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EPILEPSY BOARD REVIEW MANUAL

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Statement of Editorial Purpose

The Epilepsy Board Review Manual is a study guide for trainees and practicing physicians preparing for board examinations in epilepsy. Each manual reviews a topic essential to the current management of patients with epilepsy.

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Review of Topics: Pathophysiology and Principles of Diagnosis; Electrophysiological Diagnosis; Structural Brain Imaging; and Antiepilepsy Drugs

SEIZURES AND EPILEPSY: PATHOPHYSIOLOGY AND PRINCIPLES OF DIAGNOSIS

Thomas R. Henry, MD

[Scroll down for answers and explanations, which appear after question 5.]

QUESTIONS

1. A full-term male neonate has repeated tonic seizures and the electroencephalogram (EEG) shows a generalized burst-suppression pattern interictally. What is the likely diagnosis?

A. Benign familial neonatal epilepsy
B. Early myoclonic encephalopathy
C. Ohtahara syndrome
D. West syndrome
E. Myoclonic epilepsy in infancy

2. A full-term female infant at 10 months has normal development, single or clustered focal or massive jerks, and a normal interictal EEG. What is the likely diagnosis?

A. Epilepsy of infancy with migrating focal seizures
B. West syndrome
C. Myoclonic epilepsy in infancy
D. Dravet syndrome
E. Progressive myoclonus epilepsy

3. A 5-year-old boy has new onset of generalized tonic-clonic seizures as well as seizures with emesis and unresponsiveness. The interictal EEG shows generalized 3-per-second spike-wave bursts and bilateral occipital spikes. What is the likely diagnosis?

A. Lennox-Gastaut syndrome
B. Childhood absence epilepsy
C. Benign epilepsy with centrotemporal spikes
D. Panayiotopoulos syndrome
E. Epilepsy with myoclonic absences

4. A 25-year-old graduate student has a first generalized tonic-clonic seizure after staying up all night to study, has a negative urine toxicology screen in the emergency department, and has a normal cranial computed tomography (CT) scan. Later in the neurology clinic, on further questioning she reports that for the last year she has had multifocal jerks on mornings after staying up late. The brain magnetic resonance imaging (MRI) study shows subtle bifrontal subcortical white matter signal changes. The interictal EEG is normal except for a single brief burst of diffuse, bifrontally predominant spike-wave complexes repeating at about 4 Hz. What is the likely diagnosis?

A. Juvenile absence epilepsy
B. Juvenile myoclonic epilepsy
C. Progressive myoclonus epilepsy
D. Autosomal-dominant nocturnal frontal lobe epilepsy
E. Rasmussen syndrome

5. A 28-year-old cafeteria worker has a history of febrile convulsions in early childhood and poor school performance. No seizures have occurred for many years off antiseizure medications, until a generalized tonic-clonic seizure is observed at work. In retrospect,
the patient has had intense “daydreams” at work or home for the last year, and others often have had to repeat his name to get him to answer. The interictal EEG shows frequent delta-theta transients over the right temporal lobe and occasional right temporal spike-wave complexes. On brain MRI the right hippocampus is smaller and brighter than the left hippocampus. What is the likely diagnosis?

A. Epilepsy with generalized tonic-clonic seizures alone
B. Autosomal dominant epilepsy with auditory features
C. Lennox-Gastaut syndrome
D. Gelastic seizures with hypothalamic hamartoma
E. Mesial temporal lobe epilepsy with hippocampal sclerosis

**ANSWERS**

1. **The correct answer is (C), Ohtahara syndrome.** Only the syndromes in answers A, B, and C—benign familial neonatal epilepsy (BFNE), early myoclonic encephalopathy, and Ohtahara syndrome—occur in neonates. Of these, only BFNE and Ohtahara syndrome involve tonic seizures (although West syndrome involves tonic seizures as well). Finally, only the Ohtahara syndrome features burst-suppression on the EEG.1-3

2. **The correct answer is (C), Myoclonic epilepsy in infancy.** Only the syndromes in answers C and E—myoclonic epilepsy in infancy and progressive myoclonus epilepsy—involves myoclonus without other seizures, and of the listed syndromes, only myoclonic epilepsy in infancy features normal development. In addition, myoclonic epilepsy in infancy, along with Dravet syndrome, often has normal interictal EEGs in infancy.4

