Review of Topics: Epilepsy Surgery; Diagnosis and Management of Epilepsy in Elderly Patients; Anxiety and Depression in Patients with Epilepsy; Management of Status Epilepticus in Adults; Sudden Unexpected Death in Epilepsy; Epilepsy and Cognition

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AUTHOR INFORMATION

EPILEPSY BOARD REVIEW MANUAL

Contributors:

Amir Adeli, MD
Epilepsy Fellow, Wexner Medical Center, The Ohio State University, Columbus, OH

Amir M. Arain, MD
Associate Professor, Department of Neurology, Vanderbilt University Medical Center, Nashville, TN

William P. Cheshire Jr, MD
Professor of Neurology, Director, Clinical Neurophysiology Laboratory, Department of Neurology, Mayo Clinic, Jacksonville, FL

Sheri Cotterman-Hart, MD, PhD
Assistant Professor, The Ohio State University, Columbus, OH

Daniel L. Drane, PhD
Assistant Professor of Neurology and Pediatrics, Emory University School of Medicine, Atlanta, GA

Thomas R. Henry, MD
Professor of Neurology, Director, Comprehensive Epilepsy Center, University of Minnesota Medical School, Minneapolis, MN

Marek A. Mirski, MD, PhD
Executive Medical Director Neuroscience Critical Care Division, Professor of Anesthesiology and Critical Care Medicine, Neurology, and Neurosurgery, The Johns Hopkins Hospital, Baltimore, MD

William O. Tatum, IV, DO
Professor of Neurology, Director, Epilepsy Monitoring Unit, Department of Neurology, Mayo Clinic, Jacksonville, FL

Panayiotis N. Varelas, MD, PhD
Division Head, NeuroCritical Care Service, Senior Staff of Neurology and Neurosurgery, Henry Ford Hospital; Professor of Neurology, Wayne State University, Detroit, MI

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.

Note from the Publisher

This publication has been developed without involvement of or review by the American Board of Psychiatry and Neurology.

Publishing Staff

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Bruce M. White

SENIOR EDITOR
Robert Litchkofski

EXECUTIVE VICE PRESIDENT
Barbara T. White

EXECUTIVE DIRECTOR OF OPERATIONS
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Review of Topics: Epilepsy Surgery; Diagnosis and Management of Epilepsy in Elderly Patients; Anxiety and Depression in Patients with Epilepsy; Management of Status Epilepticus in Adults; Sudden Unexpected Death in Epilepsy; Epilepsy and Cognition

EPILEPSY SURGERY

Thomas R. Henry, MD
[Scroll down for answers and explanations, which appear after question 5.]

QUESTIONS

1. Which one of the following is MOST likely to be normal at the presurgical evaluation in a patient with temporal lobe epilepsy (TLE) who becomes seizure-free following temporal resection?

A. Extracranial video-electroencephalography (video-EEG) recording of habitual seizures
B. Intracranial video-EEG recording of habitual seizures
C. Brain magnetic resonance imaging (MRI)
D. Interictal FDG positron emission tomography (FDG PET)
E. Ictal single-photon emission computed tomography (SPECT)

2. The surgical outcomes for a patient who underwent temporal resection and then experienced only isolated auras (with no complex partial or generalized tonic-clonic seizures) following temporal resection for refractory temporal lobe epilepsy would be classified under the Engel system as which of the following?

A. Class IA
B. Class IB
C. Class IC
D. Class ID
E. Class IIA

3. When intracranial EEG recordings of multiple habitual seizures localize ictal onsets to a single small area of frontal lobe cortex, a patient with which of the following brain MRI findings would be LEAST likely to become seizure-free following resection of that small area of frontal lobe cortex together with any associated lesion?

