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9 **Missed opportunities in new onset seizures in the emergency department**

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33 New onset motor seizures, especially generalized convulsive seizures, are common but frightening to
34 patients and bystanders, and typically result in evaluation in the emergency department (ED).

35 Emergency physicians are challenged to confirm whether the event precipitating the visit was indeed a
36 seizure rather than a mimic such as stroke, syncope, non-epileptic spell, or migraine. When a true
37 seizure is suspected, the next step is to identify a precipitating cause. This is usually done by obtaining a
38 detailed medical history and performing a thorough physical examination. Sometimes diagnostic tests
39 are necessary as well. Patients in whom no underlying reason for a first lifetime seizure is found may
40 have had an isolated event, or may develop recurring seizures and a diagnosis of epilepsy. The
41 observational study by Pellinen et al, published in this issue of *Academic Emergency Medicine* serves to
42 teach us about this latter cohort of patients using a database of those subsequently diagnosed with focal
43 epilepsy after an initial ED visit.¹

44

45 Focal seizures involve ictal activities produced by electrical impulses that start in a localized region of
46 the brain. They can present with motor and non-motor manifestations that vary according to the affected
47 region of the brain originating the seizure impulses. Focal motor seizures present with subtle muscle
48 activities such as jerking, loss of muscle tone or repeated movements in isolated groups, that can also
49 rapidly generalize to involve the whole body. Focal non-motor seizures do not present with muscle
50 activity. Instead, they present with a variety of signs and symptoms of alterations in emotions, thinking
51 and sensations. Motor seizures are relatively identifiable, but subtle and non-specific non-motor focal
52 seizures are difficult to diagnose in the ED.

53

54 Pellinen et al,¹ use a registry of patients with newly diagnosed focal epilepsy to describe the
55 characteristics of a subset who presented to an ED shortly prior to their diagnosis. The authors note that
56 the first onset of epilepsy was non-motor focal seizures in slightly more than half of the patients in the
57 ED subset, but that they rarely came to the ED for these types of seizures. Indeed, the initial
58 presentation to the ED was for a first lifetime motor seizure in 90%, and for a recurring motor seizure in
59 another 5%. The patients with first lifetime motor seizures were correctly diagnosed as having had a
60 seizure 86% of the time, but in those with prior non-motor seizures the history of such events was only
61 identified 21% of the time. Identification of prior non-motor seizures did not seem to affect diagnosis or

62 treatment of patients with first time motor seizures. The authors conclude that improvement is needed in
63 the recognition of seizures, particularly non-motor focal seizures in the ED.

64

65 Accurate diagnosis and referral to specialized follow-up of patients with new onset seizures is clearly in
66 the wheelhouse of the emergency physician. The fact that patients with seizures present to the ED rather
67 than to the primary care setting is not surprising. ED utilization in lieu of primary care has risen steadily.
68 Affordability and access remain prevalent barriers to non-emergency healthcare for many. Relying on
69 primary care follow up to identify seizures missed in the ED seems unsafe. Pellilen et al, found that
70 83% of patients with first lifetime motor seizures who were later diagnosed with focal epilepsy were
71 admitted or properly referred from their ED visit. However, the remaining 17% of patients with
72 undiagnosed epilepsy who presented with a first lifetime motor seizure, and who were discharged from
73 the ED without a diagnosis, admission or proper referral, represent a substantial opportunity for
74 improvement.

75

76 First lifetime seizures are a neurological emergency warranting careful assessment and management.^{2,3}
77 Seizures could be triggered by potentially life-threatening underlying pathologies such as metabolic
78 disorders, drug toxicities, CNS infections, intracranial hemorrhage, trauma, or structural brain lesions
79 like tumors. Seizures and seizure-mimics can also result from more benign pathologies such as certain
80 types of withdrawal, syncope, migraine, or psychogenic syndromes. Since all of these presentations are
81 excluded from the cohort of epilepsy patients studied by Pellilen et al, their study does not teach us
82 anything about the relative frequency of these diagnoses as compared to those with new onset epilepsy.
83 The morbidity and mortality associated with first time seizures may also be underestimated due to
84 diagnostic challenges.

85

86 Having excluded other causes of seizure, what do emergency physicians have to do for patients with
87 first lifetime motor seizures? The findings of Pellilen et al reinforce the importance of obtaining a
88 detailed medical history and performing a thorough physical examination to identify subtle clues of prior
89 or on-going seizures, especially non-motor focal seizures. Patients may not connect prior episodes of
90 sensory, cognitive, or emotional abnormalities to their index motor seizure unless specifically
91 questioned. Subtle exam findings of myoclonus, twitching, blinking, or other automatisms and
92 extrapyramidal signs may indicate continued ictal activity. Careful clinical evaluation may help
93 diagnose epilepsy at the initial ED visit or risk stratify which patients get consultation and further
94 diagnostic testing with MRI and EEG before discharge or as an outpatient. Multiple practice guidelines

95 support outpatient testing and consultation but only if it can be obtained rapidly and reliably.³⁻⁵ Per
96 these recommendations, patients with a first lifetime seizure should be evaluated within two weeks by a
97 specialist.

