

affect qualification for Federal Aviation Administration medical certification. You also follow up with the pediatrician and he is also fully recovered and informs you that he has not treated a new case of hand, foot, and mouth syndrome in the recent week.

**Howard CT, Vu P. *You're the flight surgeon: hand, foot, and mouth disease*. *Aerosp Med Hum Perform*. 2015; 86(5):497–500.**

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You're the flight surgeon and sole Federal Aviation Administration (FAA) Aeromedical Examiner assigned to a U.S. Air Force base in Europe. Several hours after returning home from your fighter squadron, you are woken at 02:00 by the ring of your call phone. You immediately recognize the voice as one of the squadron wives. You know her and her husband extremely well as you have shared several common assignments over the past few years and have flown with her husband quite often. Her voice quivers with emotion as she initially apologizes for calling at such a late hour and then states that she is driving her husband to the hospital in their local village. She explains only minutes ago she was awakened by what she initially perceived as her husband's graceless attempt to get into bed. The lights were off and she was unable to observe the particulars of his movement, but she noted a rhythmic pattern to the disruption. Frustrated by his apparent lack of consideration, she turned on her bedside lamp and witnessed the last few seconds of what she describes as "uncontrollable shaking." Although his eyes were open, he was not responsive to her efforts to calm him, and her distress was made worse when she noted bright red blood seeping from his mouth. After several minutes his tremors stopped and he seemed to regain his composure, although he remained mildly confused. With inexplicably worsening left shoulder pain, he agreed to have her take him to the hospital. Now en route and fearful of overreacting, she is calling to seek reassurance from you that she is doing the right thing for her husband's health as well as his career. Furthermore, she asks you to meet them at the emergency department and then abruptly ends the call without waiting for your answer. You are out the door as quickly as you can zip your flight suit and, as you drive to the hospital, you recollect the day's events. You remember seeing her husband enjoying a few beers with his fellow fighter pilots after playing 18 holes of golf and you know for certain there was little hydration for most participants throughout the day. Having been the primary care physician for this family for several years now, you

mentally review the pilot's medical history. Thinking back to his recent annual flying physical, you cannot recall any medical conditions or prescription medication usage that might have precipitated the event she described.

### 1. Acknowledging the paucity of information, you still attempt a preliminary differential diagnosis. Based on what you know so far, what is your primary clinical suspicion?

- A. Syncope with convulsive accompaniment.
- B. Simple partial seizure.
- C. Complex partial seizure.
- D. Generalized seizure.
- E. Psychogenic nonepileptic seizure.

## ANSWER/DISCUSSION

**1. D.** Although the history provided is limited, there are several clues that provide insight to the likely diagnosis. A generalized tonic-clonic seizure is characterized as an upper extremity tonic episode lasting 10 to 20 s, followed by a brief period of flexion, then muscular rigidity of raised externally rotated arms abducted with partially flexed elbows. Back, neck, arm, and leg extension then follows, accompanied by apnea and cyanosis, with eyes open and deviated upward. In some cases, expired air results in an "epileptic cry" as it passes partially obstructed vocal cords. Finally, a clonic phase follows with characteristic alternating tone and relaxation, declining in frequency until cessation. In some cases, tongue biting and urinary incontinence may occur.<sup>4</sup> Additionally, generalized seizures are followed by a postictal state with subsequent confusion and often

DOI: 10.3357/AMHP.4235.2015

amnesia of the event. In contrast, during a simple partial seizure, consciousness is preserved and there are typically no adverse residual effects after the seizure event ends. Comparatively, while complex partial seizures often present with impaired or complete loss of consciousness similar to generalized seizure presentations, the accompanying repetitive movement is often limited focally. However, it is important to note that a partial seizure may progress to a secondary generalized seizure if the abnormal neuronal discharge progressively encompasses all regions of the cerebral cortex. Syncope with convulsive accompaniment may result in myoclonic movements or tonic posturing as a result of a lack of cortical activity rather than excessive electrical activity, as is the case during seizures. While the etiology of the seizure-like presentation is not immediately discernible without appropriate evaluation, the cause of his involuntary movement is unlikely due to syncope given his lack of adverse cardiac risk and unlikely orthostatic hypotension while in either a prone or supine sleeping position. Lastly, psychogenic nonepileptic seizures, also referred to as “pseudoseizures,” are most often caused by psychogenic emotional triggers such as stress or organic causes, including medications.<sup>1</sup> Such etiology is unlikely given he does not currently take any prescribed medications and has consistently demonstrated excellent stress management during the years you have known him.

