [anterior hypothalamus](#) is the body's primary thermoregulator. It receives afferent impulses from thermoreceptors in the [skin](#) and, in turn, modulates the activity of the organs involved in thermal regulation (e.g., [heart](#), blood vessels) to maintain a normal core body temperature. Other regions of the [hypothalamus](#) assist in thermoregulation: The [anterior hypothalamic nucleus](#) controls the cooling response (e.g., [vasodilation](#), sweating), while the [posterior hypothalamic nucleus](#) controls the warming response (e.g., vasoconstriction, shivering). Damage to the [preoptic nucleus](#) can result in either [hypothermia](#) or hyperthermia. Circulating pyrogens can also influence the [preoptic nucleus](#) to increase the thermoregulatory set point and initiate [fever](#).

E - Caudate nucleus

Image



Explanation Why

The [caudate nucleus](#) plays a role in the coordination of movement and higher cognitive function. Damage to the [caudate nucleus](#) is seen in conditions such as [Huntington disease](#) but would not cause dysfunctional thermoregulation.

Question # 8

A 46-year-old man comes to the physician because of a 2-month history of hoarseness and drooling. Initially, he had difficulty swallowing solid food, but now he has difficulty swallowing foods like oatmeal as well. During this period, he also developed weakness in both arms and has had an 8.2 kg (18 lb) weight loss. He appears ill. His vital signs are within normal limits. Examination shows tongue atrophy and pooled oral secretions. There is diffuse muscle atrophy in all extremities. Deep tendon reflexes are 3+ in all extremities. Sensation to pinprick, light touch, and vibration is intact. An esophagogastroduodenoscopy shows no abnormalities. Which of the following is the most likely cause of this patient's symptoms?

	Answer	Image
A	Multiple cerebral infarctions	
B	Autoimmune destruction of acetylcholine receptors	
C	Demyelination of peripheral nerves	
D	Destruction of upper and lower motor neurons	
E	Dilation of the central spinal canal	Syringomyelia - Lesion at C4-C5 - Syrinx: - Structures less affected depend on degree of severity - Anterolateral tract - Posterior tract: - Somatosensory arrangement: - Cervical segments medial-lateral; - Sacral segments lateral-medial - Anterior horn Damaged region - Discolored sensory loss (of temperature and pain): - from damage to pathways of proprioceptive sensitivity crossing at segment level - Flaccid paralysis: - from bilateral damage to anterior horns at segment level - Spastic paralysis: - from damage of the medial portion of lateral horn Note: Both the loss of sensation and the effects on motor function are mapped according to the associated dermatomes. Since most muscles are innervated by several segments, they are usually spared, but not always. Autonomic disorders (e.g., Horner's syndrome, bladder dysfunction) can also occur if the lateral horns (C8-T12/L1) are involved.

Hint

This patient's progressive dysphagia, weakness, diffuse muscle atrophy, and intact sensation suggest a diffuse polyneuropathy that spares the sensory fibers.

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Correct Answer

A - Multiple cerebral infarctions

Explanation Why

Multiple cerebral infarctions would be characteristic of embolic [strokes](#) and could explain the [upper motor neuron](#) symptoms that involve muscles in the face and upper and lower extremities, like this patient's [dysphagia](#) and [hyperreflexia](#). However, [strokes](#) typically result in asymmetric rather than bilateral muscle weakness and would not cause [LMN signs](#) (muscle [atrophy](#) and [fasciculations](#)).

B - Autoimmune destruction of acetylcholine receptors

Explanation Why

Autoimmune destruction of acetylcholine receptors is seen in [myasthenia gravis](#). Individuals with MG usually have muscle weakness that is worse at the end of the day or during periods of activity. Although this patient also has muscle weakness, he has signs of [UMN](#) involvement ([hyperreflexia](#)), which are not seen in MG. In addition, more than 50% of patients with MG have ocular symptoms ([ptosis](#) and [diplopia](#)), which is also lacking here.

C - Demyelination of peripheral nerves

Explanation Why

Peripheral nerve [demyelination](#) is the mechanism of [Guillain-Barre syndrome](#), which classically manifests with ascending weakness and can also involve the bulbar and facial muscles. However, it typically presents over the course of a few days, rather than the months seen in this patient. GBS also causes [hyporeflexia](#) due to [lower motor neuron demyelination](#), not [hyperreflexia](#), as seen here. In addition, about two-thirds of patients with GBS report a preceding upper respiratory or gastrointestinal infection, which is absent here.

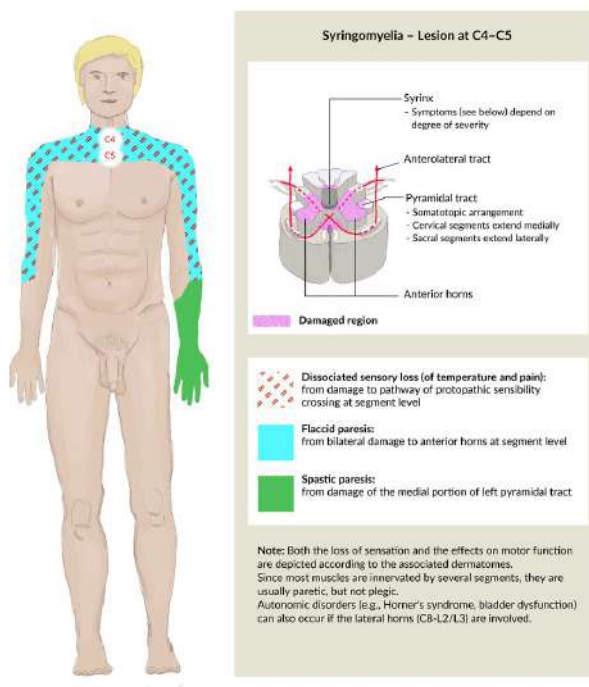
D - Destruction of upper and lower motor neurons

Explanation Why

Progressive destruction of [upper motor neurons \(UMN\)](#) and [lower motor neurons \(LMN\)](#) in multiple body segments ([cranial](#), cervical, thoracic, and lumbosacral) is characteristic of [amyotrophic lateral sclerosis](#). [UMN](#) destruction manifests as [hyperreflexia](#), increased muscle tone, and [spasticity](#). [LMN](#) damage has caused this patient's [dysphagia](#) and muscle [atrophy](#).

E - Dilation of the central spinal canal

Image



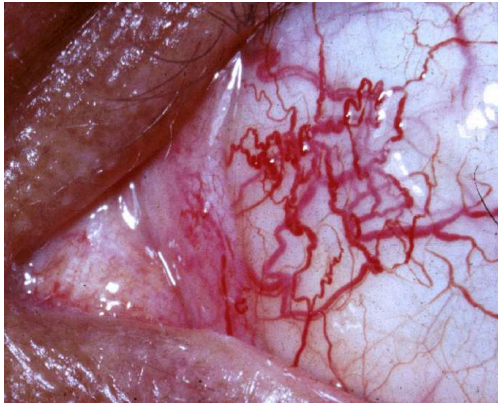
Explanation Why

Dilation of the central [spinal canal](#) is characteristic of [syringomyelia](#), which causes progressive damage to the [spinothalamic tract](#) and manifests with [dermatomal](#) loss of [pain](#) and temperature sensation ([dissociated sensory loss](#)). [Syringomyelia](#) can also damage the [corticospinal tracts](#) and

[anterior horns](#), and cause weakness, but would not explain the multiple segments involved in this patient. Moreover, [syringomyelia](#) would not explain this patient's [hyperreflexia](#).

Question # 9

A 12-year-old boy is brought to the physician for multiple bruises. He has fallen multiple times over the past 4 months and has difficulty walking without assistance. His speech is slow and difficult to understand. Neurological examination shows bilateral nystagmus, decreased muscle strength, 1+ reflexes bilaterally, and a wide-based gait with irregular and uneven steps. His proprioception and vibration senses are absent. The remainder of the examination shows kyphoscoliosis and foot inversion with hammertoes. This patient is most likely to die from which of the following complications?

	Answer	Image
A	Leukemia	
B	Renal cell carcinoma	
C	Heart failure	
D	Liver failure	

	Answer	Image
E	Posterior fossa tumors	
F	Hypoglycemia	
G	Aspiration pneumonia	

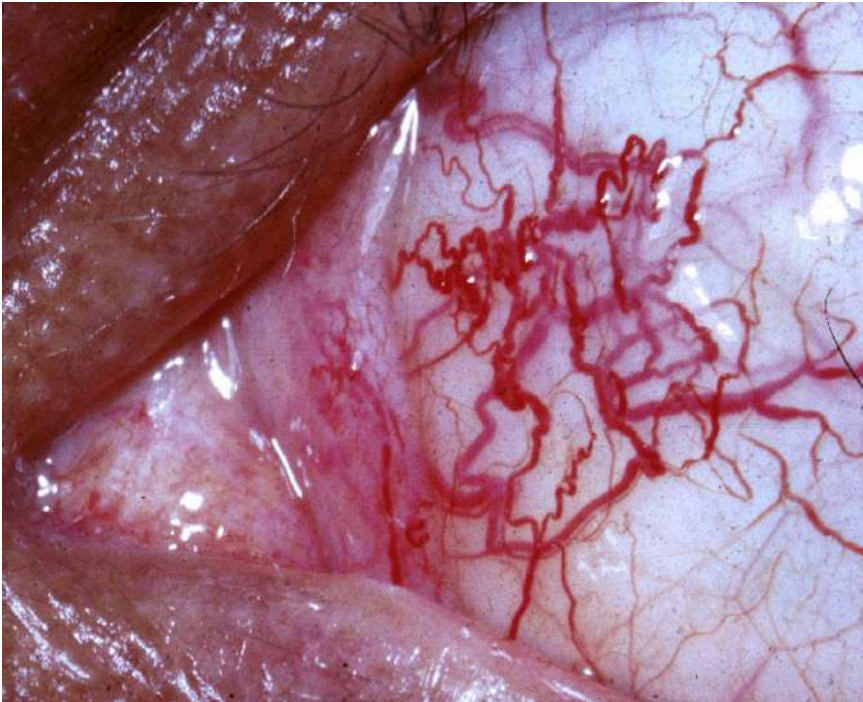
Hint

This patient presents with progressive bilateral limb ataxia and weakness, loss of deep tendon reflexes, paresthesia, dysarthria, and skeletal deformities, indicating Friedreich ataxia (FA). Pes cavus (inverted feet), hammertoes, and kyphoscoliosis are all typical skeletal deformities seen in FA.

Correct Answer

A - Leukemia

Image



Explanation But

Nystagmus as seen in this patient is distinct from oculomotor apraxia. Nystagmus involves abnormal movements that are present at rest or only with [eye](#) movement, whereas oculomotor apraxia is induced by head (not just [eye](#)) movement.

Explanation Why

Patients with [ataxia-telangiectasia](#) are at increased risk of [malignancy](#) (usually leukemia or [lymphoma](#)). Patients with AT present with [ataxia](#) and oculocutaneous [telangiectasias](#), as well as gaze abnormalities (most often oculomotor apraxia), around the age of 5 years. While this patient has an abnormal gait and abnormal [eye](#) movements, he is much older than would be expected for AT diagnosis, lacks [telangiectasias](#) and gaze abnormalities, and has musculoskeletal abnormalities that are not seen in AT.

B - Renal cell carcinoma

Explanation Why

Patients with [von Hippel-Lindau disease](#) are at increased risk of (often bilateral) [renal cell carcinoma](#). The hallmark feature of [VHL disease](#) is [central nervous system hemangioblastomas](#), particularly in the [cerebellum](#) and [brainstem](#). While an [infratentorial hemangioblastoma](#) could cause progressive [ataxia](#), [dysarthria](#), weakness, sensory loss, and [hyporeflexia](#), [VHL](#) would not cause this patient's skeletal changes (i.e., [kyphoscoliosis](#) and [hammertoes](#)).

C - Heart failure

Explanation Why

[Heart failure](#) is the most common cause of death in patients with [Friedreich ataxia](#). Almost all patients (> 95%) with FA have abnormal cardiologic findings, the most common being (usually [hypertrophic](#)) [cardiomyopathy](#) and/or [arrhythmia](#). The degree of cardiac dysfunction does not appear to correlate with neurologic disease progression. Most patients with FA do not live past the age of 30–40.

D - Liver failure

Image



Explanation Why

The majority of patients with untreated [Wilson disease](#) die of [acute liver failure](#) or [cirrhosis](#). While patients with [Wilson disease](#) often have neurologic abnormalities such as [ataxia](#) and [dysarthria](#), they also have signs of [liver](#) disease (e.g., [jaundice](#), [hepatomegaly](#), abdominal [pain](#)) and characteristic ophthalmic findings ([Kayser-Fleischer rings](#)). Moreover, [Wilson disease](#) would not explain this patient's musculoskeletal abnormalities. Finally, [Wilson disease](#) is associated with [hyperreflexia](#), not [hyporeflexia](#).

E - Posterior fossa tumors

Explanation But

[NF-2](#) could cause [dysarthria](#) if a [tumor](#) affected the bulbar muscles, but this symptom is not common.

Explanation Why

Bilateral [vestibular schwannomas](#) (in the [posterior](#) fossa) are characteristic of [neurofibromatosis type 2 \(NF-2\)](#). Patients with [NF-2](#) usually have severe [hearing loss](#) due to [CN VIII](#) compression. Moreover, [NF-2](#) would not explain this patient's musculoskeletal abnormalities.

F - Hypoglycemia

Explanation Why

Patients with [Friedreich ataxia](#) are at increased risk of [hyperglycemia](#) and [diabetes mellitus](#). If this patient were to develop [diabetes mellitus](#) in the future and overdose on an anti-diabetic agent, this could cause [hypoglycemia](#) and death. However, another cause of death is much more likely.

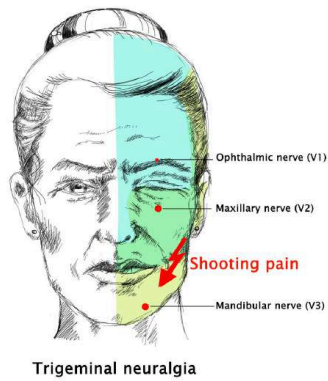
G - Aspiration pneumonia

Explanation Why

Patients with [Friedreich ataxia](#) are at increased risk of [aspiration pneumonia](#) if they have bulbar [cranial nerve](#) involvement, which leads to impaired [airway](#) protection. While this patient has evidence of [cranial nerve](#) involvement ([dysarthria](#)), [aspiration pneumonia](#) is often curable, making another cause of death more likely in a patient with FA.

Question # 10

A 31-year-old woman comes to the physician because of intermittent episodes of stabbing right lower jaw pain for 6 weeks. The pain is severe, sharp, and lasts for a few seconds. These episodes commonly occur when she washes her face, brushes her teeth, or eats a meal. She does not have visual disturbances, weakness of her facial muscles, or hearing loss. Five weeks ago, she had an episode of acute bacterial sinusitis, which was treated with antibiotics. Which of the following is the most appropriate initial treatment for this patient's condition?

	Answer	Image
A	Microvascular decompression	
B	Dextromethorphan	
C	Botulinum toxin injection	
D	Amoxicillin	
E	Carbamazepine	 Trigeminal neuralgia
F	Oxygen supplementation	

	Answer	Image
G	Valacyclovir	
H	Doxepin	

Hint

The history of intermittent episodes of severe, stabbing, unilateral facial pain lasting several seconds is consistent with trigeminal neuralgia.

Correct Answer

A - Microvascular decompression

Explanation Why

While [microvascular decompression](#) is used to provide relief in cases of refractory [trigeminal neuralgia](#), it is an invasive procedure. As such, it entails a risk of nerve damage, which may lead to [hearing loss](#), facial numbness, or [diplopia](#) ([double vision](#)) and is not used as first-line therapy.

B - Dextromethorphan

Explanation Why

[Dextromethorphan](#) is an [NMDA receptor antagonist](#) that is used as a [cough suppressant](#). Although [NMDA receptor antagonists](#) can reduce [neuropathic pain](#), [dextromethorphan](#) has little or no [analgesic](#) efficacy in the [treatment of pain](#) due to [trigeminal neuralgia](#).

C - Botulinum toxin injection

Explanation Why

[Botulinum toxin](#) injection into a facial muscle is indicated for [blepharospasm](#), and some studies also support the use of this therapy for refractory [trigeminal neuralgia](#). However, there is not enough evidence supporting the use of [botulinum toxin](#) in the management of [trigeminal neuralgia](#) for it to be considered a first-line treatment.

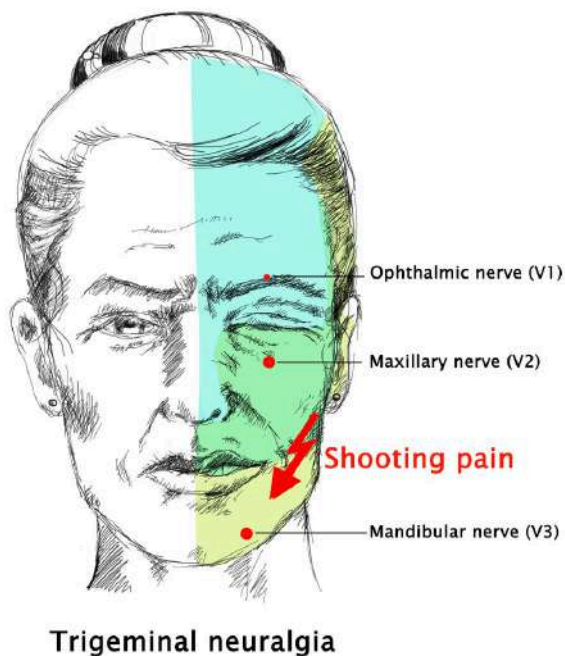
D - Amoxicillin

Explanation Why

[Amoxicillin](#) is used in the treatment of acute bacterial [sinusitis](#), which can present with a facial [pain](#). However, this [pain](#) is constant and localized to sinuses rather than the patient's intermittent, stabbing [jaw pain](#). Furthermore, the absence of [fever](#), nasal congestion, and [rhinorrhea](#) in this patient makes [acute bacterial sinusitis](#) unlikely.

E - Carbamazepine

Image



Explanation Why

[Carbamazepine](#) is recommended as first-line treatment for [trigeminal neuralgia](#) and [epilepsy](#). Side effects of [carbamazepine](#) include [vertigo](#), sedation, and [diplopia](#). Nevertheless, it has proven effective in the treatment of [trigeminal neuralgia](#) and may be used as a monotherapy.

F - Oxygen supplementation

Explanation Why

Administration of 100% oxygen is effective in terminating acute episodes of [cluster headache](#), which can also cause repeated attacks of unilateral facial [pain](#). However, patients with [cluster headache](#) typically present with [pain](#) in the orbital, supraorbital, or temporal region that is associated with ipsilateral [cranial](#) autonomic symptoms (e.g., [conjunctival injection](#), lacrimation, [rhinorrhea](#)), which this patient does not have.

G - Valacyclovir

Explanation Why

[Valacyclovir](#) is used in the treatment of [shingles](#), which can present with a unilateral, stabbing facial [pain](#), as seen in this patient. However, an [erythematous](#), [maculopapular](#) rash that quickly evolves into vesicular lesions would be expected to follow the [pain](#). Furthermore, [shingles](#) typically causes [fever](#), [headache](#), and fatigue, which are absent in this patient.

H - Doxepin

Explanation Why

[Doxepin](#), a [tricyclic antidepressant](#), can be used as an adjuvant [analgesic](#) in the treatment of [neuropathic pain](#). However, it has no known effect in the treatment of [trigeminal neuralgia](#) and is therefore not recommended.

Question # 11

Four days after delivery, a 1400-g (3-lb 1-oz) newborn has a tonic seizure that lasts for 30 seconds. Over the past 24 hours, he has become increasingly lethargic. He was born at 31 weeks' gestation. Antenatal period was complicated by chorioamnionitis. Apgar scores were 4 and 5 at 1 and 5 minutes, respectively. He appears ill. His pulse is 130/min, respirations are 53/min and irregular, and blood pressure is 67/35 mm Hg. Examination shows a bulging anterior fontanelle. The pupils are equal and react sluggishly to light. Examination shows slow, conjugate back and forth movements of the eyes. Muscle tone is decreased in all extremities. The lungs are clear to auscultation. Which of the following is the most likely underlying cause?

	Answer	Image
A	Galactose-1-phosphate uridylyltransferase deficiency	
B	Apoptosis of lower motor neurons	
C	Congenital hydrocephalus	
D	Phenylalanine hydroxylase deficiency	
E	Germinal matrix hemorrhage	

Hint

The condition described here is a serious complication of preterm birth.

Correct Answer

A - Galactose-1-phosphate uridylyltransferase deficiency

Explanation But

[Galactosemia](#) can cause [coagulopathy](#) and increased risk of bleeding, which may predispose children to the condition of this patient.

Explanation Why

Galactose-1-[phosphate](#) uridylyltransferase deficiency is the underlying cause of [galactosemia](#), which, if left untreated, may present with [lethargy](#), [hypotonia](#), and [seizures](#), as seen here. However, the absence of [cataracts](#) (may present within the first days of life), [jaundice](#), and [hepatomegaly](#), make this diagnosis less likely.

B - Apoptosis of lower motor neurons

Explanation Why

[Apoptosis](#) of [lower motor neurons](#) is the underlying mechanism of [spinal muscular atrophy](#), which is a possible cause of muscular [hypotonia](#) in [infants](#). The most severe type ([Werdnig-Hoffmann](#) disease) may manifest immediately after [birth](#) or up to 6 months of age. [Proximal](#) muscles, mostly of the lower extremities, are usually involved symmetrically. However, this patient's [seizures](#), bulging [anterior fontanelle](#), impaired pupillary response, and roving eye movements would not be consistent with this diagnosis.

C - Congenital hydrocephalus

Explanation Why

[Hydrocephalus](#) due to congenital causes, such as the [Arnold-Chiari malformation](#), [Dandy-Walker malformation](#), and intrauterine infections, may present in [neonates](#) with [lethargy](#), tense [fontanelles](#),

[seizures](#), and changes in vital signs due to [brain stem](#) compression (e.g., irregular breathing). However, [elevated intracranial pressure](#) usually manifests with rapidly increasing circumference of the head in [neonates](#), which is not seen in this [infant](#). Furthermore, instead of the roving eye movements, a downward deviation of the eyes ([sunset eye sign](#)) would be expected in patients with [hydrocephalus](#).

D - Phenylalanine hydroxylase deficiency

Explanation Why

Phenylalanine hydroxylase deficiency is the underlying cause of [phenylketonuria](#). While most patients are asymptomatic at [birth](#), half of patients with [phenylketonuria](#) (PKU) have [seizures](#) with cerebral foci, a lag of psychomotor development and a musty body odor by 4–6 months of age. Additional features include light, pale [hair](#) and blue eyes (due to decreased [melanin](#) production). Since most patients are asymptomatic until severe and often irreversible complications have occurred, direct measurement of [phenylalanine](#) levels is an important part of [newborn screening](#) for metabolic disorders. The [screening test](#) is performed on the second day after [birth](#) using blood obtained from a heel prick.

E - Germinal matrix hemorrhage

Explanation But

[Cranial ultrasonography](#) is the preferred method to diagnose [IVH](#) in the [newborn](#). Since most patients are asymptomatic, screening ultrasounds are routinely performed in [infants](#) with a [birth](#) weight < 1500 g and delivery before 30 weeks' [gestation](#).

Explanation Why

[Germinal matrix hemorrhage](#) is the underlying cause of [intraventricular hemorrhage](#) (IVH) in [preterm infants](#). [IVH](#) is a common complication in [preterm infants](#) that usually occurs within the first five days after [birth](#). It is typically seen in [neonates](#) weighing < 1500 g and born before 32 weeks' [gestation](#) due to the fragility of the [germinal matrix](#). Additional [risk factors](#) include periparturient [chorioamnionitis](#) and [hypoxia](#) (as suggested by this patient's low [Apgar scores](#)). Most [infants](#) with [IVH](#) are asymptomatic, but saltatory (over several days) or, more rarely, catastrophic (over minutes to hours) courses are also possible. Symptoms include [lethargy](#), [hypotonia](#), irregular respirations, [seizures](#), bulging [anterior fontanelle](#), [cranial nerve](#) abnormalities (e.g., pupil reacting sluggishly to light), and changes in [eye](#) movement (e.g., roving eye movements), all of which this patient has.

Question # 12

A 4-year-old boy is brought to the emergency department for evaluation after falling. He has fallen multiple times in the last year. His parents report that he did not walk until he was 18 months old. Examination shows a mildly swollen right ankle with no tenderness over the medial or lateral malleolus; range of motion is full with mild pain. He has marked enlargement of both calves. When standing up, the patient uses his hands against his knees and thighs to slowly push himself up into a standing position. Which of the following is the most likely underlying mechanism of this patient's fall?

	Answer	Image
A	Loss of the ATM protein	
B	Absence of dystrophin protein	
C	Myotonin protein kinase defect	
D	Arylsulfatase A deficiency	
E	SMN1 gene defect	

Hint

This boy's developmental delay in walking, enlargement of the calves (pseudohypertrophy), and use of the Gower maneuver (walking hands up thigh into a standing position) is consistent with Duchenne muscular dystrophy (X-linked recessive disorder)

Correct Answer

A - Loss of the ATM protein

Explanation Why

Loss of the ATM protein results in [ataxia-telangiectasia](#) (A-T), an [autosomal recessive neurodegenerative disorder](#). Symptoms of A-T commonly begin in childhood before the age of 5 and include difficulty walking and problems with balance and coordination, as seen in this patient. However, A-T does not result in [pseudohypertrophy of the calves](#) and the [Gower maneuver](#). Additionally, individuals with A-T have oculomotor apraxia, myoclonus, frequent infections, and [choreoathetoid movements](#), which are not seen in this child.

B - Absence of dystrophin protein

Image



Explanation Why

The absence of [dystrophin](#) protein results in [Duchenne muscular dystrophy \(DMD\)](#), an X-linked recessive disorder. [DMD](#) is diagnosed by testing muscle enzymes like [creatine kinase](#) (which are typically elevated), genetic analysis for the [dystrophin gene](#), and muscle biopsy if genetic analysis is inconclusive. Complications of [DMD](#) already arise during [adolescence](#) and include [dilated cardiomyopathy](#), [cardiac arrhythmias](#), and respiratory insufficiency.

C - Myotonic protein kinase defect

Explanation Why

Myotonic protein [kinase](#) defects result in [myotonic dystrophies](#) type 1 and type 2. Type 1 can present in childhood with progressive muscle weakness but involves the facial muscles and [intrinsic muscles of the hand](#) and not the [proximal](#) muscles seen in this child. Type 2 commonly presents with mild [proximal](#) muscle weakness but onset is usually in [adolescence](#) and not in early childhood, as seen here. Both types can present with the [Gower maneuver](#), as seen above, but they do not cause [pseudohypertrophy of the calves](#).

D - Arylsulfatase A deficiency

Explanation Why

Arylsulfatase A is an enzyme involved in [sphingolipid](#) metabolism, and a deficiency of it causes [metachromatic leukodystrophy](#) (MLD). While the onset of the late infantile form is between 1–2 years of age and it could be the cause of the muscle weakness and clumsiness seen in this child, MLD also causes muscle [rigidity](#), visual impairment, other developmental delays and [seizures](#) that this child does not display. Additionally, MLD does not cause [pseudohypertrophy of the calves](#).

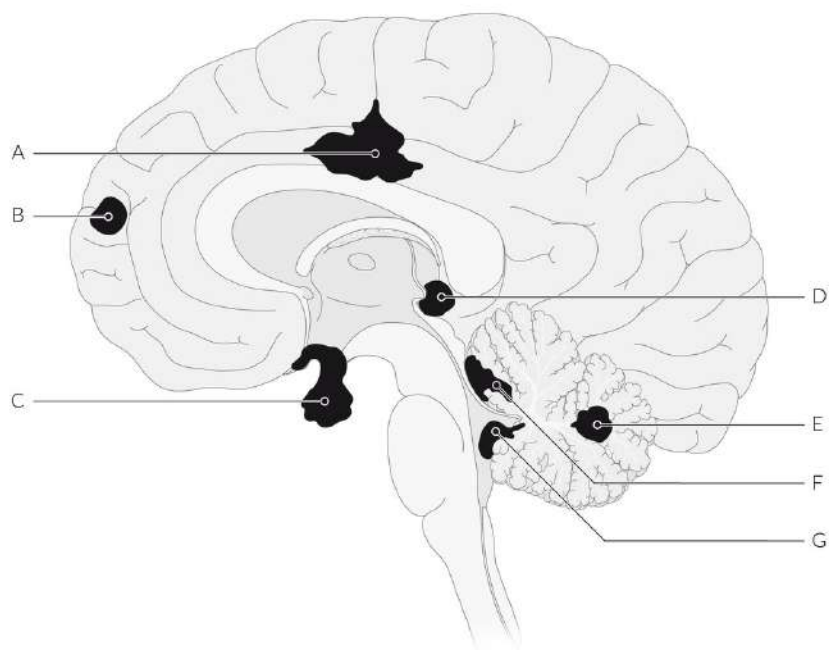
E - SMN1 gene defect

Explanation Why

An *SMN1* [gene](#) defect causes [spinal muscular atrophy](#) (SMA), a neurodegenerative [autosomal recessive](#) disorder that involves the loss of [lower motor neurons](#). While SMA can present during [infancy](#) and childhood with muscle weakness, difficulty walking, reduced reflexes, and rarely the [Gower maneuver](#) and [pseudohypertrophy of the calves](#), a patient with SMA would likely also present with [fasciculations](#), which are not present in this patient.

Question # 13

An 8-year-old boy undergoes resection of a primary brain tumor. Microscopic examination of the resected specimen shows calcifications and cystic areas filled with cholesterol crystals. This tumor was most likely located in which of the following labeled areas in the schematic overview of the brain?



	Answer	Image
A	A	
B	B	
C	C	
D	D	

	Answer	Image
E	E	
F	F	
G	G	

Hint

Calcifications and cholesterol crystals are typical histopathologic features of craniopharyngiomas.

Correct Answer

A - A

Explanation Why

[Glioblastomas](#) are highly malignant [brain tumors](#) located in the [white matter](#) of the cerebral hemispheres. In addition to being a very rare [tumor](#) in childhood, the calcifications and [cholesterol](#) crystals found in this patient's histopathologic examination are inconsistent with [glioblastoma](#). Instead, this kind of [tumor](#) is characterized by multifocal areas of [necrotic](#) and hemorrhagic lesions.

B - B

Explanation Why

The [frontal lobe](#) is the most common location of [oligodendrogliomas](#). They are notable for their “honeycomb” or “fried egg” histopathological appearance, which is due to the presence of calcification, cysts and [necrotic](#) areas. [Oligodendrogliomas](#) have a peak [incidence](#) between 40–50 years of age and are uncommon in children.

C - C

Explanation Why

[Craniopharyngiomas](#) are relatively [benign tumors](#) that are located above the [sella turcica](#) but may also expand into the [sella](#). They arise from the remnants of Rathke pouch near the [pituitary stalk](#). [Craniopharyngiomas](#) are the most common cause of [hypopituitarism](#) in children and have a bimodal age distribution with peaks at 5–14 years and 50–75 years of age.

D - D

Explanation Why

[Pinealomas](#) are expected to arise from this region, which represents the [pineal gland](#). The most common [pinealoma](#) in children is a germinoma, which would show undifferentiated germ cells on [histology](#). Calcifications and cystic areas filled with [cholesterol](#) crystals, as seen in this patient, would not be expected.

E - E

Explanation Why

The [cerebellum](#) is a frequent location of pilocytic [astrocytomas](#), the most common benign [brain tumor](#) in children. [Histopathology](#) would show microcysts, [Rosenthal fibers](#), and [GFAP](#) positive staining, none of which are seen in this patient.

F - F

Explanation Why

The [anterior cerebellum](#) is a common location of [medulloblastomas](#), the most prevalent malignant [brain tumor](#) in childhood. Histopathologic examination typically shows rosette-shaped small [tumor](#) cells (Homer-Wright rosettes). However, calcifications and cystic areas filled with [cholesterol](#) crystals as seen in this patient would not be expected. [Medulloblastomas](#) often extend into the [4th ventricle](#).

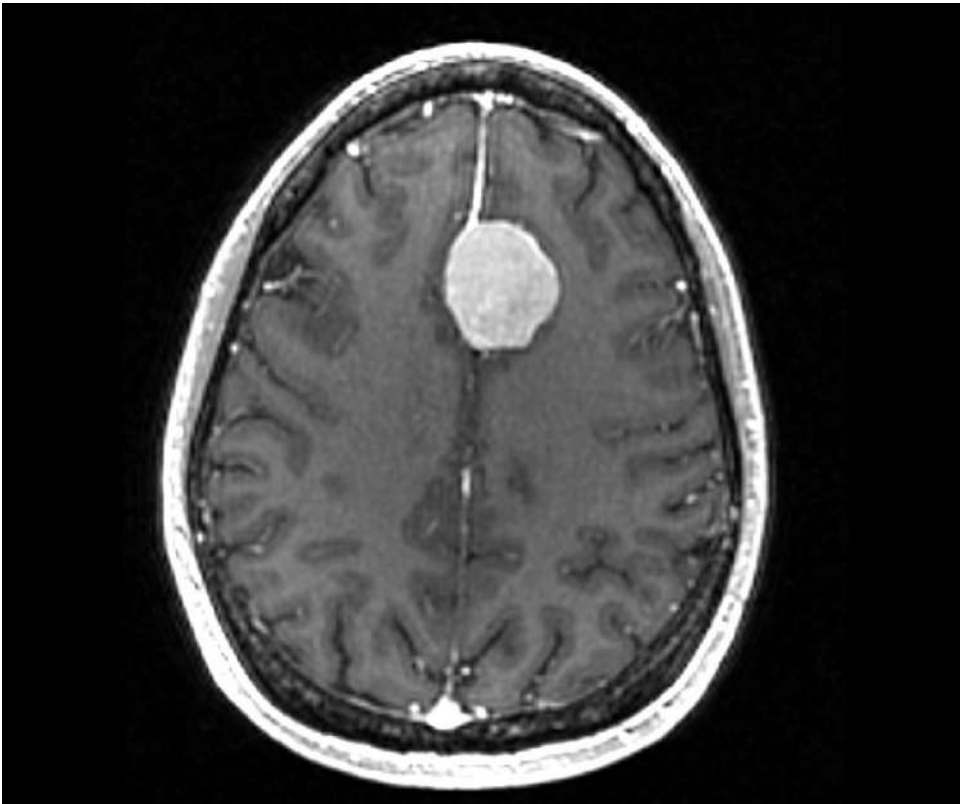
G - G

Explanation Why

[Ependymomas](#) typically arise from the floor of the [4th ventricle](#). Although calcifications and cystic areas may be present in biopsy, histopathologic examination would also show characteristic ependymal rosettes with [perivascular pseudorosettes](#). Moreover, [cholesterol](#) crystals would not be expected in [ependymomas](#).

Question # 14

A 59-year-old man is brought to the emergency department 30 minutes after having a seizure. His wife reports that the patient has been having recurrent headaches and has become increasingly irritable over the past 3 months. Physical examination shows a spastic paresis of the right lower extremity. The Babinski sign is present on the right side. An MRI of the brain is shown. Which of the following is the most likely diagnosis?



	Answer	Image
A	Pituitary adenoma	
B	Schwannoma	
C	Metastatic brain tumor	

	Answer	Image
D	Ependymoma	
E	Oligodendroglioma	
F	Meningioma	
G	Glioblastoma multiforme	

Hint

Brain tumors that present with seizures are most often supratentorial. The image shows a dural tail sign. The narrow rim of cerebrospinal fluid around this patient's tumor indicates that it is most likely extra-axial (external to the brain parenchyma).

Correct Answer

A - Pituitary adenoma

Explanation Why

[Pituitary adenomas](#) typically manifest between 35 and 60 years of age. [Headaches](#) and [seizures](#) may occur, depending on the size and location of the [tumor](#). However, the motor weakness experienced by this patient would be unusual, and [pituitary adenomas](#) with a secretory function would cause endocrine disorders. Additionally, imaging would reveal an intrasellar [hyperintense](#) mass with foci of calcification and/or [necrosis](#).

B - Schwannoma

Explanation Why

[Schwannomas](#) are [benign tumors](#) that arise from [Schwann cells](#) of the [cranial](#) and/or peripheral nerves. [Acoustic neuroma](#), the most common [schwannoma](#), typically manifests with [sensorineural hearing loss](#), [tinnitus](#), and [facial nerve palsy](#). However, [seizures](#) are uncommon. Additionally, [schwannomas](#) appear as heterogeneously [hyperintense](#) extra-axial lesions on [MRI](#) that are most commonly localized to the [cerebellopontine angle](#). The parasagittal location of this patient's [tumor](#) makes [schwannoma](#) an unlikely diagnosis.

C - Metastatic brain tumor

Explanation Why

[Metastatic brain tumors](#) may manifest with [headache](#), neurological deficits, and/or [seizures](#). However, they are typically circumscribed, multifocal, intra-axial [brain tumors](#), not extra-axial tumors, as seen in this patient.

D - Ependymoma

Explanation Why

[Ependymomas](#) are intra-axial tumors that arise from [ependymal cells](#) that line the walls of the cerebral ventricles and central [spinal canal](#). They most commonly manifest with signs of [hydrocephalus](#) due to their location near the [fourth ventricle](#) (in children) or the [spinal canal](#) (in adults). On imaging, they appear as intra-axial heterogeneous masses with areas of [necrosis](#), calcification, cystic changes, and hemorrhage.

E - Oligodendroglioma

Explanation Why

[Oligodendrogliomas](#) are most common among individuals 40–60 years of age and can manifest with [seizures](#), as seen in this patient. However, on CT imaging, they usually appear as [hypodense](#), intra-axial tumors containing focal [hyperdense](#) regions (due to calcification and/or hemorrhage). The [hyperdense](#), extra-axial mass seen in this patient makes [oligodendroglioma](#) an unlikely diagnosis.

F - Meningioma

Explanation Why

[Meningioma](#) is the most common kind of primary [CNS tumor](#) with a [median](#) age of diagnosis of 65 years. Around half of all cases have a [supratentorial](#) location (e.g., near the [falx cerebri](#), convex cerebral surface, or olfactory groove). On imaging, they appear as a round, well-circumscribed, extra-axial mass that is usually [hyperdense](#) on CT and [isointense](#) to [gray matter](#) on plain [MRI](#). On [MRI](#), they appear intense with homogeneous enhancement (as shown in the accompanying image). Most [meningiomas](#) show a marginal dural thickening that tapers peripherally (the "tail sign"). They cause symptoms due to extrinsic compression of brain tissue (i.e., [mass effect](#)). Parasagittal [meningiomas](#) may cause contralateral [spastic paralysis](#) due to compression of the motor cortex.

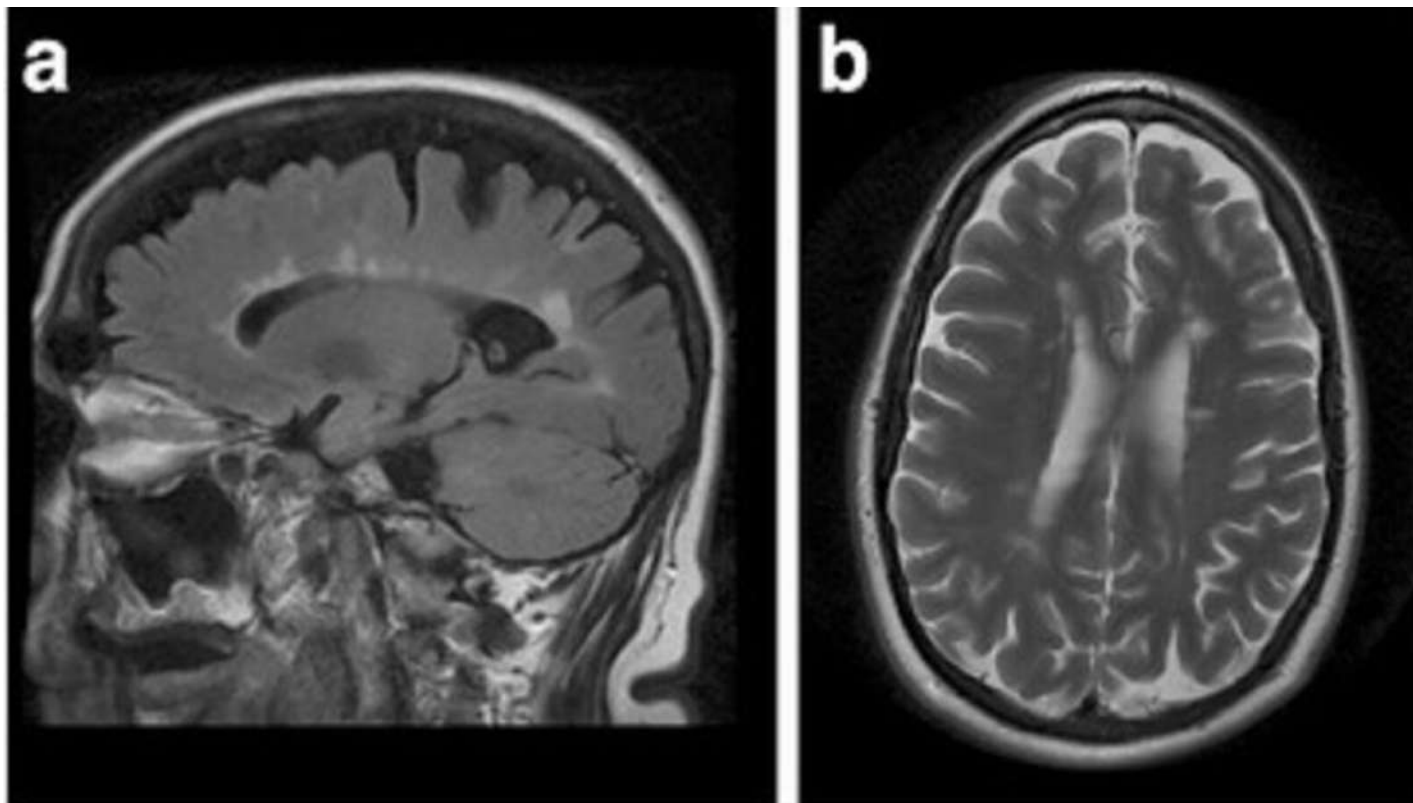
G - Glioblastoma multiforme

Explanation Why

[Glioblastoma multiforme](#) almost always occurs in patients over the age of 40 and may manifest with [seizures](#). However, on [CT scan](#), [glioblastoma multiforme](#) appears as a poorly demarcated, [hypodense](#), intra-axial lesion that tends to infiltrate along condensed [white matter](#) tracts such as the [corticospinal tract](#) and the corpus callosum. The presence of a [hyperdense](#), extra-axial mass in this patient makes the diagnosis of [glioblastoma multiforme](#) unlikely.

Question # 15

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



	Answer	Image
A	Positive antibody response to cardiolipin-cholesterol-lecithin antigen in the serum	
B	Oligodendrocytes that stain positive for polyomavirus proteins on brain biopsy	
C	Presence of immunoglobulin bands on cerebrospinal fluid immunofixation	

	Answer	Image
D	Identification of gram-positive cocci in groups on blood culture	
E	Detection of high-affinity antibodies to dsDNA in the serum	

Hint

This patient presents with lower leg weakness, tingling sensation exacerbated by hot shower (Uhthoff phenomenon), hyperreflexia, positive Babinski sign, and an absent abdominal reflex. All of these, especially in a woman of childbearing age, suggest multiple sclerosis. The MRI image shows periventricular hyperintensities (T2 weighted), suggestive of demyelination.

Correct Answer

A -

Positive antibody response to cardiolipin-cholesterol-lecithin antigen in the serum

Explanation Why

Positive [antibody](#) response to [cardiolipin-cholesterol](#)-lecithin antigen in the serum (positive rapid plasma reagin test) is a nonspecific finding in patients with [syphilis](#). The [RPR](#) test is used to screen for [syphilis](#) as well as evaluate disease activity and monitor treatment response. Although [tertiary syphilis](#) can manifest with various neurological symptoms ([neurosyphilis](#)), it usually progresses slowly and would not be expected to show periventricular hyperintensities on [MRI](#) of the brain, as seen in this patient.

B -

Oligodendrocytes that stain positive for polyomavirus proteins on brain biopsy

Explanation Why

A finding of [oligodendrocytes](#) that stain positive for [polyomavirus proteins](#) on brain biopsy is the hallmark of [progressive multifocal leukoencephalopathy](#) (PML) due to [JC virus infection](#). [PML](#) causes progressive neurological degeneration that can mimic [multiple sclerosis](#). Diffusion-weighted MRI images would typically show asymmetric [hyperintense](#) lesions. However, [PML](#) is most commonly associated with [AIDS](#), which this patient has no evidence of.

C - Presence of immunoglobulin bands on cerebrospinal fluid immunofixation

Explanation Why

The presence of [immunoglobulin](#) bands (particularly [oligoclonal bands](#)) and increased [IgG](#) production in the [CSF](#) are highly sensitive, but nonspecific, findings that support the diagnosis of MS. [Lumbar puncture](#) is indicated for patients with suspected [multiple sclerosis](#) who have

inconclusive clinical and [MRI](#) findings. The production of multiple, nonspecific clones of [IgG](#) within the [CNS](#) is a result of intrathecal [inflammation](#).

D - Identification of gram-positive cocci in groups on blood culture

Explanation Why

Identification of [gram-positive cocci](#) (GPC) in groups on blood culture would not be seen in this patient who has no signs or symptoms of [sepsis](#) (e.g., [fever](#), chills, [hypotension](#)). In addition, her neurological symptoms and imaging cannot be explained by [sepsis](#).

E - Detection of high-affinity antibodies to dsDNA in the serum

Explanation Why

Detection of [high-affinity antibodies to dsDNA](#) in the serum would suggest a diagnosis of [SLE](#), which does occur predominantly in women of childbearing age and can cause neurological symptoms. This patient, however, does not have other classical features of [SLE](#) (e.g., [photosensitivity](#), [discoid rash](#), oral ulcers, arthritis), making another finding more likely.

Question # 16

A 7-year-old girl is brought to the emergency department because of diffuse abdominal pain and multiple episodes of vomiting for 2 hours. She started developing fever, headache, and neck pain 3 days ago. On arrival, she is unresponsive. Her temperature is 40.3°C (104.5°F) and palpable blood pressure is 45 mm Hg. Physical examination shows diffuse purpuric skin lesions. In spite of all appropriate therapy, she dies shortly thereafter. Autopsy shows massive parenchymal hemorrhage of the adrenal glands. Which of the following was the portal of entry for the most likely causal organism?

	Answer	Image
A	Nasopharynx	
B	Genital mucosa	
C	Choroid plexus	
D	Gastrointestinal tract	
E	External ear	
F	Skin	
G	Bronchial epithelium	

Hint

Signs of meningitis (fever, headache, and neck pain), diffuse purpuric skin lesions, and the post-mortem discovery of bilateral adrenal gland hemorrhage (a sign of Waterhouse-Friderichsen syndrome) suggest meningococcal septicemia as the cause of death. The most likely portal of entry for *N. meningitis* is at its point of colonization.

Correct Answer

A - Nasopharynx

Explanation Why

N. meningitidis possesses [virulence factors](#) ([pili](#) and opacity proteins) that specifically adhere to nasopharyngeal [epithelial](#) cells, allowing [colonization](#) of the nasopharynx. [IgA proteases](#) produced by the bacteria protect the established colony against the host's immune defenses. The [pili](#) and opacity proteins can then induce [receptor mediated endocytosis](#), allowing the pathogens to be taken into the host's [cells](#) and eventually invade the bloodstream, thereby causing [meningococcemia](#).

B - Genital mucosa

Explanation Why

While there are bacteria that can colonize the genital mucosa and also can cause [meningitis](#) (e.g., *N. gonorrhea*), the most likely infectious pathogen that causes both [meningitis](#) and [Waterhouse-Friderichsen](#) syndrome is *N. meningitis*. However, *N. meningitis* does not possess the [virulence factors](#) that would allow [colonization](#) of genital mucosa, making this an unlikely portal of entry.

C - Choroid plexus

Explanation Why

The [choroid plexus](#) is a specialized neuroepithelial structure lining the cerebral ventricles, which is responsible for [CSF](#) production. The plexus is highly vascularized and acts a point of entry for blood-borne pathogens into the [CSF](#) (such as *N. meningitis*). However, the [choroid plexus](#) is neither the primary point of [colonization](#) nor portal of entry for *N. meningitis*.

D - Gastrointestinal tract

Explanation Why

While there are bacteria that can colonize the [gastrointestinal tract](#) and also can cause [meningitis](#) (*E. coli*, *S. agalactiae*, *S. typhi*), the most likely infectious pathogen that causes both [meningitis](#) and [Waterhouse-Friderichsen](#) syndrome is *N. meningitis*. However, *N. meningitis* does not possess the [virulence factors](#) that would allow [colonization](#) of any portion of the [gastrointestinal tract](#), making this an unlikely portal of entry.

E - External ear

Explanation Why

The external ear is colonized by various bacteria including different species of [staphylococci](#). Infection of the external ear ([otitis externa](#)) is usually due to *P. aeruginosa*, *S. epidermidis*, or *S. aureus*. While untreated [external otitis](#) may continuously spread to the [skull](#) and the [meninges](#), neither of these pathogens is commonly associated with [Waterhouse-Friderichsen syndrome](#). The external ear is not known to be a [colonization](#) site nor portal of entry for *N. meningitis*.

F - Skin

Explanation Why

While there are bacteria that can colonize the [skin](#) and also can cause [meningitis](#) (*S. aureus*, *S. pyogenes*), the most likely infectious pathogen that causes both [meningitis](#) and [Waterhouse-Friderichsen](#) syndrome is *N. meningitis*. However, *N. meningitis* does not possess the [virulence factors](#) that would allow [colonization](#) of the [skin](#), making this an unlikely portal of entry.

G - Bronchial epithelium

Explanation But

In rare cases, [Waterhouse-Friderichsen syndrome](#) has been described in patients with [sepsis](#) due to [S. pneumoniae](#) or [H. influenzae](#).

Explanation Why

While there are bacteria that can colonize the [bronchial epithelium](#) and also can cause [meningitis](#) (e.g., [S. pneumoniae](#), *H. influenzae*, [P. aeruginosa](#)), the most likely infectious pathogen that causes both [meningitis](#) and [Waterhouse-Friderichsen syndrome](#) is *N. meningitis*. However, *N. meningitis* does not possess the [virulence factors](#) that would allow [colonization](#) of the [bronchi](#), making this an unlikely portal of entry.

Question # 17

A 60-year-old man with a 1-year history of recurrent aspiration pneumonia is brought to the emergency department by his daughter after being found unconscious and gasping for air in his bed. Despite resuscitative efforts, the patient dies. Autopsy of the patient shows degeneration of the corticospinal tracts and anterior horn cells of the upper cervical cord. There is asymmetrical atrophy of the limb muscles, the diaphragm, and the intercostal muscles. Which of the following drugs would have most likely slowed the progression of this patient's condition?

	Answer	Image
A	Levodopa	The diagram illustrates the synthesis, transport, and action of dopamine. In the Substantia nigra, dopamine is synthesized from L-DOPA by the enzyme DDC. Decarboxylase inhibitors (Carbidopa) block this step. L-DOPA is transported into the Presynaptic terminal via a transporter. Inside the terminal, it is converted to dopamine by COMT. COMT inhibitors (Tolcapone (peripheral + central), Entacapone (peripheral)) block this conversion. Dopamine is then packaged into vesicles for release into the Postsynaptic neuron. In the Blood, dopamine is metabolized by MAO-B (inhibited by Selegiline) and COMT. Dopamine acts on Dopamine receptors (D1, D2) and Dopamine agonists (Apomorphine (nonergot), Bromocriptine (ergot)). It also interacts with Anticholinergic drugs (Benztropine) at the M-cholinergic receptor and NMDA antagonists (Amantadine) at the NMDA receptor, which is involved in Ca^{2+} and Na^{+} signaling. A Glia cell is also shown.
B	Nusinersen	
C	Glatiramer acetate	
D	Corticosteroids	
E	Inactivated virus vaccine	
F	Riluzole	

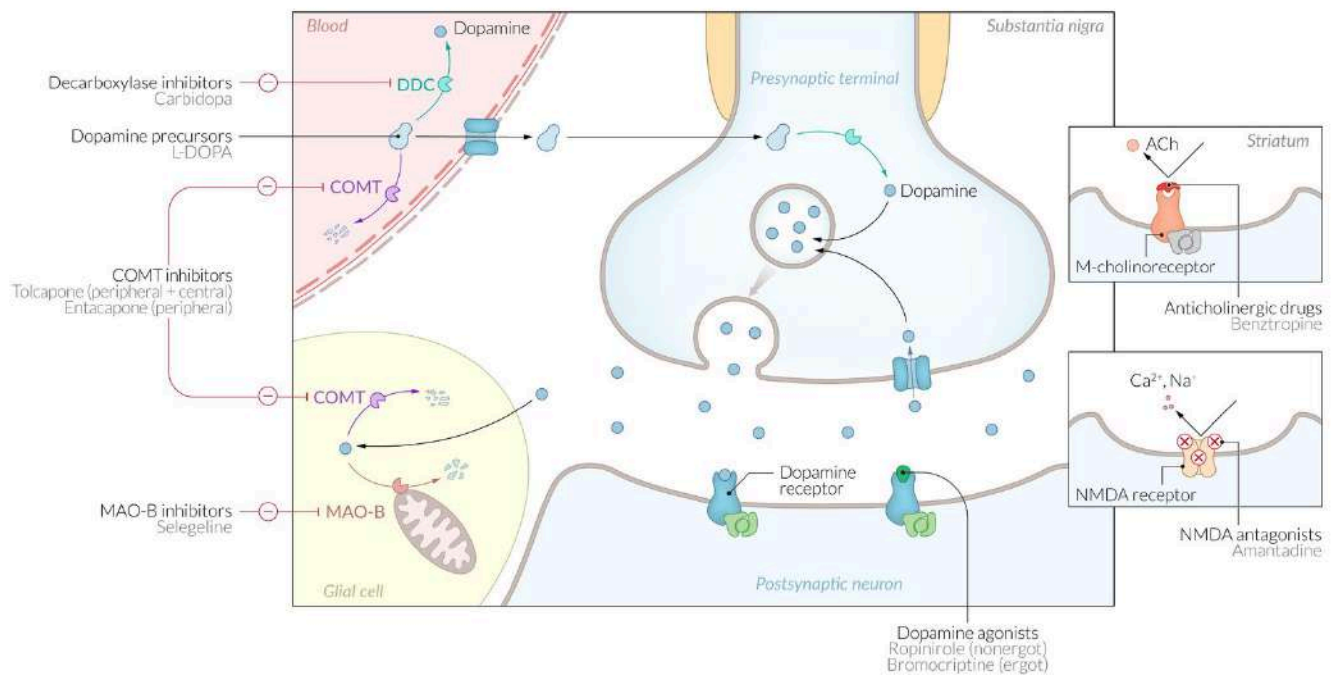
Hint

The autopsy findings of upper (corticospinal tract) and lower motor neuron (anterior horn cells, muscle atrophy) degeneration indicate amyotrophic lateral sclerosis (ALS).

Correct Answer

A - Levodopa

Image



Explanation Why

[Levodopa](#) is used in the treatment of [Parkinson disease](#), which can present with asymmetrical muscle [atrophy](#). However, in [Parkinson disease](#), autopsy would show [neuron](#) degeneration of the [substantia nigra](#), not of the [corticospinal tracts](#) and [anterior horn cells](#) of the upper cervical cord. Moreover, respiratory failure is rare in [Parkinson disease](#).

B - Nusinersen

Explanation Why

[Nusinersen](#) is used to treat [spinal muscular atrophy](#), which presents with motor weakness (also

[intercostal muscle](#) weakness, which can lead to respiratory failure) due to [apoptosis](#) of [lower motor neurons](#) (especially the [anterior horn cells](#) in the [spinal cord](#)), as seen in this patient. However, muscle [atrophy](#) would usually be symmetrical, not asymmetrical, and the onset of symptoms in [spinal muscular atrophy](#) typically occurs during [infancy](#) or childhood, not in late adulthood.

C - Glatiramer acetate

Explanation Why

[Glatiramer acetate](#) is used in the treatment of patients with [multiple sclerosis](#), a [demyelinating](#) disease that can cause [upper motor neuron](#) weakness and subsequent respiratory failure. However, autopsy would show focal [demyelination](#), loss of [axons](#), and [atrophy](#) of [oligodendrocytes](#) (plaques) that more likely involve the [dorsal spinal](#) column, causing sensory impairment (e.g., numbness, [paresthesia](#)), than the [corticospinal tracts](#) and [anterior horn cells](#). Moreover, asymmetrical [atrophy](#) of the limb muscles would not be found in patients with MS.

D - Corticosteroids

Explanation Why

[Corticosteroids](#) are used to treat chronic, inflammatory diseases like [systemic sclerosis](#), which can present with [esophageal hypomotility](#) ([gastroesophageal reflux](#) and [aspiration pneumonia](#)) and respiratory disease (and possible respiratory failure) due to abnormal growth of [connective tissue](#), leading to diffuse thickening and hardening of the [skin](#) and inner organs. Symptoms would also include cutaneous findings (e.g, thickening and hardening of the [skin](#), [sclerodactyly](#), calcinosis, Raynaud syndrome, [telangiectasia](#)) but no motor weakness or muscle [atrophy](#). In addition, autopsy would show [fibroblast proliferation](#) and increased synthesis of normal [collagen](#) (inflammatory synthesis of [extracellular matrix](#)) but no [alpha motoneuron](#) degeneration.

E - Inactivated virus vaccine

Explanation Why

Inactivated virus [vaccines](#) are used in the pre-exposure prophylaxis of certain viral infections, such as

[poliomyelitis](#) or [rabies](#). [Polio](#) causes motor weakness and [atrophy](#) due to [neuron](#) degeneration of the [spinal cord](#) (particularly the [anterior horn cells](#)). Symptoms can be severe and involve the diaphragm, causing respiratory failure, but would also involve [fever](#), neck stiffness, vomiting, and muscle [pain](#). In addition, [polio](#) is extremely rare since it has been eradicated from the U.S. and most other countries. [Rabies](#) usually presents first with [flu-like](#) symptoms and then progresses to encephalopathy, which can lead to respiratory failure if the [respiratory center](#) in the [brainstem](#) is involved. However, other symptoms would include [hydrophobia](#), agitation, confusion, [hallucinations](#), [seizures](#), muscle [rigidity](#), and hypersalivation. Autopsy would show [Negri bodies](#) in the brain, not [alpha motoneuron](#) degeneration.

F - Riluzole

Explanation But

There is no definitive treatment for [ALS](#). The prognosis is generally very poor and most patients die within 3–5 years of symptom onset.

Explanation Why

By blocking sodium channels, [riluzole](#) exerts an antiexcitotoxic effect that causes the inhibition of [glutamate](#) in the [CNS](#). In patients with [ALS](#), this effect slows down the deterioration of motor function and thus increases life expectancy. [ALS](#) usually manifests in patients > 50 years old with a combination of symptoms of upper and [lower motor neuron](#) degeneration, including asymmetric limb weakness, [fasciculations](#), cramps, and muscle stiffness. Symptoms of [bulbar palsy](#), such as [dysarthria](#) as well as [atrophy](#) and [fasciculations](#) of the [tongue](#), are early features of [ALS](#) in 25% of patients. Late symptoms include cognitive impairment as well as life-threatening conditions such as respiratory failure due to paralysis of respiratory muscles and [aspiration pneumonia](#) due to bulbar weakness.

Question # 18

A 64-year-old man comes to the physician because of a 2-week history of intractable hiccups and shortness of breath on exertion. He also has a 1-month history of left shoulder pain. He has smoked one pack of cigarettes daily for 35 years. Physical examination shows decreased breath sounds at the left lung base. An x-ray of the chest shows a 3-cm perihilar mass and elevation of the left hemidiaphragm. This patient's symptoms are most likely caused by injury to a nerve that also innervates which of the following structures?

	Answer	Image
A	Fibrous pericardium	
B	Serratus anterior muscle	
C	Vocal cords	
D	Ciliary muscle	
E	C8-T1 dermatome	
F	Visceral pleura	

Hint

The patient's symptoms (hiccups, dyspnea, shoulder pain, elevated hemidiaphragm) suggest compression of the phrenic nerve, which arises from the C3–C5 nerve roots.

Correct Answer

A - Fibrous pericardium

Explanation But

The [phrenic nerve](#) originates from the C3–C5 [nerve roots](#). Remember: “C-three, four, five keeps the diaphragm alive!”

Explanation Why

The [phrenic nerve](#) could be compressed by a [mediastinal lung tumor](#), a diagnosis of high clinical suspicion in this patient, given his smoking history and the perihilar mass seen on imaging. Each [phrenic nerve](#) provides motor and sensory supply to the ipsilateral hemidiaphragm as well as sensory supply to the fibrous [pericardium](#) and the [mediastinal](#) and diaphragmatic [pleura](#). [Pericarditis pain](#) is often referred to the shoulder due to common innervation via the [phrenic nerve](#).

B - Serratus anterior muscle

Explanation Why

The [serratus anterior](#) muscle is innervated by the [long thoracic nerve](#) that arises from the C5–C7 [nerve roots](#). Damage to this nerve would cause [winging of the scapula](#), not elevation of the hemidiaphragm as seen in this patient.

C - Vocal cords

Explanation Why

The [vocal cords](#) are innervated by the [recurrent laryngeal nerve](#). [Vocal cord](#) palsies can present with hoarseness, [dyspnea](#), weak [cough](#), and recurrent [aspiration](#). An elevated hemidiaphragm, hiccups, and shoulder [pain](#) would not be seen.

D - Ciliary muscle

Explanation Why

The [ciliary muscle](#) is innervated by the [sympathetic trunks](#) through the [stellate ganglion](#). Although an apical tumors [lung tumor](#) can cause compression of the [sympathetic trunks](#) ([Horner syndrome](#)), a [mediastinal lung tumor](#), as seen here, could not.

E - C8-T1 dermatome

Explanation Why

The C8–T1 [dermatome](#) is innervated by the lower part of the [brachial plexus](#). While the [brachial plexus](#) may be disrupted by apical [lung tumors](#), potentially resulting in shoulder [pain](#), damage to this structure would not result in an elevated hemidiaphragm, [cough](#), or hiccups.

F - Visceral pleura

Explanation Why

The [visceral pleura](#) is innervated by the [vagus nerve](#) and [sympathetic](#) nerves, not the [phrenic nerve](#). Furthermore, both the [lung](#) parenchyma and [visceral pleura](#) are insensitive to most painful stimuli, those mediated by stretch fibers being the exception. As a result, visceral pleuritic [pain](#) tends to be vague and poorly localized.

Question # 19

A 10-year-old boy is brought to the physician because of recurring episodes of achy muscle pain in his legs. He has a history of poor school performance despite tutoring and has been held back two grades. He is at the 40th percentile for height and 30th percentile for weight. Examination shows ptosis, a high-arched palate, and muscle weakness in the face and hands; muscle strength of the quadriceps and hamstrings is normal. Sensation is intact. Percussion of the thenar eminence causes the thumb to abduct and then relax slowly. Which of the following is the most likely underlying cause?

	Answer	Image
A	Apoptosis of lower motor neurons	
B	Defect of voltage-gated sodium channels of the sarcolemmal membrane	
C	Deficiency of muscle phosphorylase	
D	Complete impairment of the dystrophin protein	
E	Partial impairment of the dystrophin protein	
F	Humoral immune attack against the endothelium of capillaries	
G	CTG trinucleotide expansion in the DMPK gene	

Hint

Other common features of this autosomal dominant condition include arrhythmias and testicular atrophy.

Correct Answer

A - Apoptosis of lower motor neurons

Explanation Why

[Apoptosis](#) of [lower motor neurons](#) is the underlying cause of [spinal muscular atrophy](#). Certain mild forms of [spinal muscular atrophy](#) (e.g., [Kugelberg-Welander disease](#)) may present during late childhood with limb weakness and muscle [pain](#) (due to cramps). However, unlike in this patient, [proximal](#) muscles of the lower limb are usually more severely affected. Also, the upper [cranial nerve](#) nuclei are typically spared in patients with SMA and [ptosis](#) would therefore not be present. Although certain motor milestones may be delayed, cognitive development is typically normal in children with [spinal muscular atrophy](#).

B - Defect of voltage-gated sodium channels of the sarcolemmal membrane

Explanation Why

A defect of voltage-gated sodium channels of the sarcolemmal membrane is the underlying cause of hyperkalemic periodic paralysis. Patients with hyperkalemic periodic paralysis may present with [myotonia](#). However, the [myotonia](#) in patients with hyperkalemic periodic paralysis characteristically increases with fasting, after exercise, or in cold weather. Moreover, patients typically present with dramatic episodes of weakness that predominantly affect [proximal](#) muscles rather than the insidiously developing [distal](#) muscle weakness seen in this patient.

C - Deficiency of muscle phosphorylase

Explanation Why

Deficiency of muscle phosphorylase is the underlying cause of [McArdle disease](#), which may result in muscle weakness, myalgia, and exercise intolerance. However, [McArdle's disease](#) usually presents during late [adolescence](#) or early adulthood and results in generalized muscle weakness or weakness that affects [proximal](#) muscles more than [distal](#) ones. One characteristic feature of [McArdle disease](#) is the [second wind phenomenon](#), the relief of muscle [pain](#) and weakness after a brief episode of rest,

which is absent in this patient.

D - Complete impairment of the dystrophin protein

Explanation But

Although facial muscle weakness may occur in [DMD](#) (resulting in a typical facies with wide [palpebral fissures](#), loss of [nasolabial folds](#), and a staring lack of expression), it is usually a very late feature.

Explanation Why

Complete impairment of the [dystrophin](#) protein is the underlying cause of [Duchenne muscular dystrophy](#). Patients with [Duchenne muscular dystrophy \(DMD\)](#) would present with muscle weakness and symptoms of intellectual impairment in boys. However, weakness typically appears before the age of 5 years and predominantly affects the [hip](#) and thigh muscles (positive [Gower's sign](#) and/or waddling gait). [Pseudohypertrophy of the calves](#) is another important sign that is present in 60% of children with [DMD](#). [Extraocular muscles](#) and [distal](#) muscles of the upper limb are almost always spared, even in the late stages of the disease (unlike this child who has [ptosis](#) and hand weakness).

E - Partial impairment of the dystrophin protein

Explanation Why

Partial impairment of the [dystrophin](#) protein is the underlying cause of [Becker muscular dystrophy](#), which presents with muscle weakness in boys between the ages of 5–10. However, this weakness typically involves the [proximal](#) muscles of the lower limb (thigh and [hip](#) muscles). [Extraocular muscles](#) and [distal](#) muscles of the upper limb are almost always spared.

F - Humoral immune attack against the endothelium of capillaries

Explanation Why

[Humoral](#) immune attack against the [endothelium](#) of [capillaries](#) is the underlying cause of

[dermatomyositis](#). Juvenile-onset [dermatomyositis](#) would present with lower limb weakness in children between the ages of 5 and 10 years. However, cutaneous manifestations such as a [heliotrope rash](#) over the eyelids and cheeks, or a dry scaly eruption over the knuckles (Gotton sign) would also be present.

G - CTG trinucleotide expansion in the DMPK gene

Explanation But

The diagnosis of [myotonic dystrophy](#) can be established by [electromyography](#) and genetic testing.

Explanation Why

CTG trinucleotide expansion in the [DMPK gene](#) is the underlying cause of [myotonic dystrophy](#). [Abduction](#) of the thumb followed by slow relaxation upon percussion indicates [myotonia](#). [Myotonia](#) in a 10-year-old boy with muscle aches and weakness in the [distal](#) muscles (hand and/or foot), face, and [extraocular muscles](#) is highly suggestive of type 1 [myotonic dystrophy](#). Reduced fetal [temporalis](#) and pterygoid muscle growth result in a high-arched [palate](#). About 50% of patients with [myotonic dystrophy](#) have some degree of cognitive impairment, which likely explains his poor school performance. Other clinical features that are commonly associated with [myotonic dystrophy](#) include frontal balding, which develops typically during [adolescence](#), and bilateral [cataracts](#).

Question # 20

A 41-year-old man is brought to the emergency department 3 hours after falling while mountain biking and hitting his head. Initially, he refused treatment, but an hour ago he began to develop a severe headache, nausea, and left leg weakness. He has no visual changes and is oriented to person, time, and place. His temperature is 37°C (98.6°F), pulse is 68/min, respirations are 17/min and regular, and blood pressure is 130/78 mm Hg. Examination shows a 5-cm bruise on the right side of his skull. The pupils are equal, round, and reactive to light and accommodation. Muscle strength is 0/5 in his left knee and foot. Which of the following is the most likely cause of this patient's presentation?

	Answer	Image
A	Upward brainstem herniation	
B	Uncal herniation	
C	Tonsillar herniation	
D	Subfalcine herniation	
E	Central transtentorial herniation	
F	Extracranial herniation	

Hint

Focal deficits involving the lower limbs indicate involvement of the superior segment of the motor cortex.

Correct Answer

A - Upward brainstem herniation

Explanation Why

Upward brainstem herniation is rare and usually results from a [brainstem](#) mass (e.g., [tumor](#)), rather than [intracranial hemorrhage](#), which is suspected in this patient. Typical findings include [miossis](#), [decerebrate posturing](#), doll's eyes, and altered mental status. This patient has pupils that appear normal, normal mental status, and no abnormal posturing, making upward brainstem herniation unlikely.

B - Uncal herniation

Explanation Why

[Uncal herniation](#) leads to compression of the ipsilateral [oculomotor nerve](#) (causing a fixed and dilated pupil), the ipsilateral [posterior cerebral artery](#) (causing cortical blindness with contralateral [homonymous hemianopia](#)), and the contralateral cerebral peduncle (causing ipsilateral paralysis). While this patient is at risk of [uncal herniation](#) and has [hemiplegia](#), he has a normal pupillary exam and has no visual symptoms.

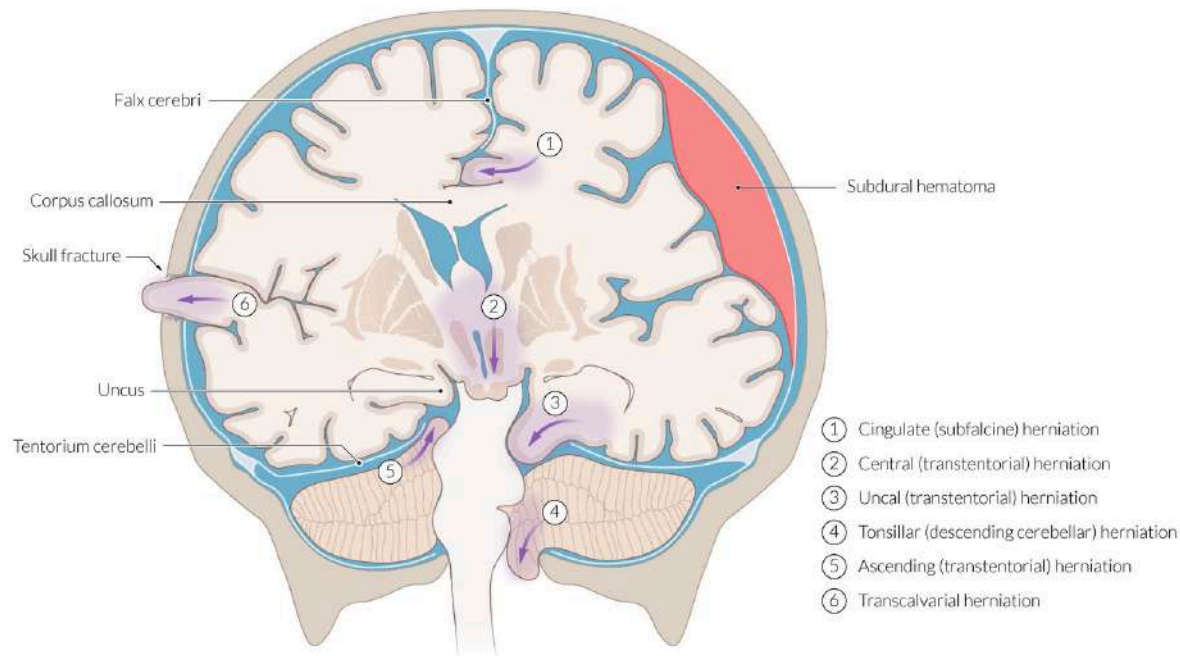
C - Tonsillar herniation

Explanation Why

[Tonsillar herniation](#) can occur due to any [mass effect](#) in the superior part of the [skull](#) (e.g., [intracranial hemorrhage](#)) and presents with symptoms of [cerebellar](#) and medullary compression (e.g., altered mental status, cardiorespiratory depression). While this patient likely has [intracranial hemorrhage](#), he has a normal mental and cardiorespiratory status. Moreover, his [hemiplegia](#) suggests an alternative diagnosis.

D - Subfalcine herniation

Image



Explanation But

The next steps would be confirmation of the diagnosis with emergency noncontrast head CT and neurosurgical consultation for likely craniectomy.

Explanation Why

[Subfalcine herniation](#) is the most common [cerebral herniation syndrome](#) and is usually due to [cingulate gyrus](#) herniation under the [falx cerebri](#), causing compression of the [foramen of Monro](#) (leading to [hydrocephalus](#) and consequent [headache](#)) and branches of the [anterior cerebral artery](#) (causing [infarction](#) in the ACA territory and consequent contralateral lower limb weakness). This patient's herniation is most likely due to traumatic [intracranial hemorrhage](#) (e.g., [subdural hemorrhage](#)), given his recent fall involving [head trauma](#). Without emergent diagnosis and treatment, expanding [intracranial hemorrhage](#) can rapidly progress to [brainstem](#) herniation and death.

E - Central transtentorial herniation

Explanation Why

Central transtentorial herniation is caused by global [cerebral edema](#) and causes herniation of the [diencephalon](#) and [midbrain](#). Typical findings include altered mental status, pupillary abnormalities, and [extensor posturing](#). This patient presents with normal mental status and has a normal ocular exam, making central transtentorial herniation unlikely. Moreover, his unilateral motor symptoms suggest an alternative diagnosis.

F - Extracranial herniation

Explanation Why

Extracranial herniation occurs when brain tissue passes through a defect in the [skull](#) (e.g., [fracture](#)), with neurologic deficits due to compression of the tissue as it passes through the defect. While this patient has a focal neurologic deficit, there is no evidence of skull fracture (e.g., focal tenderness or [skull](#) depression) or brain tissue herniating through the [skull](#) (e.g., bulge near area of [fracture](#)).

Question # 21

A 68-year-old man is brought to the emergency department 30 minutes after collapsing on the street. On arrival, he is obtunded. His pulse is 110/min and blood pressure is 250/120 mm Hg. A CT scan of the head shows an intracerebral hemorrhage involving bilateral thalamic nuclei and the third ventricle. Cortical detection of which of the following types of stimuli is most likely to remain unaffected in this patient?

	Answer	Image
A	Facial fine touch	
B	Gustatory	
C	Visual	
D	Auditory	
E	Olfactory	
F	Proprioception	

Hint

With the exception of one pathway, all sensory information pathways are relayed by thalamic neurons before reaching functionally distinct areas of the cortex. The pathway in question projects to the cortical area that is often the first to be affected in patients with Alzheimer disease.

Correct Answer

A - Facial fine touch

Explanation Why

Facial fine touch is conveyed via the [ventral posteromedial nucleus](#) of the [thalamus](#), the relay center for the [trigeminal nerve](#) pathway. The [ventral posteromedial nucleus](#) receives afferent input from the [trigeminal](#) nucleus and projects to the [primary somatosensory cortex](#). Hence, a bilateral thalamic lesion would affect facial fine touch.

B - Gustatory

Explanation Why

Gustatory information is conveyed via the [ventral posteromedial nucleus](#), the thalamic relay center for [taste](#). The [ventral posterior medial](#) nucleus receives afferent input from the [trigeminal](#) nucleus and projects to the [primary somatosensory cortex](#). Hence, a bilateral thalamic lesion would affect [taste](#).

C - Visual

Explanation Why

Visual information is conveyed via the [lateral geniculate body](#), the thalamic relay center for the optic pathway. The [lateral geniculate body](#) receives afferent input from [optic nerve](#) via the [superior colliculus](#) and projects to the [primary visual cortex](#). Therefore, a bilateral thalamic lesion would affect vision.

D - Auditory

Explanation Why

Auditory information is conveyed via the [medial geniculate nucleus](#), the thalamic relay center for the [auditory pathway](#). The [medial geniculate nucleus](#) receives afferent input from the [inferior colliculus](#) and the [superior olivary nucleus](#) and projects to the [primary auditory cortex](#). Therefore, a bilateral thalamic lesion would affect auditory sensation.

E - Olfactory

Explanation But

Olfactory dysfunction is a common finding on [neurologic examination](#) in patients with [Alzheimer disease](#).

Explanation Why

The [olfactory bulb](#) is the first central relay station for the olfactory pathway, which processes odor information. It receives afferent input from the [olfactory nerve](#) and projects to the [primary olfactory cortex](#). Although the olfactory sensory [neurons](#) do not project directly to the [thalamus](#), the mediodorsal thalamic nucleus receives and sends information to the olfactory cortex. Damage to the mediodorsal thalamic nucleus does not impair cortical olfactory detection (which would result in [anosmia](#)), but it does impair other olfactory functions, such as olfactory identification or discrimination (which may result in dysosmia).

F - Proprioception

Explanation Why

[Proprioception](#) is conveyed by the [ventral posterolateral nucleus](#) of the [thalamus](#), the relay center for the [dorsal columns](#). The [ventral posterolateral nucleus](#) receives afferent input from the [gray matter](#) of the [spinal cord](#) via the [dorsal columns](#) and projects to the [primary somatosensory cortex](#). Therefore, a

bilateral thalamic lesion would affect [proprioception](#).

Question # 22

A previously healthy 57-year-old man is brought to the emergency department because of a 3-day history of fever and headache. He also has nausea and vomited twice in the past 24 hours. His temperature is 39.1°C (102.4°F). He is lethargic but oriented to person, place, and time. Examination shows severe neck rigidity with limited active and passive range of motion. A lumbar puncture is performed; cerebrospinal fluid analysis shows a neutrophilic pleocytosis and a decreased glucose concentration. A Gram stain of the patient's cerebrospinal fluid is most likely to show which of the following?

	Answer	Image
A	Non-encapsulated, gram-negative cocci in pairs	
B	Gram-negative coccobacilli	
C	Encapsulated, gram-negative cocci in pairs	
D	Gram-positive cocci in clusters	
E	Gram-negative bacilli	
F	Encapsulated, gram-positive cocci in pairs	
G	Gram-positive bacilli	

Hint

This patient has bacterial meningitis, a life-threatening infection that causes a characteristic triad of fever, headache, and neck stiffness. *Streptococcus pneumoniae* is the most common cause of bacterial meningitis among adults of all ages.

Correct Answer

A - Non-encapsulated, gram-negative cocci in pairs

Explanation Why

Non-encapsulated, [gram-negative cocci](#) in pairs such as [Moraxella catarrhalis](#) and [Neisseria gonorrhoeae](#) have been identified only in rare reports as causes of bacterial [meningitis](#). They are not the most likely cause of [meningitis](#) in this previously healthy 57-year-old patient.

B - Gram-negative coccobacilli

Explanation Why

[Haemophilus influenzae](#) is the most common [gram-negative coccobacillus](#) that can cause bacterial [meningitis](#). However, the [incidence](#) of [H. influenzae meningitis](#) has significantly decreased since the introduction of the Hib vaccine. [H. influenzae](#) causes < 10% of all cases of bacterial [meningitis](#) among adults and is not the most likely cause of [meningitis](#) in this previously healthy 57-year-old patient.

C - Encapsulated, gram-negative cocci in pairs

Explanation Why

[Neisseria meningitidis](#) is an encapsulated, [gram-negative coccus](#) that arranges in pairs and the most common cause of bacterial [meningitis](#) among children and [adolescents](#) between 10–18 years of age. However, it is only the second most common cause of bacterial [meningitis](#) among adults.

D - Gram-positive cocci in clusters

Explanation Why

[*Staphylococcus aureus*](#) is the most common [gram-positive coccus](#) that arranges in clusters that can cause bacterial [meningitis](#). Cases of [S. aureus meningitis](#) are rare but can develop in the setting of recent otitis, [mastoiditis](#), [sinusitis](#), [cellulitis](#), [infective endocarditis](#), and/or neurosurgical procedures. These organisms are not the most likely cause of [meningitis](#) in this previously healthy 57-year-old patient.

E - Gram-negative bacilli

Explanation Why

[Gram-negative bacilli](#) such as [*Pseudomonas aeruginosa*](#) and [*Escherichia coli*](#) are rare causes of bacterial [meningitis](#). Cases of bacterial [meningitis](#) caused by [gram-negative bacilli](#) are more common among [infants](#), elderly patients, patients who have recently undergone neurosurgical procedures, and patients who are [immunocompromised](#). [Gram-negative bacilli](#) are not the most likely cause of [meningitis](#) in this previously healthy 57-year-old patient.

F - Encapsulated, gram-positive cocci in pairs

Explanation Why

[*Streptococcus pneumoniae*](#) is an encapsulated, [gram-positive coccus](#) that arranges in pairs and the most common cause of bacterial [meningitis](#) among adults of all ages in the US (> 50% of all reported cases). Initial therapy for [S. pneumoniae meningitis](#) includes intravenous [vancomycin](#) plus a [third-generation cephalosporin](#) (e.g., [ceftriaxone](#), [cefotaxime](#)).

G - Gram-positive bacilli

Explanation Why

[*Listeria monocytogenes*](#) is the most common [gram-positive bacillus](#) that can cause bacterial [meningitis](#). Cases of [L. monocytogenes meningitis](#) are most common among [infants](#), elderly patients, and patients who are [immunocompromised](#). [Gram-positive bacilli](#) are not the most likely cause of [meningitis](#) in this previously healthy 57-year-old patient.

Question # 23

A 10-year-old girl is brought to the emergency department by her mother 30 minutes after having had a seizure. When her mother woke her up that morning, the girl's entire body stiffened and she started shaking vigorously for several minutes. Her mother also reports that over the past few months, her daughter has had multiple episodes of being unresponsive for less than a minute, during which her eyelids were fluttering. The girl did not recall these episodes afterwards. Upon arrival, she appears drowsy. Neurologic examination shows no abnormalities. Which of the following is the most appropriate pharmacotherapy to prevent recurrence of this patient's symptoms?

	Answer	Image
A	Phenytoin	
B	Lorazepam	
C	Ethosuximide	
D	Topiramate	
E	Valproate	

Hint

Multiple episodes of unresponsiveness lasting less than a minute with eyelid fluttering and concomitant early morning tonic-clonic seizures is suggestive of juvenile absence epilepsy. The first-line medication for long-term management is an antiepileptic drug that can also be used as a mood stabilizer in bipolar disorder.

Correct Answer

A - Phenytoin

Explanation Why

[Phenytoin](#) is an [antiepileptic drug](#) that inhibits [voltage-gated sodium channels](#) in the brain, thereby reducing the excitability of [neurons](#). It is used primarily for [tonic-clonic](#) and [focal seizure](#) prophylaxis and in [status epilepticus](#) as an initial therapy in combination with [benzodiazepines](#). However, it is not very effective against [absence seizures](#), which this patient also has.

B - Lorazepam

Explanation Why

[Lorazepam](#) is an intermediate-acting [benzodiazepine](#) that is used in acute [seizure](#) treatment to abort [status epilepticus](#). However, it is not effective in the management of [seizure disorders](#). In addition, long-term [benzodiazepine](#) use can lead to tolerance and dependency, which makes it inappropriate for [seizure disorder](#) management.

C - Ethosuximide

Explanation Why

[Ethosuximide](#) is an [antiepileptic](#) medication that reduces excitability in the brain by blocking thalamic [T-type calcium channels](#). It is first-line treatment in [childhood absence seizures](#), which usually presents with multiple episodes of unresponsiveness lasting less than a minute, as seen in this patient. However, [childhood absence seizures](#) usually have an earlier onset, at around age 6. Furthermore, this patient had an early morning [tonic-clonic seizure](#), against which [ethosuximide](#) would be ineffective.

D - Topiramate

Explanation Why

[Topiramate](#) is an [anticonvulsant](#) that blocks sodium channels and increases [GABA](#) action, which reduces excitability in the brain. It is used in the treatment of partial (focal) and [tonic-clonic seizures](#). However, it is ineffective against [absence seizures](#), which this patient also has.

E - Valproate

Explanation But

Other indications for [valproate](#) include [bipolar disorder](#) and prevention of [migraine](#) and [cluster headaches](#).

Explanation Why

[Valproate](#) is an [anticonvulsant](#) that inhibits GABA transaminase and sodium channels. It is first-line treatment in [juvenile absence epilepsy](#). [Absence seizures](#) can occur on their own, in which case they can be successfully treated with [ethosuximide](#). However, 75% of patients with [juvenile absence epilepsy](#) have concomitant [tonic-clonic seizures](#) for which [ethosuximide](#) is ineffective.

Question # 24

A 72-year-old man with a 4-year history of Parkinson disease comes to the physician for evaluation of his medication. Since his last visit one year ago, he has had increased tremor and bradykinesia up to an hour before his next scheduled dose and sometimes feels like he does not respond to some doses at all. One week ago, he was entirely unable to move for about a minute when he wanted to exit an elevator. The physician prescribes a drug that increases the bioavailability of levodopa by preferentially preventing its peripheral methylation. This patient was most likely prescribed which of the following drugs by the physician?

	Answer	Image
A	Carbidopa	
B	Entacapone	The diagram illustrates the synthesis, release, and metabolism of dopamine in the brain. Dopamine is synthesized from L-DOPA by the enzyme DDC (Dopa Decarboxylase) in the substantia nigra. L-DOPA is transported from the blood into the neuron. Decarboxylase inhibitors (Carbidopa) block DDC. Dopamine is then transported into the presynaptic terminal and released into the synaptic cleft. In the cleft, dopamine can be taken back up into the neuron or metabolized by COMT (Catechol-O-methyltransferase) or MAO-B (Monoamine oxidase B). COMT inhibitors (Tolcapone, Entacapone) block COMT. MAO-B inhibitors (Selegiline) block MAO-B. Dopamine binds to dopamine receptors on the postsynaptic neuron, which can be blocked by dopamine antagonists (Risperidone, Haloperidol). Dopamine agonists (Ropinirole, Pramipexole) bind to these receptors. Dopamine is also metabolized by AChE (Acetylcholinesterase) in the striatum, which can be blocked by anticholinergic drugs (Benztropine). Dopamine also interacts with the NMDA receptor, which can be blocked by NMDA antagonists (Amantadine).
C	Ropinirole	
D	Trihexyphenidyl	
E	Amantadine	
F	Rasagiline	

Hint

The patient is experiencing typical symptoms of long-term treatment with levodopa including a wearing-off effect and increasing motor fluctuations (known as on-off phenomenon and freezing). The drug prescribed by the physician inhibits the enzyme catechol-O-methyltransferase, which may reduce these symptoms by keeping the bioavailability of levodopa more stable.

Correct Answer

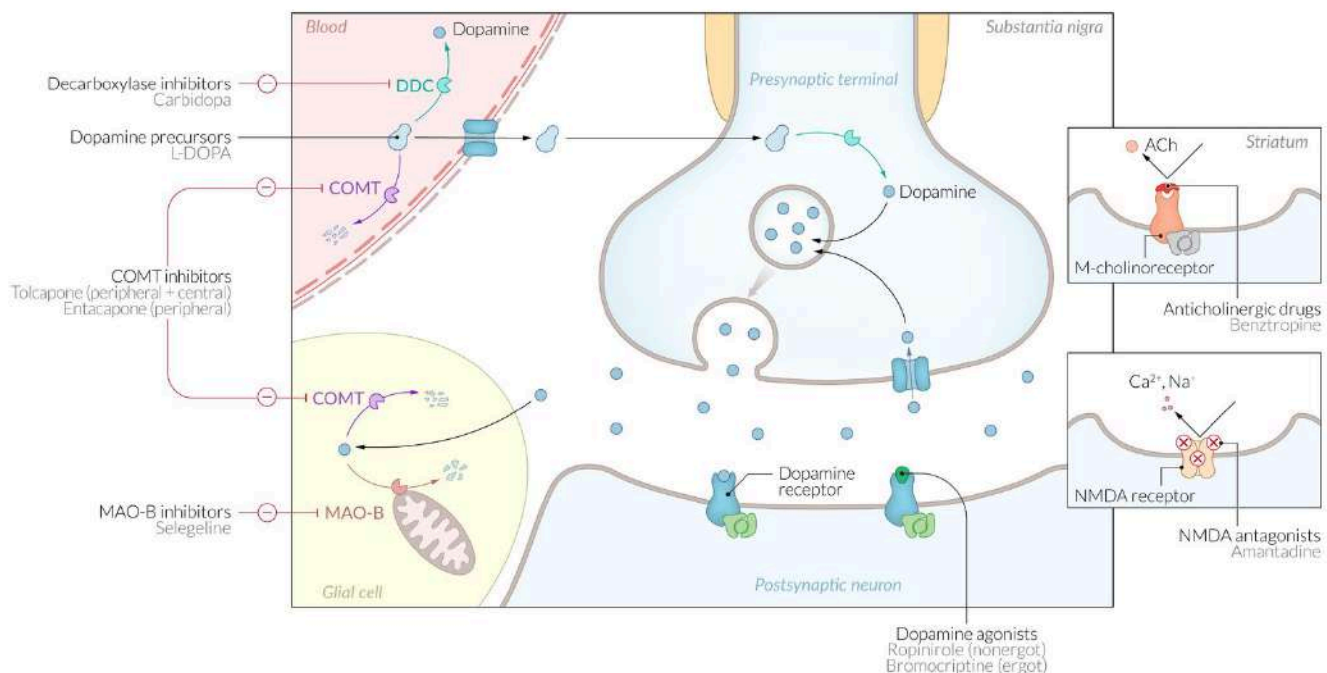
A - Carbidopa

Explanation Why

[Carbidopa](#) is a [decarboxylase inhibitor](#) that is often given as a combined [levodopa/carbidopa](#) formulation. Although [carbidopa](#) increases the [bioavailability](#) of [levodopa](#) like the drug prescribed by the physician, it acts by decreasing the peripheral conversion of [levodopa](#) to [dopamine](#). Additionally, this reduces the peripheral side effects of [levodopa](#) (e.g., [orthostatic hypotension](#), nausea, and vomiting). [Carbidopa](#) cannot cross the [blood-brain barrier](#), so it does not negatively affect [dopamine](#) production in the brain. Since [levodopa/carbidopa](#) is typically the first-line treatment of [Parkinson disease](#) in patients > 65 years of age, this patient is likely already receiving this medication.