A. Normal brain MRI
B. Brain MRI with focal cortical dysplasia near that area of frontal cortex
C. Brain MRI with cavernous malformation under that area of frontal cortex
D. Brain MRI with a small mass consistent with a ganglioglioma near that area of frontal cortex
E. Brain MRI with a small site of encephalomalacia adjacent to that area of frontal cortex

4. Select the SINGLE correct statement regarding patients with Lennox-Gastaut syndrome and multiple types of refractory seizures:

A. Anterior two-thirds corpus callosotomy is more effective in controlling atypical absence seizures than other seizure types
B. Anterior two-thirds corpus callosotomy is more effective in controlling generalized tonic-clonic seizures than other seizure types
C. Anterior two-thirds corpus callosotomy is more effective in controlling complex partial seizures than other seizure types
D. Anterior two-thirds corpus callosotomy is more effective in...
controlling generalized tonic or atonic seizures than other seizure types
E. Anterior two-thirds corpus callosotomy is more effective in controlling focal motor seizures than other seizure types

5. Multiple subpial transection is most often used to produce a limited lesion that is expected to do which of the following?

A. Interrupt seizure spread in subcortical fibers underlying a focal cortical dysplasia that is the site of ictal onsets
B. Interrupt seizure spread in epicortical fibers overlying an unresectable vascular malformation near the site of ictal onsets
C. Interrupt seizure spread in subcortical fibers underlying insular cortex that is the site of ictal onsets
D. Interrupt seizure spread in subcortical fibers underlying entorhinal cortex that is adjacent to a sclerotic hippocampus
E. Interrupt seizure spread in subcortical fibers underlying eloquent cortex that is the site of ictal onsets

ANSWERS

1. The correct answer is (C), Brain magnetic resonance imaging (MRI). Normal brain MRI is frequently encountered in patients who have efficacious temporal resection for refractory TLE. The other listed studies are rarely normal in patients whose seizures cease following temporal resection.

2. The correct answer is (B), Class IB. Occurrence of only isolated auras postoperatively would constitute a class IB (“nondisabling simple partial seizures only since surgery”) outcome.

3. The correct answer is (A), Normal brain MRI. Any of the listed lesions is associated with a greater than 50% occurrence of seizure-freedom, but a normal brain MRI is associated with less than 50% occurrence of seizure-freedom following resection of any lesion along with the area of cortex associated with initial ictal changes on intracranial recording.

4. The correct answer is (D), Anterior two-thirds corpus callosotomy is more effective in controlling generalized tonic or atonic seizures than other seizure types. This procedure is most effective in controlling epileptic drop attacks (generalized tonic or atonic seizures), compared with other seizure types.

5. The correct answer is (E), Interrupt seizure spread in subcortical fibers underlying eloquent cortex that is the site of ictal onsets. Multiple subpial transection was developed specifically to leave eloquent cortex undamaged while interrupting subcortical fibers that may support seizure propagation. This procedure has not been developed for other indications.

References


DIAGNOSIS AND MANAGEMENT OF EPILEPSY IN ELDERLY PATIENTS

Amir M. Arain, MD

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

QUESTIONS

1. An elderly patient with epilepsy presents to the emergency department (ED) because of nausea and dizziness. He was recently transferred to a nursing home from another facility. On examination in the ED, he is severely ataxic. He is maintained on Dilantin 300 mg every night at bedtime and has been seizure-free for several years. His brand name Dilantin recently has been switched to generic phenytoin. What should be the next step in management?

A. Check complete blood count
B. Check phenytoin total level
C. Check phenytoin total and free level
D. Spinal tap
E. EEG

2. The wife of an otherwise healthy elderly patient with epilepsy calls your office to report that her husband has been sick with dizziness, nausea, and vomiting. He has been seizure-free for years on carbamazepine 200 mg 3 times daily. Recently, he changed his diet, adding daily grapefruit juice to his breakfast. Which of the following evaluations should be done?

A. Perform EEG
B. Perform brain MRI
C. Check prolactin level
D. Check carbamazepine level

3. In the workup of an elderly patient with new-onset epilepsy, which of the following has the highest yield for finding the etiology?

A. Somatosensory evoked potentials
B. Brain computed tomography (CT)
C. Brain MRI
D. Lumbar puncture
E. Positron emission tomography (PET) scan of the brain

4. Which of the following antiepileptic drugs is the most appropriate for an elderly patient with new-onset epilepsy who is taking multiple medications?