98

99 The authors also imply that if emergency physicians had diagnosed epilepsy more often, by identifying a
100 history of prior non-motor focal seizures, emergency physicians could initiate treatment with
101 antiepileptic drugs (AED) more often. It is more prudent, however, to defer the decision on initiation of
102 an AED and the most appropriate AED to a neurologist. As usually described in the literature, “early
103 initiation” of an AED typically refers to starting medication after the first neurology clinic visit, but
104 could also refer to starting an AED in the ED. In either case, there is no evidence of long term patient
105 benefit from early initiation.⁶ Guidelines suggest deferring initiation even if epilepsy can be diagnosed
106 in the ED, especially if consultation can be conducted in an expeditious outpatient follow up. Initiating
107 an AED can be complex, involving confirmation of the diagnosis, titration of doses and agents, and
108 management of adverse drug reactions. This assessment also should take into consideration the patients’
109 preferences and circumstances. Indeed, the high rate of AED initiation reported by Pellilen et al, after
110 first lifetime seizure seems at variance with practice guidelines (even if it was based on the
111 recommendation of a neurology consultant in the ED), and reducing this practice represents another
112 opportunity for improving ED management of these patients.

113

114 There is much that the study by Pellilen et al cannot teach us because of many limitations. It is
115 susceptible to spectrum bias, since it only includes patients subsequently diagnosed with epilepsy and
116 referred to specialty epilepsy clinics. Because it only enrolled patients whose seizure treatment started
117 within 4 months of enrollment, the study systematically excludes patients experiencing long delays in
118 diagnosis and treatment, potentially underestimating the magnitude of the problem. It is disappointing
119 that this study did not include any data on the timing of diagnostic testing, especially EEG, in this
120 patient population. There is evidence that acquisition of EEG closer to the time of a first lifetime seizure
121 has a higher diagnostic yield than studies obtained further out.⁷ Lastly, the study only enrolled patients
122 within the age range of 12 to 60. Therefore, the findings might not be generalizable to young children or
123 elderly patients.

124

125 What we can learn from Pellilen et al, is that there may be opportunities to improve several dimensions
126 of emergency care for patients with first lifetime seizures that subsequently end up having focal
127 epilepsies. These include the potential to improve how often we correctly diagnose seizures and even

128 epilepsy. It also includes more reliable and timely referral to neurology, fewer prescriptions (counter to
129 the authors' insinuation), and better adherence to clinical guidelines on initiation of antiepileptic drugs.
130 The path to improvement is less clear. There have been long-standing calls in the literature to improve
131 neurological training through emergency medicine residencies,^{8,9} or through professional development
132 programs such as the Emergency Neurological Life Support program.¹⁰ There may also be opportunities
133 for improvement associated with technological innovations such as increased availability of smaller, less
134 expensive, rapid emergency EEG systems.^{11,12}

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136 One way or another, these data suggest we owe it to our patients with new onset epilepsy to do better.

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139 References:

- 140 1. Pellinen J, Tafuro E, Baehr A, et al. The Impact of Clinical Seizure Characteristics on Recognition
141 and Treatment of New-onset Focal Epilepsy in Emergency Departments. *Acad Emerg Med*
142 [Internet] 2020; Available from: <http://dx.doi.org/10.1111/acem.14114>
- 143 2. Teran F, Harper-Kirksey K, Jagoda A. Clinical decision making in seizures and status epilepticus.
144 *Emerg Med Pract* 2015;17(1):1–24.
- 145 3. Huff JS, Melnick ER, Tomaszewski CA, et al. Clinical policy: critical issues in the evaluation and
146 management of adult patients presenting to the emergency department with seizures. *Ann Emerg*
147 *Med* 2014;63(4):437–47.e15.
- 148 4. Krumholz A, Shinnar S, French J, Gronseth G, Wiebe S. Evidence-based guideline: Management of
149 an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the
150 American Academy of Neurology and the American Epilepsy Society. *Neurology*.
151 2015;85(17):1526–7.
- 152 5. Overview | Epilepsies: diagnosis and management | Guidance | NICE. Available at:
153 <https://www.nice.org.uk/guidance/cg137>. Last accessed November 4, 2020
- 154 6. Leone MA, Giussani G, Nolan SJ, Marson AG, Beghi E. Immediate antiepileptic drug treatment,
155 versus placebo, deferred, or no treatment for first unprovoked seizure. *Cochrane Database Syst Rev*
156 2016;(5):CD007144.

- 157 7. Debicki DB. Electroencephalography after a single unprovoked seizure. *Seizure* 2017;49:69–73.
- 158 8. Wira CR 3rd, Madsen TE, Chang BP, et al. Is There a Neurologist in the House? A Summary of the
159 Current State of Neurovascular Rotations for Emergency Medicine Residents. *AEM Educ Train*
160 2018;2(Suppl Suppl 1):S56–67.
- 161 9. Stettler BA, Jauch EC, Kissela B, Lindsell CJ. Neurologic education in emergency medicine
162 training programs. *Acad Emerg Med* 2005;12(9):909–11.
- 163 10. O’Phelan KH, Miller CM. Emergency Neurological Life Support: Third Edition, Updates in the
164 Approach to Early Management of a Neurological Emergency. *Neurocrit Care* 2017;27(Suppl 1):1–
165 3.
- 166 11. Zehtabchi S, Abdel Baki SG, Omurtag A, et al. Prevalence of non-convulsive seizure and other
167 electroencephalographic abnormalities in ED patients with altered mental status. *Am J Emerg Med*
168 2013;31(11):1578–82.
- 169 12. Vespa PM, Olson DM, John S, et al. Evaluating the Clinical Impact of Rapid Response
170 Electroencephalography: The DECIDE Multicenter Prospective Observational Clinical Study. *Crit*
171 *Care Med* 2020;48(9):1249–57.

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