B - Entacapone

Image



Explanation But

Motor fluctuations increase during long-term therapy with [levodopa](#) because the [neurons](#) gradually lose their capacity to store and release [dopamine](#). The severity of symptoms is directly related to the drug dose.

Explanation Why

[Entacapone](#) is a peripherally acting [COMT inhibitor](#) that reduces the [methylation](#) of [levodopa](#) and [dopamine](#), thus allowing a more stable and long-lasting plasma concentration of the drug. This results in fewer periods of [end-of-dose akinesia](#) and less variability of symptoms during the day. [Tolcapone](#) is a centrally acting [COMT inhibitor](#) that is used for refractory [Parkinson disease](#).

C - Ropinirole

Explanation Why

[Ropinirole](#) is a [non-ergot dopamine agonist](#) that acts directly at the striatal [dopamine](#) receptors. [Non-ergot dopamine agonists](#) (e.g., [pramipexole](#)) do not increase the [bioavailability](#) of [levodopa](#) but are used as first-line treatment of Parkinson in patients under the age of 65 and for treatment of primary [restless legs syndrome](#).

D - Trihexyphenidyl

Explanation Why

[Trihexyphenidyl](#), as well as [benztropine](#), are centrally acting [anticholinergic agents](#) that inhibit excitatory cholinergic [neurons](#), thus decreasing the concentration of [ACh](#). Lowering [ACh](#) levels proportionately to [dopamine](#) levels improves Parkinson symptoms by reestablishing the balance of [ACh](#) sensitivity in the [basal ganglia](#). [Trihexyphenidyl](#) does not increase the [bioavailability](#) of [levodopa](#) but is used as monotherapy in patients under the age of 65 with [tremor](#) as the main complaint.

E - Amantadine

Explanation Why

[Amantadine](#) is an [NMDA antagonist](#) whose mechanism of action is not yet fully understood. However, it is known to increase the [bioavailability](#) of [dopamine](#), not [levodopa](#), by increasing its release and decreasing its reuptake in central presynaptic terminals. Moreover, it may exert central [anticholinergic effects](#). [Amantadine](#) is the drug of choice during [akinetic crises](#) and can be used for reduction of [levodopa](#)-induced [dyskinesia](#) as in this patient.

F - Rasagiline

Explanation Why

[Rasagiline](#), as well as [selegiline](#), are selective [MAO-B inhibitors](#) that decrease [dopamine](#) degradation in the brain, thus prolonging the effect of [dopamine](#). [Rasagiline](#) also appears to have a neuroprotective effect by preventing the [free radical damage](#) caused by oxidative metabolism of [dopamine](#). [MAO-B inhibitors](#) do not increase the [bioavailability](#) of [levodopa](#) but can be used as monotherapy in patients with Parkinson under the age of 65 with no significant comorbidities.

Question # 25

A 17-year-old boy is brought to the emergency department after being stabbed with a knife during an altercation. Physical examination shows a 4-cm stab wound on the right lateral border of the T1 spinous process. An MRI of the spinal cord shows damage to the area of the right lateral corticospinal tract at the level of T1. Further evaluation will most likely show which of the following findings?

	Answer	Image
A	Absence of left-sided proprioception below T1	
B	Absence of right-sided temperature sensation below T1	
C	Presence of left-sided Babinski sign	
D	Absence of left-sided fine touch sensation below T1	
E	Absence of right-sided motor function below T1	Posterior tract Anterolateral tract Anterior horn Pyramidal tract ■ Damaged region ■ Dissociated sensory loss (of temperature and pain): from damage to the contralateral anterolateral tract ■ Spastic paresis: from damage to the pyramidal tract ■ Flaccid paresis: from damage to the anterior horn and segment level ■ Complete loss of sensation: from damage to protopathic and epicritic sensibility at segment level ■ Loss of proprioception and epicritic sensibility: from damage to the ipsilateral posterior tract

Hint

This patient's mechanism of injury and imaging findings are consistent with a partial Brown-Sequard syndrome. The lateral corticospinal tract originates at the precentral gyrus and decussates at the level of the medulla.

Correct Answer

A - Absence of left-sided proprioception below T1

Explanation But

An absence of ipsilateral [proprioception](#) below the lesion would be expected if the right [dorsal column](#) were involved in this patient's injury.

Explanation Why

An absence of left-sided (contralateral to the injury) [proprioception](#) below T1 would be consistent with injury to the left [dorsal column](#), which is unlikely given this patient's imaging findings of [lateral corticospinal tract](#) injury on the right side. [Proprioception](#) is transmitted via ascending sensory [neurons](#) in the [dorsal column](#) ipsilaterally, until decussation at the level of the medulla.

B - Absence of right-sided temperature sensation below T1

Explanation Why

An absence of right-sided temperature sensation below T1 would be most consistent with a left [lateral spinothalamic tract](#) injury at the level of T1. Sensory fibers from the [lateral spinothalamic tract](#) transmit input about [pain](#) and temperature and ascend two segments before decussating in the [spinal cord](#) and ascending contralaterally until they reach the sensory cortex. However, this patient's [MRI](#) shows damage to the right [lateral corticospinal tract](#) at T1, making this finding unlikely.

C - Presence of left-sided Babinski sign

Explanation Why

The [Babinski sign](#) usually takes 1–2 weeks to appear after an [upper motor neuron lesion](#) occurs. This finding would be unlikely immediately following an acute injury. Furthermore, a [Babinski sign](#) would be expected ipsilateral to the injury (in this case, on the right side), as the [upper motor neuron](#)

for the [lateral corticospinal tract](#) has been disrupted here and decussation of this tract occurs at a higher level.

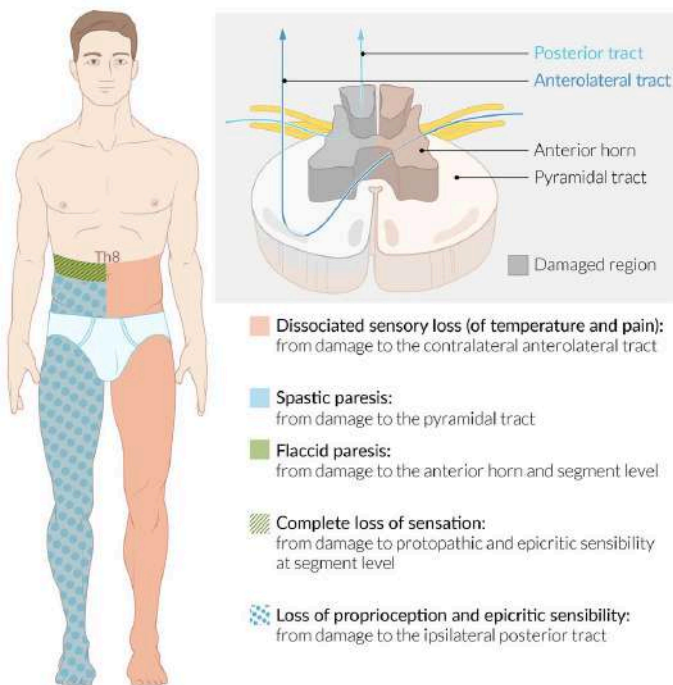
D - Absence of left-sided fine touch sensation below T1

Explanation Why

An absence of left-sided fine touch below T1 would be expected with an injury to the left [dorsal column](#), which is unlikely given this patient's imaging findings of [lateral corticospinal tract](#) injury on the right side. Fine touch is transmitted via ascending sensory [neurons](#) in the [dorsal column](#) ipsilaterally, until decussation at the level of the medulla.

E - Absence of right-sided motor function below T1

Image



Explanation Why

A right [lateral corticospinal tract](#) injury (e.g., partial [Brown-Sequard syndrome](#)) would result in the absence of ipsilateral motor function below the level of the injury. The [lateral corticospinal tract](#) decussates at the level of the medulla. An injury [distal](#) to the decussation (e.g., at the level of T1) would, therefore, affect ipsilateral motor function below the level of the injury. In a full [Brown-Sequard syndrome](#) (e.g., hemisection of the [spinal cord](#)), there would also be ipsilateral loss of vibration and [proprioception](#) below T1 ([dorsal column](#)), ipsilateral [Babinski sign](#) ([lateral corticospinal tract](#)), and contralateral loss of [pain](#) and temperature sensation beginning two levels below the lesion ([lateral spinothalamic tract](#)).

Question # 26

A 22-year-old woman is brought to the emergency department because of diplopia, slurred speech, progressive upper extremity weakness, and difficulty swallowing for the past several hours. She had mild abdominal pain that resolved spontaneously after returning from her father's farm yesterday. Her temperature is 37°C (98.6°F), respirations are 11/min and labored, and blood pressure is 110/70 mm Hg. Examination shows bilateral nystagmus and ptosis. The pupils are dilated and not reactive to light or accommodation. Muscle strength of the facial muscles and bilateral upper extremities is decreased. Which of the following is the strongest risk factor for this patient's condition?

	Answer	Image
A	Oral ingestion of preformed toxin	The diagram illustrates the mechanism of botulinum toxin. Panel 1 shows normal synaptic transmission: an action potential (AP) arrives at the presynaptic terminal, causing Ca²⁺ influx. This triggers the fusion of a vesicle containing ACh with the presynaptic membrane, releasing ACh into the synaptic cleft. ACh then binds to receptors on the postsynaptic membrane, leading to an endplate potential (EPSP). Panel 2 shows the effect of botulinum toxin: the toxin binds to and cleaves the SNARE complex proteins, preventing vesicle fusion and ACh release. This results in no fusion and no ACh release, leading to flaccid paralysis. The postsynaptic membrane shows no response (RP) to the released ACh.
B	Skin bite by Ixodes tick	
C	Exposure to bacterial spores	
D	Lack of immunization with polysaccharide fragments	
E	Gastroenteritis caused by comma-shaped rod	

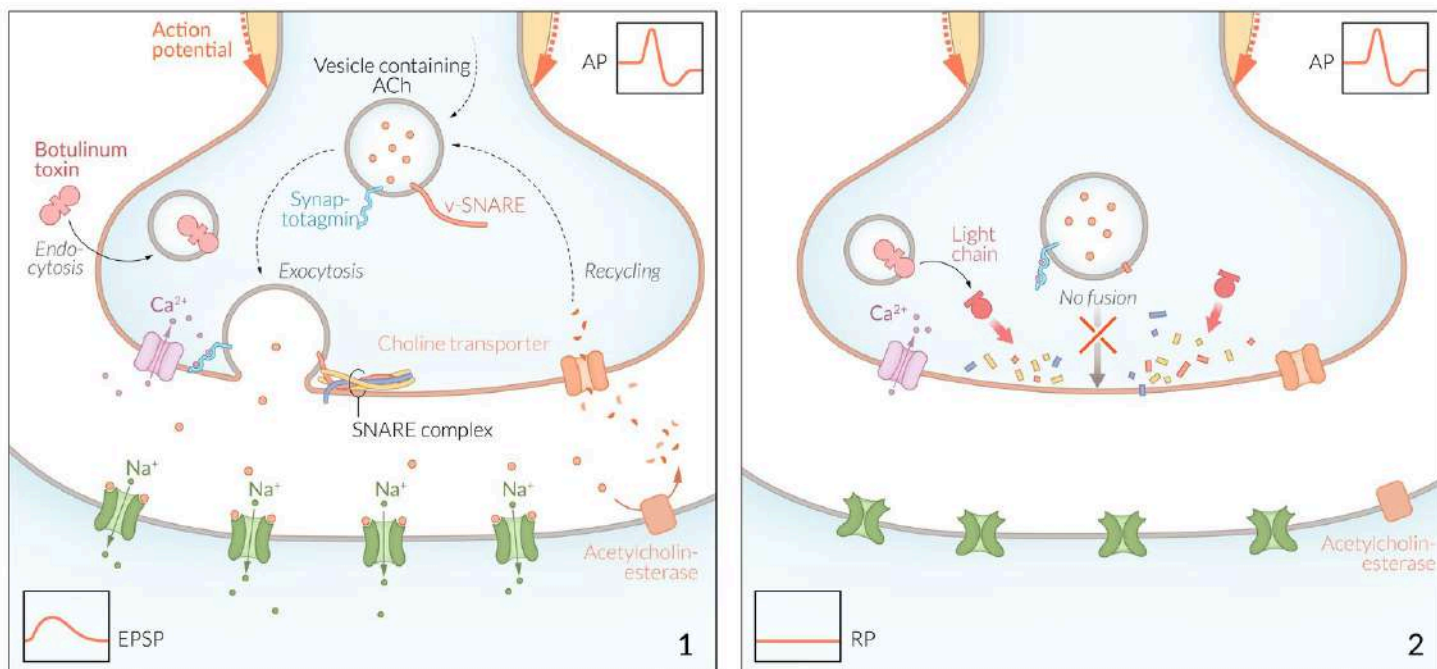
Hint

This patient presents with sudden onset of bilateral cranial neuropathies (dilated pupils, ptosis, facial weakness, speech and swallowing difficulties) and descending flaccid paralysis with possible involvement of the diaphragm (labored breathing). Her normal level of consciousness and lack of fever or sensory deficits make botulism the most likely diagnosis.

Correct Answer

A - Oral ingestion of preformed toxin

Image



Explanation Why

Oral ingestion of a preformed toxin of *Clostridium botulinum* (botulinum toxin), most commonly found in canned food (e.g., home-canned vegetables), can cause [foodborne botulism](#). The incubation period usually ranges from 12 to 36 hours and, as in this patient, gastrointestinal complaints such as abdominal [pain](#), nausea, and vomiting may precede neurological symptoms. Life-threatening respiratory complications can occur if the [phrenic nerve](#) is affected and patients may require [mechanical ventilation](#). Treatment consists of close monitoring, promoting bowel emptying, and administration of [botulism](#) antitoxin.

B - Skin bite by Ixodes tick

Explanation Why

A [skin](#) bite by *Ixodes* tick is the cause of [Lyme disease](#). Early neurological symptoms such as [cranial nerve palsies](#) (most commonly [Bell palsy](#)) may be the first disease manifestation. However, [Lyme disease](#) is not associated with acute descending [flaccid paralysis](#). Even though this patient might have been infected at her father's farm, symptoms of disseminated [Lyme disease](#) would not be expected at this stage of disease. Moreover, other characteristic features of [Lyme disease](#), such as [fever](#), rash, and [joint pain](#), are not present.

C - Exposure to bacterial spores

Explanation Why

Exposure of wounds to [Clostridium botulinum](#) spores can cause [wound botulism](#) due to in-vivo production of [botulinum toxin](#). [Wound botulism](#) presents with [cranial](#) neuropathies and descending paralysis as seen in this patient. However, it is not associated with GI symptoms but commonly involves [fever](#) and [leukocytosis](#). Although this patient might have been exposed to [C. botulinum](#) spores at her father's farm, an infected wound would be expected to be seen. Moreover, [wound botulism](#) manifests after a longer incubation period (~10 days).

D - Lack of immunization with polysaccharide fragments

Explanation Why

Lack of [immunization](#) with [polysaccharide](#) fragments would not increase the risk of [botulism](#), as there is no effective [vaccine](#) against [Clostridium botulinum](#). [Polysaccharide conjugate vaccines](#) are helpful for prevention of infection with bacteria such as [Haemophilus influenzae B](#) and [Streptococcus pneumoniae](#).

E - Gastroenteritis caused by comma-shaped rod

Explanation Why

Gastroenteritis caused by [*Campylobacter jejuni*](#), a comma-shaped rod, is the most common disease associated with [Guillain-Barré syndrome](#) (GBS). GBS presents with bilateral [cranial](#) neuropathies and [flaccid paralysis](#) that may involve the respiratory muscles, as seen in this patient. However, paralysis usually spreads from the lower to the upper limbs in a “stocking-glove” distribution, unlike this patient's descending paralysis. Moreover, initial symptoms of GBS typically include peripheral [paresthesias](#), whereas this patient has no sensory deficits.

Question # 27

A 28-year-old woman is admitted to the hospital for treatment of a displaced fracture of the femoral neck following a high-speed motor vehicle collision. She is given pentazocine for pain relief. This drug binds to heptahelical transmembrane receptors. Which of the following is the most likely effect of this drug?

	Answer	Image
A	Release of presynaptic acetylcholine	
B	Release of presynaptic substance P	
C	Opening of presynaptic Ca^{2+} channels	
D	Release of presynaptic norepinephrine	
E	Opening of postsynaptic Na^{+} channels	
F	Opening of postsynaptic K^{+} channels	

Hint

Pentazocine is an opioid that binds to G-protein coupled receptors (i.e., heptahelical transmembrane receptors). Opioids produce their analgesic action by causing hyperpolarization of neurons.

Correct Answer

A - Release of presynaptic acetylcholine

Explanation Why

Binding of [pentazocine](#) to presynaptic [opioid](#) receptors inhibits the stimulatory signal that induces the release of presynaptic [acetylcholine](#). Consequently, release of this [neurotransmitter](#) is inhibited as an effect of [opioid](#) administration.

B - Release of presynaptic substance P

Explanation Why

Binding of [pentazocine](#) to presynaptic [opioid](#) receptors inhibits the stimulatory signal that induces the release of presynaptic substance P. Consequently, release of this [neurotransmitter](#) is inhibited as an effect of [opioid](#) administration.

C - Opening of presynaptic Ca^{2+} channels

Explanation Why

Opening of presynaptic [Ca²⁺](#) channels increases calcium influx, which enhances release of [neurotransmitters](#) and thus synaptic transmission. Administration of [opioids](#), however, decreases synaptic transmission.

D - Release of presynaptic norepinephrine

Explanation Why

Binding of [pentazocine](#) to presynaptic [opioid](#) receptors inhibits the stimulatory signal that induces the release of presynaptic [norepinephrine](#). Consequently, release of this [neurotransmitter](#) is inhibited as an effect of [opioid](#) administration.

E - Opening of postsynaptic Na⁺ channels

Explanation Why

Opening of postsynaptic Na⁺ channels increases inward movement of sodium, which leads to [depolarization](#) of the [neuron](#) and an increase in synaptic transmission. Administration of [opioids](#), however, decreases synaptic transmission.

F - Opening of postsynaptic K⁺ channels

Explanation Why

[Pentazocine](#) is a synthetic [opioid](#) that acts as a weak antagonist at [μ receptors](#) and as an [agonist](#) at [κ receptors](#). [Agonism](#) at the [opioid](#) receptors has two effects: first, opening of postsynaptic K⁺ channels increases outward movement of potassium, which leads to [hyperpolarization](#) of the [neuron](#) and a subsequent decrease in synaptic transmission; and second, concurrent closing of [Ca²⁺](#) channels inhibits presynaptic release of [neurotransmitters](#) ([acetylcholine](#), [noradrenaline](#), [serotonin](#), [glutamate](#), [nitric oxide](#), and substance P).

Question # 28

A 22-year-old man is brought to the physician by his mother because of concerns about his recent behavior. Three months ago, the patient first reported hearing loud voices coming from the ceiling of his room. During this time, he has also become increasingly worried that visitors to the house were placing secret surveillance cameras. Mental status examination shows tangential speech with paranoid thoughts. Treatment for this patient's condition predominantly targets which of the following dopaminergic pathways?

	Answer	Image
A	Mesolimbic pathway	
B	Thalamocortical pathway	
C	Mesocortical pathway	
D	Corticostriatal pathway	
E	Nigrostriatal pathway	
F	Tuberoinfundibular pathway	

Hint

This patient shows several of the classic positive symptoms of schizophrenia (auditory hallucinations, disorganized speech, delusions). The first-line treatment for schizophrenia inhibits dopaminergic activity primarily within a brain pathway that is also important in mediating reward and addiction.

Correct Answer

A - Mesolimbic pathway

Explanation Why

The [positive symptoms of schizophrenia](#) are thought to occur at least in part due to increased [dopaminergic](#) activity within the [mesolimbic pathway](#). [Antipsychotics](#) are antagonists at the [dopaminergic D2 receptors](#) within this pathway and are the first-line treatment for this disorder. However, they show little benefit for the negative symptoms of schizophrenia, which are very difficult to treat.

B - Thalamocortical pathway

Explanation Why

The thalamocortical pathway is a glutamatergic pathway, not a [dopaminergic](#) pathway. It connects the [thalamus](#) to the cortex and is not significantly affected by [antipsychotics](#).

C - Mesocortical pathway

Explanation Why

Reduced [dopaminergic](#) activity in the [mesocortical pathway](#) (also known as the prefrontal cortical pathway) is thought to be involved in causing the negative symptoms of schizophrenia, such as reduced emotional expression and [apathy](#), which this patient does not exhibit.

D - Corticostriatal pathway

Explanation Why

The corticostriatal pathway is a glutamatergic pathway, not a [dopaminergic](#) pathway. It connects the cortex to the [basal ganglia](#) and is involved in the control of movement. It is not significantly affected by [antipsychotics](#).

E - Nigrostriatal pathway

Explanation Why

The nigrostriatal pathway arises from the substantia nigra, and hypofunction of [dopaminergic](#) activity in this pathway is responsible for the motor symptoms of [Parkinson disease](#). [Extrapyramidal symptoms](#), including [parkinsonism](#), are a common side effect of [antipsychotic](#) drugs as these inhibit [dopaminergic](#) activity in this pathway, but treatment for [positive symptoms of schizophrenia](#) does not target the nigrostriatal pathway.

F - Tuberoinfundibular pathway

Explanation Why

Normal [dopaminergic](#) activity in the [tuberoinfundibular pathway](#) is responsible for the control of [prolactin](#) release from the [anterior pituitary](#). [Hyperprolactinemia](#) is a common side effect of [antipsychotic](#) drugs due to inhibition of [dopaminergic](#) activity in this pathway, but treatment for [positive symptoms of schizophrenia](#) does not target the [tuberoinfundibular pathway](#).

Question # 29

A 43-year-old man is brought to the physician for a follow-up examination. He has a history of epilepsy that has been treated with a stable dose of phenytoin for 15 years. He was recently seen by another physician who added a drug to his medications, but he cannot recall the name. Shortly after, he started noticing occasional double vision. Physical examination shows slight vertical nystagmus and gait ataxia. Which of the following drugs was most likely added to this patient's medication regimen?

	Answer	Image
A	Modafinil	
B	Nafcillin	
C	Cimetidine	
D	St. John's wort	
E	Theophylline	
F	Carbamazepine	
G	Rifampin	

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Hint

This patient has been safely treated with phenytoin for many years but is now presenting with subtle signs of phenytoin toxicity (diplopia, nystagmus, and ataxia) shortly after having been prescribed a new drug. Since phenytoin is metabolized by the hepatic cytochrome-P450 system (CYP450), the toxicity is likely due to the addition of a CYP450 inhibitor.

Correct Answer

A - Modafinil

Explanation Why

[Modafinil](#) is an inducer of the [CYP450](#). When taken concurrently with [phenytoin](#), patients will have subtherapeutic levels of [phenytoin](#) and likely present with poorly controlled [seizures](#).

B - Nafcillin

Explanation Why

[Nafcillin](#) is an inducer of [CYP450](#). When taken concurrently with [phenytoin](#), patients will have subtherapeutic levels of [phenytoin](#) and likely present with poorly controlled [seizures](#).

C - Cimetidine

Explanation But

Since [phenytoin](#) itself is an inducer of [CYP450](#), [half-life](#) of this drug is dependent upon its own serum concentration. In therapeutic doses, a fixed percentage of [phenytoin](#) is eliminated over a given time. However, at higher concentrations, [CYP450](#) reaches saturation, leading to elimination of only a fixed amount of [phenytoin](#) over a given time. This results in a longer [half-life](#) of [phenytoin](#) and contributes to drug toxicity.

Explanation Why

Cimetidine is an inhibitor of [CYP450](#) and a commonly prescribed drug for relief of [GERD](#) symptoms. Concurrent intake of cimetidine and [phenytoin](#) will lead to increased serum levels of [phenytoin](#) that are causing the toxicity seen in this patient. There are numerous drugs that affect [CYP450](#) and careful revision of a patient's medication list is imperative prior to any changes.

D - St. John's wort

Explanation Why

[St. John's wort](#) (*Hypericum perforatum*) is an inducer of [CYP450](#). When taken concurrently with [phenytoin](#), patients will have subtherapeutic levels of [phenytoin](#) and likely present with poorly controlled [seizures](#).

E - Theophylline

Explanation Why

[Theophylline](#) is a substrate of [CYP450](#). When taken concurrently with [phenytoin](#), patients show no changes to their serum levels of [phenytoin](#). However, since [phenytoin](#) is a [CYP450](#) inducer itself, levels of [theophylline](#) may be decreased.

F - Carbamazepine

Explanation Why

[Carbamazepine](#) acts as an inducer and a substrate of [CYP450](#). When taken concurrently with [phenytoin](#), patients will have subtherapeutic levels of [phenytoin](#) and likely present with poorly controlled [seizures](#).

G - Rifampin

Explanation Why

[Rifampin](#) is a strong inducer of [CYP450](#). When taken concurrently with [phenytoin](#), patients will have

subtherapeutic levels of [phenytoin](#) and likely present with poorly controlled [seizures](#).

Question # 30

A 35-year-old man is brought to the emergency department by his wife because of a 1-week history of progressive confusion, myalgia, and nausea. His wife says that he first reported headaches and fatigue 10 days ago, and since then “he has not been himself”. He has refused to drink any liquids for the last day. Two months ago, he helped his neighbor remove a raccoon's den from her backyard. He appears agitated. His temperature is 100.8°F (38.2°C). Examination shows excessive drooling. Muscle tone and deep tendon reflexes are increased bilaterally. Administration of which of the following is most likely to have prevented this patient's condition?

	Answer	Image
A	RNA-dependent DNA polymerase inhibitor	
B	Chemically-inactivated virus	<pre> graph TD A[Potential rabies exposure] --> B[Wild, high-risk animal] A --> C[Domestic carnivore] A --> D[Indoor domestic herbivore] A --> E[Livestock, outdoor, domestic herbivore, other wild animal] B --> F{Available to test?} F -- Yes --> G[Test animal] G -- Animal positive --> H[PEP] F -- No --> H C --> I{Unavailable for observation} I --> H C --> J{Symptoms of rabies within the next 10 days?} J -- Yes --> K[Start PEP + test animal Stop PEP if test is negative] J -- No --> L[No PEP] D --> L E --> M[Contact local health department] </pre>
C	Live attenuated vaccine	
D	Immunoglobulin against a bacterial protein	
E	NF-κB inhibitor	

	Answer	Image
F	Inosine monophosphate dehydrogenase inhibitor	

Hint

The patient has had flulike illness followed by agitation, confusion, hydrophobia, hypersalivation, and increased muscle tone and reflexes 2 months following exposure to raccoons. These symptoms are highly suggestive of rabies infection due to a bite by a raccoon, which are a major animal reservoir of rabies.

Correct Answer

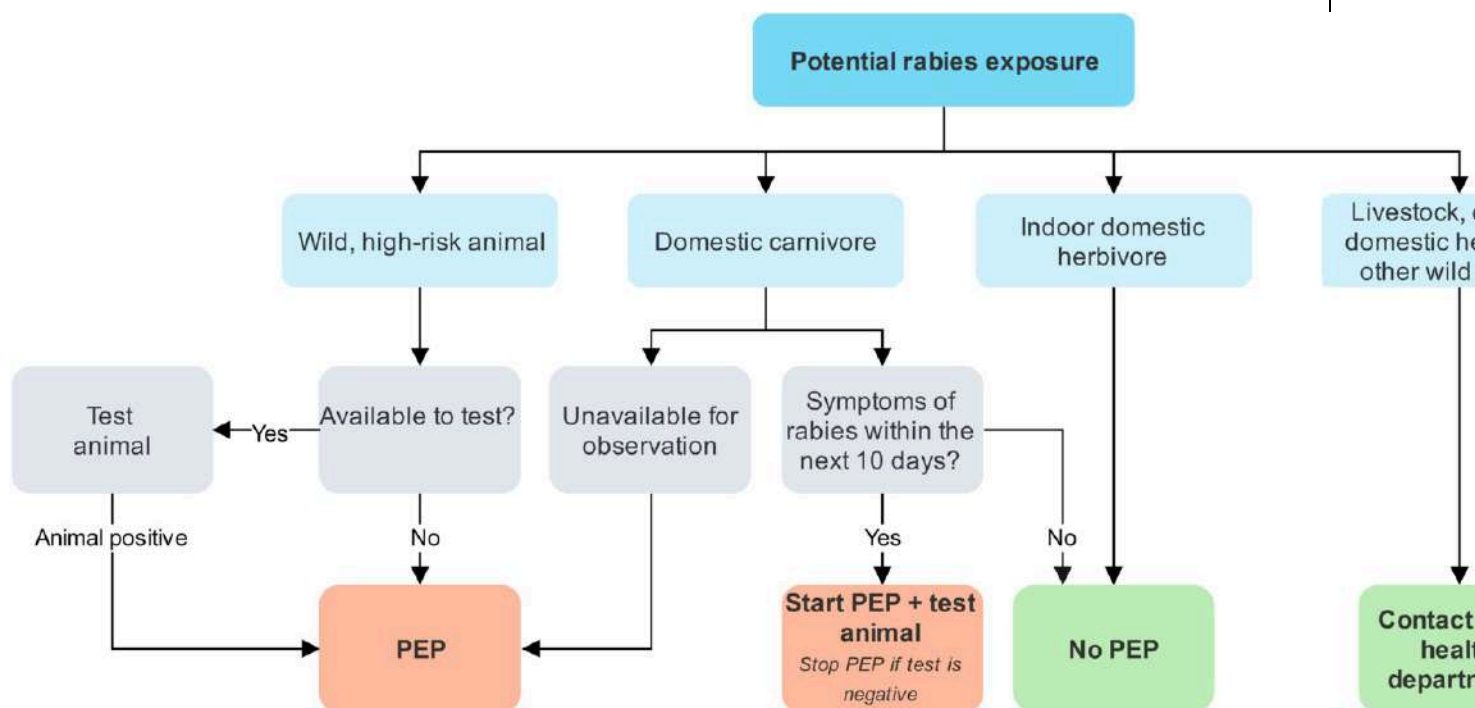
A - RNA-dependent DNA polymerase inhibitor

Explanation Why

[NRTIs](#) and [NNRTIs](#) are [RNA-dependent DNA polymerase](#) inhibitors and are used in antiretroviral HIV therapy. An acute [HIV](#) infection can manifest with [fever](#), [headache](#), and fatigue, as seen in this patient. However, [hydrophobia](#), hypersalivation, and increased muscle tone and reflexes are not associated with [HIV](#). [RNA-dependent DNA polymerase](#) inhibitors are not effective against [rabies virus](#).

B - Chemically-inactivated virus

Image



Explanation But

Treatment with postexposure prophylaxis in suspected cases of a rabid animal bite should take place immediately, as the disease is fatal once it has become symptomatic. At this patient's stage of the disease, only [palliative treatment](#) is available.

Explanation Why

Administration of a chemically-inactivated virus (i.e., [killed vaccine](#)) along with [rabies immunoglobulin](#) is recommended as postexposure prophylaxis for patients with suspected [rabies](#). The [immunoglobulin](#) provides immediate protection by binding to the [rabies virus](#) and neutralizing it (i.e., [passive immunity](#)). However, protection is only temporary, since [antibodies](#) degrade over time. Simultaneous administration of the [rabies vaccine](#) stimulates the body's [immune system](#), which reacts by producing [antibodies](#) (i.e., [active immunity](#)). Preventive [active immunization](#) with [rabies vaccine](#) is indicated for people with frequent occupational contact with potentially rabid animals and travelers to regions in which [rabies](#) is widespread.

C - Live attenuated vaccine

Explanation Why

[Immunization](#) with [live attenuated vaccine](#) usually provides lifelong protection against a virus or bacterium (e.g., [MMR vaccine](#)). However, there is no [live vaccine](#) available against [rabies virus](#).

D - Immunoglobulin against a bacterial protein

Explanation Why

Administration of [immunoglobulins](#) is an integral part of [rabies](#) postexposure prophylaxis; [immunoglobulins](#) provide immediate protection by binding to the [rabies virus](#) and thereby neutralizing it. However, [rabies](#) is a virus that belongs to the [Rhabdoviridae](#). Therefore, an [immunoglobulin](#) against a bacterial protein would not be effective.

E - NF-κB inhibitor

Explanation Why

[Corticosteroids](#) are NF-κB inhibitors that are usually administered for a variety of autoimmune conditions, as well as to prevent complications due to scarring after community-acquired bacterial [meningitis](#). However, the clinical presentation of this patient is consistent with encephalitic [rabies](#), which is not treated with [corticosteroids](#), as they cannot halt the neurological damage caused by the [rabies virus](#).

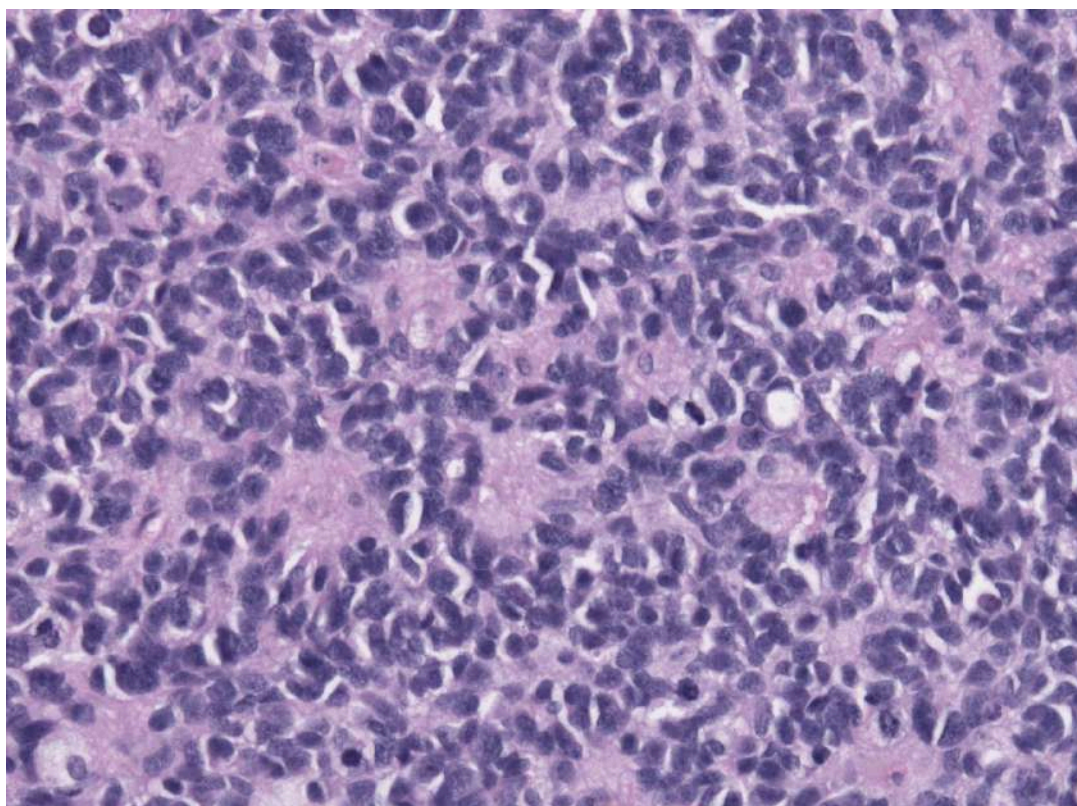
F - Inosine monophosphate dehydrogenase inhibitor

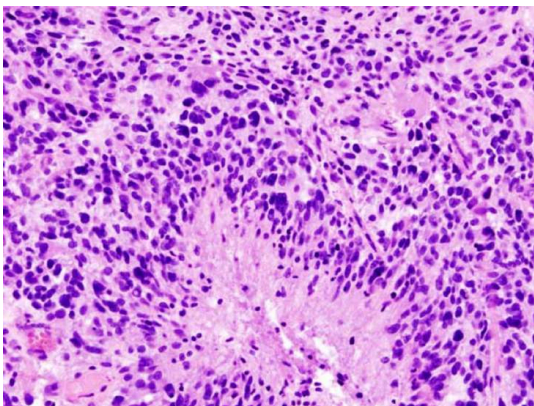
Explanation Why

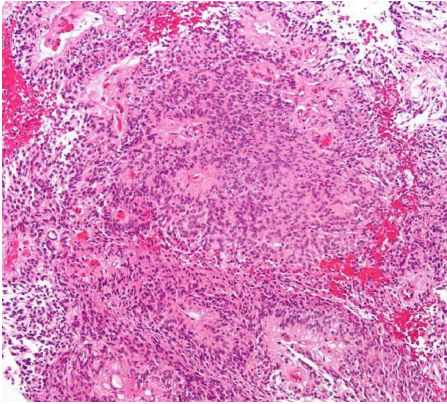
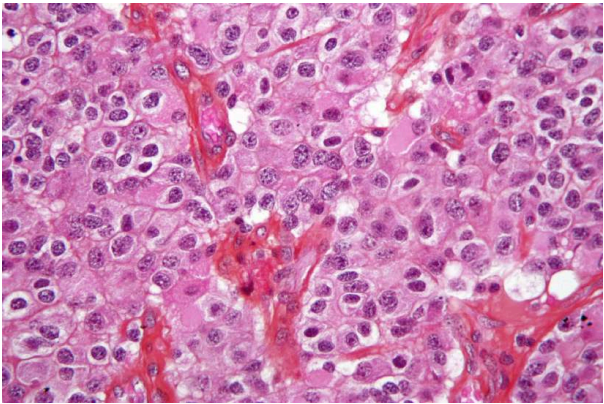
[Ribavirin](#), an [inosine monophosphate dehydrogenase](#) inhibitor, is used for the treatment of [hepatitis C](#) and [RSV](#) infection. None of these conditions is consistent with this patient's clinical presentation, which is suggestive of encephalitic [rabies](#). There is no available antiviral therapy that stops the replication of [rabies virus](#).

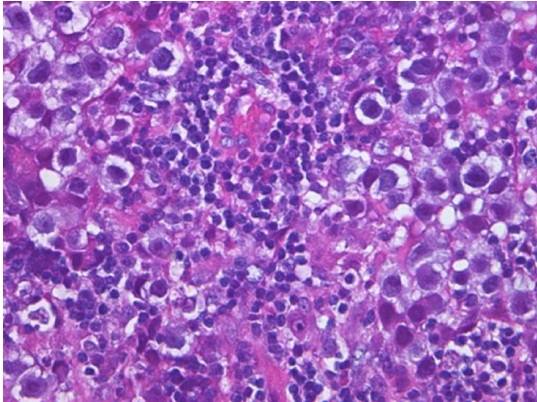
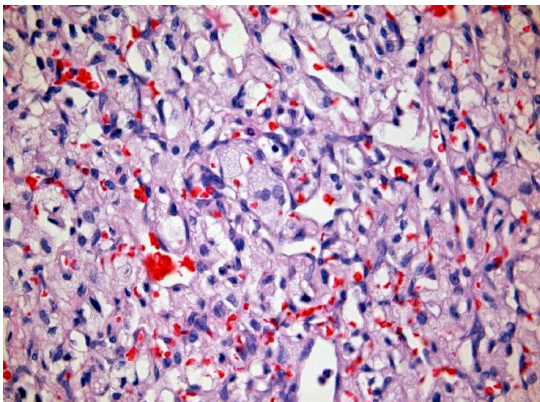
Question # 31

A previously healthy 4-year-old girl is brought to the physician for evaluation of a 3-week history of recurrent vomiting and difficulty walking. Examination shows a broad-based gait and bilateral optic disc swelling. An MRI shows an intracranial tumor. A ventriculoperitoneal shunt is placed, and surgical excision of the tumor is performed. A photomicrograph of a section of the tumor is shown. Which of the following is the most likely diagnosis?



	Answer	Image
A	Glioblastoma multiforme	

	Answer	Image
B	Ependymoma	 A histological section of an ependymoma, showing a dense population of cells with perivascular pseudorosettes, where tumor cells are arranged in a ring around a central blood vessel.
C	Medulloblastoma	 A sagittal T1-weighted MRI scan of the brain. A large, dark, heterogeneous mass is visible in the posterior fossa, posterior to the brainstem, characteristic of a medulloblastoma. The mass is labeled with '[A]' on the left and '[P]' on the right.
D	Oligodendroglioma	 A histological section of an oligodendroglioma, showing a dense population of cells with round, uniform nuclei and a 'fried egg' appearance, where the cell body is surrounded by a clear halo of myelin.

	Answer	Image
E	Pinealoma	
F	Pilocytic astrocytoma	
G	Hemangioblastoma	

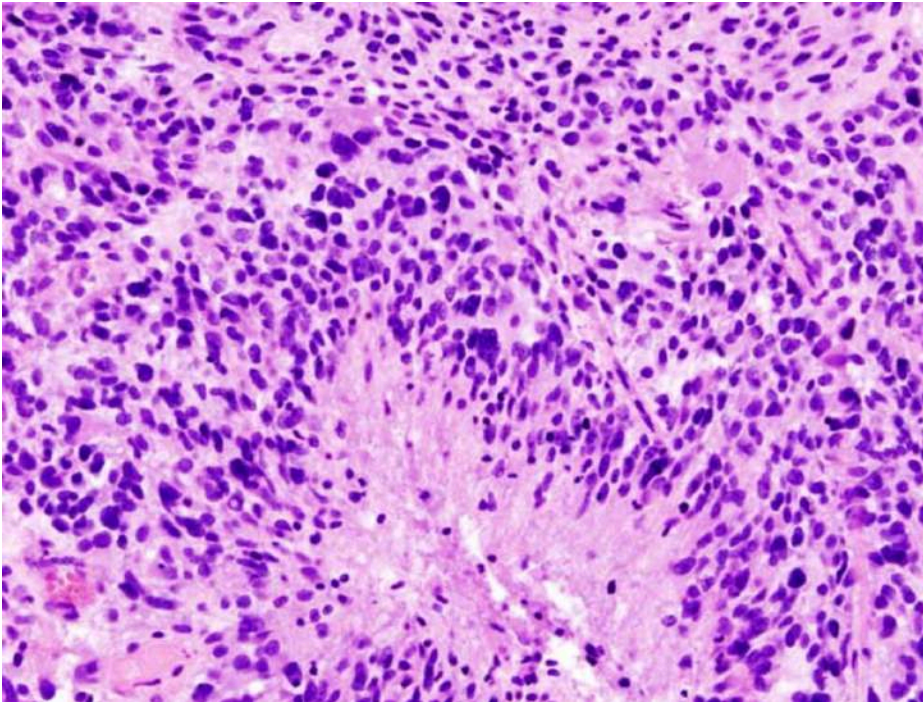
Hint

The photomicrograph shows Homer Wright rosettes, which consist of differentiated tumor cells around a central region of nerve fibers.

Correct Answer

A - Glioblastoma multiforme

Image

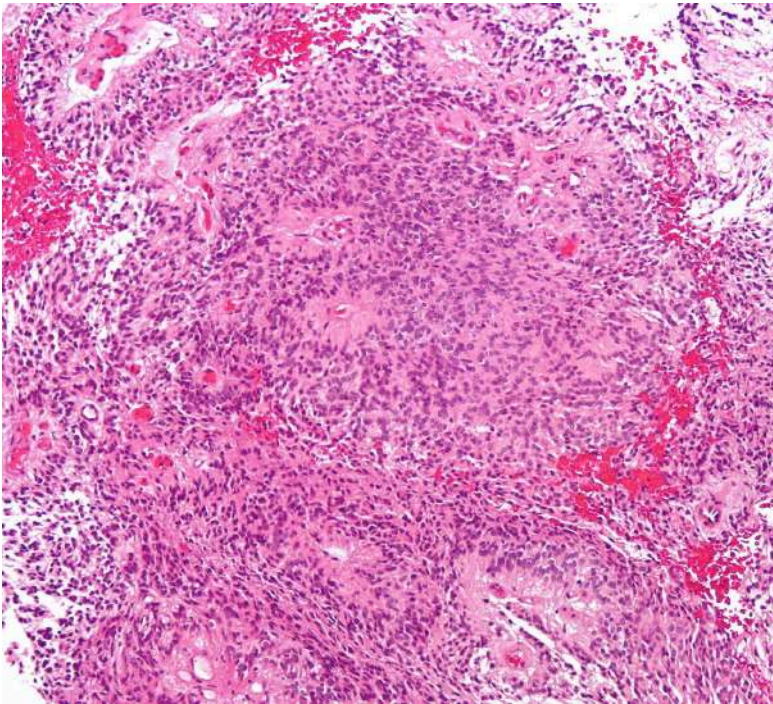


Explanation Why

[Glioblastoma multiforme](#), which predominantly develops in adults, most commonly arises in the cerebral hemispheres ([supratentorial region](#)). Biopsy of this [tumor](#) shows pleomorphic cells with hyperchromatic and irregular nuclei that aggregate around a [necrotic](#) center (pseudopalisading necrosis), not the histopathologic findings seen in this patient.

B - Ependymoma

Image

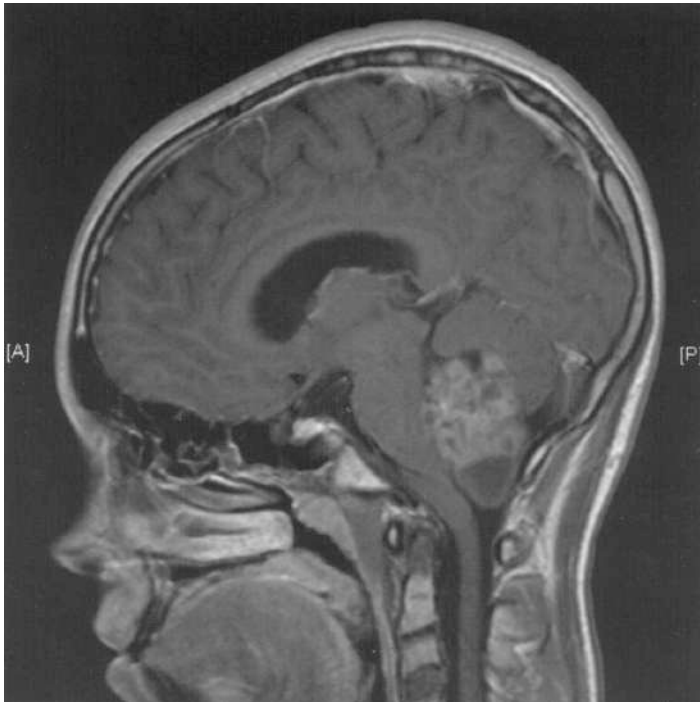


Explanation Why

Intracranial [ependymoma](#), which predominantly develops in children, most commonly arises in the [fourth ventricle](#) and can cause [symptoms of increased intracranial pressure](#). However, biopsy of this [tumor](#) shows cells with abundant [cytoplasm](#) arranged around a central vascular core ([perivascular pseudorosettes](#)), not the histopathologic findings seen in this patient.

C - Medulloblastoma

Image

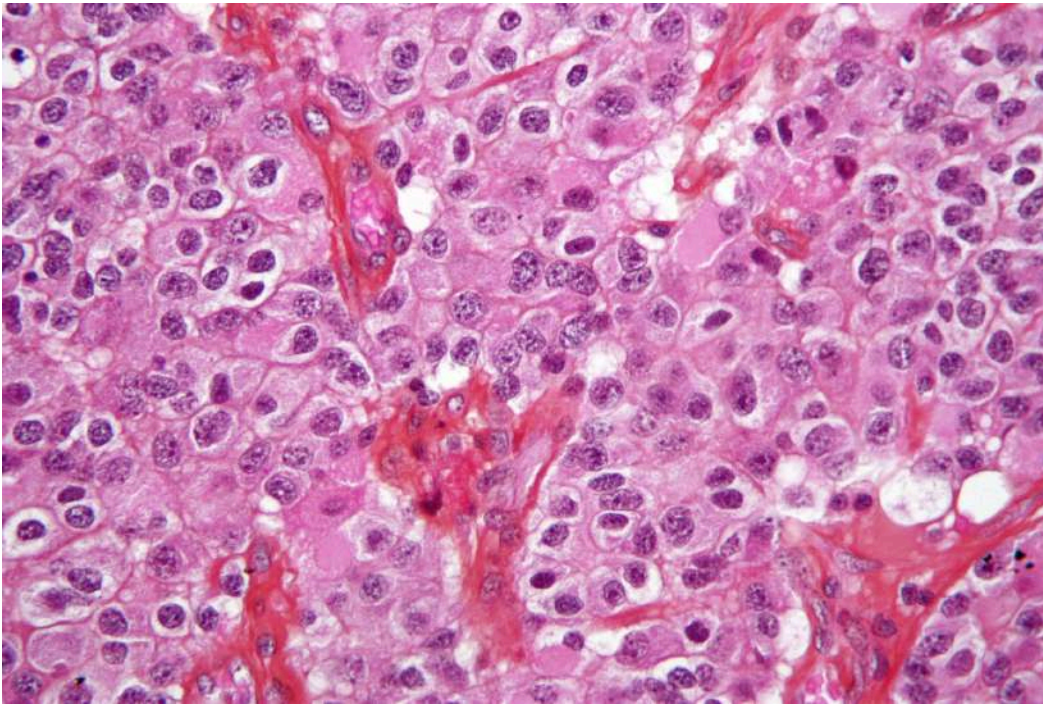


Explanation Why

[Medulloblastoma](#) is the most common primary malignant [brain tumor](#) of childhood and has a peak [incidence](#) between 3–5 years of age. This [tumor](#) typically develops in the [cerebellum](#). Destruction of the [cerebellar vermis](#) causes [truncal ataxia](#), and compression of the [fourth ventricle](#) by the [tumor](#) causes [noncommunicating hydrocephalus](#) and [symptoms of increased intracranial pressure](#) as seen in this patient. The main histopathologic feature of [medulloblastoma](#) is the presence of small round blue cells (primitive [neuroectoderm](#) cells) that surround a central, fibril-rich neuropil ([Homer Wright rosettes](#)).

D - Oligodendroglioma

Image

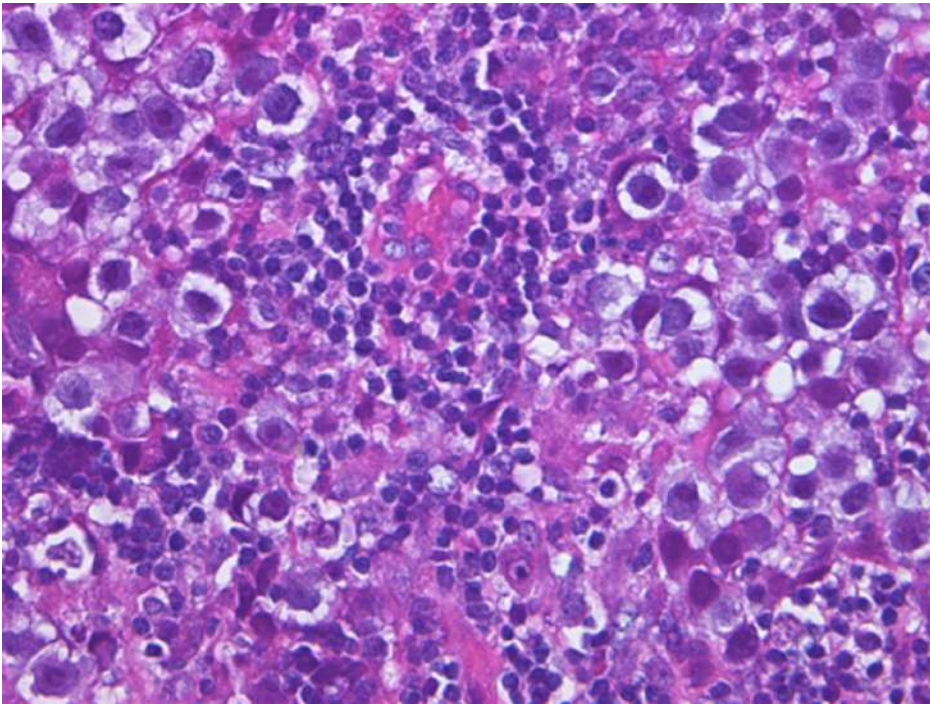


Explanation Why

[Oligodendroglioma](#), which predominantly develops in adults, most commonly arises in the [frontal lobe \(supratentorial region\)](#). Biopsy of this [tumor](#) shows round cells with clear [cytoplasm](#) (fried-egg cells) and a chicken-wire pattern formed by anastomosing [capillaries](#), not the histopathologic findings seen in this patient.

E - Pinealoma

Image

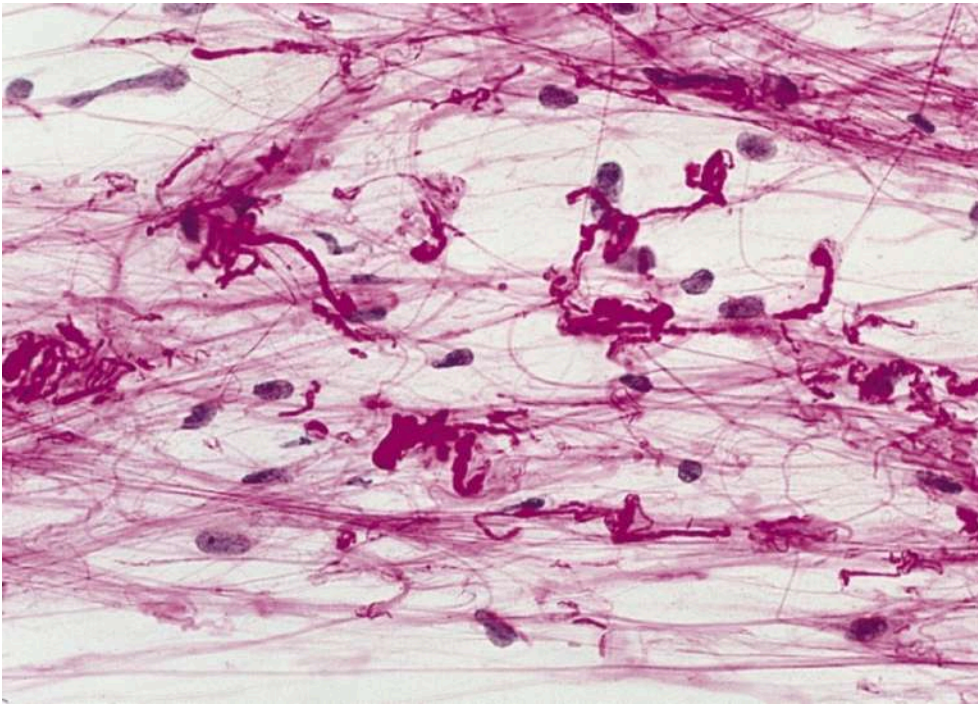


Explanation Why

[Pinealoma](#), which predominantly develops in children, typically arises near the [tectum](#) of the [midbrain](#) and can cause [symptoms of increased intracranial pressure](#) due to compression of the [cerebral aqueduct](#). However, most pediatric [pinealomas](#) are germinomas characterized histologically by a lymphoid stroma and large, vacuolated cells with enlarged oval nuclei, not the histopathologic findings seen in this patient. Moreover, this patient does not have other manifestations associated with [pinealomas](#) such as [Parinaud syndrome](#) and [precocious puberty](#).

F - Pilocytic astrocytoma

Image

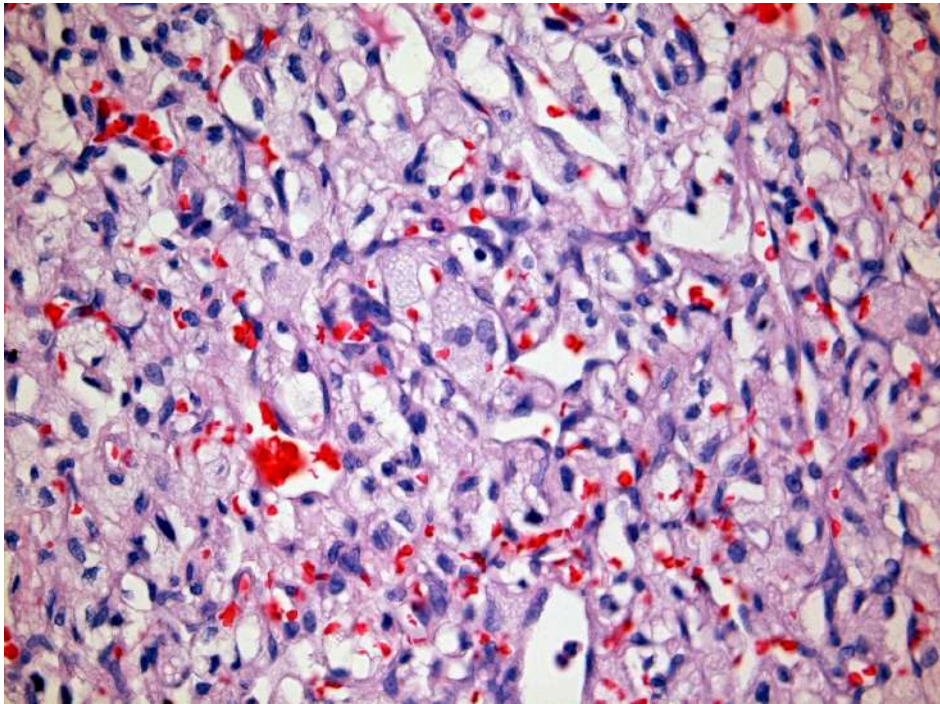


Explanation Why

Pilocytic astrocytoma, which is the most common pediatric primary brain tumor, typically arises in the cerebellum and can cause symptoms of increased intracranial pressure and truncal ataxia. However, biopsy of this tumor shows cells with eosinophilic, corkscrew-like processes (Rosenthal fibers), not the histopathologic findings seen in this patient.

G - Hemangioblastoma

Image



Explanation Why

[Hemangioblastoma](#), which predominantly develops in adults, typically arises in the [cerebellum](#) and can cause [symptoms of increased intracranial pressure](#) and [truncal ataxia](#). Biopsy of this [tumor](#) shows closely packed, thin-walled vessels with minimal intervening brain parenchyma, not the histopathologic findings seen in this patient.

Question # 32

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

	Answer	Image
A	Carbamazepine	
B	Tiagabine	
C	Valproate	
D	Vigabatrin	
E	Phenytoin	
F	Ethosuximide	
G	Diazepam	

Hint

The combination of myoclonic jerks that occur shortly after awakening, generalized tonic-clonic seizures, and a vague history that could indicate absence seizures (“he often daydreams”) in this teenager is suggestive of juvenile myoclonic epilepsy.

Correct Answer

A - Carbamazepine

Explanation Why

[Carbamazepine](#) is an [antiepileptic drug](#) that inhibits voltage-gated sodium channels in the brain, which reduces the excitability of [neurons](#). [Carbamazepine](#) is not used in patients with [juvenile myoclonic epilepsy](#) as it may induce absence status epilepticus.

B - Tiagabine

Explanation Why

[Tiagabine](#) is an [anticonvulsant](#) that inhibits [GABA](#) reuptake. [Tiagabine](#) is typically used to treat [focal seizures](#), with or without impairment of consciousness. [Tiagabine](#) is not used in patients with [juvenile myoclonic epilepsy](#) because of its potential to aggravate [generalized seizure](#) types (such as myoclonic or absence status epilepticus).

C - Valproate

Explanation But

[Carbamazepine](#), [phenytoin](#), and oxcarbazepine should be avoided in patients with [juvenile myoclonic epilepsy](#) as they may aggravate [absence seizures](#) and myoclonic jerks. These medications may control [generalized tonic-clonic seizures](#) in some refractory cases.

Explanation Why

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

D - Vigabatrin

Explanation Why

[Vigabatrin](#) is an [antiepileptic](#) medication that reduces excitability in the brain by inhibiting the [catabolism](#) of [GABA](#). It is primarily used to treat [infantile spasms](#) and refractory [complex partial seizures](#). It is contraindicated in patients with [juvenile myoclonic epilepsy](#) due to its potential to aggravate it or induce absence status epilepticus.

E - Phenytoin

Explanation Why

[Phenytoin](#) inhibits [voltage-gated sodium channels](#) in the brain, which reduces the excitability of [neurons](#). [Phenytoin](#) is used primarily for [tonic-clonic](#) and [focal seizure](#) prophylaxis and may also be used as a second-line drug in [status epilepticus](#). [Phenytoin](#) is not used in patients with [juvenile myoclonic epilepsy](#) because it may aggravate [absence seizures](#) and myoclonic jerks.

F - Ethosuximide

Explanation Why

[Ethosuximide](#) is the first line treatment for [absence seizures](#). This medication reduces excitability in the brain by blocking thalamic [T-type calcium channels](#). Although this patient has a vague history that could indicate [absence seizures](#) (“he often daydreams”), the combination of myoclonic jerks that occur shortly after awakening and [generalized tonic-clonic seizures](#) are more suggestive of [juvenile myoclonic epilepsy](#).

G - Diazepam

Explanation Why

[Diazepam](#) is a long-acting [benzodiazepine](#) that acts by binding [GABA](#)-A receptors and increasing the frequency at which they are open and inhibiting neuronal excitability. [Benzodiazepines](#) are used in patients with [status epilepticus](#), but they are not indicated as first-line agents in patients with [juvenile myoclonic epilepsy](#).

Question # 33

A 55-year-old woman comes to the physician because of involuntary rhythmic shaking of both hands for several months. More recently, she also noticed involuntary head nodding movements. The shaking seems to improve after having one or two glasses of wine. Her father had similar symptoms starting at the age of 60. Neurologic examination shows a symmetric hand tremor that worsens with voluntary movement of the respective extremity. The most appropriate pharmacotherapy for this patient's symptoms is also recommended for the treatment of which of the following conditions?

	Answer	Image
A	Motion sickness	
B	Restless legs syndrome	
C	Sleepwalking	
D	Huntington disease	
E	Hyperthyroidism	
F	Malignant hyperthermia	

Hint

The combination of symmetric bilateral hand tremor and head-nodding tremor that are alleviated by alcohol in a patient with a family history of similar symptoms is highly suggestive of essential tremor.

Correct Answer

A - Motion sickness

Explanation Why

First-generation [antihistamines](#), such as [diphenhydramine](#) or [meclizine](#), are labyrinthine sedatives. They are effective at managing motion sickness but have no effect on [essential tremor](#).

B - Restless legs syndrome

Explanation Why

[Dopamine agonists](#) ([pramipexole](#), [ropinirole](#)) and [levodopa](#) are first-line drugs used in the management of [restless leg syndrome](#). While efficacious in mitigating [tremor](#) associated with [Parkinson disease](#), they are not useful in [essential tremor](#).

C - Sleepwalking

Explanation Why

[Benzodiazepines](#), such as [clonazepam](#), are used in managing [parasomnia](#) (such as [sleepwalking](#)) when no underlying triggers are found. [Benzodiazepines](#) have not been proven to be useful in treating [essential tremor](#).

D - Huntington disease

Explanation Why

[Huntington disease](#) is associated with [dyskinesia](#) and [choreiform movements](#) and can be treated with monoamine-depleting drugs (e.g., [tetrabenazine](#)), [atypical neuroleptics](#) (e.g., [clozapine](#)), and [NMDA-receptor antagonists](#) (e.g., [amantadine](#)). None of these drugs are used in the treatment of [essential tremor](#).

E - Hyperthyroidism

Explanation Why

[Propranolol](#) would be the most appropriate pharmacotherapy in this patient with features suggestive of [essential tremor](#). [Propranolol](#) is also used in the management of [hyperthyroidism](#). As a non-selective [beta blocker](#), it reduces the [sympathetic](#) effects of [hyperthyroidism](#) ([diaphoresis](#), [tachycardia](#), etc), and also inhibits the peripheral conversion of T4 to the more active T3. Other indications include treatment of [hypertension](#) and [atrial fibrillation](#) and [migraine](#) prophylaxis.

F - Malignant hyperthermia

Explanation Why

[Dantrolene](#), a central [muscle relaxant](#), is used to treat [malignant hyperthermia](#), which may be associated with [rigidity](#), coarse [tremors](#), [autonomic dysfunction](#), and hyperthermia. Additionally, this condition is associated with the administration of [volatile anesthetics](#) or [succinylcholine](#). [Dantrolene](#) is not used in [essential tremor](#).

Question # 34

An 81-year-old man comes to the emergency department with severe left ear pain and drainage for 3 days. He has a history of poorly-controlled type 2 diabetes mellitus. He appears uncomfortable. Physical examination of the ear shows marked periauricular erythema, exquisite tenderness on palpation, and granulation tissue in the external auditory canal. The most likely causal pathogen produces an exotoxin that acts by a mechanism most similar to a toxin produced by which of the following organisms?

	Answer	Image
A	<i>Corynebacterium diphtheriae</i>	
B	<i>Bordetella pertussis</i>	
C	<i>Shigella dysenteriae</i>	
D	<i>Staphylococcus aureus</i>	
E	<i>Clostridium tetani</i>	
F	<i>Bacillus anthracis</i>	

Hint

Unilateral severe ear pain and drainage with granulation tissue in the external auditory canal in a patient with poorly controlled diabetes mellitus are highly suggestive of malignant otitis externa caused by *Pseudomonas aeruginosa*. This organism produces exotoxin A, which induces host cell death via inhibition of elongation factor 2.

Correct Answer

A - *Corynebacterium diphtheriae*

Explanation Why

Corynebacterium diphtheriae produces [diphtheria toxin](#), which inhibits [protein synthesis](#) and induces [cell death](#) by the same mechanism as Pseudomonas exotoxin A, via inactivation of [elongation factor 2](#). *C. diphtheriae* causes [diphtheria](#). Other [virulence factors](#) produced by *P. aeruginosa* include [phospholipase C](#), [endotoxins](#), and pigments (pyoverdinin and [pyocyanin](#)).

B - *Bordetella pertussis*

Explanation Why

Bordetella pertussis produces [pertussis toxin](#), which increases the level of [cAMP](#) and impairs [phagocytosis](#) by overactivating [adenylate cyclase](#). *B. pertussis* causes [whooping cough](#) (pertussis). *P. aeruginosa* does not produce an [exotoxin](#) with a similar mechanism of action to [pertussis toxin](#).

C - *Shigella dysenteriae*

Explanation Why

Shigella dysenteriae produces [Shiga toxin](#), which inhibits [protein synthesis](#) by inactivating the [60S ribosome](#) (cleaves [adenine](#) from the [ribosomal RNA](#)) and causes [cell death](#). *S. dysenteriae* causes bloody [diarrhea](#) and [hemolytic uremic syndrome](#). *P. aeruginosa* does not produce an [exotoxin](#) with a similar mechanism of action to [Shiga toxin](#).

D - Staphylococcus aureus

Explanation Why

Staphylococcus aureus produces [toxic shock syndrome toxin 1 \(TSST-1\)](#), which binds to [MHC II](#) and [T-cell receptors](#), resulting in polyclonal [T-cell](#) activation and massive release of [cytokines](#). This leads to the development of [toxic shock syndrome](#), which is characterized by sudden onset of [fever](#), rash, [hypotension](#), [renal failure](#), and changes in mental status. *P. aeruginosa* has an [endotoxin](#) that can induce [fever](#) and [shock](#), but it does not produce an [exotoxin](#) with a similar mechanism of action to [TSST-1](#).

E - Clostridium tetani

Explanation Why

Clostridium tetani produces [tetanospasmin](#), a [protease](#) that cleaves SNARE proteins, thereby preventing the release of inhibitory [neurotransmitters](#) and causing [tetanus](#). *P. aeruginosa* does not produce an [exotoxin](#) with a similar mechanism of action to [tetanospasmin](#).

F - Bacillus anthracis

Explanation Why

Bacillus anthracis produces edema toxin, which mimics [adenylyl cyclase](#) and increases the level of [cAMP](#). This results in tissue [edema](#) and impaired [chemotaxis](#) of [macrophages](#) and [neutrophils](#). *B. anthracis* can cause cutaneous, inhalational, or intestinal [anthrax](#). *P. aeruginosa* does not produce an [exotoxin](#) with a similar mechanism of action to edema toxin.

Question # 35

A 24-year-old man is brought to the emergency department because of violent jerky movements of his arms and legs that began 30 minutes ago. His father reports that the patient has a history of epilepsy. He is not responsive. Physical examination shows alternating tonic jerks and clonic episodes. There is blood in the mouth. Administration of intravenous lorazepam is begun. In addition, treatment with a second drug is started that alters the flow of sodium ions across neuronal membranes. The second agent administered was most likely which of the following drugs?

	Answer	Image
A	Topiramate	
B	Fosphenytoin	
C	Lamotrigine	
D	Phenobarbital	
E	Propofol	
F	Carbamazepine	

Hint

This patient's history of epilepsy and ongoing seizure for > 5 minutes is diagnostic of status epilepticus. Lorazepam was given to abort the seizure and the second agent was given to prevent recurrence of the seizure in the acute period.

Correct Answer

A - Topiramate

Explanation Why

[Topiramate](#) is an [anticonvulsant](#) that acts by blocking sodium channels and increasing the action of [GABA](#), which leads to an increased flow of [chloride](#) ions. It can be used in both partial (focal) and [tonic-clonic generalized seizures](#), but it does not play a role in the treatment of [status epilepticus](#).

B - Fosphenytoin

Explanation Why

[Fosphenytoin](#) is an intravenous prodrug of [phenytoin](#) with a more favorable safety profile than [phenytoin](#) preparations delivered via other routes. It is converted to [phenytoin](#), the active moiety of this drug, by hydrolyzation. Once activated, it reduces the influx and increases the efflux of sodium ions across neuronal membranes in the motor cortex. It is indicated for the prevention of [seizure](#) recurrence in [status epilepticus](#) and for short-term (< 5 days) treatment of [epilepsy](#).

C - Lamotrigine

Explanation Why

[Lamotrigine](#) is an [antiepileptic drug](#) that inhibits [voltage-gated sodium channels](#) and [glutamate](#) release in the brain. It may be used in partial (focal) [seizures](#), [tonic-clonic generalized seizures](#), and in [absence seizures](#). However, it is not used in the treatment of [status epilepticus](#).

D - Phenobarbital

Explanation Why

[Phenobarbital](#) is a [barbiturate](#) that can be used in the treatment of [status epilepticus](#), but it is not first-line because of its suboptimal safety profile. Furthermore, [barbiturates](#) act by binding [GABA](#)-A receptors, increasing the duration of [chloride](#) channel opening. This patient has, however, received a drug that alters the flow of sodium ions.

E - Propofol

Explanation Why

[Propofol](#) is an [intravenous anesthetic](#) that is thought to act on sodium channels and [GABA](#)-A receptors of the reticular formation. It is typically used for intravenous anesthesia induction or [total intravenous anesthesia](#) (TIVA) as well as for [status epilepticus](#), albeit only in refractory cases that neither respond to [benzodiazepines](#) nor nonbenzodiazepine [antiseizure drugs](#).

F - Carbamazepine

Explanation Why

[Carbamazepine](#) is an [antiepileptic drug](#) that inhibits [voltage-gated sodium channels](#) in the brain. It is used in the treatment of partial (focal) [seizures](#), [tonic-clonic generalized seizures](#), and in [trigeminal neuralgia](#). It is not indicated for treatment of [status epilepticus](#).

Question # 36

An investigator is studying cellular repair mechanisms in various tissues. One of the samples being reviewed is from the anterior horn of the spinal cord of a patient who was involved in a snowboard accident. Pathologic examination of the biopsy specimen shows dispersion of the Nissl bodies, swelling of the neuronal body, and a displacement of the nucleus to the periphery in numerous cells. Which of the following is the most likely explanation for the observed findings?

	Answer	Image
A	Neurodegenerative changes	
B	Early ischemic damage	
C	Wallerian degeneration	
D	Central chromatolysis	
E	Reactive astrogliosis	
F	Neuronal aging	

Hint

This reaction is most commonly seen in neurons following injury to their axons.

Correct Answer

A - Neurodegenerative changes

Explanation Why

Neurodegenerative changes occur in response to the loss of function and structure of [neurons](#) in neurodegenerative diseases (e.g., [Parkinson disease](#), [Alzheimer disease](#), [Huntington disease](#)). These changes manifest in many different ways depending on the neurodegenerative diseases. Mechanisms include genetic mutations, [protein misfolding](#), intracellular defects (e.g., of [protein degradation](#) pathways, [mitochondria](#), membrane, [DNA](#), or [axons](#)), defective programmed [cell death](#), and transglutaminases. However, the described findings in this question suggest another etiology.

B - Early ischemic damage

Explanation Why

Early [ischemic](#) damages manifest with [retraction](#) of the cellular outlines, [pyknosis](#), disappearance of the [Nissl bodies](#), and eosinophilic condensation of the [cytoplasm](#), unlike the biopsy findings here.

C - Wallerian degeneration

Explanation Why

[Wallerian degeneration](#) is a process that occurs in response to a [proximal](#) axonal or neuronal cell body injury. It is characterized by degeneration of the [distal](#) segment of the transected nerve fiber and axonal [retraction](#) proximally but does not cause the changes described in the biopsy findings here.

D - Central chromatolysis

Explanation Why

[Central chromatolysis](#) is a reaction of a neuronal cell body (also known as the [soma](#)) in response to an axonal injury. It is characterized by swelling of the neuronal body, dispersion of the [Nissl bodies](#), and displacement of the nucleus to the periphery. These changes reflect an increase in [protein synthesis](#) aimed at restoring the integrity of the damaged [axon](#). [Chromatolysis](#) occurs concurrently with [Wallerian degeneration](#).

E - Reactive astrogliosis

Explanation Why

Reactive astrogliosis is a nonspecific reactive change in response to damage in the [central nervous system](#). [Proliferation](#) of various [glial cell](#) lineages, including [astrocytes](#), [microglia](#), and [oligodendrocytes](#), can be seen. The hypothesized function of this response is to control oxidative damage to the remaining [neurons](#), quickly reestablish the [blood-brain barrier](#), and to lay down acute [scar](#) tissue. The changes observed in this tissue sample are within [neurons](#), not [glial cells](#).

F - Neuronal aging

Explanation Why

Neuronal [aging](#) is characterized by [lipofuscin](#) deposition in the neuronal cell body. The clinical consequences of this histologic finding are not known.

Question # 37

A 33-year-old woman with a history of multiple sclerosis is brought to the physician because of dizziness, urinary incontinence, loss of vision in her right eye, and numbness and weakness of the left leg. She has had recurrent episodes of neurological symptoms despite several changes in her medication regimen. An MRI of the brain shows several new enhancing lesions in the periventricular white matter and the brainstem. Treatment with a drug that binds to CD52 is initiated. Which of the following agents was most likely prescribed?

	Answer	Image
A	Eculizumab	
B	Bevacizumab	
C	Alemtuzumab	
D	Basiliximab	
E	Rituximab	
F	Omalizumab	
G	Abciximab	
H	Cetuximab	

	Answer	Image
I	Natalizumab	

Hint

CD52 is a surface glycoprotein expressed on mature lymphocytes. Treatment with the monoclonal antibody that binds to CD52 is used in cases of refractory MS and B-cell chronic lymphocytic leukemia.

Correct Answer

A - Eculizumab

Explanation Why

[Eculizumab](#) is a [monoclonal antibody](#) that binds [complement protein](#) C5 to prevent its cleavage to C5a and C5b. This impairs formation of the [membrane attack complex](#). [Eculizumab](#) is used in the treatment of [paroxysmal nocturnal hemoglobinuria](#) because it reduces [intravascular hemolysis](#). It does not bind [CD52](#) glycoproteins and would not be indicated as a treatment for this patient's [multiple sclerosis](#).

B - Bevacizumab

Explanation Why

[Bevacizumab](#) is a [monoclonal antibody](#) that binds [VEGF](#) receptors and is used to treat neovascular [age-related macular degeneration](#), [colorectal cancer](#), and [renal cell carcinoma](#). This [antibody](#) does not target [CD52](#) glycoproteins and would not be the treatment of choice in this patient with a history of [multiple sclerosis](#).

C - Alemtuzumab

Explanation Why

[Alemtuzumab](#) is a humanized [monoclonal antibody](#) that targets cells expressing [CD52](#) glycoproteins on their surface ([T cells](#), [B cells](#), [NKT cells](#), and [monocytes](#)). Eliminating these cells limits immune-mediated injury to [oligodendrocytes](#). [Alemtuzumab](#) is used to treat refractory [multiple sclerosis](#) (MS), which is consistent with this patient's history of persistent MS symptoms that have failed to respond to various medication regimes.

D - Basiliximab

Explanation Why

[Basiliximab](#) is a [monoclonal antibody](#) that binds to the [CD25 alpha chain](#) of the [IL-2](#) receptor on the surface of [T cells](#), which prevents [T-cell proliferation](#). This mechanism makes the [antibody](#) useful as a prophylactic treatment to prevent post-[transplantation kidney](#) rejection. [Basiliximab](#) has no role in treating [multiple sclerosis](#).

E - Rituximab

Explanation Why

[Rituximab](#) is a humanized [monoclonal antibody](#) that causes the depletion of cells that express [CD20](#) glycoproteins on their surface ([B lymphocytes](#)). [Rituximab](#) is used to treat [rheumatoid arthritis](#), [immune thrombocytopenic purpura](#), [chronic lymphocytic leukemia](#), [B-cell non-Hodgkin lymphoma](#), and symptomatic [Waldenstrom macroglobulinemia](#). It does not bind [CD52](#) glycoproteins and would not be the treatment of choice in this patient with a history of refractory [multiple sclerosis](#).

F - Omalizumab

Explanation Why

[Omalizumab](#) is an anti-[IgE monoclonal antibody](#) that binds free and [B-cell](#) membrane-bound [IgE](#). It is used in the treatment of moderate to severe allergic asthma, which is associated with high levels of [IgE](#) and is refractory to treatment with [inhaled steroids](#) and long-acting [β2-agonists](#). [Omalizumab](#) does not bind [CD52](#) glycoproteins and would not be the treatment of choice in this patient with a history of refractory [multiple sclerosis](#).

G - Abciximab

Explanation Why

[Abciximab](#) is a chimeric [antibody](#) that targets [platelet](#) glycoprotein IIb/IIIa receptors and inhibits [platelet aggregation](#). It is used as an [antiplatelet medication](#) following percutaneous coronary interventions. It does not bind [CD52](#) glycoproteins and would not be the treatment of choice in this patient with a history of refractory [multiple sclerosis](#).

H - Cetuximab

Explanation Why

[Cetuximab](#) is a chimeric [epidermal growth factor receptor](#) (EGFR) [antibody](#) that causes EGFR internalization. [Cetuximab](#) is used in the treatment of colorectal and head and neck cancers. It does not bind to [CD52](#) glycoproteins and would not be the treatment of choice in this patient with a history of refractory [multiple sclerosis](#).

I - Natalizumab

Explanation Why

[Natalizumab](#) is a recombinant [monoclonal antibody](#) that targets [integrin](#) alpha-4 surface subunits on inflammatory [lymphocytes](#) and [monocytes](#), impairing the ability of cells to adhere to blood vessels and preventing auto-[inflammation](#). This [antibody](#) is used to treat [multiple sclerosis](#), but it is not the drug prescribed to this patient because it does not target [CD52](#) glycoproteins.

Question # 38

A 72-year-old woman comes to the emergency department 1 hour after the sudden onset of a diffuse, dull, throbbing headache. She also reports blurred vision, nausea, and one episode of vomiting. She has a history of poorly controlled hypertension. A photograph of her fundoscopic examination is shown. Which of the following is the most likely underlying cause of this patient's symptoms?



	Answer	Image
A	Hemorrhagic lacunar stroke	
B	Idiopathic intracranial hypertension	
C	Migraine headache	

	Answer	Image
D	Giant cell arteritis	
E	Hypertensive emergency	Hypertensive urgency Rapid and critical rise in blood pressure ≥ 180 and/or ≥ 120 with no signs of organ damage Headache Lightheadedness, vertigo Epistaxis Restlessness, insomnia Hypertensive emergency ⚠️ Rapid and critical increase in blood pressure ≥ 180 and/or ≥ 120 with signs of organ damage Intracranial hemorrhage, apoplexy Hypertensive encephalopathy Retinal hemorrhages Hypertensive acute heart failure, myocardial infarction Hypertensive pulmonary edema Aortic dissection Renal failure Potential triggers - Nonadherence to antihypertensive therapy - Medication that may exacerbate hypertension, e.g.: NSAIDs, MAO inhibitors, TCAs, cocaine, amphetamines, ecstasy, stimulant diet pills - Acute and rapidly progressing renal disorders - Pregnancy, eclampsia - Pheochromocytoma - Collagen vascular diseases (e.g., SLE) - Seizures
F	Epidural hematoma	
G	Transient ischemic attack	

Hint

Fundoscopy examination shows obscured disc margins, engorged retinal veins, and small hemorrhages around the optic disc margins, which are typical findings of papilledema.

Correct Answer

A - Hemorrhagic lacunar stroke

Explanation Why

A hemorrhagic [lacunar stroke](#) is possible given this patient's age and history of poorly controlled [hypertension](#). However, [lacunar strokes](#) manifest with one of five classic [stroke](#) syndromes, depending on the location of the [infarct](#) ([basal ganglia](#), [internal capsule](#), [thalamus](#), [corona radiata](#), or [pons](#)), each of which has characteristic motor and/or sensory findings. This patient does not have focal neurological signs on examination. Moreover, [papilledema](#) is not associated with [lacunar strokes](#) as these [infarcts](#) are, by definition, very small (< 15 mm) in size.

B - Idiopathic intracranial hypertension

Explanation Why

[Idiopathic intracranial hypertension \(IIH\)](#) typically manifests with [headache](#) in women of childbearing age; [obesity](#) is also a significant [risk factor](#). [IIH](#) would be very unlikely in this 72-year-old patient. While [IIH](#) can manifest with additional symptoms such as [papilledema](#), nausea, and vomiting, which are seen in this patient, its onset would not be acute. Furthermore, [IIH](#) often manifests with [visual field](#) loss and [abducens nerve palsy](#), neither of which are present here.

C - Migraine headache

Explanation Why

[Migraine headaches](#) are usually recurrent, acute, unilateral, throbbing/pulsatile [headaches](#) that sometimes include an [aura](#) and can also manifest with [nausea and vomiting](#). While this patient has nausea, vomiting, and [headache](#), she has no history of [migraine](#) or recurrent [headache](#), and new [migraine](#) in the elderly is unlikely. Moreover, [migraine](#) would not explain this patient's [papilledema](#).

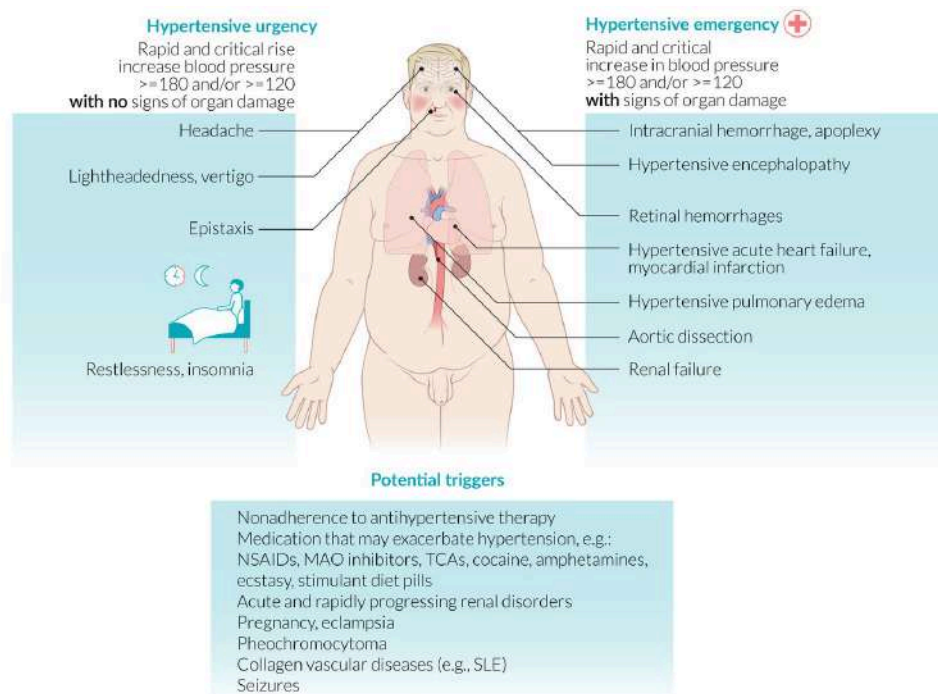
D - Giant cell arteritis

Explanation Why

[Giant cell arteritis \(GCA\)](#) is an important cause of [headache](#) in older patients. While this patient is 72 years of age and presents with acute end-organ, she does not have other expected findings of [GCA](#) (e.g., [jaw claudication](#), temporal tenderness, and constitutional symptoms). Furthermore, [GCA](#) is associated with acute visual loss due to retinal [artery](#) occlusion, not blurred vision and [papilledema](#).

E - Hypertensive emergency

Image



Explanation But

Although this patient presents with a dull, throbbing [headache](#) as opposed to the classic severe [thunderclap headache](#) of [subarachnoid hemorrhage \(SAH\)](#), her overall presentation is also concerning for [SAH](#), which must be promptly investigated and ruled out.

Explanation Why

[Hypertensive emergency](#) is the most likely diagnosis in this patient presenting with signs and symptoms of both severe [hypertensive retinopathy](#) and [hypertensive encephalopathy](#) (headache, nausea, and vomiting). Given her fundoscopic examination and history of poorly controlled [hypertension](#), a significantly [elevated blood pressure](#) would be expected in this patient ([systolic](#) $\geq$ 180 mm Hg and/or [diastolic](#) $\geq$ 120 mm Hg). Acute [hypertensive nephrosclerosis](#) (formerly referred to as [malignant nephrosclerosis](#)) is also commonly seen in [hypertensive emergency](#) and manifests with (usually microscopic) [hematuria](#) and elevated serum [creatinine](#). Her [hypertensive emergency](#) requires immediate treatment (often with [labetalol](#) or [nitroprusside](#)) to prevent further end-organ damage.

F - Epidural hematoma

Explanation Why

[Epidural hematoma](#) (blood between the [skull](#) and [dura mater](#)) end-organ in [head trauma](#) that damages the [middle meningeal artery](#). History of [epidural hematoma](#) classically involves a sudden loss of consciousness, transient return to normal sensorium (the [lucid interval](#)), then neurological compromise with the development of focal deficits. Diagnosis is most commonly made with a head CT that shows a biconvex, [hyperdense](#) collection. This patient, however, has no history of trauma, making an epidural bleed unlikely.

G - Transient ischemic attack

Explanation Why

[Transient ischemic attack](#) (TIA) manifests with acute focal neurological deficits (e.g., unilateral facial weakness) that spontaneously resolve in less than 24 hours (most last < 1 hour). Although this patient is at high risk for [TIA](#) (given her age and history of [hypertension](#)), she does not present with focal neurological deficits. Furthermore, [TIA](#) would not cause [papilledema](#).

Question # 39

A 57-year-old man is brought to the emergency department by his wife 20 minutes after having had a seizure. He has had recurrent headaches and dizziness for the past 2 weeks. An MRI of the brain shows multiple, round, well-demarcated lesions in the brain parenchyma at the junction between gray and white matter. This patient's brain lesions are most likely comprised of cells that originate from which of the following organs?

	Answer	Image
A	Breast	
B	Colon	
C	Thyroid	
D	Prostate	
E	Kidney	
F	Lung	
G	Skin	

Hint

The junction between the gray and white matter is the typical location for brain metastases, the most common type of intracranial tumors, which visualize as round, well-demarcated intraparenchymal lesions on MRI.

Correct Answer

A - Breast

Explanation Why

Although [breast cancers](#) have a tendency to [metastasize](#) to the brain, they are not the most common origin of [brain metastases](#). Moreover, cancers of the [breast](#) rarely occur in men.

B - Colon

Explanation Why

[Colon cancer](#) classically [metastasizes](#) hematogenously first to the [liver](#), as venous blood from the [colon](#) drains into the [portal vein](#) and the [hepatic sinusoids](#), seeding the [tumor](#) emboli within the [liver](#) parenchyma. Although [colon cancers](#) have a tendency to [metastasize](#) to the brain, they are not the most common origin of [brain metastases](#).

C - Thyroid

Explanation Why

[Thyroid cancers](#) that spread hematogenously (i.e., [follicular thyroid cancer](#), [anaplastic thyroid cancer](#), and [medullary thyroid cancer](#)) predominantly [metastasize](#) to the bone and [lung](#) but rarely to the brain. [Papillary thyroid cancer](#) [metastasizes](#) predominantly through [lymphatics](#) to the regional [lymph nodes](#); distant [metastases](#) from [papillary thyroid cancer](#) are uncommon.

D - Prostate

Explanation Why

[Prostate cancer](#) cells have a high affinity for [bone marrow endothelial](#) cells and, therefore, [metastasize](#) hematogenously primarily to bone (especially in the lumbosacral [spine](#) and [pelvis](#)). The [prostate](#) is unlikely to be the site of the primary [tumor](#) in a patient with [brain metastases](#).

E - Kidney

Explanation Why

[Renal cell carcinoma](#) most frequently [metastasizes](#) to the [lungs](#) as the [tumor](#) emboli enter the [renal vein](#) and [inferior vena cava](#) and reach the [lungs](#) via the [pulmonary artery](#). Although [kidney](#) cancers may rarely [metastasize](#) to the brain, they are not the most common origin of [brain metastases](#).