A. Carbamazepine
B. Ezogabine
C. Levetiracetam
D. Phenytoin
E. Topiramate

5. The wife of an elderly patient with epilepsy brings him to your clinic because he has been acting different for the past 3 weeks. He seems to have word finding difficulty, and she is worried that he is developing Alzheimer’s disease. You had seen him last month for new-onset epilepsy and had started him on topiramate. What should be the next course of action?

A. Perform brain MRI
B. Perform lumbar puncture
C. Perform echocardiography
D. Taper off topiramate and start levetiracetam
E. Stop topiramate

**ANSWERS**

1. The correct answer is (C), Check phenytoin total and free level.

The phenytoin total and free level should be checked because the free level is the most accurate measure of the active drug in the elderly. This patient is likely toxic on phenytoin because of the change in phenytoin formulation.

2. The correct answer is (D), Check carbamazepine level.

Grapefruit juice is a strong inhibitor of the cytochrome P450 enzyme system and can increase carbamazepine levels significantly. The best course of action would be to evaluate the patient in clinic, checking his carbamazepine level and holding the carbamazepine dose if the level is high.

3. The correct answer is (C), Brain MRI. The most common etiology for new-onset epilepsy in elderly patients is cerebrovascular accident. MRI provides the best yield in the evaluation for abnormalities associated with cerebrovascular accident. Lumbar puncture and PET scan are of limited utility in elderly patients with epilepsy. Somatosensory evoked potentials are not helpful in the workup of epilepsy.

4. The correct answer is (C), Levetiracetam. Levetiracetam would be most appropriate because it has no drug-drug interaction and is not highly protein bound. Its add-on efficacy was established in the KEEPER trial in elderly patients with partial-onset epilepsy, and a recent comparative trial found its efficacy to be equivalent to carbamazepine in newly diagnosed epilepsy.
5. The correct answer is (D), Taper off topiramate and start levitetiracetam. Topiramate is well known to cause word finding difficulty and other cognitive side effects. It is appropriate to taper him off topiramate and add levetiracetam as the risk of seizure recurrence is high in elderly patients.

References

ANXIETY AND DEPRESSION IN PATIENTS WITH EPILEPSY

Sheri Cotterman-Hart, MD, PhD, and Amir Adeli, MD

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

QUESTIONS

1. A 55-year-old man with a history of dysthymia presents to your clinic for evaluation of spells. He is accompanied by his wife, who has witnessed multiple similar episodes. She reports, “He looks frightened and his eyes get huge, and afterwards, he is covered in sweat and has no idea what happened.” The patient himself reports a sensation that he describes as “my heart is racing and I feel like I’m out of my mind” but is unable to provide further details. These events have occurred during the day and night. What further history would suggest a possible diagnosis of primary panic attack?

A. History of febrile seizures
B. Identifiable precipitating stressor
C. Associated loss of consciousness

2. When describing the presentation of depression in patients with epilepsy, which statement is most correct?

A. Major depressive disorder is rarely seen in patients with epilepsy
B. Clinical depression is a normal reaction anyone would have to the diagnosis of epilepsy
C. Atypical depression is the most common presentation in patients with epilepsy
D. Depression always lags after seizure onset by several years
E. Ictal depressive symptoms are common

3. Which of the following statements regarding detection of depression in patients with epilepsy is true?

A. Use of screening tools can increase the detection rate significantly in patients with epilepsy
B. Use of screening tools is discouraged as none have been validated in the population of patients with epilepsy
C. Use of screening tools is not needed as the clinical detection rate of depression is high in patients with epilepsy
D. Screening tools like the Neurologic Disorders Depression Inventory for Epilepsy have low sensitivity and specificity

4. Which of the following medications would be a first-line treatment for depression in patients with epilepsy?

A. Bupropion
B. Clomipramine
C. Escitalopram
D. Fluoxetine

5. Which of the following statements regarding the treatment of depression in patients with epilepsy is true?

A. Antidepressants greatly increase risk of seizures
B. Electroconvulsive therapy is contraindicated
C. Cognitive behavioral therapy has no demonstrated efficacy
D. An antiepileptic regimen with favorable mood effects can be chosen