3. **The correct answer is (D), Panayiotopoulos syndrome.** Nonconvulsive seizures with ictal emesis are rare except in the Panayiotopoulos syndrome. Interictal generalized 3-per-second spike wave bursts and bilateral occipital spikes can occur in benign epilepsy with centrotemporal spikes (BECTS) and Panayiotopoulos syndrome, but the absence of centrotemporal spikes excludes BECTS.5

4. **The correct answer is (B), Juvenile myoclonic epilepsy.** Juvenile myoclonic epilepsy (JME) most often features generalized tonic-clonic seizures and myoclonus on wakening; each of the other listed syndromes requires at least one additional type of seizure that this patient does not have. Generalized fast spike-wave and polyspike-waves discharges are most characteristic of JME, and not of the other syndromes. Onset of myoclonus in JME occasionally occurs in early adulthood, although onset of myoclonus usually is earlier.6

5. **The correct answer is (E), Mesial temporal lobe epilepsy with hippocampal sclerosis.** The brain MRI is described as showing the findings of hippocampal sclerosis, and these together with the ipsilateral interictal temporal EEG spikes are compatible only with mesial temporal lobe epilepsy (TLE) with hippocampal sclerosis. Many patients with mesial TLE can provide a more definite description of auras and other ictal and postictal phenomena, but subjective symptoms of the partial seizures in mesial TLE also can be quite vague.7

**References**


SEIZURES AND EPILEPSY: ELECTROPHYSIOLOGICAL DIAGNOSIS

Thomas R. Henry, MD, and Zhiyi Y. Sha, MD, PhD

[Scroll down for answers and explanations, which appear after question 5.]

QUESTIONS

1. A waking and drowsy scalp EEG in a 12-year-old girl is abnormal due to occasional 2- to 4-Hz focal polymorphic delta transients of F7-T3 (F7-T7 in the new nomenclature) maximum in waking, and to rare F7-T3-maximum spike-wave complexes in drowsiness. You have not seen the patient and the non-neurologist who ordered the test stated only “syncope versus seizure” on the order form. The EEG abnormalities in themselves are known to be most often associated with which of the following?

A. The interictal state of TLE based on spikes recorded from the left hippocampus on the scalp EEG
B. The interictal state of TLE, based on spikes recorded from the left perisylvian neocortex on the scalp EEG
C. The interictal state of benign Rolandic epilepsy, based on spikes recorded from the left perisylvian neocortex on the scalp EEG
D. Psychogenic nonepileptic events, based on spikes that are likely to represent benign epileptiform transients of sleep (BETS)
E. Absence of epilepsy, based on spikes that are likely to represent BETS

2. A waking and drowsy scalp EEG in a 12-year-old boy is abnormal due to occasional generalized 3-Hz spike-wave discharges lasting up to 3 seconds in waking and drowsiness, with a photoconvulsive response at 15- and 16-Hz photic stimulation; the patient refused to perform hyperventilation. You have not seen the patient and the non-neurologist who ordered the test stated only “ADHD versus petit mal versus oppositional-defiant disorder” on the order form. The EEG abnormalities are LEAST likely to be associated with which of the following?

A. The interictal state of childhood absence epilepsy
B. The interictal state of juvenile absence epilepsy
C. The interictal state of JME
D. The interictal state of benign Rolandic epilepsy
E. Oppositional-defiant disorder