F - Lung

Explanation Why

Primary cancers of the [lung](#) (particularly [small cell lung cancer](#) and [adenocarcinoma of the lung](#)) are the most common origin of [brain metastases](#). The 2nd most common origin of [brain metastases](#) are cancers of the [breast](#) followed by [melanoma](#) and cancers of the [kidney](#) and [colon](#). [Metastatic](#) disease accounts for approx. 50% of all [brain tumors](#).

G - Skin

Explanation Why

Although [melanomas](#) have a tendency to [metastasize](#) to the brain, they are not the most common origin of [brain metastases](#).

Question # 40

A 70-year-old man with hypertension and type 2 diabetes mellitus is admitted to the hospital 8 hours after the onset of impaired speech and right-sided weakness. Two days after admission, he becomes confused and is difficult to arouse. His pulse is 64/min and blood pressure is 166/96 mm Hg. Pulse oximetry on room air shows an oxygen saturation of 95%. Fundoscopic examination shows bilateral optic disc swelling. He is intubated and mechanically ventilated. A CT scan of the brain shows hypoattenuation in the territory of the left middle cerebral artery with surrounding edema and a 1-cm midline shift to the right. Which of the following interventions is most likely to result in a decrease in this patient's intracranial pressure?

	Answer	Image
A	Decrease the blood pressure	
B	Increase the respiratory rate	
C	Increase the fraction of inhaled oxygen	
D	Increase the positive end-expiratory pressure	
E	Decrease the heart rate	

Hint

Patients with large strokes are at increased risk of developing cerebral edema in the early post-stroke period. An increase in intracranial pressure (ICP) due to cerebral edema can cause impaired consciousness, papilledema, and an increase in blood pressure with a reduction in heart rate (Cushing reflex).

Correct Answer

A - Decrease the blood pressure

Explanation Why

The [cerebral perfusion pressure](#) (CPP), depends on the ICP and the [mean arterial pressure](#) (CPP = [MAP](#) – ICP). In acute [strokes](#), vasoregulation is often lost and adequate cerebral oxygenation depends directly on the [mean arterial pressure](#). Aggressive blood pressure reduction in this patient should be avoided as it may result in reduced perfusion and increased secondary neurologic injury.

B - Increase the respiratory rate

Explanation Why

Cerebral perfusion is regulated by [pCO₂](#) and patients with raised [intracranial pressure](#) who are mechanically ventilated can be managed with therapeutic [hyperventilation](#). [Hyperventilation](#) leads to a reduction in the [partial pressure](#) of carbon dioxide ([pCO₂](#)) which leads to vasoconstriction with subsequent reduction in cerebral blood flow and fall in [intracranial pressure](#). Current guidelines recommend titrating the [respiratory rate](#) to achieve a target [pCO₂](#) of between 28–32 mm Hg.

C - Increase the fraction of inhaled oxygen

Explanation Why

A pO₂ < 55 mmHg would increase the [cerebral perfusion pressure](#) and subsequently aggravate the existing [cerebral edema](#) in this patient. However, the pO₂ only plays an important role in cerebral perfusion regulation in cases of severe [hypoxia](#), which this patient does not have evidence of (normal [pulse oximetry](#) findings). Increasing the inhaled oxygen concentration (e.g., [FiO₂](#)) would be unlikely to affect his ICP.

D - Increase the positive end-expiratory pressure

Explanation Why

Increasing [positive end-expiratory pressure \(PEEP\)](#) is a strategy used with mechanically ventilated patients to prevent end-expiratory alveolar collapse and improve oxygenation. However, increasing [PEEP](#) reduces [venous return](#), including the [venous return](#) from the brain, and may be detrimental to this patient with [cerebral edema](#). Increasing [PEEP](#) is commonly used to manage [acute respiratory distress syndrome](#) but is not recommended for [cerebral edema](#).

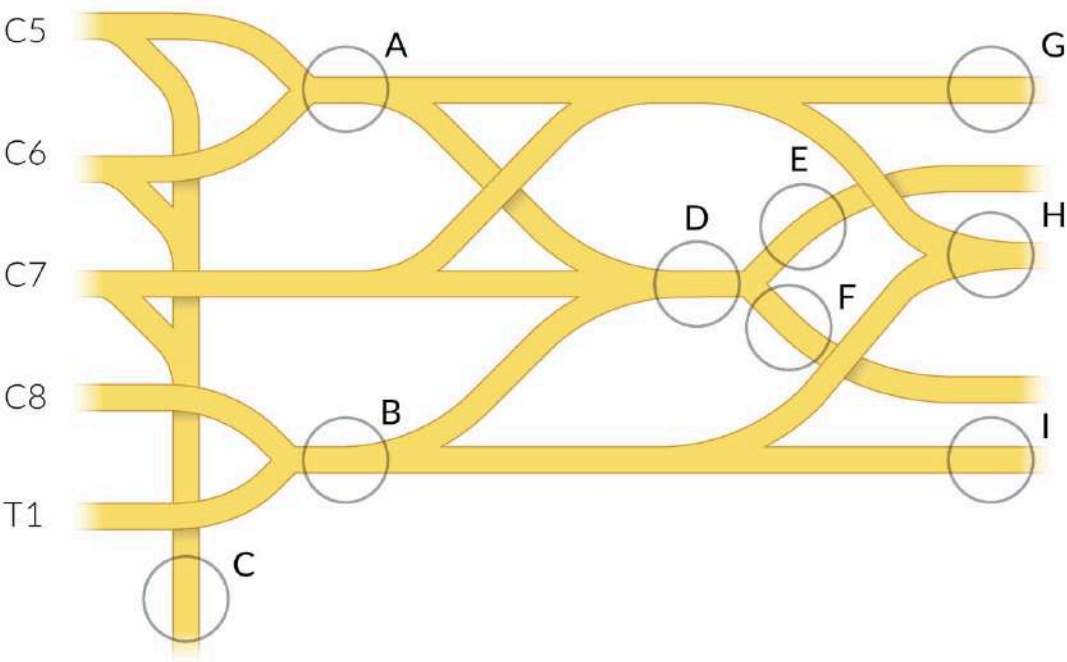
E - Decrease the heart rate

Explanation Why

Decreasing the [heart rate](#) is a management strategy that may be employed in certain clinical scenarios such as [acute myocardial infarction](#) or [decompensated heart failure](#). However, the [cerebral perfusion pressure](#) (CPP) depends primarily on the ICP and the [mean arterial pressure](#) ($CPP = MAP - ICP$); the [heart rate](#) does not play an important role unless it is affecting the [mean arterial pressure](#). Furthermore, this patient already has a borderline low [heart rate](#) due to the [Cushing reflex](#).

Question # 1

A 24-year-old man is brought to the emergency room after he was involved in a motor vehicle accident. He complains of pain in his right shoulder. Physical examination shows bruising and tenderness to palpation just below the right coracoid process. He is unable to flex the right elbow or supinate the right forearm against resistance. There is decreased sensation to light touch over the anterolateral forearm. Which of the following labeled structures of the brachial plexus is most likely to be injured?



	Answer	Image
A	A	
B	B	
C	C	

	Answer	Image
D	D	
E	E	
F	F	
G	G	
H	H	
I	I	

Hint

Weakness with elbow flexion and forearm supination along with decreased sensation over the anterolateral forearm is consistent with an injury to the musculocutaneous nerve.

Correct Answer

A - A

Explanation Why

Traumatic damage to the [upper trunk of the brachial plexus](#) (C5–C6) manifests with [Erb palsy](#), which also presents with impaired [flexion](#) and [supination](#) of the forearm. However, the sensory loss expected would not only occur over the [lateral](#) arm but extend to the thumb. Moreover, impaired [external rotation](#), [abduction](#), and wrist extension would also be expected.

B - B

Explanation Why

Damage to the [lower trunk of the brachial plexus](#) (C8–T1) occurs through hyperabduction trauma. It results in Klumpke deformity and a characteristic [claw hand](#), which results in impaired [flexion](#) of the [MCP](#) with an inability to extend the DIP and PIP [joints](#). Moreover, damage to the plexus is accompanied by a sensory loss over the little finger and [medial](#) surface of forearm and arm. This patient's presentation is not consistent with an injury to the [lower trunk of the brachial plexus](#).

C - C

Explanation Why

Damage to the [long thoracic nerve](#) (C5–C7) is seen in trauma to the [posterior](#) scapular and axillary regions (e.g., in [mastectomies](#) with axillary node dissection). It results in impairment of the [serratus anterior muscle](#) and a [winged scapula](#). Another feature is impaired arm [abduction](#) beyond 90 degrees. This patient's presentation is not consistent with [long thoracic nerve injury](#).

D - D

Explanation Why

Damage to the [posterior cord of the brachial plexus](#) (C5–T1) is seen in forceful traction injuries. This structure gives rise to the radial nerve and the [axillary nerve](#). The radial nerve innervates wrist extensors and the [axillary nerve](#) innervates the deltoid and [teres minor](#). Damage to the [posterior cord](#) commonly manifests with [wrist drop](#) due to radial nerve damage, and with loss of upper limb [abduction](#) above 15 degrees and decreased sensation over the [deltoid muscle](#) due to [axillary nerve](#) damage. This patient's presentation is not consistent with [posterior cord](#) injury.

E - E

Explanation Why

Damage to the [axillary nerve](#) (C5–C6) is commonly seen in [surgical neck fractures](#) of the [humerus](#) and results in impairment of the [deltoid muscle](#). The clinical presentation includes a loss of [abduction](#) of the upper limb above 15 degrees and decreased sensation over the [deltoid muscle](#). This patient's presentation is not consistent with [axillary nerve](#) damage.

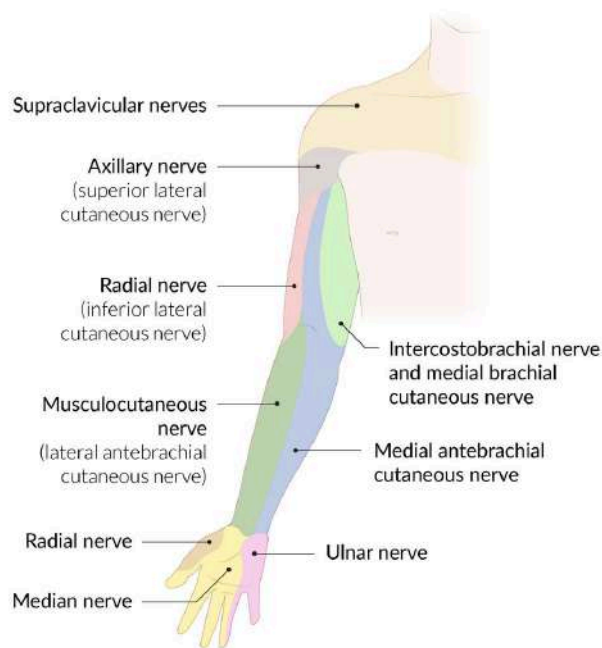
F - F

Explanation Why

Traumatic damage to the radial nerve (C5–T1) is seen in midshaft humeral [fractures](#) or prolonged axillary compression, causing, e.g., [Saturday night palsy](#). Clinical presentation includes [wrist drop](#), weakened hand grip, and loss of sensation over the [posterior](#) aspect of the upper limb. This patient's presentation is not consistent with radial nerve damage.

G - G

Image



Explanation Why

The [musculocutaneous nerve](#) arises from the [lateral cord](#) of the [brachial plexus](#) (union of C5–C7 [nerve roots](#)). Damage to this nerve can arise from upper limb compression or laceration to the [lateral](#) aspect of the arm. This patient's inability to flex the right [elbow](#) and [supinate](#) the right forearm in conjunction with a history of trauma is highly suggestive of an [injury to the musculocutaneous nerve](#).

H - H

Explanation Why

Traumatic [median nerve palsy](#) (C5–T1) most commonly occurs with [supracondylar fractures](#) of the [humerus](#). The clinical presentation includes impaired wrist [pronation](#) and [flexion](#), impaired [lateral flexion](#) of the index and middle finger, loss of thumb opposition ([hand of benediction](#), [ape hand](#)

deformity), and sensory loss over the index and middle finger and the radial side of the ring finger. This patient's presentation is not consistent with [median nerve injury](#).

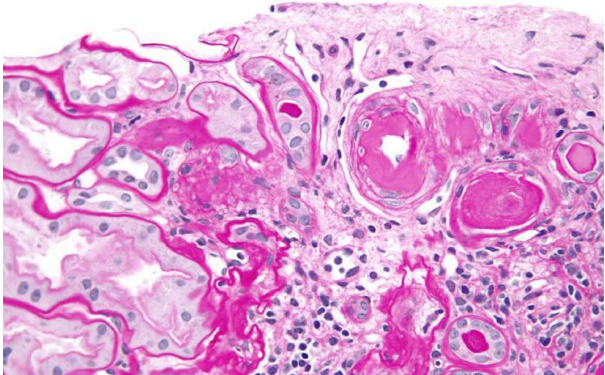
I - I

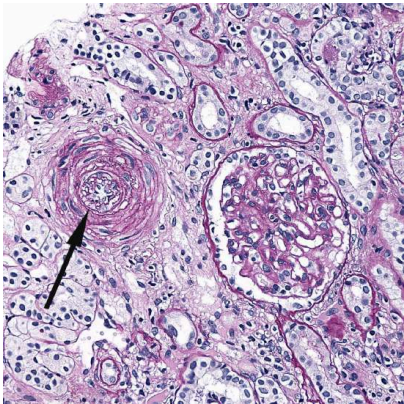
Explanation Why

Traumatic damage to the ulnar nerve (C8–T1) is seen in [fractures](#) of the [medial epicondyle](#) of the [humerus](#) or the hook of the [hamate](#). It results in impaired [flexion](#) of the ring and little finger ([ulnar claw](#) deformity) as well as loss of sensation over the little finger and the [medial](#) side of the ring finger. This patient's presentation is not consistent with [ulnar nerve injury](#).

Question # 2

A 61-year-old woman comes to the physician for evaluation of numbness and a burning sensation in her feet for the past 5 months. She has type 2 diabetes mellitus and hypercholesterolemia. Her blood pressure is 119/82 mm Hg. Neurologic examination shows decreased sensation to pinprick, light touch, and vibration over the soles of both feet. There is a nontender ulcer on the plantar surface of her left foot. Pedal pulses are strong bilaterally. Her hemoglobin A1c concentration is 8.6%. Which of the following processes is most likely involved in the pathogenesis of this patient's current symptoms?

	Answer	Image
A	Demyelination of posterior columns and lateral corticospinal tracts	
B	Accumulation of lipids and foam cells in arteries	
C	Increased protein deposition in endoneurial vessel walls	
D	Dystrophic calcification of arterial media and intima	

	Answer	Image
E	Osmotic damage to oligodendrocyte nerve sheaths	
F	Elevated hydrostatic pressure in arteriolar lumen	

Hint

In a diabetic individual with elevated blood sugar ($\uparrow$ HbA1c), the presence of symmetric distal sensory neuropathy and a painless foot ulcer is highly suggestive of diabetic neuropathy.

Correct Answer

A - Demyelination of posterior columns and lateral corticospinal tracts

Explanation Why

[Vitamin B12 deficiency](#) can cause [demyelination](#) of the [posterior column](#) and [lateral corticospinal tracts](#) through a process called [subacute combined degeneration](#) (SCD). The neuropathy that results is clinically similar to [diabetic peripheral neuropathy](#), with symptoms that include [hyporeflexia](#), decreased sensation, and [pain](#). However, this patient has neither [upper motor neuron signs](#) of the [corticospinal tract](#) degeneration of SCD ([spasticity](#), [hyperreflexia](#), and extensor [plantar reflex](#)), nor any other [signs of vitamin B12 deficiency](#) ([macrocytic anemia](#), [glossitis](#), or [cheilitis](#)).

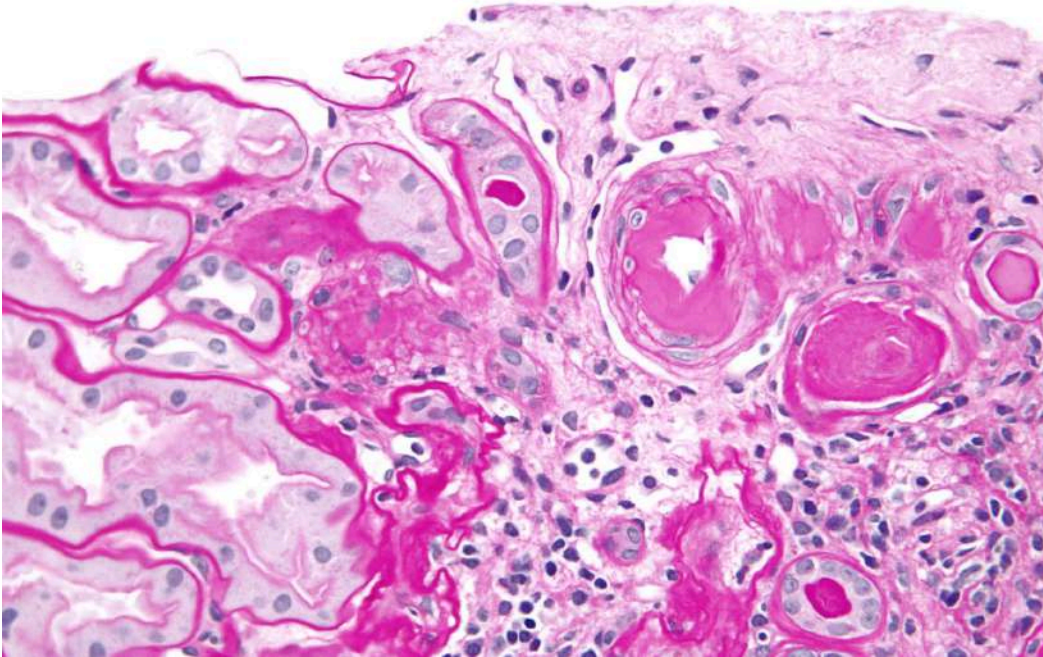
B - Accumulation of lipids and foam cells in arteries

Explanation Why

Accumulation of lipids and [foam cells](#) in [arteries](#) is one of the major steps in the pathophysiology of [atherosclerosis](#). [Foam cells](#) and [platelets](#) promote [smooth muscle cell](#) migration to large extracellular lipid cores. By consuming lipids, the [smooth muscle cells](#) proliferate in conjunction with [fibrosis](#) and [foam cell](#) deposition, further expanding the atherosclerotic lesion. While this process may lead to [peripheral vascular disease](#), in this case, the uncontrolled diabetic patient is more likely to develop [hyaline arteriolosclerosis](#), which does not involve lipids and [foam cells](#).

C - Increased protein deposition in endoneural vessel walls

Image



Explanation Why

Although there are multiple pathophysiological mechanisms that play a role in the development of [diabetic peripheral neuropathy](#), [microvascular](#) disease is a key contributing factor. Chronic [hyperglycemia](#) leads to the formation of nonenzymatically glycosylated plasma and tissue [proteins](#), which leads to [hyalinization](#) of the [basal lamina](#) and thickening of the [basement membrane](#) of endoneural vasculature. As a result, nerve [ischemia](#) occurs, leading to a reduction of [intraepidermal](#) nerve fiber density.

D - Dystrophic calcification of arterial media and intima

Image



Explanation Why

[Dystrophic calcification](#) of arterial media and [intima](#) is seen in patients with [Mönckeberg sclerosis](#). While this process is generally age-related, diabetics are predisposed to it as well. However, Mönckeberg media sclerosis is more common in larger [arteries](#), not the small peripheral vessels affected by this diabetic patient's [peripheral vascular disease](#).

E - Osmotic damage to oligodendrocyte nerve sheaths

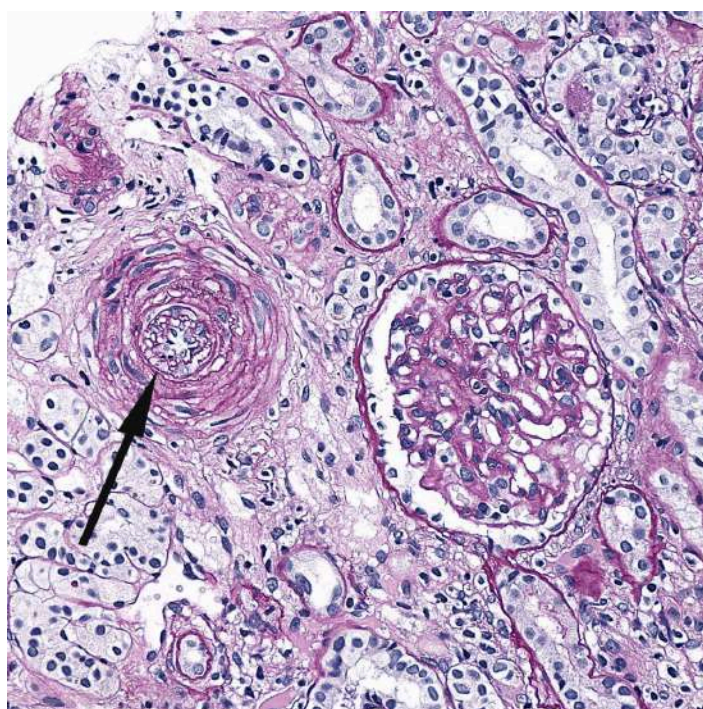
Explanation Why

Osmotic damage to [oligodendrocytes](#), solely located in the [central nervous system](#), occurs during [central pontine myelinolysis](#). The resulting cell damage leads to encephalopathy-like symptoms, such as nausea, [headaches](#), confusion, and [seizures](#), none of which are seen in this patient. However,

chronic [hyperglycemic](#) patients may have osmotic-related peripheral nerve damage due to [sorbitol](#) accumulation. Glucose is often trapped within cells through conversion to [sorbitol](#) via [aldose reductase](#). Although some tissues then convert [sorbitol](#) to fructose via [sorbitol dehydrogenase](#), insufficient activity or concentration of the enzyme leads to the accumulation of [sorbitol](#), raising the osmolality of the cell and resulting in osmotic damage to peripheral nerve fibers.

F - Elevated hydrostatic pressure in arteriolar lumen

Image



Explanation Why

Elevated intraluminal [hydrostatic pressure](#) in the arteriolar lumen is observed in patients with [high blood pressure](#). Chronically [elevated blood pressures](#) (such as in [malignant hypertension](#)) can lead to [hyperplastic arteriosclerosis](#). While diabetics are predisposed to [hyperplastic arteriosclerosis](#), this patient has normal blood pressure, so it is an unlikely etiology for her neuropathy.

Question # 3

A 64-year-old man is brought to the emergency department because of dull lower abdominal pain for 3 hours. He has not urinated for 24 hours and has not passed stool for over 3 days. He was diagnosed with herpes zoster 4 weeks ago and continues to have pain even after his rash resolved. He has hypertension, benign prostatic hyperplasia, and coronary artery disease. Physical examination shows a tender, palpable suprapubic mass. Bowel sounds are hypoactive. Abdominal ultrasound shows a large anechoic mass in the pelvis. Which of the following drugs most likely accounts for this patient's current symptoms?

	Answer	Image
A	Simvastatin	
B	Pregabalin	
C	Dutasteride	
D	Tamsulosin	
E	Amlodipine	
F	Valproate	
G	Desipramine	

Hint

Severe lower abdominal pain, anuria, and a palpable anechoic lower abdominal mass suggest acute urinary retention (AUR). Given this patient's concurrent constipation and hypoactive bowel sounds, he is most likely taking a drug with strong anticholinergic side effects.

Correct Answer

A - Simvastatin

Explanation Why

[Simvastatin](#) is an [HMG-CoA reductase inhibitor](#) indicated for the treatment of [coronary heart disease](#), which this patient has. While [simvastatin](#) can cause [constipation](#), it does not possess [anticholinergic](#) effects and therefore would not explain this patient's [acute urinary retention](#) or hypoactive bowel sounds.

B - Pregabalin

Explanation Why

[Pregabalin](#) is an [anticonvulsant](#) that can be used in the treatment of polyneuropathies such as [postherpetic neuralgia](#), which this patient has. It is a structural analog of the [GABA neurotransmitter](#) and binds to presynaptic [neurons](#), reducing calcium currents and decreasing [neurotransmitter](#) release. While [pregabalin](#) can cause [constipation](#), it does not possess [anticholinergic](#) effects and therefore would not explain this patient's [acute urinary retention](#) or hypoactive bowel sounds.

C - Dutasteride

Explanation Why

Dutasteride is a [5-alpha-reductase inhibitor](#) that can be used in the treatment of [benign prostatic hyperplasia](#), which this patient has. It decreases intraprostatic [DHT](#) levels, reducing [prostate](#) size and thereby relieving [prostatic](#) obstruction of the [urethra](#). Dutasteride does not possess [anticholinergic](#) effects and therefore would not explain this patient's acute symptoms.

D - Tamsulosin

Explanation Why

[Tamsulosin](#) is a selective [alpha-1 adrenergic receptor](#) antagonist used in the treatment of [benign prostatic hyperplasia](#), which this patient has. [Tamsulosin](#) acts on [alpha-1 receptors](#), relaxing the [smooth muscle](#) of the [internal urethral sphincter](#) to facilitate [bladder](#) voiding. [Tamsulosin](#) does not possess [anticholinergic](#) effects and therefore would not explain this patient's acute symptoms.

E - Amlodipine

Explanation Why

[Amlodipine](#) is a dihydropyridine [calcium channel blocker](#) used in the treatment of [hypertension](#), which this patient has. However, it does not possess [anticholinergic](#) effects and therefore would not explain this patient's acute symptoms

F - Valproate

Explanation Why

[Valproate](#) is a classic [anticonvulsant](#) that offers only limited benefits for the treatment of [postherpetic neuralgia](#). While [valproate](#) can cause [constipation](#), it does not possess [anticholinergic](#) effects and therefore would not explain this patient's [acute urinary retention](#) or hypoactive bowel sounds.

G - Desipramine

Explanation But

The treatment of choice for patients with [AUR](#) is relief of the overfilled [bladder](#) via transurethral catheterization.

Explanation Why

[Desipramine](#) is a [tricyclic antidepressant](#) (TCA) used for the treatment of neuropathies such as [postherpetic neuralgia](#). This class of drugs has alpha-reductase [anticholinergic](#) effects that explain this patient's [acute urinary retention](#) and [constipation](#). Because of their [anticholinergic effects](#), TCAs should be used cautiously in patients with conditions that predispose to [acute urinary retention](#), such as [benign prostatic hyperplasia](#), as well as in elderly patients.

Question # 4

A 61-year-old woman comes to the emergency department because of a 2-hour history of headache, nausea, blurred vision, and pain in the left eye. She has had similar symptoms in the past. Her vital signs are within normal limits. The left eye is red and is hard on palpation. The left pupil is mid-dilated and nonreactive to light. Administration of which of the following drugs should be avoided in this patient?

	Answer	Image
A	Acetazolamide	
B	Epinephrine	
C	Pilocarpine	

	Answer	Image
D	Apraclonidine	The diagram illustrates the effects of Apraclonidine on the eye. It shows the drainage of aqueous humor through the trabecular meshwork and Schlemm's canal. Apraclonidine, an α_1 agonist, causes vasoconstriction of the ciliary muscle, leading to a decrease in aqueous humor production. It also causes relaxation of the episcleral veins, leading to a decrease in episcleral venous pressure, which in turn increases the outflow of aqueous humor through the trabecular meshwork. The diagram also shows the effects of other drugs: PGF 2a (widening of trabecular meshwork), Cholinimetics (contraction of ciliary muscle), and beta-blockers (depression of ciliary epithelial cells, leading to decreased aqueous humor production).
E	Timolol	The diagram illustrates the effects of Timolol on the eye. It shows the drainage of aqueous humor through the trabecular meshwork and Schlemm's canal. Timolol, a β-blocker, causes depression of the ciliary epithelial cells, leading to a decrease in aqueous humor production. It also causes relaxation of the episcleral veins, leading to a decrease in episcleral venous pressure, which in turn increases the outflow of aqueous humor through the trabecular meshwork. The diagram also shows the effects of other drugs: PGF 2a (widening of trabecular meshwork), Cholinimetics (contraction of ciliary muscle), and α_1 agonists (vasoconstriction of the ciliary muscle, leading to decreased aqueous humor production).

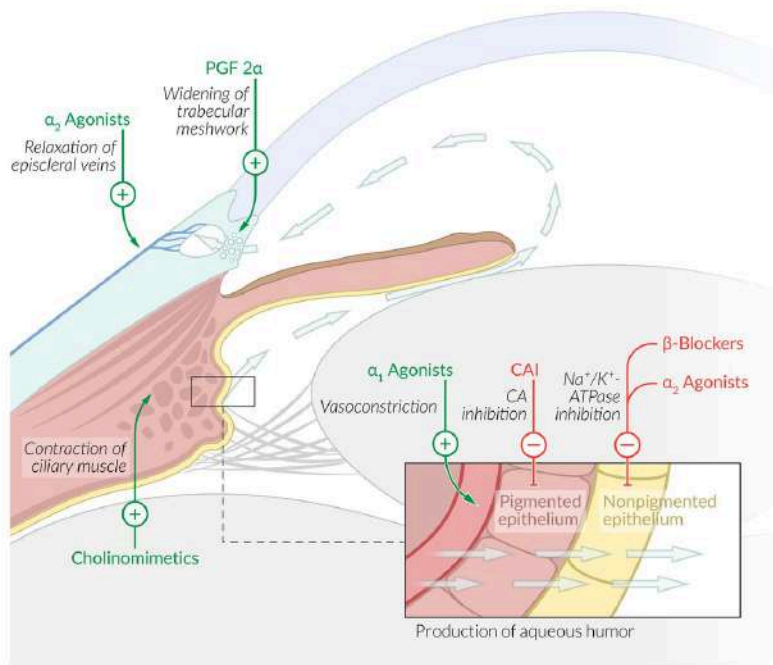
Hint

This patient has a unilateral red, hard, severely painful eye with a mid-dilated, nonreactive pupil as well as frontal headaches, vomiting, and nausea. These features are consistent with acute angle-closure glaucoma.

Correct Answer

A - Acetazolamide

Image

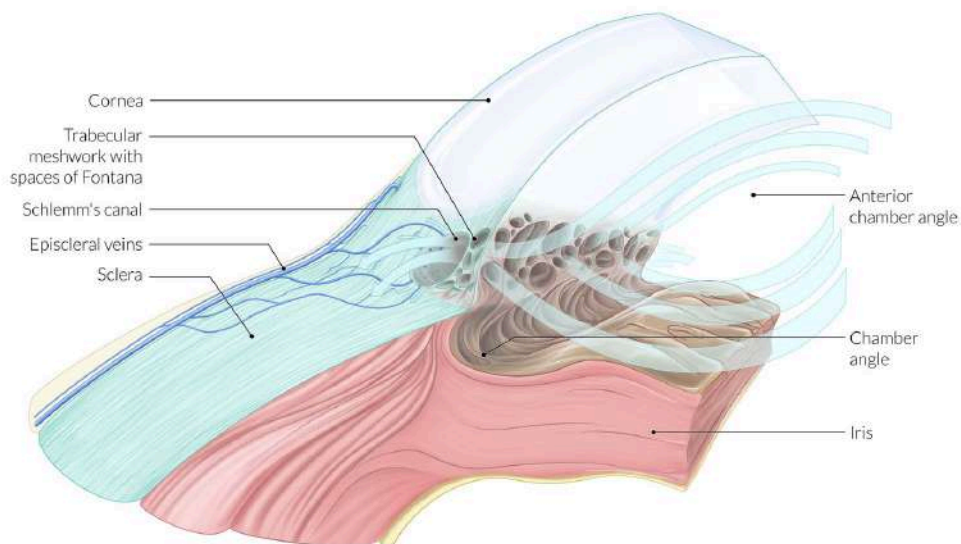


Explanation Why

[Acetazolamide](#) reduces [aqueous humor](#) production via [carbonic anhydrase](#) inhibition and is often given in conjunction with other medications for the treatment of acute [angle-closure glaucoma](#). [Acetazolamide](#) should be avoided in individuals with [sulfa drug allergy](#), [cirrhosis](#), or severe [hypokalemia](#).

B - Epinephrine

Image

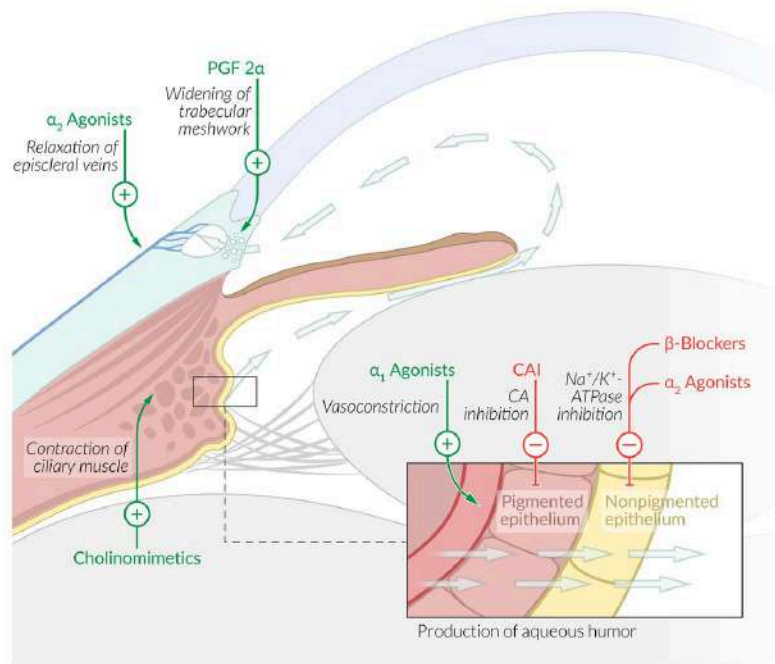


Explanation Why

[Epinephrine](#) is an [alpha-adrenergic](#) and [beta-adrenergic](#) receptor [agonist](#). [Epinephrine](#) is used topically to treat [open-angle glaucoma](#) because [alpha-1 receptor](#) stimulation induces vasoconstriction and subsequently decreases [aqueous humor](#) production. Alpha-1 receptor [agonism](#) also causes pupillary dilation ([mydriasis](#)), which decreases the iridocorneal angle and subsequently decreases [aqueous humor](#) outflow. In individuals with [angle-closure glaucoma](#) such as this patient, [mydriasis](#) can rapidly increase [intraocular pressure](#) and lead to permanent loss of vision. Therefore, [epinephrine](#) is contraindicated in this patient. [Mydriatic](#) eyedrops (e.g., [atropine](#), [homatropine](#), and [tropicamide](#)), which are often used for ophthalmologic examination, should also be avoided in patients suspected to have angle-closure [glaucoma](#) for the same reason.

C - Pilocarpine

Image

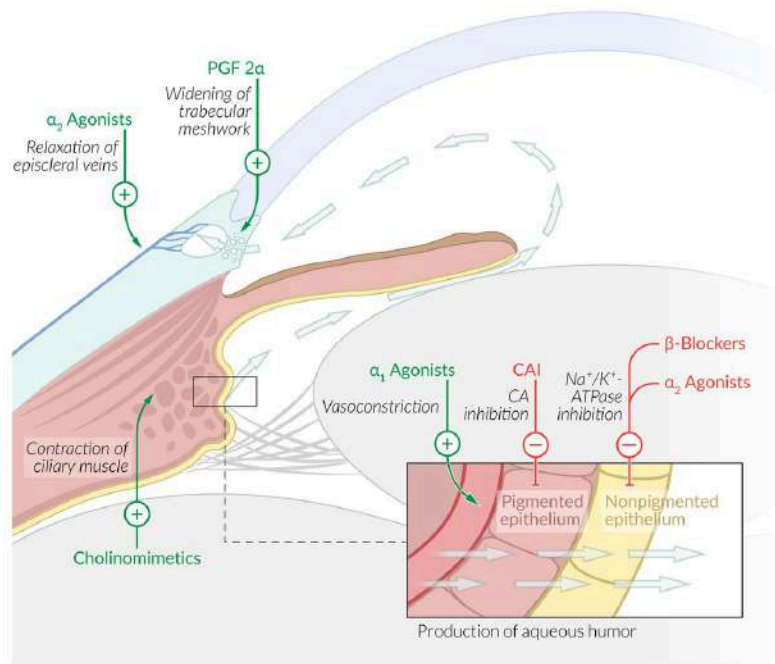


Explanation Why

Pilocarpine, a muscarinic agonist, is used to treat primary angle-closure glaucoma. M3 receptor stimulation causes miosis, which opens the iridocorneal angle and subsequently reduces intraocular pressure by increasing aqueous humor outflow. Pilocarpine is contraindicated in patients with asthma or COPD, and in cases of angle-closure glaucoma secondary to iritis or lens luxation because miosis can worsen eye pain or glaucoma. The history of similar symptoms in the past suggests primary rather than secondary angle-closure glaucoma.

D - Apraclonidine

Image

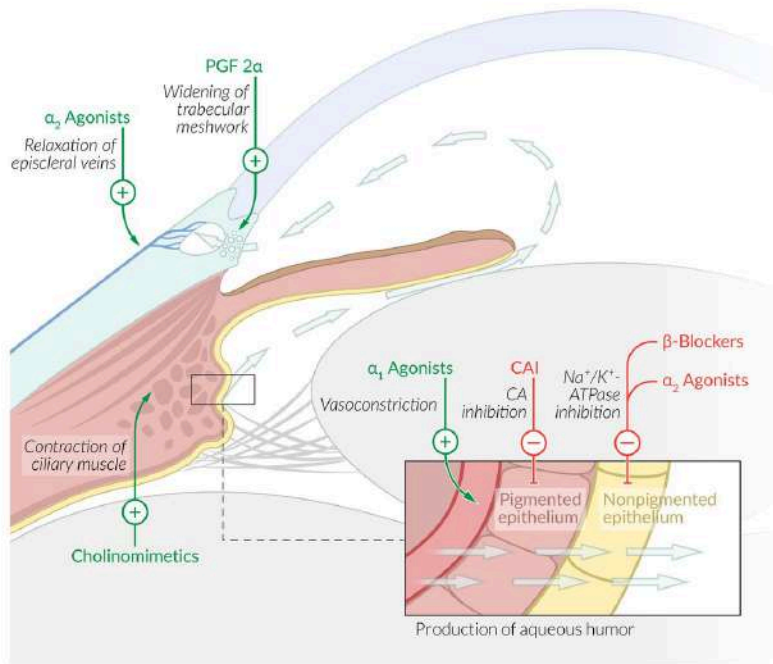


Explanation Why

[Apraclonidine](#), an alpha-2 agonist, is commonly used to acutely reduce [intraocular pressure](#) because it decreases [aqueous humor](#) production. [Apraclonidine](#) is a component of the treatment regimen for individuals with acute [angle-closure glaucoma](#) and would be indicated in this patient. This alpha-2 [agonist](#) should be avoided in individuals with hypersensitivity to [apraclonidine](#) or [clonidine](#) and in patients taking [MAO inhibitors](#).

E - Timolol

Image

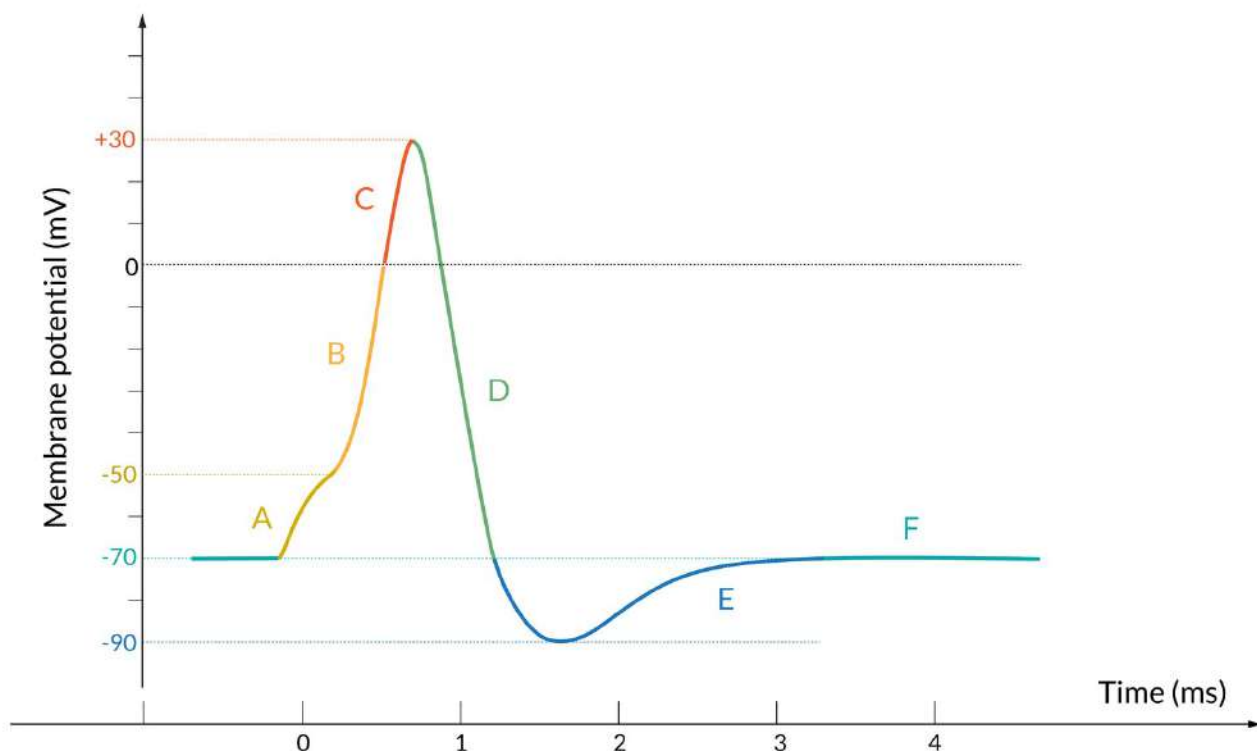


Explanation Why

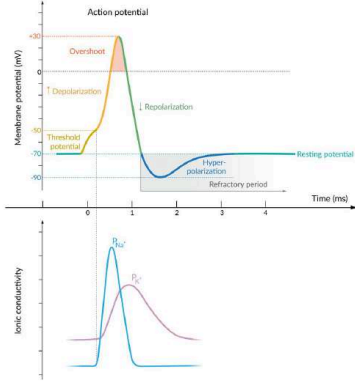
Timolol, a nonselective beta blocker, is commonly used in the treatment of acute angle-closure glaucoma because the inhibition of beta-2 receptors decreases aqueous humor production and leads to contraction of the ciliary muscle. This process increases the pore size of trabecular meshwork and subsequently increases aqueous outflow. Timolol should be avoided in individuals with asthma, COPD, or a heart block.

Question # 5

An investigator is studying the reaction of mutated voltage-gated potassium channel subunits. The mutation alters gating properties by reducing the potassium conductance through these channels, which manifests on ECG with a prolongation of the QT interval. Which of the following labeled phases of the action potential will be most affected by this mutation?



	Answer	Image
A	A	
B	B	
C	C	

	Answer	Image
D	D	
E	E	
F	F	

Hint

QT interval prolongation (long QT syndrome) is often a result of a reduction in efflux of potassium from the cell through the voltage-gated K^+ channels during the repolarization phase of the action potential.

Correct Answer

A - A

Explanation Why

A represents the phase leading up to the [threshold potential](#) (-50 mV), the all-or-nothing cutoff at which enough current is administered to the cell to begin membrane [depolarization](#). Reaching this potential is contingent upon sufficient [neurotransmitter](#) binding to receptors to trigger the opening of Na^+ channels and generate a full [action potential](#). It does not involve [voltage-gated \$\text{K}^+\$ channels](#).

B - B

Explanation Why

B represents the [depolarization](#) phase of the [action potential](#), characterized by a rapid rise in membrane potential. It occurs via the massive influx of Na^+ ions through [voltage-gated \$\text{Na}^+\$ channels](#) that drive the membrane potential towards the [equilibrium potential](#) for Na^+ (+60 mV). During this phase, all [voltage-gated \$\text{K}^+\$ channels](#) remain closed. Therefore, the properties of the [depolarization](#) phase are determined solely by sodium channels, and alterations to voltage-gated K^+ channels will have no effect on this phase of the [action potential](#).

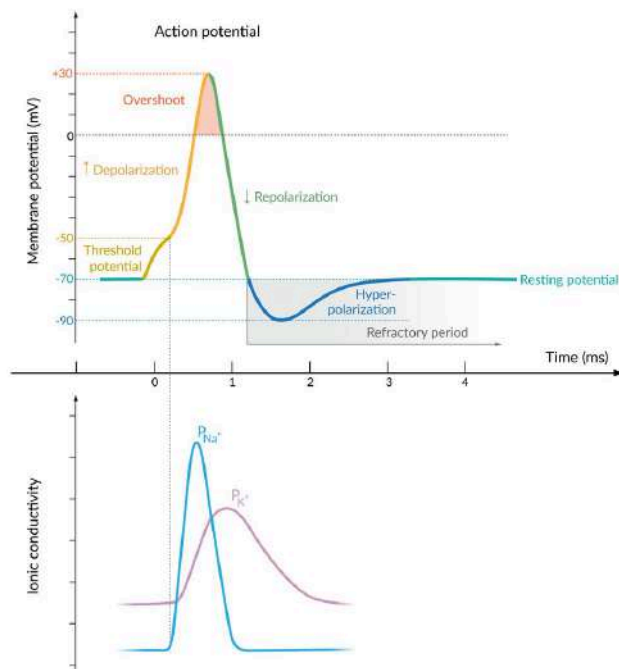
C - C

Explanation Why

C represents the overshoot phase, the point at which the membrane potential passes neutral (0 mV) and continues to depolarize until the peak [action potential](#) is reached (approx. +30 mV). During this period, most Na^+ channels are open, but the [voltage-gated \$\text{K}^+\$ channels](#) are almost entirely closed. While this mutation, which reduces the voltage-gated K^+ channel current, may then have a small effect on the overshoot section due to the few K^+ channels that begin to open at this point, it will have a much more profound effect on a different phase of the [action potential](#).

D - D

Image



Explanation Why

D represents the [repolarization](#) phase of the [action potential](#), where the cell is driven back towards the resting default state. This phase is primarily driven by potassium efflux from [voltage-gated \$K^+\$ channels](#) as the voltage-gated Na^+ channels are now closed. This mutation in the voltage-gated K^+ channels alters gating properties so that there is a reduction in the repolarizing K^+ current. This decrease in [repolarization](#) current will prolong the period of time during which the ventricles are fully depolarized. This manifests as a prolonged [QT interval](#) on [ECG](#).

E - E

Explanation Why

E represents the [hyperpolarization](#) phase of the [action potential](#), the point at which membrane potential drives below the [resting potential](#) on its return to baseline. It is caused by the continued efflux of some K^+ channels after [repolarization](#) such that the membrane potential approaches the equilibrium potential of K^+ (-90 mV). During this period, Na^+ channels are briefly inactivated, preventing a new [action potential](#) from being generated. This is known as the [refractory period](#). This mutation will not greatly affect this phase of the [action potential](#) because it does not affect the [equilibrium potential](#) for K^+ .

F - F

Explanation Why

F represents the return to the default excitable state of the cell, the [resting membrane potential](#), following a full [action potential](#) (AP). At this resting voltage, determined by the relative intracellular and extracellular concentrations of Na^+ and K^+ , Voltage-gated K^+ and Na^+ channels are closed but can be activated again to initiate a new AP. Since this mutation is specific to [voltage-gated \$K^+\$ channels](#), it will not affect the [resting membrane potential](#).

Question # 6

An investigator is studying the principles of cell-to-cell signaling of the autonomic nervous system. It is found that the adrenal medulla has receptors that, when activated, result in the immediate opening of Na^+ , Ca^{2+} , and K^+ channels, which subsequently leads to the secretion of epinephrine and norepinephrine. These receptors are structurally most similar to which of the following receptors?

	Answer	Image
A	H ₂ receptors of the stomach	
B	Beta 2 receptors of the lungs	
C	M ₃ receptors of the sweat glands	
D	Alpha 1 receptors of the bladder neck	
E	M ₂ receptors of heart	
F	D ₂ receptors of the basal ganglia	
G	N _M receptors of the quadriceps femoris muscle	

Hint

The studied receptors in the adrenal medulla are ligand-gated ion channels of the sympathetic nervous system.

Correct Answer

A - H₂ receptors of the stomach

Explanation Why

[H₂ receptors](#) of the [stomach](#) are [histamine](#) receptors that increase [gastric acid](#) secretion by [parietal cells](#). In contrast to the [ligand](#)-gated channel structure seen in the receptors of the [adrenal medulla](#), [H₂ receptors](#) are [chronotropic](#) receptors, meaning they act via the [cAMP](#) pathway to stimulate [adenylate cyclase](#) and increase its activity.

B - Beta 2 receptors of the lungs

Explanation Why

[Beta 2 receptors](#) (β_2) of the [lungs](#) are adrenergic receptors responsible for the relaxation of bronchial [smooth muscles](#). In contrast to the [ligand](#)-gated channel structure seen in the receptors of the [adrenal medulla](#), [\$\beta_2\$ receptors](#) are [Gs protein](#)-coupled receptors, meaning they act via the [cAMP](#) pathway to stimulate [adenylate cyclase](#) and increase its activity.

C - M₃ receptors of the sweat glands

Explanation Why

[M₃](#) receptors of the [sweat glands](#) are muscarinic [acetylcholine](#) receptors of the [sympathetic](#) pathway that promote [diaphoresis](#). In contrast to the [ligand](#)-gated channel structure seen in the receptors of the [adrenal medulla](#), [M₃ receptors](#) are Gq protein-coupled receptors, meaning they act via the [inositol triphosphate](#) pathway to increase intracytoplasmic calcium concentration.

D - Alpha 1 receptors of the bladder neck

Explanation Why

[Alpha 1 receptors](#) (α_1) of the [bladder neck](#) are adrenergic receptors that promote contraction of [smooth muscles](#), enhancing urinary continence. In contrast to the [ligand](#)-gated channel structure seen in the receptors of the [adrenal medulla](#), [\$\alpha_1\$ receptors](#) are Gq protein-coupled receptors, meaning they act via the [inositol triphosphate](#) pathway to increase intracytoplasmic calcium concentration.

E - M₂ receptors of heart

Explanation Why

M₂ receptors of the [heart](#) are muscarinic [acetylcholine](#) receptors that have a negative [chronotropic](#) effect and reduce atrial contractility. In contrast to the [ligand](#)-gated channel structure seen in the receptors of the [adrenal medulla](#), M₂ receptors are Gi protein-coupled receptors, meaning they act via the [cAMP](#) pathway to decrease [adenylate cyclase](#) activity.

F - D₂ receptors of the basal ganglia

Explanation Why

D₂ receptors of the [basal ganglia](#) are [dopaminergic](#) receptors that inhibit the [indirect pathway of movement](#). In contrast to the [ligand](#)-gated channel structure seen in the receptors of the [adrenal medulla](#), [D₂ receptors](#) are [Gi protein-coupled receptors](#), meaning they act via the [cAMP](#) pathway to decrease [adenylate cyclase](#) activity.

G - N_M receptors of the quadriceps femoris muscle

Explanation Why

N_M receptors at the [neuromuscular junction](#) of the [skeletal muscle](#) are structurally similar to the N_N receptors of the autonomic [ganglia](#) and [adrenal medulla](#). N_M and N_N both belong to a subclass of receptors known as [nicotinic acetylcholine receptors](#) (i.e., [acetylcholine](#) receptors that contain [ligand](#)-gated Na⁺/K⁺ channels that are activated by [nicotine](#)). Activation of N_M receptors of the [quadriceps femoris muscle](#) results in [depolarization](#) at the [motor end plate](#) and, subsequently, muscle contraction.

Question # 7

A 19-year-old woman comes to the physician because of increased sweating for the past 6 months. She experiences severe sweating that is triggered by stressful situations and speaking in public. She is failing one of her university classes because of her avoidance of public speaking. She has not had any fevers, chills, weight loss, or night sweats. Her temperature is 36.6°C (98°F). Physical examination shows moist skin in the axillae and on the palms, soles, and face. Which of the following drugs is most likely to be effective for this patient's condition?

	Answer	Image
A	Pilocarpine	
B	Oxytocin	
C	Physostigmine	
D	Phenylephrine	
E	Glycopyrrolate	

Hint

Sweating is an autonomic reflex primarily mediated by acetylcholine receptors of the sympathetic nervous system.

Correct Answer

A - Pilocarpine

Explanation Why

[Pilocarpine](#) is a [direct parasympathomimetic](#) (direct [agonist](#)) that binds directly to muscarinic [ACh](#) receptors, which in turn increases the secretion of sweat. [Pilocarpine](#) would worsen this patient's condition.

B - Oxytocin

Explanation Why

[Oxytocin](#) stimulates uterine contractions and milk expression. It does not play a role in [sweat gland](#) secretion and would have no effect on this patient's condition.

C - Physostigmine

Explanation Why

[Physostigmine](#) is an [indirect parasympathomimetic](#) (indirect [agonist](#)) that decreases the breakdown of [ACh](#), which in turn increases the secretion of sweat. [Physostigmine](#) would worsen this patient's condition.

D - Phenylephrine

Explanation Why

[Phenylephrine](#) is a [sympathomimetic](#) agent that mainly affects [\$\alpha\$ -1 adrenergic receptors](#), causing vasoconstriction, nasal decongestion, and [mydriasis](#). It does not play a role in [sweat gland](#) secretion and would have no effect on this patient's condition.

E - Glycopyrrolate

Explanation But

[Botulinum toxin](#), which also inhibits [ACh](#) release, can be used to treat focal hyperhidrosis (e.g., hyperhidrosis limited to the [axillae](#)).

Explanation Why

[Glycopyrrolate](#) is an [anticholinergic agent](#) used to treat hyperhidrosis. This drug blocks [ACh](#) at [muscarinic receptors](#), which temporarily reduces sweat production. As with any [anticholinergic drug](#), careful dosing is required to avoid adverse effects of excessive [ACh](#) inhibition (e.g., flushed [skin](#), cycloplegia, dry mouth, [constipation](#)).

Question # 8

A 57-year-old man comes to the physician for a follow-up examination. During the last 6 months, he has had recurring pneumonia after undergoing a surgical operation. He reports that, when food has gone down his windpipe, he has not automatically coughed. Examination shows normal voluntary coughing, but an impaired cough reflex. The nerve responsible for this patient's symptoms is most likely damaged at which of the following anatomical sites?

	Answer	Image
A	Carotid sheath	
B	Infratemporal fossa	
C	Foramen magnum	
D	Aortic arch	
E	Piriform recess	
F	Parotid gland	

Hint

An intact cough reflex depends primarily on afferent fibers of the internal laryngeal nerve (a branch of the vagus nerve), which transmit sensations of the larynx above the vocal cords, and on efferent fibers of the vagus, phrenic, and spinal motor nerves. This patient is able to cough voluntarily (indicating an intact efferent pathway) but has an impaired cough reflex (indicating a defect in the afferent pathway).

Correct Answer

A - Carotid sheath

Explanation Why

In the [carotid sheath](#), [anterior](#) to the [internal carotid artery](#), a branch of the [glossopharyngeal nerve \(CN IX\)](#) runs to the [carotid sinus](#). This branch maintains blood pressure by relaying [baroreceptor](#) impulses from the [carotid sinus](#) to the vasomotor center in the [brainstem](#) ([carotid sinus](#) reflex). Injury to the [CN IX](#) can also cause loss of [gag reflex](#) (afferent limb) and mild [dysphagia](#), which can lead to [aspiration pneumonia](#) as seen in this patient. However, the [CN IX](#) is not responsible for the absent laryngeal [cough reflex](#) seen in this patient, and the [internal laryngeal nerve](#) does not pass through the [carotid sheath](#).

B - Infratemporal fossa

Explanation Why

Through the [infratemporal fossa](#) runs the [mandibular nerve \(CN V3\)](#), the third branch of the [trigeminal nerve](#). Injury to [CN V3](#) can lead to weakness of the [mastication](#) muscles as well as hyperesthesias of the chin, lower lip, and inside of the cheek. However, this nerve is not responsible for the absent laryngeal [cough reflex](#) seen in this patient, and the [internal laryngeal nerve](#) does not pass through the [infratemporal fossa](#).

C - Foramen magnum

Explanation Why

Through the foramen magnum travels the [accessory nerve \(CN XI\)](#), which innervates the [sternocleidomastoid](#) and [trapezius](#) muscles. Injury to [CN XI](#) would result in weakness of head-turning (contralateral side) and shoulder elevation (ipsilateral side). This nerve is not responsible for the absent laryngeal [cough reflex](#) seen in this patient, and the [internal laryngeal nerve](#) does not pass through the [foramen magnum](#).

D - Aortic arch

Explanation Why

Under the [aortic arch](#) travels the left [recurrent laryngeal nerve](#), a branch of the [vagus nerve \(CN X\)](#). [Recurrent laryngeal nerve](#) dysfunction can lead to hoarseness or [dyspnea](#) (due to paralysis of the [posterior cricoarytenoid muscle](#), which opens the [vocal cords](#)). However, this nerve is not responsible for the absent laryngeal [cough reflex](#) seen in this patient, and the [internal laryngeal nerve](#) does not pass through the [aortic arch](#).

E - Piriform recess

Explanation Why

The [superior laryngeal nerve](#) divides into an internal and external branch beneath the [internal carotid artery](#). The [internal laryngeal nerve](#) runs directly beneath the mucosa of the piriform recess, along with the [recurrent laryngeal nerve](#), and is distributed to the mucous membrane of the [larynx](#). The [internal laryngeal nerve](#) can be injured during surgery (e.g., [thyroidectomy](#)) or damaged by food items (e.g., a fishbone) being trapped in the piriform fossa. Damage to this nerve classically manifests with an impaired [cough reflex](#), which increases the risk for recurrent [aspiration pneumonia](#).

F - Parotid gland

Explanation Why

Through the [parotid gland](#) runs the [facial nerve \(CN VII\)](#), which is commonly injured during [parotid](#) resections or oncologic procedures (e.g., vestibular [schwannoma](#) surgery). Injury to [CN VII](#) can lead to the ipsilateral loss of facial expression, impaired function of the submandibular, sublingual, and [lacrimal glands](#), [hyperacusis](#), and impaired [taste](#) perception of the [anterior](#) $\frac{2}{3}$ of the [tongue](#). However, this nerve is not responsible for the absent laryngeal [cough reflex](#) seen in this patient, and the [internal laryngeal nerve](#) does not pass through the [parotid gland](#).

Question # 9

A 17-year-old high school student is brought to the emergency department because of irritability and rapid breathing. He appears agitated and is diaphoretic. His temperature is 38.3°C (101°F), pulse is 129/min, respirations are 28/min, and blood pressure is 158/95 mmHg. His pupils are dilated. An ECG shows sinus tachycardia. Which of the following substances is used to make the drug this patient has most likely taken?

	Answer	Image
A	Ergotamine	
B	Pseudoephedrine	
C	Homatropine	
D	Sodium oxybate	
E	Codeine	

Hint

Amphetamines can be synthesized from certain over-the-counter cold medicines.

Correct Answer

A - Ergotamine

Explanation Why

[Ergotamine](#), which can be used to treat acute [migraine](#) attacks, can be used illicitly to prepare [lysergic acid diethylamide \(LSD\)](#). In rare cases, an overdose of [LSD](#) can cause features of [sympathetic](#) overactivity due to the effects of the drug itself or due to [serotonin syndrome](#). However, an [LSD](#) overdose is typically associated with visual or [auditory hallucinations](#), [depersonalization](#), and/or [flashbacks](#), none of which have been reported in this patient. Although [ergotamine](#) has some of the pharmacological effects of [amphetamine](#) or [cocaine](#) (e.g., peripheral vasoconstriction), [ergotamine](#) does not have a chemical structure similar to either of these compounds.

B - Pseudoephedrine

Explanation Why

This patient presents with clinical features of [sympathetic](#) overactivity such as [tachycardia](#), [hypertension](#), [tachypnea](#), [mydriasis](#), [fever](#), and [diaphoresis](#). A toxidrome of [sympathetic](#) overactivity is typically caused by an overdose of stimulants such as [amphetamines](#). [Pseudoephedrine](#) and [ephedrine](#), which are used in nasal decongestant preparations, can be used illicitly to synthesize [amphetamines](#).

C - Homatropine

Explanation Why

[Homatropine](#), which is used in certain [cough suppressant](#) medications, can be used to synthesize other tropane alkaloids such as [scopolamine \(hyoscine\)](#). [Scopolamine](#) overdose can result in features of [anticholinergic syndrome](#) such as [fever](#), [tachycardia](#), [mydriasis](#), and altered mental status. However, patients with [anticholinergic syndrome](#) would have dry rather than sweaty [skin](#).

D - Sodium oxybate

Explanation Why

[Sodium oxybate](#), which is used to treat [narcolepsy](#), can be used to synthesize [gamma-hydroxybutyrate](#) (GHB). An overdose of [GHB](#) would manifest with symptoms of [CNS](#) depression such as loss of consciousness and [bradypnea](#) rather than the agitation and [tachypnea](#) seen here.

E - Codeine

Explanation Why

[Codeine](#), which is used as a [cough suppressant](#), can be used illicitly to prepare heroin and other [opiates](#). An overdose of [opiates](#) would result in [bradypnea](#) (due to respiratory depression) and [miosis](#) rather than the [tachypnea](#) and [mydriasis](#) seen in this patient.

Question # 10

A 38-year-old woman comes to the emergency department because of progressive headache, blurry vision, and nausea for 1 day. Four days ago, she was diagnosed with a right middle ear infection. She appears lethargic. Her temperature is 39.1°C (102.3°F), and blood pressure is 148/95 mm Hg. Ophthalmologic examination shows bilateral swelling of the optic disc. The corneal reflex in the right eye is absent. Sensation to touch is reduced on the upper right side of the face. Serum studies show increased concentrations of fibrin degradation products. Which of the following is the most likely diagnosis?

	Answer	Image
A	Cerebral venous thrombosis	
B	Hypertensive emergency	
C	Subarachnoid hemorrhage	
D	Migraine headache	
E	Idiopathic intracranial hypertension	
F	Viral meningitis	

Hint

This patient has manifestations of increased intracranial pressure (e.g., headache, papilledema, focal neurologic deficits).

Correct Answer

A - Cerebral venous thrombosis

Explanation Why

[Cerebral venous thrombosis \(CVT\)](#) is a condition of impaired blood drainage from the brain due to thrombosis of cerebral [veins](#) or the [dural sinus](#), which can lead to tissue [ischemia](#). [CVT](#) can cause manifestations of [increased intracranial pressure](#) (e.g., [headache](#), altered mental status, [papilledema](#), focal neurologic deficits) as seen in this case. [Risk factors](#) for the development of [CVT](#) include [hypercoagulability](#) (e.g., due to [oral contraceptive](#) use, [pregnancy](#), and the [puerperium](#)), [malignancy](#), and infection. In particular, local infections of the sinuses, mouth, face, neck, and/or ears (like this patient's recent episode of [acute otitis media](#)) can precipitate [CVT](#). An increased serum concentration of [D-dimer](#), which is a fibrin degradation product produced during clot breakdown, supports a diagnosis of [CVT](#). Urgent imaging studies are required to confirm the diagnosis.

B - Hypertensive emergency

Explanation Why

[Hypertensive emergency](#) is defined as an acute increase in blood pressure $> 180/120$ mm Hg with manifestations of end-organ damage, which can include neurologic symptoms such as [headache](#), blurry vision, and [papilledema](#). This patient's blood pressure is 148/95 mm Hg and thus does not meet the threshold for [hypertensive emergency](#). In addition, [hypertensive emergency](#) does not cause [fever](#) or focal neurologic deficits and would not typically result in increased serum concentrations of fibrin degradation products (e.g., [D-dimer](#)).

C - Subarachnoid hemorrhage

Explanation Why

[Subarachnoid hemorrhage](#) can cause [headache](#), nausea, [fever](#) (from blood irritating the [meninges](#)), and focal neurologic deficits (as a result of [mass effect](#)). Though some patients with this condition can have a [prodromal headache](#) due to [sentinel leak](#), the characteristic manifestation of [subarachnoid](#)

[hemorrhage](#) is a sudden-onset, severely painful [headache](#) (i.e., [thunderclap headache](#)), which this patient does not have. [Papilledema](#), as seen in this case, is uncommon. In addition, [subarachnoid hemorrhage](#) does not cause increased serum concentrations of fibrin degradation products (e.g., [D-dimer](#)).

D - Migraine headache

Explanation Why

[Migraine headache](#) can cause visual disturbances (e.g., blurry vision, [photopsia](#), distorted color perception) and nausea. In severe cases, focal neurologic deficits can be present. However, [migraine headache](#) does not cause [fever](#), [papilledema](#), or increased serum concentrations of fibrin degradation products (e.g., [D-dimer](#)) as seen in this case.

E - Idiopathic intracranial hypertension

Explanation Why

[Idiopathic intracranial hypertension](#) can cause [headache](#), visual disturbances (e.g., transient vision loss, [photopsia](#)), nausea, bilateral [papilledema](#), and focal neurologic deficits. However, [idiopathic intracranial hypertension](#) does not cause [fever](#) or increased serum concentrations of fibrin degradation products (e.g., [D-dimer](#)) as seen in this case.

F - Viral meningitis

Explanation But

Cases of bacterial [meningitis](#) caused by [Neisseria meningitidis](#) can be complicated by [disseminated intravascular coagulation](#) (which causes increased serum concentrations of fibrin degradation products). In contrast to viral [meningitis](#), [meningococcal meningitis](#) typically manifests with a [petechial](#) rash, [septic shock](#), and is often life-threatening.

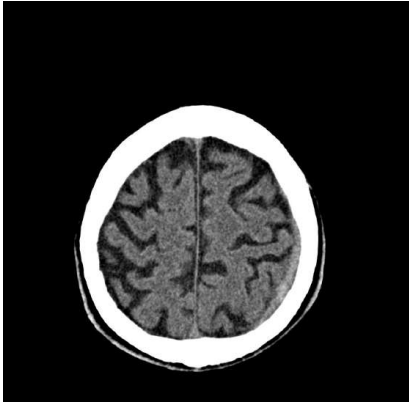
Explanation Why

Viral [meningitis](#) can cause [fever](#), nausea, and manifestations of [increased intracranial pressure](#) (e.g., [headache](#), altered mental status, [papilledema](#), focal neurologic deficits). However, this condition does not cause increased serum concentrations of fibrin degradation products (e.g., [D-dimer](#)).

Question # 11

A 2-month-old boy is brought to the emergency department by his mother because of an 8-hour history of difficulty feeding and decreased arousability. His mother says that the symptoms began after he rolled over and fell from the bed. His vital signs are within normal limits. Examination shows regions of purple discoloration in the T4–T10 dermatomes bilaterally and tense fontanelles. Fundoscopy shows bilateral optic disc swelling with dot-and-blot hemorrhages extending to the ora serrata. Which of the following is the most likely diagnosis?

	Answer	Image
A	Basilar skull fracture	
B	Lobar hemorrhage	
C	Epidural hematoma	
D	Bacterial meningitis	
E	Periventricular hemorrhage	

	Answer	Image
F	Subdural hematoma	

Hint

Infants do not begin to roll on their own until the age of 4–6 months. Nonaccidental trauma in children should be suspected when an implausible or inconsistent history is given by the caretaker, as in this case, the claim that a 2-month-old infant rolled off a bed.

Correct Answer

A - Basilar skull fracture

Explanation Why

Common manifestations of a [basilar skull fracture](#) include [periorbital ecchymosis](#) with [CSF rhinorrhea](#), [CSF otorrhea](#), [mastoid ecchymosis](#), and otorrhagia, which are not seen in this patient. Therefore, a [skull base fracture](#) is very unlikely in this patient.

B - Lobar hemorrhage

Explanation Why

Lobar hemorrhage is associated with [cerebral amyloid angiopathy](#). This type of hemorrhage is typically seen in adults. This pediatric patient was most likely injured as a result of [nonaccidental trauma](#), which does not typically cause lobar hemorrhage.

C - Epidural hematoma

Image



Explanation Why

An [epidural hematoma](#) usually results from rupture of the [middle meningeal artery](#) due to a traumatic skull fracture. Although this patient has evidence of altered mental status (decreased feeding and [arousability](#)), and it is likely that he sustained some form of [head trauma](#), the fundoscopic findings would be less likely to occur in patients with [epidural hematoma](#). Furthermore, [epidural hematomas](#) are not the most common type of [intracranial hemorrhage](#) in cases of pediatric [nonaccidental trauma](#).

D - Bacterial meningitis

Explanation Why

Bacterial [meningitis](#) is typically accompanied by altered mental status (AMS), which, in [infants](#), can manifest subtly with symptoms ranging from irritability to [lethargy](#). Although this patient's decreased

[arousability](#) indicates acute AMS, he does not have [fever](#) or signs of meningism. This patient's presentation should raise concern for [nonaccidental trauma](#).

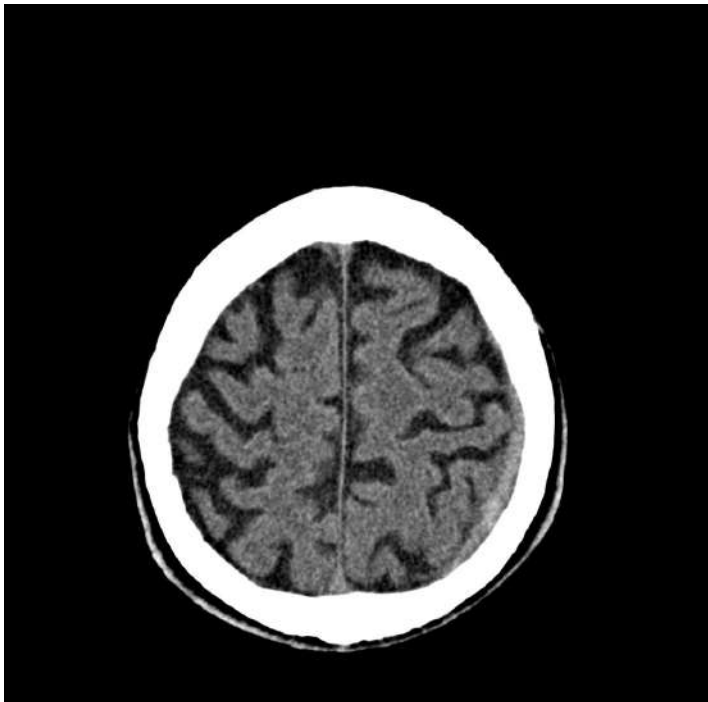
E - Periventricular hemorrhage

Explanation Why

Periventricular hemorrhage (PVH) is a major cause of neurological disabilities and most commonly occurs in [preterm infants](#) due to [germinal matrix hemorrhage](#). However, this boy was born at [full term](#). Furthermore, symptoms would be expected to arise within the first 1–5 days of life, not 2 months after [birth](#). This patient was most likely injured as a result of [nonaccidental trauma](#), which does not typically lead to PVH.

F - Subdural hematoma

Image



Explanation But

Any case of suspected [child maltreatment](#) should be immediately reported to Child Protective Services.

Explanation Why

A [subdural hematoma](#) is a type of [intracranial hemorrhage](#) frequently seen in [infants](#) with [shaken baby syndrome](#). In [shaken baby syndrome](#), which is caused by violent shaking of a baby, whiplash and rapid rotational head movements can lead to tearing of the intracerebral [bridging veins](#) and [diffuse axonal injury](#). Characteristic [physical exam](#) findings of [shaken baby syndrome](#) include irritability, [lethargy](#), retinal hemorrhages (due to rupture of the retinal [veins](#)), and bulging [fontanelles](#), all of which are seen in this patient. Other injuries indicative of [child abuse](#) include [posterior rib fractures](#), [fractures](#) at multiple stages of healing, [bruises](#) to the upper torso caused by forceful grip (like the purple discoloration in the T4–T10 [dermatomes](#) seen in this patient), and complex, [long bone fractures](#) (e.g., of the spiral [humerus fractures](#)).

Question # 12

A 73-year-old man is brought to the emergency department 30 minutes after the sudden onset of right-sided body weakness. His wife reports that he does not seem to understand simple questions. He has type 2 diabetes mellitus and has smoked 1 pack of cigarettes daily for 45 years. The patient speaks fluently, but he answers questions with nonsensical phrases and cannot repeat single words. Which of the following is the most likely diagnosis?

	Answer	Image
A	Broca aphasia	
B	Conduction aphasia	
C	Transcortical motor aphasia	
D	Global aphasia	
E	Wernicke aphasia	
F	Transcortical sensory aphasia	

	Answer	Image
G	Anomic aphasia	

Hint

In conjunction with meaningless speech and impaired comprehension, sudden onset of right-sided body weakness should raise concern for a cerebral lesion located in the posterior part of the left superior temporal gyrus (i.e., an occlusion of the left middle cerebral artery).

Correct Answer

A - Broca aphasia

Explanation Why

[Broca aphasia](#) is caused by lesions in the inferior frontal [gyrus](#) of the dominant (usually left) hemisphere (e.g., due to an [infarct](#) in the superior division of the [middle cerebral artery](#)). In patients with [Broca aphasia](#), language production is greatly affected, resulting in nonfluent, telegraphic, and grammatically incorrect [speech](#). Patients are aware of their impaired [speech](#) and can become frustrated during the [physical examination](#). This patient cannot repeat single words and has impaired language comprehension. However, he speaks fluently and is unaware of his language deficits.

B - Conduction aphasia

Explanation Why

[Conduction aphasia](#) is usually caused by damage to the [arcuate fasciculus](#). This type of [aphasia](#) is characterized by impaired repetition with fluent [speech](#) and intact comprehension. This patient has poor repetition with fluent [speech](#) but impaired comprehension.

C - Transcortical motor aphasia

Explanation Why

Transcortical motor [aphasia](#) is characterized by nonfluent [aphasia](#) with good comprehension and intact repetition. This patient speaks fluently but has impaired comprehension and poor repetition.

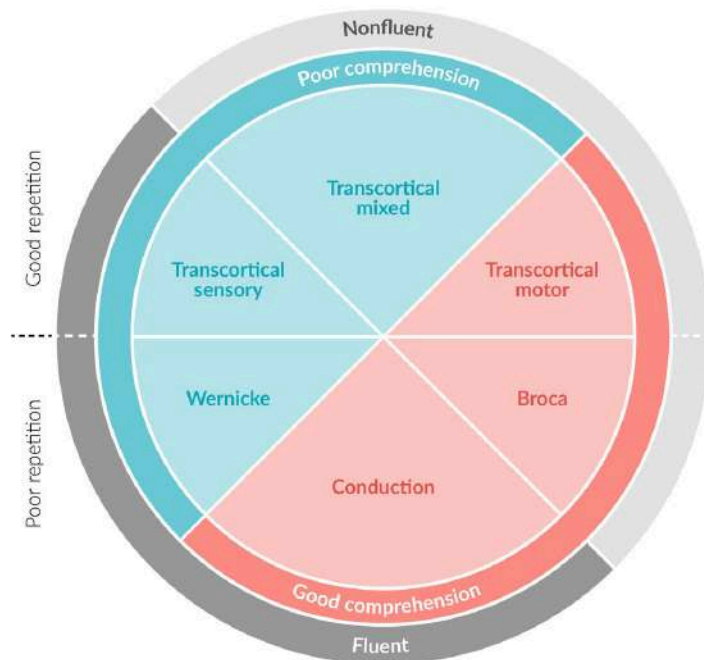
D - Global aphasia

Explanation Why

[Global aphasia](#) is a neurologic insult that involves nonfluent [aphasia](#) and impaired comprehension. [Global aphasia](#) is usually caused by a large lesion affecting the [Broca area](#), the [Wernicke area](#), and the [arcuate fasciculus](#). This patient has impaired comprehension and repetition but speaks fluently.

E - Wernicke aphasia

Image



Explanation Why

[Wernicke aphasia](#) is caused by lesions in the [superior temporal gyrus](#) of the dominant (usually left) hemisphere, usually along the left [MCA](#) distribution. Patients with [Wernicke aphasia](#) typically present with impaired language comprehension and repetition; although they can speak fluently, they produce nonsensical phrases. Furthermore, these patients lack awareness of their impairment, as is

the case here. In addition to [Wernicke aphasia](#), signs of an [MCA stroke](#) include gaze deviation towards the side of the [infarction](#) and contralateral [homonymous hemianopia](#) without [macular sparing](#).

F - Transcortical sensory aphasia

Explanation Why

Transcortical sensory [aphasia](#) is characterized by impaired auditory comprehension with intact repetition and fluent [speech](#). This patient has fluent [speech](#) with impaired comprehension, but his repetition is poor.

G - Anomic aphasia

Explanation Why

[Anomic aphasia](#) is a type of expressive [aphasia](#) characterized by word-finding difficulties, particularly in relation to nouns and verbs. Patients with [anomic aphasia](#) usually have fluent [speech](#) and intact comprehension. This patient speaks fluently but has impaired comprehension and poor repetition.

Question # 13

A 56-year-old woman is brought to the physician by her husband because of a two-day history of fever, malaise, headaches, and confusion. She recently immigrated from rural China and her immunization status is unknown. Her temperature is 39.1°C (102.4°F). Physical examination shows nuchal rigidity and photophobia. Cerebrospinal fluid analysis shows a neutrophil count of 1,500/mm³. Cerebrospinal fluid cultured on Thayer-Martin agar and normal sheep blood agar shows no growth. However, when the sheep blood agar sample is heated, numerous non-hemolytic, opaque, cream-colored colonies grow. Which of the following characteristics best describes the most likely causal pathogen?

	Answer	Image
A	Gram-negative coccobacillus	
B	Gram-negative, facultative intracellular bacillus	
C	Gram-positive, lancet-shaped diplococcus	
D	Gram-negative diplococcus	
E	Gram-positive, facultative intracellular bacillus	

Hint

This patient has symptoms and laboratory findings consistent with bacterial meningitis. Chocolate agar is sheep blood that is slowly heated until red blood cells lyse and release factors V (NAD) and X (hematin).

Correct Answer

A - Gram-negative coccobacillus

Explanation Why

Haemophilus influenzae is a gram-negative coccobacillus that requires [factors X](#) (hematin) and V ([NAD](#)) for growth. Because this organism is incapable of [hemolysis](#) on its own, [red blood cells](#) must be lysed by slow heating in order to release these molecules into the growth medium and make them available for bacterial metabolism. Without [factors X](#) and V, *H. influenzae* will not grow. When exposed to these factors, the bacteria can reproduce, which can be seen as the growth of cream-colored colonies. [Meningitis](#) caused by this organism is most common in patients who have not received the Hib vaccine.

B - Gram-negative, facultative intracellular bacillus

Explanation Why

Gram-negative, facultative intracellular [bacillus](#) describes *Legionella pneumophila*. Unlike the organism isolated from the [CSF](#) cultures here, *L. pneumophila* is unable to grow on [chocolate agar](#). *L. pneumophila* is best grown on [charcoal yeast extract agar](#).

C - Gram-positive, lancet-shaped diplococcus

Explanation Why

Gram-positive, lancet-shaped diplococcus is characteristic of *Streptococcus pneumoniae* ([pneumococcus](#)). *S. pneumoniae* is an [α-hemolytic](#) bacterium and is able to grow on both normal agar and [chocolate agar](#). The bacteria in question that has infected this patient is [non-hemolytic](#) and cannot grow on conventional blood agar.

D - Gram-negative diplococcus

Explanation Why

[*Neisseria meningitidis*](#) is a gram-negative diplococcus that can cause bacterial [meningitis](#). [Thayer-Martin agar](#) is a selective medium that favors the growth of [Neisseria](#) species because it contains [vancomycin](#) (which inhibits the growth of gram-positive organisms) and [nystatin](#) (which inhibits the growth of fungi), along with [trimethoprim](#) and [colistin](#) (which together inhibit the growth of other gram-negative organisms). The organism isolated from the [CSF](#) cultures of the patient here did not grow on [Thayer-Martin agar](#), making [Neisseria](#) infection unlikely.

E - Gram-positive, facultative intracellular bacillus

Explanation Why

Gram-positive, facultative intracellular [bacillus](#) describes [Listeria monocytogenes](#). Unlike the organism isolated from the [CSF](#) cultures of this patient, *L. monocytogenes* is a [β-hemolytic](#) bacterium and can grow on both normal agar and [chocolate agar](#).

Question # 14

A previously healthy 67-year-old man comes to the physician for routine health maintenance evaluation. He works at a community center and volunteers at a local homeless shelter. A tuberculin skin test shows an induration of 14 mm. An x-ray of the chest is normal. Treatment with an antimycobacterial drug is initiated. Two months later, he has numbness and burning over both feet and an unsteady gait. Physical examination shows decreased sensation to light touch extending from the soles of the feet to the mid-shin bilaterally. This patient's condition is most likely to result in which of the following?

	Answer	Image
A	Impaired synthesis of neurotransmitters	
B	Intracellular accumulation of sorbitol	
C	Segmental demyelination of peripheral axons	
D	Impaired breakdown of glucose to ATP	
E	Degeneration of the dorsal columns	

Hint

Isoniazid is a commonly used monotherapy for latent tuberculosis. Adverse effects of isoniazid include peripheral polyneuropathy due to pyridoxine deficiency.

Correct Answer

A - Impaired synthesis of neurotransmitters

Explanation But

Dietary [vitamin B6 deficiency](#) is rare, but can occur in patients with certain [risk factors](#) such as advanced age, as seen here, as well as [obesity](#), [pregnancy](#), [preeclampsia](#), [eclampsia](#), and malabsorptive states. [Pyridoxine deficiency](#) is more commonly associated with medication interactions that impair [vitamin B6](#) metabolism, such as [isoniazid](#), [penicillamine](#), and [hydralazine](#).

Explanation Why

[Pyridoxine deficiency](#) causes impaired synthesis of [neurotransmitters](#), as [pyridoxine](#) is an important [cofactor](#) for multiple enzymes, including those that take part in the synthesis of [GABA](#), [serotonin](#), [epinephrine](#), [norepinephrine](#), and [dopamine](#). Decreased levels of [GABA](#) can cause hyperirritability and [seizures](#). In addition, [vitamin B6](#) is an important [cofactor](#) of the enzyme [cystathionine synthase](#), which is needed for the conversion of [homocysteine](#) to [cysteine](#). When this enzyme is impaired, (e.g., during [isoniazid](#) treatment), [homocysteine](#) is increasingly metabolized to [S-adenosylmethionine](#) (SAM) via [methionine synthase](#). SAM inhibits the synthesis of [sphingolipids](#) and [myelin](#), which can lead to irreversible nerve damage.

B - Intracellular accumulation of sorbitol

Explanation Why

Intracellular accumulation of [sorbitol](#) is the mechanism of action of [diabetic neuropathy](#), which can result in [paresthesias](#), loss of sensation in a stocking pattern, and an unsteady gait due to impaired [proprioception](#) ([sensory ataxia](#)). However, [isoniazid](#) is not associated with [sorbitol](#) accumulation.

C - Segmental demyelination of peripheral axons

Explanation Why

[Segmental demyelination](#) of peripheral [axons](#) is seen in certain peripheral neuropathies such as [Guillain-Barré syndrome](#), chronic inflammatory demyelinating neuropathy, [metachromatic leukodystrophy](#), and type 1 [Charcot-Marie-Tooth disease](#). These peripheral neuropathies can also result in [paresthesias](#), loss of light touch sensation, and an unsteady gait due to impaired [proprioception](#) ([sensory ataxia](#)). However, the [peripheral neuropathy](#) caused by [pyridoxine deficiency](#) is the result of a degenerative axonal neuropathy and not a [demyelinating](#) neuropathy.

D - Impaired breakdown of glucose to ATP

Explanation Why

Deficiency of [ATP](#) due to an impaired breakdown of glucose is the mechanism of neuropathy in patients with [thiamine deficiency](#) ([dry beriberi](#)), because [thiamine](#) is an essential [cofactor](#) for the enzymes [pyruvate dehydrogenase](#) and [α-ketoglutarate dehydrogenase](#). [Isoniazid](#) causes a deficiency of [pyridoxine](#) ([vitamin B₆](#)), not [thiamine](#) ([vitamin B₁](#)).

E - Degeneration of the dorsal columns

Explanation Why

Degeneration of the [dorsal column](#) is seen in [subacute combined degeneration](#) (SCD), which is caused by [vitamin B₁₂ deficiency](#) and can manifest with decreased light touch sensation as well as an unsteady gait due to impaired [proprioception](#) ([sensory ataxia](#)). [Peripheral neuropathy](#) due to [vitamin B₁₂ deficiency](#) could also explain the [paresthesias](#) in this patient. However, while long-term use of [metformin](#) can cause [vitamin B₁₂ deficiency](#), [isoniazid](#) is not known to cause it.

Question # 15

A 41-year-old man comes to the physician because of a 3-week history of fatigue, cough, and a 4.5-kg (10-lb) weight loss. He does not smoke or drink alcohol. He appears emaciated. A chest x-ray shows a calcified nodule in the left lower lobe and left hilar lymphadenopathy. The physician initiates therapy for the condition and informs him that he will have to return for monthly ophthalmologic examination for the next 2 months. These examinations are most likely to evaluate the patient for an adverse effect of a drug with which of the following mechanisms of action?

	Answer	Image
A	Impaired protein synthesis due to binding to 30S ribosomes	
B	Impaired synthesis of cell wall polysaccharides	
C	Impaired synthesis of mycolic acids	
D	Impaired protein synthesis due to binding to 50S ribosomes	
E	Impaired production of hemozoin from heme	
F	Impaired activity of DNA-dependent RNA polymerase	

Hint

This patient presents with features that suggest primary pulmonary tuberculosis (e.g., fatigue, cough, weight loss, Ghon complex on chest x-ray). The first-line therapy for tuberculosis is a multidrug regimen consisting of rifampin, isoniazid, ethambutol, and pyrazinamide. Because optic neuropathy is an adverse effect that affects approximately 5% of patients taking ethambutol, monthly examination of visual acuity and color vision is recommended.

Correct Answer

A - Impaired protein synthesis due to binding to 30S ribosomes

Explanation Why

Impaired [protein synthesis](#) due to binding to 30S [ribosomal](#) subunits is the mechanism of action of [aminoglycosides](#) (e.g., [streptomycin](#)) and [tetracyclines](#). [Streptomycin](#) can be part of the multidrug regimen used to treat [tuberculosis](#). However, it is not used as a first-line treatment and has rarely been reported to cause optic neuropathy. [Tetracyclines](#) are not administered for [treatment of tuberculosis](#). Moreover, while they can cause GI upset and [photosensitivity](#), they are not associated with optic neuropathy.

B - Impaired synthesis of cell wall polysaccharides

Explanation Why

The mechanism of action of [ethambutol](#) is the inhibition of [arabinosyltransferase](#), which subsequently inhibits the synthesis of arabinogalactan, an important [mycobacterial cell wall polysaccharide](#). [Polysaccharides](#) on the outer surface of bacteria are the principal antigens in most pathogenic bacteria, including *M. tuberculosis*. By inhibiting [arabinosyltransferase](#), the [bacterial cell wall](#) becomes more permeable. A common side effect of [ethambutol](#) is reversible optic neuropathy with [red-green color blindness](#).

C - Impaired synthesis of mycolic acids

Explanation Why

Impaired synthesis of [mycolic acids](#) is the mechanism of action of [isoniazid](#). Isoniazid is part of the multidrug regimen used to treat [tuberculosis](#) but it is not commonly associated with optic neuropathy. A well-known adverse effect of [isoniazid](#) is [peripheral neuropathy](#) due to [vitamin B6](#) deficiency.

D - Impaired protein synthesis due to binding to 50S ribosomes

Explanation Why

Impaired [protein synthesis](#) due to binding to 50S [ribosomal](#) subunits is the mechanism of action of [linezolid](#), [chloramphenicol](#), [clindamycin](#), and [macrolides](#). [Linezolid](#) can be part of the multidrug regimen used to treat [tuberculosis](#). However, it is not used as a first-line treatment and it is not associated with optic neuropathy. [Macrolides](#) can be used to treat diseases caused by [M. avium-intracellulare](#), but they are not effective in treating [M. tuberculosis](#) infections.

E - Impaired production of hemozoin from heme

Explanation Why

Impaired production of [hemozoin](#) from [heme](#) is the mechanism of action of [chloroquine](#). A potential adverse effect of [chloroquine](#) is optic neuropathy. However, [chloroquine](#) is not part of the multidrug regimen used to treat [tuberculosis](#).

F - Impaired activity of DNA-dependent RNA polymerase

Explanation Why

Impaired activity of [DNA-dependent RNA polymerase](#) is the mechanism of action of [rifampin](#). [Rifampin](#) is part of the multidrug regimen used to treat [tuberculosis](#) but it is not associated with optic neuropathy. Adverse effects of treatment with [rifampin](#) include hepatotoxicity and orange discoloration of body fluids. Furthermore, [rifampin](#) induces [CYP450](#) activity, leading to interaction with various other drugs (e.g., [clarithromycin](#)).

Question # 16

A 32-year-old man is admitted to the hospital for evaluation of a 3-month history of insomnia, odynophagia, and irritability. He works in a metal refinery. He appears distracted and irritable. Oral examination shows inflammation of the gums and buccal mucosa with excessive salivation. Neurological examination shows a broad-based gait and an intention tremor in both hands. After treatment with dimercaprol is begun, his symptoms slowly improve. This patient was most likely exposed to which of the following?

	Answer	Image
A	Mercury	
B	Cyanide	
C	Arsenic	
D	Iron	
E	Copper	

Hint

Dimercaprol is a thiol-based chelating agent used to treat metal toxicity.

Correct Answer

A - Mercury

Explanation But

[Lead poisoning](#) would manifest with symptoms very similar to the ones in this case, including neuropsychiatric disturbances and anorexia. Dimercaprol is also the first-line treatment. However, this patient's prominent excess salivation, [odynophagia](#), and gingival [inflammation](#) would not be expected in cases of [lead poisoning](#).