ANSWERS

1. The correct answer is (B), Identifiable precipitating stressor. An identifiable precipitating stressor is more likely associated with a panic attack rather than a seizure, in which the feelings of fear are more typically out of context. A history of febrile seizures is associated with temporal lobe epilepsy. Alteration in consciousness, confusion, and bladder incontinence are symptoms associated with seizures rather than panic attacks.¹

2. The correct answer is (C), Atypical depression is the most common presentation in patients with epilepsy. Atypical depression, with moods of sudden onset/offset, brief duration, markedly increased irritability, and more chronic dysthymia, is the most common presentation in patients with epilepsy. Other predominant symptoms include anhedonia, anergy, pain, insomnia, fear, and anxiety.²³ Although patients with epilepsy do not always meet DSM criteria for major depressive disorder, it remains a common problem for these patients.⁴⁵ Depression does not have to follow and can even precede the onset of seizures.⁶ Ictal depressive symptoms occur in approximately 1% of patients.⁷

3. The correct answer is (A), Use of screening tools can increase the detection rate significantly in patients with epilepsy. Depression is frequently underrecognized in patients with epilepsy. The use of reliable and valid screening tools during normal care increases the rate of detection of depression by 10% to 47%.⁸ The Beck Depression Inventory, Center for Epidemiologic Studies Depression Scale, and Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) are all validated in this population.⁹ The NDDI-E is 81% sensitive and 90% specific for detecting depression in patients with epilepsy.¹⁰

4. The correct answer is (C), Escitalopram. Selective serotonin reuptake inhibitors (SSRIs) are first-line therapy for depression in patients with epilepsy. Although both escitalopram and fluoxetine are SSRIs, escitalopram has fewer pharmacokinetic interactions with antiepileptic drugs and is thus preferred. The data regarding the effect of the norepinephrine-dopamine reuptake inhibitor bupropion on seizure threshold is mixed and it therefore is not a first-line option. The tricyclic antidepressant clomipramine carries a higher risk for provoking seizures and is therefore not a first-line therapy.¹¹

5. The correct answer is (D), An antiepileptic regimen with favorable mood effects can be chosen. Most antidepressants are safe for use in patients with epilepsy. Electroconvulsive therapy is a safe and effective treatment for patients with medication-resistant depression. Cognitive behavioral therapy has demonstrated efficacy in treating depression in patients with epilepsy. Antiepileptic drugs can be selected for positive affective profiles in a step toward treating depression in patients with epilepsy.¹²¹³

References


MANAGEMENT OF STATUS EPILEPTICUS IN ADULTS

Panayiotis N. Varelas, MD, PhD, and Marek A. Mirski, MD, PhD

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

QUESTIONS

1. A 43-year-old woman who had a parafalcine meningioma resected 5 years ago with subsequent epilepsy and is on phenytoin at home presents to the ED with 6 generalized tonic-clonic seizures lasting approximately 45 to 60 seconds each. She was previously intact and working until this morning when she developed seizures at work. The last seizure happened 1 minute ago and she has not regained consciousness since prior to the first seizure. She weighs 85 kg. Her heart rate is 110 beats/min, systolic blood pressure is 146/59 mm Hg, respiratory rate is 21 breaths/min, and oxygen saturation is 100% on 2 L nasal cannula. What is the best first step in managing this patient?

A. Draw blood for electrolytes, phenytoin levels, complete blood count, and blood gases and administer lorazepam 1 mg intravenously (IV) once
B. Insert a peripheral venous catheter; draw blood for electrolytes, complete blood count, and blood gases; and administer lorazepam 1 mg IV once
C. Insert a peripheral venous catheter; draw blood for glucose and phenytoin levels, electrolytes, complete blood count, and liver function tests; and administer lorazepam 2 mg IV once
D. Insert peripheral catheter and administer midazolam 10 mg intramuscularly (IM) and phenytoin 1 g IV once
E. Administer midazolam 10 mg IM; draw blood for glucose, phenytoin levels, ionized calcium, and electrolytes; and order a CT scan of the head without contrast and prepare to intubate the patient

2. The patient continues to have generalized tonic-clonic seizures and is noncommunicative. The phenytoin level is 3 µg/mL and the remainder of the blood test results are normal. She is now desaturating (oxygen saturation, 86%) despite receiving oxygen supplementation via a nonrebreather face mask. What is the next best step in the management of this patient?