You arrive at the emergency department just in time to listen to the history provided by the pilot himself, with assistance from his wife when necessary. Without prompting, he is quick to note that his mother has taken seizure medications for as long as he can remember, but he is unable to provide specifics. When asked to describe the event, he apologizes that he does not remember much. However, with a little patience and prompting by the medical staff, he does recall experiencing a visual aura prior to the event that he describes as a “moving blur.” He thought nothing of it since he’s had them since college and considered them to be the “floaters” he’s read about online. Cautiously, he admits he never volunteered their presence before for fear of losing his pilot status. Otherwise his personal medical history is unremarkable. He is a healthy aviator without history of head trauma or chronic health conditions such as diabetes. He denies history of febrile seizures in childhood and his medical records confirm that he has never previously experienced any similar seizure-like event. Although he denies illicit drug use, he admits to occasional bouts of heavy alcohol use as you had witnessed throughout the preceding day. However, he emphatically denies alcohol dependency, which is known to decrease the seizure threshold for individuals predisposed to epilepsy.<sup>10</sup> Otherwise he is unable to answer any additional questions regarding the actual event. His wife offers more details, including urinary incontinence, which they masked by changing his boxers prior to leaving for the hospital. At present, his chief complaint is generalized muscle soreness with focal tenderness in both of his shoulders, as well as a moderate headache and touch of nausea. His physical examination is unremarkable with the exception of tongue lacerations secondary to biting and an abnormal anterior location of the humeral head on his left shoulder. After sending him to radiology for plain films of his shoulders, the attending physician confers with you about what else you would like ordered in addition to a blood alcohol concentration.

**2. You are now confident of your initial clinical suspicion of generalized seizure. Which laboratory serum study to help confirm or “rule in” the diagnosis would not be included in your request?**

- A. Prolactin (PRL).
- B. Neuron-specific enolase.
- C. Sequential multiple analysis-7/CHEM-7.
- D. Creatine kinase.

**ANSWER/DISCUSSION**

**2. B.** In any event where generalized seizure is clinically suspected, a thorough general and neurological medical history is the primary means of confirmation. A careful reconstruction of preceding events helps to ascertain whether the seizure was provoked or unprovoked in nature; this is a critical discriminator affecting the ultimate aeromedical disposition. Attention should be focused on assessing sleep deprivation status, medication use, illicit drug use, and/or alcohol use. In combination or singularly, these elements have the potential to lower the seizure threshold and manifest a sentinel seizure episode. Withdrawal from moderate to heavy alcohol consumption, defined as three to four or more drinks per occasion, lowers the seizure threshold and may reveal metabolic disorders that result in similar presentations, with the greatest risk for seizure onset between 7 to 48 h after the last drink.<sup>6</sup> As an adjunct evaluation, laboratory serum studies are often reassuring. Elevated serum creatine kinase is supportive for the diagnosis of generalized seizure and may be made more sensitive by waiting at least 3 h after the event to take the serum sample.<sup>7</sup> Likewise, elevated serum PRL can help distinguish between generalized seizures and psychogenic nonepileptic seizures.<sup>3</sup> However, PRL elevations after a seizure are short-lived, with PRL levels returning to baseline within about 90 min postictally. It is important to note that seizure disorders can be manifested by abnormal electrolyte imbalances, including hypocalcemia and hypomagnesemia, and abnormal glucose levels leading to hyper- or hypoglycemia.<sup>11</sup> The CHEM-7 panel evaluates blood serum for four electrolytes (sodium, potassium, chloride, bicarbonate) as well as blood urea nitrogen, creatinine, and glucose. Given acute electrolyte changes are often typical of seizure activity, it is a worthwhile study to help rule out other potential etiologies that might be easily corrected and may show metabolic acidosis changes that could support the diagnosis of seizure. Less certain, neuron-specific enolase may serve as an equally effective postictal biomarker, but more studies are needed for confirmation.<sup>2</sup>

The plain films indeed confirm that his left shoulder is anteriorly dislocated secondary to the intensity of the tonic-clonic process. After reducing his shoulder, the labs return, demonstrating an elevation in both prolactin and creatine kinase, with a blood alcohol concentration of  $0.02 \text{ g} \cdot \text{dl}^{-1}$ . He is discharged home with pain medications, his left shoulder splinted, and a presumptive diagnosis of generalized seizure likely provoked by the prior day’s activities, including lack of sleep, dehydration, and excess alcohol intake. On your drive back to your office, you consider the best course of action regarding his continued medical management. It’s obvious you’ll have to ground him immediately, but then what? Just as you arrive at

your office, your phone rings again. It's your pilot and he asks, "Are you going to take away my wings?" You explain to him that there is more to be done before you can definitively answer his question and encourage him to get some sleep. You determine that you will have a plan ready for him when he wakes later in the day to best manage his expectations regarding the impact this will have on his flying career.

### 3. Which ancillary study should not be ordered to facilitate comprehensive evaluation of your pilot's medical condition?

- A. Brain magnetic resonance imaging (MRI) with/without gadolinium contrast and attention to temporal lobe structures.
- B. Routine electroencephalogram (EEG) study.
- C. Sleep-deprived EEG study with recording of sleep and wakefulness.
- D. Computed tomography (CT) with/without contrast.