Explanation Why

[Mercury poisoning](#) is the most likely explanation for this patient's presentation. Chronic [mercury](#) toxicity manifests with neuropsychiatric symptoms including anxiety, [erethism](#) mercurialis (abnormal irritability), [ataxia](#), and [tremor](#). Various degrees of [polyneuropathy](#) may also be observed. Another common sign is gingival and/or buccal [inflammation](#) with a characteristic bluish-violet discoloration. This patient's history of working in a metal refinery further supports this diagnosis. Finally, treatment includes administering dimercaprol, a [chelating agent](#) used to reduce serum [mercury](#) levels. The [chelating agents](#) 2,3 dimercaptopropane-1-sulfonate (DMPS) and dimercaptosuccinic acid (DMSA) can also be used to lower [mercury](#) levels.

B - Cyanide

Explanation Why

[Cyanide](#) intoxication manifests acutely as confusion, [vertigo](#), [headache](#), nausea, and vomiting, which can progress to [seizures](#) and [coma](#) in severe cases. Affected patients are initially hypertensive and [tachycardic](#) but then develop [hypotension](#) and [bradycardia](#) as peripheral [oxygen delivery](#) deteriorates. Chronic toxicity most often causes non-specific symptoms such as abdominal [pain](#), nausea, [chest pain](#), and [headache](#). Neither acute nor chronic exposure cause gingivobuccal [inflammation](#), [tremor](#), or [ataxia](#). Finally, [cyanide toxicity](#) is usually treated with [sodium thiosulfate](#) and [hydroxocobalamin](#), or [amyl nitrite](#), [sodium nitrite](#), and [sodium thiosulfate](#), but not with dimercaprol.

C - Arsenic

Explanation Why

[Arsenic toxicity](#) can occur after an acute exposure or following years of chronic exposure. In either case, the most prominent feature of toxicity is symmetrical [peripheral neuropathy](#) that can involve motor and sensory nerves. Chronic exposure will often cause characteristic white lines to appear in the fingernails; acute [poisoning](#) typically manifests with garlic-scented breath, [seizures](#), and [coma](#). Although dimercaprol is indicated in cases of [arsenic poisoning](#), this patient's presentation is not consistent with acute or chronic [arsenic poisoning](#).

D - Iron

Explanation Why

[Iron toxicity](#) is most commonly seen in children, usually due to accidental ingestion of [iron](#) tablets. [Acute iron toxicity](#) typically manifests with hemorrhagic gastroenteritis, anion gap [metabolic acidosis](#), respiratory depression, and altered consciousness, none of which this patient has. [Chronic iron toxicity](#) may cause renal and/or [liver](#) failure. Finally, [iron toxicity](#) is managed with [deferoxamine](#), not dimercaprol.

E - Copper

Explanation Why

Acute [copper](#) toxicity usually manifests with vomiting, [diarrhea](#), [melena](#), and abdominal [pain](#). More severe or continued exposure may result in [hemolytic anemia](#) along with renal and/or hepatic failure. This patient's symptoms include neuropsychiatric components and gingivobuccal [inflammation](#), neither of which are expected in [copper](#) toxicity. Furthermore, [penicillamine](#) is the first-line treatment for [copper](#) toxicity; dimercaprol is used less frequently.

Question # 17

A 4-year-old girl is brought to the pediatrician by her parents for a 1-year history of gradual loss of speech and motor skills. Pregnancy and delivery were uncomplicated, and development was normal until the age of 3 years. Her parents say she used to run and speak in short sentences but now is only able to walk slowly and cannot form sentences. She avoids eye contact and constantly rubs her hands together. There are no dysmorphic facial features. Neurologic examination shows marked cognitive and communicative delay. She has a broad-based gait and is unable to hold or pick up toys on her own. Which of the following mutations is the most likely underlying cause of this patient's condition?

	Answer	Image
A	Microdeletion of methyl-CpG binding protein 2 on X-chromosome	
B	Microdeletion on chromosome 15q11-q13	
C	CGG trinucleotide repeat in FMR1 gene on X-chromosome	
D	CTG trinucleotide repeat in DMPK gene on chromosome 19	
E	Partial deletion of long arm of chromosome 7	
F	Partial deletion of short arm of chromosome 5	

Hint

This girl's progressive loss of motor and cognitive skills with hand stereotypy (e.g., hand-wringing) and a history of prior normal development make Rett syndrome a likely diagnosis.

Correct Answer

A - Microdeletion of methyl-CpG binding protein 2 on X-chromosome

Explanation Why

[Rett syndrome](#) is a rare neurocognitive disorder that is most commonly caused by a mutation in the MECP2 [gene](#) on the X [chromosome](#), which codes for a methyl-CpG binding protein 2 (MeCP2). This condition manifests almost exclusively in girls because affected males die in-utero. Patients with [Rett syndrome](#) typically present with regression of motor, [speech](#), and cognitive abilities starting between the ages of 1 and 4 years, specific stereotypical behaviors (e.g., hand-wringing, vocal grunting), [ataxia](#), [seizures](#), and [failure to thrive](#).

B - Microdeletion on chromosome 15q11-q13

Explanation But

[Angelman syndrome](#) is caused by a maternal microdeletion on [chromosome](#) 15q11-q13 and is characterized by hyperexcitability, happy demeanor, [intellectual disability](#), and [epileptic seizures](#).

Explanation Why

A microdeletion on the paternal [gene](#) copy at the long arm of [chromosome](#) 15 (at the 15q11-q13 [gene loci](#)) causes [Prader-Willi](#) syndrome. This rare genetic condition manifests with muscular [hypotonia](#) during [infancy](#), genital [hypoplasia](#), [short stature](#), [hyperphagia](#), and aggressive behavior, none of which are seen in this patient. This patient's progressive loss of motor and cognitive skills and her hand-wringing are characteristic of [Rett syndrome](#), which is a result of a [point mutation](#) at a different [gene locus](#).

C - CGG trinucleotide repeat in FMR1 gene on X-chromosome

Explanation Why

A CGG [trinucleotide repeat](#) in the [FMR1 gene](#) of the x-[chromosome](#) is the cause of [fragile X syndrome](#), which would cause features of an [autism spectrum disorder](#) (e.g., stereotypy, impairment of cognitive ability and [speech](#)). However, motor development is usually spared, and most patients present with symptoms by the age of 2 years. A normal development until the age of 3 years followed by regression of previously attained [developmental milestones](#) is not consistent with [fragile X syndrome](#). Furthermore, this condition predominantly occurs in boys and presents with features such as a long narrow face with large ears and postpubertal [macro-orchidism](#).

D - CTG trinucleotide repeat in DMPK gene on chromosome 19

Explanation Why

CTG [trinucleotide repeats](#) in the [DMPK](#) region of [chromosome](#) 19 is responsible for type 1 [myotonic muscular dystrophy](#). The severe, early-onset [phenotype](#) of this condition can present during childhood with cognitive impairment as well as impairment of motor and [speech](#) skills due to wasting of all muscles including the muscles of the face and [tongue](#), which are needed for [speech](#) articulation. However, the weakness associated with the early-onset [phenotype](#) would typically start during [infancy](#) and often improve during childhood before worsening during adulthood, unlike this child who had a period of normal motor development during [infancy](#) and subsequently had regression of [developmental milestones](#). Furthermore, other characteristic features such as [myotonia](#), [cataracts](#), and hypersomnolence would be seen.

E - Partial deletion of long arm of chromosome 7

Explanation Why

A partial deletion of the long arm of [chromosome](#) 7 is the cause of [Williams syndrome](#), which would cause cognitive impairment. However, motor development is usually spared and regression of previously attained [developmental milestones](#) would not be expected. Moreover, poor [eye](#) contact would not be expected. Rather, patients with this condition are gregarious and often engage with

strangers. They would also have features such as an [elfin facies](#) and a cardiac [murmur](#) (due to [supravalvular aortic stenosis](#)) on examination.

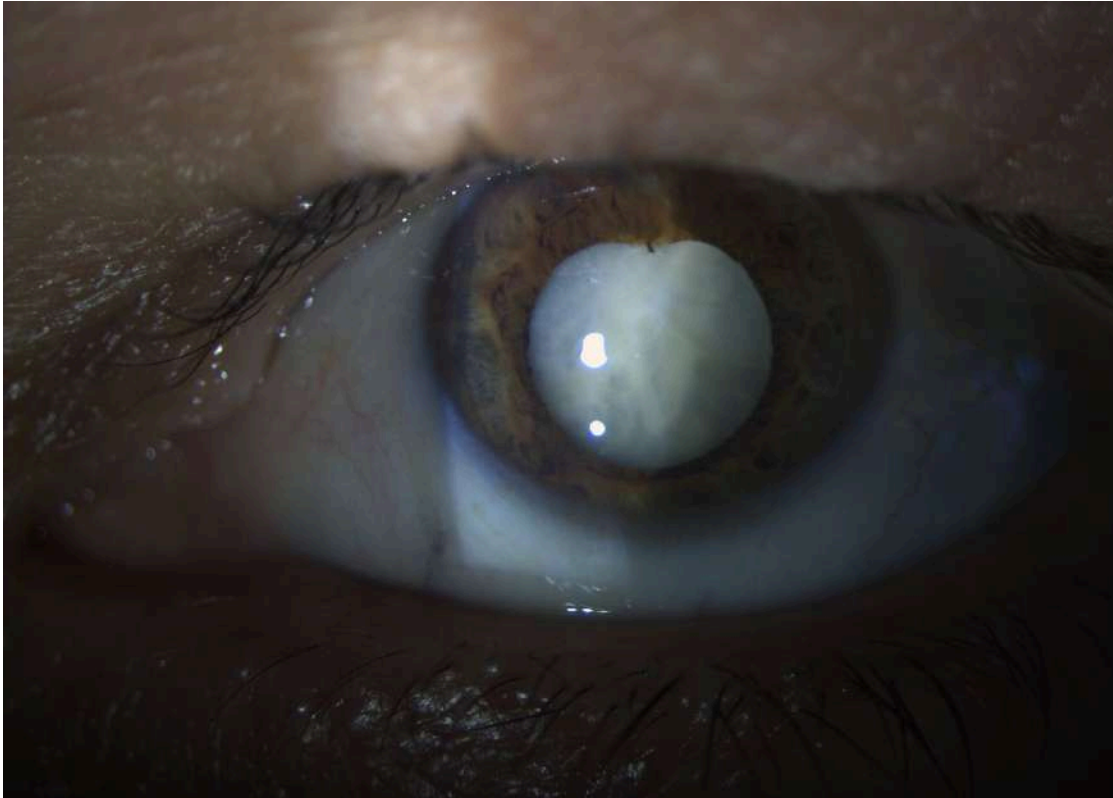
F - Partial deletion of short arm of chromosome 5

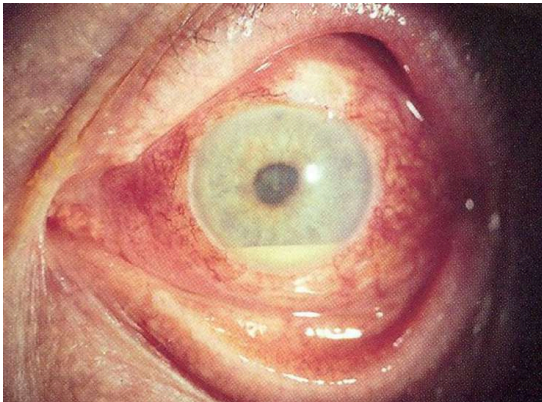
Explanation Why

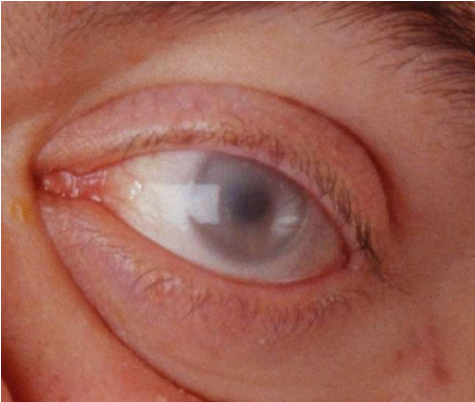
A partial deletion of the short arm of [chromosome](#) 5 is the cause of [cri-du-chat](#) syndrome. This rare genetic condition would manifest with stereotypical behaviors and impairment of cognitive, [speech](#), and motor skills. However, the stereotypical behaviors associated with this condition are typically aggressive and self-mutilating (e.g. head-banging, self-biting) instead of the benign hand-wringing stereotypy seen here. Also, regression of previously attained [developmental milestones](#) would not be expected, and other features such as epicanthal folds, [hypertelorism](#), and a characteristic high-pitched cry would be expected.

Question # 18

A 56-year-old man comes to the physician because of progressive worsening of vision in both his eyes over the past 6 months. He reports that he first noticed some blurring of his vision and glare in the evenings, which have both gotten worse in this period. He works as a tower crane operator and spends most of his day outdoors. Ophthalmologic examination shows visual acuity of 20/100 in both eyes. A photograph of the eye is shown. Damage to which of the following structures is most likely responsible for this patient's current symptoms?



	Answer	Image
A	Aqueous humor	

	Answer	Image
B	Cornea	
C	Vitreous body	
D	Lens	
E	Retina	

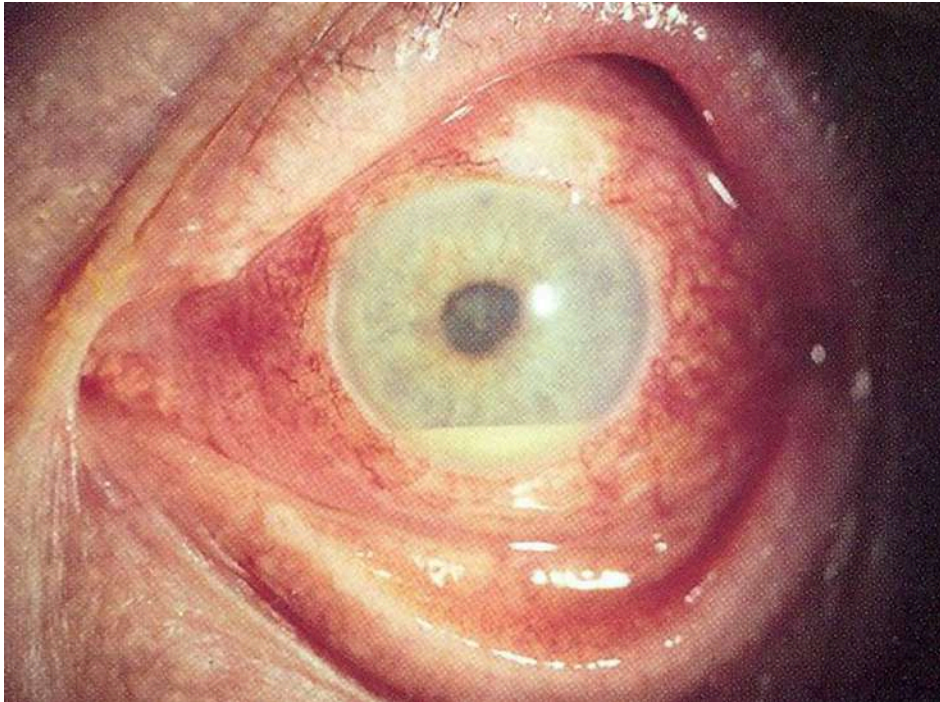
Hint

This photograph shows leukocoria (white pupillary reflex). Chronic UV exposure due to working outdoors is a risk factor for this condition.

Correct Answer

A - Aqueous humor

Image

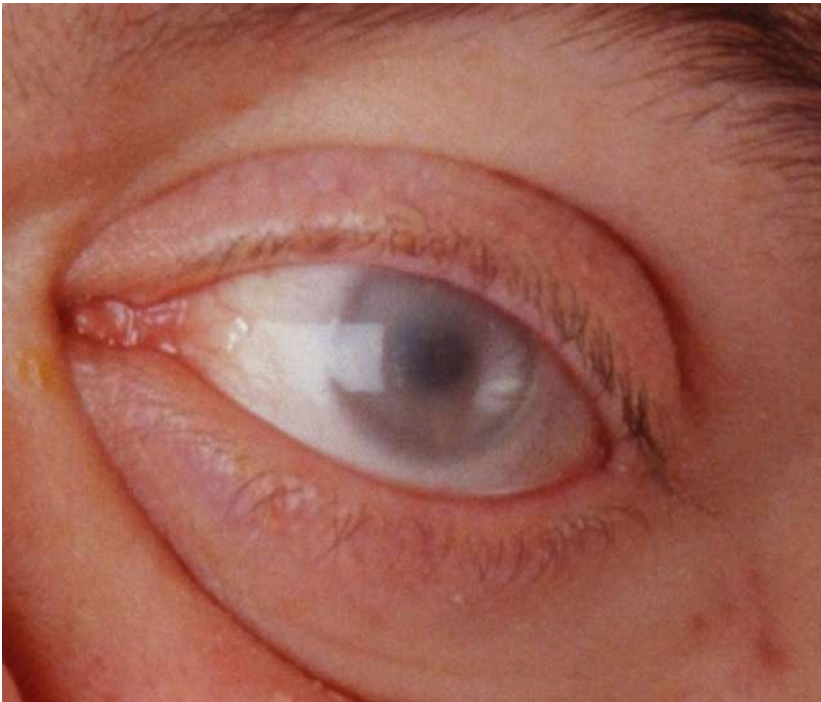


Explanation Why

Opacification of the aqueous humor typically occurs in acute [uveitis](#), a condition in which [pus](#) accumulates in the [anterior](#) chamber ([hypopyon](#)). However, opacification would not be restricted to the pupillary area, as seen here. Instead, it would be present in the inferior region of the [anterior](#) chamber and obscure the underlying [iris](#). Moreover, the chronic nature of the patient's symptoms and the absence of [pain](#) and [conjunctival injection](#) make a different kind of ocular damage more likely.

B - Cornea

Image



Explanation Why

Corneal edemas, which can be caused by [keratitis](#), [anterior uveitis](#), acute congestive [glaucoma](#), and certain metabolic disorders (e.g., [mucopolysaccharidoses](#)), would appear as opacifications on slit-lamp examination and cause impaired visual acuity. However, such opacifications would not be restricted to the pupillary area, as is the case here. Instead, opacification would be present throughout the [cornea](#) and obscure the underlying [iris](#).

C - Vitreous body

Explanation Why

[Vitreous body](#) pathologies, such as [persistent hyperplastic primary vitreous \(PHPV\)](#) and chronic ocular [toxocariasis](#), can result in impaired visual acuity and [leukocoria](#). However, [PHPV](#) typically

occurs during childhood, and [toxocariasis](#) is accompanied by ocular [pain](#). Moreover, both conditions are typically unilateral, whereas both eyes are affected in this patient.

D - Lens

Explanation Why

Gradual painless loss of vision with [leukocoria](#) in an adult suggests [cataract](#) formation. [Cataracts](#) are the most common cause of impaired vision in patients over 40 years of age. [Risk factors](#) for [cataract](#) formation include advanced age, [diabetes mellitus](#), smoking, heavy alcohol consumption, chronic [corticosteroid](#) therapy, ocular trauma, and UV exposure. Conditions associated with congenital and juvenile [cataracts](#) include [galactosemia](#), [chromosomal trisomies](#), certain [TORCH infections](#) (e.g., [rubella](#), [toxoplasmosis](#)), [Marfan syndrome](#), [Alport syndrome](#), [myotonic dystrophy](#), and [neurofibromatosis type II](#).

E - Retina

Image



Explanation Why

Retinal pathologies such as [retinoblastoma](#), [retrolental fibroplasia](#), and [Coats disease](#) can cause [leukocoria](#) with impaired visual acuity. However, these conditions typically occur in the pediatric population, not in adults.

Question # 19

An 8-year-old girl is brought to the physician by her parents for a 10-month history of disturbing dreams and daytime sleepiness. She has difficulty falling asleep and says she sometimes sees ghosts just before falling asleep at night. She has had a 7-kg (15-lb) weight gain during this period despite no changes in appetite. She is alert and oriented, and neurologic examination is unremarkable. During physical examination, she spontaneously collapses after the physician drops a heavy book, producing a loud noise. She remains conscious after the collapse. Polysomnography with electroencephalogram is most likely to show which of the following?

	Answer	Image
A	Periodic sharp waves	
B	Slow spike-wave pattern	
C	Rapid onset of beta waves	
D	Decreased delta wave sleep duration	
E	Diffuse slowing of waves	

Hint

This patient's symptoms of visual hypnagogic hallucinations (hallucinations while falling asleep), excessive daytime sleepiness, abrupt loss of postural tone in response to a frightening stimulus (cataplexy), and weight gain for over 10 months make narcolepsy the most likely diagnosis.

Correct Answer

A - Periodic sharp waves

Explanation Why

[Periodic sharp-wave complexes \(PSWC\)](#) are seen in the early stages of sporadic [Creutzfeldt-Jakob disease \(CJD\)](#) if the EEG is performed during the wakeful state. However, [CJD](#) presents with progressive [dementia](#), startle myoclonus, and [ataxia](#). In addition [CJD](#) is extremely rare and is almost never seen in children. [PSWCs](#) are not seen in patients with [narcolepsy](#).

B - Slow spike-wave pattern

Explanation Why

A diffuse, slow spike-wave activity is seen on EEG in patients with [Lennox-Gastaut syndrome \(LGS\)](#). Patients with [LGS](#) present between 1 and 7 years of age with repeated [seizures](#) (e.g., tonic [seizures](#) during sleep, [atonic seizures](#), [atypical absence seizures](#)) as well as cognitive and behavioral changes. Nocturnal [hallucinations](#), daytime sleepiness, [cataplexy](#), and weight gain are not features of [LGS](#).

C - Rapid onset of beta waves

Explanation Why

[EEG beta waves](#) are seen during the wakeful state and during [REM sleep](#). The diagnosis of [narcolepsy](#) can be confirmed by the rapid onset of [beta waves](#) (i.e., shortened [REM sleep latency](#)) during [polysomnography](#) or by decreased levels of [hypocretin](#) in [CSF](#). [Narcolepsy](#) is treated with good [sleep hygiene](#) measures, daytime stimulant therapy (e.g., [amphetamines](#), [modafinil](#)), and nighttime [sodium oxybate](#) therapy.

D - Decreased delta wave sleep duration

Explanation Why

[EEG delta waves](#) occur during the [N3 stage](#) of [non-REM sleep](#). Decreased [EEG delta wave](#) sleep duration occurs in old age and with the use of [benzodiazepines](#), [barbiturates](#), or alcohol. This would not be expected in patients with [narcolepsy](#).

E - Diffuse slowing of waves

Explanation Why

A diffuse slowing of the EEG waveforms is characteristic of [delirium](#) due to metabolic or toxic encephalopathies, which could cause increased daytime [somnolence](#) and [hallucinations](#) that are worse at night. However, an abrupt collapse in response to a frightening stimulus ([cataplexy](#)) is not a feature of [delirium](#). Moreover, [delirium](#) typically occurs acutely, unlike the condition that has been affecting this patient for 10 months, and would be associated with abnormal findings on [mental status examination](#) (e.g., [disorientation](#), [memory](#) impairment, blunted affect).

Question # 20

A 26-year-old woman is admitted to the hospital because of a 3-day history of tingling and weakness in the lower extremities. Neurologic examination shows areflexia of the ankle and knee joints bilaterally. Motor strength is 1/5 in both lower legs. Over the next 3 weeks, the patient's condition progresses to involve both upper extremities, and she requires ventilatory support. Six weeks after admission, deep tendon reflexes are 1+ in the ankles, and she is able to wiggle her toes. Which of the following is most likely responsible for the improvement in this patient's neurological status?

	Answer	Image
A	Synthesis of monoamine neurotransmitters	
B	Remyelination of peripheral nerves	
C	Replication of oligodendrocyte precursor cells	
D	Accumulation of S-adenosylmethionine	
E	Lymphocytic infiltration in the endoneurium	

Hint

This patient had Guillain-Barré syndrome, a condition that causes acute-onset distal paresthesias with symmetrical, ascending lower motor neuron weakness.

Correct Answer

A - Synthesis of monoamine neurotransmitters

Explanation Why

The synthesis of monoamine neurotransmitters is impaired in patients with neuropsychiatric disorders such as [major depressive disorder](#). [Neurotransmitter](#) synthesis is not involved in the recovery process from [Guillain-Barré syndrome](#).

B - Remyelination of peripheral nerves

Explanation But

In addition to supportive management, high doses of intravenous immunoglobulins and plasmapheresis can be used to shorten the time to recovery.

Explanation Why

The underlying pathology of [Guillain-Barré syndrome](#) is a postinfectious, autoimmune reaction that generates cross-reactive [antibodies](#) that [demyelinate](#) peripheral nerve [axons](#). Disease progression peaks 2–4 weeks after the onset of symptoms. Peripheral nerve [axons](#) then undergo remyelination by [Schwann cells](#) over a duration of weeks to months, and symptoms recede in reverse order of their development (i.e., functionality is restored in a descending pattern, in contrast to the ascending pattern of paralysis).

C - Replication of oligodendrocyte precursor cells

Explanation Why

[Oligodendrocyte](#) precursor cells replicate during the recovery process after an exacerbation of [multiple sclerosis](#), a condition that causes [hyperreflexia](#) (not the [hyporeflexia](#) seen in this case). [Oligodendrocytes](#) synthesize [myelin](#) in the [central nervous system](#) and are not involved in the

recovery process from [Guillain-Barré syndrome](#), which affects the [peripheral nervous system](#).

D - Accumulation of S-adenosylmethionine

Explanation Why

The accumulation of [S-adenosylmethionine](#) is part of the underlying pathology of [peripheral neuropathy](#) caused by [vitamin B₆](#) deficiency, a condition that can be induced by [isoniazid](#) therapy and [oral contraceptive](#) use. It is not involved in the recovery process from [Guillain-Barré syndrome](#).

E - Lymphocytic infiltration in the endoneurium

Explanation Why

[Lymphocytic](#) infiltration in the [endoneurium](#) of peripheral nerves is part of the underlying pathology of [Guillain-Barré syndrome](#). This autoimmune reaction generates cross-reactive [antibodies](#) that damage peripheral nerve [axons](#). [Lymphocytic](#) infiltration is not involved in the recovery process from this condition.

Question # 21

A 26-year-old woman, gravida 1, para 0, at 22 weeks' gestation is brought to the emergency department by her husband because of a 2-day history of confusion and falls. Pregnancy has been complicated by excessive vomiting and an 8-kg (17-lb) weight loss over the past 10 weeks. Physical examination shows vertical nystagmus and a wide-based gait. Muscle tone and tendon reflexes are diminished in all extremities. An MRI of the brain shows periventricular diffusion abnormalities. Treatment is initiated with a vitamin followed by a dextrose infusion. The primary reason to administer the vitamin first is to ensure the function of which of the following enzymes?

	Answer	Image
A	Pyruvate carboxylase	
B	Methionine synthase	
C	α -Ketoglutarate dehydrogenase	
D	Aminolevulinate synthase	
E	Fatty acid synthase	
F	Succinate dehydrogenase	
G	γ -Glutamyl carboxylase	

Hint

This woman has Wernicke encephalopathy, a condition caused by severe thiamine (vitamin B₁) deficiency. Manifestations of this condition include confusion, oculomotor dysfunction, gait ataxia, peripheral polyneuropathy, and periventricular lesions on MRI. Symptoms can be precipitated by administration of dextrose prior to thiamine.

Correct Answer

A - Pyruvate carboxylase

Explanation Why

[Pyruvate carboxylase](#) converts [pyruvate](#) to [oxaloacetate](#) for [gluconeogenesis](#) and the [TCA cycle](#). This reaction, as well as several other [carboxylation](#) reactions, requires [biotin](#) ([vitamin B7](#)), not [thiamine](#) ([vitamin B1](#)), as a [cofactor](#).

B - Methionine synthase

Explanation Why

[Methionine synthase](#) converts [homocysteine](#) to [methionine](#) by transferring CH₃ groups as methylcobalamin. This reaction, as well as the conversion of [methylmalonyl-CoA](#) to [succinyl-CoA](#) by [methylmalonyl-CoA mutase](#), requires [cobalamin](#) ([vitamin B12](#)), not [thiamine](#) ([vitamin B1](#)), as a [cofactor](#).

C - α -Ketoglutarate dehydrogenase

Explanation But

Other enzymes that require [TPP](#) as a [cofactor](#) include [pyruvate dehydrogenase complex](#) (which converts [pyruvate](#) to [acetyl-CoA](#) for use in cellular respiration) and [transketolase](#) (which converts [ribulose-5-phosphate](#) to fructose-6-phosphate in the [pentose phosphate pathway](#)). Impairment of these reactions also contributes to cellular damage when dextrose is administered prior to [thiamine](#) in patients with [Wernicke encephalopathy](#).

Explanation Why

[\$\alpha\$ -Ketoglutarate dehydrogenase](#) complex converts [\$\alpha\$ -ketoglutarate](#) to [succinyl-CoA](#) in the [TCA cycle](#) and requires [thiamine](#), in the form of [thiamine pyrophosphate](#) ([TPP](#)), as a [cofactor](#). This patient

developed [Wernicke encephalopathy](#) due to increased metabolic demand for [thiamine](#) during [pregnancy](#) in combination with increased loss and inadequate intake due to [hyperemesis gravidarum](#). Patients with suspected [thiamine deficiency](#) should receive [thiamine](#) prior to dextrose to avoid the risk of developing severe [lactic acidosis](#), which can result when [pyruvate](#) is unable to enter the [TCA cycle](#) and undergoes [anaerobic glycolysis](#) to form [lactate](#).

D - Aminolevulinate synthase

Explanation Why

[Aminolevulinate synthase](#) converts [succinyl-CoA](#) and [glycine](#) into [aminolevulinic acid](#) within [mitochondria](#). This reaction is the rate-limiting step of [heme synthesis](#) and requires [pyridoxine](#) ([vitamin B6](#)), not [thiamine](#) ([vitamin B1](#)), as a [cofactor](#).

E - Fatty acid synthase

Explanation Why

Fatty acid synthase catalyzes the formation of [long-chain fatty acids](#) from [acetyl-CoA](#) and malonyl-CoA. The synthesis of this enzyme requires [pantothenic acid](#) ([vitamin B5](#)), not [thiamine](#) ([vitamin B1](#)), as a [cofactor](#).

F - Succinate dehydrogenase

Explanation Why

[Succinate dehydrogenase](#) converts [succinate](#) to [fumarate](#) in the [TCA cycle](#) and oxidizes [FADH₂](#) to [FAD](#) in the [electron transport chain](#). [Redox reactions](#) often use [riboflavin](#) ([vitamin B2](#)) derivatives such as [FAD](#) and [FMN](#), not [thiamine](#) ([vitamin B1](#)) derivatives, as [cofactors](#).

G - γ -Glutamyl carboxylase

Explanation Why

γ -Glutamyl carboxylase activates procoagulative factors of the [coagulation cascade](#), including [factors II](#), VII, IX, X, [protein C](#), and [protein S](#). It requires [vitamin K](#), not [thiamine](#), as a [cofactor](#).

Question # 22

A 53-year-old man is brought to the emergency department by his wife after the sudden onset of dizziness, nausea, and left-sided weakness. His blood pressure is 165/95 mm Hg. Neurological examination shows decreased muscle tone and hyperreflexia in the right upper and lower extremities. His gait is unsteady, and he falls to the left when attempting to walk. Finger-to-nose testing shows dysmetria on the left side. A CT scan of the head shows a small lesion in the left lateral pons that involves the nucleus of a cranial nerve that exits the brain at the middle cerebellar peduncle. Which of the following additional findings is most likely in this patient?

	Answer	Image
A	Ptosis and inability to look up with the right eye	
B	Hoarseness and deviation of the uvula to the right	

	Answer	Image
C	Deviation of the tongue to the left when protruded	Labels on the left side of the diagram: - Optic chiasm - Pituitary stalk - Cerebral crus - Mammillary body - Interpeduncular fossa - Basilar sulcus - Pons - Pontomedullary sulcus - Olivary body - Pyramid - Pyramidal decussation - Anterior median fissure Labels on the right side of the diagram: - Optic nerve (II) - Optic tract - Oculomotor nerve (III) - Trochlear nerve (IV) - Trigeminal nerve (V) - Abducens nerve (VI) - Facial nerve (VII) - Vestibulocochlear nerve (VIII) - Glossopharyngeal nerve (IX) - Vagus nerve (X) - Accessory nerve (XI) - Hypoglossal nerve (XII)
D	Winging of the left scapula and weakness turning the head to the right	Labels on the left side of the diagram: - Optic chiasm - Pituitary stalk - Cerebral crus - Mammillary body - Interpeduncular fossa - Basilar sulcus - Pons - Pontomedullary sulcus - Olivary body - Pyramid - Pyramidal decussation - Anterior median fissure Labels on the right side of the diagram: - Optic nerve (II) - Optic tract - Oculomotor nerve (III) - Trochlear nerve (IV) - Trigeminal nerve (V) - Abducens nerve (VI) - Facial nerve (VII) - Vestibulocochlear nerve (VIII) - Glossopharyngeal nerve (IX) - Vagus nerve (X) - Accessory nerve (XI) - Hypoglossal nerve (XII)
E	Impaired vision and absent direct pupillary light reflex of the left eye	Labels on the left side of the diagram: - Optic chiasm - Pituitary stalk - Cerebral crus - Mammillary body - Interpeduncular fossa - Basilar sulcus - Pons - Pontomedullary sulcus - Olivary body - Pyramid - Pyramidal decussation - Anterior median fissure Labels on the right side of the diagram: - Optic nerve (II) - Optic tract - Oculomotor nerve (III) - Trochlear nerve (IV) - Trigeminal nerve (V) - Abducens nerve (VI) - Facial nerve (VII) - Vestibulocochlear nerve (VIII) - Glossopharyngeal nerve (IX) - Vagus nerve (X) - Accessory nerve (XI) - Hypoglossal nerve (XII)

	Answer	Image
F	Difficulty chewing and deviation of the jaw to the left	The diagram illustrates the efferent and afferent pathways of the trigeminal nerve (CN V) in the brainstem. The left side shows efferent pathways, and the right side shows afferent pathways. The legend indicates: Efferent: General somatic efferent (red), General visceral efferent (yellow), Special visceral efferent (orange). Afferent: General somatic afferent (green), General visceral afferent (blue), Special visceral afferent (purple). Efferent Pathway: The motor nucleus of the trigeminal nerve (V) is located in the midbrain. It gives rise to the motor root of the trigeminal nerve, which branches into the ophthalmic, maxillary, and mandibular divisions. The mandibular division innervates the muscles of mastication (masseter, temporalis, pterygoid). Afferent Pathway: The principal sensory nucleus of the trigeminal nerve (V) is located in the midbrain. It receives sensory input from the trigeminal ganglion. The motor nucleus of the trigeminal nerve (V) also receives input from the principal sensory nucleus (V). Other Nuclei and Nerves: The diagram also shows the following nuclei and nerves: Oculomotor nucleus, Edinger-Westphal nucleus, Mesencephalic nucleus of trigeminal nerve, Trochlear nucleus, Abducens nucleus, Facial motor nucleus, Salivatory nuclei (superior/inferior), Nucleus ambiguus, Hypoglossal nucleus, Dorsal nucleus of vagus nerve, Nucleus of solitary tract, Spinal trigeminal nucleus, and Spinal nucleus of accessory nerve.
G	Inability to smell vanilla or coffee	The diagram illustrates the olfactory pathway. The olfactory nerve (I) is shown entering the brainstem from the olfactory bulb. The olfactory bulb is located above the nasal cavity. The olfactory nerve (I) is shown entering the brainstem from the olfactory bulb. The olfactory bulb is located above the nasal cavity. The olfactory nerve (I) is shown entering the brainstem from the olfactory bulb. The olfactory bulb is located above the nasal cavity.

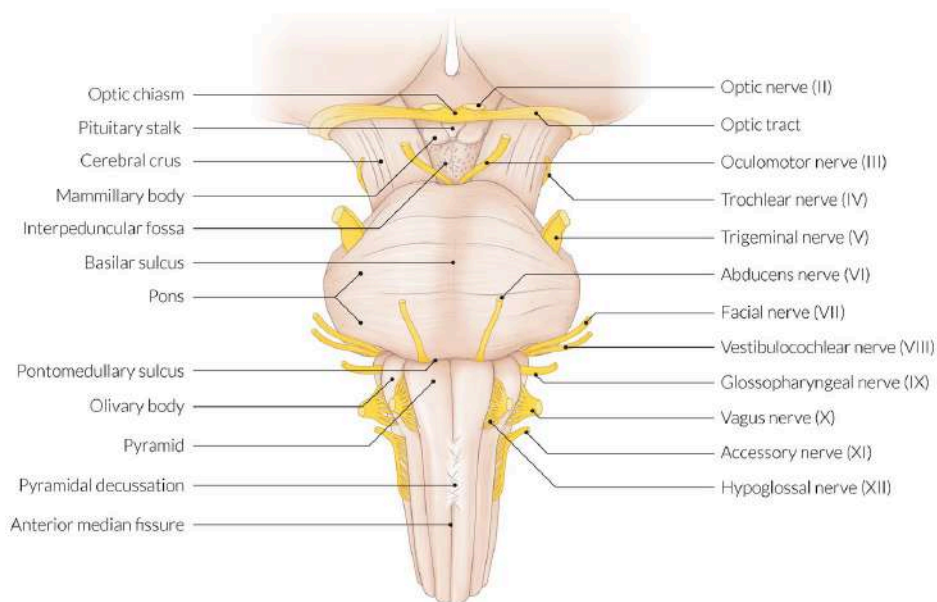
Hint

This patient's symptoms (contralateral hemiparesis and ipsilateral limb ataxia) and imaging findings indicate a diagnosis of lateral pontine syndrome. The trigeminal nerve (CN V) exits the brainstem on the anterior aspect of the pons at the middle cerebellar peduncle.

Correct Answer

A - Ptosis and inability to look up with the right eye

Image

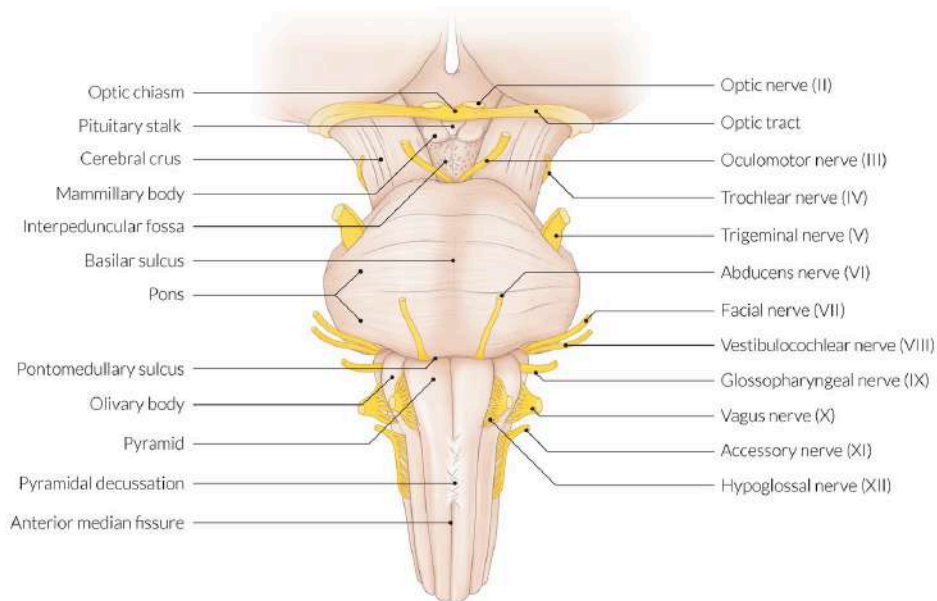


Explanation Why

Ptosis (due to weakness of the levator palpebrae superioris muscle) and the inability to look up (due to weakness of the **superior rectus muscle**) can occur in patients who have a lesion of the **oculomotor nerve (CN III)**. This nerve arises from the **midbrain** and would not be affected by a **pontine** lesion.

B - Hoarseness and deviation of the uvula to the right

Image

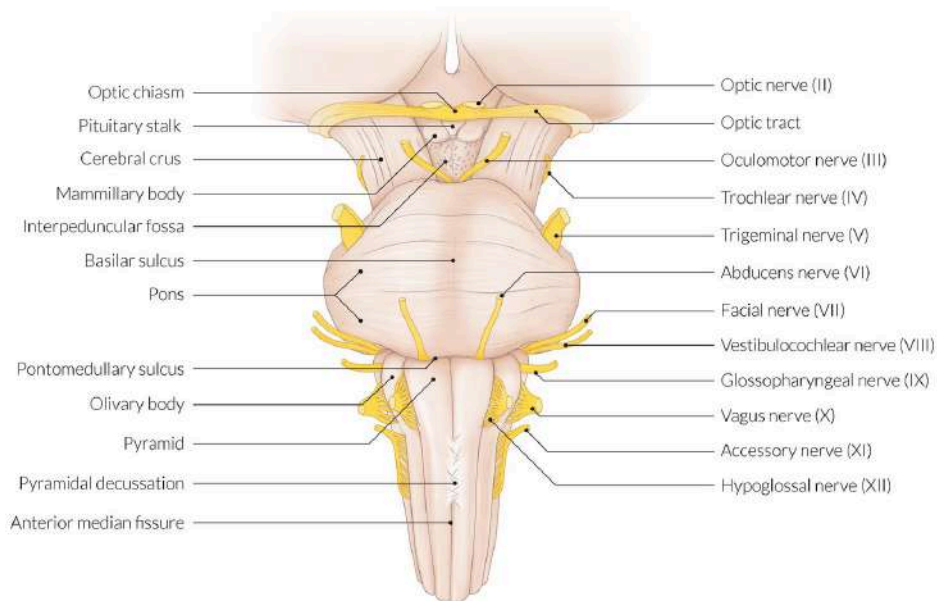


Explanation Why

Hoarseness and deviation of the uvula to the right can occur in patients who have a lesion of the left [vagus nerve \(CN X\)](#). This nerve arises from the medulla and would not be affected by a [pontine](#) lesion.

C - Deviation of the tongue to the left when protruded

Image

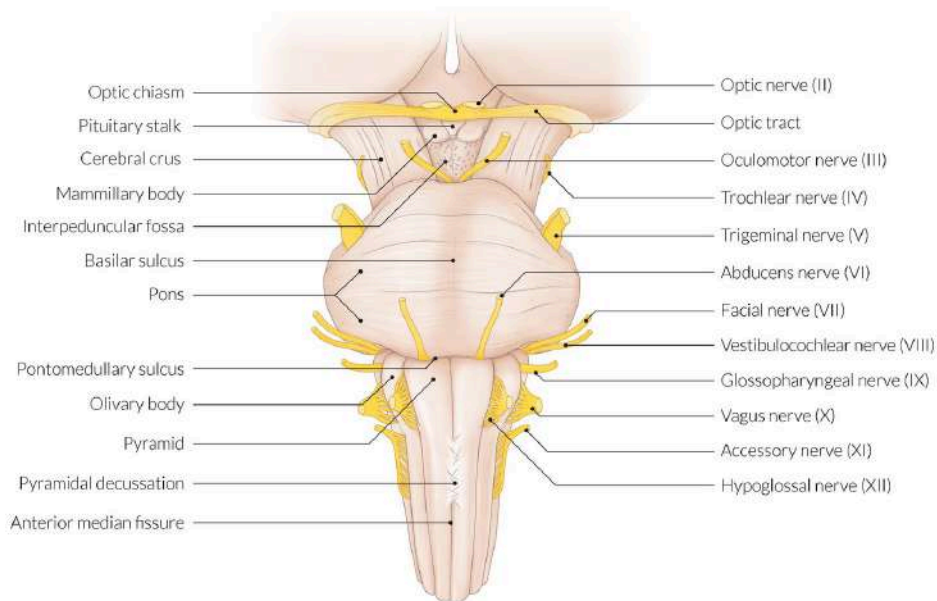


Explanation Why

Deviation of the [tongue](#) to the left when protruded can occur in patients who have a lesion of the left [hypoglossal nerve](#) ([CN XII](#)). This nerve arises from the medulla and would not be affected by a [pontine](#) lesion.

D - Winging of the left scapula and weakness turning the head to the right

Image

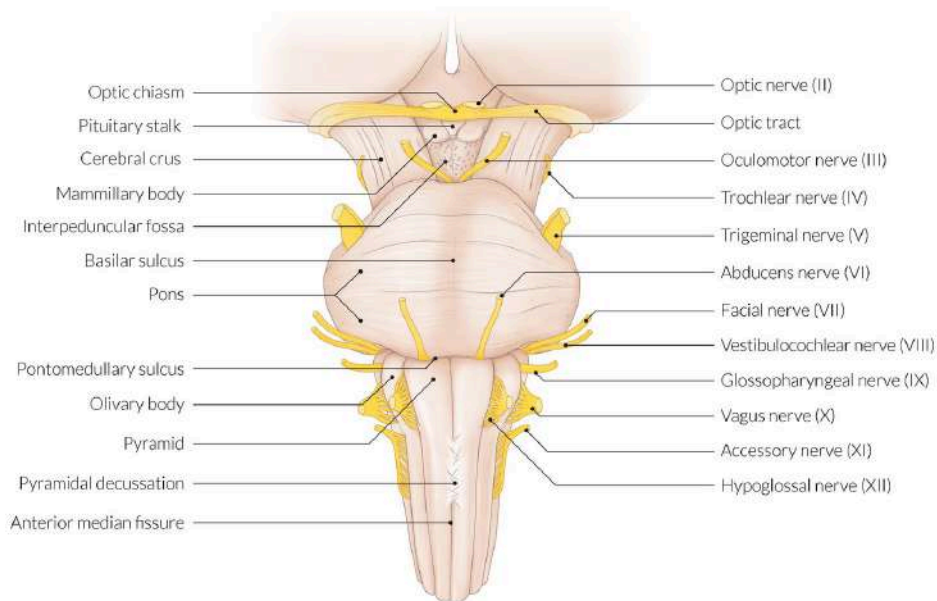


Explanation Why

Winging of the scapula and weakness turning the head to the right are caused by weakness of the left sternocleidomastoid muscle, which can occur in patients who have a lesion of the left spinal accessory nerve (CN XI). This nerve arises from the upper cervical spine (C1–C5) and would not be affected by a pontine lesion.

E - Impaired vision and absent direct pupillary light reflex of the left eye

Image

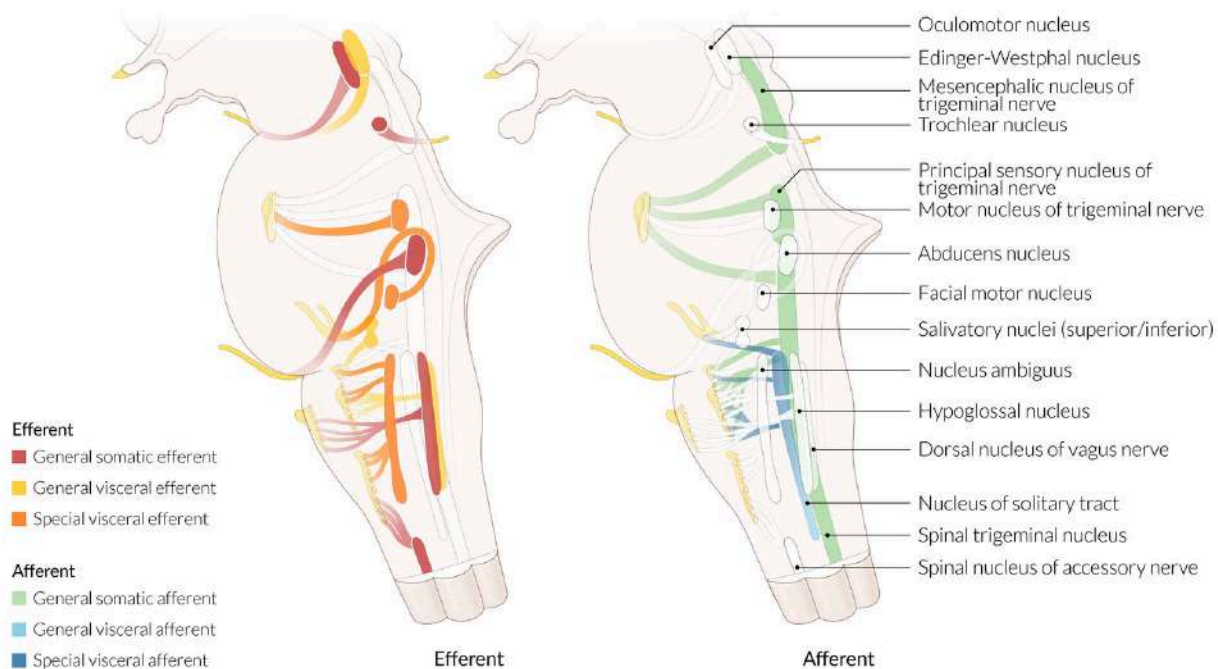


Explanation Why

Impaired vision and absent [direct pupillary light reflex](#) of the left [eye](#) can occur in patients who have a lesion of the left [optic nerve \(CN II\)](#), which transmits visual information from the [retina](#) to the [optic chiasm](#), from which it continues on in the [optic tract](#). The [optic nerve](#) and its continuations arise directly from the forebrain and would not be affected by a [pontine](#) lesion.

F - Difficulty chewing and deviation of the jaw to the left

Image



Explanation But

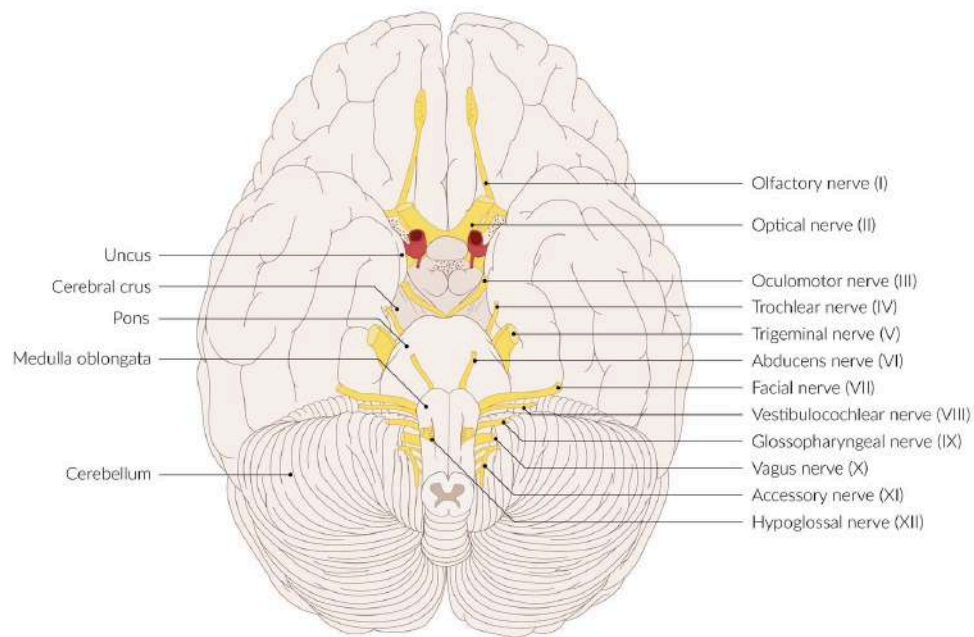
A lesion of the left [lateral pons](#) can also affect the nuclei of the [facial nerve \(CN VII\)](#) and [vestibulocochlear nerve \(CN VIII\)](#). Therefore, patients with [lateral pontine syndrome](#) can also develop ipsilateral facial paralysis ([CN VII](#)) and ipsilateral [hearing loss](#), [vertigo](#), and nystagmus ([CN VIII](#)). The nucleus of the [abducens nerve \(CN VI\)](#) is located in the [medial](#) portion of the [pons](#) and is therefore not typically affected in individuals with [lateral pontine syndrome](#).

Explanation Why

The [trigeminal nerve \(CN V\)](#) exits the brain at the [middle cerebellar peduncle](#), and its motor nucleus is located in the [lateral](#) portion of the upper [pons](#). This patient has an [infarct](#) of the left [lateral pons](#) that involves this nucleus. As a result, the [mandibular branch of the trigeminal nerve \(CN V₃\)](#), which innervates the [muscles of mastication](#) (e.g., the [lateral pterygoid muscle](#)), could be affected and result in difficulty chewing and ipsilateral deviation of the [jaw](#).

G - Inability to smell vanilla or coffee

Image

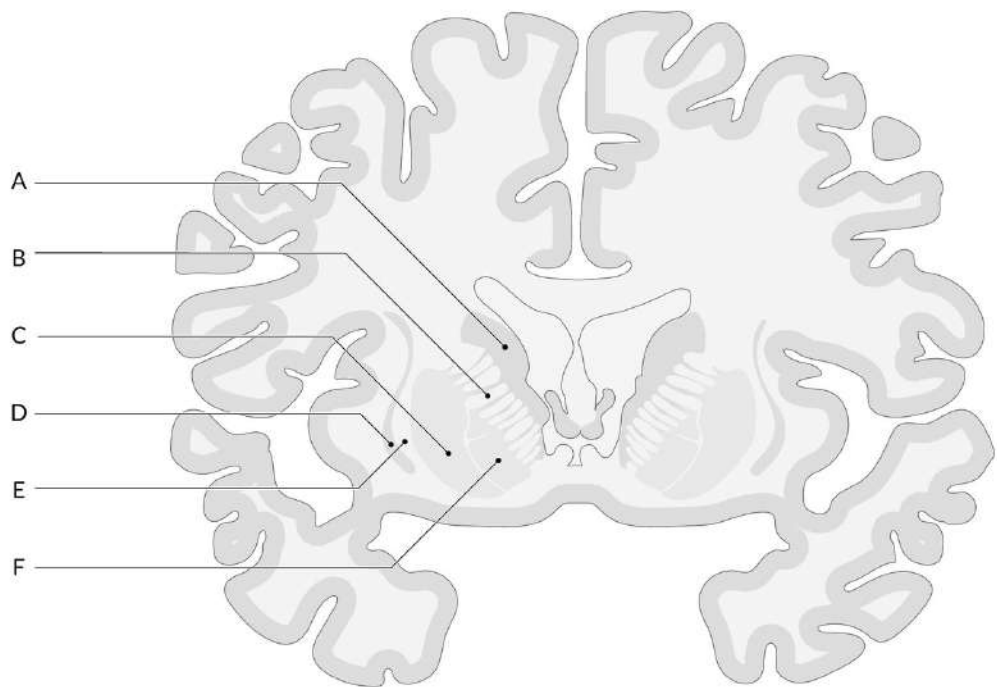


Explanation Why

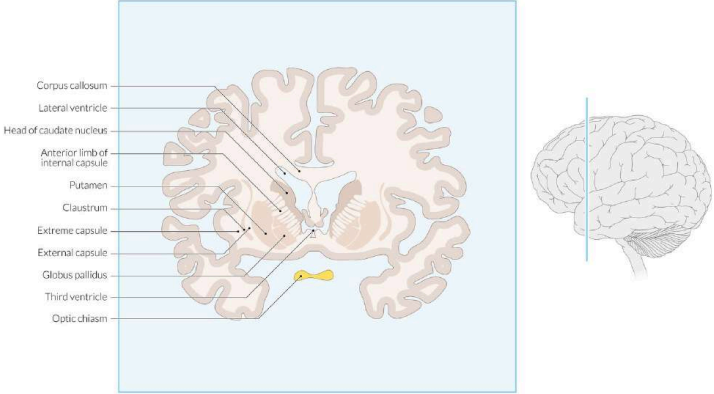
The inability to [smell](#) vanilla or coffee suggests a lesion of the [olfactory nerve \(CN I\)](#). This nerve arises directly from the forebrain and would not be affected by a [pontine](#) lesion.

Question # 23

A 48-year-old man is brought to the emergency department by his wife because of the sudden onset of slurred speech and left-side weakness that began about an hour ago. His wife says the symptoms were preceded by a progressively worsening headache and visual disturbances. He has a history of alcohol use disorder and has smoked 2 packs of cigarettes daily for 20 years. His blood pressure is 210/92 mm Hg. He is only oriented to self and has difficulty answering questions. A CT scan of the head without contrast shows a large hyperdense fluid collection in the right putamen. Which of the following labeled structures most likely represents the affected location?



	Answer	Image
A	A	
B	B	

	Answer	Image
C	C	
D	D	
E	E	
F	F	

Hint

The putamen is the most lateral part of the basal ganglia.

Correct Answer

A - A

Explanation Why

This structure is the head of the [caudate nucleus](#), not the [putamen](#). Lesions of the [caudate nucleus](#) have been implicated in the pathogenesis of [Parkinson disease](#) (depletion of [dopaminergic neurons](#) that [synapse](#) here), [Huntington disease](#) ([atrophy](#) of the caudate), and [schizophrenia](#) (reduced volume of the caudate).

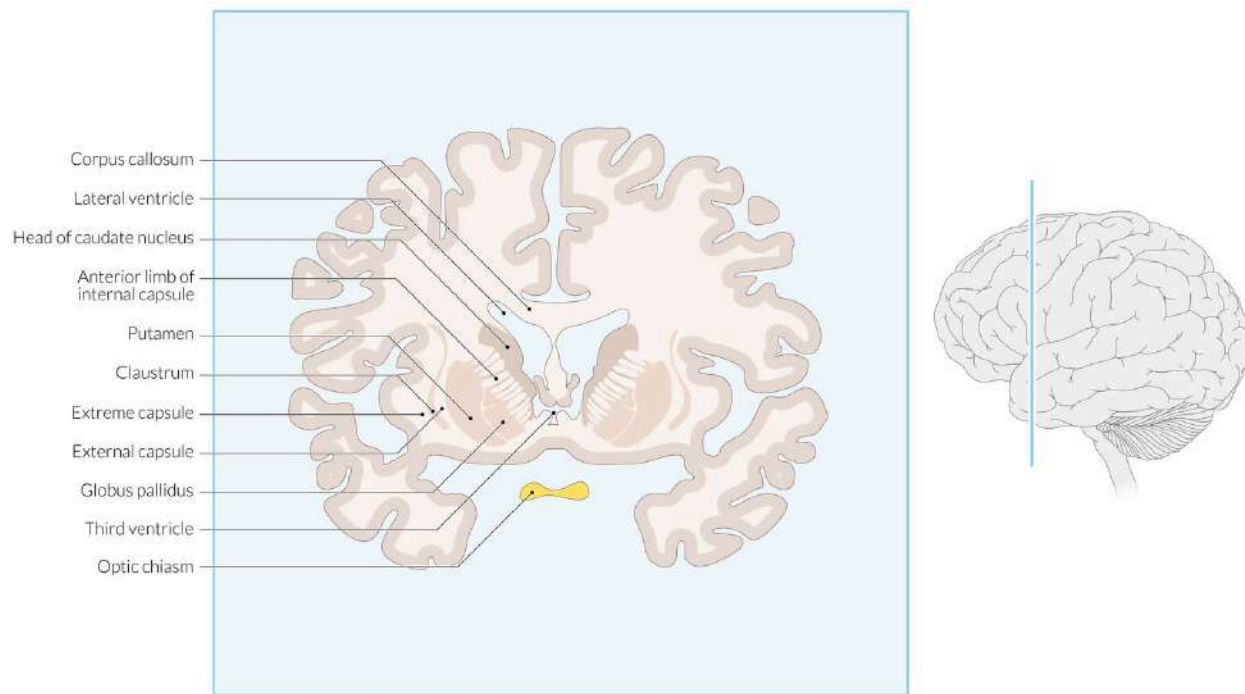
B - B

Explanation Why

This structure is the [anterior](#) limb of the [internal capsule](#), not the [putamen](#). Lesions of the [internal capsule](#) (e.g., due to a [lacunar stroke](#) from occlusion of the [lenticulostriate artery](#)) manifest with contralateral paralysis without cortical signs.

C - C

Image



Explanation But

The acute features of putaminal hemorrhage can vary widely and are usually attributed to the involvement of the surrounding structures. Patients with a small putaminal bleed may be asymptomatic or report features of a [lacunar stroke](#) syndrome (e.g., pure [sensorimotor stroke](#)). With large putaminal hemorrhage, patients can develop [aphasia](#) (dominant side) or [hemineglect](#) (non-dominant side), [intraventricular hemorrhage](#), and raised intracranial tension.

Explanation Why

This structure is the [putamen](#). It forms the [lentiform nucleus](#) with the [globus pallidus](#) and the [striatum](#) with the [caudate nucleus](#). The [putamen](#) has [gabaminergic neurons](#) that project onto the [globus pallidus](#). It receives [dopaminergic](#) input from the [substantia nigra](#) pars compacta and [glutaminergic](#) input from the cortex. The [putamen](#), which receives blood from the [lenticulostriate arteries](#), is the most common location for hypertensive hemorrhage. This typically occurs due to rupture of [Charcot-Bouchard microaneurysms](#). The [putamen](#) is also affected by degenerative conditions such as [Huntington disease](#) and [Wilson disease](#).

D - D

Explanation Why

This structure is the claustrum, not the [putamen](#). Lesions of the claustrum have been implicated in some cases of [epilepsy](#).

E - E

Explanation Why

This structure is the external capsule, not the [putamen](#). Lesions of the external capsule are rare, with [infarction](#) being the most common lesion at this site (manifesting with [cranial nerve palsies](#) and [dysarthria](#)).

F - F

Explanation Why

This structure is the [globus pallidus](#), not the [putamen](#). Dysfunction of the [globus pallidus](#) has been implicated in the pathogenesis of [Huntington disease](#) and [Parkinson disease](#). Furthermore, bilateral lesions of the [globus pallidus](#) may be seen in [carbon monoxide poisoning](#).

Question # 24

An investigator is studying the pattern of glutamate release from presynaptic nerve terminals in human volunteers with Alzheimer disease. The concentration of glutamate in the CA1 region of the hippocampus is measured using magnetic resonance spectroscopy after Schaffer collateral fibers are electrically stimulated. Which of the following events most likely occurs immediately prior to the release of neurotransmitters?

	Answer	Image
A	Activation of G protein-coupled receptors	
B	Synthesis of glutamine	
C	Accumulation of cAMP	
D	Opening of ligand-gated ion channels	
E	Packaging of synaptic vesicles	

	Answer	Image
F	Influx of calcium	The diagram illustrates the three stages of synaptic transmission at a cholinergic synapse: Panel 1: A presynaptic action potential (AP) arrives at the terminal, causing the opening of voltage-gated calcium channels (Ca^{2+}). This leads to the influx of Ca^{2+} ions into the cytoplasm. The presynaptic neuron contains vesicles containing acetylcholine (ACh). Synaptotagmin is located on the vesicle membrane, and v-SNARE proteins are on the vesicle membrane. t-SNARE proteins are on the presynaptic membrane. The synaptic cleft is between the presynaptic and postsynaptic neurons. The postsynaptic neuron has ACh receptors. A resting potential (RP) graph is shown. Panel 2: The influx of Ca^{2+} ions triggers the formation of the SNARE complex, leading to the exocytosis of ACh-containing vesicles into the synaptic cleft. ACh molecules are released and bind to ACh receptors on the postsynaptic membrane, causing the opening of sodium channels (Na^{+}). This results in the influx of Na^{+} ions, generating an endplate potential (EPSP). An action potential (AP) graph is shown. Panel 3: The ACh molecules are broken down by cholinesterase in the synaptic cleft. The resulting choline is taken up by the presynaptic neuron via a choline transporter. The vesicle containing ACh is recycled. A resting potential (RP) graph is shown.

Hint

Activation of the membrane fusion machinery precedes the release of neurotransmitters.

Correct Answer

A - Activation of G protein-coupled receptors

Explanation Why

Activation of [G protein-coupled receptors](#) (GPCRs) modulates the intensity of signaling between presynaptic and postsynaptic [neurons](#), but it does not immediately precede the release of [neurotransmitters](#).

B - Synthesis of glutamine

Explanation Why

[Glial cells](#) facilitate the clearance of [glutamate](#) after it has been released into the [synaptic cleft](#) by converting this [neurotransmitter](#) to [glutamine](#). [Glutamine](#) is then taken up by the presynaptic nerve [axon](#), converted back to [glutamate](#), and packaged into postsynaptic vesicles.

C - Accumulation of cAMP

Explanation Why

The accumulation of [cAMP](#) in presynaptic [neurons](#) results in activation of the PKA signaling pathway, which ultimately increases neuronal plasticity and induces the long-term potentiation of [axons](#). While the accumulation of [cAMP](#) modulates neuronal firing, it does not immediately precede the release of [neurotransmitters](#).

D - Opening of ligand-gated ion channels

Explanation Why

After [glutamate](#) is released from a presynaptic [axon](#), it binds and thus stimulates the opening of [ligand](#)-gated ion channels on the [dendrites](#) of a postsynaptic [neuron](#). [Ligand](#)-gated ion channels open after, not before, the release of the [glutamate neurotransmitter](#).

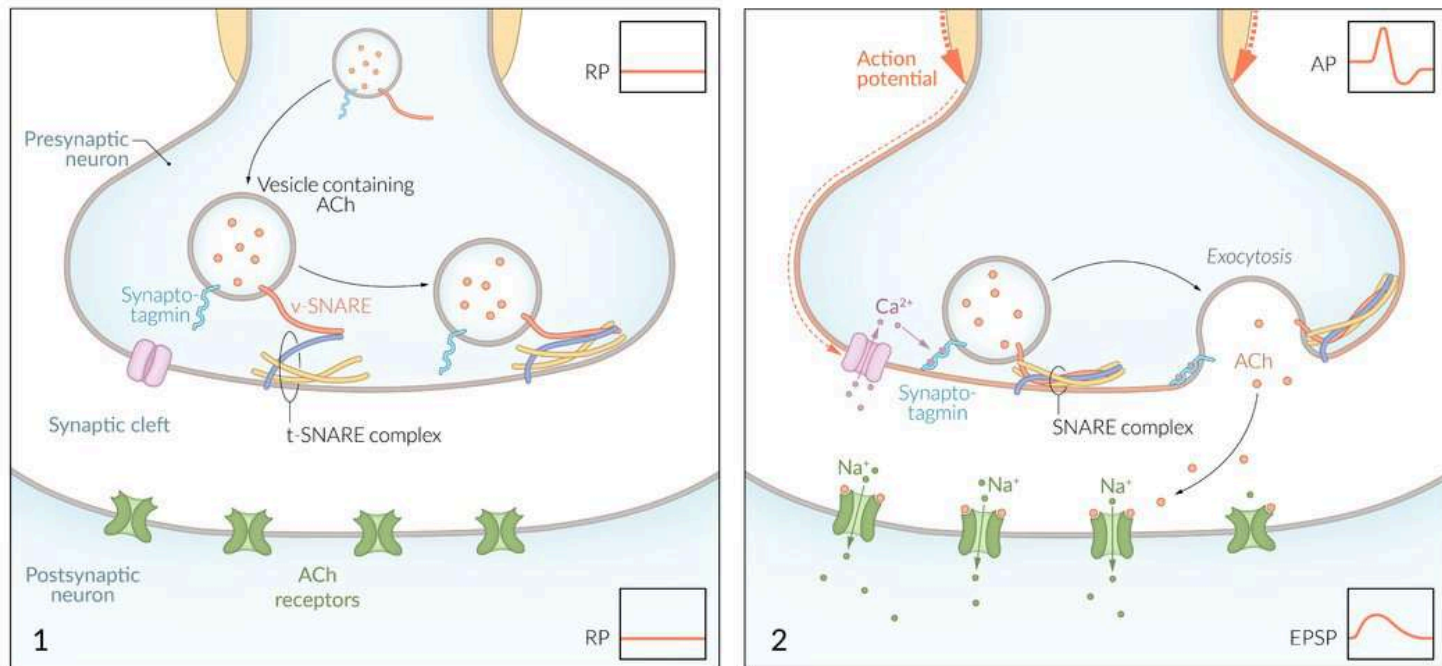
E - Packaging of synaptic vesicles

Explanation Why

[Neurotransmitters](#) are continuously packaged inside synaptic vesicles via specific transporter [proteins](#) expressed on the membranes. Packaging of synaptic vesicles occurs regardless of whether the nerve is depolarized and does not immediately precede the release of [neurotransmitters](#).

F - Influx of calcium

Image



Explanation Why

The release of [neurotransmitters](#) (e.g., [glutamate](#), [catecholamines](#), or [acetylcholine](#)) is immediately preceded by the influx of extracellular calcium into the presynaptic [neurons](#). [Depolarization](#) of the [axon](#) causes voltage-gated calcium channels to open at the terminus of the presynaptic [neurons](#). The increase in calcium facilitates the release of [neurotransmitters](#) by promoting the fusion of vesicles that contain [neurotransmitters](#) with the presynaptic [neuron](#) membrane.

Question # 25

An autopsy is performed on a 39-year-old man 5 days after he was found pulseless at his apartment by his neighbor. Examination of the brain shows liquefactive necrosis in the distribution of the right middle cerebral artery with surrounding edema. Immunophenotyping of a sample of the affected brain tissue shows numerous cells that express CD40 on their surface. On further histopathological evaluation, the morphology of these cells is not readily discernible with Nissl stain. These histological findings are most consistent with which of the following cell types?

	Answer	Image
A	Radial glial cells	
B	Microglia	
C	Astrocytes	
D	Oligodendrocytes	
E	Neurons	
F	Schwann cells	

Hint

These CD40 positive cells in the brain are derived from the mesoderm and are activated in response to tissue damage. The gross findings present on autopsy suggest an ischemic stroke as a cause of his death.

Correct Answer

A - Radial glial cells

Explanation Why

Radial glial cells are progenitor cells that line the ventricles in the brain. Radial glial cells do not stain positive for [CD40](#), rather for [vimentin](#), nestin, and [GFAP](#).

B - Microglia

Explanation But

In general, all [neurons](#) and [glial cells](#) stain with [Nissl stain](#), which is why it is useful for determining [ratios](#) or counts of [neurons](#) and [glial cells](#) but not for identifying specific cell types within that population.

Explanation Why

[Microglia](#) are responsible for the removal of cellular debris and [apoptotic](#) cells in the brain parenchyma and can be seen within 3–5 days after an injury, such as in the case of the [ischemic stroke](#) seen in this patient. Following activation, [microglia](#) express [CD40](#) and other markers, including CD11b, CD68, and [CD45](#).

C - Astrocytes

Explanation Why

[Astrocytes](#) are essential for [reactive gliosis](#), which typically occurs 5–15 days after a [CNS](#) injury and is characterized by the [proliferation](#) of [astrocytes](#), [microglia](#), and [oligodendrocytes](#), creating a [glial scar](#). [Astrocytes](#) stain positive for [GFAP](#) and [glutamine synthetase](#) but not for [CD40](#) as the cells seen in this patient's sample.

D - Oligodendrocytes

Explanation Why

[Oligodendrocytes](#) are involved in [reactive gliosis](#), which typically occurs 5–15 days after a [CNS](#) injury and is characterized by the [proliferation](#) of [astrocytes](#), [microglia](#), and [oligodendrocytes](#), creating a [glial scar](#). [Oligodendrocytes](#) stain positive for [platelet-derived growth factor](#) receptor alpha and SOX10 but not for [CD40](#) as the cells seen in this patient's sample.

E - Neurons

Explanation Why

[Neurons](#) may be present in the sample of this patient's brain tissue, but they would stain positive for [CD45](#) and [GFAP](#), not for [CD40](#).

F - Schwann cells

Explanation Why

[Schwann cells](#) are [neural crest](#)-derived cells that are responsible for the myelination of peripheral nerves. They are not part of the [CNS](#) and would therefore not be expected to be present in this patient's histologic sample. Moreover, they [Schwann cells](#) stain positive for [S100](#) but not for [CD40](#).

Question # 26

One week after starting a new medication, a 16-year-old girl is brought to the emergency department by her mother because of a painful, blistering rash. She has a history of bipolar disorder. Her temperature is 39°C (102°F). Physical examination shows numerous coalescing bullae with epidermal detachment covering the face, trunk, and extremities. There are hemorrhagic erosions on the hard palate and buccal mucosa. When lateral pressure is applied to healthy-appearing skin at the edge of a bulla, a blister starts to form. Which of the following drugs is most likely responsible for this patient's current condition?

	Answer	Image
A	Quetiapine	
B	Topiramate	
C	Valproic acid	
D	Lamotrigine	
E	Lithium	

Hint

This girl's fever, blistering rash, positive Nikolsky sign, and recent medication change are consistent with a diagnosis of Stevens-Johnson syndrome (SJS). Toxic epidermal necrolysis is a severe form of this condition that involves $> 30\%$ of the skin.

Correct Answer

A - Quetiapine

Explanation Why

[Quetiapine](#) is an [atypical antipsychotic](#) that is used with first-line [mood stabilizers](#) to treat refractory [bipolar disorder](#). However, cases of [SJS](#) attributed to [quetiapine](#) therapy have not been reported. More common adverse effects of [quetiapine](#) therapy include [hyperprolactinemia](#), weight gain, [hyperlipidemia](#), [hyperglycemia](#), [prolonged QT interval](#), and [extrapyramidal symptoms](#).

B - Topiramate

Explanation Why

[Topiramate](#) is an [antiepileptic drug](#) with [mood-stabilizing](#) properties that is sometimes used in conjunction with other agents to treat refractory [bipolar disorder](#). However, cases of [SJS](#) attributed to [topiramate](#) therapy have not been reported. More common adverse effects of [topiramate](#) therapy include [glaucoma](#), weight loss, [nephrolithiasis](#), and cognitive impairment.

C - Valproic acid

Explanation Why

[Valproic acid](#) is an [antiepileptic drug](#) with [mood-stabilizing](#) properties that is used to treat [bipolar disorder](#). However, [valproic acid](#) is an extremely rare cause of [SJS](#). More common adverse effects of [valproic acid](#) therapy include hepatic [necrosis](#), [pancreatitis](#), drug interactions due to [CYP450](#) inhibition, weight gain, and gastrointestinal distress.

D - Lamotrigine

Explanation But

Other commonly implicated triggers of [SJS](#) include [allopurinol](#), [sulfamethoxazole](#), [sulfa drugs](#), and [phenobarbital](#). Other [antiepileptic drugs](#), such as [phenytoin](#), [carbamazepine](#), and [ethosuximide](#), can also cause [SJS](#) but are less frequently implicated than [lamotrigine](#).

Explanation Why

[Lamotrigine](#) is an [antiepileptic drug](#) with [mood-stabilizing](#) properties that is used to treat [bipolar disorder](#). It is one of the most commonly implicated triggers of [SJS](#). Most cases of [SJS](#) develop within 2–8 weeks of initiating the offending medication. The risk of developing [SJS](#) induced by [lamotrigine](#) therapy is greatest when high doses are used, so the initial dose should be low and increased slowly. In addition, about 10% of patients treated with [lamotrigine](#) develop a benign [skin](#) rash that is difficult to differentiate from early [SJS](#); accordingly, all patients should be advised to discontinue [lamotrigine](#) therapy at the first sign of a rash.

E - Lithium

Explanation Why

[Lithium](#) is a [mood stabilizer](#) used to treat [bipolar disorder](#). However, cases of [SJS](#) attributed to [lithium](#) therapy have not been reported. More common adverse effects of [lithium](#) therapy include gastrointestinal distress, neurologic symptoms (e.g., slurred [speech](#), [ataxia](#), hand [tremors](#), [seizures](#)), [nephrogenic diabetes insipidus](#), [thyroid](#) dysfunction ([hyperthyroidism](#) or [hypothyroidism](#)), and [teratogenesis](#) ([Ebstein anomaly](#)).

Question # 27

A 33-year-old man is brought to the emergency department 20 minutes after he fell from the roof of his house. On arrival, he is unresponsive to verbal and painful stimuli. His pulse is 72/min and blood pressure is 132/86 mm Hg. A CT scan of the head shows a fracture in the anterior cranial fossa and a 1-cm laceration in the left anterior orbital gyrus. If the patient survives, which of the following would ultimately be the most common cell type at the injured region of the frontal lobe?

	Answer	Image
A	Schwann cells	
B	Neurons	
C	Astrocytes	
D	Microglia	
E	Fibroblasts	
F	Oligodendrocytes	

Hint

These cells are derived from the neuroectoderm, are GFAP-positive and are a component of the blood-brain barrier.

Correct Answer

A - Schwann cells

Explanation Why

[Schwann cells](#) are support cells within the nervous system that facilitate the [regeneration](#) of damaged nerves. However, they are solely found in the [peripheral nervous system](#).

B - Neurons

Explanation Why

[Neurons](#) are outnumbered by [glial cells](#) in the brain. Furthermore, [neurons](#) are post-[mitotic](#) and therefore cannot carry out [mitosis](#) in response to neuronal damage.

C - Astrocytes

Explanation Why

Following [CNS](#) damage (e.g., [stroke](#), [traumatic brain injury](#)), [astrocytes](#) at the margin of the damaged region proliferate and enlarge ([reactive gliosis](#)) to form a permanent [glial scar](#). The process of [reactive gliosis](#) usually begins 1–2 weeks after the injury.

D - Microglia

Explanation Why

[Microglia](#), which are the [macrophages](#) of the brain, are activated in response to brain injury. They

would [phagocytose](#) the dead neuronal tissue, but they would not be a major component of the [glial scar](#) that ultimately forms at the site of injury.

E - Fibroblasts

Explanation Why

[Fibroblasts](#), which synthesize [collagen](#), are important for healing and [scar](#) formation following injury. However, [fibroblasts](#) would not be the most common cell type in [scar](#) tissue within the [CNS](#).

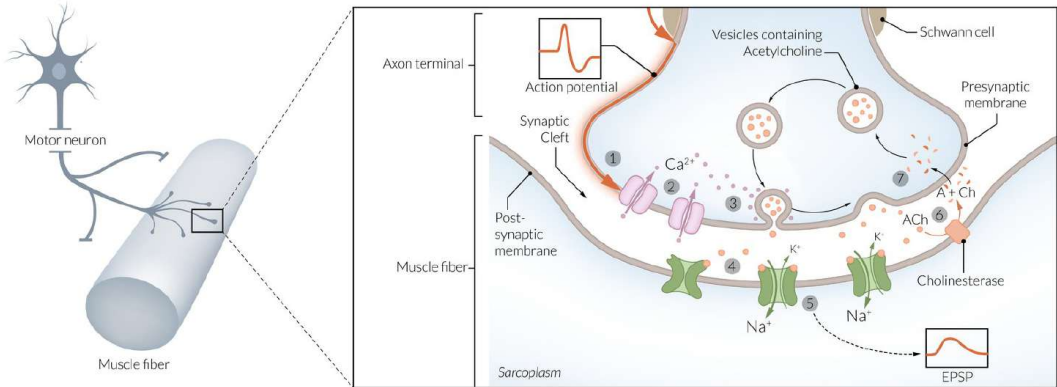
F - Oligodendrocytes

Explanation Why

[Oligodendrocytes](#) are part of the supportive tissue of the [CNS](#) and are important for remyelinating damaged [axons](#). However, [oligodendrocytes](#) are not the most common cell type of the [glial scar](#) that ultimately forms at the site of injury.

Question # 28

An investigator is developing a drug that results in contraction of the pupillary dilator muscle when instilled topically. The drug works by increasing neurotransmitter release from the presynaptic nerve terminal. When administered intravenously, this drug is most likely to have which of the following additional effects?

	Answer	Image
A	Contraction of skeletal muscles	 The diagram illustrates the process of a neuromuscular junction. On the left, a motor neuron is shown with its axon extending to a muscle fiber. A dashed box highlights the axon terminal, which is shown in a larger, detailed view on the right. In the axon terminal, an action potential (represented by a red line graph) travels down the axon. This triggers the opening of voltage-gated calcium channels (labeled 1 and 2), allowing Ca2+ ions to enter the terminal. The influx of Ca2+ causes vesicles containing acetylcholine (ACh) to fuse with the presynaptic membrane (labeled 3), releasing ACh into the synaptic cleft. ACh then binds to receptors on the post-synaptic membrane (labeled 4), which opens sodium channels (labeled 5) and closes potassium channels (labeled 6). This results in a net inward current, leading to an end-plate potential (EPSP), shown as a red line graph. The EPSP triggers an action potential in the muscle fiber, which then contracts. The diagram also shows a Schwann cell surrounding the axon terminal and cholinesterase enzymes in the synaptic cleft that break down ACh into acetate (A-) and choline (Ch).
B	Acceleration of gut peristalsis	
C	Relaxation of the bladder neck sphincter	

	Answer	Image
D	Release of epinephrine by the adrenal medulla	
E	Secretion of sweat by exocrine glands	
F	Increase in pyloric sphincter tone	

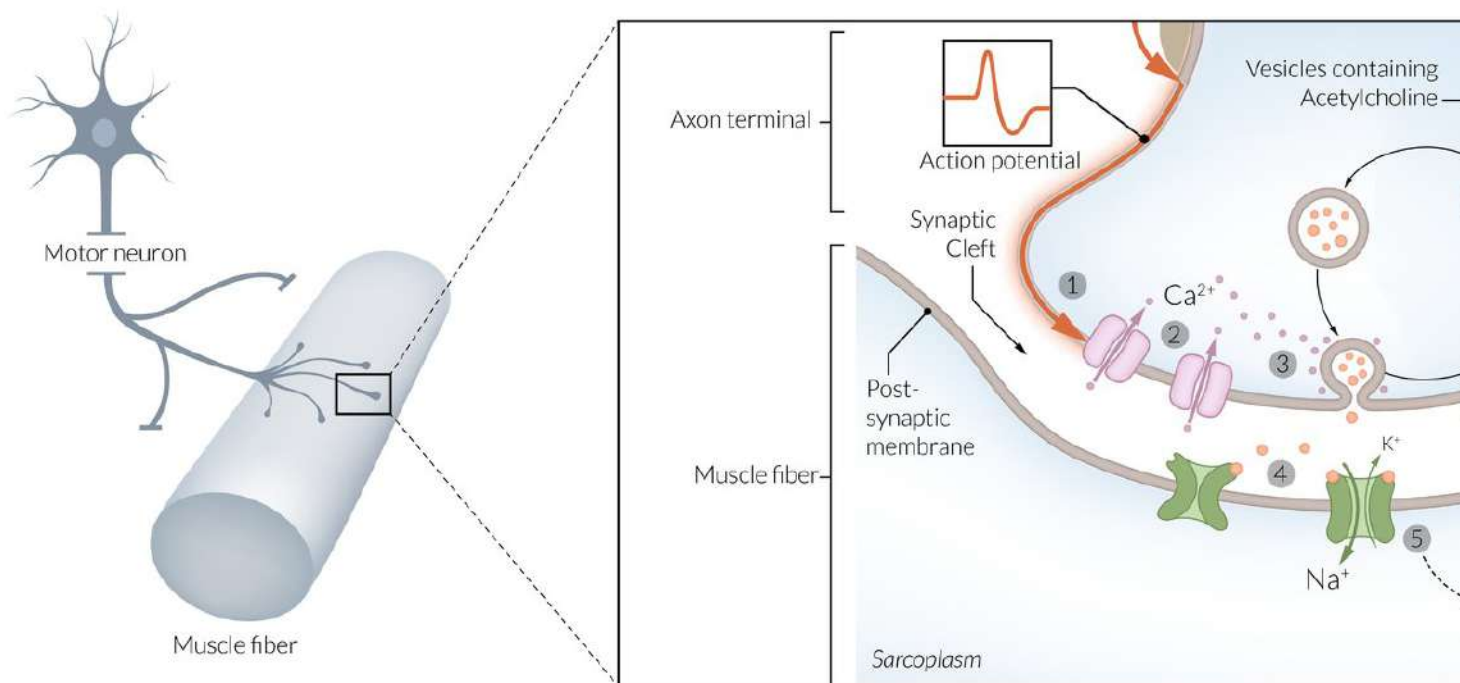
Hint

The pupillary dilator muscle is a smooth muscle that is innervated by sympathetic fibers.

Correct Answer

A - Contraction of skeletal muscles

Image



Explanation Why

[Skeletal muscle](#) contraction occurs in response to [acetylcholine](#) release from somatic nerves. The drug described here works by increasing [norepinephrine](#) release from the ends of [postganglionic sympathetic](#) fibers, which is not involved in the contraction of [skeletal muscles](#).

B - Acceleration of gut peristalsis

Explanation Why

Increased gut [peristalsis](#) occurs in response to [acetylcholine](#) release from the [postganglionic parasympathetic](#) fibers in the muscularis externa ([Auerbach plexus](#)). The drug mentioned here works

by increasing [norepinephrine](#) release from the ends of [postganglionic sympathetic](#) fibers, which would be expected to cause a decrease in [peristalsis](#).

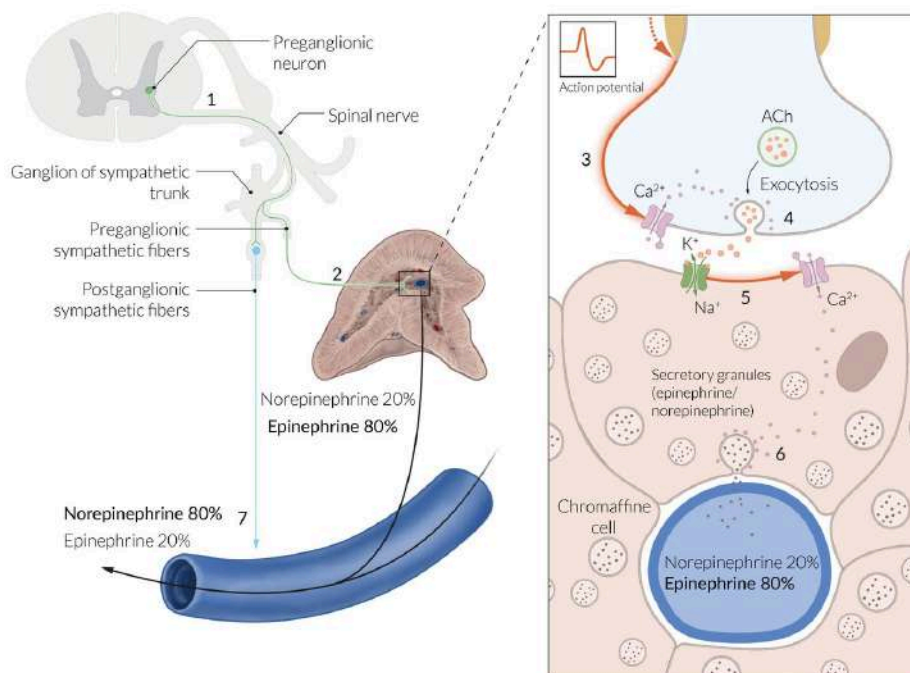
C - Relaxation of the bladder neck sphincter

Explanation Why

Relaxation of the [bladder neck sphincter](#) occurs in response to decreased release of [norepinephrine](#) from the ends of [postganglionic sympathetic](#) fibers or blockade of the [norepinephrine](#) receptors ([alpha-1 receptors](#)) found on the [bladder neck](#). The drug in question, which increases [norepinephrine](#) release from [postganglionic sympathetic](#) fibers, would have the opposite effect and cause contraction of the [bladder neck sphincter](#).

D - Release of epinephrine by the adrenal medulla

Image



Explanation Why

The release of [epinephrine](#) by the [adrenal medulla](#) occurs in response to the release of [acetylcholine](#) from [preganglionic sympathetic](#) fibers. [Epinephrine](#) then acts on target tissues to produce a [sympathetic](#) response. The drug in question works by directly increasing [norepinephrine](#) release from the ends of [postganglionic sympathetic](#) fibers.

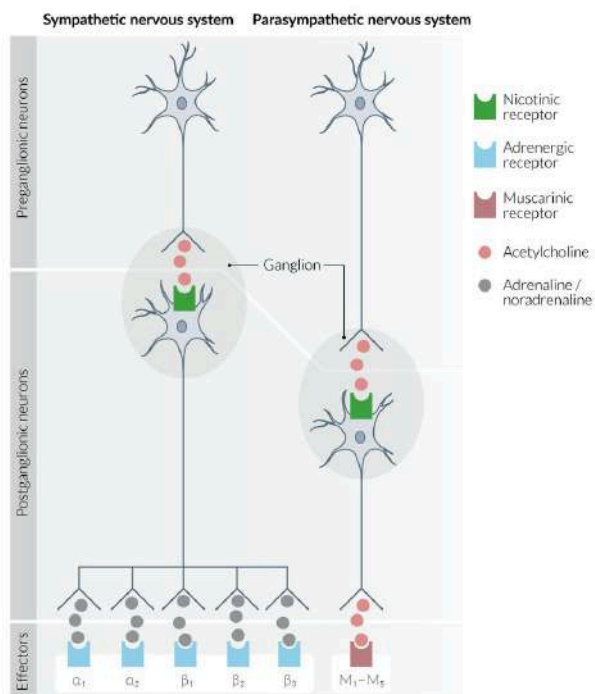
E - Secretion of sweat by exocrine glands

Explanation Why

Secretion of sweat by [exocrine glands](#) occurs in response to increased [acetylcholine](#) release from the ends of [postganglionic sympathetic](#) fibers. The drug in question also works by increasing the release of a [neurotransmitter](#) from [postganglionic sympathetic](#) fibers, but the [neurotransmitter](#) is [norepinephrine](#) rather than [acetylcholine](#).

F - Increase in pyloric sphincter tone

Image



Explanation Why

Contraction of the [pupillary dilator](#) occurs in response to increased [acetylcholine](#) release from the ends of [preganglionic sympathetic](#) fibers at the [superior cervical ganglion](#) and, subsequently, increased [norepinephrine](#) release from the ends of [postganglionic sympathetic](#) fibers within the [pupillary dilator](#) muscle. Since this drug caused [pupillary dilator](#) contraction when instilled topically, its most likely mechanism of action is the direct stimulation of [norepinephrine](#) release.

[Norepinephrine](#), which is an adrenergic [agonist](#), has the highest affinity for [alpha-1 receptors](#).

Besides [pupillary dilator](#) contraction, the other effects of alpha-1 stimulation include vasoconstriction, contraction of the [bladder](#) sphincter, and contraction of all intestinal sphincters including the [pyloric sphincter](#).

Question # 29

A 72-year-old man comes to the physician for a 5-month history of hoarseness, exertional dyspnea, and fatigue. He does not smoke or drink alcohol. His pulse is 98/min and irregular. His voice is coarse in quality. Physical examination shows a liver span of 16 cm and a soft diastolic murmur heard best at the apex. Which of the following is the most likely cause of this patient's hoarseness?