3. A 25-year-old woman has had brief events with paresthesias of the left face and hand at least weekly for the past year; during these events, others observe no change in her behavior. Her boyfriend reported that she also has had brief events with confusion and unresponsiveness at other times, at least once per week, but that she does not seem to be aware that these have occurred; she does not remember what he says to her during these moments when she acts confused. Her referring neurologist obtains a normal routine EEG and a normal brain MRI scan. She is given levetiracetam, but over the next month experiences 2 convulsive seizures with unconsciousness and falling. The neurologist admits her for diagnostic video-EEG monitoring “with a high suspicion of pseudoseizures.” Levetiracetam is stopped on the neurologist’s orders on the day before admission. The interictal EEG is normal for several hours, and the patient marks an event of her habitual left face and hand paresthesias. During this event, the EEG is technically well recorded and shows continuously normal waking EEG activities. Video analysis of the event reveals that the patient was sitting up in bed and staring up in the direction of the television, then she reached over to the event marker and pressed the button, after which she returned to staring up in the direction of the television, with no visible movements of the face or body. A nurse is seen to enter the room after about 15 seconds and to call the patient by name, to which the patient immediately responded by reporting that she was having one of her usual events; they converse and after 10 second she reports that she now feels normal again. The nurse calls you to ask for the diagnosis, as the patient wants to start a new medication and to go home now. You answer that it would be preferable for the patient to continue monitoring in order to gather more data.
before possibly starting a new medication. Why is further video-EEG monitoring recommended for this patient?

A. The patient had normal EEG activity during her habitual event, which on this basis is diagnostic of a psychogenic nonepileptic event; she should stay until the psychiatric consultant sees her to recommend a treatment other than antiseizure medication

B. The patient had normal EEG activity during her habitual event, which on this basis is diagnostic of a psychogenic nonepileptic event; she should stay for further video-EEG monitoring because many patients with nonepileptic events also have epileptic seizures

C. The patient had normal EEG activity during her habitual event, which on this basis is diagnostic of a psychogenic nonepileptic event; she should stay for further video-EEG monitoring because patients with convulsions always need to have these recorded on EEG in order to plan therapy

D. The patient had normal EEG activity during a habitual event, but this type of event cannot consistently be definitively diagnosed with extracranial EEG recordings; her other types of habitual events are more likely to be fully diagnosed with extracranial EEG recordings

E. The EEG recordings cannot be adequately interpreted because she continues to have levetiracetam effects in her brain; recordings should continue until the levetiracetam level is undetectable and before any diagnoses are made

4. A neurologist who has been in practice in a small town for many years calls you to request urgent transfer of a 68-year-old woman who has had gradual onset of memory, word-finding, fluency, and judgment deficits over the past 5 years. She was admitted to their small hospital after she fell down in a store. He had thought that she had Alzheimer's disease, but he decided to have their respiratory therapist run an EEG “just in case.” He was chagrined to find that she was having bilateral independent temporal lobe seizures, which he must have been missing for all of these years. He got her loaded with phenytoin, but the seizures continued. You ask him to describe the seizures, and he notes that during drowsiness she had 5- to 10-second runs of rhythmic sharp waves that stay at about 5 Hz occurring over the left and right temporal areas independently once or twice per minute. She can still talk and answer simple questions accurately, as her behavior does not change much during the seizures. His paper EEG machine cannot transmit a digital EEG file to you, but you ask him to fax several pages of the seizure recordings to you. Which of the following do you expect to find on this patient’s EEG?

A. Repeated brief electrographic seizures from each temporal lobe
B. An EEG consistent with nonconvulsive status epilepticus
C. Rhythmic midtemporal theta of drowsiness
D. An EEG consistent with normal REM sleep
E. Runs of pulse artifacts shifting from right to left

5. A 29-year-old right-handed man with refractory complex partial seizures is undergoing resection of a lesion in white matter that underlies the left dorsolateral temporoparietal junction area, and you are extraoperatively mapping language function by stimulating with an 8-by-8 subdural grid of electrodes (with 1 cm interelectrode spacing). The lesion has MRI characteristics of a cavernoma. The grid was placed 5 days earlier, and post-placement MRI showed that the grid covered all cortex overlying the lesion and extended at least 3 cm beyond the edge of the overlying cortex in all directions. After placement of the grid, 5 habitual complex partial seizures were recorded, and earliest changes of ictal discharges consistently began on the left superior temporal gyrus as focal beta activities at contacts 27 and 28 with subsequent spread to adjacent contacts and then over the entire grid as the frequency of continuous sinusoidal discharges gradually slowed.