## ANSWER/DISCUSSION

3. D. Necessary studies following a suspected seizure require MRI of the brain with and without gadolinium as well as wake and sleeping sleep-deprived EEG studies. As seizures commonly arise from the temporal lobes, the MRI should also specifically assess this region (often ordered as "seizure protocol"). CT of any type is not sufficient to determine likely anatomic etiologies,<sup>4</sup> although an unenhanced CT may prove useful when evaluating for life-threatening emergent conditions such as hemorrhage.<sup>8</sup> In the case of an initial focal presentation, it is critical that potential precipitating factors, including a gliotic scar, tumor, or abscess, be identified if present.<sup>4</sup> While a definitive diagnosis of generalized seizure can be made with a positive EEG demonstrating epileptiform discharges, negative (normal) readings do not rule out such a diagnosis, as nearly 40% of individuals with confirmed epilepsy demonstrate normal EEG studies throughout their lives.<sup>4</sup> It is important to remember that a single seizure episode does not establish the diagnosis of epilepsy. Such a definitive diagnosis requires two or more unprovoked events.<sup>4</sup> However, it is worth noting that recurrence risk from unprovoked seizures ranges from 26 to 33% over 5 yr.<sup>4</sup>

## AEROMEDICAL DISPOSITION

Your pilot returns to the emergency department of the local hospital 3 d later to be treated for an identical presentation. However, this occurrence happened during the day and his wife witnessed the entire event from initial symptom onset. In addition to the observations previously reported, she noted a cyanotic appearance and recounted the initial presentation was global without any sign of a preliminary focal phase. Consequently, he was started on Keppra (levetiracetam) for seizure prevention and diagnosed with epilepsy. Pre/postcontrast brain MRI is read as unremarkable. EEG studies show intermittent left midposterior temporal spikes and sharp waves, more prominent in drowsiness and light sleep. As his primary care physician, your focus is effectively managing his disease, restoring his quality of life, and ensuring his safety as well as the safety of those around him. The goal is to effectively

titrate his medication under the guidance of a neurologist and encourage lifestyle habits intended to maintain a high seizure threshold, such as ensuring regular fluid and nutritional intake and avoiding excessive/binge ethanol intake, prolonged sleep deprivation, and medications that have seizures as a potential adverse effect. Secondly, it is your responsibility to advise your patient's state motor vehicle administration (especially if required by his state) of his diagnosis and recommend his driver's license be temporarily revoked for medical reasons until he remains seizure free for the appropriate time period specified by the state. As his flight surgeon, you are responsible for informing him of his permanent disqualification from flying duties with a definitive diagnosis of epilepsy now that a second unprovoked seizure occurred greater than 24 h apart. While this will surely be difficult, he wouldn't want to hear it from anyone else.

According to the Air Force Waiver Guide, "epilepsy is unequivocally disqualifying for all flying duties."<sup>12</sup> Likewise, the Army Aeromedical Policy Letters<sup>\*</sup> and the U.S. Navy Aeromedical Reference and Waiver Guide<sup>9</sup> state epileptic seizures are disqualifying and not waivable. The key considerations when addressing any aeromedical neurological concern include the degree of incapacitation and the predictability of such occurrence. The diagnosis of epilepsy is wholly incompatible with military aviation duties in both respects and most definitely constitutes an unacceptable safety risk. Likewise, as the sole Aeromedical Examiner on the base, you have a duty to inform the FAA of the epilepsy diagnosis and submit all required documentation to facilitate an FAA disposition. Current FAA guidance for recurrent seizures advises the patient have a 10-yr seizure-free period and be off all anticonvulsant medication for at least 3 yr before being considered for medical recertification.<sup>5</sup>

A final thought about evaluating seizure-like episodes—given the significant adverse impact an epilepsy diagnosis has on the life and career of an aviator, it is imperative that you make every effort to make a definitive diagnosis. Unfortunately, an erroneous epilepsy diagnosis is relatively common, with approximately 25% of those improperly diagnosed later found to have syncope or psychogenic nonepileptic seizures.<sup>1</sup> As the diagnosis of seizure is primarily based on historical information, you owe it to yourself and your patient to perform a thorough assessment.

**Woolford JS. You're the flight surgeon: epilepsy. *Aerosp Med Hum Perform.* 2015; 86(5):500–503.**

## ACKNOWLEDGMENTS

The author would like to thank Col. (Dr.) Roger Hesselbrock, U.S. Air Force School of Aerospace Medicine, Aeromedical Consultation Service, Neurology, Wright-Patterson Air Force Base, OH, for his review of this article. The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Air Force, the Department of Defense, or the U.S. Government.

<sup>\*</sup> U.S. Army Aeromedical Activity. Flight surgeon's aeromedical checklists. Aeromedical policy letters and aeromedical technical bulletins. Ft. Rucker, AL: U.S. Army Aeromedical Activity; 2014 Aug 10. [Accessed 15 Oct. 2014]. Available from [https://vfso.rucker.amedd.army.mil/public/downloads/Army\\_APLs\\_10aug2014.pdf](https://vfso.rucker.amedd.army.mil/public/downloads/Army_APLs_10aug2014.pdf) to those with access.

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