	Answer	Image
A	Carcinoma arising from the mucosa of the larynx	
B	Extrinsic impingement of the recurrent laryngeal nerve	
C	Bacterial infection of the vocal folds	
D	Occlusion of the posterior inferior cerebellar artery	

	Answer	Image
E	Laryngeal inflammation due to chemical irritant	
F	Circulating acetylcholine receptor antibodies	

Hint

This patient's fatigue, exertional dyspnea, irregular heart rhythm, and hepatomegaly suggest atrial fibrillation and congestive heart failure (CHF). In this setting, the diastolic murmur at the apex is concerning for mitral stenosis, which commonly leads to left atrial dilation.

Correct Answer

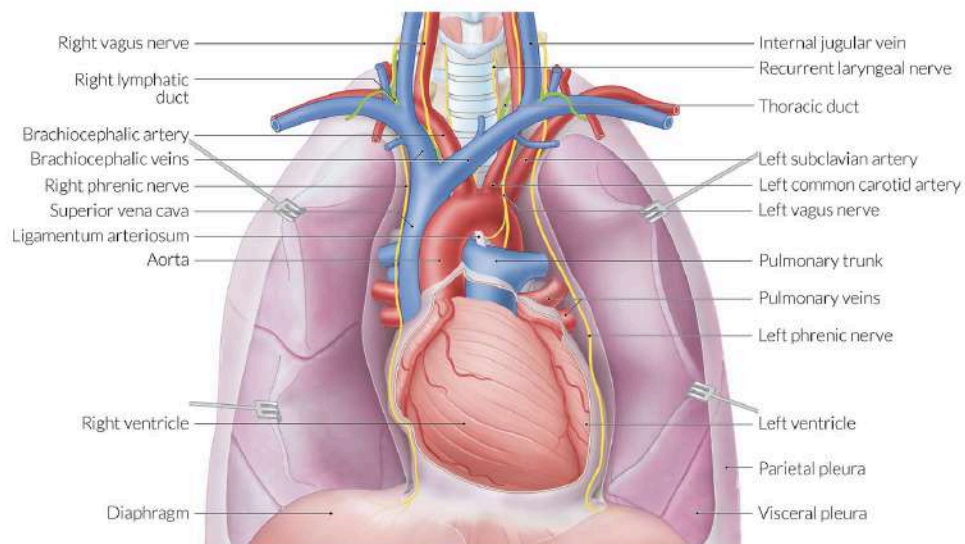
A - Carcinoma arising from the mucosa of the larynx

Explanation Why

A [squamous cell carcinoma](#) arising from laryngeal mucosa can cause hoarseness, fatigue, [dyspnea](#) due to [lung metastases](#) and, rarely, [hepatomegaly](#) due to [liver metastases](#). However, a laryngeal [malignancy](#) would not explain the [atrial fibrillation](#) and the [diastolic murmur](#) in this patient without [risk factors](#) for laryngeal [malignancy](#) such as smoking and alcohol consumption.

B - Extrinsic impingement of the recurrent laryngeal nerve

Image



Explanation Why

The left [recurrent laryngeal nerve](#) winds around the [arch of the aorta](#). Massive enlargement of the [left](#)

[atrium](#) (and potentially also the [pulmonary artery](#)) in patients with [mitral stenosis](#) can compress this nerve resulting in hoarseness (Ortner syndrome). Other rare complications associated with massive [left atrial enlargement](#) are massive [hemoptysis](#) due to erosion of the [bronchial arteries](#) and esophageal compression (dysphagia megalatriensis).

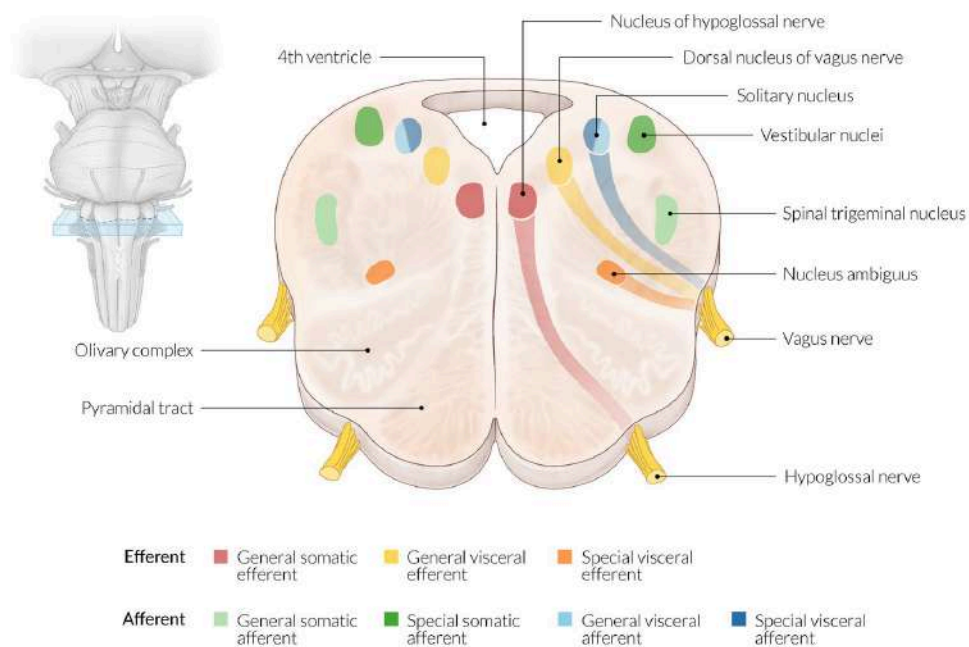
C - Bacterial infection of the vocal folds

Explanation Why

Infection of the [vocal folds](#) ([laryngitis](#)) with bacteria such as [Moraxella catarrhalis](#), [Hemophilus influenzae](#), and [Streptococcus pneumoniae](#) can cause hoarseness and fatigue, but the onset of symptoms would be acute, unlike in this patient, who has had symptoms for the past 5 months, and would likely include [sore throat](#) or a dry [cough](#). Moreover, [laryngitis](#) would not cause exertional dyspnea, fatigue, [hepatomegaly](#), or a [diastolic murmur](#).

D - Occlusion of the posterior inferior cerebellar artery

Image



Explanation Why

Patients with [atrial fibrillation](#) are at increased risk for a [thromboembolic stroke](#), and a [stroke](#) in the region of the [posterior inferior cerebellar artery](#) ([lateral medullary syndrome](#)) could cause hoarseness due to [nucleus ambiguus infarction](#) and [dyspnea](#) due to [dorsal vagal nucleus infarction](#) as well as fatigue. However, hoarseness and [dyspnea](#) would have been acute and preceded the onset of fatigue by weeks to months (post-[stroke](#) fatigue). Moreover, a PICA [stroke](#) would also cause other clinical features such as [dysphagia](#), [vertigo](#), nystagmus, ipsilateral [ataxia](#), ipsilateral [Horner syndrome](#), and decreased [pain](#) and temperature sensation in one side of the face and the contralateral half of the body.

E - Laryngeal inflammation due to chemical irritant

Explanation Why

Laryngeal [inflammation](#) from acidic gastric contents, which occurs in [gastroesophageal reflux disease](#) ([GERD](#)), can cause persistent hoarseness, but it would not cause exertional dyspnea, fatigue, [hepatomegaly](#), or a [diastolic murmur](#). Furthermore, this patient does not have other common features of [GERD](#) such as postprandial [chest pain](#), belching, or dry [cough](#).

F - Circulating acetylcholine receptor antibodies

Explanation Why

Circulating [acetylcholine receptor antibodies](#) are seen in patients with [myasthenia gravis](#) (MG), which can cause fluctuating fatigue, hoarseness, [stridor](#), and, rarely, [dyspnea](#). The classic presentation of this condition includes [diplopia](#) and [ptosis](#) that worsen as the day progresses, neither of which have been reported by this patient. In addition, MG would not cause [atrial fibrillation](#), a [diastolic murmur](#), or [hepatomegaly](#).

Question # 30

A 73-year-old man is brought to the physician by his daughter for evaluation of increasing forgetfulness during the past 6 months. The daughter reports that he recently got lost while walking home from the grocery store. He has also been more irritable recently. On mental status examination, he has a normal affect. He is oriented to person and place but cannot recall which month it is. He recalls memories from more than 20 years ago in great detail but cannot state his home address or the name of his recently born grandson. His gait is normal and there is no nystagmus. An MRI of the brain is shown. Which of the following is the most likely underlying cause of the radiologic findings?



	Answer	Image
A	Inflammation of the choroid plexus	
B	Atrophy of the cortex	
C	Demyelination of periventricular structures	

	Answer	Image
D	Bleeding into the ventricular system	
E	Obstruction of the foramen of Monro	

Hint

This elderly patient has progressively worsening memory loss (especially of recently formed memories), mood alterations, and disorientation, which are all suggestive of dementia. Alzheimer disease is the most common cause of dementia in individuals aged > 65 years.

Correct Answer

A - Inflammation of the choroid plexus

Explanation Why

[Inflammation](#) of the [choroid plexus](#) (choroid plexitis), which is most commonly caused by [CNS](#) infection (e.g., [tuberculosis](#), [cryptococcosis](#)) can result in increased [CSF](#) production and thereby cause [lateral ventricle](#) enlargement, as seen here on the [T2 weighted MRI](#). However, this patient does not have any clinical features of [CNS](#) infection (e.g., [fever](#), [headache](#), meningism) and there is no enlargement of the [choroid plexus](#) in the [lateral ventricles](#) on imaging to suggest choroid plexitis.

B - Atrophy of the cortex

Explanation Why

[Atrophy](#) of the cortex of the brain (especially the [medial temporal lobe](#) structures) with narrowing of the [gyri](#) and widening of the sulci are characteristic neuroradiological findings in patients with [Alzheimer disease](#). The ventricular dilation seen on imaging is a consequence of cerebral loss, with the ventricles expanding to fill the volume formerly occupied by the cortex. This phenomenon is known as [hydrocephalus ex vacuo](#) but unlike true [hydrocephalus](#), there is no primary pathology of [cerebrospinal fluid](#) production or outflow in patients with [Alzheimer disease](#). This patient's normal gait and lack of urinary symptoms are important in differentiating this presentation of [Alzheimer disease](#) from the classic presentation of [hydrocephalus](#), given that the neuroimaging findings in both conditions are similar.

C - Demyelination of periventricular structures

Explanation Why

[Demyelination](#) of periventricular areas is seen in [multiple sclerosis](#) and [Wernicke encephalopathy](#). Patients affected by either of these conditions can develop irreversible [memory](#) loss and personality changes, as seen here. However, the onset of [memory](#) loss and personality changes would be preceded by a history of fatigue and episodic neurological deficits in the case of [multiple sclerosis](#),

and the triad of confusion, [ataxia](#), and [ophthalmoplegia](#) (due to mamillary body [atrophy](#)) in the case of [Wernicke encephalopathy](#). Furthermore, the [T2 weighted MRI](#) of this patient does not show any evidence of periventricular [demyelination](#).

D - Bleeding into the ventricular system

Explanation Why

Bleeding into the [ventricular system](#) can cause [obstructive hydrocephalus](#) and thereby result in ventricular enlargement, as seen here in the [T2 weighted MRI](#). However, [intraventricular hemorrhage](#) usually presents acutely with a severe [headache](#) and features of raised [intracranial pressure](#) (e.g., nausea, vomiting, blurred vision), unlike this patient who presents with cognitive impairment and [mood](#) changes that have progressively worsened over the past 6 months. Furthermore, there is no radiological evidence of an [intraventricular hemorrhage](#) on this patient's [MRI](#) (e.g., mixed fluid attenuation)

E - Obstruction of the foramen of Monro

Explanation Why

Obstruction of the [foramen of Monro](#), which is typically caused by a [tumor](#) (e.g., colloid cyst), would result in unilateral (asymmetrical) [lateral ventricle](#) enlargement, unlike this patient who has symmetrical enlargement of both the [lateral ventricles](#) on the [T2 weighted MRI](#).

Question # 31

A 29-year-old man comes to the emergency department because of progressively worsening fatigue and shortness of breath for the past 2 weeks. His only medication is insulin. Examination shows elevated jugular venous distention and coarse crackles in both lungs. Despite appropriate life-saving measures, he dies. Gross examination of the heart at autopsy shows concentrically thickened myocardium and microscopic examination shows large cardiomyocytes with intracellular iron granules. Examination of the spinal cord shows atrophy of the lateral corticospinal tracts, spinocerebellar tracts, and dorsal columns. Which of the following is the most likely underlying cause of this patient's condition?

	Answer	Image
A	SOD1 gene mutation on chromosome 21	
B	CTG trinucleotide repeat expansion on chromosome 19	
C	Dystrophin gene mutation on the X chromosome	
D	GAA trinucleotide repeat expansion on chromosome 9	
E	HFE gene mutation on chromosome 6	
F	SMN1 gene mutation on chromosome 5	

Hint

In a patient of this age, the combination of spinal cord degeneration, insulin-dependence, and hypertrophic cardiomyopathy suggests Friedreich ataxia.

Correct Answer

A - SOD1 gene mutation on chromosome 21

Explanation Why

An *SOD1* [gene](#) mutation on [chromosome](#) 21 is the underlying genetic pathology of familial [amyotrophic lateral sclerosis](#) (ALS). Although [ALS](#) can manifest with degeneration of the [lateral corticospinal tracts](#) ([upper motor neuron](#)), [atrophy](#) of the [spinocerebellar tracts](#) and [dorsal columns](#) would not be expected. In addition, [ALS](#) would also cause degeneration of the [anterior horn cells](#) ([lower motor neuron](#)), which is not seen here. Furthermore, [ALS](#) is not associated with [diabetes mellitus](#) or [hypertrophic cardiomyopathy](#), and respiratory failure is the most common cause of death, not [heart failure](#).

B - CTG trinucleotide repeat expansion on chromosome 19

Explanation Why

A CTG [trinucleotide repeat expansion](#) on the *DMPK* [gene](#) on [chromosome](#) 19 is the underlying genetic pathology of [myotonic dystrophy type 1](#) (MD1). MD1 is associated with [cardiomyopathies](#) and may be accompanied by multiple endocrinopathies, including insulin resistance, but frank [diabetes mellitus](#) would be unusual. More importantly, MD1 does not manifest with [spinal cord atrophy](#).

C - Dystrophin gene mutation on the X chromosome

Explanation Why

A *DMD* [gene](#) ([dystrophin](#)) mutation on the X [chromosome](#) is the underlying genetic pathology of Duchenne and Becker [muscular dystrophies](#) (DMD and BMD). Neither [DMD](#) nor BMD manifests with the [spinal cord atrophy](#) seen in this patient. Moreover, neither disease is associated with [diabetes mellitus](#) or [hypertrophic cardiomyopathy](#).

D - GAA trinucleotide repeat expansion on chromosome 9

Explanation But

A similar pattern of [spinal cord](#) degeneration is seen in [subacute combined degeneration](#) due to [vitamin B₁₂ deficiency](#).

Explanation Why

A GAA [trinucleotide repeat expansion](#) on [chromosome](#) 9 results in defective [frataxin](#) production, which causes [Friedreich ataxia](#). [Frataxin](#) is involved in the synthesis of [iron](#)-sulfur clusters, which are used in the [mitochondrial respiratory chain](#). A deficiency of the protein causes [iron](#) to accumulate within cells, including in the [heart](#), resulting [hypertrophic cardiomyopathy](#), in [pancreatic islets](#), which explains the patient's need for [insulin therapy](#), and in the [spinal cord](#), causing neurologic dysfunction.

E - HFE gene mutation on chromosome 6

Explanation Why

An [HFE gene](#) mutation on [chromosome](#) 6 is the underlying genetic pathology of [hemochromatosis](#), which can manifest with [cardiomyopathy](#) (either [dilated cardiomyopathy](#) or [restrictive cardiomyopathy](#)) and [diabetes mellitus](#), both of which are caused by [iron overload](#). However, [hypertrophic cardiomyopathy](#) would not be expected, and [hemochromatosis](#) would not explain the [spinal cord atrophy](#) found in this patient's autopsy.

F - SMN1 gene mutation on chromosome 5

Explanation Why

An [SMN1 gene](#) mutation on [chromosome](#) 5 is the underlying genetic pathology of [spinal muscular atrophy](#) (SMA). SMA results in congenital degeneration of the [anterior horn](#) in the [gray matter](#) of the [spinal cord](#); the [lateral corticospinal tracts](#), [spinocerebellar tracts](#), and [dorsal columns](#) would not be

affected. Furthermore, SMA is not associated with [diabetes mellitus](#) or [hypertrophic cardiomyopathy](#).

Question # 32

A 26-year-old man is brought to the emergency department by ambulance after being involved in a motor vehicle collision. He does not open his eyes on command or respond to verbal cues. A CT scan of the head shows a hyperdense fluid collection in the right medial temporal lobe with medial displacement of the uncus and parahippocampal gyrus of the temporal lobe. Which of the following cranial nerves is most likely to be injured as a result of this patient's lesion?

	Answer	Image
A	Facial	
B	Vagus	
C	Vestibulocochlear	
D	Abducens	
E	Oculomotor	
F	Trigeminal	

Hint

The findings from this patient's radiological imaging indicate a transtentorial uncal herniation.

Correct Answer

A - Facial

Explanation Why

The [facial nerve \(CN VII\)](#) exits the [brainstem](#) at the [pons](#), which is situated too low to be affected by [uncal herniation](#), which is seen on this patient's [CT scan](#). [CN VII](#) is in close proximity to the [anterior inferior cerebellar artery](#), and it can be injured by bleeds or [aneurysms](#) of this vessel.

B - Vagus

Explanation Why

The [vagus nerve \(CN X\)](#) exits the [brainstem](#) at the medulla, which is situated too low to be affected by [uncal herniation](#), which is seen on this patient's [CT scan](#). [CN X](#) can be injured by direct neck trauma. Injury to this nerve can also occur because of compression by an [aortic aneurysm](#).

C - Vestibulocochlear

Explanation Why

The [vestibulocochlear nerve \(CN VIII\)](#) exits the [brainstem](#) at the [pons](#), which is situated too low to be affected by [uncal herniation](#), which is seen on this patient's [CT scan](#). [CN VIII](#) is in close proximity to the [anterior inferior cerebellar artery](#), and it can be injured by bleeds or [aneurysms](#) of this vessel.

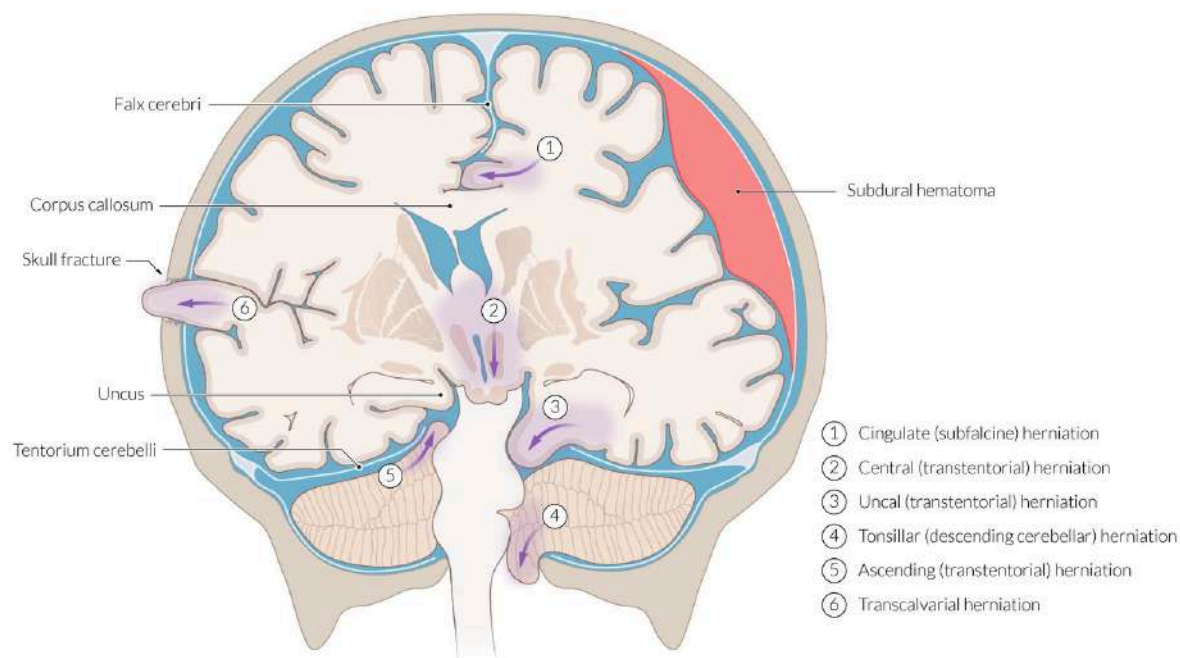
D - Abducens

Explanation Why

The [abducens nerve](#) (CN VI) exits the [brainstem](#) at the [pons](#), which is situated too low to be affected by [uncal herniation](#), which is seen on this patient's [CT scan](#). [CN VI](#) is local to the [basilar artery](#), and it can be injured by a [basilar artery aneurysm](#).

E - Oculomotor

Image



Explanation But

A [CN III](#) injury can also be caused by an [aneurysm](#) or bleed of the [posterior communicating artery](#) or [posterior cerebral artery](#), both of which are in close proximity to this nerve.

Explanation Why

The [oculomotor nerve \(CN III\)](#) is most likely to be injured by [uncal herniation](#), which manifests with an [abducted](#) and depressed ipsilateral [eye](#) (due to damage to motor fibers that innervate most of the extraocular [eye muscles](#)) with a [fixed, dilated pupil](#) (due to damage to [parasympathetic](#) fibers). Other features of [uncal herniation](#) include cortical blindness with contralateral [homonymous hemianopia](#) due to compression of the [posterior cerebral artery](#), and [Kernohan phenomenon](#) due to compression of the contralateral cerebral peduncle. A downward shift of the [brainstem](#) causes hemorrhages and compression of the reticular formation, which can lead to impaired consciousness and, ultimately, death.

F - Trigeminal

Explanation Why

The [trigeminal nerve \(CN V\)](#) exits the [brainstem](#) at the [pons](#), which is situated too low to be affected by [uncal herniation](#), which is seen on this patient's [CT scan](#). [CN V](#) can be injured by a [lateral pontine](#) lesion. Injury to this nerve can also occur because of compression by a [superior cerebellar artery aneurysm](#).

Question # 33

A 40-year-old woman comes to the physician for a preoperative examination before undergoing a planned elective cholecystectomy. She has a history of myasthenia gravis, for which she takes oral pyridostigmine. She has had occasional episodes of muscle weakness, blurred vision, and slurred speech recently. Physical examination shows mild ptosis bilaterally. The pupils are normal in size and reactive bilaterally. Muscle strength is 3/5 at the hips and shoulders. Sensory examination shows no abnormalities. After the administration of 10 mg of edrophonium, her ptosis resolves, and her proximal muscle strength improves to 5/5. This patient is most likely to benefit from which of the following interventions?

	Answer	Image
A	Administer timed doses of edrophonium	
B	Increase the dose of pyridostigmine	
C	Discontinue treatment with pyridostigmine	
D	Initiate treatment with intravenous atropine	
E	Add glycopyrrolate as needed	

Hint

This patient has episodes of facial muscle and extremity weakness despite treatment with pyridostigmine, an anticholinesterase inhibitor.

Correct Answer

A - Administer timed doses of edrophonium

Explanation Why

Timed doses of [edrophonium](#), an [acetylcholinesterase inhibitor](#) that prolongs the presence of [acetylcholine](#) in the [neuromuscular junction](#) for a very limited amount of time (approx. 5–10 minutes), can be used for diagnostic purposes in patients suspected of having [myasthenia gravis](#). Improvement of this patient's symptoms following administration supports the diagnosis of [myasthenia gravis](#). However, the very short [half-life](#) of the effect of the drug makes it unsuited for the treatment for [myasthenia gravis](#).

B - Increase the dose of pyridostigmine

Explanation Why

Despite receiving treatment with [pyridostigmine](#), this patient still exhibits typical symptoms of [myasthenia gravis](#) (e.g., weakness, [ptosis](#)). The improvement of her symptoms after receiving [edrophonium](#) confirms that the persisting symptoms are still due to her underlying [myasthenia gravis](#), rather than an alternate diagnosis (e.g., [cholinergic crisis](#)). The dose of [pyridostigmine](#) she is currently receiving is most likely insufficient to control her myasthenic symptoms and should be increased. Other treatment options for [myasthenia gravis](#) include [glucocorticoids](#), [immunosuppressive agents](#), plasmapheresis, intravenous immune globulin injection, and thymectomy.

C - Discontinue treatment with pyridostigmine

Explanation Why

Discontinuing [pyridostigmine](#) would be appropriate if there was concern for [cholinergic excess](#) causing [cholinergic crisis](#), which can also manifest with muscle weakness in a patient taking an [acetylcholine](#) esterase inhibitor such as [pyridostigmine](#). However, this patient's signs and symptoms are more consistent with persistent [myasthenia gravis](#) symptoms (mild [ptosis](#), blurry vision, bulbar

weakness) and she lacks typical symptoms of [cholinergic excess](#) such as [miosis](#), bronchospasm, and lacrimation. The resolution of her symptoms with administration of [edrophonium](#) is further evidence that this patient is not suffering from [cholinergic excess](#) and discontinuing [pyridostigmine](#) would not be appropriate.

D - Initiate treatment with intravenous atropine

Explanation Why

Intravenous [atropine](#) can be used for the treatment of [cholinergic crisis](#), which can also manifest with diffuse weakness. This patient is at risk of [cholinergic crisis](#) due to her use of a [cholinesterase inhibitor](#) ([pyridostigmine](#)). However, she lacks other typical signs and symptoms of [cholinergic excess](#), such as [miosis](#), lacrimation, [diarrhea](#), salivation, and bronchospasm. Moreover, the improvement of her symptoms after administration of [edrophonium](#) further argues against [cholinergic excess](#). [Atropine](#) would most likely worsen her current condition rather than improve it.

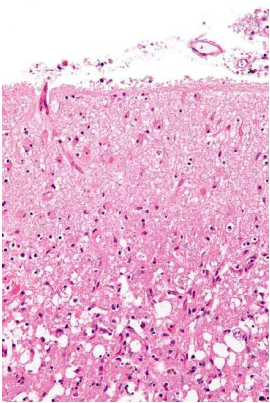
E - Add glycopyrrolate as needed

Explanation Why

[Glycopyrrolate](#) is a [muscarinic antagonist](#) that blocks the release of [acetylcholine](#) and can be used for patients with cholinergic side effects attributable to [cholinesterase inhibitor](#) therapy. This patient's use of [pyridostigmine](#) and diffuse weakness raises the possibility of [cholinergic excess](#), but the absence of other typical signs or symptoms of [cholinergic excess](#) (e.g., lacrimation, [miosis](#), [diarrhea](#), salivation, and bronchospasm) make this unlikely. The improvement of her symptoms after [edrophonium](#) administration make this even more unlikely and administration of [glycopyrrolate](#) would be expected to worsen her symptoms.

Question # 34

An 87-year-old woman is admitted to the intensive care unit after a neighbor found her lying on the floor at her home. Her respirations are 13/min and shallow. Despite appropriate therapy, the patient dies. Gross examination of the brain at autopsy shows neovascularization and liquefactive necrosis without cavitation in the distribution of the left middle cerebral artery. Histological examination of a brain tissue sample from the left temporal lobe shows proliferation of neural cells that stain positive for glial fibrillary acidic protein. Based on these findings, approximately how much time has most likely passed since the initial injury in this patient?

	Answer	Image
A	10 days	
B	12 hours	
C	25 days	
D	2 hours	
E	2 days	

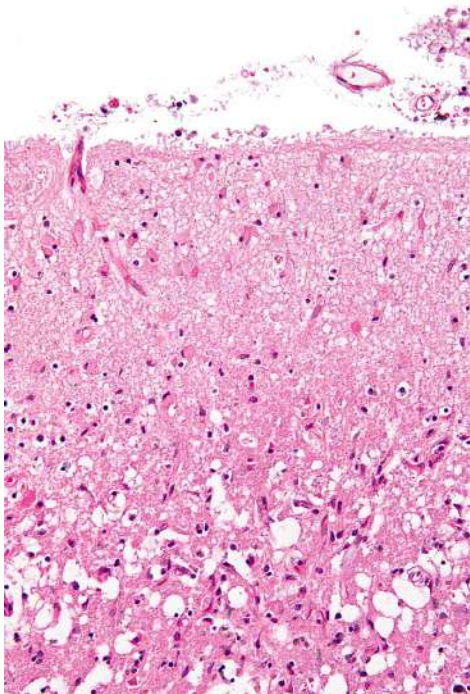
Hint

This patient has had a massive ischemic stroke. The GFAP-positive cells described here are most likely astrocytes, which are derived from the neuroectoderm.

Correct Answer

A - 10 days

Image



Explanation Why

This patient's histological examination shows [astrocyte proliferation](#) and [neovascularization](#). [Reactive gliosis](#), which is characterized by [astrocyte proliferation](#), is the attempt of brain tissue to fill the [necrotic](#) area with [glial cells](#). These histological examination findings are usually seen 1–2 weeks after [ischemic](#) brain injury.

B - 12 hours

Explanation Why

Initial cellular changes can be seen approximately 12 hours after an [ischemic stroke](#). Findings would

include red neurons caused by [cytoplasmic eosinophilia](#). [Reactive gliosis](#), which is seen here at autopsy, is typically not present at this time.

C - 25 days

Explanation Why

Although [astrocyte proliferation](#) can still be found 25 days after an [ischemic stroke](#), histological examination at this point would also show [glial scarring](#) with cerebral cavitation, which is not seen here.

D - 2 hours

Explanation Why

Initial cellular changes include electrolyte diffusion alterations, which can be radiologically detected as early as 3 minutes after the initial injury (e.g., with diffusion-weighted [MRI](#)). However, histological changes like the ones seen here at autopsy are typically not present 2 hours after injury.

E - 2 days

Explanation Why

Common histological findings 2 days after [ischemic](#) brain injury include cell [necrosis](#) and the infiltration of [neutrophils](#). [Neovascularization](#), which is seen here at autopsy, is typically not present at this time.

Question # 35

A 55-year-old man with atrial fibrillation is brought to the emergency department by his wife 6 hours after the acute onset of right arm weakness and slurred speech. An MRI of the brain shows a thrombus in the left middle cerebral artery. Twelve hours later, the patient develops ventricular tachycardia. Despite appropriate care, he dies. Which of the following histopathologic changes are most likely to be seen on a biopsy specimen from the affected brain tissue?

	Answer	Image
A	Neutrophilic infiltration with central necrosis	
B	Reactive gliosis with vascular proliferation	
C	Glial scarring with fibrous tissue hypertrophy	
D	Eosinophilic neuronal cytoplasm with pyknotic nuclei	
E	Microglial infiltration with local tissue destruction	
F	Normal brain parenchyma	

Hint

This patient died 18 hours after developing an ischemic stroke, which is a common complication of atrial fibrillation.

Correct Answer

A - Neutrophilic infiltration with central necrosis

Explanation Why

Neutrophilic infiltration with central [necrosis](#) is seen on histopathologic examination of brain tissue taken 1–3 days after [ischemic stroke](#). This patient's [stroke](#) occurred < 24 hours ago.

B - Reactive gliosis with vascular proliferation

Explanation Why

[Reactive gliosis](#) (due to activation of [astrocytes](#) and [microglia](#)) with vascular [proliferation](#) (due to the release of [proinflammatory cytokines](#), [chemokines](#), and [VEGF](#) in [necrotic](#) brain tissue) is seen on histopathologic examination of brain tissue taken 5–15 days after [ischemic stroke](#). This patient's [stroke](#) occurred approximately 18 hours ago.

C - Glial scarring with fibrous tissue hypertrophy

Explanation Why

[Glial scarring](#) with fibrous tissue [hypertrophy](#) is seen on histopathologic examination of brain tissue taken > 2 weeks after [ischemic stroke](#). This patient's [stroke](#) occurred approximately 18 hours ago.

D - Eosinophilic neuronal cytoplasm with pyknotic nuclei

Explanation Why

In patients who have had an [ischemic stroke](#), the tissue changes seen on histopathologic examination of brain tissue depend on the time of presentation following [ischemia](#). Within 12–24 hours after [ischemia](#), histopathologic examination shows [neurons](#) with eosinophilic [cytoplasm](#) and [pyknotic](#) nuclei. Hyper eosinophilia causes a red appearance on [hematoxylin-eosin staining](#) of affected tissue, which gives the appearance of red neurons.

E - Microglial infiltration with local tissue destruction

Explanation Why

Infiltration of [macrophages](#) ([microglia](#)) with local tissue destruction is seen on histopathologic examination of brain tissue taken 3–5 days after [ischemic stroke](#). This patient's [stroke](#) occurred < 24 hours ago.

F - Normal brain parenchyma

Explanation Why

Up to 12 hours after [ischemic stroke](#), histopathologic examination of brain tissue can appear normal. This patient's [stroke](#) occurred > 12 hours ago.

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

The diagram illustrates the synthesis, release, and effects of dopamine. In the **Substantia nigra**, dopamine is synthesized from **Dopamine precursors L-DOPA** by the enzyme **DDC** (Dopa decarboxylase). This process is inhibited by **Decarboxylase inhibitors** like **Carbidopa**. L-DOPA is also converted to dopamine by **COMT** (Catechol-O-methyltransferase), which is inhibited by **COMT inhibitors** such as **Tolcapone** (peripheral) and **Entacapone** (peripheral). Within the **Presynaptic terminal**, dopamine is packaged into vesicles. It is released into the synaptic cleft and binds to **Dopamine receptors** on the **Postsynaptic neuron**. Inside the terminal, dopamine is also broken down by **MAO-B** (Monoamine oxidase B), which is inhibited by **MAO-B inhibitors** like **Selegiline**. In the **Glial cell**, dopamine is broken down by **COMT**. Dopamine can also be taken up into the **Blood** via a transporter. On the postsynaptic side, dopamine interacts with **ACh** (Acetylcholine) receptors and **NMDA receptors**. **Anticholinergic drugs** like **Benztrapine** block ACh receptors, while **NMDA antagonists** like **Amantadine** block NMDA receptors. **Dopamine agonists** such as **Ropinirole** (nonergot), **Bromocriptine** (ergot), and **Levodopa** (neurotoxic) are shown at the bottom.

Hint

This patient has classic symptoms of Parkinson disease (shuffling gait, hypomimia, cogwheel rigidity) and is being treated with levodopa (L-DOPA) and carbidopa. Carbidopa is a peripheral decarboxylase inhibitor, which decreases the peripheral conversion of L-DOPA to dopamine and, thus, increases the amount of L-DOPA that enters the central nervous system.

Correct Answer

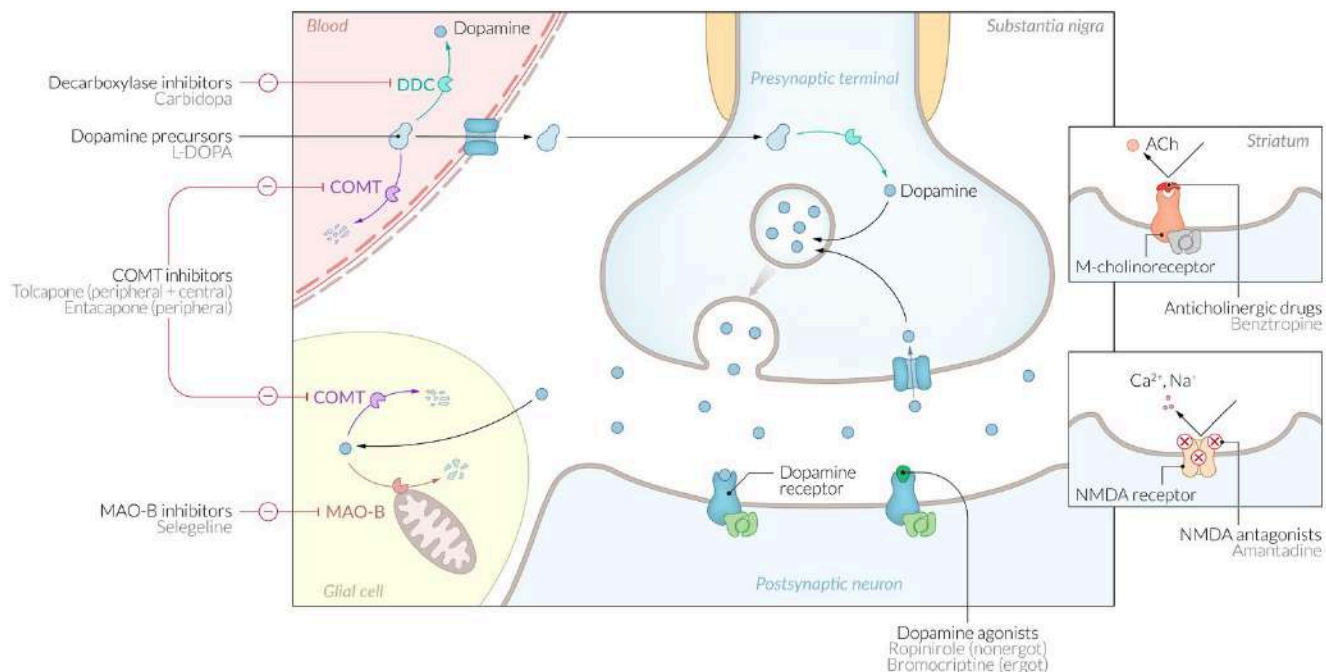
A - Resting tremor

Explanation Why

Resting tremor is reduced by L-DOPA therapy. The addition of carbidopa is likely to further reduce the incidence of resting tremor because a combination of these drugs would increase the amount of centrally available dopamine. However, resting tremor is a feature of Parkinson disease and not an adverse effect of L-DOPA therapy.

B - Orthostatic hypotension

Image



Explanation Why

Following administration, L-DOPA is absorbed into the systemic circulation where it is partially

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

C - Urinary retention

Explanation Why

[Urinary retention](#) is a common side effect of [anticholinergic](#) medications, such as [benztropine](#), that are used to treat [Parkinson disease](#). However, [L-DOPA](#) and [carbidopa](#) are not associated with [urinary retention](#).

D - Visual hallucinations

Explanation Why

[Visual hallucinations](#) are a central side effect of [L-DOPA](#) therapy and they correlate to the concentration of [dopamine](#) in the [central nervous system](#). By decreasing the peripheral conversion of [L-DOPA](#) to [dopamine](#), [carbidopa](#) increases the fraction of the administered drug that crosses the [blood-brain](#) barrier. Therefore, [visual hallucinations](#) would be expected to increase rather than decrease.

E - Dyskinesia

Explanation Why

[Dyskinesia](#) is a [central nervous system](#) side effect of [L-DOPA](#) that typically occurs with long-term therapy. By decreasing the peripheral conversion of [L-DOPA](#) to [dopamine](#), [carbidopa](#) increases the fraction of the administered drug that crosses the [blood-brain](#) barrier. Therefore, symptoms of [dyskinesia](#) would be expected to increase rather than decrease.

Question # 37

A 56-year-old woman is admitted to the hospital for progressive bilateral lower extremity weakness and absent deep tendon reflexes. Cerebrospinal fluid analysis shows an elevated protein concentration and a normal cell count. Treatment with plasmapheresis is initiated, after which her symptoms start to improve. Four weeks after her initial presentation, physical examination shows normal muscle strength in the bilateral lower extremities and 2+ deep tendon reflexes. Which of the following changes in neuronal properties is the most likely explanation for the improvement in her neurological examination?

	Answer	Image
A	Increase in length constant	
B	Decrease in nerve conduction velocity	
C	Decrease in transmembrane resistance	
D	Increase in axonal capacitance	
E	Increase in axial resistance	
F	Decrease in action potential amplitude	

Hint

Increased cerebrospinal protein content with normal cell count (e.g., cytoalbuminologic dissociation) in the context of progressive lower extremity weakness and areflexia is consistent with Guillain-Barré syndrome (GBS).

Correct Answer

A - Increase in length constant

Explanation But

Other factors that increase the [length constant](#) include decreased axonal resistance and increased axonal diameter.

Explanation Why

Recovery from GBS involves remyelination of the [demyelinated](#) nerve segments. Remyelinated nerves have an increased transmembrane resistance compared to [demyelinated](#) nerves because the [myelin](#) sheath functions as an electrical insulator, thereby permitting the electrical [action potentials](#) in myelinated nerves to travel further before decaying. This increased resistance produces an increase in [length constant](#).

B - Decrease in nerve conduction velocity

Explanation Why

Nerve conduction velocity is most significantly impacted by the presence or absence of [myelin](#) on a given nerve. In the presence of [myelin](#), [saltatory conduction](#) is possible and nerve conduction velocities are much higher than in nerves that lack [myelin](#) sheaths. In patients with GBS, nerve conduction velocity is much slower as a result of significant [demyelination](#). The recovery process involves restoration of the [myelin](#) sheath so nerve conduction velocities would be expected to increase.

C - Decrease in transmembrane resistance

Explanation Why

Decreased transmembrane resistance results from [demyelination](#) of nerve fibers, which accounts for

the symptoms observed in this patient with GBS. The results of this patient's [neurological examination](#) four weeks after her initial presentation are significantly improved, indicating that the nerves have undergone remyelination. Transmembrane resistance increases as a result of remyelination.

D - Increase in axonal capacitance

Explanation Why

Recovery from GBS involves the restoration of the normal [myelin](#) sheath surrounding the [axons](#) of peripheral nerves. The presence of [myelin](#) increases nerve [cell membrane](#) resistance because it is an electrical insulator. Resistance is inversely proportional to capacitance. Therefore, the [axonal capacitance](#) is likely to be reduced in the recovery phase of GBS.

E - Increase in axial resistance

Explanation Why

[Axial resistance](#) refers to the intrinsic quality of a given [axon](#) and it derives from the specific [cytoplasmic](#) makeup of a [neuron](#) and the [cross-sectional](#) area of [cytoplasm](#). [Axons](#) with a larger [cross-sectional](#) area as well as those with increased [cytoplasm](#) conductivity are able to facilitate greater ion transfer and, therefore, have lower [axial resistance](#). Neither the pathophysiology of GBS or the recovery process affects the diameter or [cytoplasmic](#) content of an [axon](#) so a change in [axial resistance](#) would not be expected.

F - Decrease in action potential amplitude

Explanation Why

GBS has been associated with near normal or slightly decreased [action potential](#) amplitude. Therefore, [action potential](#) amplitude would be expected to remain constant or increase slightly in this recovered patient.

Question # 38

A 23-year-old man comes to the physician because of recurrent episodes of chest pain, shortness of breath, palpitations, and a sensation of choking. The symptoms usually resolve with deep breathing exercises after about 5 minutes. He now avoids going to his graduate school classes because he is worried about having another episode. Physical examination is unremarkable. Treatment with lorazepam is initiated. The concurrent intake of which of the following drugs should be avoided in this patient?

	Answer	Image
A	Levocetirizine	
B	Diphenhydramine	
C	Venlafaxine	
D	Phenelzine	
E	Naloxone	
F	Fluoxetine	
G	Ondansetron	

Hint

Lorazepam is a benzodiazepine that works as a GABA_A agonist.

Correct Answer

A - Levocetirizine

Explanation Why

[Levocetirizine](#) is a [second-generation antihistamine](#) most commonly used in the treatment of [seasonal allergies](#) and [allergic rhinitis](#). The most common adverse effects of [levocetirizine](#) include [pharyngitis](#) and [hypersensitivity reactions](#) in adults and GI disturbances, [fever](#), and [otitis media](#) in children. However, there is no contraindication for concurrent administration of [levocetirizine](#) and [lorazepam](#).

B - Diphenhydramine

Explanation Why

This patient's symptoms are consistent with [panic disorder](#), for which he was prescribed [lorazepam](#), an oral [benzodiazepine](#) that has [CNS](#) depressant effects. Simultaneous administration of other drugs that possess [CNS](#) depressant properties, such as [first-generation antihistamines](#) (e.g., [diphenhydramine](#), [promethazine](#), [hydroxyzine](#)), [opioids](#), and [barbiturates](#), should be avoided because of the synergistic effects and risk of respiratory depression.

C - Venlafaxine

Explanation Why

[Venlafaxine](#) is an [SNRI](#) that is commonly used to treat generalized anxiety and [panic disorder](#). The concurrent use of [SNRIs](#) and drugs that increase synaptic [serotonin](#) levels (e.g., [MAOI](#)) is contraindicated because it can cause [serotonin syndrome](#). However, [benzodiazepines](#) (e.g., [lorazepam](#)) do not alter [serotonin](#) levels and concurrent use of an [SNRI](#) is not contraindicated.

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D - Phenelzine

Explanation Why

[Phenelzine](#) belongs to the class of [antidepressant](#) drugs known as [MAOIs](#). The concomitant use of [MAOIs](#) and other drugs that increase synaptic [serotonin](#) levels should be avoided because it can cause [serotonin syndrome](#). Additionally, the combination of an [MAOI](#) and [tyramine](#)-rich food (e.g., cheese, wine) can result in a [hypertensive crisis](#). However, the concurrent use of [benzodiazepines](#) and [MAOIs](#) is not contraindicated.

E - Naloxone

Explanation Why

[Naloxone](#) is an [opioid](#) antagonist most commonly used to treat acute [opioid intoxication](#). Concomitant use of [opioids](#) and [benzodiazepines](#) can result in synergistic [CNS](#) depression but this effect is unlikely to be seen with administration of [naloxone](#) due to its antagonist properties.

F - Fluoxetine

Explanation Why

[Fluoxetine](#) is an [SSRI](#) that is commonly used in generalized anxiety and [panic disorder](#). The concurrent use of [SSRI](#) and drugs that increase synaptic [serotonin](#) levels (e.g., [SNRI](#), [MAOI](#)) can cause [serotonin syndrome](#) and is therefore contraindicated. However, [benzodiazepines](#) (e.g., [lorazepam](#)) do not alter [serotonin](#) levels. The combination of [SSRIs](#) and [benzodiazepines](#) is common in the treatment of [panic disorder](#).

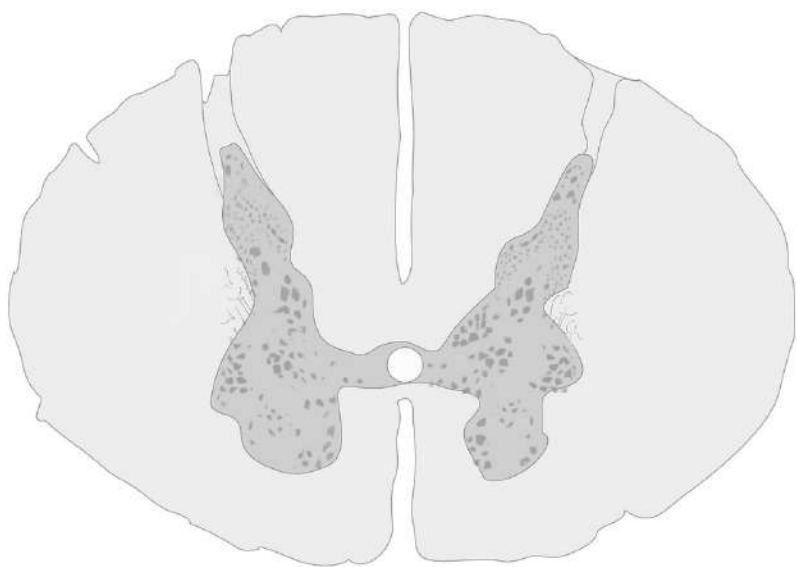
G - Ondansetron

Explanation Why

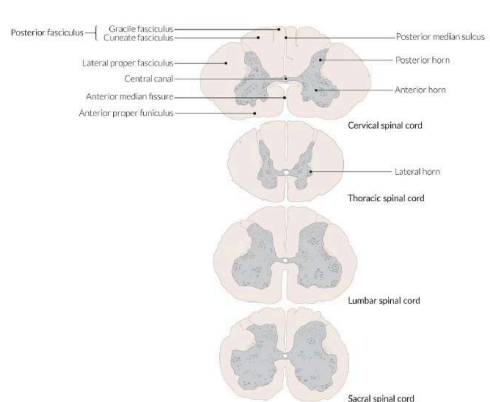
[Ondansetron](#) is a [5-HT₃ antagonist](#) that inhibits the binding of [serotonin](#) to its receptor, which increases the amount of [serotonin](#) at the [synapse](#). Simultaneous administration of [ondansetron](#) and other drugs that increase synaptic [serotonin](#) (e.g., [SSRIs](#), [SNRIs](#)) can result in [serotonin syndrome](#). However, [benzodiazepines](#) (e.g., [lorazepam](#)) do not alter [serotonin](#) levels. There are currently no contraindications for the concurrent use of [5-HT₃ antagonists](#) and [benzodiazepines](#).

Question # 39

A 45-year-old man is brought to the emergency department by ambulance after a motor vehicle collision. He is not responsive to verbal commands and is unable to provide any history. His pulse is 108/min and regular. Physical examination shows ecchymoses over the neck and back. Neurological examination indicates damage to the spinal cord at the level shown in the illustration. This patient's injury is most likely located at which of the following levels of the spinal cord?



	Answer	Image
A	L4	
B	C2	
C	S4	

	Answer	Image
D	S2	
E	T6	

Hint

The illustration shows a segment of the spinal cord that contains prominent lateral projections between the dorsal and ventral horns. These projections are lateral horns, which contain neuronal cell bodies of the sympathetic nervous system.

Correct Answer

A - L4

Explanation Why

The [spinal cord](#) level of L4 generally has more [gray matter](#), less [white matter](#), and larger [ventral horns](#) compared to the cervical and thoracic segments and does not contain [lateral horns](#) as seen in the illustration.

B - C2

Explanation Why

The [spinal cord](#) level of C2 generally has less [gray matter](#) and more [white matter](#) compared to the other [spinal](#) segments and does not contain [lateral horns](#) as seen in the illustration.

C - S4

Explanation Why

Though the [spinal cord](#) levels S2–S4 contain [lateral horns](#), they do not form prominent [lateral](#) projections between the [dorsal](#) and [ventral horns](#) as seen in the illustration. In addition, the sacral portions of the [spinal cord](#) contain much less [white matter](#) than the [spinal](#) segment in the illustration. [White matter](#) contains the [axons](#) of [neurons](#) as they travel between the brain and the rest of the body; at the sacral level, there are fewer [axons](#) traveling up to the brain compared to more superior levels of the [spinal cord](#). Thus, [gray matter](#) forms a greater [proportion](#) of the sacral [spinal cord](#).

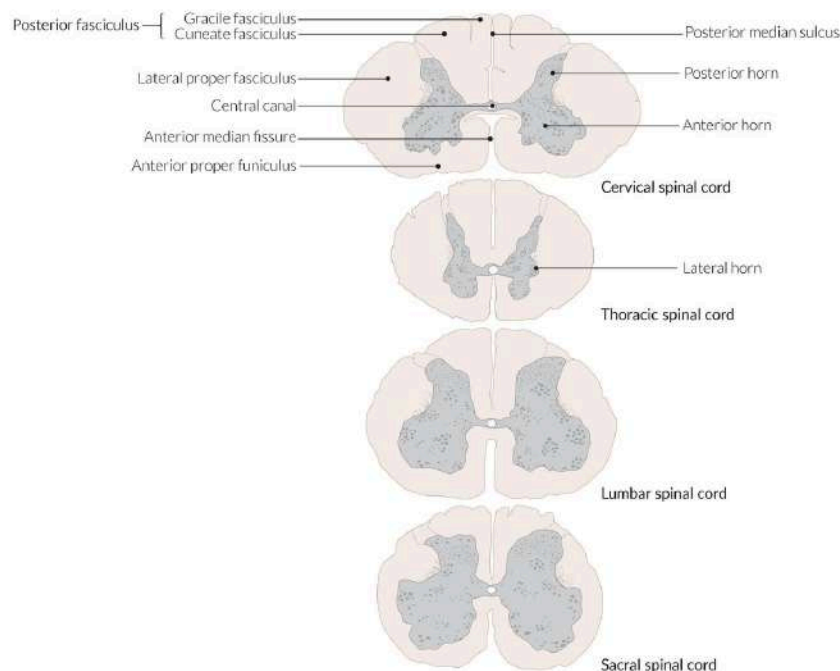
D - S2

Explanation Why

Though the [spinal cord](#) levels S2–S4 contain [lateral horns](#), they do not form prominent [lateral](#) projections between the [dorsal](#) and [ventral horns](#) as seen in the illustration. In addition, the sacral portions of the [spinal cord](#) contain much less [white matter](#) than the [spinal](#) segment in the illustration. [White matter](#) contains the [axons](#) of [neurons](#) as they travel between the brain and the rest of the body; at the sacral level, there are fewer [axons](#) traveling up to the brain compared to more superior levels of the [spinal cord](#). Thus, [gray matter](#) forms a greater [proportion](#) of the sacral [spinal cord](#).

E - T6

Image



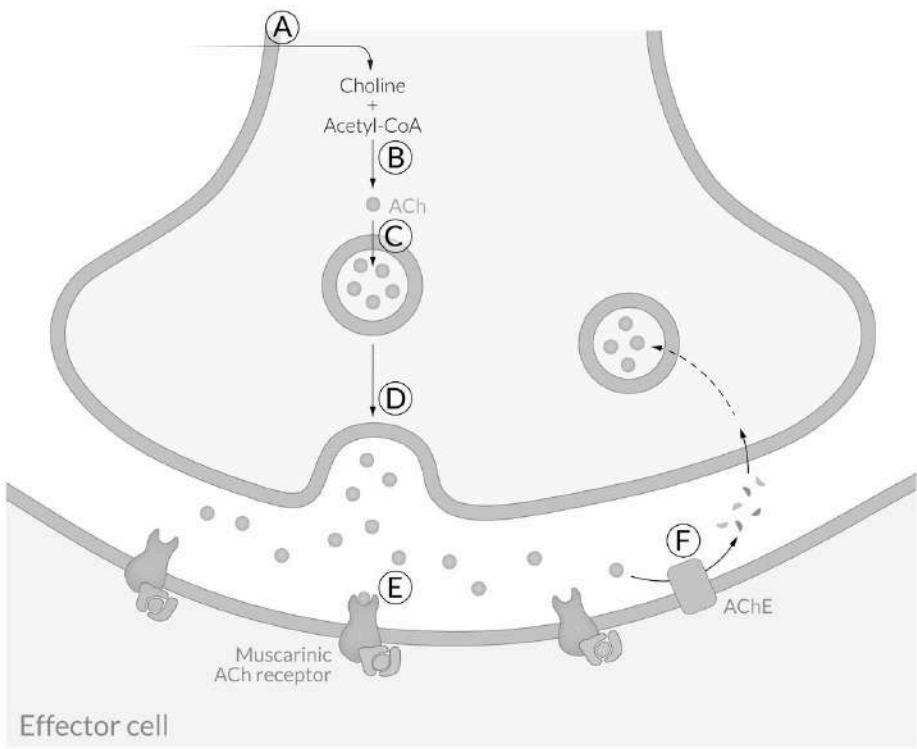
Explanation Why

Cross-sections of the [spinal cord](#) show butterfly-shaped [gray matter](#) with surrounding [white matter](#).

[Gray matter](#) contains the cell bodies of [neurons](#); [white matter](#) contains the [axons](#) of [neurons](#) as they travel between the brain and the rest of the body. In general, [gray matter](#) is divided into three regions: [dorsal horns](#), [ventral horns](#), and [lateral horns](#). [Dorsal](#) and [ventral horns](#) are found throughout the [spinal cord](#). Though [lateral horns](#) are present between segments T1–L3 and segments S2–S4, only segments T1–L3 have the prominent [lateral](#) projections between the [dorsal](#) and [ventral horns](#) as seen in the illustration. Thus, this patient's injury must be located within these segments.

Question # 40

A 6-month-old boy is brought to the emergency department by his mother because of poor feeding, especially when trying to breastfeed. The mother also reports that the boy's grip is weak and that he is constipated. He has met all developmental milestones and his immunizations are up-to-date. His diet consists primarily of breast milk, applesauce, and oatmeal sweetened with honey. Physical examination shows diffuse weakness and decreased breath sounds bilaterally. Deep tendon reflexes are decreased throughout. Which of the following labeled processes in the cholinergic synapse is most likely directly affected in this patient?



	Answer	Image
A	A	
B	B	
C	C	

	Answer	Image
D	D	The diagram illustrates the mechanism of action for various drugs at a cholinergic synapse. A PNS neuron is shown on the left, releasing ACh into the synaptic cleft. Inside the presynaptic terminal, Choline and Acetyl-CoA combine to form ACh, which is then packaged into vesicles. These vesicles release ACh into the cleft. ACh binds to muscarinic receptors on the effector cell, triggering a response. ACh is also broken down by AChE in the cleft. Muscarinic antagonists (e.g., atropine) block the receptors. Indirect parasympathomimetics (e.g., neostigmine) inhibit AChE, increasing ACh levels. Direct parasympathomimetics (e.g., pilocarpine) activate the receptors.
E	E	
F	F	

Hint

This patient's diffuse weakness and constipation are most likely caused by the ingestion of *C. botulinum* spores that produce a potent neurotoxin. These spores are frequently found in honey.

Correct Answer

A - A

Explanation Why

A shows choline being transported into the presynaptic [neuron](#), which is the rate-limiting step in the synthesis of [acetylcholine](#). This process is inhibited e.g., by hemicholinium. [Botulinum toxin](#), however, does not affect the uptake of choline.

B - B

Explanation Why

B shows the synthesis of [acetylcholine](#) from choline and [acetyl-CoA](#) by the enzyme choline acetyltransferase. This enzyme is inhibited e.g., by bromoacetylcholine. [Botulinum toxin](#), however, does not affect choline acetyltransferase.

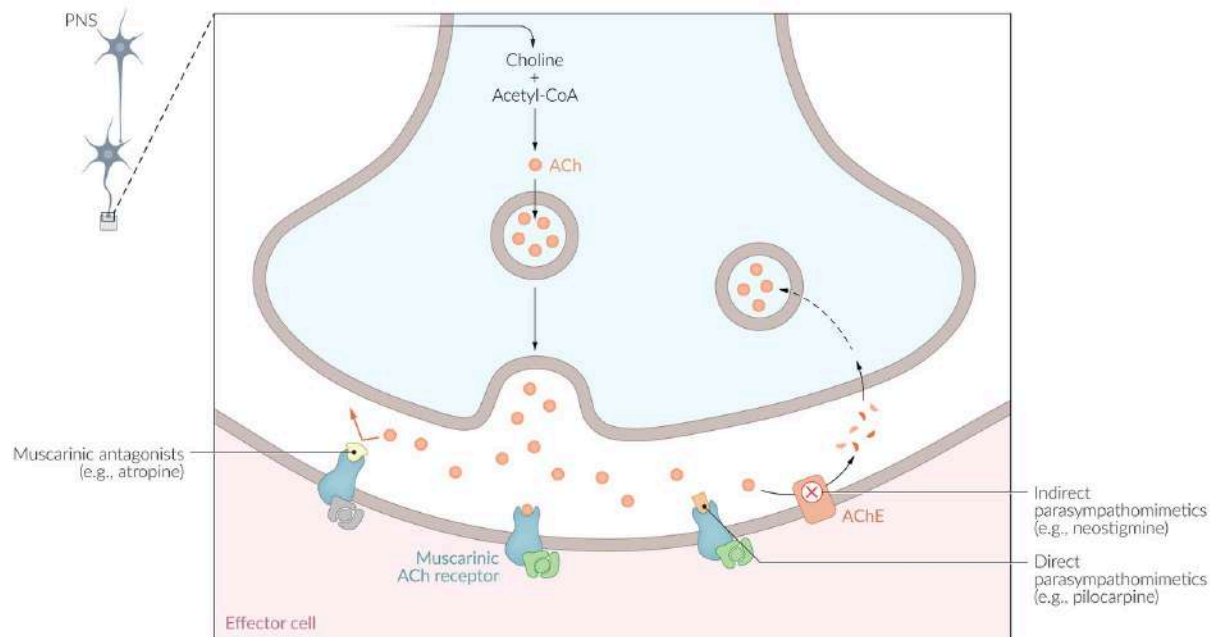
C - C

Explanation Why

C shows the uptake of [acetylcholine](#) into synaptic vesicles via the vesicular [acetylcholine](#) transporter. This process is inhibited e.g., by vesamicol. [Botulinum toxin](#), however, does not affect the vesicular [acetylcholine](#) transporter.

D - D

Image



Explanation Why

D shows exocytosis of [acetylcholine](#)-filled vesicles into the [synaptic cleft](#). [Botulinum toxin](#) inhibits this process by cleaving the SNAP-25 SNARE protein that mediates the fusion of vesicles with the presynaptic membrane in response to a rise in intracellular Ca^{2+} concentration, which is caused by [neuron depolarization](#). Without [acetylcholine](#) release into the [synaptic cleft](#), muscle cells will not contract, leading to [flaccid paralysis](#). Because [botulinum toxin](#) can inhibit cholinergic innervation of both nicotinic and muscarinic [neurons](#), autonomic innervation of tear, sweat, and salivary glands can also be affected.

E - E

Explanation Why

E shows the binding of [acetylcholine](#) to acetylcholine receptors on the postsynaptic [neuron](#). At the [neuromuscular junction](#), this process is inhibited by neuromuscular-blocking drugs (e.g., [suxamethonium](#), [rocuronium](#), or [cisatracurium](#)), which are used during anesthesia to cause paralysis. [Muscarinic acetylcholine receptors](#) can be blocked by [atropine](#). [Botulinum toxin](#), however, does not affect [acetylcholine](#) binding to the acetylcholine receptor.

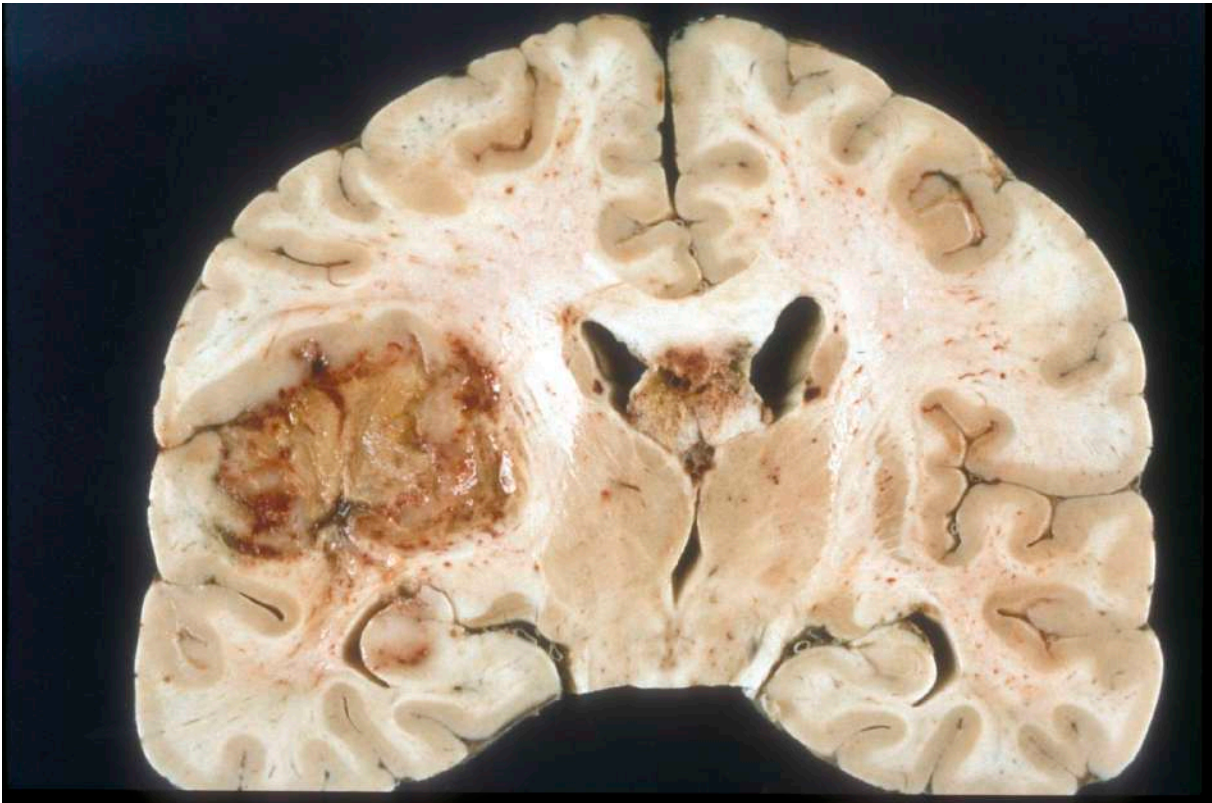
F - F

Explanation Why

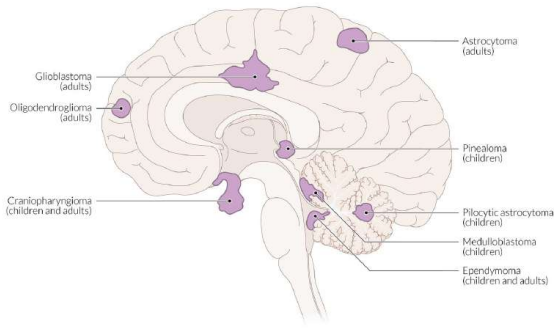
F shows the action of acetylcholinesterase; this enzyme breaks down [acetylcholine](#) into choline and acetate for recycling by the presynaptic [neuron](#), terminating stimulation of the postsynaptic [neuron](#). At peripheral cholinergic [neurons](#), acetylcholinesterase is inhibited reversibly by the drugs [physostigmine](#), [neostigmine](#) and [pyridostigmine](#), and irreversibly by [organophosphates](#). [Botulinum toxin](#), however, does not affect acetylcholinesterase.

Question # 1

A 56-year-old woman is brought to the emergency department by her husband 30 minutes after a generalized tonic-clonic seizure. Over the past 3 months, she has had recurrent headaches and worsening early-morning vomiting. She has no personal or family history of a seizure disorder. An MRI of the brain shows a central mass; surgical resection is planned. One day before the surgery, the patient has another generalized seizure and, despite resuscitative efforts, she dies. Gross examination of the brain at autopsy is shown. Which of the following was the most likely cause of this patient's symptoms?



	Answer	Image
A	Oligodendroglioma	
B	Hemangioblastoma	

	Answer	Image
C	Glioblastoma	 A sagittal section of the human brain with several purple-colored tumors highlighted. Labels with leader lines point to the following tumors: Glioblastoma (adults) in the cerebral cortex; Oligodendroglioma (adults) in the white matter; Craniopharyngioma (children and adults) at the base of the brain near the hypothalamus; Astrocytoma (adults) in the cerebral cortex; Pinealoma (children) in the pineal gland region; Pilocytic astrocytoma (children) in the cerebellum; Medulloblastoma (children) in the cerebellum; and Ependymoma (children and adults) near the ventricles.
D	Schwannoma	
E	Brain metastasis	
F	Meningioma	

Hint

This patient presented with nonspecific neurological symptoms (seizures, headaches, early-morning vomiting), most likely caused by a tumor derived from astrocytes.

Correct Answer

A - Oligodendroglioma

Explanation Why

[Oligodendrogliomas](#) are slow-growing tumors that arise from [oligodendrocytes](#). While these tumors can manifest with the nonspecific neurological symptoms seen here, the disease course of [oligodendrogliomas](#) is often much less rapid. Additionally, [oligodendrogliomas](#) are usually found in the [frontal lobe](#), while this patient's [tumor](#) is located temporally. On gross pathological examination, [oligodendrogliomas](#) may show areas of [necrosis](#), but hemorrhage and [microvascular proliferation](#), which are seen here, are not characteristic.

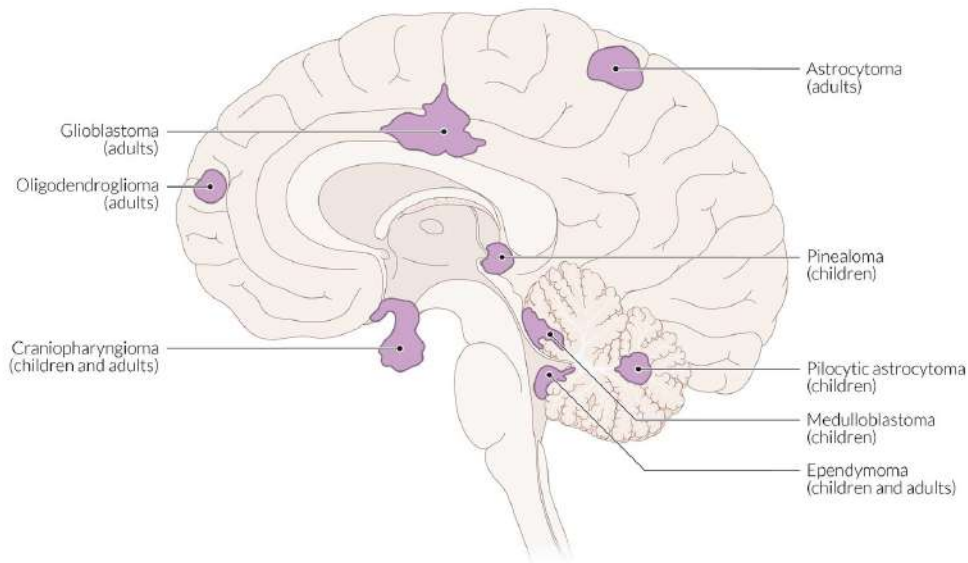
B - Hemangioblastoma

Explanation Why

[Hemangioblastomas](#) are benign, slow-growing, highly vascularized tumors. Unlike this patient's [supratentorial tumor](#), [hemangioblastomas](#) are typically located in the [cerebellum](#) ([infratentorial](#)), which is why symptoms often include [cerebellar defects](#) (e.g., [ataxia](#)). [Features of increased intracranial pressure](#) (e.g., [headaches](#), vomiting) may occur if the [tumor](#) compresses the [fourth ventricle](#). On gross pathological examination, these tumors appear red due to their high vascularity and they are often located within a cyst.

C - Glioblastoma

Image



Explanation Why

[Glioblastomas](#) are highly malignant, rapidly progressive [brain tumors](#) that commonly manifest with nonspecific neurological symptoms, as seen in this patient. In keeping with the autopsy findings here, [glioblastomas](#) are typically located in the [white matter](#) of the cerebral hemispheres (e.g., left [temporal lobe](#)), although they can cross the midline ([butterfly glioma](#)). Gross hemorrhage, central [necrosis](#), and [microvascular proliferation](#) are further pathological characteristics. On [MRI](#), the [tumor](#) would appear as a [ring-enhancing](#) mass due to central [necrosis](#).

D - Schwannoma

Explanation Why

[Schwannomas](#) are [benign tumors](#) that arise from the [Schwann cells](#) of peripheral nerves. Unlike this

patient's [supratentorial tumor](#), [Schwannomas](#) are usually located in the [cerebellopontine angle \(infratentorial\)](#) because they primarily arise within the vestibular portion of the [vestibulocochlear nerve \(CN VIII\)](#). Symptoms depend on the nerves affected by the [tumor](#) (e.g., [dizziness](#), [hearing loss](#), [facial nerve palsy](#)); however, [headaches](#), vomiting, and [seizures](#) would not be characteristic. On gross examination, [schwannomas](#) may be visible as calcifications, cystic components, [necrosis](#), and hemorrhage.

E - Brain metastasis

Explanation Why

[Brain metastases](#) of [carcinomas](#) (e.g., [lung](#), [melanoma](#), renal) are the most common type of [intracranial tumors](#) in adults. While [metastases](#) can also manifest with the nonspecific neurological symptoms seen here, additional features of a primary [malignancy](#) would be expected. Moreover, gross pathological examination of [brain metastases](#) usually reveals multiple, well-circumscribed lesions at the gray-white junction.

F - Meningioma

Explanation Why

[Meningiomas](#) are benign, slow-growing tumors that arise from arachnoid cells. While these tumors can manifest with the nonspecific neurological symptoms seen here, they are usually asymptomatic and found incidentally on imaging. [Meningiomas](#) typically develop outside of the brain parenchyma, while this patient's [tumor](#) is within the [temporal lobe](#). Gross pathological examination of [meningiomas](#) shows a round, encapsulated, grayish-white [tumor](#) with a firm to hard texture.

Question # 2

A 12-year-old boy is brought to the physician because of difficulty in walking for 5 months. His mother reports that he has trouble keeping his balance and walking without support. Over the past year, he has started to have difficulty seeing in the dark and his hearing has been impaired. Examination shows marked scaling of the skin on the face and feet and a shortened 4th toe. Muscle strength is 3/5 in the lower extremities and 4/5 in the upper extremities. Sensation to pinprick is symmetrically decreased over the legs. Fundoscopy shows peripheral pigment deposits and retinal atrophy. His serum phytanic acid concentration is markedly elevated. The patient's condition is most likely caused by a defect in which of the following cellular structures?

	Answer	Image
A	Peroxisomes	
B	Mitochondria	
C	Smooth endoplasmic reticulum	
D	Myofilaments	
E	Proteasomes	
F	Lysosomes	

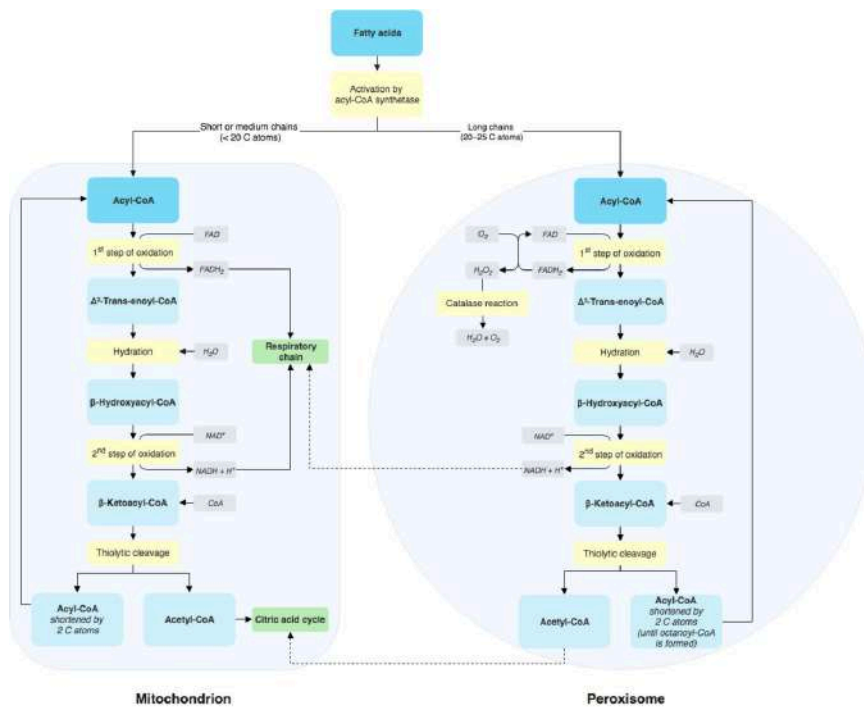
Hint

Phytanic acid is a branched-chain fatty acid that is normally converted to pristanic acid by α -oxidation. An autosomal recessive defect in α -oxidation is responsible for Refsum disease, which can manifest with scaly skin, shortening of the 4th toe, impaired vision (due to cataracts or retinitis pigmentosa), sensorineural hearing loss, ataxia, and peripheral neuropathy.

Correct Answer

A - Peroxisomes

Image



Explanation But

Other peroxisomal disorders include [X-linked adrenoleukodystrophy](#), which is caused by defective [VLCFA \$\beta\$ -oxidation](#) and [Zellweger syndrome](#), in which the cells completely lack [peroxisomes](#) and all peroxisomal functions are impaired.

Explanation Why

[Mitochondria](#) are the primary site for the [\$\beta\$ -oxidation](#) of unbranched long-chain, medium-chain, and short-chain [fatty acids](#), but [mitochondrial](#) enzymes cannot break down branched-chain fatty acids (BCFAs) or [very long-chain fatty acids](#) (VLCFAs). BCFAs (e.g., phytanic acid) must first undergo [\$\alpha\$ -oxidation](#), a process that occurs exclusively in [peroxisomes](#) and removes the side groups from BCFA. Similarly, [VLCFAs](#) must first be shortened to [long-chain fatty acids](#) by peroxisomal [\$\beta\$ -oxidation](#). [Refsum disease](#), as seen here, is caused by defective [\$\alpha\$ -oxidation](#) of BCFAs in [peroxisomes](#). Other processes that occur in [peroxisomes](#) include [catalase](#) enzyme reactions (e.g., ethanol [catabolism](#)), [D-amino acid catabolism](#), and the synthesis of [cholesterol](#), [plasmalogen](#), and [bile acids](#).

B - Mitochondria

Explanation Why

[Mitochondria](#) are the primary site for the [\$\beta\$ -oxidation](#) of [fatty acids](#). Further processes carried out by [mitochondria](#) include [oxidative phosphorylation](#), the [Krebs cycle](#), [gluconeogenesis](#), [heme synthesis](#), [ketogenesis](#), and the [urea cycle](#). Examples of diseases caused by defective [mitochondrial](#) function include [systemic primary carnitine deficiency](#), medium-chain acyl-CoA [dehydrogenase](#) deficiency, and [mitochondrially inherited](#) diseases (e.g., [MELAS syndrome](#), [Leber hereditary optic neuropathy](#)). This patient presents with elevated phytanic acid concentrations; this branched-chain fatty acid can only be metabolized by [\$\alpha\$ -oxidation](#), which occurs in a different cellular structure.

C - Smooth endoplasmic reticulum

Explanation Why

The [smooth endoplasmic reticulum](#) ([SER](#)) is the major site for [steroid hormone](#) synthesis, drug metabolism ([CYP450 system](#)), and [glucose-6-phosphatase](#) activity. [Congenital adrenal hyperplasia](#), [aromatase deficiency](#), and [von Gierke disease](#) are examples of impaired [SER](#) function. This patient has increased levels of phytanic acid, which is catabolized by a different cellular structure.

D - Myofilaments

Explanation Why

[Myofilaments](#), which are composed of [actin](#) and [myosin](#) molecules, are functional and structural units of skeletal and [cardiac muscle](#). Familial [hypertrophic cardiomyopathy](#) and [Duchenne muscular dystrophy](#) are associated with impaired [myofilament](#) function. A different cellular structure is defective in this patient with increased serum phytanic acid levels.

E - Proteasomes

Explanation Why

[Proteasomes](#) degrade ubiquitinated [proteins](#) and are involved in the elimination of viral components. Decreased [proteasomal](#) activity is implicated in the pathogenesis of certain cases of [Parkinson disease](#), and increased [proteasomal](#) activity is responsible for tissue [atrophy](#) as well as certain cancers (e.g., [multiple myeloma](#)). This patient has increased levels of phytanic acid, which is catabolized by a different cellular structure.

F - Lysosomes

Explanation Why

[Lysosomes](#) contain enzymes that are involved in the hydrolytic breakdown of several biomolecules. Diseases caused by defective [lysosomal](#) function result in the accumulation of [sphingolipids](#) (e.g., [Gaucher disease](#), [Tay-Sachs disease](#)), [mucopolysaccharides](#) (e.g., [Hurler syndrome](#)), glycoproteins (e.g., [I-cell disease](#)), or glycogen (e.g., [Pompe disease](#)). This patient has increased levels of phytanic acid, which is catabolized by a different cellular structure.

Question # 3

A 23-year-old man comes to the emergency department with palpitations, sweating, and shortness of breath that began 10 minutes ago. He says, "Please help me, I don't want to die." He has experienced several similar episodes over the past 2 months, which occurred without warning in situations including open spaces or crowds and resolved gradually after 10 to 20 minutes. He has been staying at home as much as possible out of fear of triggering another episode. He has no history of serious illness and takes no medications. He drinks 2 bottles of beer daily. He appears anxious and has a flushed face. His pulse is 104/min, respirations are 20/min, and blood pressure is 135/82 mm Hg. Cardiopulmonary examination shows no abnormalities. An ECG shows sinus tachycardia. Which of the following is the most appropriate initial action by the physician?

	Answer	Image
A	Administer oral propranolol	
B	Administer intravenous thiamine	
C	Measure plasma metanephrine levels	
D	Administer oral buspirone	
E	Administer oral alprazolam	
F	Perform a cardiac stress test	
G	Administer oral venlafaxine	

	Answer	Image
H	Perform long-term ECG monitoring	

Hint

This patient's history of 10–20 minute episodes of palpitations, sweating, shortness of breath, and fear of dying that occur in both crowded and open spaces is suggestive of panic attacks. The presence of recurrent panic attacks for ≥ 1 month with behavior modification due to fear of subsequent episodes is consistent with panic disorder.

Correct Answer

A - Administer oral propranolol

Explanation Why

Oral [propranolol](#), a nonselective [beta blocker](#), is an appropriate treatment for [performance-only social anxiety disorder](#), which may manifest with [palpitations](#) and sweating. This patient's fear, however, is not restricted to performing in front of others (e.g., public speaking), which is characteristic of this disorder.

B - Administer intravenous thiamine

Explanation Why

Intravenous [thiamine](#) ([vitamin B₁](#)) is part of the initial management of suspected [alcohol withdrawal](#) to prevent or treat [Wernicke encephalopathy](#). This patient drinks 2 bottles of beer daily and anxiety, [palpitations](#), and sweating may be symptoms of minor [alcohol withdrawal](#). However, symptoms of minor [alcohol withdrawal](#) typically last 24–48 hours rather than 10–20 minutes.

C - Measure plasma metanephrine levels

Explanation Why

Plasma [metanephrines](#) are the most appropriate initial diagnostic study for suspected [pheochromocytoma](#), which may cause [palpitations](#), sweating, and anxiety. Other features of this [tumor](#) include [headaches](#), pallor, and episodic [hypertension](#), none of which are seen here. Furthermore, fear of dying and change in behavior because of fear of triggering another episode are not typical features of [pheochromocytoma](#).

D - Administer oral buspirone

Explanation Why

Oral [buspirone](#) is a long-term treatment option for individuals with [anxiety disorder](#) (e.g., [generalized anxiety disorder](#)). Although this patient has some anxiety-related symptoms (e.g., [palpitations](#) and sweating), [generalized anxiety disorder](#) is characterized by ≥ 6 months of excessive and persistent worry that is nonspecific or revolves around certain themes (e.g., work, health, money), not anticipatory fear of [panic attacks](#).

E - Administer oral alprazolam

Explanation Why

An oral [benzodiazepine](#) such as [alprazolam](#) is the most appropriate initial treatment option for the management of suspected [panic attack](#) in the acute setting. For long-term management, patients with [panic disorder](#) may benefit from [cognitive behavioral therapy](#) and/or [antidepressants](#) (e.g., [SSRIs](#), [SNRIs](#)). [Benzodiazepines](#) are not recommended as maintenance therapy because of the risk of dependence. However, [benzodiazepines](#) can be used alongside [antidepressants](#) for acute-phase treatment until the [antidepressants](#) begin to have a therapeutic effect, which typically takes several weeks.

F - Perform a cardiac stress test

Explanation Why

A [cardiac stress test](#) may be an appropriate initial step in the evaluation of suspected episodes of [angina pectoris](#). Based on this patient's age and lack of [risk factors for atherosclerosis](#) (e.g., smoking, [diabetes mellitus](#), [hypertension](#)), he has a very low [pretest probability](#) for [coronary artery disease](#).

G - Administer oral venlafaxine

Explanation Why

Oral [venlafaxine](#) is an appropriate long-term pharmacotherapy for [panic disorder](#). However, it typically takes weeks before oral [venlafaxine](#) has an effect, which is why it is not useful in acute settings.

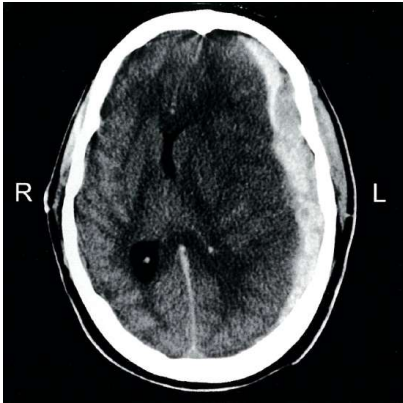
H - Perform long-term ECG monitoring

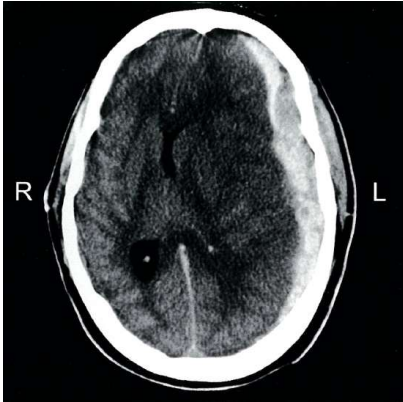
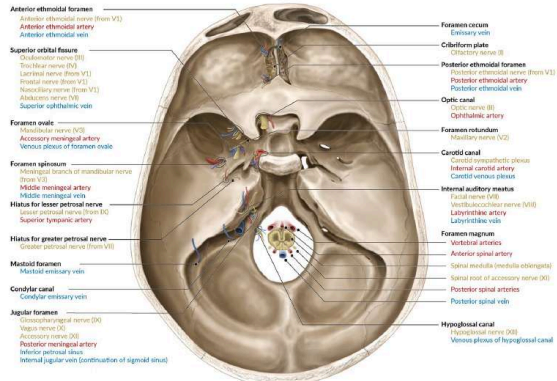
Explanation Why

Long-term [ECG](#) monitoring ([Holter monitoring](#)) is the most appropriate next step in evaluating a suspected [arrhythmia](#). [Palpitations](#) and [shortness of breath](#) are possible features of an [arrhythmia](#). However, this patient's cardiopulmonary examination findings are normal and [ECG](#) findings show [sinus tachycardia](#). Furthermore, fear of dying and change in behavior because of fear of triggering another episode, which is seen in this patient, are not typical features of [arrhythmia](#).

Question # 4

A 45-year-old man is brought to the emergency department 30 minutes after falling off a staircase and hitting his head on the handrail. He was unconscious for 10 minutes and vomited twice. On arrival, he is drowsy. Examination shows a fixed, dilated left pupil and right-sided flaccid paralysis. A CT scan of the head shows a skull fracture in the region of the pterion and a biconvex hyperdensity overlying the left frontotemporal lobe. This patient's condition is most likely caused by damage to a vessel that enters the skull through which of the following foramina?

	Answer	Image
A	Foramen lacerum	
B	Jugular foramen	
C	Foramen rotundum	
D	Foramen magnum	

	Answer	Image
E	Foramen ovale	
F	Foramen spinosum	

Hint

This patient has signs of an acute epidural hematoma (unconsciousness, vomiting, fixed dilated pupil following trauma), which the CT findings confirm. This condition is most commonly due to rupture of the middle meningeal artery.

Correct Answer

A - Foramen lacerum

Image



Explanation Why

The [foramen lacerum](#) serves as the opening for the [artery](#) and nerve of the pterygoid canal as well as for emissary veins. Rupture of an emissary vein can occur after [head trauma](#) and cause an [acute subdural hematoma](#). This condition presents similar to [epidural hematoma](#), the main symptoms being severe [headaches](#), nausea, vomiting, and fluctuating consciousness. Focal neurologic signs may also be present. However, a [CT scan](#) would show a crescent-shaped lesion that is not limited by suture lines in contrast to the biconvex [hyperdensity](#) seen in this patient.

B - Jugular foramen

Explanation Why

The [jugular foramen](#) is the opening for the [internal jugular vein](#) and occipital [artery](#), as well as the [cranial nerves](#) IX, X, and XI. Traumatic aneurysms of either the [internal jugular vein](#) or occipital [artery](#) are rare but could occur following [blunt head trauma](#) as in this patient. However, neither would present with pupil dilation, [flaccid paralysis](#), or the finding of a biconvex [hyperdensity](#) on CT. Instead, they often present as a painless non-pulsatile scalp mass.

C - Foramen rotundum

Explanation Why

No blood vessel passes through the [foramen rotundum](#). Instead, it serves as the opening for the maxillary division of the [trigeminal nerve](#). Compression of this nerve at the [foramen rotundum](#) could occur from [head trauma](#). However, damage to the [maxillary nerve](#) would present with anesthesia to the midface and not pupil dilation or [flaccid paralysis](#). Moreover, the biconvex [hyperdensity](#) seen in this patient's [CT scan](#) cannot be explained by a [maxillary nerve](#) lesion.

D - Foramen magnum

Explanation Why

The [foramen magnum](#) serves as an opening for the medulla of the [brainstem](#) and the [vertebral arteries](#). Dissection of a [vertebral artery](#) could follow [blunt head trauma](#), as in this patient. However, ipsilateral pupil dilation, contralateral [flaccid paralysis](#), and biconvex [hyperdensity](#) in a [CT scan](#) would not be present. Instead, [vertebral artery dissection](#) would cause [stroke](#)-like symptoms including ipsilateral facial [pain](#) and numbness, [dysphagia](#), [dysarthria](#), [vertigo](#), and possibly [Wallenberg syndrome](#).