While you are stimulating the electrode pair 27-28, no behavioral response occurs until the current is increased to 10 milliamperes (in a 5-second train at a rate of 50 phases/second with each phase lasting 0.3 ms), at which point there is speech arrest during the continuous language performance task. The speech arrest lasts for the duration of the stimulus train and then another 5 seconds, after which the patient has no evident language dysfunction. During and for 5 seconds after the stimulation, there is occurrence of rhythmically repetitive 2- to 3-Hz focal spike-wave complexes at the electrode pair 25-26 (which also appears to be located on the left superior
temporal gyrus on the post-placement MRI), which suddenly stops without spreading to other electrodes and with immediate return to prior baseline electrocorticographic activities at all electrode sites. What is your interpretation and response to these observations?

A. Interpretation: A speech arrest occurred on stimulation of the left superior temporal gyrus in association with a focal afterdischarge at adjacent electrodes. Language interference was clearly due to stimulation directly at this site, and this site cannot be resected (even though habitual seizures appeared to begin there on spontaneous seizure recording) because it is Wernicke’s area in this patient. Response: Stop the procedure and inform the neurosurgeon that this site cannot be resected because of a high risk of permanent language deficits.

B. Interpretation: A speech arrest occurred on stimulation of the left superior temporal gyrus in association with a focal afterdischarge at adjacent electrodes. Language interference was due either to stimulation directly at this site (which therefore must represent Wernicke’s area in this patient) or to effects of local spread of the afterdischarge to another area about 2 cm away from the stimulation site. Response: In order to more adequately define the site of Wernicke’s area, you hope to continue mapping without further induction of afterdischarges. This might be accomplished by stimulating the electrode pair 27-28 at a current lower than 10 milliamperes repeatedly, so long as afterdischarges do not occur at this lower current, and then to return to stimulation at a current of 10 milliamperes.

C. Interpretation: A speech arrest occurred on stimulation of the left superior temporal gyrus due to induction of a focal afterdischarge. It is dangerous to continue electrical stimulation in this patient as a generalized tonic-clonic seizure is likely to ensue. Response: Stop the procedure and inform the neurosurgeon that this technique will not be adequate for mapping of eloquent cortex.

D. Interpretation: A speech arrest occurred on stimulation of the left superior temporal gyrus due to induction of a seizure. Because Wernicke’s area is found only in the left angular gyrus or left supramarginal gyrus, you know that the speech arrest did not occur due to stimulation of Wernicke’s area. Response: Stop the procedure and inform the neurosurgeon of these results, indicating that this area should be resected to control seizures and this resection will not damage eloquent cortex.

E. Interpretation: This speech arrest occurred due to poor cooperation by the patient. Response: The patient confirmed that he would try harder next time, so you decide to increase the current to 15 milliamperes for the next stimulation trials at electrode pair 27–28.

ANSWERS

1. The correct answer is (B), The interictal state of TLE, based on spikes recorded from the left perisylvian neocortex on the scalp EEG. Pathological spikes of F7-T3 maximum are generated by neocortex near the sylvian fissure and are very highly associated with TLE. Hippocampal spikes cannot be recorded with extracranial electrodes. Benign Rolandic epilepsy is associated with centrotemporal spikes and is not associated with interictal focal polymorphic delta slowing. BETS occur in sleep (not in drowsiness or waking) and are not associated with interictal focal polymorphic delta slowing co-localized with spike maximum.1–5

2. The correct answer is (E), Oppositional-defiant disorder. Classic generalized 3-Hz spike-wave discharges often occur in the conditions listed in options A to D, although JME is more strongly associated with generalized fast spike-wave discharges, and benign Rolandic epilepsy usually has centrottemporal spikes occurring together with any generalized 3-Hz spike-wave discharges. None of the personality disorders is associated with specific interictal epileptiform activities.4–6

3. The correct answer is (D), The patient had normal EEG activity during a habitual event, but this type of event cannot consistently be definitively diagnosed with extracranial EEG recordings; her other types of habitual events are more likely to be fully diagnosed with extracranial EEG recordings. The patient had one type of habitual event that consisted of paroxysmal left face-hand paresthesias, which in general could be consistent with a simple partial seizure with sensory phenomena. She also had habitual events with nonconvulsive and convulsive behaviors and impaired awareness. Simple partial seizures frequently
Review of Topics

are unassociated with scalp EEG changes, so options A, B, and C are incorrect. Presence or absence of ictal EEG discharges can be interpreted diagnostically without regard to antiseizure medication use, so answer E is incorrect. In this case, recording of a habitual event with global impairment of awareness likely could establish a diagnosis of an epileptic seizure or nonepileptic event, which is a reason to continue monitoring.7,8