A. Give phenytoin 1600 mg IV once and additional lorazepam 2 mg IV once and order a continuous EEG
B. Give valproate 1600 mg IV once and order a continuous EEG
C. Give levetiracetam 2000 mg IV once and intubate/mechanically ventilate the patient
D. Intubate/mechanically ventilate the patient and start propofol infusion 50 µg/kg/min
E. Intubate/mechanically ventilate the patient, give phenytoin 1600 mg IV once and additional lorazepam 4 mg IV once, and order a continuous EEG

3. The patient has stopped convulsing and has been transferred to the neuro-ICU. She is withdrawing bilaterally, left slightly less than right, but also is not waking up (Glasgow coma scale score: motor 4, eyes 1, verbal 1T). There is no neck rigidity.

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Levetiracetam 1000 mg IV is given once. Continuous EEG shows 2 runs of right frontomedial 15-second seizures within the next 15 minutes and interictal discharges in between. Phenytoin load has been completed. What is the next best management step?

A. Load with pentobarbital to a 20-second burst-suppression pattern and start pentobarbital infusion
B. Order a CT of the head and start midazolam infusion at 5 mg/hr
C. Order a CT of the head, start midazolam infusion at 5 mg/hr, remove the EEG leads for the CT of the head and replace them after, and draw blood gases
D. Prepare for lumbar puncture, give additional 2000 mg levetiracetam IV once, and start acyclovir for potential herpetic encephalitis
E. Order a CT of the head and perform lumbar puncture afterwards to exclude viral encephalitis

4. CT scan of the head does not show any new abnormality. The EEG shows no more seizures after the midazolam infusion was started. It is already 9 PM and there is no further EEG reading available overnight, unless on emergency. The resident who is covering the neuro-ICU does not feel comfortable reading EEGs. A plan is made to keep the patient on continuous EEG and midazolam infusion overnight and stop it in the morning at 6 AM. Upon return to the ICU at 7 AM, what should you do if the patient is drowsy but follows commands bilaterally?

A. Check a random phenytoin level upon arrival in the ICU in order to decide if more drug is needed
B. If the EEG during the night and after stopping the infusion does not show any seizures, extubate the patient, stop the EEG, and watch her in the ICU for the next 12 to 24 hours while continuing both phenytoin and levetiracetam maintenance dosing
C. Keep the patient sedated for another 24 hours on midazolam to allow time for the brain to recuperate from status epilepticus (SE), check phenytoin and levetiracetam levels, and adjust maintenance doses
D. Perform an MRI of the brain after removing the EEG leads, as the patient is still intubated and sedated which will help to avoid movement artifacts
E. Immediately stop the levetiracetam administration and the midazolam infusion; continue only with phenytoin and extubate the patient

5. Risk factors for refractory status epilepticus include which one of the following?

A. Low antiepileptic drugs levels
B. Short period of time since onset
C. History of absence seizures
D. Encephalitis as a cause
E. Seizure at head injury onset

ANSWERS

1. The correct answer is (C), Insert a peripheral venous catheter; draw blood for glucose and phenytoin levels, electrolytes, complete blood count, and liver function tests; and administer lorazepam 2 mg IV once. The patient is in generalized tonic-clonic status epilepticus (SE). Securing a peripheral vein in order to draw blood or administer intravenous medications is very important. Checking blood, including glucose levels and antiepileptic drug levels, in parallel with treating the patient are also important diagnostic steps. The patient is epileptic, so the most common etiology of SE would be drug noncompliance. Therefore, CT of the head would be appropriate only if new neurologic findings are present or antiepileptic drug levels are therapeutic. Based on the vital signs, the patient does not need immediate intubation and mechanical ventilation. The dose of lorazepam should be 0.07 to 0.1 mg/kg. Because of multiple in-succession seizures, 2 mg IV seems a more reasonable initial dose than the smaller 1 mg dose. Midazolam IM would have been a choice in the prehospital setting or if there were no available intravenous route in the emergency department.14