E - Foramen ovale

Image

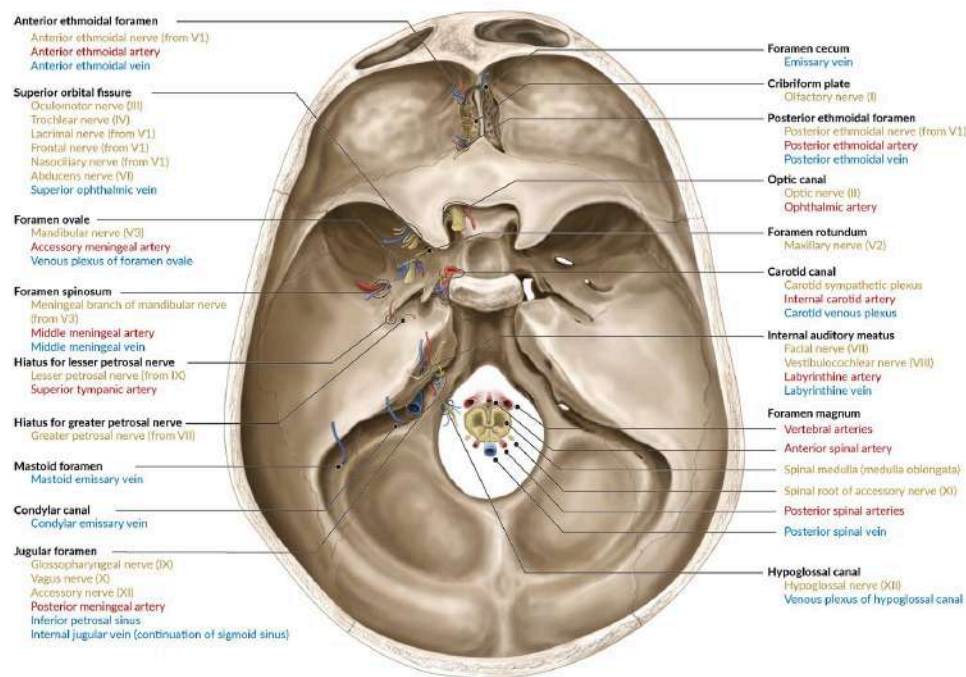


Explanation Why

The foramen ovale serves as an opening for the [mandibular nerve](#) and emissary veins. Rupture of an emissary vein can occur after [head trauma](#) and cause an [acute subdural hematoma](#). This condition presents similar to [epidural hematoma](#), the main symptoms being severe [headaches](#), nausea, vomiting, and fluctuating consciousness. Focal neurologic signs may also be present. However, a [CT scan](#) would show a crescent-shaped lesion that is not limited by suture lines in contrast to the biconvex [hyperdensity](#) seen in this patient.

F - Foramen spinosum

Image



Explanation Why

The [middle meningeal artery](#) enters the [skull](#) through the [foramen spinosum](#) in the greater wing of the [sphenoid bone](#). This vessel's [anterior](#) division runs in close proximity to the pterion, a very thin area of the [skull](#). Subsequently, it can easily rupture secondary to a skull fracture involving the pterion, as seen in this patient. An [epidural hematoma](#) is a medical emergency in which urgent craniotomy is essential.

Question # 5

A 51-year-old man is brought to the physician by his wife because of a 3-week history of abnormal behavior. His wife reports he has been preoccupied with gambling at the local casino. He becomes restless and irritable when his wife attempts to restrict his gambling. Four months ago, he was diagnosed with Parkinson disease and treatment was initiated. Which of the following best describes the mechanism of action of the drug that was most likely prescribed for this patient?

	Answer	Image
A	Peripheral inhibition of DOPA decarboxylase	
B	Inhibition of dopamine reuptake	
C	Direct activation of dopamine receptors	The diagram illustrates the dopamine pathway and various pharmacological interventions. In the Substantia nigra, L-DOPA is converted to Dopamine by DDC (DOPA decarboxylase). Dopamine is then transported into the Presynaptic terminal via a transporter. Inside the terminal, it can be stored in vesicles or metabolized by COMT (catechol-O-methyltransferase). Dopamine is released into the synaptic cleft and binds to Dopamine receptors on the Postsynaptic neuron. It can also be taken up by the Presynaptic terminal via a transporter. In the Glial cell, Dopamine can be metabolized by MAO-B (monoamine oxidase B). The diagram also shows the interaction of Dopamine with ACh (acetylcholine) receptors and NMDA receptors in the Striatum. Various drugs are shown inhibiting different components: Decarboxylase inhibitors (Carbidopa) inhibit DDC; COMT inhibitors (Tolcapone, Entacapone) inhibit COMT; MAO-B inhibitors (Selegiline) inhibit MAO-B; Dopamine agonists (Ropinirole, Levodopa, Bromocriptine, Ergot) activate Dopamine receptors; Anticholinergic drugs (Benztropine) block ACh receptors; and NMDA antagonists (Amantadine) block NMDA receptors.
D	Selective inhibition of monoamine oxidase B	
E	Inhibition of catechol-O-methyl transferase	

Hint

Pramipexole, a non-ergot alkaloid used in the treatment of Parkinson disease, is known to cause impulse control disorder (e.g., pathological gambling).

Correct Answer

A - Peripheral inhibition of DOPA decarboxylase

Explanation Why

[Carbidopa](#), a [DOPA decarboxylase](#) inhibitor, is administered in combination with [levodopa](#) to inhibit its peripheral conversion to [dopamine](#). This reduces the side effects of [levodopa](#) that result from increased systemic [dopamine](#) levels (e.g., [postural hypotension](#), nausea). [Carbidopa-levodopa](#) is the preferred first-line therapy in [Parkinson disease](#) patients > 65 years of age or younger patients presenting with moderate to severe symptoms. Impulse control disorder, which is seen here, is not associated with [carbidopa](#) use.

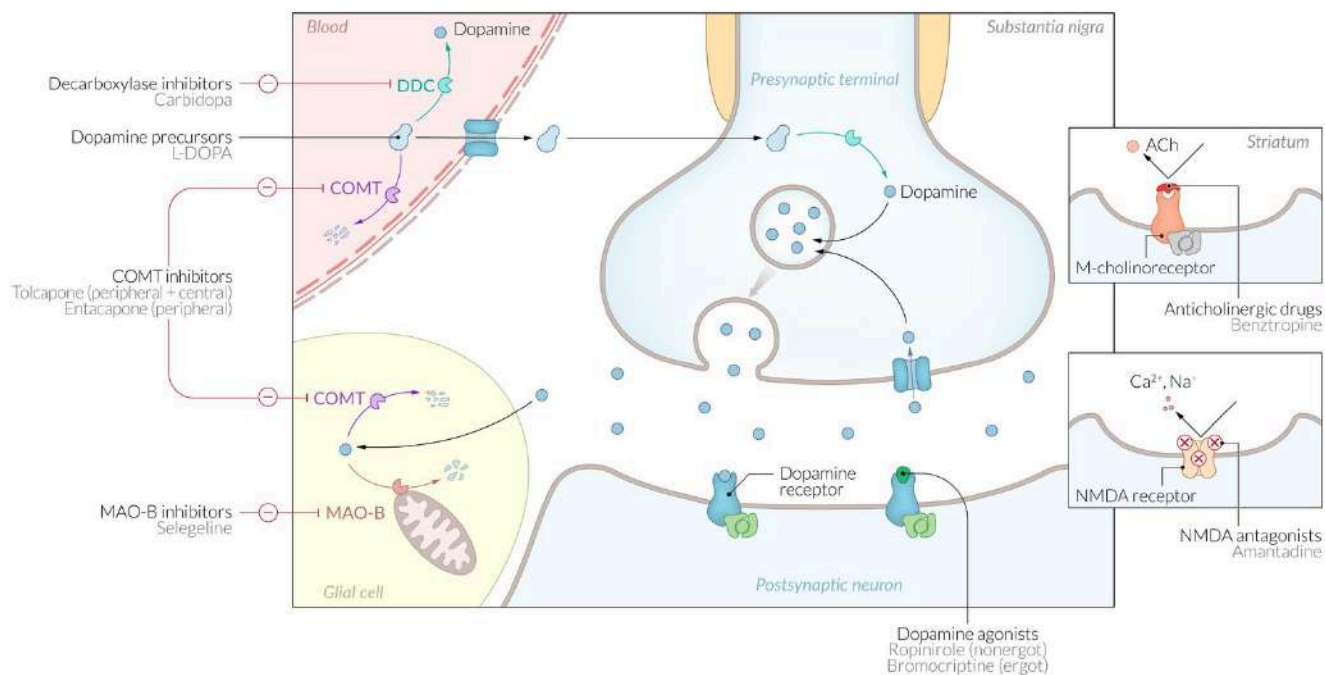
B - Inhibition of dopamine reuptake

Explanation Why

[Amantadine](#) is thought to increase the [bioavailability](#) of [dopamine](#) by enhancing presynaptic release and inhibiting reuptake. In addition, [amantadine](#) acts as a weak [NMDA receptor antagonist](#). It has some efficacy in treating [Parkinson disease](#), particularly mild symptoms, and resolving [akinetiic crises](#). [Amantadine](#) is usually well tolerated but side effects include peripheral [edema](#), [livedo reticularis](#), confusion, and [hallucinations](#). Although [amantadine](#) is not a direct [anticholinergic agent](#), it also exhibits [anticholinergic side effects](#) (dry mouth, [urinary retention](#), and [constipation](#)). Recent evidence has suggested that its antihyperglutamatergic activity can help to treat the impulse control disorders associated with the use of a different class of antiparkinsonian drugs.

C - Direct activation of dopamine receptors

Image



Explanation But

Patients may also develop compulsive use of these drugs (termed [dopaminergic dysregulation syndrome](#)). A withdrawal syndrome resembling cocaine withdrawal (e.g., anxiety, depression, sweating, nausea, fatigue, and drug craving) may occur if the drug is abruptly discontinued.

Explanation Why

Direct [dopamine receptor agonists](#) (e.g., [pramipexole](#), [ropinirole](#)) are the first-line treatment for [Parkinson disease](#) patients < 65 years of age. They are, however, associated with the development of impulse control disorders (e.g., compulsive gambling, hypersexuality, excessive spending of money), which occurs in up to 50% of patients with long-term use. This adverse effect is presumably due to decreased neuronal activity in brain areas responsible for impulse and inhibitory control. [Risk factors](#) include high doses, long duration of treatment, young age, and male sex. Other common side effects of [dopamine agonists](#) include nausea, drowsiness, [orthostatic hypotension](#), confusion, and [hallucinations](#).

D - Selective inhibition of monoamine oxidase B

Explanation Why

Selective [monoamine oxidase B inhibitors](#) (e.g., [rasagiline](#), [safinamide](#), [selegiline](#)) reduce [dopamine](#) degradation in the brain and are a treatment option for early-stage mild [Parkinson disease](#). Common side effects include nausea, [headache](#), confusion, and [hallucinations](#). Impulse control disorder, which is seen here, has been associated with the use of [rasagiline](#) in a few [case reports](#); however, a different group of drugs is more likely to cause this adverse effect.

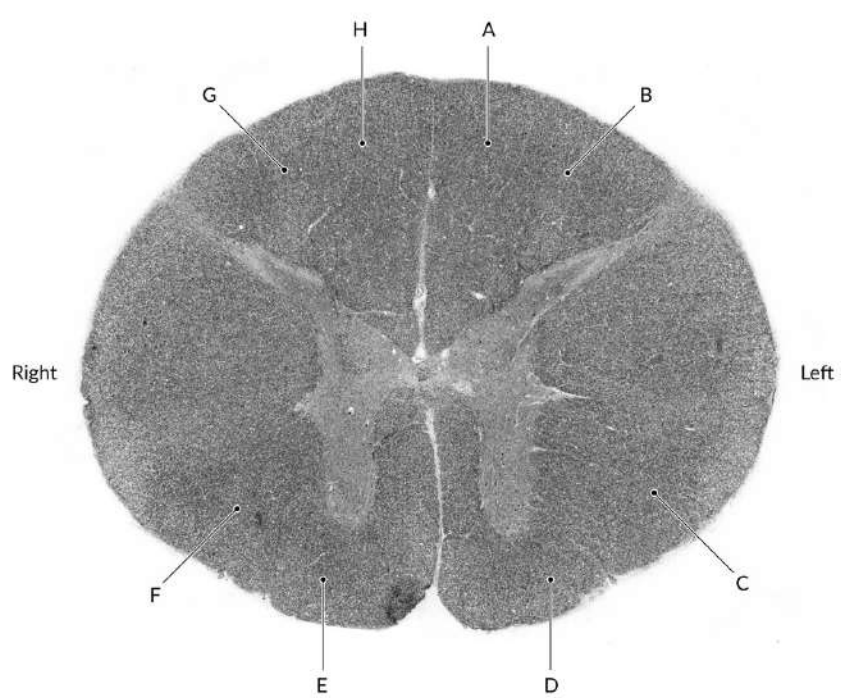
E - Inhibition of catechol-O-methyl transferase

Explanation Why

[Entacapone](#) and [tolcapone](#), which are [catechol-O-methyl transferase \(COMT\)](#) inhibitors, can prolong the action of [levodopa](#) by reducing its degradation. As they are always used in combination with [levodopa](#) and [carbidopa](#), [COMT inhibitors](#) are effective in patients with a decreasing response to [levodopa](#) or a fluctuation in motor symptoms. Common side effects include [dyskinesia](#), [hallucinations](#), confusion, nausea, [orthostatic hypotension](#), [diarrhea](#), and an orange discoloration of the [urine](#). Impulse control disorder, which is seen here, is not associated with this group of drugs.

Question # 6

A 78-year-old woman comes to the physician for a follow-up examination. Three weeks ago, she was diagnosed with herpes zoster in the right T10 dermatome. The rash has since resolved, but she now reports continuous burning and stabbing pain in the affected area. During the neurologic examination, the physician tests the patient's pain and temperature sensation on the right lower abdomen. Which of the following labeled parts of the upper thoracic spinal cord is responsible for transmitting this sensory information?



	Answer	Image
A	A	
B	B	

Hint

Sensation to pain and temperature is transmitted to the thalamus by the lateral spinothalamic tract.

Correct Answer

A - A

Explanation Why

A is the left [gracile fasciculus](#), which carries impulses from the lower body. Together with the [cuneate fasciculus](#), it ascends ipsilaterally in the [dorsal column](#), conveying [proprioception](#), vibration, and fine touch.

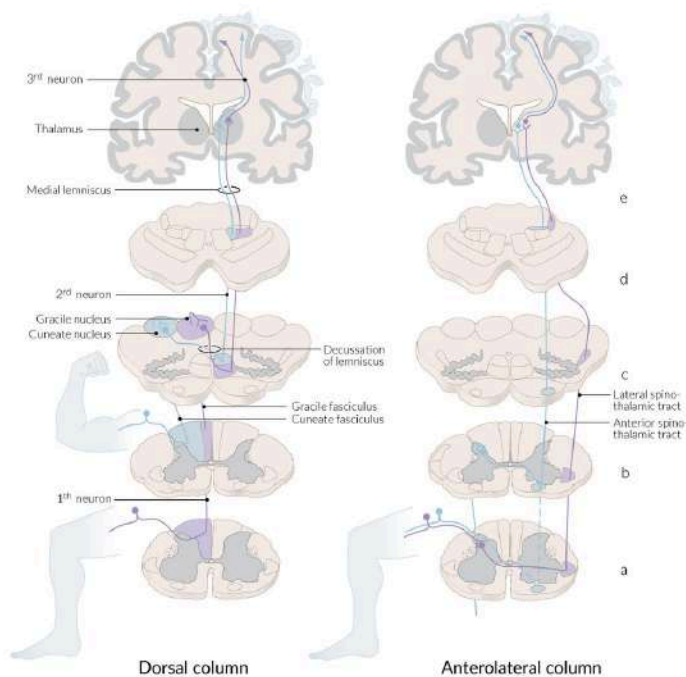
B - B

Explanation Why

B is the left [cuneate fasciculus](#), which carries impulses from the upper body (excluding the face and ear). Together with the [gracile fasciculus](#), it ascends ipsilaterally in the [dorsal column](#), conveying [proprioception](#), vibration, and fine touch.

C - C

Image



Explanation Why

C is the left [lateral spinothalamic tract](#). The [spinothalamic tract](#) consists of ascending sensory nerve fibers, which transmit the sensations of [pain](#) and temperature ([lateral](#) tract) as well as the sensations of pressure and crude touch ([anterior](#) tract). First-order [neurons](#) are located within the [dorsal root ganglia](#), where their [axons](#) enter the [spinal cord](#) and ascend or descend 1–2 segments to form [synapses](#) with the second-order [neurons](#), which are located in the [posterior horn](#) of the [gray matter](#). [Axons](#) of the second-order [neurons](#) cross to the contralateral side of the [spinal cord](#) within the [anterior](#) white commissure to ascend contralaterally in the [spinothalamic tract](#) to the [thalamus](#). Accordingly, the left [spinothalamic tract](#) in an upper thoracic segment transmits the sensations of [pain](#) and temperature from the right T10 [dermatome](#).

D - D

Explanation Why

D is the left [anterior spinothalamic tract](#), which contains ascending sensory nerves that transmit the sensations of crude touch and pressure.

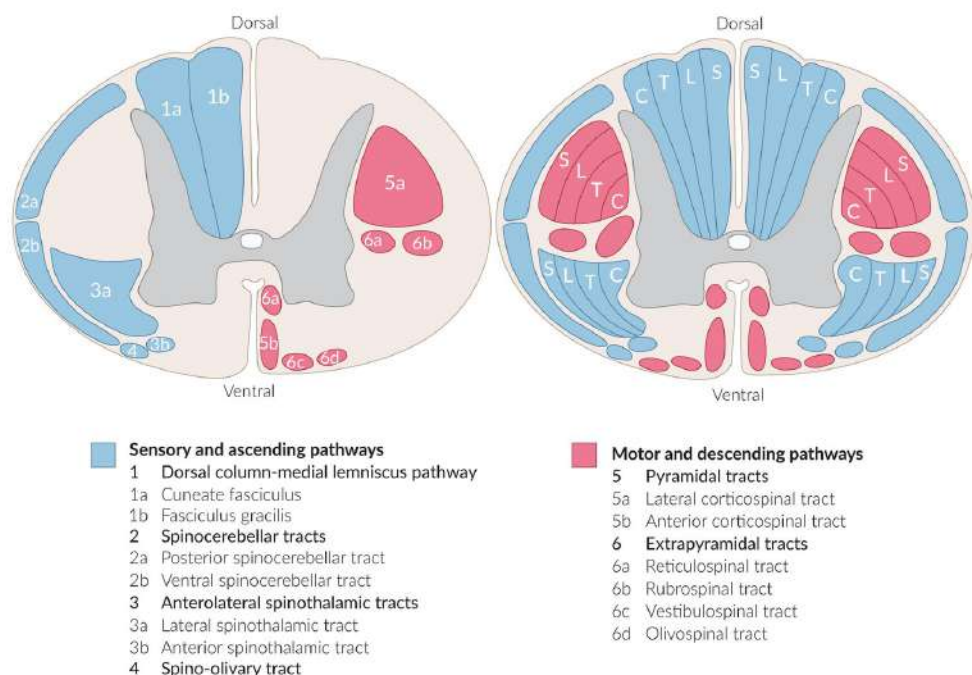
E - E

Explanation Why

E is the right [anterior spinothalamic tract](#), which contains ascending sensory nerves that transmit the sensations of crude touch and pressure.

F - F

Image



Explanation Why

F is the right [lateral spinothalamic tract](#), which contains sensory nerves that transmit [pain](#) and temperature. The [axons](#) of the first-order [neurons](#) of the [lateral spinothalamic tract](#) enter the ipsilateral [spinal cord](#) and ascend or descend several segments before they form [synapses](#) with second-order [neurons](#). Then [axons](#) of the second-order [neurons](#) cross to the contralateral side of the [spinal cord](#) to ascend contralaterally in the [spinothalamic tract](#). This patient's [pain](#) and temperature sensation in the right T10 [dermatome](#) is tested. The ipsilateral [lateral spinothalamic tract](#) would not be affected in this patient because the cross-section of the [spinal cord](#) shown is at the upper thoracic level. Therefore, the second-order [neuron](#) rather than the first-order [neuron](#) would be affected.

G - G

Explanation Why

G is the right [cuneate fasciculus](#), which carries impulses from the upper body (excluding the face and ear). Together with the [gracile fasciculus](#), it ascends ipsilaterally in the [dorsal column](#), conveying [proprioception](#), vibration, and fine touch.

H - H

Explanation Why

H is the right [gracile fasciculus](#), which carries impulses from the lower body. Together with the [cuneate fasciculus](#), it ascends ipsilaterally in the [dorsal column](#), conveying [proprioception](#), vibration, and fine touch.

Question # 7

A 48-year-old homeless man is brought to the emergency department 2 hours after his right arm was burned by a fire. He is diagnosed with extensive third-degree burns of the right forearm and upper arm and is admitted to the hospital for debridement and grafting. During his stay in the hospital, he suddenly develops confusion and agitation. Neurologic examination shows horizontal nystagmus and a broad-based gait. Laboratory studies show decreased erythrocyte transketolase activity. Administration of which of the following most likely caused this patient's current condition?

	Answer	Image
A	Cobalamin	
B	Glucose	
C	Aspirin	
D	Disulfiram	
E	Hypertonic saline	
F	Clindamycin	
G	Haloperidol	

Hint

The triad of confusion, ophthalmoplegia, and ataxia suggests Wernicke encephalopathy, which is due to thiamine (vitamin B₁) deficiency (most commonly seen in patients with alcohol use disorder).

Decreased activity of the enzyme erythrocyte transketolase, which uses thiamine as a cofactor, is diagnostic of Wernicke encephalopathy.

Correct Answer

A - Cobalamin

Explanation Why

[Cobalamin](#) ([vitamin B₁₂](#)) serves as a [cofactor](#) in enzymatic reactions responsible for [red blood cell](#) formation and myelination of the nervous system. Deficiency is seen in [malnourished](#) patients (e.g., due to chronic [alcoholism](#)) and manifests with chronic neurologic symptoms, including gait abnormalities. However, supplementation of [cobalamin](#) would improve symptoms, not worsen them. Moreover, [cobalamin](#) is not known to precipitate [Wernicke encephalopathy](#). Other features of [cobalamin deficiency](#) include [macrocytic anemia](#), mild [icterus](#), and [glossitis](#), as well as symmetric [peripheral neuropathy](#), [subacute combined degeneration of the spinal cord](#), and neuropsychiatric disease.

B - Glucose

Explanation But

As a [cofactor](#) for the [transketolase](#) reaction of the [NADPH](#)-producing [pentose phosphate pathway](#), [TPP](#) is also essential for [regeneration](#) of the antioxidant [glutathione](#). Decreased [glutathione regeneration](#) due to [thiamine deficiency](#) impairs [free radical](#) neutralization, causing further cell damage.

Explanation Why

The active form of [thiamine](#), [thiamine pyrophosphate](#) ([TPP](#)), serves as a [cofactor](#) for [dehydrogenases](#) such as [pyruvate dehydrogenase](#) and [α-ketoglutarate dehydrogenase](#), both enzymes that are essential for [ATP](#) generation. [Thiamine deficiency](#) (e.g., due to chronic [alcoholism](#) or [malnutrition](#)) leads to [ATP](#) depletion, which primarily damages highly aerobic tissues such as [CNS neurons](#). Infusing glucose in a patient with [thiamine deficiency](#) without administering [thiamine](#) beforehand precipitates [Wernicke encephalopathy](#) because the little [TPP](#) available is used to break down glucose to [pyruvate](#). Since [pyruvate](#) cannot enter the [citric acid cycle](#) due to an impaired [pyruvate dehydrogenase](#) reaction, cytotoxic amounts of [lactate](#) build up, whereas [ATP](#) generation remains depleted.

C - Aspirin

Explanation Why

[Aspirin](#) is an [NSAID](#) and, if administered during viral infections, may in rare cases cause [acute encephalopathy](#) ([Reye syndrome](#)). Typical early manifestations include vomiting, [lethargy](#), and signs of hepatic failure. Agitation, [horizontal nystagmus](#), or gait disorders would not be expected. Moreover, this condition is generally considered a childhood disease, and [laboratory studies](#) would not show decreased erythrocyte transketolase activity. Finally, [aspirin](#) is not known to cause [Wernicke encephalopathy](#).

D - Disulfiram

Explanation Why

Disulfiram can be used to treat patients with [alcohol use disorder](#). This drug increases the negative side effects of alcohol ingestion by inhibiting [acetaldehyde dehydrogenase](#). Rapid accumulation of acetaldehyde after alcohol consumption results in intoxication symptoms such as nausea, [vertigo](#), and confusion. However, nystagmus or gait disturbances would not be expected. Administration of disulfiram is not known to precipitate [Wernicke encephalopathy](#).

E - Hypertonic saline

Explanation Why

Overly rapid correction of severe [hyponatremia](#) with hypertonic saline infusions can cause [osmotic demyelination syndrome](#). Symptoms appear a few days after correction of [hyponatremia](#) and include an altered [level of consciousness](#), [coma](#), [locked-in syndrome](#), [dysarthria](#), [dysphagia](#), [diplopia](#), and/or worsening quadriparesis. Agitation, [horizontal nystagmus](#), or gait disorders would not be expected. Administration of hypertonic saline does not cause [Wernicke encephalopathy](#).

F - Clindamycin

Explanation Why

[Clindamycin](#) is an [antibiotic](#) mainly used in the treatment of infections with [anaerobes](#). Adverse effects include [pseudomembranous colitis](#), which manifests with watery [diarrhea](#), abdominal [pain](#), and [fever](#). However, neurological symptoms would not be expected. Moreover, [clindamycin](#) does not precipitate [Wernicke encephalopathy](#).

G - Haloperidol

Explanation Why

[Haloperidol](#) is occasionally used in the management of severe agitation during [alcohol withdrawal](#). [Extrapyramidal symptoms](#), including gait disturbances, are common side effects. However, confusion, agitation, and [horizontal nystagmus](#) would not be seen. [Haloperidol](#) is not a known precipitant of [Wernicke encephalopathy](#).

Question # 8

A 32-year-old homeless woman is brought to the emergency department by ambulance 30 minutes after the police found her on the sidewalk. On arrival, she is unresponsive. Her pulse is 76/min, respirations are 6/min, and blood pressure is 110/78 mm Hg. Examination shows cool, dry skin. The pupils are pinpoint and react sluggishly to light. Intravenous administration of a drug is initiated. Two minutes after treatment is started, the patient regains consciousness and her respirations increase to 12/min. The drug that was administered has the strongest effect on which of the following receptors?

	Answer	Image
A	M ₁ receptor	
B	Ryanodine receptor	
C	μ-receptor	
D	GABA _A receptor	
E	α-receptor	
F	5-HT _{2A} receptor	

Hint

Respiratory depression and miosis in an unresponsive patient strongly suggest opioid overdose.

Correct Answer

A - M₁ receptor

Explanation Why

[Atropine](#) is a [competitive antagonist](#) with activity against [muscarinic receptors](#) M₁–[M₃](#) and can be used as an [antidote](#) for the muscarinic effects of acetylcholinesterase inhibitor poisoning (e.g., [organophosphate](#) and carbamate insecticides). [Miosis](#) and altered consciousness are consistent with acetylcholinesterase inhibitor poisoning; however, additional symptoms such as sweating, [hypotension](#), and [bradycardia](#) would be expected. Furthermore, [atropine](#) is not used in [opioid overdose](#).

B - Ryanodine receptor

Explanation Why

[Dantrolene](#) is a [ryanodine receptor](#) antagonist that acts as an [antidote](#) for [malignant hyperthermia](#) by preventing the release of calcium from the [sarcoplasmic reticulum](#). However, this patient does not show signs of [malignant hyperthermia](#) (e.g, hyperthermia, [rigidity](#), [tachypnea](#), [tachycardia](#)). Furthermore, [dantrolene](#) is not used in the treatment of [opioid overdose](#).

C - μ-receptor

Explanation Why

[Naloxone](#) is the treatment of choice for [opioid overdose](#), given its action as a competitive [opioid](#) receptor antagonist with a quick onset of action (2–5 minutes). Although [naloxone](#) has the highest affinity for the [μ-receptor](#), it is a nonselective [opioid](#) receptor antagonist and binds all major [opioid](#) receptors (μ-, κ-, and [δ-opioid receptors](#)). As [naloxone](#) binds and displaces [opioids](#) from [opioid](#) receptors, it reverses the symptoms of [opioid intoxication](#), as seen by this patient's almost immediate improvement in breathing and [level of consciousness](#) after drug administration. Because [naloxone](#) has a shorter duration of action than most [opioids](#), patients should be monitored for the ongoing

effects of [opioid intoxication](#) as [naloxone](#) is metabolized.

D - GABA_A receptor

Explanation Why

[Flumazenil](#) competitively inhibits [benzodiazepine](#) activity at the [GABA_A receptor](#) and can be used as a treatment for [benzodiazepine toxicity](#). While [benzodiazepine toxicity](#) can present with respiratory depression and altered consciousness, [miosis](#) would not be expected. Furthermore, [flumazenil](#) is not used to treat [opioid overdose](#).

E - α -receptor

Explanation Why

Phentolamine is a nonselective [\$\alpha\$ -adrenergic receptor](#) antagonist that can be used to treat a [hypertensive crisis](#) caused by [methamphetamine](#) or [cocaine](#) overdose. However, this patient is not in [hypertensive crisis](#), with a [systolic](#) blood pressure < 180 mm Hg and a [diastolic](#) blood pressure < 120 mm Hg. Moreover, [amphetamine](#) overdose typically results in agitation, hyperthermia, dilated pupils, [hyperventilation](#), [tachycardia](#), and [diaphoresis](#), none of which are seen in this patient. Phentolamine is not used in the treatment of [opioid overdose](#).

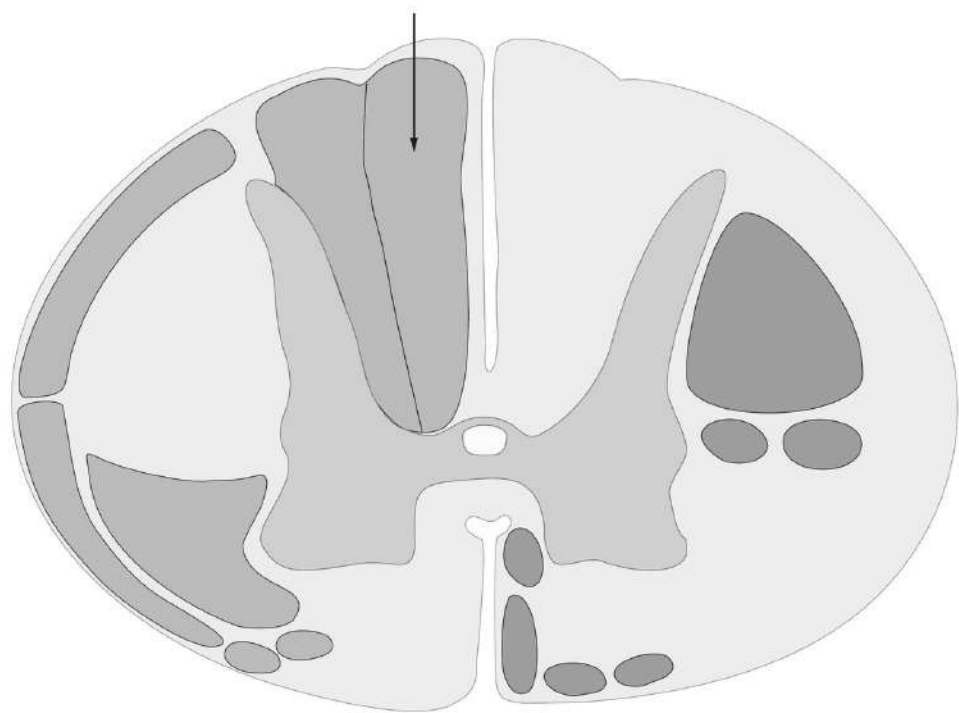
F - 5-HT_{2A} receptor

Explanation Why

[Cyproheptadine](#) is a nonspecific antagonist of H₁, 5-HT_{1A}, and [5-HT_{2A} receptors](#) and can be used as an [antidote](#) for [serotonin syndrome](#). Although [serotonin syndrome](#) may manifest with [coma](#) in later stages, patients typically present with neuromuscular excitability (e.g., hypertonia, [hyperreflexia](#), myoclonus) and [autonomic dysfunction](#). Furthermore, [miosis](#) and respiratory depression would not be expected in [serotonin syndrome](#) and [cyproheptadine](#) is not used to treat [opioid overdose](#).

Question # 9

A 52-year-old man with a history of gastric cancer that was treated with subtotal gastrectomy dies in a motor vehicle collision. At autopsy, examination of the spinal cord shows unilateral atrophy of the neurons in the area indicated by the arrow. Neurological examination of the patient when he was still alive would most likely have shown which of the following findings?



	Answer	Image
A	Decreased sense of pain in the contralateral leg	
B	Decreased sense of temperature in the ipsilateral arm	
C	Decreased strength of the contralateral leg	

	Answer	Image
D	Decreased vibratory sense in the ipsilateral arm	
E	Decreased positional sense in the ipsilateral leg	Sensory and ascending pathways 1 Dorsal column-medial lemniscus pathway 1a Cuneate fasciculus 1b Fasciculus gracilis 2 Spinocerebellar tracts 2a Posterior spinocerebellar tract 2b Ventral spinocerebellar tract 3 Anterolateral spinothalamic tracts 3a Lateral spinothalamic tract 3b Anterior spinothalamic tract 4 Spino-olivary tract Motor and descending pathways 5 Pyramidal tracts 5a Lateral corticospinal tract 5b Anterior corticospinal tract 6 Extrapyramidal tracts 6a Reticulospinal tract 6b Rubrospinal tract 6c Vestibulospinal tract 6d Olivospinal tract
F	Decreased sense of crude touch in the contralateral arm	

Hint

The region of the spinal cord indicated in the image is affected by vitamin B₁₂ deficiency, which occurs in about 15% of patients with prior subtotal gastrectomy (due to insufficient intrinsic factor synthesis).

Correct Answer

A - Decreased sense of pain in the contralateral leg

Explanation Why

The sensations of [pain](#) and temperature are carried by the afferent [neurons](#) that run in the [lateral spinothalamic tract](#) of the [spinal cord](#). These [neurons](#) decussate 1–2 [spinal](#) nerve segments above the point of entry. Therefore, [atrophy](#) of these [neurons](#) can result in decreased sensitivity to [pain](#) and temperature on the ipsilateral side of the body at the level of the lesion and on the contralateral side two segments below the lesion. However, the [atrophic](#) area in this patient does not correspond to the [lateral spinothalamic tract](#).

B - Decreased sense of temperature in the ipsilateral arm

Explanation Why

The sensations of [pain](#) and temperature are carried by the afferent [neurons](#) that run in the [lateral spinothalamic tract](#) of the [spinal cord](#). These [neurons](#) decussate 1–2 [spinal](#) nerve segments above the point of entry. Therefore, [atrophy](#) of these [neurons](#) can result in decreased sensitivity to [pain](#) and temperature on the ipsilateral side of the body at the level of the lesion and on the contralateral side two segments below the lesion. However, the [atrophic](#) area in this patient does not correspond to the [lateral spinothalamic tract](#).

C - Decreased strength of the contralateral leg

Explanation Why

Voluntary limb movement is controlled by the [lateral corticospinal tract](#), which is formed by the [axons](#) of [pyramidal neurons](#) located in the [primary motor cortex](#). The [axons](#) decussate at the [caudal](#) medulla. Lesions above the [caudal](#) medulla result in contralateral limb weakness, while lesions in the [spinal cord](#) result in ipsilateral weakness. However, the [atrophic](#) area in this patient does not correspond to the [lateral corticospinal tract](#).

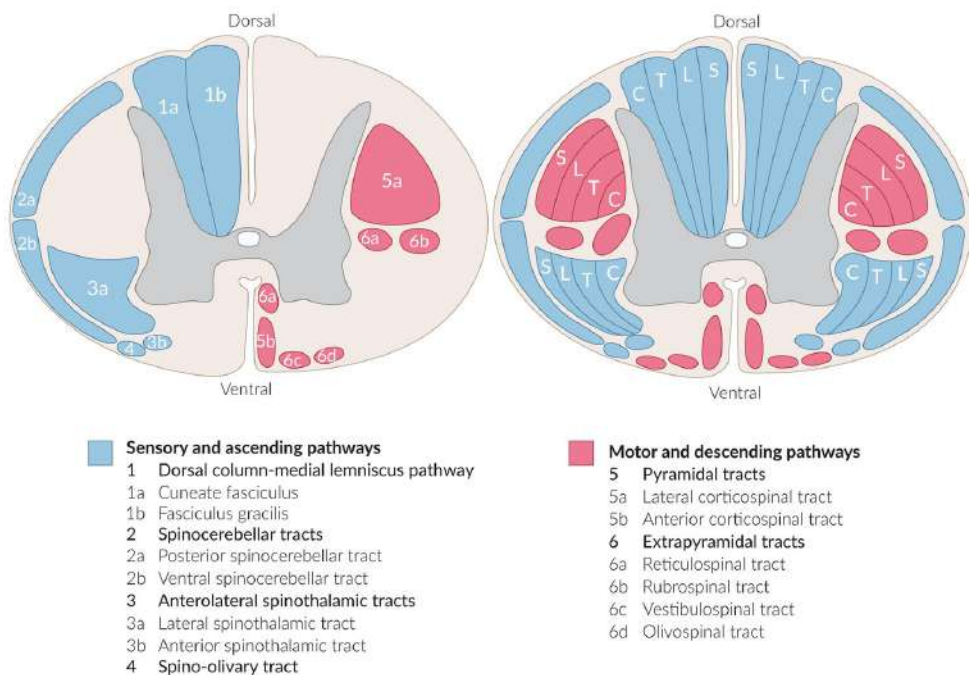
D - Decreased vibratory sense in the ipsilateral arm

Explanation Why

[Atrophy](#) of the [fasciculus cuneatus](#) can result in decreased [proprioception](#), vibration, pressure, and fine touch sensation in the ipsilateral arm and upper trunk. However, the [atrophic](#) area in this patient does not correspond to the [fasciculus cuneatus](#).

E - Decreased positional sense in the ipsilateral leg

Image



Explanation But

[Vitamin B₁₂ deficiency](#) can also lead to combined degeneration of the [dorsal](#) and [lateral columns](#) of the [spinal cord](#) (i.e., [subacute combined degeneration of spinal cord](#)), which classically manifests with decreased [proprioception](#) and vibratory sensation, [spasticity](#), and [ataxia](#).

Explanation Why

The area indicated by the arrow corresponds to the [fasciculus gracilis](#) of the [dorsal column](#). This part of the [spinal cord](#) consists of afferent [neurons](#), which transmit the sensations of [proprioception](#), vibration, pressure, and fine touch from the ipsilateral lower trunk and extremities. [Atrophy](#) of this area due to neuronal [demyelination](#) can be caused by [vitamin B12 deficiency](#) and results in decreased function of these [neurons](#), leading to decreased positional sense (i.e., [proprioception](#)) and vibratory sensation in the ipsilateral leg.

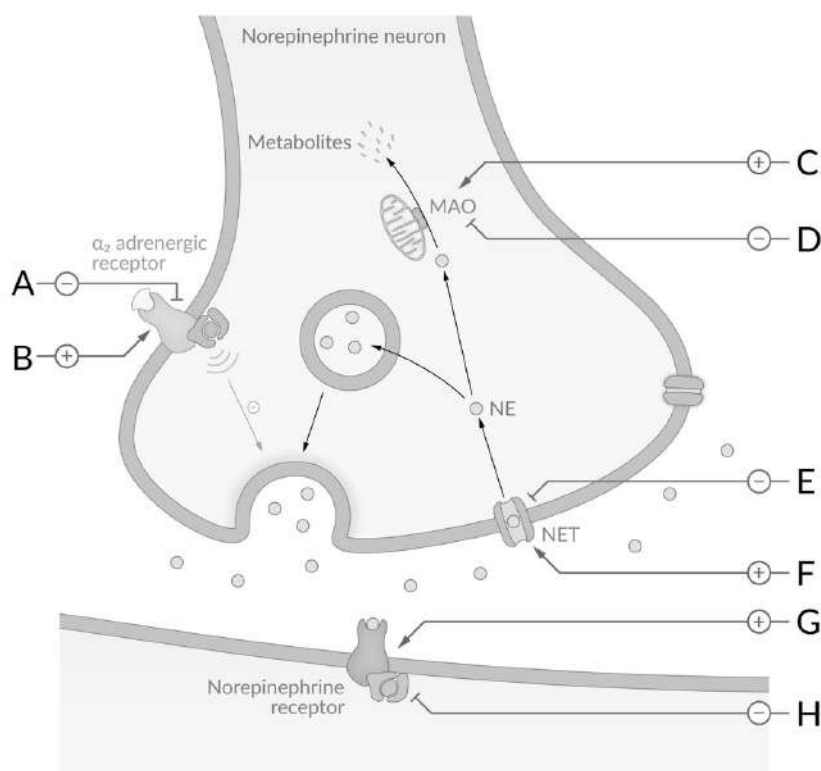
F - Decreased sense of crude touch in the contralateral arm

Explanation Why

The sensations of crude touch and pressure are transmitted through afferent [neurons](#) that run in the [anterior spinothalamic tract](#). These [neurons](#) decussate 1–2 [spinal](#) nerve segments above the point of entry. Therefore, [atrophy](#) of these [neurons](#) can result in decreased sensitivity to [pain](#) and temperature on the contralateral side of the body. However, the [atrophic](#) area in this patient does not correspond to the [anterior spinothalamic tract](#).

Question # 10

A 38-year-old woman comes to the physician because of a 3-week history of fatigue, difficulty sleeping, and feeling sad. She has been unable to concentrate recently and is no longer interested in spending time with her friends. She has a history of anorexia nervosa, for which she attends weekly psychotherapy. She has had a persistently decreased appetite for 3 months. Mental status examination shows a depressed mood and flat affect. Treatment with a drug is begun that treats both her depressed mood and her decreased appetite. An overview of a noradrenergic synapse is shown. The prescribed drug most likely has which of the following labeled mechanisms of action?



	Answer	Image
A	A	
B	B	
C	C	

	Answer	Image
D	D	
E	E	
F	F	
G	G	
H	H	

Hint

This patient has a history of anorexia nervosa and symptoms of major depressive disorder (e.g., depressed mood, fatigue, sleep disturbances, anhedonia). Mirtazapine is an antidepressant that also stimulates appetite.

Correct Answer

A - A

Explanation But

[Mirtazapine](#) also causes sedation (which may be useful in patients with comorbid [insomnia disorder](#)) and dry mouth.

Explanation Why

Inhibition of α_2 -[adrenergic receptors](#) (as well as 5-HT₂ receptors, 5-HT₃ receptors, and [H₁ receptors](#)) is the mechanism of action of [mirtazapine](#). These mechanisms increase the synaptic release of [norepinephrine](#) and [serotonin](#). Although [mirtazapine](#) is typically considered a second-line [antidepressant](#) for [major depressive disorder](#), it stimulates appetite and can cause weight gain, which is desirable in a patient with comorbid [anorexia nervosa](#).

B - B

Explanation Why

Activation of α_2 -[adrenergic receptors](#) is the mechanism of action of [clonidine](#), α -[methyldopa](#), and [brimonidine](#). [Clonidine](#) is used to treat [attention-deficit hyperactivity disorder](#) and [hypertensive urgency](#), while α -[Methyldopa](#) is used to treat [hypertension](#) during [pregnancy](#). [Brimonidine](#) is used to treat [open-angle glaucoma](#). None of these drugs is indicated in [major depressive disorder](#) or [anorexia nervosa](#).

C - C

Explanation Why

Activation of [monoamine oxidase](#) (along with inhibition of sodium channels and GABA transaminase) is the mechanism of action of [valproic acid](#). This drug is used to treat [seizures](#),

[migraines](#), and [bipolar disorder](#) but is not indicated in [major depressive disorder](#) or [anorexia nervosa](#).

D - D

Explanation Why

Inhibition of [monoamine oxidase](#) (MAO) is the mechanism of action of [MAO inhibitors](#) (e.g., [phenelzine](#)). This group of drugs reduces the breakdown of intrasynaptic amine [neurotransmitters](#) (e.g., [serotonin](#), [norepinephrine](#), [dopamine](#)). [MAO inhibitors](#) are rarely used as first-line or second-line [antidepressants](#) because of their potentially severe side effects, which include [hypertensive crisis](#) and [serotonin syndrome](#). They are most commonly used to treat [atypical depression](#) and anxiety and would not be the most appropriate choice for a patient with [major depressive disorder](#) and [anorexia nervosa](#).

E - E

Explanation Why

Inhibition of [norepinephrine](#) reuptake is part of the mechanism of action of [serotonin-norepinephrine reuptake inhibitors](#) (SNRIs), [tricyclic antidepressants](#) (TCAs), and [bupropion](#). SNRIs and TCAs (which also inhibit [serotonin](#) reuptake) can be used to treat [major depressive disorder](#) but are not the most appropriate pharmacotherapy for a patient with comorbid [anorexia nervosa](#). [Bupropion](#) (which also inhibits [dopamine](#) reuptake) reduces the [seizure](#) threshold and is therefore contraindicated in individuals with increased [seizure](#) risk, which include patients with [anorexia nervosa](#).

F - F

Explanation Why

Activation of [norepinephrine](#) reuptake is a mechanism that is of interest for the treatment of depression. However, there are no approved substances that currently target this mechanism.

G - G

Explanation Why

Activation of [norepinephrine](#) receptors is a mechanism that is of interest for the treatment of depression. However, there are no approved substances that currently target this mechanism.

H - H

Explanation Why

Inhibition of [norepinephrine](#) receptors is a mechanism that is of interest for the treatment of depression. However, there are no approved substances that currently target this mechanism.

Question # 11

An investigator is studying brachial artery reactivity in women with suspected coronary heart disease. The brachial artery diameter is measured via ultrasound before and after intra-arterial injection of acetylcholine. An increase of 7% in the vascular diameter is noted. The release of which of the following is most likely responsible for the observed effect?

	Answer	Image
A	Nitric oxide from endothelial cells	
B	Endothelin from the peripheral vasculature	
C	Serotonin from neuroendocrine cells	
D	Norepinephrine from the adrenal medulla	
E	Atrial natriuretic peptide from atrial myocytes	
F	Neuropeptide Y from sympathetic nerve endings	

Hint

Acetylcholine is released from cholinergic nerve fibers. While the parasympathetic nervous system does not directly innervate the peripheral vasculature, it can cause vasodilation via the release of another substance, which in turn induces the relaxation of smooth muscle cells in the vessel wall via the action of cGMP.

Correct Answer

A - Nitric oxide from endothelial cells

Explanation Why

The release of [nitric oxide](#) (an endothelial-derived relaxation factor) from [endothelial](#) cells is caused by [acetylcholine](#) and is responsible for the [vasodilatory](#) effect seen here. The binding of [acetylcholine](#) to its receptors on [endothelial](#) cells results in the activation of [nitric oxide synthase](#), which catalyzes the production of [nitric oxide](#) from L-[arginine](#). [Nitric oxide](#), in turn, activates [guanylyl cyclase](#), which increases [cGMP](#) synthesis. The end result of this cascade is arterial [smooth muscle](#) relaxation and subsequent dilation of the vessel.

B - Endothelin from the peripheral vasculature

Explanation Why

The release of endothelin from the peripheral vasculature (e.g., secondary to vascular damage) results in vasoconstriction (rather than [vasodilation](#)) of the peripheral vessels.

C - Serotonin from neuroendocrine cells

Explanation Why

The release of [serotonin](#) from neuroendocrine cells, such as intestinal [enterochromaffin cells](#), results in vasoconstriction (rather than [vasodilation](#)) of peripheral vessels. Moreover, the release of [serotonin](#) is not stimulated by [acetylcholine](#). Further effects of [serotonin](#) include increased gastrointestinal motility, bronchoconstriction, and [platelet aggregation](#).

D - Norepinephrine from the adrenal medulla

Explanation Why

The release of [norepinephrine](#) from the [adrenal medulla](#) occurs in response to the release of [acetylcholine](#) from [preganglionic sympathetic](#) fibers. However, [norepinephrine](#) causes vasoconstriction (rather than [vasodilation](#)) due to the activation of α_1 -[adrenergic receptors](#).

E - Atrial natriuretic peptide from atrial myocytes

Explanation Why

The release of [atrial natriuretic peptide \(ANP\)](#) from atrial [myocytes](#) causes peripheral [vasodilation](#) mediated by an increase in [cGMP](#) concentrations in [smooth muscle cells](#). Although this experiment showed peripheral [vasodilation](#), [ANP](#) release is not stimulated by [acetylcholine](#) but is, rather, a result of increased stretch on the [atrium](#) (e.g., due to [arterial hypertension](#)). Further effects of [ANP](#) include decreased renal sodium reabsorption and increased diuresis.

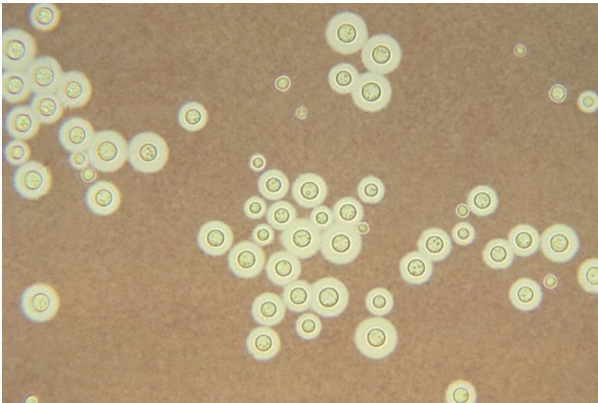
F - Neuropeptide Y from sympathetic nerve endings

Explanation Why

The release of [neuropeptide Y](#) from [sympathetic](#) nerve endings results in appetite stimulation, regulation of anxiety-related behaviors, neuronal excitability, and vasoconstriction (rather than [vasodilation](#)) of peripheral vessels.

Question # 12

A 32-year-old man with HIV infection is brought to the emergency department by his roommate because of a 2-week history of progressively worsening headache and vomiting. Current medications include trimethoprim-sulfamethoxazole, dolutegravir, and tenofovir-emtricitabine. His temperature is 38.5°C (101.3°F). Physical examination shows nuchal rigidity. Kernig and Brudzinski signs are present. A lumbar puncture is performed and shows an opening pressure of 32 cm H₂O (N: < 20). The pathogen isolated from the cerebrospinal fluid (CSF) can be cultured on Sabouraud agar. Further evaluation of this patient's CSF is most likely to show which of the following additional findings?

	Answer	Image
A	Presence of gram-positive diplococci	
B	Positive latex agglutination test	
C	Positive PCR for HSV-2 DNA	
D	Presence of tachyzoites	
E	Presence of gram-positive rods	
F	Increased adenosine deaminase concentration	

	Answer	Image
G	Positive PCR for JC virus DNA	

Hint

This patient most likely has cryptococcal meningoencephalitis, an opportunistic infection that typically causes progressive fever and meningism over a period of 1–2 weeks.

Correct Answer

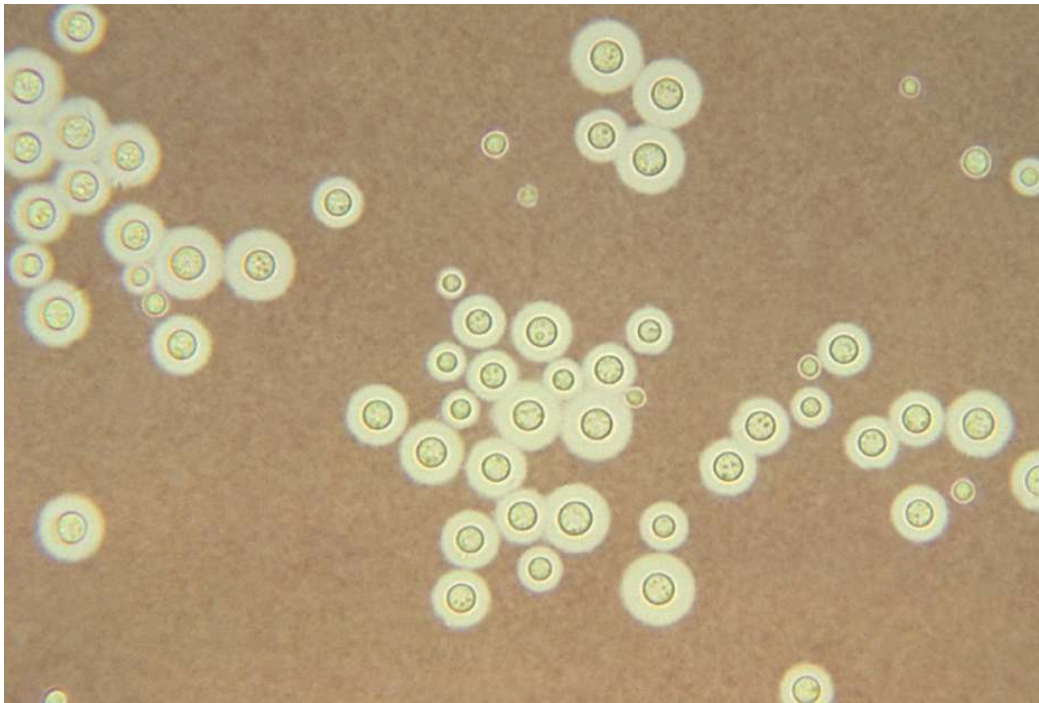
A - Presence of gram-positive diplococci

Explanation Why

The presence of gram-positive diplococci in the [CSF](#) is seen in patients with bacterial [meningitis](#) caused by [Streptococcus pneumoniae](#), which is the most common causal bacterial pathogen of [meningitis](#) among adults of all ages. [S. pneumoniae meningitis](#) causes progressive [headache](#), nausea, [fever](#), meningism, and a significantly increased opening pressure on [lumbar puncture](#). However, this condition typically manifests acutely over hours to days and would be an unlikely diagnosis for this patient whose symptoms have progressed across 2 weeks. In addition, [S. pneumoniae](#) cannot grow on [Sabouraud agar](#); this organism can be cultured on bacterial media such as blood agar.

B - Positive latex agglutination test

Image



Explanation But

Treatment of [cryptococcal meningoencephalitis](#) includes induction therapy with [amphotericin B](#) and [flucytosine](#) and consolidation therapy with [fluconazole](#).

Explanation Why

The detection of cryptococcal antigen in the [CSF](#) by a latex agglutination test is highly sensitive for a diagnosis of [cryptococcal meningoencephalitis](#). Like several other fungi, *Cryptococcus* spp. can grow on [Sabouraud agar](#). Staining techniques also aid in the identification of this pathogen; [India ink staining](#) shows encapsulated [yeast](#) surrounded by clear halos, and [mucicarmine staining](#) shows [yeast](#) with a red inner capsule.

C - Positive PCR for HSV-2 DNA

Explanation Why

A positive [PCR](#) for [HSV-2 DNA](#) in the [CSF](#) is seen in patients with herpes simplex [meningitis](#). This condition can manifest with progressive [headache](#), nausea, [fever](#), and meningism. However, the opening pressure on [lumbar puncture](#) of patients with viral [meningitis](#) is typically normal or only slightly increased; this patient's opening pressure was significantly increased. In addition, viruses cannot be cultured on [Sabouraud agar](#).

D - Presence of tachyzoites

Explanation Why

The presence of [tachyzoites](#) in the [CSF](#) confirms a diagnosis of [toxoplasmic encephalitis](#). This condition is caused by reactivation of [Toxoplasma gondii](#) in patients who are [immunocompromised](#) and can manifest with progressive [headache](#), nausea, [fever](#), and meningism. However, [T. gondii](#) cannot grow on [Sabouraud agar](#); diagnostic testing for this organism includes serologic testing, [PCR](#) for [T. gondii DNA](#), and histopathologic examination of tissue and/or fluid.

E - Presence of gram-positive rods

Explanation Why

The presence of gram-positive rods in the [CSF](#) is seen in patients with bacterial [meningitis](#) caused by [Listeria monocytogenes](#). [L. monocytogenes meningitis](#) is more common among [neonates](#) and adults > 60 years of age but can develop in patients who are [immunocompromised](#). This condition can manifest subacutely with progressive [headache](#), nausea, [fever](#), meningism, and a significantly increased opening pressure on [lumbar puncture](#). However, [L. monocytogenes](#) cannot grow on [Sabouraud agar](#); this organism can be cultured on bacterial media such as blood agar.

F - Increased adenosine deaminase concentration

Explanation Why

An increased [adenosine deaminase](#) concentration in the [CSF](#) is seen in [tuberculous meningitis](#). This condition can manifest with progressive [headache](#), nausea, [fever](#), meningism, and a significantly increased opening pressure on [lumbar puncture](#). However, [Mycobacterium tuberculosis](#) cannot grow on [Sabouraud agar](#); this organism can be cultured on [Löwenstein-Jensen agar](#).

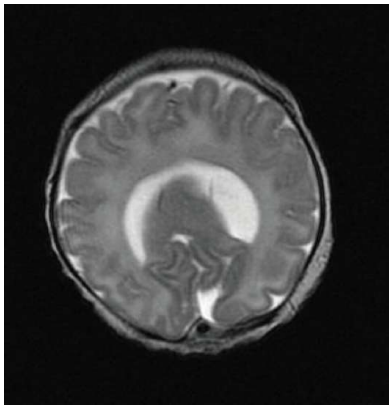
G - Positive PCR for JC virus DNA

Explanation Why

A positive [PCR](#) for [JC virus DNA](#) in the [CSF](#) confirms a diagnosis of [progressive multifocal leukoencephalopathy \(PML\)](#). This condition is caused by reactivation of the [JC virus](#) in patients who are [immunocompromised](#) and typically causes focal neurologic deficits (e.g., motor deficits, visual deficits). [PML](#) does not typically cause nausea, [fever](#), meningism, or a significantly increased opening pressure on [lumbar puncture](#). In addition, viruses cannot be cultured on [Sabouraud agar](#).

Question # 13

A male newborn delivered at 32 weeks' gestation to a 41-year-old woman dies shortly after birth. The mother did not receive prenatal care and consistently consumed alcohol during her pregnancy. At autopsy, examination shows microcephaly, an eye in the midline, a cleft lip, and a single basal ganglion. Failure of which of the following processes is the most likely cause of this condition?

	Answer	Image
A	Fusion of the lateral palatine shelves	
B	Disjunction of chromosome 18	
C	Closure of the rostral neuropore	
D	Formation of the 1 st branchial arch	
E	Development of the metencephalon	
F	Cleavage of the forebrain	

Hint

This condition has been associated with disruption of the sonic hedgehog signaling pathway.

Correct Answer

A - Fusion of the lateral palatine shelves

Explanation Why

Failed fusion of the [lateral](#) palatine shelves results in a [cleft palate](#), which was not observed on this [newborn](#)'s autopsy. Rather, the autopsy showed a [cleft lip](#), which occurs when the [medial](#) nasal process fails to fuse with the maxillary process. Furthermore, failed fusion of the [lateral](#) palatine shelves would not account for the other anomalies observed.

B - Disjunction of chromosome 18

Explanation Why

[Nondisjunction](#) of [chromosome](#) 18 leads to [trisomy 18](#), also called [Edwards syndrome](#). Typical features include clenched fists, low-set ears, [micrognathia](#), prominent occiput bone, and [rocker-bottom](#) feet, none of which were described in this [newborn](#)'s autopsy.

C - Closure of the rostral neuropore

Explanation Why

Failed closure of the [rostral neuropore](#) results in [anencephaly](#), which is characterized by the absence of the forebrain and severe [cranial](#) anomalies (e.g., an open [calvarium](#) or an [encephalocele](#)). Because brain development does not occur, this condition is virtually always incompatible with life. This [newborn](#) was born alive and has findings consistent with forebrain development on autopsy (the presence of a [basal ganglion](#) and an [eye](#) in the midline, both of which originate from the forebrain).

D - Formation of the 1st branchial arch

Explanation Why

The [1st branchial arch](#) is the origin of the [maxilla](#), the [mandible](#), the [zygomatic bone](#), and the [Meckel cartilage](#). Other derivatives of this arch include the [malleus](#), the [incus](#), and the [sphenomandibular ligament](#). Errors in the formation of the [1st branchial arch](#) lead to facial abnormalities such as [micrognathia](#), [cleft palate](#), and [glossoptosis](#) and/or mandibular [hypoplasia](#), none of which were seen on this [newborn](#)'s autopsy. [Pierre Robin sequence](#) and [mandibulofacial dysostosis](#) (Treacher-Collins syndrome) are characterized by [first branchial arch](#) misdevelopment.

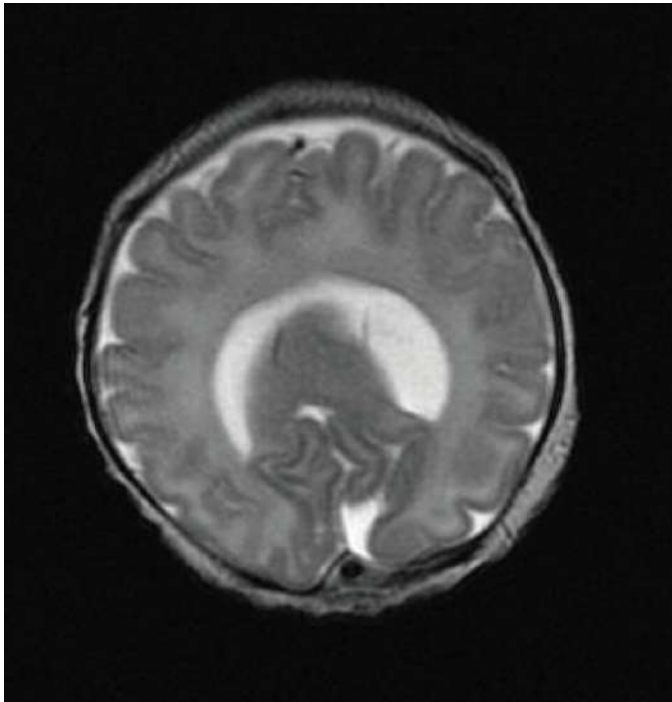
E - Development of the metencephalon

Explanation Why

Errors in the development of the [metencephalon](#) cause [malformations](#) of the [pons](#) and [cerebellum](#). They are furthermore associated with a spectrum of conditions that manifest with [Dandy-Walker malformation](#), the key features of which are an enlarged [fourth ventricle](#), an aplastic [cerebellar vermis](#), and an enlarged [posterior](#) fossa. This [newborn](#)'s autopsy showed neither [malformations](#) of the [pons](#) or [cerebellum](#) nor [Dandy-Walker malformations](#), but rather severe craniofacial anomalies, which would not be expected with abnormal development of the [metencephalon](#).

F - Cleavage of the forebrain

Image



Explanation But

[Holoprosencephaly](#) is also associated with [trisomy 13](#).

Explanation Why

Failed forebrain cleavage (i.e., the separation into a left and right hemisphere) leads to [holoprosencephaly](#), which manifests with severe maxillofacial anomalies (e.g., [cleft lip](#), nasal deformities, or cyclopia), a singular [basal ganglion](#), and a singular ventricle (monoventricle), most of which can be seen on this [newborn's](#) autopsy. The separation of the two hemispheres usually occurs during the fifth or sixth week of [pregnancy](#); failure to do so most typically results in a [first trimester spontaneous abortion](#), but fetuses occasionally survive to the [third trimester](#), as was the case here. Maternal alcohol consumption is a strong [risk factor](#) for [holoprosencephaly](#) as well as [fetal alcohol syndrome](#).

Question # 14

A 36-year-old man is brought to the emergency department by his wife 20 minutes after having a seizure. Over the past 3 days, he has had a fever and worsening headaches. This morning, his wife noticed that he was irritable and demonstrated strange behavior; he put the back of his fork, the salt shaker, and the lid of the coffee can into his mouth. He has no history of serious illness and takes no medications. His temperature is 39°C (102.2°F), pulse is 88/min, and blood pressure is 118/76 mm Hg. Neurologic examination shows diffuse hyperreflexia and an extensor response to the plantar reflex on the right. A T2-weighted MRI of the brain shows edema and areas of hemorrhage in the left temporal lobe. Which of the following is most likely the primary mechanism of the development of edema in this patient?

	Answer	Image
A	Release of vascular endothelial growth factor	
B	Cellular retention of sodium	
C	Breakdown of endothelial tight junctions	
D	Degranulation of eosinophils	
E	Increased hydrostatic pressure	

Hint

The patient's history of fever, headaches, seizure, focal neurologic findings (e.g., hyperreflexia and extensor response to plantar reflex), and MRI showing edema and hemorrhage in the temporal lobe suggest HSV encephalitis.

Correct Answer

A - Release of vascular endothelial growth factor

Explanation Why

Release of [vascular endothelial growth factor](#) is one of the pathologic mechanisms of [edema](#) in [brain tumors](#). This patient's [headache](#), [seizure](#), and focal neurologic deficits are early signs of a [brain tumor](#). However, an acute onset of symptoms and [fever](#) are more consistent with an infectious etiology.

B - Cellular retention of sodium

Explanation Why

Cellular retention of sodium leading to fluid retention and cellular swelling is the pathologic mechanism of cytotoxic [edema](#), a complication of acute [ischemic stroke](#). [Ischemic stroke](#) can manifest with [headache](#), [seizure](#), and focal neurologic findings (e.g., [hyperreflexia](#) and extensor response to [plantar reflex](#)). However, [T2-weighted MRI](#) in acute [ischemic stroke](#) typically shows [hyperintensity](#) with no hemorrhages. Furthermore, an acute [ischemic stroke](#) would not explain this patient's [fever](#).

C - Breakdown of endothelial tight junctions

Explanation But

The patient's behavioral change (putting the fork, salt shaker, and coffee can lid in his mouth) is characteristic of [hyperorality](#), a finding in [Kluver-Bucy syndrome](#). This condition is a possible complication of [HSV encephalitis](#).

Explanation Why

Breakdown of [endothelial tight junctions](#) causing damage to the [blood-brain barrier](#) (BBB) is the

pathologic mechanism underlying vasogenic [edema](#). Disruption of the BBB leads to extravasation of fluid and [proteins](#) into the extracellular space of the cerebral parenchyma, leading to [increased intracranial pressure](#) and neuronal dysfunction. This mechanism of [edema](#) development can also be due to other inflammatory conditions, [metastasis](#), trauma, or [lead poisoning](#).

D - Degranulation of eosinophils

Explanation Why

Degranulation of [eosinophils](#) is part of the pathologic mechanism of a [type 1 hypersensitivity reaction](#). This reaction is characterized by tissue swelling and [edema](#) due to increased [histamine](#) release and increased vascular permeability. However, this mechanism does not play a role in the pathophysiology of [cerebral edema](#).

E - Increased hydrostatic pressure

Explanation Why

Increased [hydrostatic pressure](#) is the pathologic mechanism underlying [hypertensive encephalopathy](#), which causes severe [headaches](#), [seizures](#), and focal neurologic symptoms (e.g., [hyperreflexia](#) and extensor response to [plantar reflex](#)). However, [hypertensive encephalopathy](#) does not typically cause [fever](#). Furthermore, this patient's blood pressure is within the normal range.

Question # 15

A 29-year-old primigravid woman at 18 weeks' gestation comes to the physician for her first prenatal visit. She works as a paralegal and lives with her husband. Her current pregnancy was unexpected, and she did not take any prenatal medications or supplements. Physical examination shows a uterus 2 inches above the umbilicus. The concentration of α -fetoprotein in the maternal serum and concentrations of both α -fetoprotein and acetylcholinesterase in the amniotic fluid are elevated. Ultrasonography of the uterus shows an increased amniotic fluid volume. The fetus most likely has which of the following conditions?

	Answer	Image
A	Holoprosencephaly	
B	Lissencephaly	
C	Spina bifida occulta	
D	Myelomeningocele	
E	Anencephaly	

Hint

This fetus's condition results from failure of closure of the rostral neuropore during embryogenesis. The increased amniotic fluid volume (i.e., polyhydramnios) seen here is due to impaired fetal swallowing.

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Correct Answer

A - Holoprosencephaly

Explanation Why

[Holoprosencephaly](#) results from failure of the embryonic [prosencephalon](#) to separate into two cerebral hemispheres, leading to brain [malformation](#) of varying severity as well as midline craniofacial defects. The etiology is thought to be multifactorial, including both genetic (e.g., [trisomy 13](#), mutations in [sonic hedgehog](#) signaling pathway) and environmental (e.g., alcohol and [retinoic acid](#) exposure in utero) components. [Holoprosencephaly](#) can be diagnosed on prenatal [ultrasonography](#) and fetal [MRI](#); however, [polyhydramnios](#) is not a characteristic finding. Moreover, this defect is not associated with increased [α-fetoprotein](#) and acetylcholinesterase levels in the maternal serum or [amniotic fluid](#).

B - Lissencephaly

Explanation Why

[Lissencephaly](#) results from failure of neuronal cell migration, thereby inhibiting development of the [gyri](#) and sulci. This [malformation](#) is typically genetic but may also be caused by viral infections or insufficient intrauterine perfusion in early [pregnancy](#). [Lissencephaly](#) is often diagnosed at [birth](#) or soon after via imaging; however, [polyhydramnios](#) on prenatal [ultrasonography](#) is not a characteristic finding. Moreover, [lissencephaly](#) is not associated with increased [α-fetoprotein](#) and acetylcholinesterase levels in the maternal serum or [amniotic fluid](#).

C - Spina bifida occulta

Explanation Why

[Spina bifida occulta](#) is a [neural tube defect \(NTD\)](#) that results from failure of the [caudal neuropore](#) to close. [Folate deficiency](#), which this patient likely has (lack of prenatal supplements), is associated with an increased risk of [NTDs](#). However, [spina bifida occulta](#) is a closed [NTD](#) and would, therefore, not show increased [α-fetoprotein](#) and acetylcholinesterase levels in the maternal serum or [amniotic](#)

[fluid](#). Moreover, this defect is not associated with [polyhydramnios](#) on prenatal [ultrasonography](#). [Spina bifida occulta](#) is most commonly diagnosed postnatally based on typical cutaneous findings (i.e., small dimple or tuft of [hair](#) in the lumbosacral region).

D - Myelomeningocele

Image



Explanation Why

[Myelomeningocele](#) is a [neural tube defect](#) (NTD) that results from failure of the [caudal neuropore](#) to close. [Folate deficiency](#), which this patient likely has (lack of prenatal supplements), is associated with an increased risk of NTDs. [Myelomeningocele](#) is an open NTD that would show increased [α-fetoprotein](#) and acetylcholinesterase levels in the maternal serum or [amniotic fluid](#), as seen here. However, this defect is not associated with [polyhydramnios](#) but is rather diagnosed based on [vertebral](#) irregularities (e.g., U-shaped [vertebral body](#), bulging of the fetal back) on prenatal [ultrasonography](#).

E - Anencephaly

Explanation Why

[Anencephaly](#) is a lethal [neural tube defect \(NTD\)](#) characterized by an open [cranial](#) vault and absence of the forebrain. The most important [risk factor](#) associated with [NTDs](#) is [folate deficiency](#), either due to dietary shortage or the consumption of [folic acid](#) antagonists (e.g., [valproate](#), [carbamazepine](#)). Because [anencephaly](#) is an open [NTD](#) that leaves the [neural tube](#) exposed, [α-fetoprotein \(AFP\)](#) and acetylcholinesterase (AChE) can diffuse freely into the [amniotic fluid](#) and maternal serum. If both [AFP](#) and AChE are elevated in the [amniotic fluid](#), fetal [NTDs](#) can be diagnosed with high [accuracy](#), even if [ultrasonography](#) is inconclusive.

Question # 16

A 21-year-old woman comes to the physician for a follow-up examination. Four months ago, she underwent posterior arthrodesis for thoracolumbar scoliosis. She has recovered well from the surgery but noticed difficulties combing her hair with her right hand. A photograph of the patient's back is shown. The nerve that was most likely injured in the surgery originates from which of the following spinal roots?



	Answer	Image
A	C8-T1	Sensitivity: affected regions Motor function: Froment sign Motor function: claw hand Proximal lesion Distal lesion

	Answer	Image
B	C6-C8	
C	C1-C3	
D	C3-C5	
E	T2-T5	
F	C5-C7	I) Long thoracic nerve II) Upper trunk III) Middle trunk IV) Lower trunk V) Lateral cord VI) Posterior cord VII) Medial cord VIII) Axillary nerve IX) Radial nerve X) Musculocutaneous nerve XI) Median nerve XII) Ulnar nerve

Hint

The image shows winging of the scapula, which is characteristic of long thoracic nerve injury.

Correct Answer

A - C8-T1

Image



Explanation Why

The [lower trunk of the brachial plexus](#) and the ulnar nerve receive nerve fibers from C8–T1 [spinal](#) roots. In surgeries that require the patient to be in a [prone position](#) (e.g., [spinal](#) surgery), improper positioning of the arms can injure the lower trunk (due to arm hyperabduction) or the ulnar nerve (due to pressure on the cubital tunnel). However, [lower brachial plexus palsy](#) ([Klumpke palsy](#)) would manifest with weakness of all the [intrinsic muscles of the hand](#) and sensory deficits on the [medial](#) side of the corresponding upper limb. [Ulnar nerve injury](#) results in weakness of the fourth and fifth [lumbricals](#) and sensory deficits in the fourth and fifth digit. [Scapular winging](#) would not be expected in either condition.

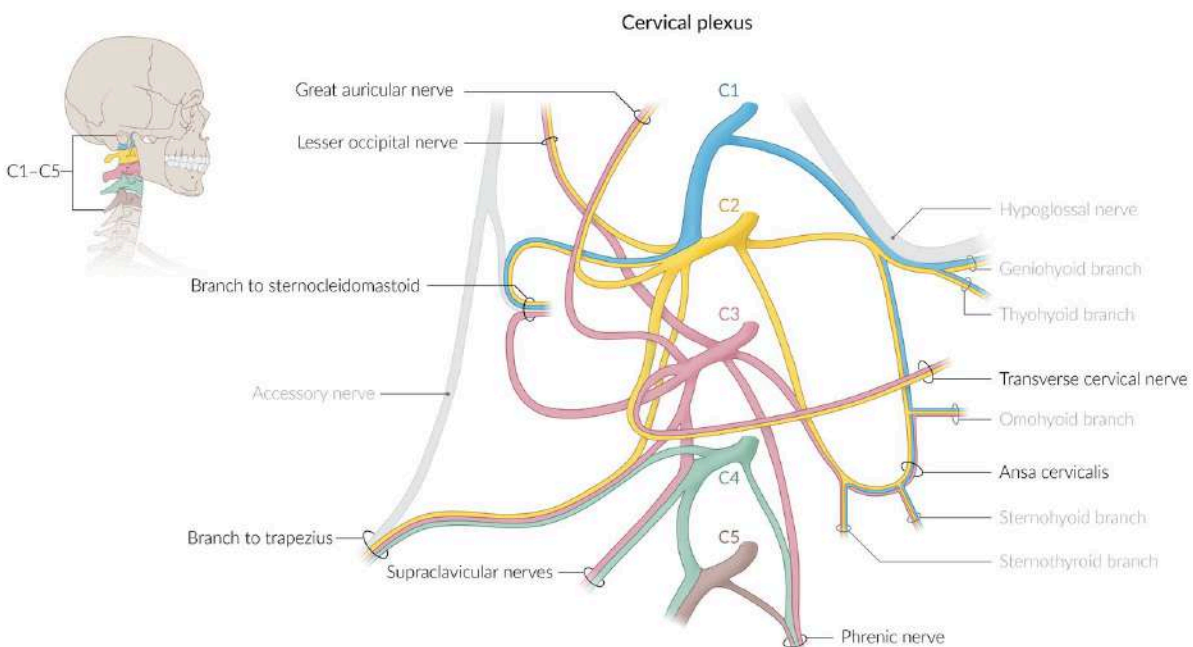
B - C6-C8

Explanation Why

The [thoracodorsal nerve](#) receives nerve fibers from the C6–C8 [spinal](#) roots. It lies along the [posterior](#) axillary wall, making it vulnerable to injury during axillary lymph node dissection. Injury to this nerve causes weakness of the [latissimus dorsi](#) and [teres major](#) and manifests with impaired [internal rotation](#) and [adduction](#) of the arm. [Scapular winging](#) or difficulty with combing [hair](#) would not be expected.

C - C1-C3

Image



Explanation Why

The [ansa cervicalis](#) receives nerve fibers from C1–C3 [spinal](#) roots. It lies in the [carotid triangle](#) of the neck and primarily innervates the [infrahyoid muscles](#). Damage to the [ansa cervicalis](#) can occur

during [neck dissection](#) or trauma to the [cervical spine](#) and results in a change in voice and [swallowing](#) difficulties. [Scapular winging](#) or difficulty with combing [hair](#) would not be expected.

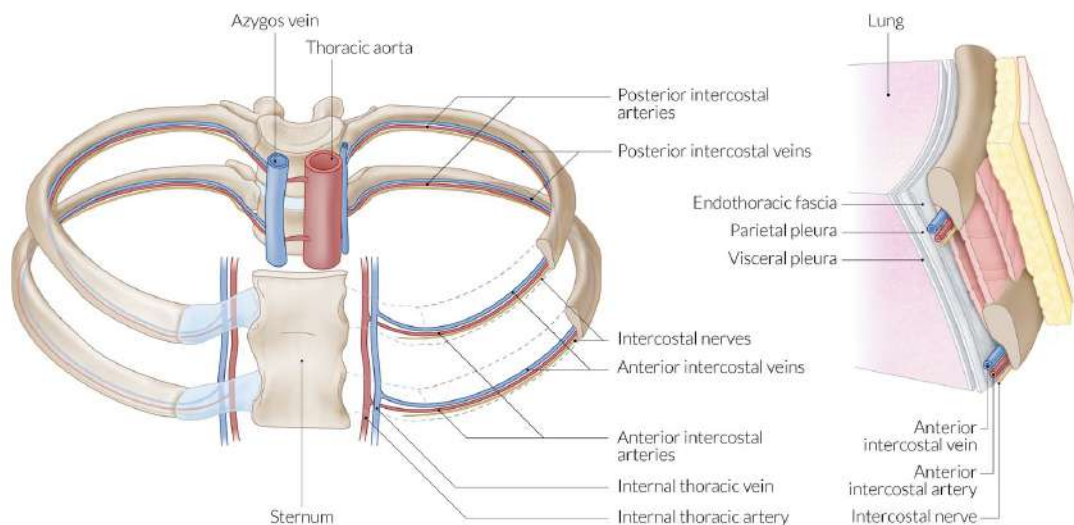
D - C3-C5

Explanation Why

The [phrenic nerve](#) arises from the C3–C5 [spinal](#) roots and innervates the diaphragm and [pericardium](#). It can be injured during anterior scalenectomy, open [heart](#) or thoracoscopic [mediastinal](#) surgery, [pulmonary vein radiofrequency ablation](#), and [IVC](#) clamping during hepatectomy or [liver transplantation](#). [Phrenic nerve injury](#) manifests with [dyspnea](#) and, in the case of unilateral palsy, asymmetric chest movement. [Scapular winging](#) or difficulty with combing [hair](#) would not be expected.

E - T2-T5

Image

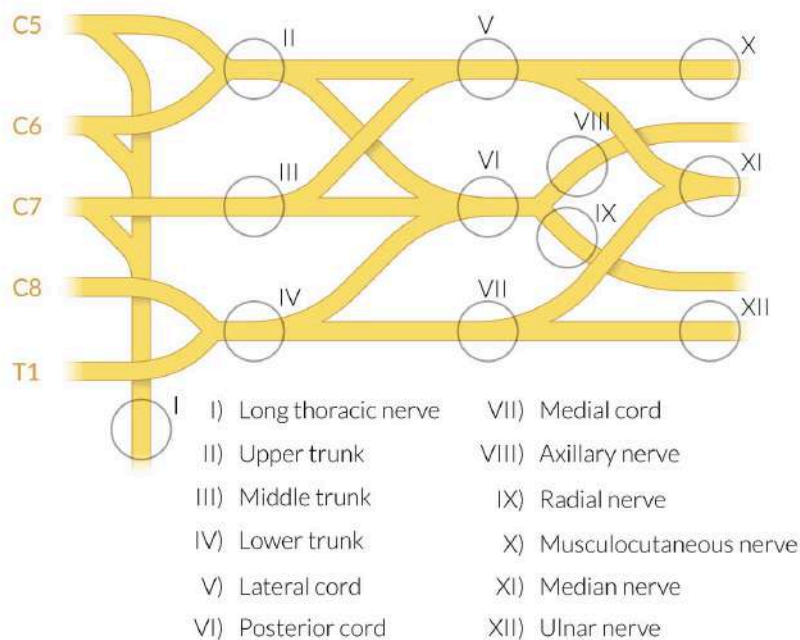


Explanation Why

Each thoracic [intercostal nerve](#) arises from the corresponding [spinal](#) root (e.g., second [intercostal nerve](#) from T2 [spinal](#) root) and innervates the corresponding [intercostal muscle](#). The second to fifth [intercostal nerves](#) also innervate the [serratus posterior superior muscle](#). [Intercostal nerve](#) injury typically occurs during the placement of a [chest drain](#) or thoracotomy. However, the muscles innervated by these nerves are accessory respiratory muscles, and their paralysis is clinically insignificant as long as the diaphragm functions. Neuralgic [pain](#) is the only significant symptom following [intercostal nerve](#) injury.

F - C5–C7

Image



Explanation But

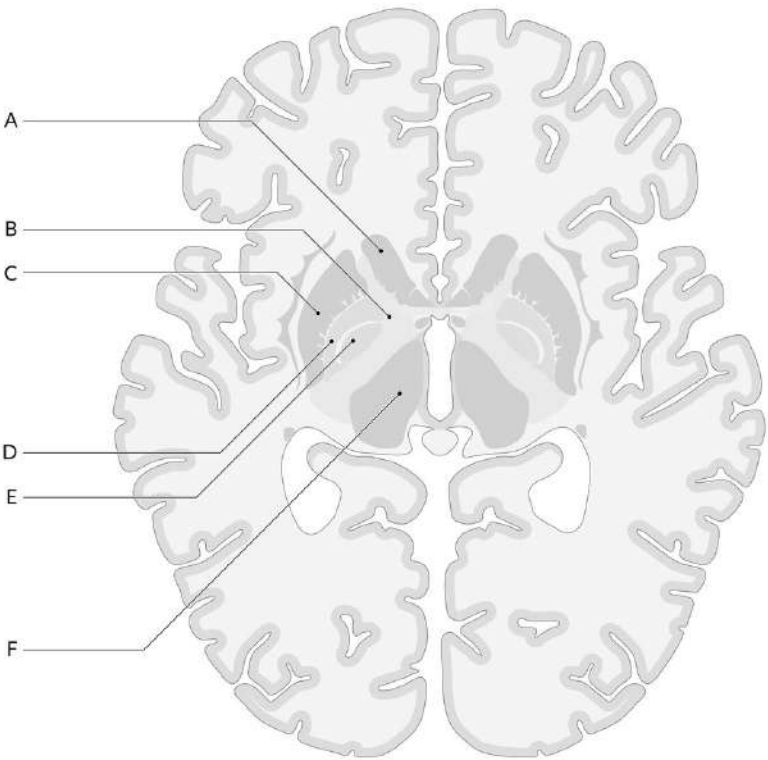
The [musculocutaneous nerve](#) also receives nerve fibers from C5–C7 [spinal](#) roots, but it arises as a branch of the [lateral cord of the brachial plexus](#) rather than directly from the [spinal](#) roots. [Injury to the musculocutaneous nerve](#) (e.g., a [gunshot wound](#) in the arm) manifests with loss of sensation over the [lateral](#) forearm and impaired [flexion](#) and [supination](#) of the forearm.

Explanation Why

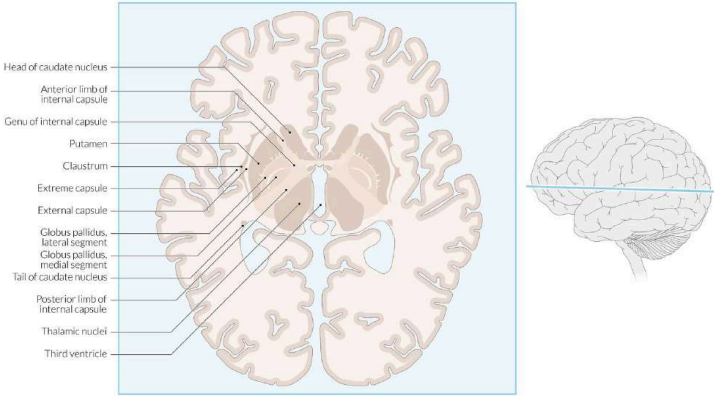
The [long thoracic nerve](#) originates directly from the C5–C7 [anterior spinal](#) roots, enters the axillary cavity, and descends together with the [lateral thoracic artery](#) along the [lateral](#) surface of the thoracic cage. In surgeries that require the patient to be in a [prone position](#) (e.g., [spinal](#) surgery), improper positioning of the arms can compress and injure this nerve. This injury leads to paralysis of the [serratus anterior muscle](#), which manifests with [medial winging of the scapula](#) and weakened [abduction](#) of the shoulder above 90° (manifesting, e.g., during [hair](#) combing), as seen here. Further common causes of [long thoracic nerve injury](#) include invasive procedures (e.g., axillary lymph node dissection), direct trauma to the shoulder, and prolonged nerve compression (e.g., carrying a heavy backpack).

Question # 17

A 21-year-old man comes to his physician because he has been having problems during track practice. He has become increasingly clumsy, even falling during his race last week, and seems to be moving much slower than last year. During this period, his mother reports that he has also become more irritable and he is having trouble in his classes. He has no history of serious medical illness and takes no medications. He does not use illicit drugs or drink alcohol. Vital signs are within normal limits. He is alert and oriented but has a flat affect. His speech is slurred and monotonous. Examination shows rigidity and an unsteady, broad-based gait. Abdominal examination shows hepatosplenomegaly. An MRI of the brain shows cavitory degeneration of the putamen. Which of the following labeled structures corresponds to the lesions seen in this patient?



	Answer	Image
A	A	
B	B	

	Answer	Image
C	C	
D	D	
E	E	
F	F	

Hint

The combination of parkinsonism, personality changes (irritability, flat affect), dysarthria, rigidity, broad-based ataxic gait, and hepatosplenomegaly in a young patient suggests Wilson disease. The putamen is located medial to the insular lobe.

Correct Answer

A - A

Explanation Why

This structure is the [caudate nucleus](#), which is part of the [striatum](#). The [striatum](#) is affected in patients with [Huntington disease](#) (HD). HD can cause personality changes, movement abnormalities, and [dysarthria](#). Also, in the case of [genetic anticipation](#), HD can manifest in patients in their early twenties. However, the movement abnormality characteristic of early HD is [chorea](#), which is not present in this patient. Moreover, there is no [family history](#) of HD to suggest anticipation. A different part of the [striatum](#) is affected in this patient.

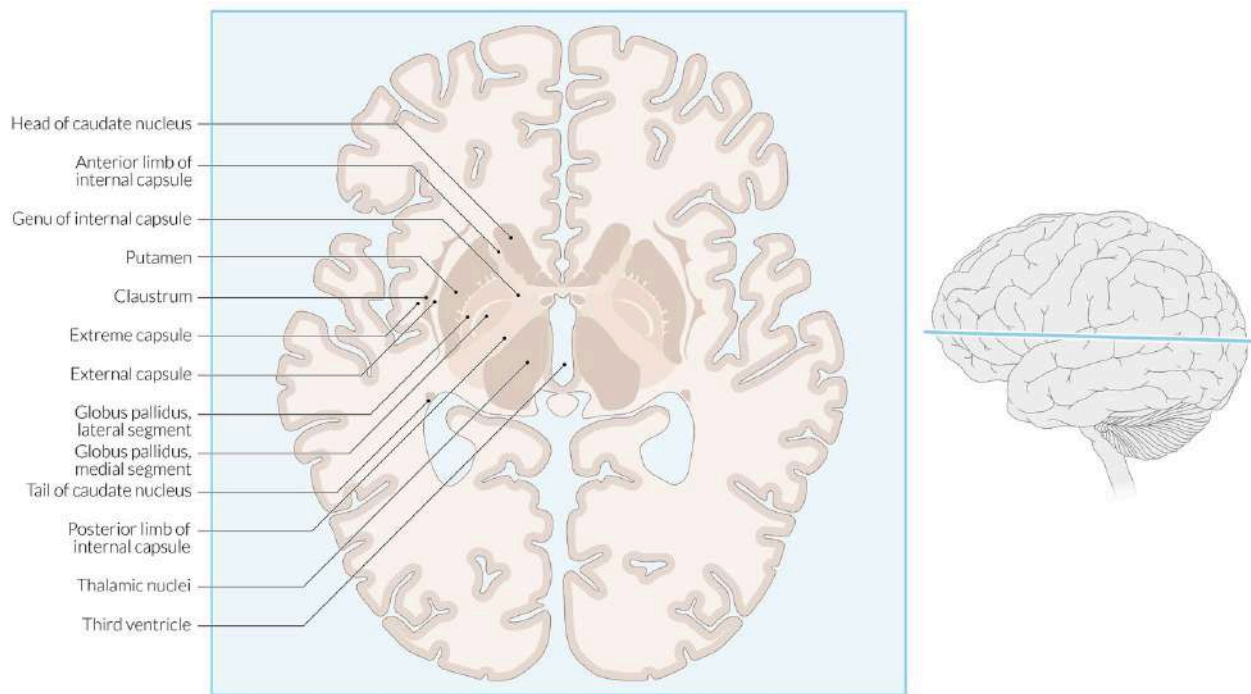
B - B

Explanation Why

This structure is the [internal capsule](#), a subcortical structure that contains motor and somatosensory projection fibers. A lesion affecting this site (e.g., an [infarct](#)) manifests with contralateral motor deficits. A different structure is affected in this patient.

C - C

Image



Explanation Why

This structure is the [putamen](#), which is typically affected early in the course of [Wilson disease](#). In [Wilson disease](#) ([hepatolenticular degeneration](#)), damage to a component of the [basal ganglia](#) called the [lentiform nucleus](#) ([putamen](#) and [globus pallidus](#)) occurs as a result of [copper](#) accumulation. Damage to this area is the cause of this patient's [parkinsonism](#), personality changes (irritability, flat affect), [dysarthria](#), [rigidity](#), and broad-based [ataxic gait](#).

D - D

Explanation Why

This structure is the external [globus pallidus](#), a component of the [lentiform nucleus](#). While the external [globus pallidus](#) is often affected in [Wilson disease](#), the structure that is affected in this

patient is a different part of the [lentiform nucleus](#).

E - E

Explanation Why

This structure is the internal [globus pallidus](#), a component of the [lentiform nucleus](#). While the internal [globus pallidus](#) is often affected in [Wilson disease](#), the structure that is affected in this patient is a different part of the [lentiform nucleus](#).