4. **The correct answer is (C), Rhythmic midtemporal theta of drowsiness.** The neurologist essentially described rhythmic midtemporal theta of drowsiness (RMTD), a monorhythmic theta discharge of temporal maximum in drowsiness; further details, including a midtemporal maximum, are likely to be noted on further review. Partial seizures evolve in field, frequency, and morphology, which excludes options A and B. The patient is answering simple questions accurately during the theta activities, and thus cannot be in REM sleep (excluding D). A pulse at 5 Hz (300 beats per minute) would cause cerebral hypoperfusion with EEG unconsciousness; the respiratory therapist would have checked the pulse and called for cardiac resuscitation (excluding E). Unrecognized RMTD is the most common cause of falsely diagnosed “subclinical temporal lobe seizures” on scalp EEG among neurologists with inadequate training or inadequate ongoing EEG experience.9

5. **The correct answer is (B), Interpretation: A speech arrest occurred on stimulation of the left superior temporal gyrus in association with a focal afterdischarge at adjacent electrodes. Language interference was due either to stimulation directly at this site (which therefore must represent Wernicke’s area in this patient) or to effects of local spread of the afterdischarge to another area about 2 cm away from the stimulation site.** Response: In order to more adequately define the site of Wernicke’s area, you hope to continue mapping without further induction of afterdischarges. This might be accomplished by stimulating the electrode pair 27-28 at a current lower than 10 milliamperes repeatedly, so long as afterdischarges do not occur at this lower current, and then to return to stimulation at a current of 10 milliamperes. When behavioral alterations occur with stimulation that induces an afterdischarge, it is not clear whether the behavioral alteration occurred due to transitory stimulation-induced dysfunction at the site of stimulation or to transitory afterdischarge-induced dysfunction with spread of the afterdischarge to sites other than the site of stimulation. In order to stimulate at a site that has had an afterdischarge, the afterdischarge threshold can often be elevated by repeated stimulation of that site at a lower current than the one which induced the afterdischarge, before returning later to this higher current.10–12

References


SEIZURES AND EPILEPSY: STRUCTURAL BRAIN IMAGING IN CHRONIC EPILEPSIES

Alexander M. McKinney, IV, MD, and Thomas R. Henry, MD

[Scroll down for answers and explanations, which appear after question 5.]

QUESTIONS

1. A 24-year-old patient with right face-arm focal motor and secondarily generalized tonic-clonic seizures undergoes brain MRI with FLAIR (Figure 1, left image) and postcontrast T1-weighted (Figure 1, right image) sequences. Which of the following conditions do these findings likely represent?

A. Focal cortical dysplasia
B. A ganglioglioma
C. A grade 3 astrocytoma
D. Periventricular nodular heterotopia
E. Unilateral perisylvian polymicrogyria

2. A 58-year-old patient with complex partial and secondarily generalized tonic-clonic seizures undergoes brain MRI with a FLAIR sequence (Figure 2). Which of the following conditions does this MRI finding likely represent?

A. A cavernous malformation
B. Focal cortical dysplasia
C. A grade 2 astrocytoma
D. Hippocampal sclerosis
E. A watershed infarction

3. A 28-year-old patient with complex partial and secondarily generalized tonic-clonic seizures undergoes brain MRI; an image obtained on the T2-weighted sequence is shown in Figure 3. Which of the following conditions does this MRI finding likely represent?

A. A grade 2 astrocytoma of the hippocampus on the left side of the image
B. Hippocampal dysplasia on the left side of the image
4. An 11-year-old patient with complex partial and secondarily generalized tonic-clonic seizures undergoes brain MRI; an image obtained on the T1-weighted sequence is shown in Figure 4. Which of the following conditions does this MRI finding (arrow) likely represent?

A. Ectopia of the cingulate cortex
B. Focal cortical dysplasia
C. A grade 2 astrocytoma
D. Hippocampal sclerosis
E. Periventricular nodular heterotopias bilaterally

ANSWERS

1. The correct answer is (C), A grade 3 astrocytoma. The lesion has mass effect, surrounding edema on the FLAIR image, internal inhomogeneity of signal, and a rim of enhancement. Among the lesions listed, only a grade 3 astrocytoma would have these features.