2. The correct answer is (E), Intubate/mechanically ventilate
the patient, give phenytoin 1600 mg IV once and additional lorazepam 4 mg IV once, and order a continuous EEG. Protection of the airway, better oxygenation and treatment of the ensuing metabolic acidosis, and mechanical ventilation in case of respiratory compromise from additional benzodiazepines or general anesthetics seems a reasonable strategy at this stage of SE. Since phenytoin levels were low, noncompliance becomes a reasonable etiologic hypothesis, and since this antiepileptic has been working before, loading with phenytoin seems a more reasonable therapy than valproate, levetiracetam, or propofol. Since the patient is already intubated, an additional larger dose of lorazepam may control the seizures until the phenytoin is infused. Ordering an EEG at this point is also reasonable to exclude nonconvulsive status development.3,4

3. The correct answer is (C), Order a CT of the head, start midazolam infusion at 5 mg/hr, remove the EEG leads for the CT of the head and replace them after, and draw blood gases. The patient has refractory SE. Since there is slight focality in the neurologic exam and there are still electrographic seizures on the EEG, it is reasonable to exclude any new structural abnormalities as a cause of the SE (eg, new stroke, recurrence of tumor, intracranial bleed). Removal of the EEG leads temporarily is important because of the artifact they produce on the CT. Starting an anesthetic infusion, such as midazolam, is a reasonable next step for a patient with refractory SE (failure to control after benzodiazepine and 2 first-line antiepileptics). Lumbar puncture would be reasonable after the CT is done if there are signs of meningitis or encephalitis, which this patient does not have per history and exam.5

4. The correct answer is (B), If the EEG during the night and after stopping the infusion does not show any seizures, extubate the patient, stop the EEG, and watch her in the ICU for the next 12 to 24 hours while continuing both phenytoin and levetiracetam maintenance dosing. Despite the fact that the patient’s condition has improved clinically, she did develop refractory SE after both levetiracetam and phenytoin loads. It would be prudent before extubating her to have no evidence of nonconvulsive ictal activity on the EEG and continue for the short-term both antiepileptics after extubating her. Trough antiepileptic levels are better checked before the next dose of the drug and not randomly. Although an MRI of the brain may be ordered as follow-up by the neurosurgeon who operated on her, this may be done as an outpatient and there is no reason to delay her extubation or discharge from the ICU for the test to be done. There is also no reason for longer sedation-intubation in the ICU since she is not clinically or electroencephalographically seizing anymore and she is waking up.

5. The correct answer is (D), Encephalitis as a cause. Risk factors that have been identified for refractory SE are encephalitis as a cause, severe consciousness impairment, de novo episodes of SE, delay in initiation of treatment, nonconvulsive SE, and focal motor seizures at onset.5–9

References

SUDDEN UNEXPECTED DEATH IN EPILEPSY

William P. Cheshire Jr, MD, and William O. Tatum, IV, DO

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

QUESTIONS

1. Which of the following seizure types imparts the highest risk for sudden unexpected death in epilepsy (SUDEP)?
   A. Convulsive syncope
   B. Myoclonic seizures
   C. Focal seizures with dyscognitive features
   D. Generalized tonic-clonic seizures
   E. Acute repetitive absence seizures

2. Which of the following interventions is most likely to reduce the risk for SUDEP?
   A. Reduction of antiseizure medications
   B. Night-time supervision
   C. Bedtime snack
   D. Sleeping in the prone position
   E. Bedtime dosing of sedating medication