F - F

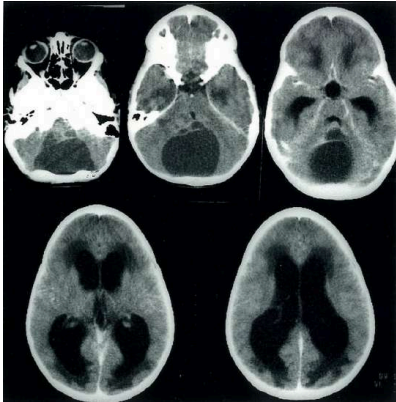
Explanation Why

The nuclei of the [thalamus](#) (structure F) are responsible for relaying and processing various types of sensory information; they are not involved in motor function. The [thalamus](#) is not commonly affected in [Wilson disease](#).

Question # 18

An 8-year-old boy is brought to the physician because of headaches for the past 2 weeks. His headaches tend to occur in the morning and are associated with nausea and vomiting. One month ago, the patient was admitted to the hospital because of fever, irritability, and neck rigidity, and he was successfully treated with antibiotics. His temperature today is 37.5°C (98.5°F). An MRI of the brain shows bilateral ventricular enlargement and enlargement of the subarachnoid space. Which of the following is the most likely explanation of the patient's condition?

	Answer	Image
A	Increased CSF production by the choroid plexus	
B	Impaired CSF flow through the arachnoid granulations	
C	Impaired CSF drainage into the subarachnoid space	

	Answer	Image
D	Impaired CSF drainage into the fourth ventricle	
E	Compensatory enlargement of CSF spaces	

Hint

The combination of fever, irritability, and neck rigidity is characteristic of meningitis. This patient's current symptoms and MRI findings indicate communicating hydrocephalus, which can be a complication of meningitis.

Correct Answer

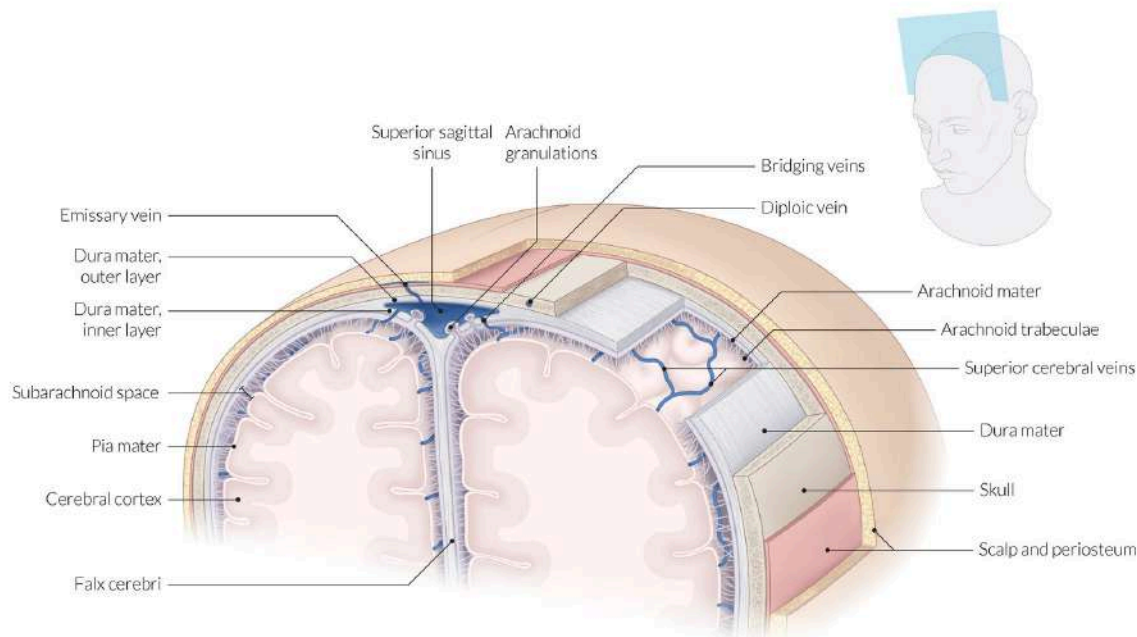
A - Increased CSF production by the choroid plexus

Explanation Why

Increased [CSF](#) production by the [choroid plexus](#) is seen in [choroid plexus papilloma](#), a rare benign pediatric [tumor](#) that can manifest with [features of increased intracranial pressure](#) (e.g., [headache](#), nausea, vomiting) as well as enlargement of both the ventricular and subarachnoid spaces ([communicating hydrocephalus](#)). However, a history of [fever](#) and neck [rigidity](#) would not be expected with a [choroid plexus papilloma](#), and the [MRI](#) would also show a well-defined, intraventricular, lobulated mass that enhances brilliantly because of its high vascularization.

B - Impaired CSF flow through the arachnoid granulations

Image

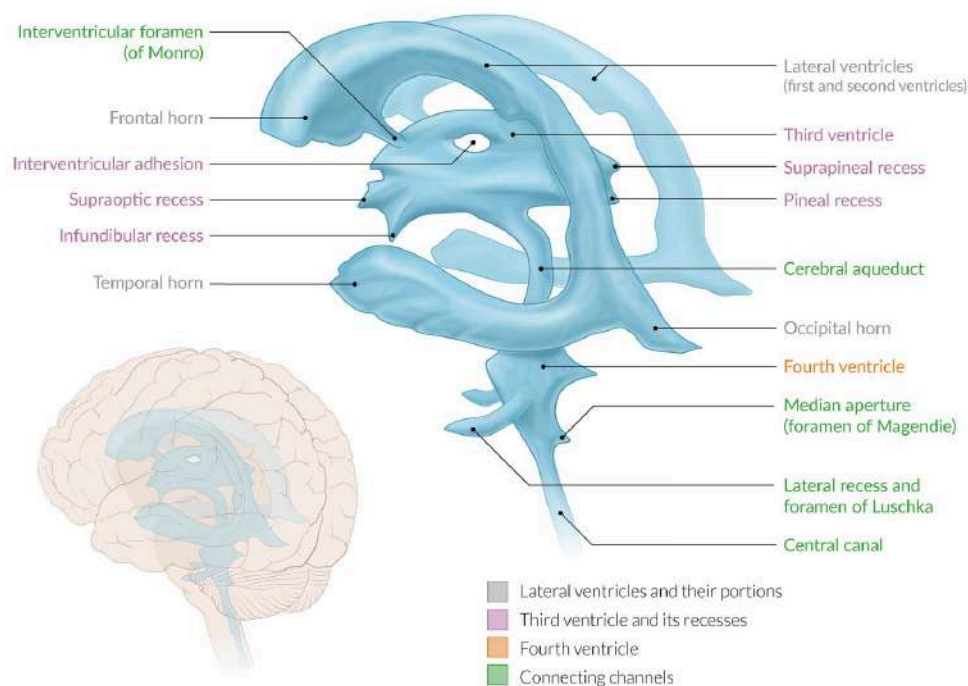


Explanation Why

CSF drains from the 4th ventricle into the subarachnoid space and from the subarachnoid space into dural venous sinuses via arachnoid granulations. The blockage of arachnoid granulations by degenerating neutrophils and proliferating fibroblasts (i.e., arachnoid scarring) is a complication of bacterial meningitis. This blockage results in the accumulation of CSF in the subarachnoid space and the ventricular spaces, the subsequent symmetric enlargement of the entire ventricular system (communicating hydrocephalus), and features of raised intracranial pressure (e.g., early-morning headaches, nausea, vomiting). Communicating hydrocephalus can also be a complication of subarachnoid hemorrhage.

C - Impaired CSF drainage into the subarachnoid space

Image



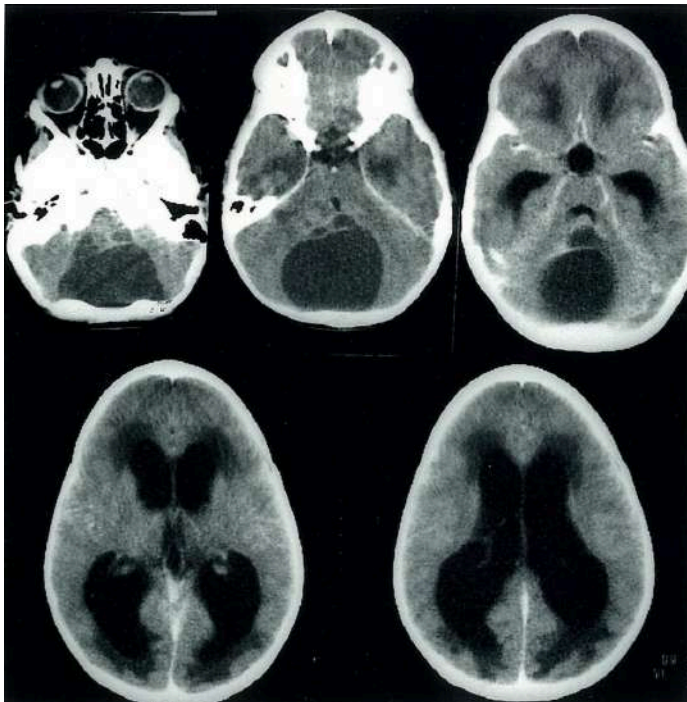
Explanation Why

Drainage of CSF into the subarachnoid space would be impaired upon blockage of the median foramen of Magendie or the lateral foramina of Luschka, which connect the 4th ventricle with the subarachnoid space. This blockage can occur as a complication of bacterial meningitis and lead to bilateral ventricular enlargement, as seen here. However, obstructive hydrocephalus only causes

dilation of the ventricles upstream of the obstruction, which is why the [subarachnoid space](#) would not be enlarged in this case. Enlargement of the [subarachnoid space](#) in this patient suggests a different pathological process.

D - Impaired CSF drainage into the fourth ventricle

Image



Explanation Why

Impaired [CSF](#) drainage from the [3rd ventricle](#) into the [4th ventricle](#) is caused by obstruction of the [cerebral aqueduct](#), which can occur as a complication of bacterial [meningitis](#) and lead to bilateral ventricular enlargement, as seen here. However, [obstructive hydrocephalus](#) only causes dilation of the ventricles upstream of the obstruction, so the [subarachnoid space](#) would not be enlarged due to aqueductal stenosis. Enlargement of the [subarachnoid space](#) in this patient suggests a different pathological process.

E - Compensatory enlargement of CSF spaces

Explanation Why

Compensatory enlargement of [CSF](#) spaces, which is seen in [hydrocephalus ex vacuo](#), occurs secondary to loss of brain volume in neurodegenerative diseases or [stroke](#). An [MRI](#) would show biventricular enlargement and enlargement of the [subarachnoid space](#), as seen here. However, [hydrocephalus ex vacuo](#) does not cause any symptoms because it does not affect intracerebral pressure, and it is not typically seen in children.

Question # 19

A 79-year-old woman is brought to the emergency department because of a 1-hour history of hoarseness. Her pulse is 85/min and blood pressure is 142/90 mm Hg. Physical examination shows a diminished gag reflex and loss of pain and temperature over the left face and right trunk and extremities. There is no facial asymmetry and the tongue does not deviate when protruded. Her strength is 5/5 bilaterally in both the upper and lower extremities. Ophthalmologic examination shows involuntary, rhythmic ocular movements. There is left-sided miosis and ptosis. This patient's condition is most likely caused by occlusion of which of the following vessels?

	Answer	Image
A	Basilar artery	
B	Posterior cerebral artery	Diagram illustrating the brainstem and midbrain structures, including the Cerebral aqueduct, Superior colliculus, Edinger-Westphal nucleus, Mesencephalic nucleus of trigeminal nerve, Oculomotor nucleus, Medial lemniscus, Red nucleus, Corticospinal tract (occipitospinal, temporo-spinal, and parieto-pontine fibers), and Pyramidal tract. The diagram also shows the Substantia nigra and Periaqueductal gray matter. A legend indicates Efferent pathways (General somatic efferent, General visceral efferent) and Afferent pathways (General somatic afferent, General visceral afferent).
C	Anterior spinal artery	Diagram illustrating the brainstem and midbrain structures, including the Edinger-Westphal nucleus, Oculomotor nucleus, Trochlear nucleus, Motor nucleus of trigeminal nerve, Abducens nucleus, Facial motor nucleus, Salivatory nuclei (superior/inferior), Nucleus ambiguus, Hypoglossal nucleus, Dorsal nucleus of vagus nerve, and Spinal nucleus of accessory nerve. The diagram also shows the Mesencephalic nucleus of trigeminal nerve, Principal sensory nucleus of trigeminal nerve, Cochlear nuclei, Vestibular nuclei, Nucleus of tractus solitarius (superior portion), Spinal nucleus of trigeminal nerve, and Nucleus of tractus solitarius (inferior portion). A legend indicates Efferent pathways (General somatic efferent, General visceral efferent, Special visceral efferent) and Afferent pathways (General somatic afferent fibers, Special somatic afferent, General visceral afferent, Special visceral afferent).

	Answer	Image
D	Posterior inferior cerebellar artery	Efferent: ■ General somatic efferent ■ General visceral efferent ■ Special visceral efferent Afferent: ■ General somatic afferent ■ Special somatic afferent ■ General visceral afferent ■ Special visceral afferent
E	Anterior inferior cerebellar artery	Efferent: ■ General somatic efferent ■ Special visceral efferent Afferent: ■ General somatic afferent ■ Special somatic afferent
F	Posterior communicating artery	

Hint

This patient presents with features of damage to the nucleus ambiguus (hoarseness and diminished gag reflex), spinal trigeminal nucleus (loss of pain and temperature sensations in the face ipsilaterally), spinothalamic tract (loss of (loss of pain and temperature sensations in the contralateral trunk and extremities), vestibular nucleus (nystagmus), and hypothalamospinal tract (ipsilateral ptosis and miosis). This constellation of features suggests that the infarction is located in the lateral medulla.

Correct Answer

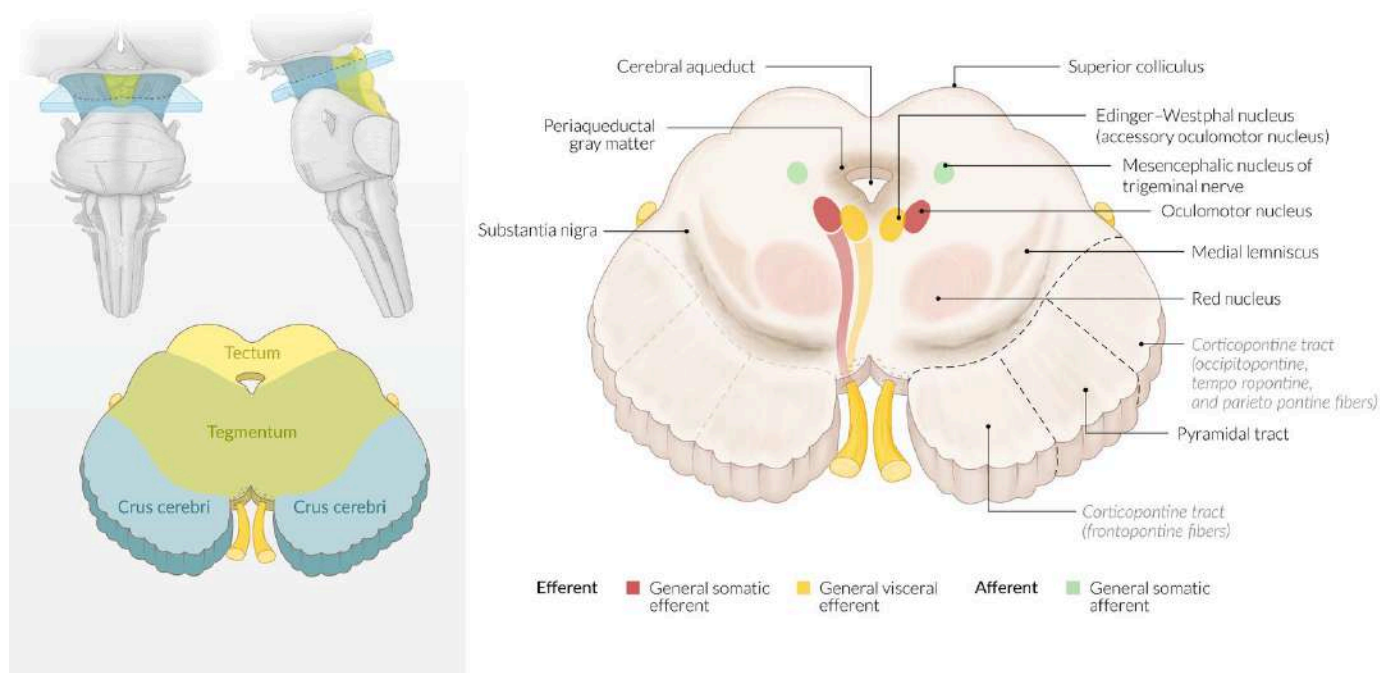
A - Basilar artery

Explanation Why

The [basilar artery](#) supplies the ventromedial parts of the [pons](#), [caudal midbrain](#), and [rostral medulla](#) via its paramedian and circumferential branches. The clinical features of [basilar artery](#) occlusion (BAO) vary depending on the site at which the [basilar artery](#) is occluded. Presentations specific to BAO include [inferior medial pontine syndrome](#) ([Foville syndrome](#)) and [locked-in syndrome](#). [Foville syndrome](#) manifests as [middle alternating hemiplegia](#) (ipsilateral [lateral rectus palsy](#) due to [CN VI](#) palsy and contralateral [hemiparesis](#) due to [corticospinal tract](#) damage) and contralateral loss of fine touch, [proprioception](#), and vibration sensations (due to [medial lemniscus](#) damage). [Locked-in syndrome](#) manifests as quadriplegia and [bulbar palsy](#) with preserved consciousness, blinking, and vertical [eye](#) movements. This patient's clinical features allow the [infarct](#) to be localized to the [lateral medulla](#), which receives blood from a different vessel.

B - Posterior cerebral artery

Image

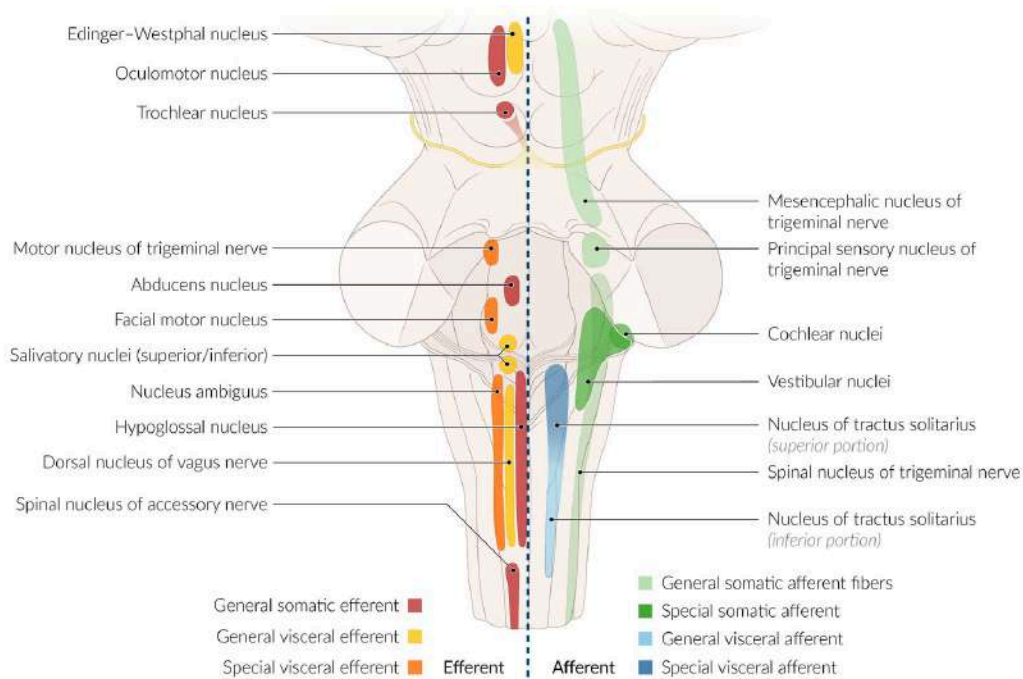


Explanation Why

Occlusion of a [posterior cerebral artery](#) can cause [infarction](#) of the [rostral midbrain](#), [thalamus](#), and/or [occipital lobe](#) ipsilaterally and manifest as unilateral [ptosis](#) (due to [infarction](#) of the [CN III](#) nucleus and/or hypothalamospinal tract) and unilateral sensory deficits of the trunk and extremities (due to [infarction](#) of the [ventral posterolateral nucleus](#) or the ascending sensory tracts), which are seen here. However, all types of sensations (not just [pain](#) and temperature) would be impaired, and sensory deficits in the face would occur on the same side as those of the trunk and extremities. Moreover, [miosis](#) is usually absent because the [Edinger-Westphal nucleus](#) and/or its efferent [parasympathetic](#) fibers would also be damaged, and features such as hoarseness and diminished [gag reflex](#) would not occur. Instead, patients would present with [hemiparesis](#) and hemianopia with [macular sparing](#), which are not seen here.

C - Anterior spinal artery

Image



Explanation But

Occlusion of the [anterior spinal artery](#) below the level of the medulla causes [anterior spinal cord syndrome](#), which manifests with loss of [pain](#) and temperature sensations in the trunk and extremities (due to [lateral spinothalamic tract](#) damage) but these sensory deficits would be present bilaterally rather than unilaterally. In addition, quadriplegia or paraplegia would also be present, and features of [brain stem](#) lesions (e.g., nystagmus, hoarseness, diminished [gag reflex](#), [Horner syndrome](#), loss of sensations in the face) would not be expected.

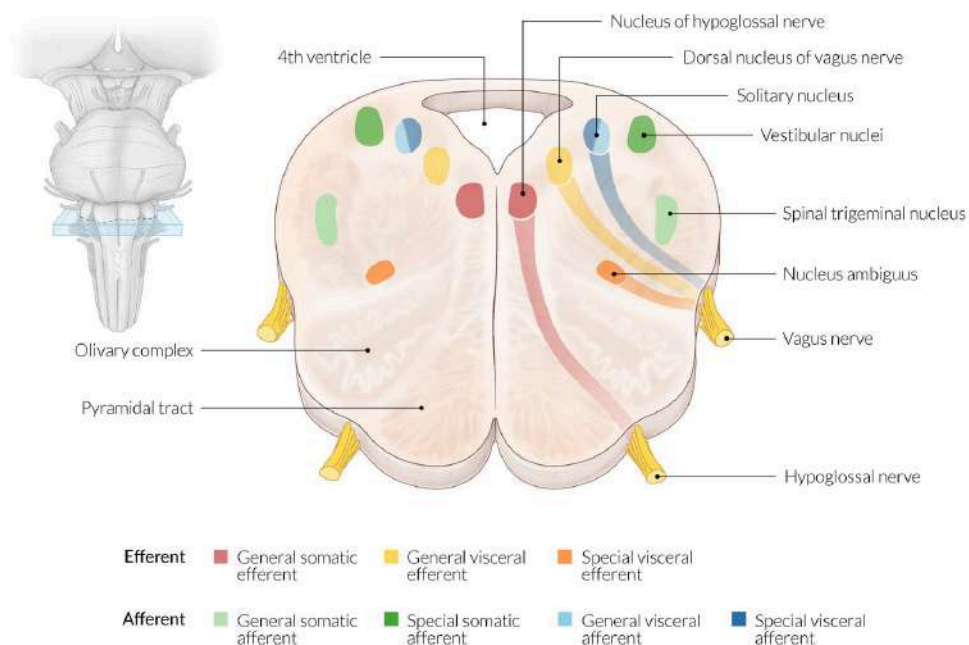
Explanation Why

Occlusion of the paramedian branches in the [cranial](#) segment of the [anterior spinal artery](#) causes [medial medullary syndrome](#) (MMS), which manifests with unilateral sensory deficits of the trunk and extremities, which are seen here. However, [proprioception](#), vibration, and fine touch are impaired (due to [medial lemniscus](#) damage) instead of temperature and [pain](#) sensations. Sensory loss in the face, hoarseness, diminished [gag reflex](#), nystagmus, and [Horner syndrome](#) would not be expected. Instead, patients with MMS have [inferior alternating hemiplegia](#) (ipsilateral paralysis of the [tongue](#) due to [hypoglossal nerve palsy](#) and contralateral [hemiparesis](#) due to [corticospinal tract](#)

damage), which is not seen here.

D - Posterior inferior cerebellar artery

Image



Explanation But

Blood is supplied to the [brainstem](#) through the following vessels: [anterior spinal artery](#) ([medial medulla](#)), [posterior inferior cerebellar artery](#) ([lateral medulla](#)), [basilar artery](#) ([medial pons](#)), [anterior inferior cerebellar artery](#) ([lateral pons](#)), [superior cerebellar artery](#) ([caudal midbrain](#)), [posterior cerebral artery](#) ([rostral midbrain](#)).

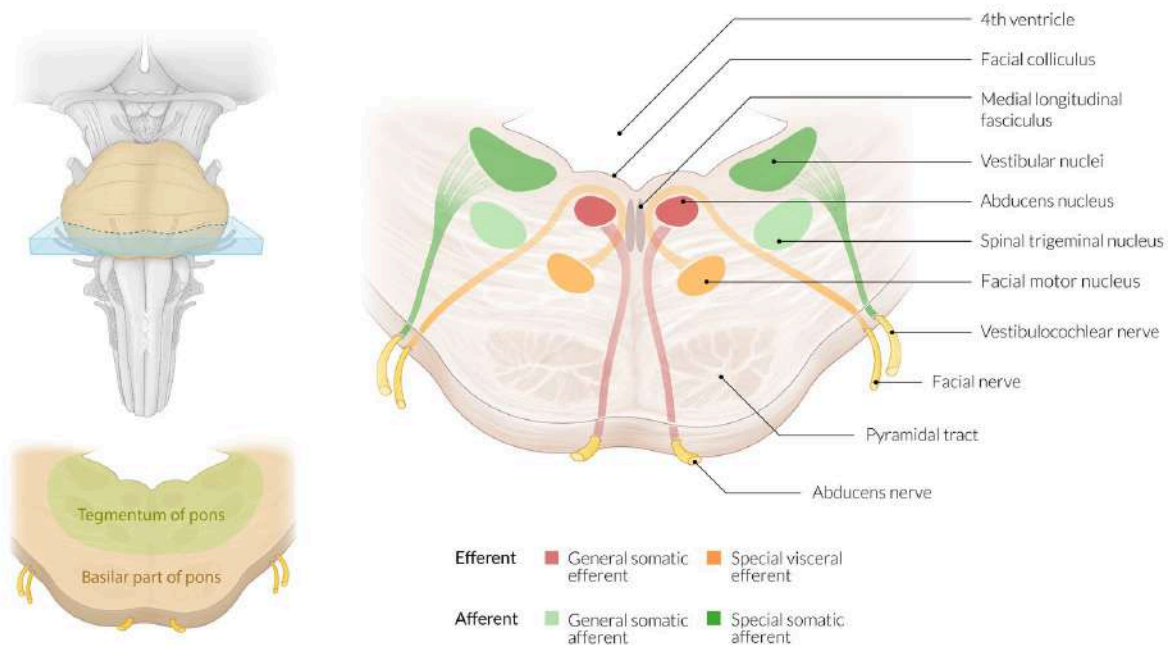
Explanation Why

The [lateral medulla](#) is supplied by the [posterior inferior cerebellar artery](#) (PICA) and the [lateral pons](#) by the [anterior inferior cerebellar artery](#) (AICA). Both [infarction](#) of the [lateral medulla](#) ([lateral medullary syndrome](#) or Wallenberg syndrome) and [lateral pons](#) ([lateral pontine syndrome](#)) manifest with loss of [pain](#) and temperature sensations in one half of the face and the contralateral trunk and extremities, as well as [vestibulocerebellar](#) symptoms (e.g., nystagmus, [vertigo](#), [ataxia](#)) and unilateral [Horner syndrome](#). The two conditions can be differentiated based on the presence or absence of certain [cranial nerve palsies](#). [Lateral medullary syndrome](#) also manifests with features of [CN IX](#) and

[CN X](#) palsies as a result of [nucleus ambiguus infarction](#), whereas [lateral pontine syndrome](#) manifests with features of [cochlear nucleus infarction](#) and [CN VII](#) palsy because of facial nucleus [infarction](#).

E - Anterior inferior cerebellar artery

Image

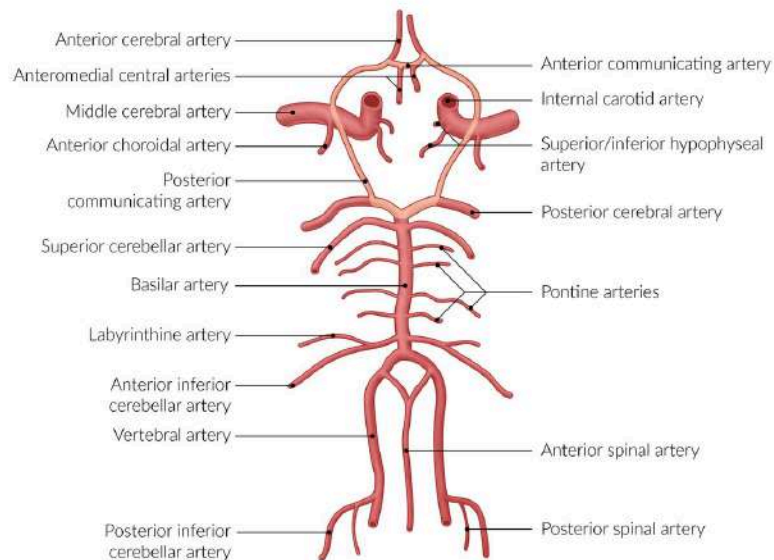


Explanation Why

Occlusion of an [anterior inferior cerebellar artery](#) (AICA) causes [lateral pontine syndrome](#), which manifests with nystagmus, ipsilateral [Horner syndrome](#), and loss of [pain](#) and temperature sensation in the ipsilateral face and contralateral trunk and extremities, all of which is seen here. However, patients with this syndrome also have facial asymmetry (due to [CN VII](#) palsy) and unilateral [sensorineural hearing loss](#) (due to [cochlear nucleus](#) palsy), which are not seen here. In addition, features of [CN IX](#) or [CN X](#) palsy (hoarseness, diminished [gag reflex](#)) would not be expected.

F - Posterior communicating artery

Image

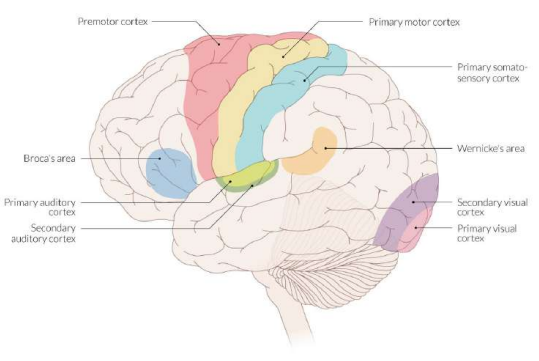
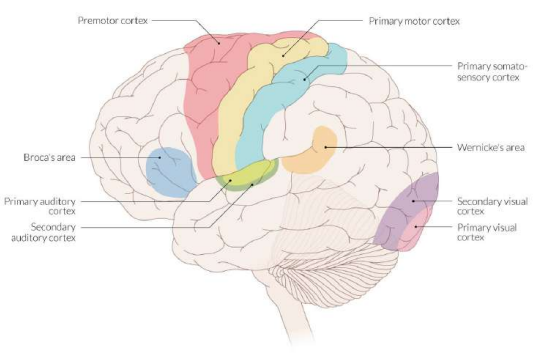


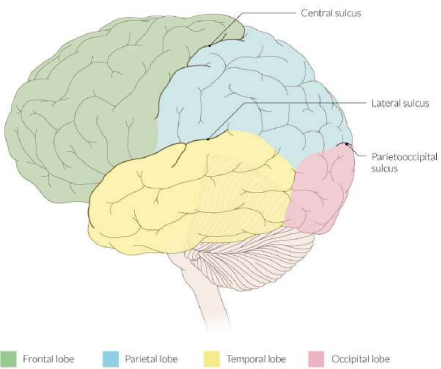
Explanation Why

Isolated occlusion of a [posterior communicating artery](#) (PCOM) typically does not cause [stroke](#). However, a [stroke](#) can occur if the ipsilateral [internal carotid artery](#) is also occluded because the PCOM provides collateral blood flow from the [posterior cerebral artery](#) to the vascular territory of the [internal carotid artery](#). Occlusion of the [internal carotid artery](#) would cause a cortical [stroke](#) and manifest with cortical deficits such as [hemispatial neglect](#), [aphasia](#), gaze preference, and [urinary incontinence](#), which are not seen here.

Question # 20

A 75-year-old woman is brought to the physician by her daughter for a 4-month history of increasing difficulty recognizing her friends and family. She has had to rely on recognizing haircuts, gait, and voices because she cannot remember their faces. Neurologic examination shows that she is able to recognize objects and name facial features such as the eyes and nose. On mental status examination, she is alert and has no deficits in cognition or short-term memory. An MRI of her head shows an inhomogenous 2-cm mass with perifocal edema in her brain. Which of the following brain regions is most likely affected?

	Answer	Image
A	Left posterior parietal cortex	
B	Right posterior superior temporal cortex	
C	Left hippocampus	
D	Right superior parietal cortex	

	Answer	Image
E	Right ventral occipitotemporal cortex	 The diagram illustrates the lateral view of the human brain, color-coded by lobe: Frontal lobe (green), Parietal lobe (blue), Temporal lobe (yellow), and Occipital lobe (pink). Key sulci are labeled: Central sulcus (separating frontal and parietal lobes), Lateral sulcus (separating temporal lobe from frontal and parietal lobes), and Parietoccipital sulcus (separating parietal and occipital lobes). A legend at the bottom identifies the colors for each lobe.

Hint

This patient presents with prosopagnosia, which is characterized by an inability to recognize familiar faces. The brain region that is typically affected in this condition is supplied by the posterior cerebral artery.

Correct Answer

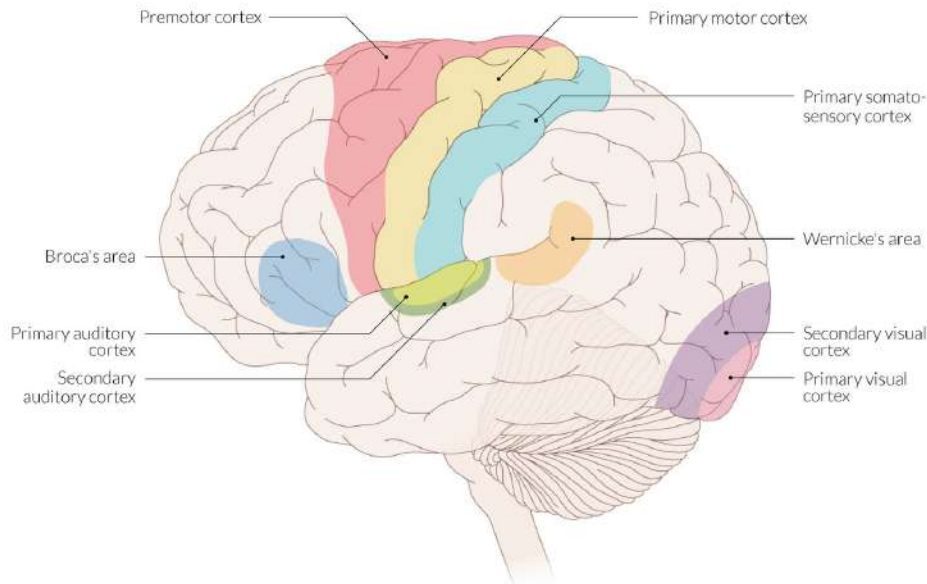
A - Left posterior parietal cortex

Explanation Why

A left [posterior](#) parietal cortex lesion in a right-handed patient would manifest with features of [Gerstmann syndrome](#) (e.g., [agraphia](#) without [alexia](#), [acalculia](#), finger [agnosia](#), right-left [disorientation](#)). A similar lesion in a left-handed patient would manifest with [constructional apraxia](#) and/or spatial [hemineglect](#). This patient presents with [prosopagnosia](#), which is not a typical feature of parietal cortex lesions.

B - Right posterior superior temporal cortex

Image



Explanation Why

A right [posterior](#) superior temporal cortex lesion would manifest with left upper quadrantanopia, a [visual field](#) defect caused by damage to the Meyer loop. A lesion in this location can also cause aprosodia in right-handed patients and [Wernicke aphasia](#) in left-handed patients. This patient presents with [prosopagnosia](#), which is not a feature of [posterior](#) superior temporal cortex lesions.

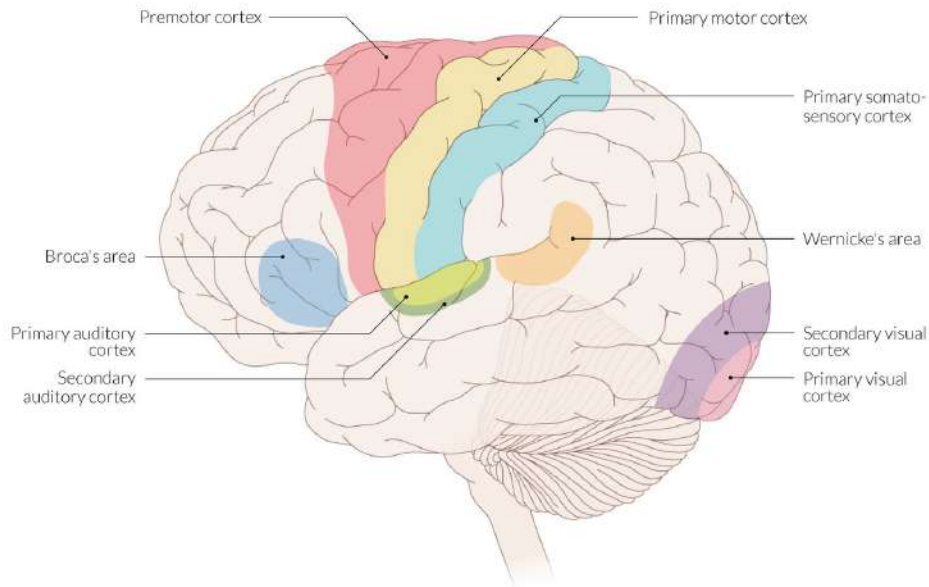
C - Left hippocampus

Explanation Why

Lesions in the [hippocampus](#) may cause [anterograde amnesia](#), which can manifest with the inability to recognize faces of recently acquainted people. However, this patient has difficulty remembering familiar faces (friends and family), and she does not present with any other [memory](#) impairments.

D - Right superior parietal cortex

Image

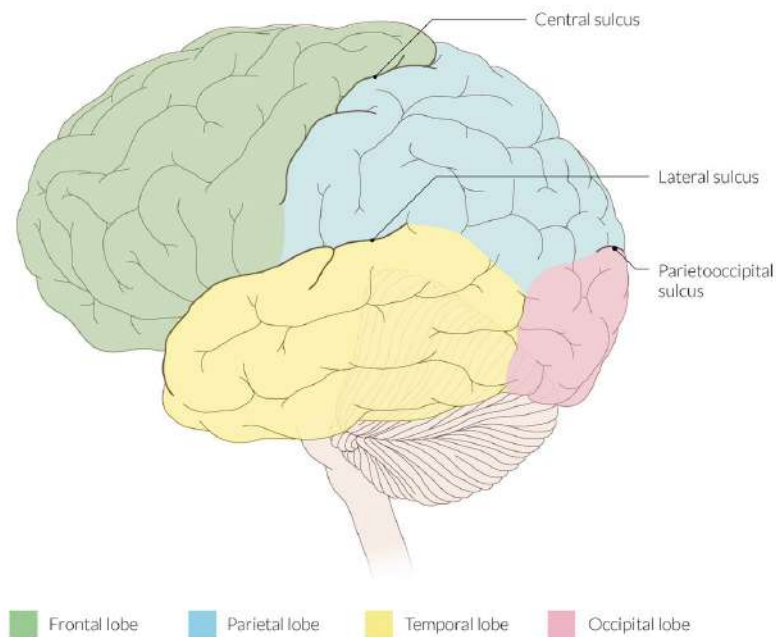


Explanation Why

The superior region of the parietal cortex contains the [somatosensory association cortex](#) and a section of the [primary somatosensory cortex](#). A lesion in the right superior parietal cortex would manifest with left-sided [astereognosis](#), [apraxia](#), and possibly left-sided sensory deficits, none of which are seen here.

E - Right ventral occipitotemporal cortex

Image

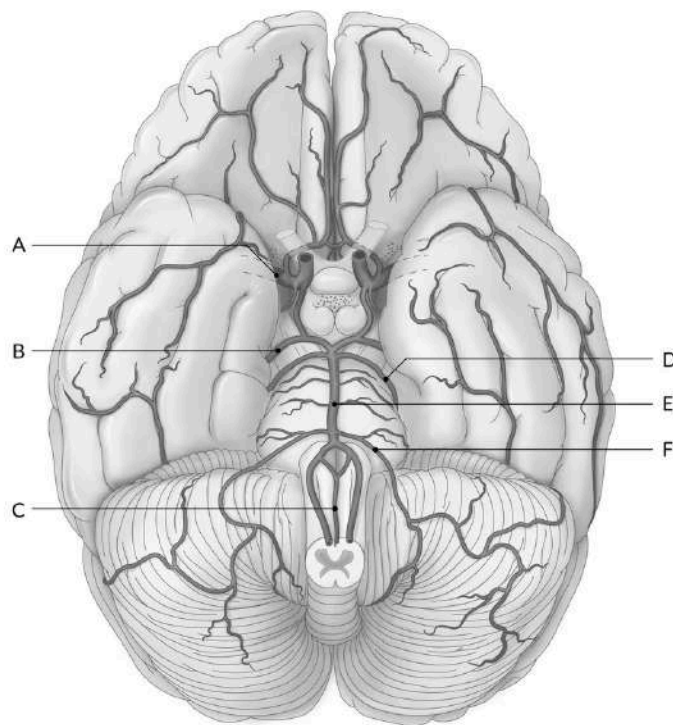


Explanation Why

[Prosopagnosia](#) is caused by bilateral lesions or large unilateral (typically right-sided) lesions (e.g., [brain tumors](#)) in the [ventral](#) occipitotemporal cortex, which includes parts of the [secondary visual cortex](#) as well as parts of the [temporal lobe](#). Individuals with [prosopagnosia](#) are able to visually perceive faces because the pathway to the [primary visual cortex](#) in the [occipital lobe](#) is still intact, but they have lost the ability to process the image properly. Affected individuals retain their ability to name parts of the face (e.g., nose, mouth) and are typically able to identify individuals by other cues (e.g., clothing, voice).

Question # 21

A 67-year-old man is brought to the emergency department 1 hour after the sudden onset of left-sided body weakness and difficulty speaking. He has a history of hypertension and coronary artery disease. He has smoked one pack of cigarettes daily for 30 years. His temperature is 36°C (96.8°F), pulse is 100/min, respirations are 18/min, and blood pressure is 151/87 mm Hg. Physical examination shows deviation of the tongue to the right, left-sided hemiparesis, and decreased proprioception on the left side of the body. Sensation to pinprick and temperature is intact. This patient's condition is most likely caused by occlusion of which of the following labeled vessels in the schematic overview of the arterial supply to the brain?



	Answer	Image
A	A	
B	B	
C	C	
D	D	
E	E	

	Answer	Image
F	F	The image contains three anatomical diagrams. The top left diagram shows a superior view of the pons with the facial colliculus and medial longitudinal fasciculus. The bottom left diagram shows a cross-section of the pons, labeling the tegmentum and basilar part. The main diagram on the right is a cross-section of the medulla oblongata, showing various cranial nerve nuclei and tracts. Labels include: 4th ventricle, Facial colliculus, Medial longitudinal fasciculus, Vestibular nuclei, Abducens nucleus, Spinal trigeminal nucleus, Facial motor nucleus, Vestibulocochlear nerve, Facial nerve, Pyramidal tract, and Abducens nerve. A legend identifies efferent and afferent pathways: General somatic efferent (red), Special visceral efferent (orange), General somatic afferent (light green), and Special somatic afferent (dark green).

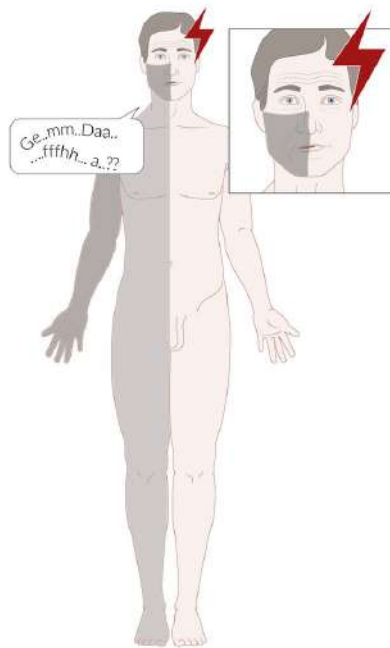
Hint

This patient presents with features of infarction in the right corticospinal tract (left-sided hemiparesis), right medial lemniscus (left-sided loss of proprioception), and right hypoglossal nucleus (deviation of the tongue to the right and difficulty speaking due to dysarthria).

Correct Answer

A - A

Image

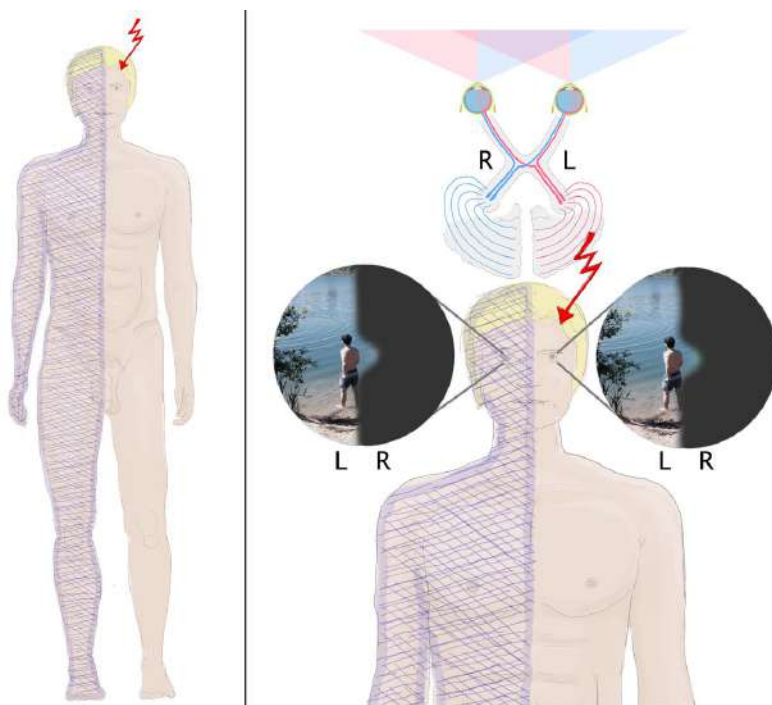


Explanation Why

This is the right [middle cerebral artery \(MCA\)](#), which supplies a large part of the [lateral](#) surface of the right (typically nondominant) [cerebral cortex](#). Occlusion of this [artery](#) can cause left-sided neurological deficits, primarily of the face and upper limbs, such as weakness (due to [primary motor cortex infarction](#)), sensory loss (due to primary sensory cortex [infarction](#)), and difficulty speaking (due to labial dysarthria caused by [upper motor neuron CN VII](#) palsy). However, all types of sensations, not just [proprioception](#), would be impaired and deviation of the [tongue](#) would not be expected. Instead, patients typically present with left [homonymous hemianopia](#) (due to [infarction](#) of the [optic radiations](#)) and left [hemineglect](#) (due to [infarction](#) of the nondominant frontal and [parietal lobes](#)).

B - B

Image

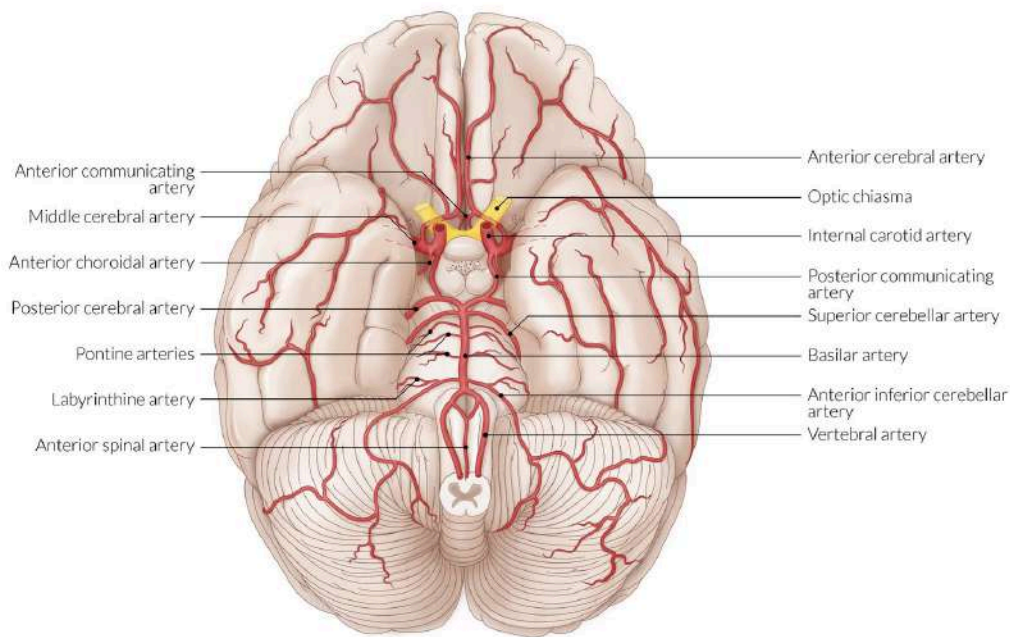


Explanation Why

This is the right [posterior cerebral artery](#) (PCA), which supplies the [rostral midbrain](#), [thalamus](#), [occipital lobe](#), and inferomedial [temporal lobe](#) ipsilaterally. Occlusion of this [artery](#) can cause left-sided sensory loss (due to [infarction](#) of the right [ventral posterolateral nucleus](#) or the right ascending sensory tracts) and left-sided [hemiparesis](#) (due to [infarction](#) of the right [corticospinal tracts](#)), which are seen here. However, in PCA occlusion, all types of sensations (not just [proprioception](#)) are impaired and features such as difficulty speaking and deviation of the [tongue](#) would not be expected. Instead, left [homonymous hemianopia](#) with [macular sparing](#), [memory](#) deficits, and [vertigo](#) would be expected.

C - C

Image



Explanation But

Occlusion of the [anterior spinal artery](#) below the level of the medulla causes [anterior spinal cord syndrome](#), which manifests with quadriplegia or paraplegia and bilateral loss of [pain](#) and temperature sensations in the trunk and extremities.

Explanation Why

This [artery](#), which is formed by the union of branches from the [vertebral artery](#) and located in the midline on the [ventral](#) surface of the medulla and [spinal cord](#), is the [anterior spinal artery](#). Occlusion of the paramedian branches of the [anterior spinal artery](#) and/or [vertebral artery](#) can lead to [medial medullary syndrome](#), which is caused by [infarction](#) of the [corticospinal tract](#), [medial lemniscus](#), and hypoglossal nucleus, as seen here. This patient's history of [coronary heart disease](#), [hypertension](#), and smoking history suggests a thrombotic [stroke](#), which is caused by plaque rupture in arteriosclerotic [arteries](#). After the exclusion of bleeding as a cause, treatment will most likely consist of reperfusion therapy, supportive care, and prevention of post-[stroke](#) complications.

D - D

Explanation Why

This is the left [superior cerebellar artery](#), which supplies the [superior cerebellar peduncle](#), [anterior cerebellar](#) lobe, and part of the [lateral tegmentum](#) ipsilaterally. Occlusion of this [artery](#) can result in difficulty speaking (due to [ataxic dysarthria](#)), and, occasionally, sensory deficits, which are seen here. However, sensory loss would occur on the right side (due to left [spinothalamic tract infarction](#)) and involve [pain](#) and temperature modalities rather than [proprioception](#). In addition, deviation of the [tongue](#) and [hemiparesis](#) are not consistent with a [superior cerebellar artery infarct](#). Instead, [cerebellar signs](#) (e.g., [vertigo](#), nystagmus, [ataxic gait](#), [dysmetria](#)) and [Horner syndrome](#) would be expected.

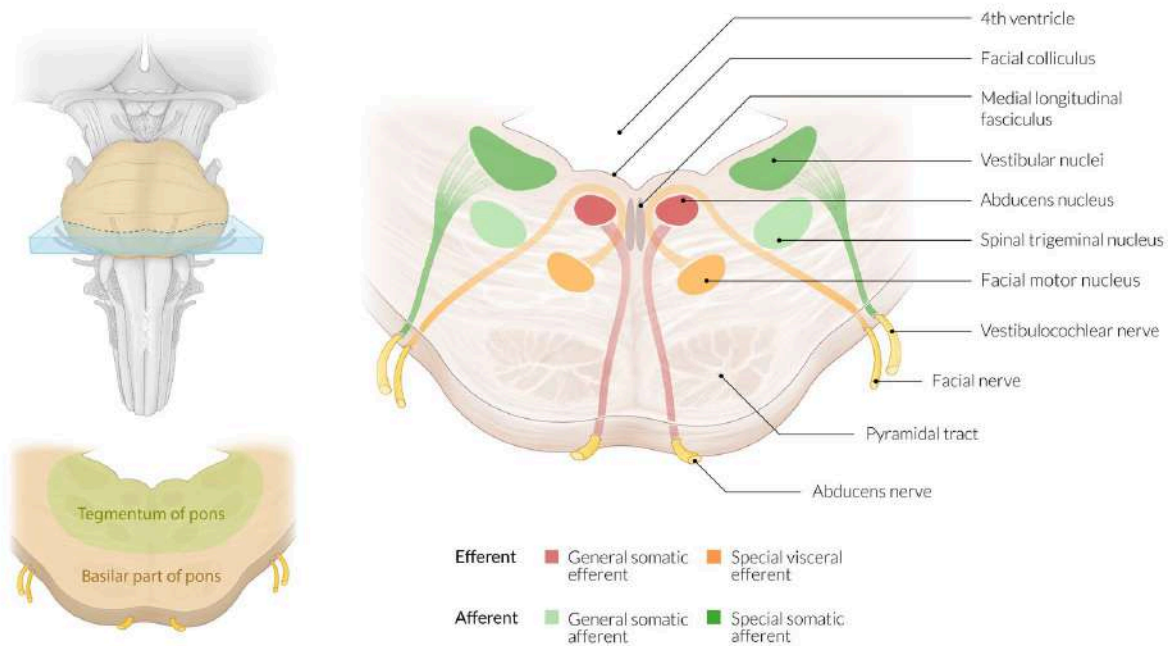
E - E

Explanation Why

This is the [basilar artery](#), which supplies the ventromedial parts of the [midbrain](#), [pons](#), and [rostral medulla](#) via its paramedian and circumferential branches. The clinical features of [basilar artery](#) occlusion vary depending on the site at which the [basilar artery](#) is occluded. The most severe manifestation is [locked-in syndrome](#), which manifests as quadriplegia and [bulbar palsy](#) with preserved consciousness, blinking, and vertical [eye](#) movements. The presence of [hypoglossal nerve palsy](#) in this patient means that the [infarct](#) can be localized to the [medial](#) part of the [caudal](#) medulla, which receives blood from a different vessel.

F - F

Image

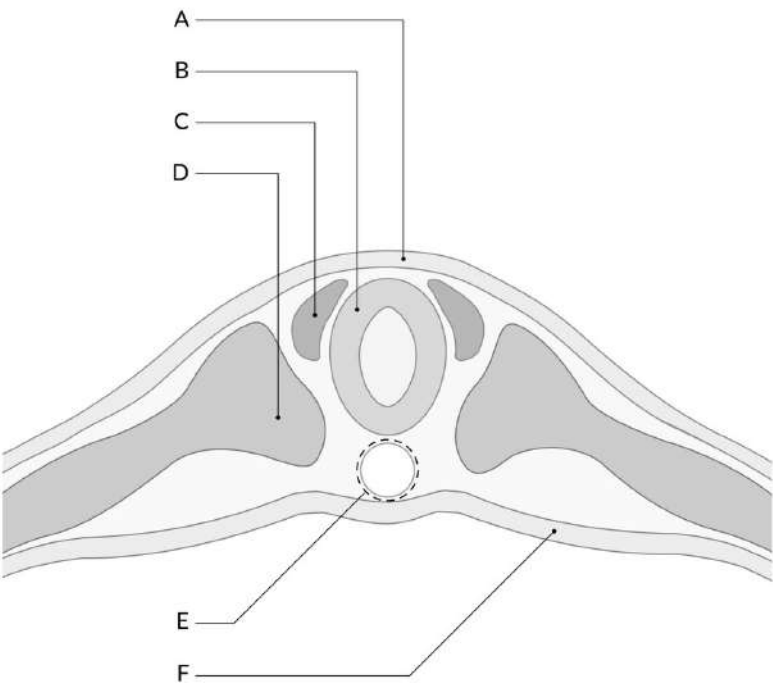


Explanation Why

This is the left [anterior inferior cerebellar artery \(AICA\)](#). The [AICA](#) supplies structures located in the [lateral pons](#) such as [CN VII](#) nucleus, [vestibular nucleus](#), [spinothalamic tract](#), spinal trigeminal nucleus, hypothalamospinal tract, and middle and [inferior cerebellar peduncles](#). Occlusion of the [AICA](#) causes features of [lateral pontine syndrome](#) such as difficulty speaking (due to labial dysarthria) and sensory deficits, which are seen here. However, sensory loss would involve [pain](#) and temperature modalities rather than [proprioception](#) and, in patients with left [AICA](#) occlusion, sensory deficits would occur on the right side. In addition, [hemiparesis](#) and deviation of the [tongue](#) would not be expected. Instead, [Horner syndrome](#), [vertigo](#), and [ataxia](#) would be seen.

Question # 22

A 2710-g (6-lb) female newborn is delivered at 37 weeks gestation to a 26-year-old primigravid woman following a spontaneous vaginal delivery. Apgar scores are 7 and 9 at 1 and 5 minutes, respectively. Physical examination shows skin dimpling and a tuft of hair over the lumbar spine. There is no herniation of meninges or neural tissue. A schematic transverse section of the embryonic disc at approximately week 3 of embryonal development is shown. This patient's condition is most likely caused by incomplete fusion of tissue derived from which of the following labeled structures?



	Answer	Image
A	A	

	Answer	Image
B	B	
C	C	
D	D	
E	E	

	Answer	Image
F	F	The diagram illustrates the development of an embryo. The top part shows a three-layered embryo with labels: Amniotic cavity (blue), Yolk sac (yellow), and Connecting stalk (green). The bottom part shows a more complex stage with various internal organs and structures labeled. The labels on the left are: (Remnants of) Buccopharyngeal membrane, Developing heart, Septum transversum, Vitelline duct, Allantois, Cloacal membrane, and Cloaca. The labels on the right are: Pharyngeal pouches, Thyroid diverticulum, Developing esophagus, Respiratory diverticulum, Developing stomach, Dorsal pancreatic bud, Hepatic diverticulum, Gut tube, and Neural tube.

Hint

This patient with a skin dimple and hair tuft in the lumbar region has spina bifida occulta, in which one or more vertebral arches fail to fuse completely while the spinal cord, meninges, and skin remain intact.

Correct Answer

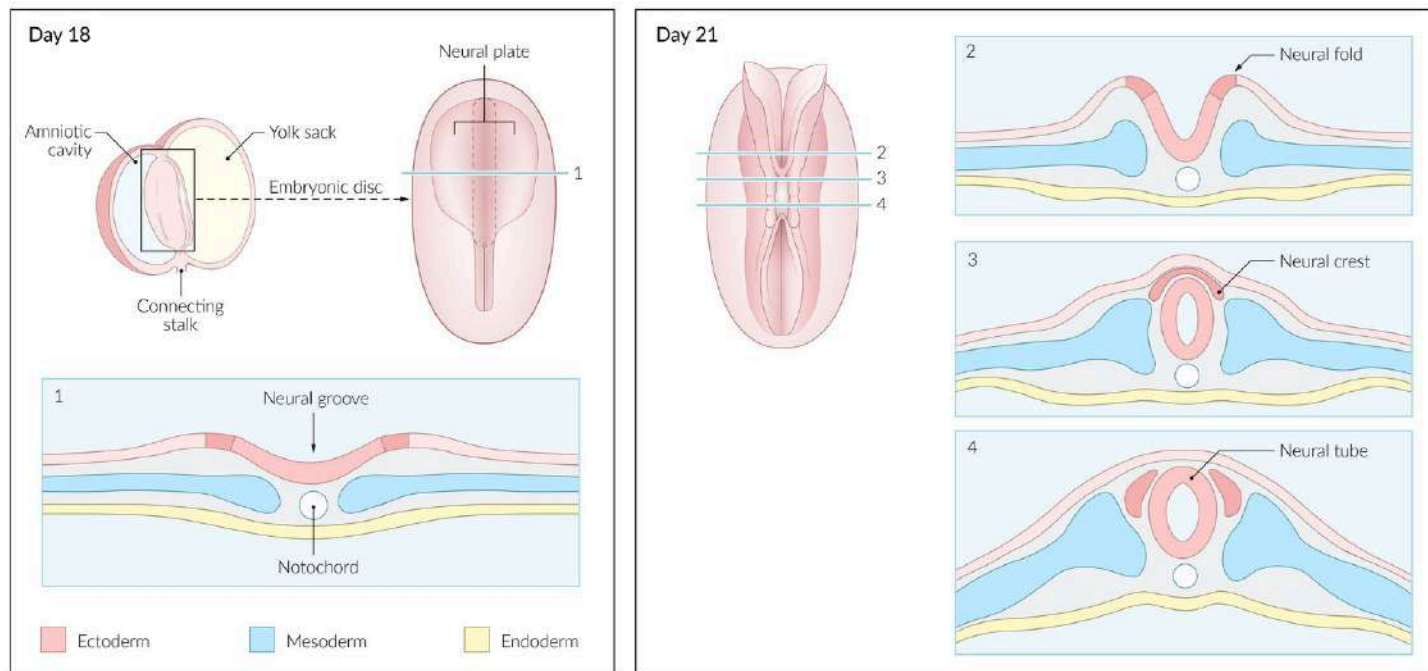
A - A

Explanation Why

This structure is the [surface ectoderm](#), which gives rise to the [epidermis](#), [hair](#), [nails](#), [dental enamel](#), [eye lens](#), and [adenohypophysis](#). A failure of the [surface ectoderm](#) to separate from the [caudal](#) part of the [neural tube](#) is responsible for the failure of [vertebral arch](#) fusion in patients with [spina bifida occulta](#). The subsequent aberrant surface ectodermal differentiation is responsible for the [skin](#) dimpling and [hair](#) tuft seen in this patient. However, the [vertebral arches](#) themselves are not derived from the [surface ectoderm](#).

B - B

Image



Explanation Why

This structure is the [neural tube](#), which forms the brain and [spinal cord](#). Incomplete fusion of the [neural tube](#)'s [caudal neuropore](#) causes [open spina bifida](#), which manifests in the lumbar region as a herniated [CSF](#)-filled meningeal sac containing the [spinal cord](#) ([myelomeningocele](#)) or an exposed [spinal cord](#) ([myeloschisis](#)). The normal development of the [vertebrae](#) requires molecular signals from the [neural tube](#), but the [vertebral arches](#) themselves are not derived from the [neural tube](#).

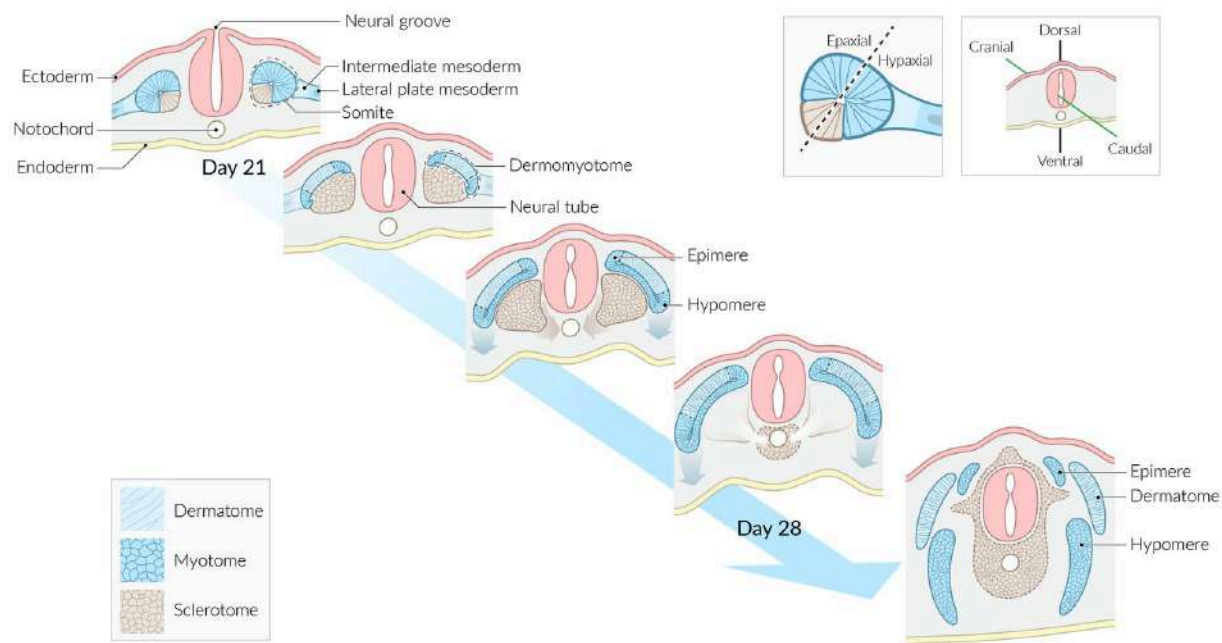
C - C

Explanation Why

This structure is the [neural crest](#), which gives rise to the [pia mater](#), the [arachnoid mater](#), and bones of the [skull](#) and face. [Dysplastic](#) development of the [pia](#) and [arachnoid mater](#) is implicated in the pathogenesis of [myeloschisis](#), a form of [open spina bifida](#) that manifests as an exposed [spinal cord](#) in the lumbar region. Unlike craniofacial bones, the [vertebral arches](#), which fail to fuse in [spina bifida occulta](#), do not arise from the [neural crest](#).

D - D

Image



Explanation But

In contrast to [spina bifida occulta](#), the primary pathology in [meningomyelocele](#) and [myeloschisis](#) is a [neural tube defect](#). Since the normal development of the [vertebrae](#) requires molecular signals from the [neural tube](#), patients with either of these conditions would also have a [vertebral arch](#) defect ([open spina bifida](#)), but the presentation in both these conditions would be different than that in this patient. A [meningomyelocele](#) would manifest as a herniated [CSF](#)-filled meningeal sac that is typically not covered by [skin](#), and [myeloschisis](#) would manifest as an exposed [spinal cord](#). In addition, both these conditions would be associated with severe neurological deficits (e.g., lower limb paralysis, bowel and [bladder incontinence](#)).

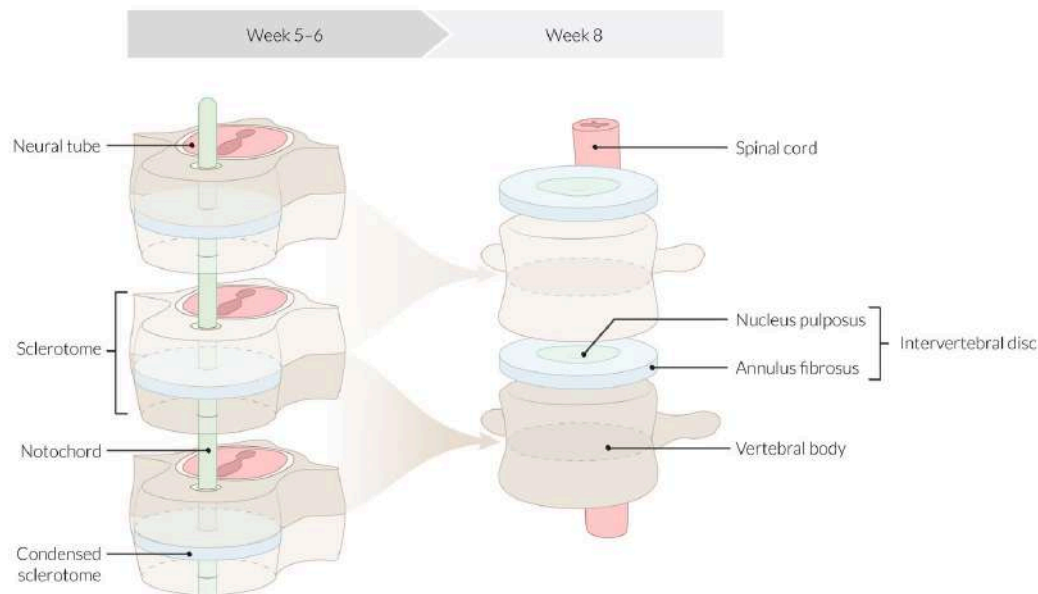
Explanation Why

This structure is the [paraxial mesoderm](#), which becomes segmented into [somites](#) during weeks 4–5 of [embryonic development](#) and subsequently differentiates into sclerotomes and [dermomyotomes](#). Normally, the sclerotomes on either side of the [neural tube](#) migrate medially and fuse between the [surface ectoderm](#) and [neural tube](#) to form [vertebral arches](#), and around the [notochord](#) to form [vertebral bodies](#). In the case of [spina bifida occulta](#), the primary defect is a failure of the [surface](#)

[ectoderm](#) to separate from the [neural tube](#) in the [caudal](#) region. This defect impairs [sclerotome](#) migration and the formation of [vertebral arches](#). The absence of sclerotomes in the [caudal](#) region can also lead to aberrant differentiation of the [surface ectoderm](#) and manifest as [skin](#) dimpling and a [hair](#) tuft, as seen here. [Spina bifida occulta](#), which affects approx. 10% of the population, is usually asymptomatic.

E - E

Image

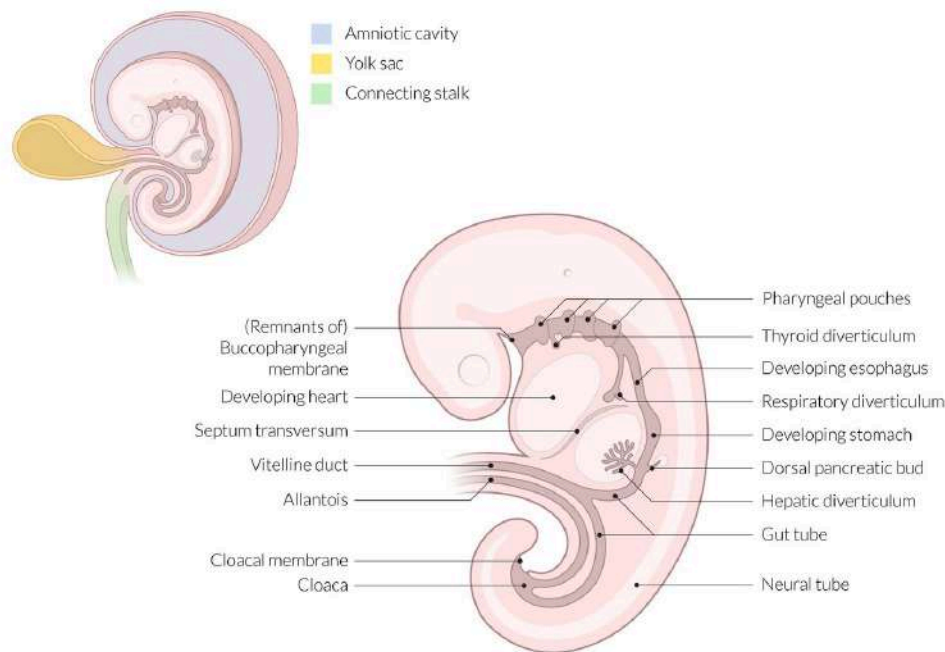


Explanation Why

This structure is the [axial mesoderm](#), which becomes the [notochord](#) and, subsequently, the [nucleus pulposus](#) of the [intervertebral discs](#). Molecular signals from the [notochord](#) play a role in the segmentation of the [spine](#) into [vertebrae](#), but the [vertebral arches](#) themselves do not arise from the [notochord](#).

F - F

Image



Explanation Why

This structure is the [endoderm](#), which gives rise to [branchial pouches](#), primordial buds of the [liver](#), [pancreas](#), and [lungs](#), and the epithelium of the gastrointestinal tract and [urogenital sinus](#). Examples of conditions caused by incomplete fusion of tissue derived from the [endoderm](#) include [pancreas divisum](#) (failure of fusion of the [ventral](#) and [dorsal pancreatic](#) buds) and ectopic parathyroid tissue (failure of fusion of the [dorsal](#) wings of the 3rd and 4th branchial pouches). Osseous structures such as the [vertebral arches](#), which fail to fuse in [spina bifida occulta](#), do not arise from the [endoderm](#).

Question # 23

A 25-year-old man comes to the physician for a consultation about drug use. Last week, he tried cocaine for the first time during a business event. Because his father had a sedative use disorder, the patient had always been cautious with addictive substances. He is now concerned about the addictive potential of this substance. It has been shown that even a single exposure to cocaine can lead to plastic changes in circuits of the limbic system, which plays a role in the development of addiction. The underlying synaptic remodeling is initiated by activation of postsynaptic receptors that act as ion channels allowing nonselective cation influx into the neuron. Activation of which of the following receptors is most likely responsible for the described synaptic remodeling process?

	Answer	Image
A	N-methyl-D-aspartate	
B	Dopamine D ₁	
C	Muscarinic M ₁	
D	γ -Aminobutyric acid A	
E	Opioid μ	
F	Histamine H ₁	

Hint

This remodeling process, long-term potentiation, is initiated by the activation of an ionotropic channel through glutamate.

Correct Answer

A - N-methyl-D-aspartate

Explanation But

Even a single use of [cocaine](#) use has been shown to cause LTP, associating [cocaine](#) intake with a pleasure response.

Explanation Why

The N-methyl-D-aspartate receptor (NMDA-R) is a postsynaptic [glutamate](#)-gated ion channel in the perforant pathway of the [hippocampus](#), which is a part of the [limbic system](#). The ion channel of NMDA-R allows the influx of a number of cations, including Ca^{2+} , but is normally blocked by an Mg^{2+} ion. A sufficiently large [excitatory postsynaptic potential](#) dislodges Mg^{2+} from the ion channel of NMDA-R, thereby allowing the influx of Ca^{2+} . Ca^{2+} acts as a [second messenger](#) with early phase effects (within a few hours), such as insertion of further [glutamate](#)-gated ion channels (AMPA receptors) in the postsynaptic membrane, and late phase effects (days to weeks), such as increased [translation](#) of AMPA-receptors and growth factors that promote the formation of new [synapses](#) (synaptic plasticity). These effects strengthen the connections between perforant pathway [neurons](#) and lead to long-term potentiation (LTP), a process that is responsible for learning, [memory](#), and addiction.

B - Dopamine D₁

Explanation Why

The [dopamine D₁ receptor](#) is present in [dopaminergic pathways](#) such as the [mesolimbic system](#) (reward pathway). [Cocaine](#) inhibits the presynaptic reuptake of [dopamine](#), and stimulation of [D₁ receptors](#) in the [mesolimbic system](#) is a part of the pathophysiology of [cocaine](#) addiction. However, the [D₁ receptor](#) is a [G-protein](#) coupled receptor, not an [ion channel-linked receptor](#).

C - Muscarinic M₁

Explanation Why

The muscarinic M₁ receptor in the [central nervous system](#) is a [G-protein](#) coupled receptor, not an [ion channel-linked receptor](#).

D - γ -Aminobutyric acid A

Explanation Why

The γ -Aminobutyric acid A receptor ([GABA_A receptor](#)) is a postsynaptic [ligand-gated ion channel](#) that is involved in long-term potentiation, synaptic remodeling, and addiction to certain drugs, such as [benzodiazepines](#). However, the [GABA_A receptor](#) selectively allows the influx of [chloride](#), which is an anion, not a cation.

E - Opioid μ

Explanation Why

The [opioid \$\mu\$ receptor](#) in the [CNS](#) is involved in long-term potentiation, synaptic remodeling, and addiction to certain drugs, such as [opiates](#). However, it is a [G-protein](#) coupled receptor, not an [ion channel-linked receptor](#).

F - Histamine H₁

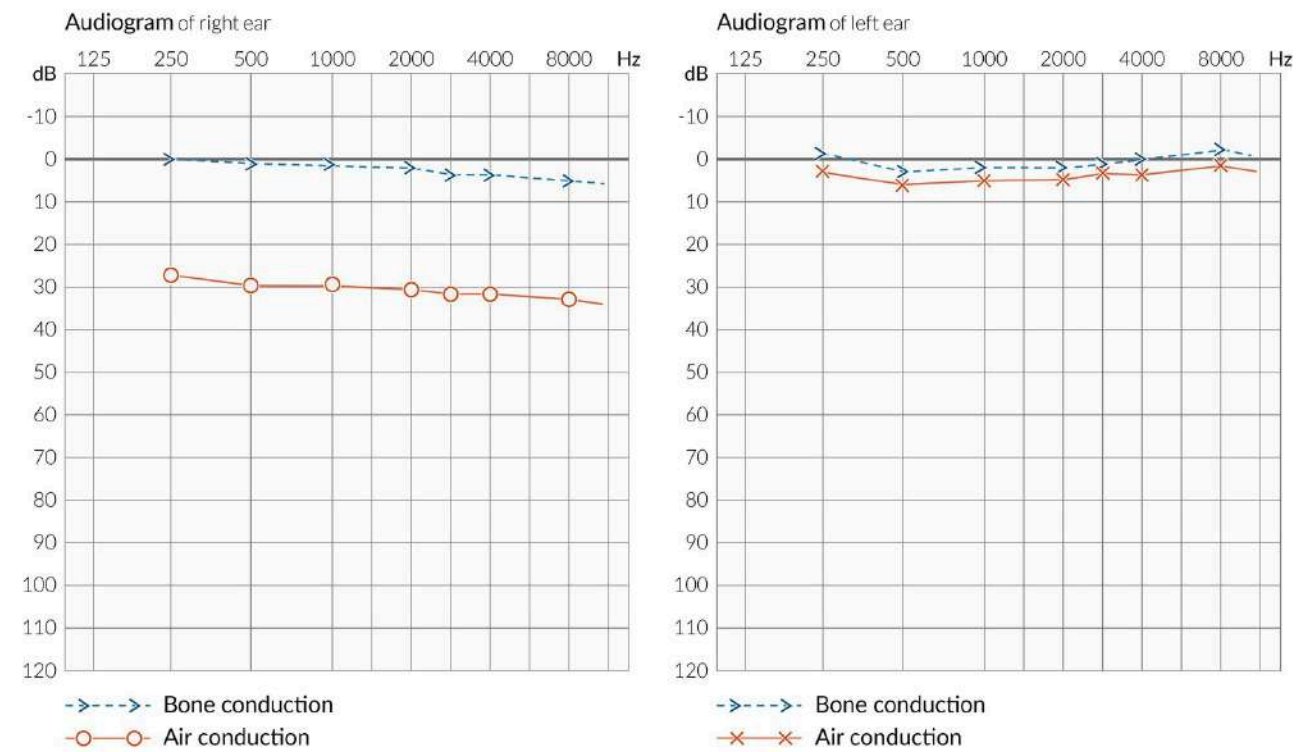
Explanation Why

The [histamine H₁ receptor](#) in the [central nervous system](#) is a [G-protein](#) coupled receptor, not an [ion](#)

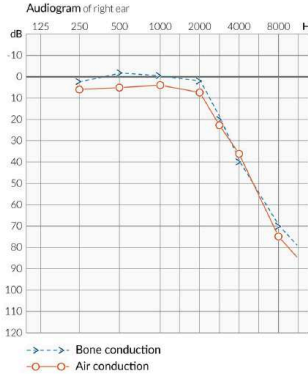
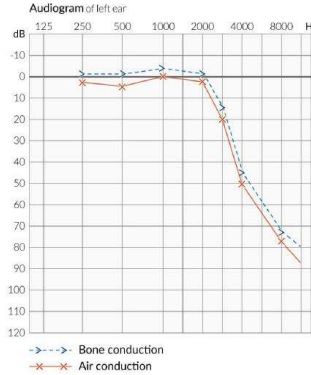
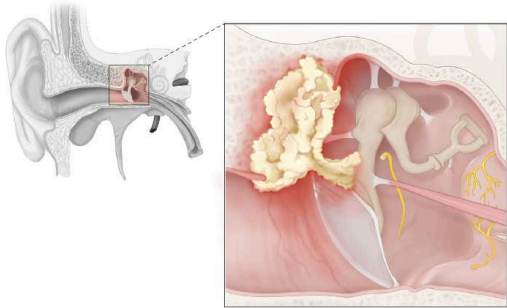
[channel-linked receptor.](#)

Question # 24

An otherwise healthy 42-year-old man comes to the physician with progressive hearing loss for the past year and painless unilateral fluid leakage from the ear for the past month. He takes no medications. His temperature is 37.1°C (98.8°F). Otoscopic examination shows a brown, irregular mass and partial retraction of the tympanic membrane. The results of an audiogram are shown. Which of the following is the most likely underlying cause of this patient's hearing loss?



	Answer	Image
A	Infection of the external ear canal on the right	

	Answer	Image
B	Accumulation of sebaceous gland secretions on the left	
C	Damage to the organ of Corti on the right	Audiogram of right ear  Audiogram of left ear 
D	Malignant squamous cell neoplasia on the left	
E	Collection of keratinizing squamous epithelium on the right	

	Answer	Image
F	Tumor of the vestibular nerve on the left	

Hint

This patient's audiogram shows an air-bone gap as a result of an increased auditory threshold in air conduction with normal bone conduction, which is typical for conductive hearing loss.

Correct Answer

A - Infection of the external ear canal on the right

Image



Explanation Why

Infection of the external ear canal ([otitis externa](#)) on the right can lead to fluid leakage from the right ear and [conductive hearing loss](#) on the right, which are seen on this patient's [audiogram](#). However, [otitis externa](#) is typically associated with severe ear [pain](#). [Otoscopy](#) in this condition would show an [erythematous](#) and [edematous](#) external ear canal, and possibly [granulation tissue](#) at the transition between the [cartilaginous](#) and the osseous parts of the [external auditory canal](#). Furthermore, [otitis externa](#) is an acute condition, whereas this patient's presentation indicates a more chronic process.

B - Accumulation of sebaceous gland secretions on the left

Image

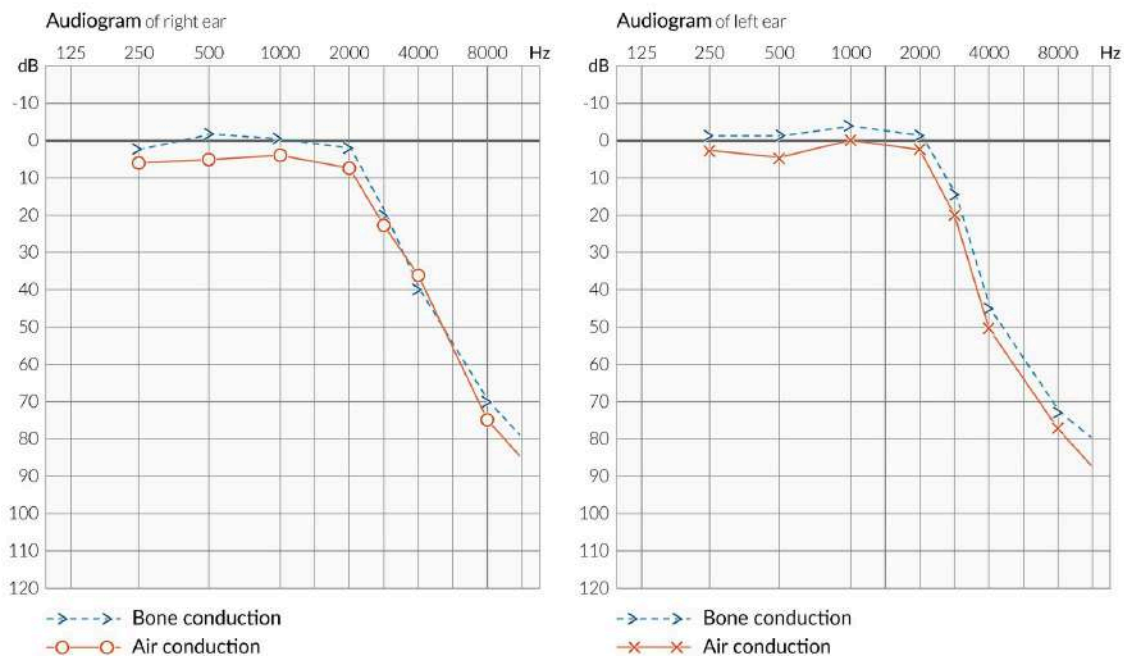


Explanation Why

Accumulation of [cerumen](#), which is secreted by the [sebaceous glands](#) in the auditory canal, can cause [cerumen impaction](#) and lead to [conductive hearing loss](#), which is seen here. However, [cerumen impaction](#) on the left would result in impaired air conduction of the left ear, whereas this patient's [audiogram](#) shows abnormal air conduction on the right side. Furthermore, [otorrhea](#) would not be expected, and [otoscopy](#) of a [cerumen](#)-impacted ear would show obstruction of the [external auditory canal](#) by a brownish-yellow, waxy plug; the [tympanic membrane](#) would most likely not be visible.

C - Damage to the organ of Corti on the right

Image



Explanation Why

Unilateral damage to the [organ of Corti](#) can occur, e.g., as a result of [labyrinthitis](#). However, damage to the [organ of Corti](#) manifests with [sensorineural hearing loss](#), which would show up on audiometry as an increase in the threshold for both air and bone conduction. Furthermore, patients with [labyrinthitis](#) also typically present acutely or subacutely, unlike this patient, who has had progressive [hearing loss](#) for the past year, and [labyrinthitis](#) is usually associated with [tinnitus](#) and/or [vertigo](#).

D - Malignant squamous cell neoplasia on the left

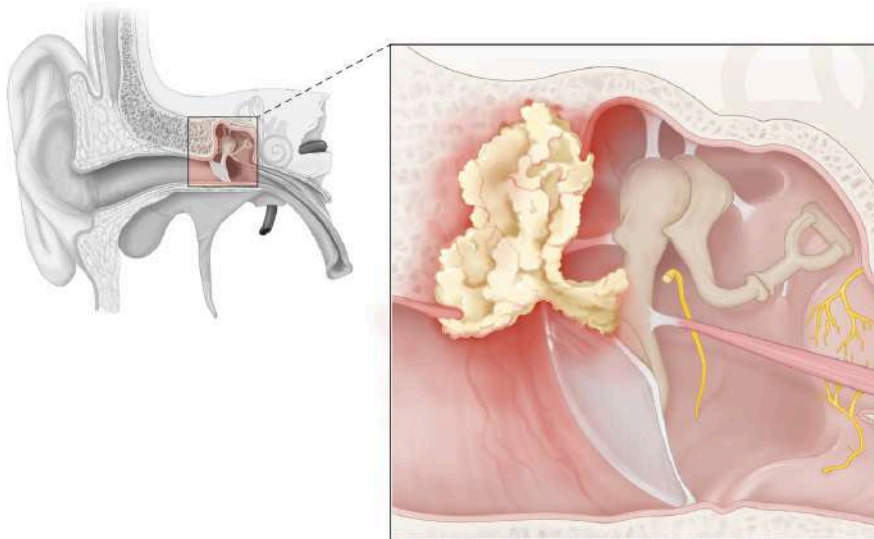
Explanation Why

[Squamous cell carcinoma](#) of the [external auditory canal](#) can manifest with [otorrhea](#) and [conductive hearing loss](#), as well as otoscopic findings similar to those seen in this patient. However, patients

would typically have severe ear [pain](#), which is not seen here, and this patient's [audiogram](#) shows [conductive hearing loss](#) in the right, not the left ear.

E - Collection of keratinizing squamous epithelium on the right

Image



Explanation Why

This patient's progressive right-sided [conductive hearing loss](#), painless [otorrhea](#), and irregular mass on [otoscopy](#) suggest a [cholesteatoma](#) of the right ear. This condition is characterized by keratinizing [squamous epithelium](#) growing from the [tympanic membrane](#) or the auditory canal into the [middle ear](#) mucosa or the mastoid, causing chronic [inflammation](#) and erosion of the auditory [ossicles](#). Cholesteatomas can be congenital or acquired. Acquired cholesteatomas can be classified as primary if caused by chronic negative [middle ear](#) pressure (due to [eustachian tube](#) dysfunction without [middle ear infection](#)) or secondary if caused by past injury to the [tympanic membrane](#) (typically due to [chronic otitis media](#)). The [retraction](#) pocket in the [tympanic membrane](#) and brown, irregular mass seen in this patient's [otoscopy](#) are characteristic of primary acquired [cholesteatoma](#). Secondary acquired cholesteatomas, on the other hand, typically appear as a pearly white mass shining through the intact [tympanic membrane](#).