2. The correct answer is (A), A cavernous malformation. The lesion has complex internal inhomogeneity of signal and a rim of signal void, which are characteristic features of cavernomas. The surrounding edema can be seen with cavernomas after recurrent seizures. The sharply demarcated rim of signal void is inconsistent with glial tumors, as well as infarctions and dysplasias. This area is not near the hippocampus.

3. The correct answer is (D), Hippocampal sclerosis on the right side of the image. The hippocampus on the right side of the image is smaller and brighter than the hippocampus on the left, and these are the principal features of hippocampal sclerosis. The hippocampus on the left side of the image has bumps on its upper surface, which are the normal digitations of the hippocampal head (and are not dysplasias); the hippocampus on the right appears to have loss of hippocampal digitations, which is an ancillary finding in hippocampal sclerosis.

4. The correct answer is (E), Periventricular nodular heterotopia. The lesion at the arrow has the same signal characteristics as the cortical ribbon (gray matter contrast, which is not the contrast expected of glial tumors such as astrocytomas) and is located in the periventricular area (not in or underlying cortex, where focal cortical dysplasias are located, and not in the hippocampus). Cingulate cortex is not known to occur ectopically.
5. The correct answer is (A), Bilateral perisylvian polymicrogyria. The lesions are bilateral, are located in the perisylvian areas, and have shallow clefts that are lined by multiple small gyri; this is pathognomonic for bilateral perisylvian polymicrogyria. While schizencephalies have clefts, the clefts usually are deeper and lined by smoother gray matter tissue than occurs with bilateral perisylvian polymicrogyria. Focal cortical dysplasias might occur in the perisylvian areas but do not have clefts and multiple small gyri. Infarctions do not increase the complexity of gyral patterns. This area is not near the hippocampus or the ventricles.

SEIZURES AND EPILEPSY: STRUCTURAL BRAIN IMAGING IN ACUTE SEIZURES AND FUNCTIONAL NEUROIMAGING IN THE EPILEPSIES

Alexander M. McKinney, IV, MD, and Thomas R. Henry, MD

[Scroll down for answers and explanations, which appear after question 5.]

QUESTIONS

1. A 57-year-old man presents to the emergency department following his first generalized tonic-clonic seizure and undergoes brain imaging, including CT scan. Which of the following conditions is shown on the noncontrast CT image presented here (Figure 6)?

A. Bilateral perisylvian polymicrogyria
B. Dystrophic intraventricular calcifications
C. Hydrocephalus ex vacuo
D. Hydrocephalus with elevated intracranial pressure
E. Periventricular nodular heterotopia

Figure 6. Noncontrast CT image of the patient in question 1.

2. A 57-year-old man presents to the emergency department following his first generalized tonic-clonic seizure and undergoes brain imaging. Which of the following conditions is shown on the noncontrast CT image presented here (Figure 7)?

A. Acute lobar cerebral hemorrhage
B. Acute subdural hemorrhage
C. Chronic subdural hemorrhage
D. Focal cortical dysplasia
E. Grade 2 astrocytoma

Figure 7. Noncontrast CT image of the patient in question 2.

3. A 32-year-old woman presents to the emergency department following her first generalized tonic-clonic seizure and undergoes brain MRI. The T2-weighted FLAIR images (Figure 8) show findings consistent with which of the following?

A. Bilateral perisylvian polymicrogyria
B. Bilateral watershed infarcts
C. Hippocampal dysplasia bilaterally
D. Hippocampal sclerosis bilaterally
E. Posterior reversible encephalopathy syndrome

Figure 8. FLAIR images of the patient in question 3.
4. A 25-year-old woman presents to the emergency department following her first generalized tonic-clonic seizure and undergoes brain imaging. The T2-weighted MRI image (Figure 9) shows findings consistent with which of the following?