3. Which of the following EEG findings is frequently associated with SUDEP?
   A. Polymorphic delta
   B. Alpha persisting during N3 sleep
   C. Wicket rhythm
   D. Generalized post-ictal EEG suppression
   E. Excessive frontal beta

4. Which of the following mechanisms has been postulated for SUDEP?
   A. Seizures involving the insular cortex
   B. Increased heart rate variability
   C. Orthostatic hypotension
   D. Shortened QT interval on electrocardiogram (ECG)
   E. Respiratory sinus arrhythmia

5. Which of the following factors has the highest risk for SUDEP?
   A. Duration of treatment less than 1 year
   B. Age greater than 50 years
   C. Sustained sobriety
   D. Physician-guided antiseizure drug transitions
   E. Obsessive-compulsive personality disorder

ANSWERS

1. The correct answer is (D), Generalized tonic-clonic seizures. Established risk factors for SUDEP consist of generalized tonic-clonic seizures, frequent uncontrolled seizures, seizures while sleeping or in bed, seizures requiring multiple antiseizure drugs, subtherapeutic antiseizure drug concentrations, younger age (20–45 years), and male sex. The other seizure types listed are associated with less intense forms of epilepsy, which are less likely to be associated with SUDEP. Convulsive syncope is not a form of epilepsy but rather a brief series of myoclonic jerks caused by global cerebral hypoperfusion during transient loss of consciousness from vasovagal syncope, which is typically followed by rapid recovery.

2. The correct answer is (B), Night-time supervision. The multicenter MORTEMUS study found that most instances of SUDEP occurred between the hours of 7:30 PM and 6:00 AM, which they attributed to more effective supervision during daylight hours. Closer night-time supervision in their study correlated with more rapid detection and more readily available resuscitation measures. Reduction of antiseizure medications and sleeping in the prone position are associated with a
greater risk for SUDEP.7,8 Accordingly, any clinical factors that might compromise the airway, such as hypnotic or sedating medications for insomnia or a full stomach with the potential for gastroesophageal reflux, could potentially contribute to apnea in a postictal patient with respiratory suppression.

3. **The correct answer is (D), Generalized post-ictal EEG suppression.** Prolonged generalized suppression on the EEG in the immediate postictal timeframe is a well-established correlate of SUDEP and the only EEG abnormality associated with SUDEP.9–11

4. **The correct answer is (A), Seizures involving the insular cortex.** Seizures involving the insular cortex have been postulated as a potential mechanism to explain some cases of SUDEP, as the insula contributes to the regulation of heart rate.12,13 Heart rate changes in some cases of mesial temporal lobe epilepsy have been attributed to insular cortex involvement.14 Decreased, not increased, heart rate variability has been associated with SUDEP.15,16 Orthostatic hypotension is not an epileptic phenomenon but is defined as an abnormal drop in blood pressure upon standing, which may cause transient loss of consciousness.17 Prolonged, not shortened, QT interval on ECG predisposes to ventricular arrhythmias and has been implicated in some cases of SUDEP.18,19 Respiratory sinus arrhythmia is a normal ECG finding in healthy individuals.20

5. **The correct answer is (D), Physician-guided antiseizure drug transitions.** Subtherapeutic antiseizure drug serum concentrations, whether resulting from the patient’s noncompliance or physician-guided antiseizure drug transition, is a recognized risk factor for SUDEP.21 The first 3 choices are the opposites of other SUDEP risk factors, which include younger age, a long history of seizures, and alcohol abuse.21,22 There is no known correlation between obsessive-compulsive disorder and SUDEP.

**References**


15. Lotufo PA, Valiengo L, Benseñor IM, Brunoni AR. A systemat-
ic review and meta-analysis of heart rate variability in epilepsy and antiepileptic drugs. Epilepsia 2012;53:272–82.