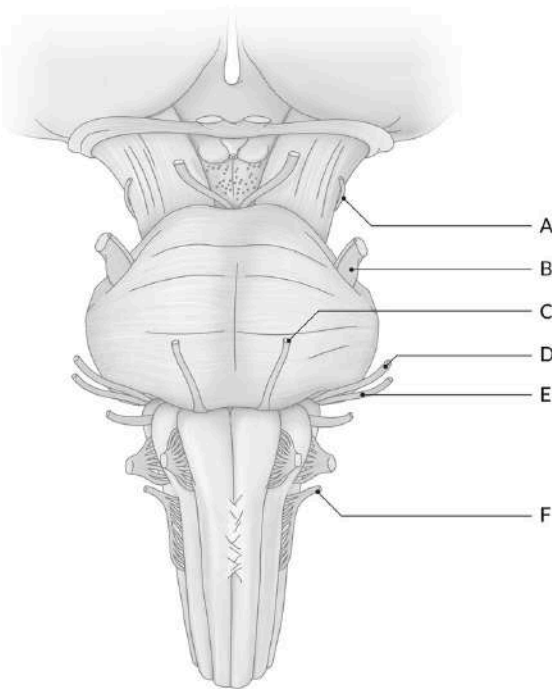
F - Tumor of the vestibular nerve on the left

Explanation Why

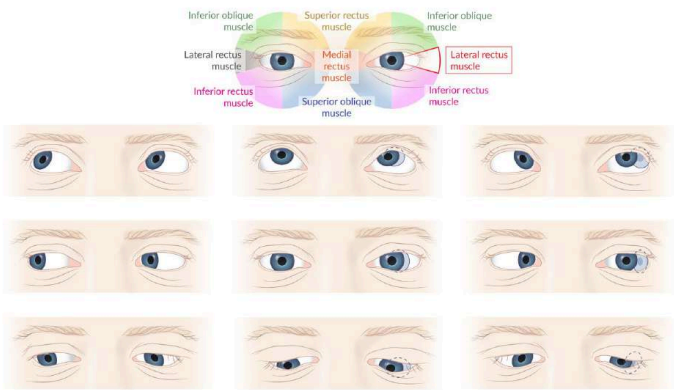
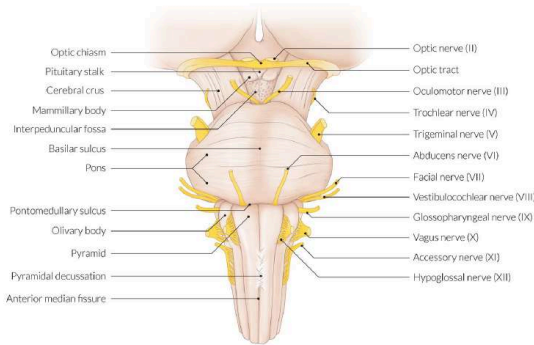
Tumors of the [vestibulocochlear nerve](#) such as [acoustic neuromas](#) can cause unilateral [hearing loss](#), which is seen in this patient. However, a [tumor](#) on the left would be evident on an [audiogram](#) as [sensorineural hearing loss](#) on the left, characteristically showing increased auditory thresholds in both air and bone conduction. This patient's [audiogram](#) shows [conductive hearing loss](#) in the right ear. Moreover, a [tumor](#) of the vestibular nerve would likely cause further symptoms, such as [vertigo](#) and [tinnitus](#), and would not explain this patient's [otorrhea](#) and otoscopic findings.

Question # 25

A 55-year-old woman comes to the physician because of a 5-month history of weakness of the left side of her face, loss of taste, as well as dryness and redness of her left eye. She has no history of serious illness and takes no medications. Physical examination shows an inability to puff the left cheek and close her left eye. An MRI of the brain shows a contrast-enhancing mass in the posterior fossa. The patient's symptoms are most likely caused by compression of which of the following structures?



	Answer	Image
A	A	

	Answer	Image
B	B	
C	C	 The diagram illustrates the extraocular muscles of the eye. The top part shows a frontal view of the eye with labels for the Inferior oblique muscle, Superior rectus muscle, Inferior oblique muscle, Lateral rectus muscle, Medial rectus muscle, Inferior rectus muscle, and Superior oblique muscle. Below this is a 3x3 grid of illustrations showing various eye movements: up, down, left, right, and combinations thereof.
D	D	 This anatomical diagram shows the brainstem and the origins of the twelve cranial nerves. Labels on the left include: Optic chiasm, Pituitary stalk, Cerebral crus, Mammillary body, Interpeduncular fossa, Basilar sulcus, Pons, Pontomedullary sulcus, Olfactory body, Pyramid, Pyramidal decussation, and Anterior median fissure. Labels on the right include: Optic nerve (II), Optic tract, Oculomotor nerve (III), Trochlear nerve (IV), Trigeminal nerve (V), Abducens nerve (VI), Facial nerve (VII), Vestibulocochlear nerve (VIII), Glossopharyngeal nerve (IX), Vagus nerve (X), Accessory nerve (XI), and Hypoglossal nerve (XII).
E	E	
F	F	

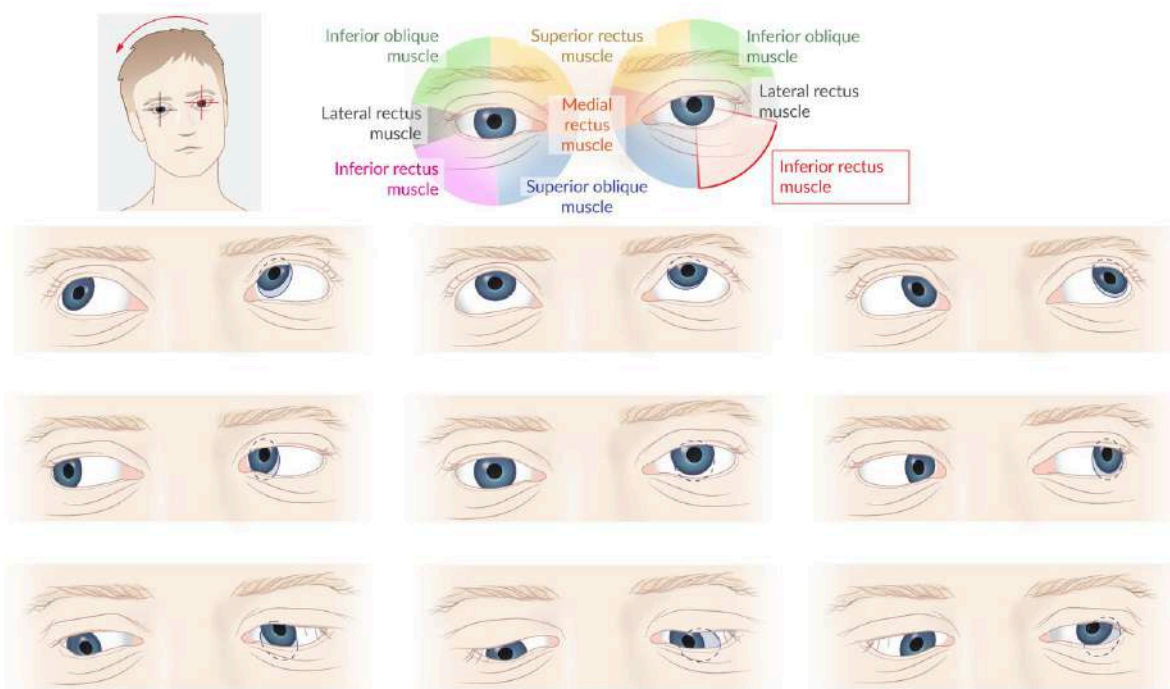
Hint

This patient presents with features of facial nerve palsy.

Correct Answer

A - A

Image



Explanation Why

This structure, which emerges from the [posterior](#) surface of the [brainstem](#), is the [trochlear nerve \(CN IV\)](#). [CN IV](#) lies in the posterior cranial fossa just below the free edge of the tentorium. Compression of [CN IV](#), which innervates the [superior oblique muscle](#), would present with [diplopia](#) and [extorsion](#) of the [eye](#).

B - B

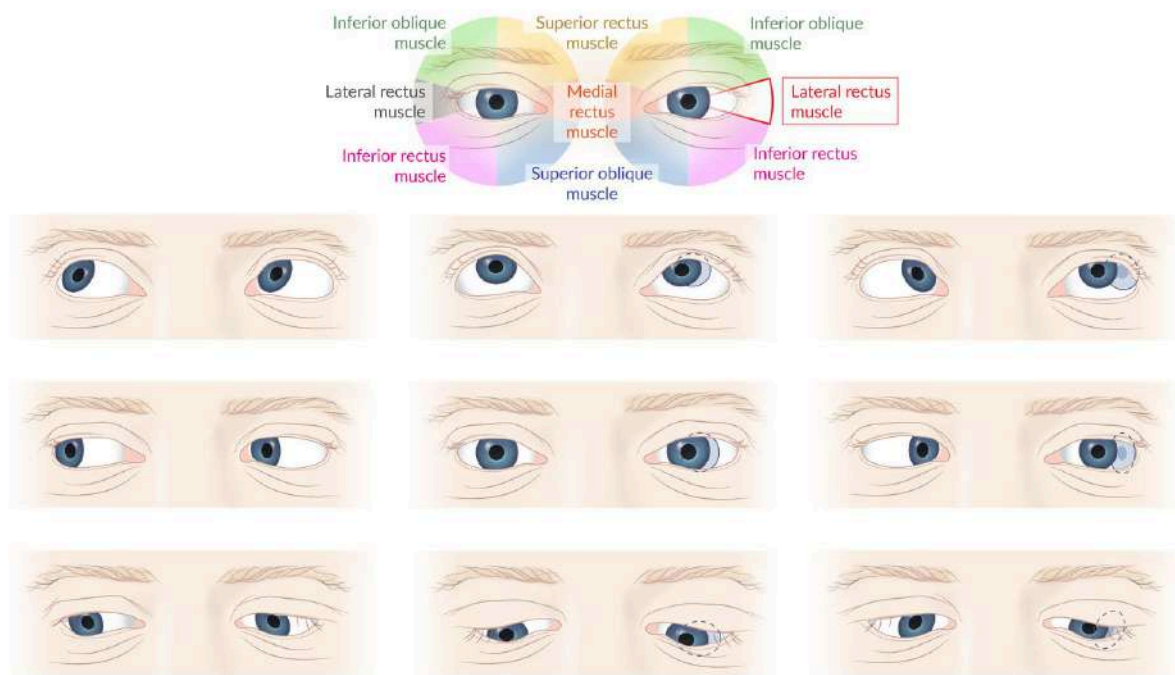
Explanation Why

B corresponds to the [trigeminal nerve \(CN V\)](#), which emerges from the anterolateral surface of the

pons. A posterior fossa tumor can compress CN V, and potentially result in redness and dryness in the eye (due to neurotrophic keratopathy) as well as sensory loss in the tongue. However, somatosensations (e.g., touch, pain, temperatures) in the tongue rather than taste sensation are lost in patients with a compressed CN V and features of facial muscle weakness (e.g., lagophthalmos, inability to puff the cheek) would not be expected. Instead, affected patients have weakness in the muscles of mastication and sensory deficits in the face.

C - C

Image

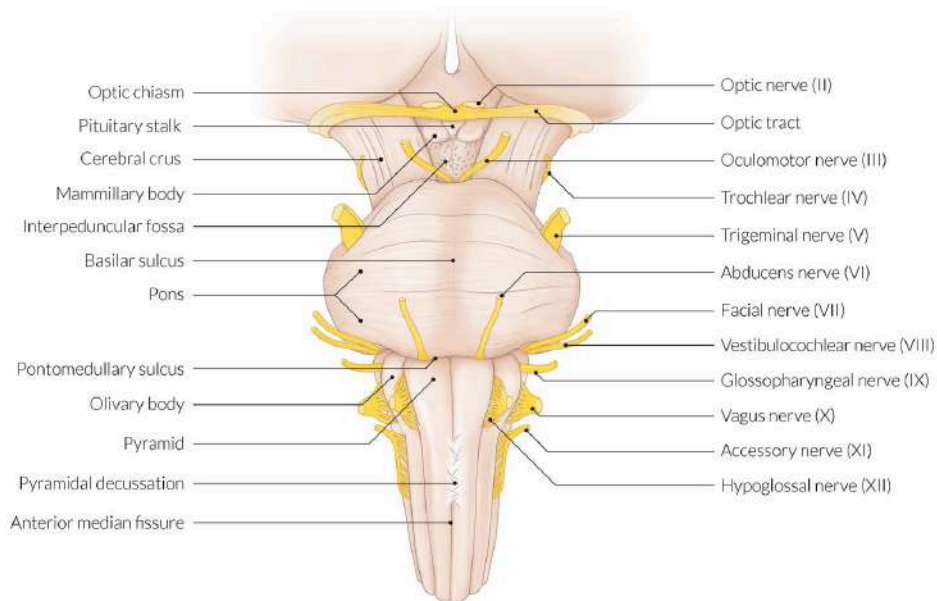


Explanation Why

The structure indicated by C is the abducens nerve (CN VI), which emerges from the anteromedial region of the pontomedullary junction. Compression of CN VI, which innervates the lateral rectus muscle, would present with diplopia and esotropia.

D - D

Image



Explanation Why

This structure is the [facial nerve \(CN VII\)](#), which emerges from the [lateral](#) part of the pontomedullary junction ([cerebellopontine angle](#)) [medial](#) to the [vestibulocochlear nerve \(CN VIII\)](#). [CN VII](#) provides innervation to the muscles of facial expression and [orbicularis oculi](#). [CN VII](#) also contains nerve fibers that relay [taste](#) sensation from the [anterior](#) $\frac{2}{3}$ of the [tongue](#) (via the [chorda tympani](#)) and [parasympathetic](#) efferents to the [lacrimal gland](#). Compression of [CN VII](#) can, therefore, cause an inability to puff the cheeks, decreased [taste](#) sensation, [lagophthalmos](#), and a dry [eye](#), as seen here. The most likely cause of [CN VII](#) compression at the [cerebellopontine angle](#) is a [schwannoma](#). [Schwannomas](#) can develop in any [cranial](#) or peripheral nerve but most commonly arises from [CN VIII](#) (i.e., [acoustic neuroma](#)/[vestibular schwannoma](#)).

E - E

Explanation Why

This structure, which emerges from the most [lateral](#) part of the pontomedullary junction ([cerebellopontine angle](#)), is the [vestibulocochlear nerve \(CN VIII\)](#). Compression of [CN VIII](#) would present with [sensorineural hearing loss](#) and vestibular symptoms (e.g., nystagmus, [vertigo](#)).

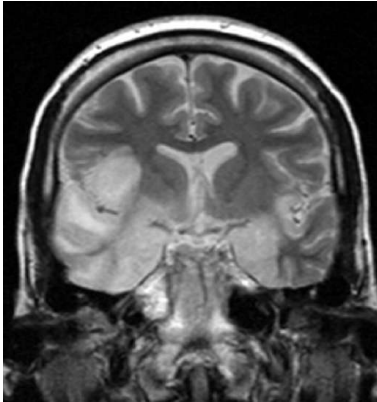
F - F

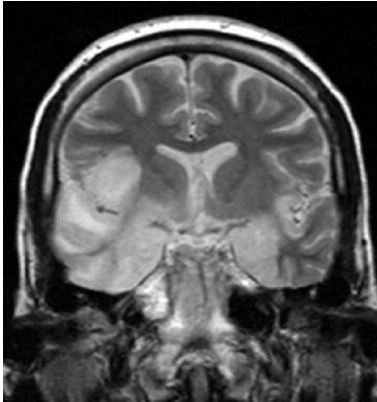
Explanation Why

F corresponds to the [accessory nerve \(CN XI\)](#), a structure that has roots emerging from the [lateral](#) region of the inferior medulla and upper cervical cord. The [accessory nerve](#) passes through the posterior cranial fossa before exiting the [skull](#) via the [jugular foramen](#). Compression of this nerve would manifest as an inability to elevate the shoulder (ipsilateral [trapezius](#) weakness) and/or an inability to turn the head away from the affected side (ipsilateral [sternocleidomastoid](#) weakness), which are not seen here.

Question # 26

A 55-year-old man is brought to the physician by his wife because of abnormal behavior for the past 3 weeks. The symptoms started after he was released from the hospital, where he was treated for herpes simplex encephalitis. His wife says that he has been eating increasing volumes of food and recently started putting nonfood items in his mouth and licking objects in the house. When they are home he often rubs his genitals on furniture, and he has also begun touching his genitals and masturbating in public. The patient appears docile. He is 185 cm (6 ft 1 in) tall and weighs 132 kg (291 lbs); BMI is 38 kg/m^2 . He is oriented to person but not to time or place. Neurological examination shows the ability to follow motor commands but an inability to name objects. The patient's symptoms are most likely caused by damage to which of the following structures?

	Answer	Image
A	Subthalamic nuclei	
B	Amygdalae	
C	Hippocampi	
D	Frontal lobe	
E	Mamillary bodies	



Hint

New onset of disinhibited behavior (i.e., hyperorality, hyperphagia, hypersexuality) and visual agnosia in an individual with a recent history of HSV-1 encephalitis raises suspicion for Kluver-Bucy syndrome.

Correct Answer

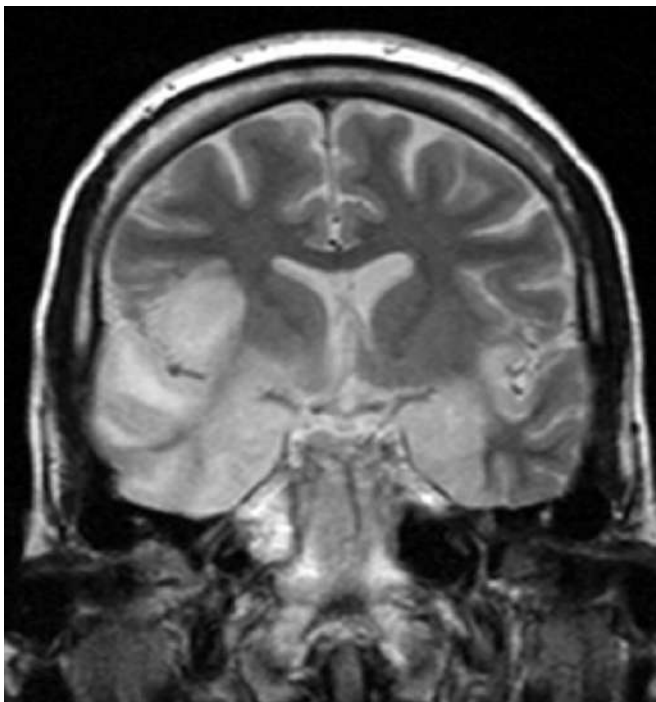
A - Subthalamic nuclei

Explanation Why

Damage to the [subthalamic nuclei](#) would not cause the disinhibited behavior (i.e., [hyperorality](#), [hyperphagia](#), hypersexuality) and [visual agnosia](#) seen here. The [subthalamic nucleus](#) is part of the [indirect pathway of the basal ganglia](#); activation of the [subthalamic nuclei](#) decreases motor activity. Lesions to the [subthalamic nucleus](#) characteristically result in contralateral [hemiballismus](#), which this patient does not have.

B - Amygdalae

Image



Explanation But

If active [HSV infection](#) is suspected, treatment is with IV [acyclovir](#); otherwise, therapy with psychotropic medications is recommended.

Explanation Why

Bilateral damage of the [medial](#) parts of the [anterior temporal lobe](#) (including the amygdalae) results in [Kluver-Bucy syndrome](#) (KBS). [HSV-1 encephalitis](#) is the most common cause of KBS as the virus shows neurotropism with a predilection for the [medial temporal lobe](#). Symptoms of KBS include [hyperorality](#), [hyperphagia](#), docility, cognitive dysfunction, and [visual agnosia](#). [MRI](#) is the most sensitive modality, particularly in the early stages of disease, and would show bilateral [hyperintense temporal lobe](#) lesions. Other causes of KBS include [head trauma](#), [stroke](#), [malignancy](#), and neurodegenerative diseases (e.g., Alzheimer, Pick, Parkinson, and [Huntington disease](#)).

C - Hippocampi

Explanation Why

Damage to the [hippocampi](#) would not cause the disinhibited behavior (i.e., [hyperorality](#), [hyperphagia](#), hypersexuality) and [visual agnosia](#) seen here. Bilateral hippocampal lesions would result in [anterograde amnesia](#), which this patient does not have.

D - Frontal lobe

Explanation Why

[Frontal lobe](#) lesions are typically associated with disinhibited behavior (e.g., sexual behavior) and deficits in [judgment](#), as seen here. However, this patient's [hyperorality](#), [visual agnosia](#), and [hyperphagia](#) would not be consistent with a [frontal lobe](#) lesion. [Frontal lobe](#) lesions may also be associated with the reemergence of [primitive reflexes](#), [Broca aphasia](#) (dominant inferior frontal gyrus), [urinary incontinence](#) (frontal micturition center), deficits in conjugate horizontal gaze ([frontal eye fields](#)), and [frontal gait disorder](#), which are also not seen here.

E - Mamillary bodies

Explanation Why

Damage to the [mammillary bodies](#) would be more likely to manifest with confusion, [disorientation](#), indifference, and inattentiveness than [hyperphagia](#), [hyperorality](#), and hypersexuality. Moreover, damage to the [mammillary bodies](#) is also associated with [ataxia](#) and [ophthalmoplegia](#) (i.e., [Wernicke encephalopathy](#)) with or without [amnesia](#) (anterograde > retrograde) and [confabulation](#) (i.e., [Korsakoff syndrome](#)), which this patient does not have. Furthermore, damage to the [mammillary bodies](#) is commonly associated with [thiamine](#) (B1) deficiency secondary to chronic heavy alcohol use, which is not consistent with this patient's history.

Question # 27

One hour after undergoing a surgical repair of a thoracic aortic aneurysm, a 70-year-old man experiences severe pain at the thoracolumbar junction and weakness and numbness in both legs. He appears pale and anxious. His temperature is 36°C (96.8°F), pulse is 95/min, respirations are 20/min, and blood pressure is 95/65 mm Hg. Physical examination shows decreased sensation to pain and temperature below the level of the umbilicus. Muscle strength is 1/5 in bilateral lower extremities. Proprioception and vibration sense are normal in both lower extremities. Sensation and motor function in the upper extremities, chest, and back are intact. Which of the following is the most likely diagnosis?

	Answer	Image
A	Leriche syndrome	
B	Anterior cord syndrome	
C	Brown-Séquard syndrome	Disassociated sensory loss (of temperature and pain): from damage to the contralateral anterolateral tract Spastic paresis: from damage to the pyramidal tract Flaccid paresis: from damage to the anterior horn and segment level Complete loss of sensation: from damage to protopathic and epicritic sensibility at segment level Loss of proprioception and epicritic sensibility: from damage to the ipsilateral posterior tract
D	Central cord syndrome	

	Answer	Image
E	Posterior cord syndrome	
F	Spinal epidural hematoma	

Hint

This patient may also experience bowel and bladder dysfunction due to bilateral damage to the lateral horns of the spinal cord.

Correct Answer

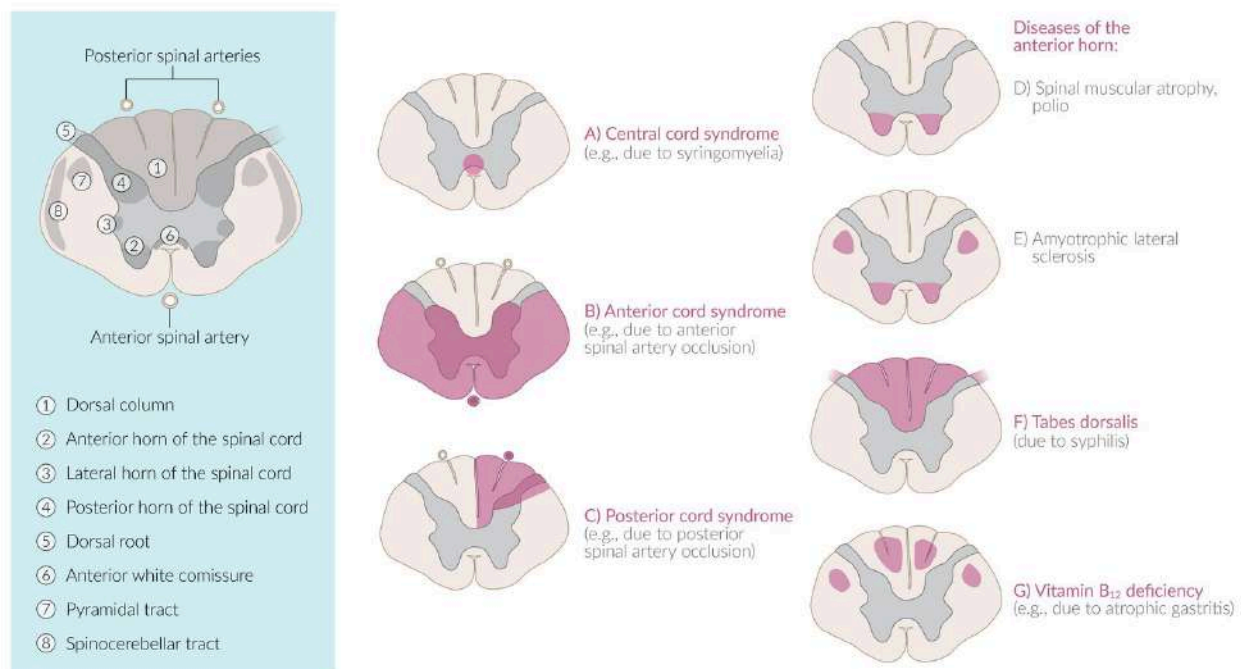
A - Leriche syndrome

Explanation Why

Leriche syndrome (i.e., **aortoiliac occlusive disease**) is caused by **peripheral artery disease** at the level of the **aortic bifurcation** or bilateral occlusion of the iliac arteries. This condition manifests as the triad of thigh/hip **claudication**, **erectile dysfunction**, and absent/diminished femoral pulses, which this patient does not have. Moreover, this patient presents with severe thoracolumbar **pain**, lower extremity numbness, and lower extremity muscle weakness, which would not be expected in **Leriche syndrome**.

B - Anterior cord syndrome

Image

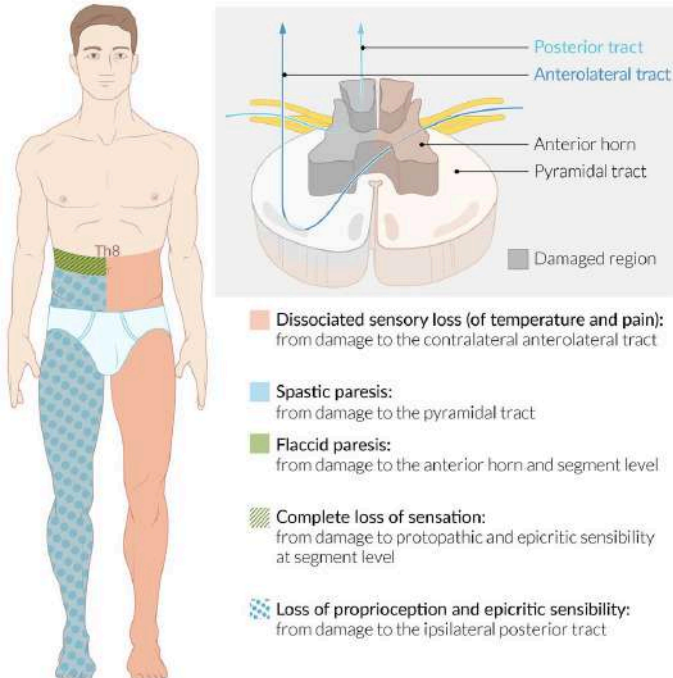


Explanation Why

[Anterior cord syndrome](#), which is caused by damage to the [anterior](#) $\frac{2}{3}$ of the [spinal cord](#), manifests bilaterally, with [lower motor neuron](#) deficit at the level of the lesion ([anterior horn](#) damage), and decreased [pain](#) and temperature sensation ([spinothalamic tract](#) damage) and [upper motor neuron](#) deficit ([lateral corticospinal tract](#) damage) below the level of the lesion. In [anterior cord syndrome](#), [proprioception](#) and [vibration sense](#) are preserved because the [posterior spinal arteries](#) provide blood supply to the [dorsal columns](#). [Anterior cord syndrome](#) may occur as a complication of an [aortic aneurysm](#) itself or [iatrogenically](#) during the repair of the [aneurysm](#) (due to damage to the [anterior spinal artery](#) and/or [artery of Adamkiewicz](#)). The thoracolumbar segment of the [spinal cord](#) is a [watershed area](#) and is, therefore, the most common site of [infarction](#), as seen here. Other causes of [anterior cord syndrome](#) include trauma (e.g., penetrating injury), [hypotension](#) (e.g., from severe hemorrhage), and compression (e.g., tumors, cervical [spondylosis](#)).

C - Brown-Séquard syndrome

Image



Explanation Why

[Brown-Séquard syndrome](#) occurs as a result of hemisection of the [spinal cord](#) and manifests as an

ipsilateral loss of [proprioception](#), fine touch, and [vibration sense](#) ([dorsal column](#) damage), contralateral loss of [pain](#) and temperature sensation ([spinothalamic tract](#) damage), ipsilateral [lower motor neuron](#) deficit at the level of the lesion ([anterior horn](#) damage), and ipsilateral [upper motor neuron](#) deficit below the level of the lesion ([corticospinal tract](#) damage). This is not consistent with the bilateral loss of [pain](#) and temperature sensation and bilateral weakness in lower extremities seen here. Moreover, this patient's [proprioception](#) and fine touch are intact bilaterally.

D - Central cord syndrome

Explanation Why

[Central cord syndrome](#) can manifest as bilateral loss of [pain](#) and temperature sensation (damage to the decussating fibers of the [spinothalamic tract](#) at the [anterior](#) white commissure) and bilateral paresis of the extremities (damage to [lateral corticospinal tracts](#)), as seen here. However, the paresis is usually worse in the upper extremities (especially the hands) when compared to the lower extremities (upper extremity tracts are more [medial](#) than lower extremity tracts). Moreover, [central cord syndrome](#) is commonly associated with [pain](#) and temperature loss in a “cape-like” distribution across the upper back and down the [posterior](#) upper extremities, which is not seen here.

E - Posterior cord syndrome

Explanation Why

[Posterior cord syndrome](#) affects the [dorsal columns](#). It would manifest as a loss of [proprioception](#), fine touch, and [vibration sense](#) below the level of the lesion, with preserved muscle strength and [pain](#) and temperature sensation, which is not consistent with this patient's presentation.

F - Spinal epidural hematoma

Explanation Why

[Spinal epidural hematoma](#) can cause acute [spinal cord compression](#) and manifest as back [pain](#) and lower extremity weakness and numbness, as seen in this patient. However, [spinal epidural hematoma](#) typically occurs following puncture of the [dura mater](#) that causes damage to the vertebral venous

plexus (e.g., following [lumbar puncture](#), after pulling a dural catheter) rather than following an [aortic aneurysm](#) repair.

Question # 28

A 41-year-old man with multiple sclerosis comes to the physician for a follow-up examination. After evaluation, the physician recommends the administration of baclofen to the patient. This drug is most likely to improve which of the following symptoms?

	Answer	Image
A	Paresthesias	
B	Spasticity	
C	Depression	
D	Erectile dysfunction	
E	Urinary incontinence	
F	Urinary retention	

Hint

Baclofen, a centrally acting γ -aminobutyric acid B (GABA_B) receptor agonist, exerts its effect on receptors in the brainstem and in the spinal cord's dorsal horn.

Correct Answer

A - Paresthesias

Explanation Why

Sudden, painful [paresthesias](#) of the face, trunk, and limbs can occur in patients with MS due to involvement of the [brainstem](#) and [dorsal spinal](#) column. [Baclofen](#) may cause [paresthesias](#), so it is not used to treat this symptom. MS-associated [paresthesias](#) are usually treated with [carbamazepine](#) and [amitriptyline](#).

B - Spasticity

Explanation But

Other [spasticity](#) treatments include [physiotherapy](#), [dantrolene](#), and [tizanidine](#).

Explanation Why

By activating the GABA_B receptors, [baclofen](#) decreases excitatory [neurotransmitter](#) release and lessens γ motor [neuron](#) excitability, which improves [spasticity](#), a common problem in patients with [multiple sclerosis](#) (MS). In individuals with MS, [spasticity](#) can cause impaired walking, make it harder to perform activities of daily living, and worsen fatigue. The aim of treatment for [spasticity](#) in patients with MS is to decrease muscle tone enough that function improves, but not reduce it to the point that safety is decreased. [Baclofen](#) is a supportive therapy (rather than a disease-modifying drug) for MS and can be administered either orally or intrathecally via a pump.

C - Depression

Explanation Why

Individuals with MS commonly have comorbid depression. Some of the factors that contribute to depression in patients with MS are anxiety, cognitive impairment, excessive sleepiness, [sexual](#)

[dysfunction](#), and [urinary incontinence](#). MS patients with depression are treated with [psychotherapy](#) and [antidepressants](#) ([SSRIs](#), [SNRIs](#), TCAs, or [bupropion](#)) instead of [baclofen](#).

D - Erectile dysfunction

Explanation Why

[Erectile dysfunction](#) is common in men with MS. Since [autonomic dysfunction](#) contributes to [erectile dysfunction](#) (and [GABA](#) is not involved), there would not be a role for [baclofen](#) in the treatment of this issue. [Erectile dysfunction](#) is treated with [phosphodiesterase-5 inhibitors](#) (e.g., [sildenafil](#)).

E - Urinary incontinence

Explanation Why

MS is associated with [bladder](#) problems such as [urinary incontinence](#), which is caused by [detrusor](#) overactivity due to impairment of the [detrusor](#) reflex. Since [GABA](#) is not involved, there would not be a role for [baclofen](#) in the treatment of [urinary incontinence](#). MS-associated [urinary incontinence](#) is treated with [antimuscarinic agents](#) (e.g., [oxybutynin](#)).

F - Urinary retention

Explanation Why

MS is associated with [bladder](#) problems such as [urinary retention](#). Since [autonomic dysfunction](#) contributes to the [urinary retention](#) (and [GABA](#) is not involved), there would not be a role for [baclofen](#) in the treatment of this issue. MS-associated [urinary retention](#) is treated with intermittent catheterization and [parasympathomimetic drugs](#) (e.g., [bethanechol](#)).

Question # 29

A 24-year-old man comes to the physician because of back pain after being severely sunburned on his upper back 3 days ago. He now experiences pain in the affected area when applying cream or putting on a shirt. Physical examination of the upper back shows erythema of the skin and some mild blistering. Sensitization of which of the following structures would best explain this patient's symptoms?

	Answer	Image
A	Glycinergic receptors of thalamic neurons	
B	Nociceptors of dorsal root	
C	Ruffini corpuscles of sensory neurons	
D	Glutaminergic receptors of ventral horn neurons	
E	Opioid synapses of interneurons	

Hint

This patient's symptoms are consistent with allodynia.

Correct Answer

A - Glycinergic receptors of thalamic neurons

Explanation Why

Glycinergic receptors on thalamic [neurons](#) play a role in the modulation of a painful stimulus. However, glycinergic receptors are inhibitory receptors and their [sensitization](#) would not contribute to [allodynia](#).

B - Nociceptors of dorsal root

Explanation Why

The nociceptors of the [dorsal](#) root are involved in the pathophysiology of dysfunctional perceptions of [pain](#), such as [allodynia](#). Although incompletely understood, [allodynia](#) is thought to result from both peripheral and [central sensitization](#). After an injury (e.g., [sunburn](#)), [cytokines](#), nerve growth factors, and other chemical mediators are released in the injured area, leading to a constant, increased input to the nociceptors. This causes an up-regulation of the ion channels in the nociceptors, making them more sensitive to chemical mediators and lowering the threshold to stimulus, consequently causing more [action potentials](#) to form. This phenomenon is known as [peripheral sensitization](#). The constant increased peripheral output is likely a significant driver to the [sensitization](#) of central [nociceptive neurons](#), which likely contributes to the persistence of [allodynia](#) long after the initial injury (e.g., in [postherpetic neuralgia](#)).

C - Ruffini corpuscles of sensory neurons

Explanation Why

[Ruffini corpuscles](#) are slow-adapting mechanoreceptors that are sensitive to mechanical pressure, [skin](#) stretching, and [joint](#)-angle changes. These receptors are not involved in the modulation of painful stimuli and would therefore not contribute to [allodynia](#). Moreover, [Ruffini corpuscles](#) are located in the fingertips and [joints](#) rather than the upper back.

D - Glutaminergic receptors of ventral horn neurons

Explanation Why

The [ventral horn](#) contains the bodies of the [lower motor neurons](#), for which the glutaminergic receptors provide excitatory stimulus. Because these [neurons](#) are involved with movement, not sensation, they do not contribute to [allodynia](#).

E - Opioid synapses of interneurons

Explanation Why

Interneurons located in the [dorsal horn](#) release endogenous [opioids](#) at their [synapses](#) to modulate painful stimuli. This process results in the inhibition of [neurotransmitter](#) release in the [synapses](#) between [dorsal horn neurons](#) and [dorsal root ganglion neurons](#). Therefore, these [synapses](#) provide inhibitory inputs and would not contribute to [allodynia](#).

Question # 30

A 65-year-old man is brought to the emergency department by his wife for the evaluation of a suspected stroke. He has a history of chronic hypertension. The patient's wife reports that he is right-handed. A noncontrast CT scan of the brain shows an acute cerebral infarction. A photograph of a transverse section of a normal brain is shown; the area that is affected by the infarction is indicated by the arrow. This patient most likely presented with which of the following findings on physical examination?



	Answer	Image
A	Weakness of the right leg	Head of caudate nucleus Anterior limb of internal capsule Genu of internal capsule Putamen Claustrum Extreme capsule External capsule Globus pallidus, lateral segment Globus pallidus, medial segment Tail of caudate nucleus Posterior limb of internal capsule Thalamic nuclei Third ventricle

	Answer	Image
B	Hemineglect of the right side	
C	Hemiballismus of the left side	
D	Paralysis of the left face	
E	Loss of sensation of the left arm	
F	Hemianopia of the right visual field	

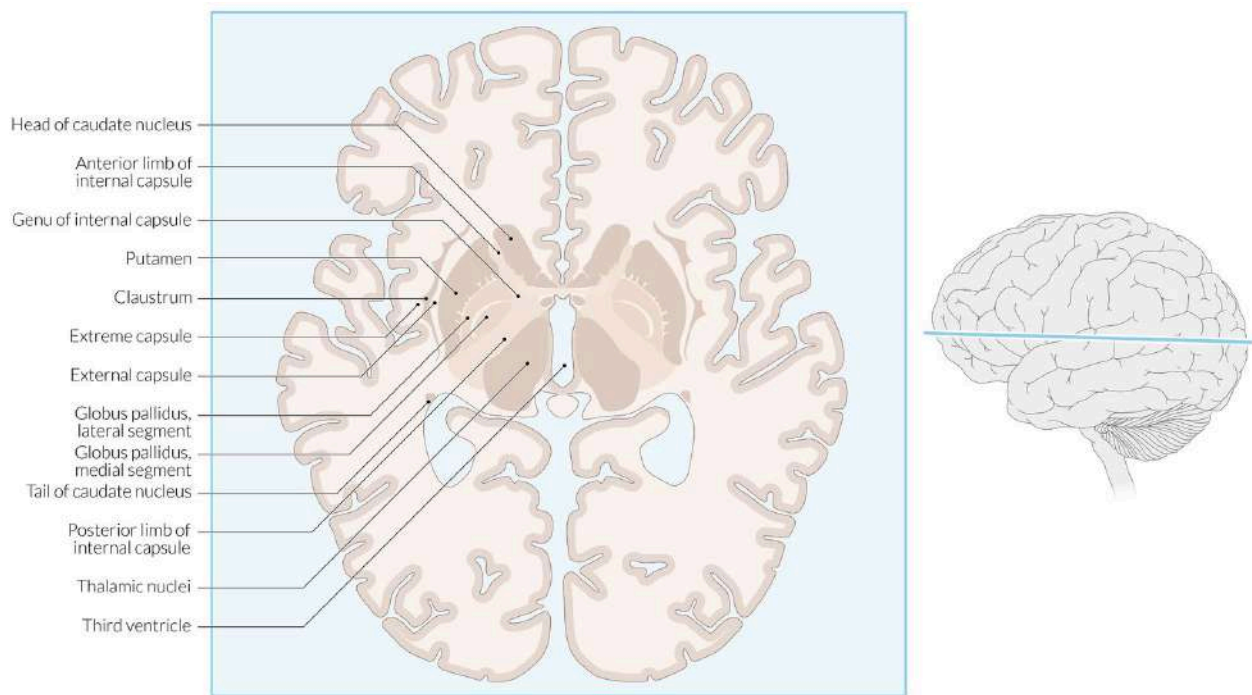
Hint

This arrow points at the posterior limb of the left internal capsule.

Correct Answer

A - Weakness of the right leg

Image



Explanation But

Other parts of the [internal capsule](#) include the [anterior](#) limb, which contains the thalamocortical tract, and the genu, which contains the corticobulbar tract.

Explanation Why

Weakness of the right leg is the most likely physical finding of a [lacunar infarction](#) of the [posterior](#) limb of the left [internal capsule](#), which is located between the [lentiform nucleus](#) ([basal ganglia](#)) and [thalamus](#) and contains the anterior corticospinal tract, [lateral corticospinal tract](#), and thalamocortical tract. Pure motor [hemiparesis](#), the most common type of [lacunar stroke](#), is caused by an isolated [infarction](#) of the [posterior](#) limb of the [internal capsule](#). Affected individuals present with contralateral [hemiparesis](#) (due to [corticospinal tract](#) damage) in the absence of cortical signs (e.g., [aphasia](#), [visual field](#) abnormalities). Chronic [hypertension](#), as seen in this patient, is a [risk factor](#) for [microatheroma](#) formation and [lipohyalinosis](#) in the poorly-collateralized small penetrating [arteries](#) of the brain (e.g., [lenticulostriate arteries](#)), which can result in [lacunar stroke](#).

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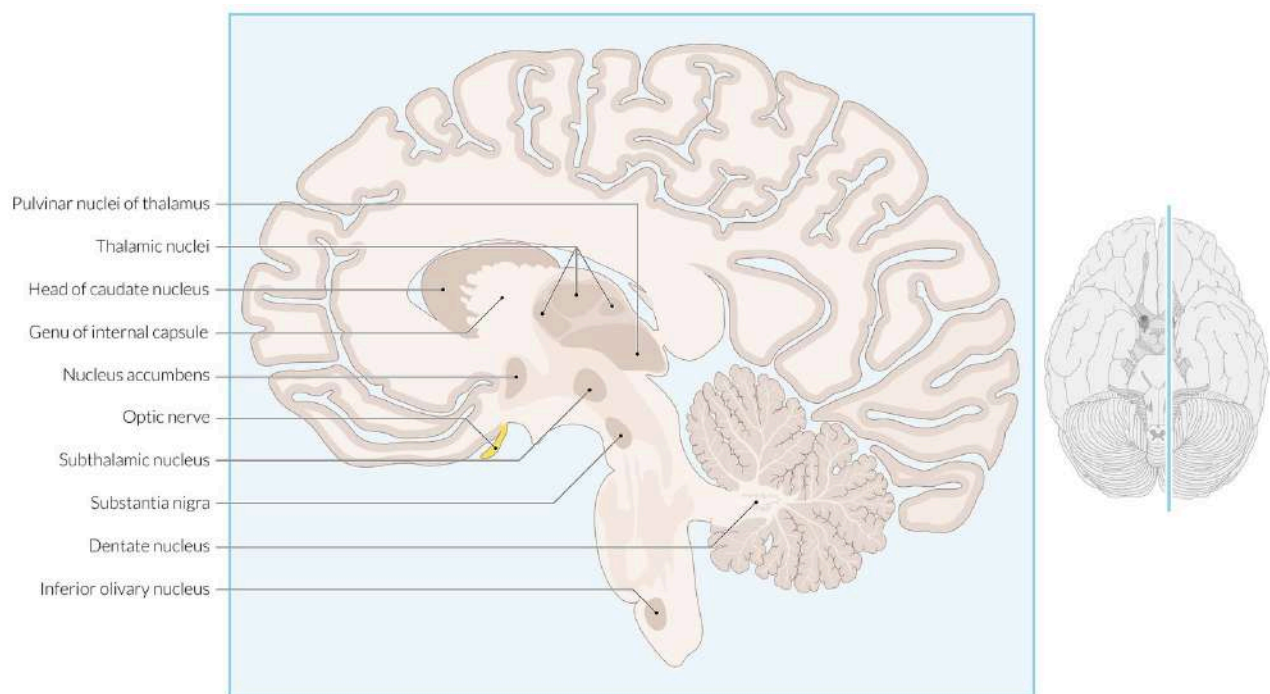
B - Hemineglect of the right side

Explanation Why

[Hemineglect](#) is most commonly caused by a lesion affecting the nondominant parietal cortex (which is typically the right parietal cortex in right-handed individuals). Consequently, right-handed individuals typically only present with [hemineglect](#) of the left side. Moreover, this patient has an [infarct](#) of a deep brain structure in the left hemisphere, not the right parietal cortex.

C - Hemiballismus of the left side

Image



Explanation Why

[Hemiballismus](#) is most commonly caused by a [lacunar stroke](#) involving the contralateral [subthalamic nucleus](#). The [subthalamic nuclei](#) are a pair of grey matter structures located [caudal](#) to the [thalamus](#),

[cranial](#) to the [substantia nigra](#) (part of the [midbrain](#)), and [medial](#) to the [internal capsule](#). The transverse section shown here is taken at the level of the [thalamus](#); the [subthalamic nuclei](#) are not visible in this section.

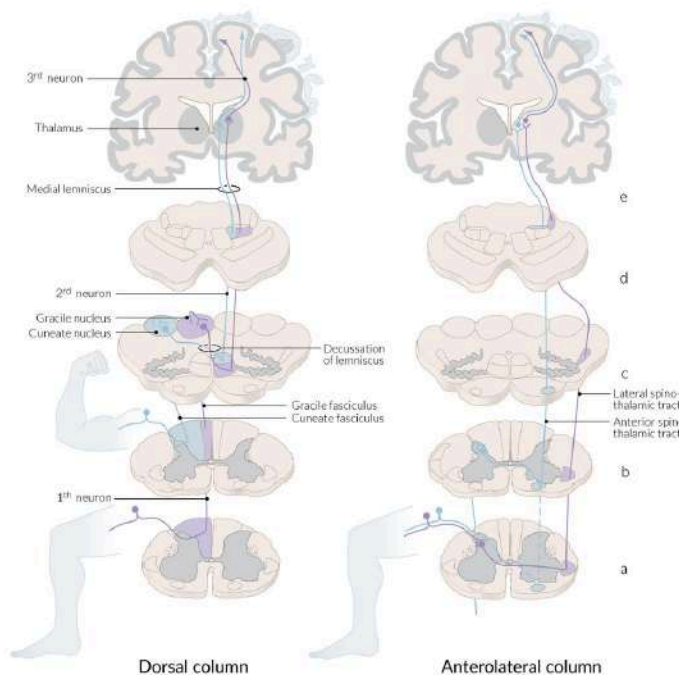
D - Paralysis of the left face

Explanation Why

An [infarct](#) of the [internal capsule](#) can manifest with hemifacial paralysis as a result of damage to the corticobulbar tracts that supply the facial motor nuclei. However, a left-sided [internal capsule infarct](#), as described here, would cause paralysis of the right rather than left lower facial muscles because the lower division of the facial nucleus receives [upper motor neuron](#) innervation from the contralateral corticobulbar tract. Moreover, corticobulbar tracts travel within the genu (flexure) of the [internal capsule](#), whereas the arrow is pointing at the [posterior](#) limb of the [internal capsule](#).

E - Loss of sensation of the left arm

Image

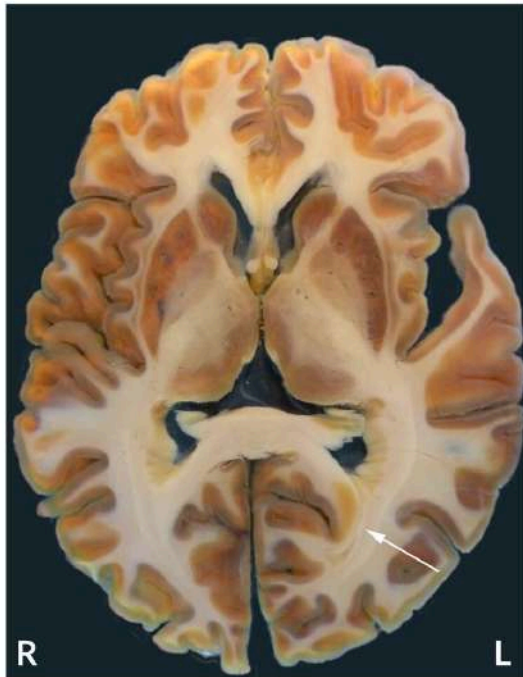


Explanation Why

An [infarct](#) involving the [posterior](#) limb of the [internal capsule](#) may manifest with a loss of arm sensation as a result of damage to the thalamocortical tract (which conveys somatosensory information from the contralateral body to the cortex). However, an [infarct](#) in the left [internal capsule](#), as depicted in the photograph, would cause loss of sensation of the right arm rather than the left.

F - Hemianopia of the right visual field

Image



Explanation Why

Hemianopia of the right [visual field](#) (i.e., right [homonymous hemianopia](#)) is most commonly caused by a post-chiasmal cortical lesion within the contralateral [optic tract](#), [optic radiation](#), or visual cortex (in the [occipital lobe](#)). Parts of the [optic radiations](#) and occipital lobes are seen on this transverse brain slice, but these structures are located in the [posterior](#) region of the slice. The arrow in the image points to a different structure.

Question # 31

A 2550-g (5 lb 10 oz) female newborn is delivered at term to a 27-year-old woman, gravida 1, para 1. Labor and delivery were uncomplicated but the mother did not receive prenatal care. Examination of the newborn shows hypotonia in the lower extremities and a red, fleshy swelling without overlying skin in the lumbosacral region. Clear yellow fluid leaks from the superior margin of the swelling. Ultrasonography of the swelling shows a fluid-filled sac containing herniated neural tissue. Which of the following best explains the pathogenesis of this patient's condition?

	Answer	Image
A	Failure of posterior neuropore closure	The diagram illustrates the pathogenesis of neural tube defects. It is divided into four columns: Normal, Spina bifida occulta, Meningocele, and Meningomyelocele. Each column shows a cross-section of the developing embryo and a corresponding longitudinal section of the spine. In the Normal column, the neural tube is shown closing properly, with labels for the vertebral arch, dura mater, spinal cord, and subarachnoid space. In the Spina bifida occulta column, a 'Dimple with hair' is shown on the skin surface, and 'Unfused laminae' are indicated in the vertebral arch. In the Meningocele column, a large fluid-filled sac is shown protruding from the vertebral arch. In the Meningomyelocele column, the sac is even larger and contains herniated neural tissue. The longitudinal sections show the progression of the defect from the skin surface down to the spinal cord and meninges.
B	Increase in cerebrospinal fluid pressure	
C	Nondisjunction of the neural tube and surface ectoderm	
D	Defect in neuronal migration	
E	Proliferation of totipotent germ cells	

	Answer	Image
F	Cystic dilation in the central canal	

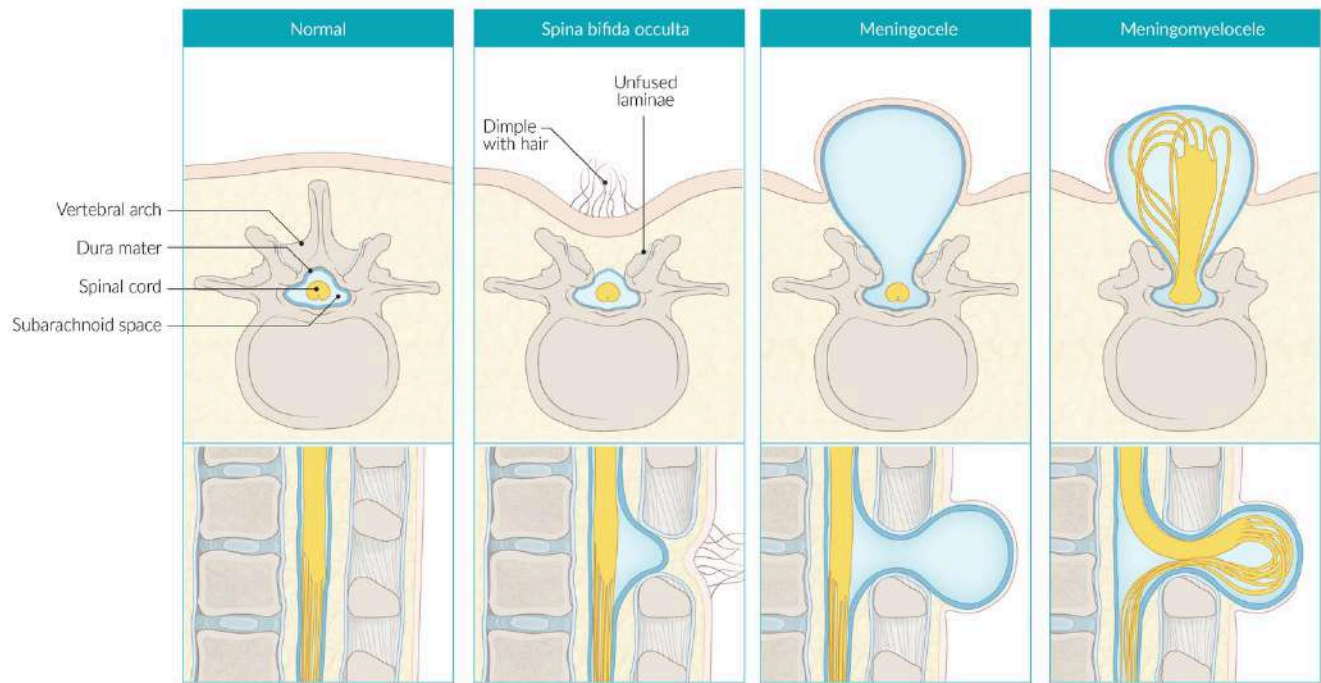
Hint

A lumbosacral swelling that is not covered by skin, leaks CSF, and contains neural tissue is suggestive of myelomeningocele.

Correct Answer

A - Failure of posterior neuropore closure

Image



Explanation But

[Anencephaly](#) is also a disorder of primary [neurulation](#), and results from the failure of the [anterior \(rostral\) neuropore](#) closure.

Explanation Why

[Myelomeningocele](#) is a disorder of primary [neurulation](#) that results from the failure of the [posterior \(caudal\) neuropore](#) to close at 3–4 weeks [gestation](#). While [myelomeningoceles](#) can usually be detected on routine prenatal [ultrasound](#) or [laboratory studies](#) (i.e., serum [α-fetoprotein](#)), this patient's mother did not receive any [prenatal care](#). Moreover, a [folate deficiency](#) due to a lack of prenatal [vitamins](#) is associated with an increased risk of [neural tube defects](#). Symptoms including lower extremity paralysis and sensory deficits, bowel and [bladder](#) dysfunction, and cognitive impairment are often present from [birth](#), as seen here. Additional evaluation, including a head [MRI](#), should be performed because approximately 95% of patients with [myelomeningocele](#) have an associated [Chiari II malformation](#).

B - Increase in cerebrospinal fluid pressure

Explanation Why

An increase in [cerebrospinal fluid](#) pressure can cause [hydrocephalus](#), which can occur concomitantly with [myelomeningocele](#) with a [Chiari II malformation](#). However, [hydrocephalus](#) alone would not explain the swelling containing neural tissue on this patient's lumbosacrum. Additionally, because the [fontanelles](#) in [infants](#) are open, neurological symptoms associated with [hydrocephalus](#) may not present at [birth](#). Moreover, once symptoms do present, [spasticity](#) and [hyperreflexia](#) would be expected, not [hypotonia](#).

C - Nondisjunction of the neural tube and surface ectoderm

Explanation Why

[Nondisjunction](#) of the [neural tube](#) and [surface ectoderm](#) would result in [spina bifida occulta](#), a disorder of secondary [neurulation](#). This [nondisjunction](#) results in failure to form the [posterior vertebral arch](#) and may result in lumbosacral swelling, as seen here. However, the [cerebrospinal fluid](#) and neural tissue are contained underneath a [skin](#) barrier in [spinal](#) bifida occulta and may only be noticeable by a dimple or tuft of [hair](#). Moreover, most patients with [spina bifida occulta](#) are asymptomatic, and [hypotonia](#) would not be expected.

D - Defect in neuronal migration

Explanation Why

Defective neuronal migration at 3–5 months [gestation](#) can cause [lissencephaly](#), which results in the underdevelopment of [gyri](#) and sulci in the brain. While [lissencephaly](#) can result in [hypotonia](#), a lumbosacral swelling containing neural tissue would not be expected. Moreover, additional signs and symptoms, including [microcephaly](#), ventriculomegaly, and craniofacial abnormalities, would be expected in a patient with [lissencephaly](#).

E - Proliferation of totipotent germ cells

Explanation Why

The [proliferation](#) of [totipotent](#) germ cells can result in the formation of germ cell tumors, which can also manifest with a protrusion. However, the most common germ cell tumors in [newborns](#) are sacrococcygeal teratomas, which manifest in the sacrococcygeal region, not the lumbosacral region. Moreover, no neural tissue would be expected to be present in the protrusion.

F - Cystic dilation in the central canal

Explanation Why

A cystic dilation in the central canal suggests [syringomyelia](#), which also causes [hypotonia](#) in the lower extremities. However, [syringomyelia](#) is most common in the cervical region, where symptoms often present in a cape-like distribution prior to manifesting in the lower extremities. Additionally, [syringomyelia](#) is not associated with a lumbosacral swelling containing neural tissue because the [syrinx](#) is most often located within the [spinal cord](#) and therefore not visible on the [skin](#). Moreover, this condition usually manifests at 30–40 years of age, rather than immediately postnatal.

Question # 32

A previously healthy 28-year-old man is brought to the emergency department 1 hour after the onset of a severe headache and sudden confusion. Five days ago, he returned from a 14-mile hike to a natural hot spring, where he spent the afternoon lounging in the water. On arrival, he is agitated and vomiting. His temperature is 39.4°C (102.9°F), pulse is 110/min, and blood pressure is 110/72 mm Hg. Physical examination shows flexion of the hips when the neck is flexed. A CT scan of the head with contrast shows basilar meningeal enhancement. A lumbar puncture is performed. Cerebrospinal fluid analysis shows:

Leukocyte count	340/mm ³
Erythrocyte count	250/mm ³
Glucose	15 mg/dL
Opening pressure	240 mm H ₂ O
Protein	45 mg/dL

A wet mount of centrifuged cerebrospinal fluid shows motile trophozoites. Which of the following is the most likely route of infection of the causal pathogen?

	Answer	Image
A	Contiguous spread to the meninges	
B	Inoculation by an arthropod vector	
C	Dissemination into the bloodstream	
D	Infiltration of intact skin	

	Answer	Image
E	Penetration of the cribriform plate	
F	Invasion of the oral mucosa	

Hint

This patient's acute onset of altered mental status, headache, fever, and physical examination showing Brudzinski sign suggests meningoencephalitis. His history of bathing in warm freshwater and the motile trophozoites seen on CSF analysis are consistent with *Naegleria fowleri* infection.

Correct Answer

A - Contiguous spread to the meninges

Explanation Why

Contiguous spread refers to the dissemination of pathogens through adjacent structures. The [meninges](#) are protected from the external environment by [cranial bones](#). A contiguous route of infection to the [meninges](#) is only possible if the [meninges](#) are exposed to the external environment by an opening in the [cranial](#) vault or fossa as a result of surgery (e.g., craniotomy), trauma, or infection (e.g., bacterial or fungal [sinusitis](#)), or if the [middle ear](#) is infected (allows contiguous spread to the [meninges](#) via the cochlear aqueduct). There is no history of recent paranasal or otologic infection, surgery, or trauma in this patient.

B - Inoculation by an arthropod vector

Explanation Why

Inoculation by an arthropod vector is the route of infection for [arboviral meningoencephalitis](#) (e.g., [St. Louis encephalitis](#), [West Nile meningoencephalitis](#)). Outdoor activities (e.g., hiking) increase risk for [arboviral](#) infections, and [arboviral meningoencephalitis](#) causes some of this patient's [CSF](#) findings (e.g., [pleocytosis](#), high opening pressure, increased protein) and similar clinical features. However, [arboviral meningoencephalitis](#) usually has a biphasic course; features of [meningoencephalitis](#) (e.g., confusion, vomiting, Brudzinksi sign) would have been preceded by several days of [flu-like](#) symptoms, which were not present in this patient. Moreover, viral [meningoencephalitis](#) typically does not cause hypoglycorrhachia or CSF erythrocytosis, and the presence of [trophozoites](#) in [CSF](#) indicates a protozoal rather than viral infection.

C - Dissemination into the bloodstream

Explanation Why

Dissemination into the bloodstream is the route of infection for pathogens that cause primary bloodstream infections (e.g., catheter-associated bloodstream infections, bloodstream infections in

injection drug users, [transfusion](#)-transmitted infections). Examples of such pathogens include certain bacteria (e.g., coagulase-negative [staphylococci](#), *S. aureus*, *Enterobacter* spp.), fungi (e.g., *Candida*), and viruses (e.g., [hepatitis C virus](#)). This patient with [trophozoites](#) in [CSF](#) has a protozoal [meningoencephalitis](#), which is not caused by dissemination in the bloodstream.

D - Infiltration of intact skin

Explanation Why

Infiltration of intact [skin](#) is the route of infection of *Schistosoma* spp., which are found in freshwater. This patient has a recent history of bathing in freshwater but patients having [schistosomiasis](#) present several weeks to months after the initial exposure with [liver fibrosis](#) and [portal hypertension](#) (*S. mansoni* infection), or [dysuria](#) and [hematuria](#) (*S. hematobium* infection), unlike this patient who presents with [meningoencephalitis](#) a few days after bathing in freshwater. Moreover, this patient has no travel history to sub-Saharan Africa, where *Schistosoma* spp. are [endemic](#). The causal pathogen in this case is not transmitted by [skin](#) infiltration.

E - Penetration of the cribriform plate

Explanation Why

Naegleria fowleri is a thermophilic amoeba that can be found in warm freshwater (e.g., hot springs). Transmission occurs when contaminated water enters the nasal cavity (e.g., during swimming or diving). [Trophozoites](#) of *N. fowleri* penetrate the olfactory mucosa and the cribriform plate to reach the [olfactory bulb](#) and subsequently spread to the brain. *N. fowleri* consumes [glial cells](#) and causes a rapidly progressing, fulminant, necrotizing [meningoencephalitis](#). [CSF analysis](#) would show features similar to those of bacterial [meningitis](#) (e.g., neutrophilic [pleocytosis](#), hypoglycorrhachia, increased [CSF](#) protein), [trophozoites](#), and possibly CSF erythrocytosis (due to hemorrhagic [necrosis](#)), as seen here. Although very rare, *N. fowleri* [meningoencephalitis](#) ([primary amebic meningoencephalitis](#)) has a [mortality rate](#) of almost 100%. [Amphotericin B](#) has been shown to be effective for a few patients.

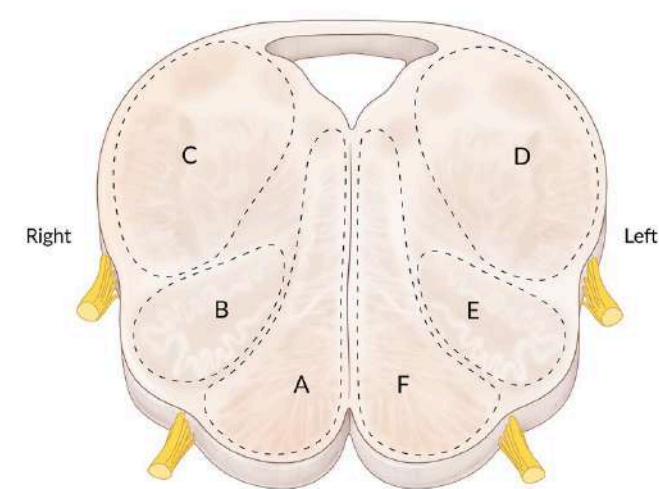
F - Invasion of the oral mucosa

Explanation Why

Invasion of the oral mucosa is the route of infection of [herpes simplex virus 1 \(HSV-1\)](#). [HSV encephalitis](#) manifests with most of this patient's [CSF](#) findings ([pleocytosis](#), high opening pressure, increased protein, CSF erythrocytosis) and similar clinical features. However, [HSV encephalitis](#) typically affects the frontal and [temporal lobe](#), and patients with this condition usually have enhancement of these brain regions on contrast imaging, as well as behavioral changes and dysphasia, none of which are seen here. Moreover, viral encephalitis typically does not cause hypoglycorrhachia, and the presence of [trophozoites](#) in [CSF](#) indicates a protozoal rather than viral infection.

Question # 33

A 69-year-old man is brought to the emergency department because of right-sided body weakness for 1 hour. Neurologic examination shows deviation of the tongue to the left when protruded and decreased sensation to vibration and position in the right extremities. Muscle strength is 2/5 in the right lower extremity and 1/5 in the right upper extremity. Plantar reflex shows an extensor response on the right side. A CT scan of the head and neck shows a brainstem lesion. A schematic section of the brainstem at the level of the medulla oblongata is shown. The patient's symptoms are most likely to be caused by a lesion in which of the following labeled areas?



	Answer	Image
A	A	
B	B	
C	C	

	Answer	Image
D	D	
E	E	
F	F	The diagram illustrates the medulla oblongata in cross-section, highlighting the nuclei of cranial nerves III, IV, V, VI, VII, VIII, IX, X, XI, and XII. It also shows the pyramidal tract and the olivary complex. A legend identifies the color coding for efferent and afferent pathways: red for general somatic efferent, yellow for general visceral efferent, orange for special visceral efferent, green for general somatic afferent, dark green for special somatic afferent, light blue for general visceral afferent, and dark blue for special visceral afferent. Labels include: 4th ventricle, Nucleus of hypoglossal nerve, Dorsal nucleus of vagus nerve, Solitary nucleus, Vestibular nuclei, Spinal trigeminal nucleus, Nucleus ambiguus, Vagus nerve, Hypoglossal nerve, Olivary complex, and Pyramidal tract.

Hint

This transverse section is taken from the cranial portion of the medulla oblongata, as evidenced by the visibility of the fourth ventricle in the posterior aspect and the emergence of hypoglossal nerves and vagus nerves (from the preolivary sulci and postolivary sulci respectively) in the anterior aspect. Occlusion of the paramedian branches of the anterior spinal artery can cause infarction of the area affected in this patient.

Correct Answer

A - A

Explanation Why

This area contains the right [pyramidal tract](#), right [medial lemniscus](#), and [axons](#) of the right hypoglossal nucleus. Opposite to the presentation seen in this patient, a lesion in this region would cause [hemiparesis](#) and hemisensory loss on the left (rather than the right) side of the body, and the [tongue](#) would deviate to the right (rather than left) upon protrusion.

B - B

Explanation Why

This area identifies the right [inferior olivary nucleus](#) (ION), which provides innervation to the contralateral (i.e., left) [cerebellar](#) nuclei. The [cerebellar](#) nuclei control motor coordination in the ipsilateral half of the body. Damage to the right ION would cause anterograde transneuronal degeneration of the left [cerebellar](#) nuclei and therefore present with left-sided hemiataxia rather than the right-sided [hemiparesis](#) and [hypoglossal nerve palsy](#) seen in this patient.

C - C

Explanation Why

This area contains the right [lateral spinothalamic tract](#), spinal trigeminal nucleus, [nucleus ambiguus](#), [vestibular nuclei](#), and [sympathetic](#) fibers. Damage to the right [lateral spinothalamic tract](#) and the right spinal trigeminal nucleus causes left-sided loss of [pain](#) and temperature sensations, unlike the right-sided loss of [proprioception](#) and vibration sensation that are seen here. In addition, [hemiparesis](#) or deviation of the [tongue](#) are inconsistent with a lesion in this region. Instead, other features of an ipsilateral [lateral medullary syndrome](#) ([Wallenberg syndrome](#)) such as right-sided [palate](#) weakness (deviation of the uvula to the left), nystagmus, [vertigo](#), and right-sided [Horner syndrome](#) would be expected.

D - D

Explanation Why

This area contains the left [lateral spinothalamic tract](#), spinal trigeminal nucleus, [nucleus ambiguus](#), [vestibular nuclei](#), and [sympathetic](#) fibers. Damage to the left [lateral spinothalamic tract](#) and the left spinal trigeminal nucleus causes contralateral (i.e., right-sided) hemisensory loss, which is seen here, but [pain](#) and temperature sensations rather than [proprioception](#) and vibration would also be affected. In addition, [hemiparesis](#) or deviation of the [tongue](#) is not consistent with a lesion in this region. Instead, other features of an ipsilateral [lateral medullary syndrome](#) ([Wallenberg syndrome](#)) such as left-sided [palate](#) weakness (deviation of the uvula to the right), nystagmus, [vertigo](#), and left-sided [Horner syndrome](#) would be expected.

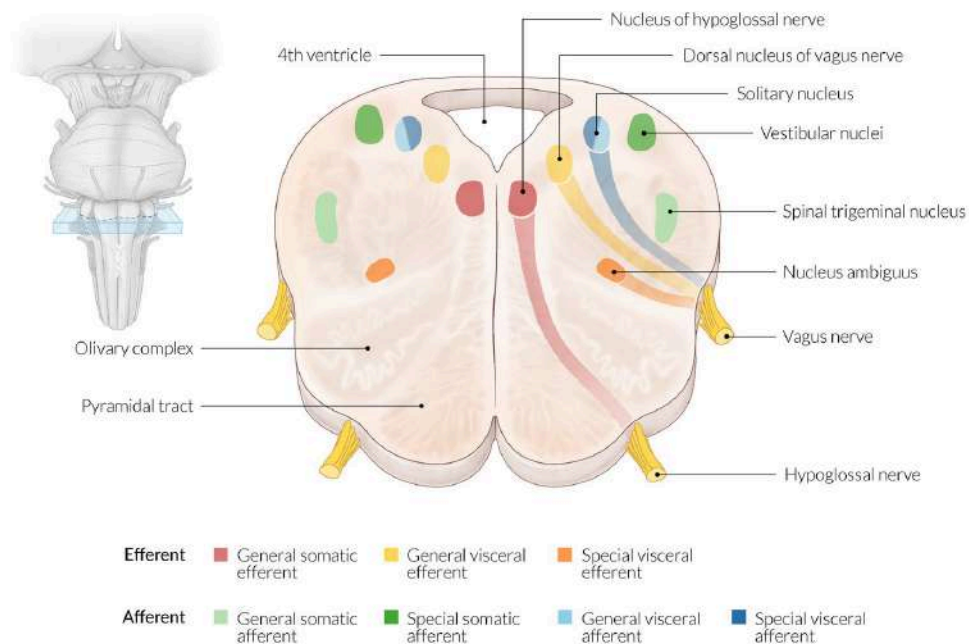
E - E

Explanation Why

This area corresponds to the left [inferior olivary nucleus](#) (ION), which provides innervation to the contralateral (i.e., right) [cerebellar](#) nuclei. The [cerebellar](#) nuclei control motor coordination in the ipsilateral half of the body. Damage to the left ION causes anterograde transneuronal degeneration of the right [cerebellar](#) nuclei and therefore presents with right-sided hemiataxia. [Hemiparesis](#) and [hypoglossal nerve palsy](#), as seen in this patient, are inconsistent with a lesion in this area.

F - F

Image



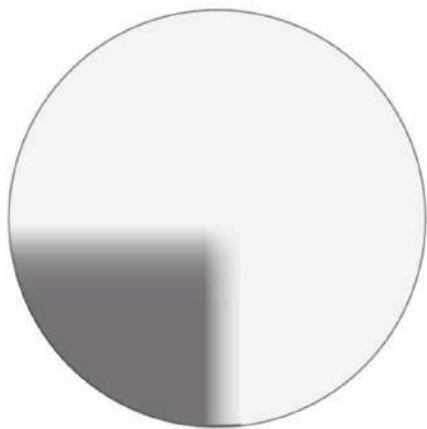
Explanation Why

This area contains the left [pyramidal tract](#) (descending motor tract) and left [medial lemniscus](#) (an ascending sensory tract) at the level of the [cranial medulla](#) (i.e., level of the [inferior olivary nuclei](#)). At this level, the [pyramidal tract](#) and [medial lemniscus](#) have not yet decussated to the contralateral side. A lesion in this area causes [medial medullary syndrome](#) with features of [upper motor neuron hemiparesis](#) as well as a loss of [proprioception](#), vibration, and fine touch in the contralateral (i.e., right) side of the body, as seen here. In addition, the [axons](#) of the ipsilateral (i.e., left) [hypoglossal nerve](#) (CN XII) pass through this area; damage to these fibers causes ipsilateral intrinsic [tongue](#) muscle weakness, which manifests as a deviation of the [tongue](#) to the side of weakness.

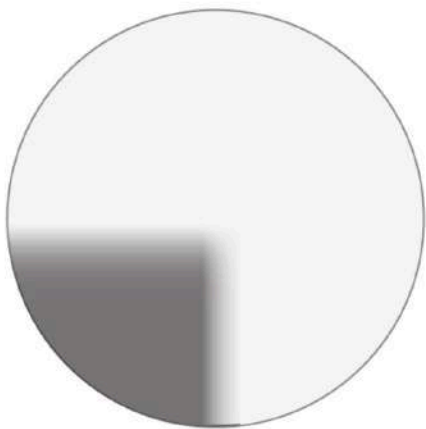
Question # 34

A 62-year-old man comes to the physician because of a 2-week history of cough, fatigue, impaired vision, and progressive headaches. He has smoked 2 packs of cigarettes daily for the last 38 years. After a thorough diagnostic workup, a diagnosis of metastatic lung cancer is made. A schematic overview of the patient's visual fields is shown. This patient is most likely to have a metastatic lesion in which of the following locations of the visual pathway?

Left eye



Right eye



	Answer	Image
A	Right Meyer loop	
B	Left Meyer loop	
C	Left dorsal optic radiation	

	Answer	Image																								
D	Left optic tract																									
E	Right dorsal optic radiation	Site of injury Visual field defects <table border="1"> <thead> <tr> <th></th> <th>L</th> <th>R</th> </tr> </thead> <tbody> <tr> <td>1 Left optic nerve</td> <td>Complete blindness</td> <td>Complete blindness</td> </tr> <tr> <td>2 Medial portion of the optic chiasm</td> <td>Superior and inferior quadrants</td> <td>Superior and inferior quadrants</td> </tr> <tr> <td>3 Left optic tract</td> <td>Complete blindness</td> <td>Complete blindness</td> </tr> <tr> <td>4 Lower bundle (Meyer's loop) of the left optic radiation</td> <td>Superior temporal quadrant</td> <td>Complete blindness</td> </tr> <tr> <td>5 Upper bundle of the left optic radiation</td> <td>Superior nasal quadrant</td> <td>Complete blindness</td> </tr> <tr> <td>6 Anterior portion of the calcarine sulcus and adjacent visual cortex</td> <td>Superior temporal quadrant</td> <td>Superior temporal quadrant</td> </tr> <tr> <td>7 Left occipital pole</td> <td>Complete blindness</td> <td>Complete blindness</td> </tr> </tbody> </table> Visual field diagram: Shows the nasal and temporal fields of vision for both eyes. Lines connect injury sites to the corresponding defects: 1 (Left optic nerve) to complete blindness; 2 (Medial portion of the optic chiasm) to superior and inferior quadrants; 3 (Left optic tract) to complete blindness; 4 (Lower bundle of the left optic radiation) to superior temporal quadrant; 5 (Upper bundle of the left optic radiation) to superior nasal quadrant; 6 (Anterior portion of the calcarine sulcus and adjacent visual cortex) to superior temporal quadrant; 7 (Left occipital pole) to complete blindness.		L	R	1 Left optic nerve	Complete blindness	Complete blindness	2 Medial portion of the optic chiasm	Superior and inferior quadrants	Superior and inferior quadrants	3 Left optic tract	Complete blindness	Complete blindness	4 Lower bundle (Meyer's loop) of the left optic radiation	Superior temporal quadrant	Complete blindness	5 Upper bundle of the left optic radiation	Superior nasal quadrant	Complete blindness	6 Anterior portion of the calcarine sulcus and adjacent visual cortex	Superior temporal quadrant	Superior temporal quadrant	7 Left occipital pole	Complete blindness	Complete blindness
	L	R																								
1 Left optic nerve	Complete blindness	Complete blindness																								
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7 Left occipital pole	Complete blindness	Complete blindness																								
F	Left macula																									
G	Right optic tract																									
H	Right macula																									

Hint

This patient's visual field defects indicate a lesion in the parietal lobe.

Correct Answer

A - Right Meyer loop

Explanation Why

The inferior bundle of right [optic radiations](#) (right Meyer loop) is located in the right [temporal lobe](#) and transmits visual information from the left superior quadrants of the [visual field](#) (i.e., from the [right lower quadrant](#) of both [retinas](#)). Therefore, damage to the right Meyer loop would result in left upper [homonymous quadrantanopsia](#) (“pie in the sky”), which does not correspond to the visual defect seen in this patient.

B - Left Meyer loop

Explanation Why

The inferior bundle of left [optic radiations](#) (left Meyer loop) is located in the left [temporal lobe](#) and transmits visual information from the right superior quadrants of the [visual field](#) (i.e., from the [left lower quadrant](#) of both [retinas](#)). Therefore, damage to the left Meyer loop would result in right upper [homonymous quadrantanopsia](#) (“pie in the sky”), which does not correspond to the visual defect seen in this patient.

C - Left dorsal optic radiation

Explanation Why

The superior bundle of left [optic radiations](#) (left dorsal optic radiation) is located in the left [parietal lobe](#) and relays information from the right inferior quadrants of the [visual field](#) (i.e., from the left superior quadrant of both [retinas](#)). Therefore, damage to the left superior bundle of [optic radiations](#) results in right lower [homonymous quadrantanopsia](#), which does not correspond to the visual defect seen in this patient.

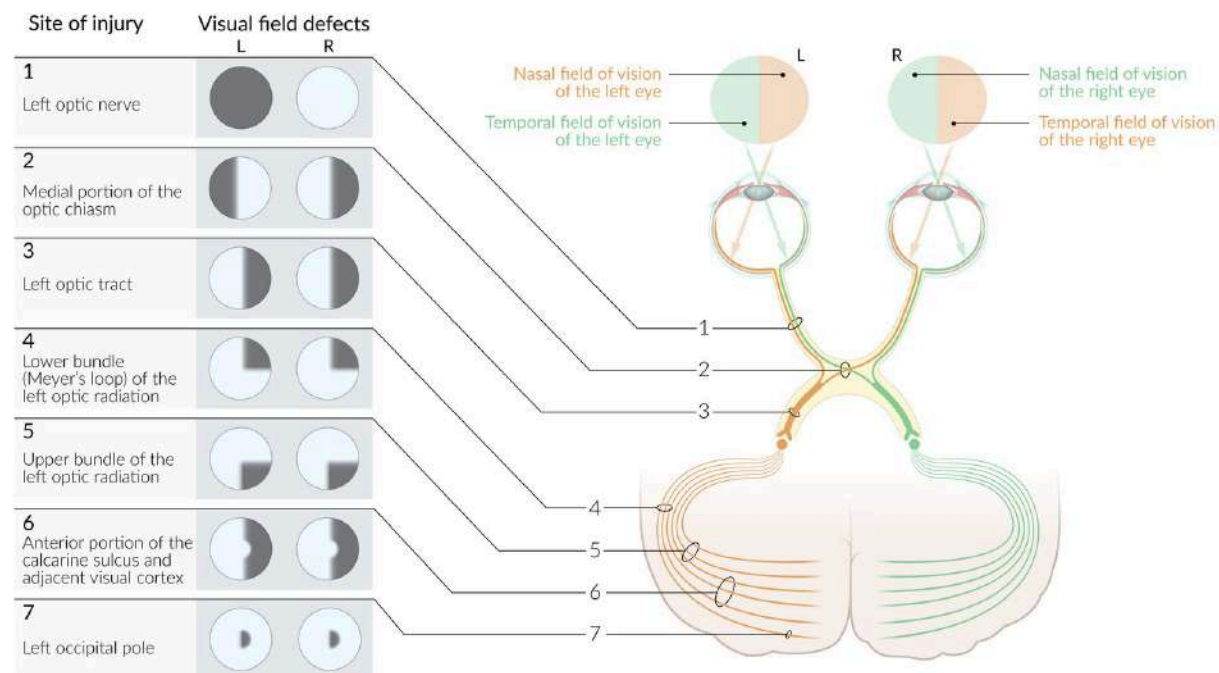
D - Left optic tract

Explanation Why

The left [optic tract](#) transmits information from the right half of each [eye's visual field](#) (i.e., from the temporal half of the left [retina](#) and nasal half of the right [retina](#)). Therefore, damage to the left [optic tract](#) would result in right [homonymous hemianopsia](#), which is not seen here.

E - Right dorsal optic radiation

Image



Explanation Why

The [visual pathway](#) transmits visual information from the [retina](#) to the visual cortex ([Brodmann area 17](#)) through the [optic nerve](#), [optic chiasm](#), [optic tract](#), [lateral geniculate nucleus](#), and [optic radiations](#). The superior bundle of right [optic radiations](#) (right dorsal optic radiation) relays information from the left inferior quadrants of the [visual field](#), i.e., from the right superior quadrant of both [retinas](#).

Therefore, damage to the right superior bundle of [optic radiations](#) would produce left lower [homonymous quadrantanopsia](#) (“pie on the floor”), as seen here.

F - Left macula

Explanation Why

The left [macula](#) transmits visual information from the center of the left [eye's visual field](#). Therefore, damage to the right [macula](#) (e.g., due to [macular degeneration](#)) would result in a left [central scotoma](#), which does not correspond to the visual defect seen in this patient.

G - Right optic tract

Explanation Why

The right [optic tract](#) transmits information from the left half of each [eye's visual field](#) (i.e., from the nasal half of the left [retina](#) and temporal half of the right [retina](#)). Therefore, damage to the right [optic tract](#) would result in left [homonymous hemianopsia](#), which is not seen here.

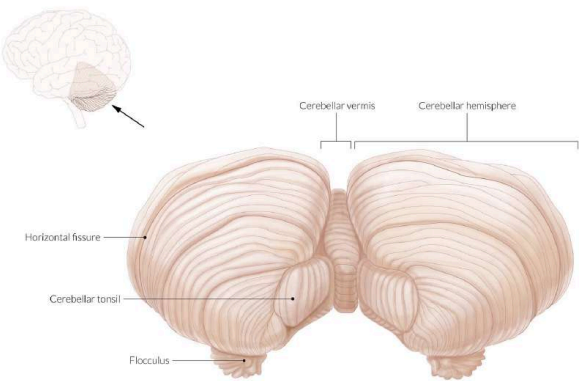
H - Right macula

Explanation Why

The right [macula](#) transmits visual information from the center of the right [eye's visual field](#). Therefore, damage to the right [macula](#) (e.g., due to [macular degeneration](#)) would result in a right [central scotoma](#), which does not correspond to the visual defect seen in this patient.

Question # 35

A 72-year-old woman is brought to the emergency department because of sudden-onset neck pain, nausea, vomiting, and difficulty walking for the past hour. She cannot sit upright without propping herself up on her hands. She has a history of hypertension, type 2 diabetes mellitus, and atrial fibrillation. She does not smoke. She drinks a glass of wine every other evening. Current medications include enalapril, hydrochlorothiazide, metformin, and warfarin. She is 162 cm (5 ft 4 in) tall and weighs 68 kg (150 lb); BMI is 27 kg/m². Her temperature is 37°C (98.6°F), pulse is 103/min, and blood pressure is 205/148 mm Hg. Neurologic examination shows downbeat nystagmus, neck stiffness, head bobbing, and a broad-based gait. She is unable to perform a balance test or Romberg test. The most likely cause of this patient's condition is an injury to which of the following areas?

	Answer	Image
A	Posterior spinal cord	
B	Pyramidal tract	
C	Cerebellar vermis	
D	Flocculonodular lobe	
E	Frontal lobe	

	Answer	Image
F	Cerebellar hemisphere	

Hint

Sudden-onset headache and nonspecific neurologic symptoms (e.g., meningismus, headache, nausea, vomiting) in a hypertensive patient on anticoagulation are highly suspicious for the development of intracerebral hemorrhage.

Correct Answer

A - Posterior spinal cord

Explanation Why

The [posterior spinal cord](#) carries the [dorsal column](#), which is responsible for [proprioception](#) and sensation of pressure, vibration, and fine touch. Injury to the [posterior spinal cord](#) can, therefore, cause [sensory ataxia](#) that is worse in dimly lit settings, where a patient's [proprioception](#) cannot compensate for the loss of visual bearings. However, this patient's broad-based gait and inability to perform a [Romberg test](#) are not environment-dependent. In addition, there is no indication that she has other sensory deficits. Moreover, [posterior spinal cord](#) injury is not associated with nystagmus, head bobbing, or [truncal ataxia](#) (e.g., inability to sit upright without propping oneself up on the hands).

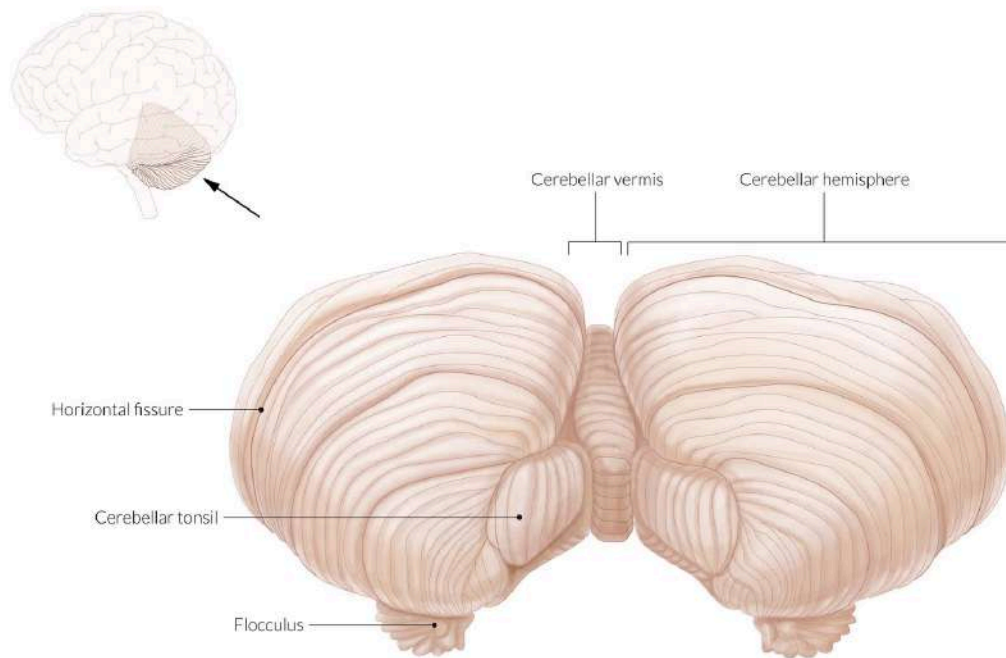
B - Pyramidal tract

Explanation Why

The [pyramidal tracts](#) control voluntary muscular movement to the face via the corticobulbar tract and to the body via the [corticospinal tract](#). Injury to the corticobulbar tract typically results in manifestations of [pseudobulbar palsy](#) (e.g., [dysarthria](#), [dysphagia](#), lack of facial expression). Injury to the [corticospinal tract](#) classically manifests with [upper motor neuron signs](#) (e.g., [spasticity](#), hypertonia, [hyperreflexia](#), [clonus](#), [Babinski sign](#)) on the contralateral side. This patient's [neurologic examination](#) is not consistent with injury to either [pyramidal tract](#).

C - Cerebellar vermis

Image



Explanation Why

The [cerebellar vermis](#) is a midline structure of the [cerebellum](#) that is involved in the coordination of the [vestibular system](#), [eye](#) movements, balance, and complex and sequential movements. This patient's findings of [downbeat nystagmus](#), head bobbing, and [truncal ataxia](#) (evidenced by her inability to sit upright without propping herself up on her hands) indicate that the site of injury is the [cerebellar vermis](#). Lesions of the [medial](#) parts of the [cerebellum](#) ([vermis](#), [flocculonodular lobe](#), and corresponding deep nuclei) affect [medial](#) structures of the body (e.g., axial and [proximal](#) limb musculature), resulting in [truncal ataxia](#) and nystagmus. Lesions of the [lateral](#) parts of [cerebellum](#) (hemispheres) affect [lateral](#) structures of the body (e.g., [distal](#) limb musculature), resulting in ipsilateral [limb ataxia](#).

D - Flocculonodular lobe

Explanation Why

The [flocculonodular lobe](#) is a midline [cerebellar](#) structure involved in regulating balance, ocular movements, and gaze stability. Midline [cerebellar](#) injury can cause head bobbing, [truncal ataxia](#) (e.g., inability to sit upright without propping oneself up on the hands), and nystagmus. However, [flocculonodular lobe](#) injury is typically associated with upbeat or rebound nystagmus, not the [downbeat nystagmus](#) seen in this patient, and usually manifests with [vertigo](#).

E - Frontal lobe

Explanation Why

The [frontal lobe](#) is involved in several processes, including motor function, [memory](#), and attention. Injury to the bilateral parts of the [frontal lobe](#) can result in a [frontal gait](#), which manifests with a broad-based gait and difficulty with balance. However, a [frontal lobe](#) injury also typically causes problems with initiating gait, slow steps, and inappropriate compensatory mechanisms for changes in posture while walking. In addition, [frontal lobe](#) injury is also associated with the reemergence of [primitive reflexes](#) and deficits in concentration and [judgment](#). Moreover, conditions that cause bilateral [frontal lobe](#) injury, such as [Alzheimer dementia](#), [frontotemporal dementia](#), and [normal pressure hydrocephalus](#), commonly manifest in a more chronic to subacute timeframe.

F - Cerebellar hemisphere

Explanation Why

The right and left [cerebellar hemispheres](#) are involved in complex motor functions that involve the limbs. [Cerebellar hemisphere](#) injury can cause loss of balance but does not typically result in downbeat nystagmus, head bobbing, or [truncal ataxia](#) (e.g., inability to sit upright without propping oneself up on the hands). Moreover, this patient does not have other common manifestations of [cerebellar hemisphere](#) injury, including [limb ataxia](#) (e.g., [dysmetria](#), [dysdiadochokinesis](#), [hypotonia](#), [intention tremor](#)), which typically affects the ipsilateral side, and [dysarthria](#).

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