A. Hippocampal sclerosis bilaterally
B. Hydrocephalus
C. Limbic encephalitis
D. Periventricular nodular heterotopia bilaterally
E. Posterior reversible encephalopathy syndrome

**Figure 9.** T2-weighted image of the patient in question 4.

ANSWERS

1. The correct answer is (D), Hydrocephalus with elevated intracranial pressure. The bilaterally enlarged ventricles are associated with diffuse effacement of cortical sulci, indicating increased intracranial pressure. In hydrocephalus ex vacuo, the ventricles are enlarged, but there is associated cortical atrophy. Normal (not dystrophic) calcification of the choroid plexi is observed in image A. Periventricular nodular heterotopia and bilateral perisylvian polymicrogyria are difficult to detect with CT and in general are not associated with ventriculomegaly.

2. The correct answer is (A), Acute lobar cerebral hemorrhage. The lesion (arrow) is intraparenchymal (not in the extra-axial subdural space) and has increased density consistent with acute bleeding. Astrocytomas and dysplasias do not have predominantly high-density signal on X-ray CT.

3. The correct answer is (E), Posterior reversible encephalopathy syndrome. Posterior reversible encephalopathy syndrome is commonly associated with acute symptomatic grand mal seizures, and these images show changes consistent with immediately subcortical edema (largely sparing the adjacent cortical ribbon) which is mainly posterior. The abnormalities are not distributed in watershed distributions, are not in the hippocampi, and are not in the perisylvian regions.

4. The correct answer is (C), Limbic encephalitis. The hippocampi are of normal volumes within the limits of assessment on transaxial images, but show signal increases that also extend into the adjacent basal frontal lobe, consistent with limbic encephalitis. Hippocampal sclerosis rarely has marked signal increase in the absence of obvious atrophy, and does not extend into the inferior frontal cortex. Ventriculomegaly is not observed here, nor are ventricles with adjacent heterotopia or the white matter edema of posterior reversible encephalopathy syndrome.

5. The correct answer is (D), Mild asymmetry of the temporal lobes with relatively lower FDG activity in the left temporal lobe.
The temporal lobes have asymmetric intensity on each image plane, with lower FDG activity on the right side of the image (the left temporal lobe). The frontal lobes (best seen on 2 images on the right) and cerebellum (best seen on the 3 images on the left) are symmetric. The occipital area (best seen on the rightmost image) has higher intensity than the temporal lobes.

**QUESTIONS**

1. Which one of the following is NOT commonly considered a putative antiseizure mechanism of one or more FDA-approved antiepilepsy medications?

   A. Decreasing excitation at AMPA/kainate receptors  
   B. Decreasing excitation at NMDA receptors  
   C. Decreasing neuronal membrane depolarization by reducing ion flux at voltage-sensitive sodium channels  
   D. Increasing inhibition at cannabinoid receptors  
   E. Increasing inhibition at GABAergic chloride channels

2. Which of the following antiepilepsy medications has predominantly hepatic metabolism as the main route of elimination?

   A. Gabapentin  
   B. Levetiracetam  
   C. Lacosamide  
   D. Perampanel  
   E. Pregabalin

3. When added to a regimen of lamotrigine at stable dosing, which one of the following drugs would cause blood levels of lamotrigine to rise due to reduced lamotrigine elimination?

   A. Carbamazepine  
   B. Levetiracetam  
   C. Phenytoin  
   D. Valproic acid  
   E. Zonisamide

4. When used as a co-medication, which antiepilepsy drug is most likely to accelerate hepatic metabolism (and thereby reduce serum levels and efficacy) of warfarin, folic acid, and estrogen- or progesterone-based contraceptives?

   A. Lamotrigine  
   B. Levetiracetam  
   C. Phenytoin  
   D. Valproic acid  
   E. Zonisamide

5. Which one of the following agents has NOT been consistently associated with lowered seizure threshold and increased seizure frequency?

   A. Atorvastatin  
   B. Bupropion  
   C. Clozapine  
   D. Dalfampridine  
   E. Tramadol

**ANSWERS**

1. The correct answer is (D), Increasing inhibition at cannabinoid receptors. Examples of most of these actions and associated antiepilepsy medications are increased inhibition at GABAergic chloride channels (phenobarbital), decreased excitation at NMDA receptors (felbamate), decreased excitation at AMPA/kainate receptors (topiramate), and decreased neuronal membrane depolarization by reducing ion flux at voltage-sensitive sodium channels (phenytoin). Endocannabinoid binding at known cerebral cannabinoid receptors acts to reduce GABA release; no FDA-approved antiepilepsy medications are thought to control seizures by interacting with cannabinoid receptors.
2. **The correct answer is (D), Perampanel.** Each of the listed agents except for perampanel has mainly renal elimination.