**Questions**

1. Which of the following variables has been associated with cognitive dysfunction in patients with epilepsy?

   A. Antiepileptic drug regimen
   B. Interictal epileptiform discharges
   C. Structural brain lesions
   D. All of the above

2. Which of the following is not true of focal seizures?

   A. The cognitive effects of focal seizures are almost always much worse than those of generalized seizures
   B. Focal seizures often cause cognitive dysfunction related to abilities controlled by regions distant from the seizure onset zone
   C. Focal seizures can result in both functional and structural brain changes
   D. Focal lobe seizures arising from the frontal lobes can cause disturbances of motor coordination and speed, attention, complex problem solving, aspects of generative fluency, and behavioral problems

3. Which of the following cognitive abnormalities is least likely to occur in temporal lobe epilepsy (TLE)?

   A. Verbal generative fluency deficits (both letter and semantic)
   B. Recognition of famous persons in patients with right anterior temporal lobe seizure onset
   C. Material-specific memory deficits
   D. Naming decline (quantitative) in patients undergoing right anterior temporal lobe surgery

4. Which of the following epilepsy syndromes is associated with language regression and autistic-like features?

   A. Dravet syndrome
   B. Landau-Kleffner syndrome
   C. Lennox-Gastaut syndrome
   D. Childhood absence epilepsy

5. Which of the following could potentially improve cognitive function in a patient with epilepsy?

   A. Reduction of seizure frequency
   B. Altering synaptic neurotransmitter availability
   C. Attempting to avoid polytherapy with antiepileptic drugs and maintaining suggested therapeutic blood levels of such medications
   D. All of the above
ANSWERS

1. **The correct answer is (D), All of the above.** Several factors can contribute to cognitive dysfunction in patients with epilepsy. Antiepileptic drug regimen, interictal epileptiform discharges, and structural brain lesions have all been associated with cognitive deficits.

2. **The correct answer is (A), The cognitive effects of focal seizures are almost always much worse than those of generalized seizures.** While the cognitive effects of focal seizures can be worse than those of generalized seizures at times, quite frequently, generalized seizures will produce a broader, more diffuse pattern of dysfunction than a focal seizure. The remaining responses are all true of focal seizures. Focal seizures often cause cognitive dysfunction involving regions distal to the seizure onset zone (see nociferous cortex hypothesis of Wilder Penfield). Focal seizures can result in both functional and structural brain changes. Examples include hippocampal atrophy, diffusion imaging abnormalities of white matter, and hypometabolism as defined by PET or SPECT scans in temporal lobe epilepsy. Finally, response E captures the wide range of cognitive functions that can be affected by focal seizures.

3. **The correct answer is (D), Naming decline (quantitative) in patients undergoing right anterior temporal lobe surgery.** Quantitative naming decline only occurs following dominant temporal lobe resection, which is most often associated with the left hemisphere. Some research suggests that speed of naming may decline following damage to either anterior temporal lobe region, but quantitative naming decline occurs only following right anterior temporal lobe surgery. Also of note, patients with nondominant TLE may have baseline naming deficits. However, these deficits will not worsen with surgery involving the nondominant hemisphere. In contrast, all of the other deficit patterns reflected in answers A through C are common cognitive deficits observed in TLE. Verbal fluency deficits can be observed in both left and right TLE cases, deficits in famous face recognition have been observed in right temporal lobe cases, and material-specific memory deficits have been a commonly reported cognitive problem observed in TLE.

4. **The correct answer is (B), Landau-Kleffner syndrome.** Core cognitive features of Landau-Kleffner syndrome include language regression and autistic-like features. Both Dravet syndrome and Lennox-Gastaut syndrome are commonly associated with mental retardation and diffuse cognitive dysfunction. Childhood absence epilepsy has more recently been associated with a number of varied cognitive limitations and poor psychosocial adjustment. However, it does not involve language regression or autistic features.

5. **The correct answer is (D), All of the above.** Reduction of seizure frequency can obviously improve cognitive function by reducing the neural disruption occurring during a seizure event. Altering neurotransmitter availability can also be beneficial to cognition and mood in some cases. Finally, avoiding polytherapy and attempting to maintain recommended therapeutic blood levels of antiepileptic drugs can also lead to optimal cognitive function. While it may not be possible to adhere to these antiepileptic drug guidelines in a given case due to the need to control seizures, research shows that patients experience better cognitive function when they are followed.

References