3. **The correct answer is (D), Valproic acid.** Valproic acid causes reduced lamotrigine clearance. Addition of carbamazepine or phenytoin causes lamotrigine levels to decline. Addition of levetiracetam or zonisamide causes no change in lamotrigine levels.

4. **The correct answer is (C), Phenytoin.** Chronic phenytoin use causes induction of multiple enzymes of the hepatic cytochrome P-450 system, which increases the elimination of warfarin, folic acid, estrogen, progesterone, and other drugs. None of the other listed agents has this effect.

5. **The correct answer is (A), Atorvastatin.** Atorvastatin has not been associated with lowered seizure threshold, unlike each of the other listed agents.

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**ANTIPELPSY DRUGS: PHARMACODYNAMICS AND PRINCIPLES OF DRUG SELECTION**

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[Scroll down for answers and explanations, which appear after question 5.]

**QUESTIONS**

1. Which one of the following antiepileptic drugs (AED) is LEAST likely to be useful in controlling absence seizures?

   A. Carbamazepine
   B. Divalproex sodium
   C. Ethosuximide
   D. Lamotrigine
   E. Valproic acid

2. Which one of the following AEDs is LEAST likely to be useful in controlling complex partial seizures?

   A. Carbamazepine
   B. Divalproex sodium
   C. Ethosuximide
   D. Lamotrigine
   E. Valproic acid

3. **Which one of the following AEDs is LEAST likely to be useful in controlling generalized-onset seizures in the Lennox-Gastaut syndrome?**

   A. Clobazam
   B. Pregabalin
   C. Rufinamide
   D. Topiramate
   E. Valproic acid

4. **Select the SINGLE correct statement from the following:**

   A. Fetal exposure to valproic acid is not associated with any detectable teratogenicity
   B. Fetal exposure to valproic acid is associated with increased risks of spina bifida and of lowered IQ
   C. Fetal exposure to valproic acid is associated with increased risks of focal cortical dysplasias and of suicidality
   D. Fetal exposure to valproic acid is associated with increased risks of periventricular nodular heterotopias and of autism
   E. Fetal exposure to valproic acid is associated with increased risks of spina bifida and of borderline personality disorder

5. **Which one of the following agents has NOT been associated with anticonvulsant hypersensitivity, including dermatitis, hepatitis, eosinophilia, and other systemic symptoms?**

   A. Carbamazepine
   B. Levetiracetam
   C. Oxcarbazepine
   D. Phenobarbital
   E. Phenytoin

**ANSWERS**

1. **The correct answer is (A), Carbamazepine.** Carbamazepine has not shown efficacy in reducing the occurrence of absence
seizures, and in fact has been reported to exacerbate absence seizures in many individuals with idiopathic or symptomatic generalized epilepsies. Each of the other listed agents has shown efficacy in controlling absence seizures.

2. **The correct answer is (C), Ethosuximide.** Ethosuximide has not shown efficacy in reducing the occurrence of complex partial seizures or other partial-onset seizures. Each of the other listed agents has shown efficacy in controlling complex partial seizures.

3. **The correct answer is (B), Pregabalin.** Pregabalin has shown efficacy only in reducing the occurrence of partial-onset seizures. Each of the other listed agents has shown efficacy in controlling generalized-onset seizures in the Lennox-Gastaut syndrome.

4. **The correct answer is (B), Fetal exposure to valproic acid is associated with increased risks of spina bifida and of lowered IQ.** Fetal exposure to valproic acid has shown statistically significant associations with spina bifida and with lowered IQ. Fetal exposure to valproic acid has not been shown to be significantly associated with focal cortical dysplasias, suicidality, periventricular nodular heterotopias, autism, or borderline personality disorder.

5. **The correct answer is (B), Levetiracetam.** Of the listed agents, only levetiracetam has not been associated with anticonvulsant hypersensitivity syndromes.

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