



SYSTEMATIC APPROACH TO NEW-ONSET SEIZURE

The lifetime risk of developing new-onset seizure is roughly 8% to 10%. Oftentimes, it can be difficult to determine the cause of seizure. A careful systematic evaluation is needed to correctly diagnose and appropriately treat those patients presenting with new onset epilepsy. This issue of *CLIPs* briefly summarizes an article that evaluates the new-onset of seizure in adults and adolescents. Topics include identifying patient characteristics and obtaining a patient history and underlying etiology of the seizure. If you need further information, please contact the Center for Healthcare Innovation and Patient Outcomes Research (CHIPOR) at chipor@samford.edu.

Gavvala JR, Schuele SU. New-onset seizure in adults and adolescents: a review. *JAMA*. 2016;316(24):2657-2668. doi:10.1001/jama.2016.18625.

Epidemiology / clinical presentation

- The lifetime risk for unprovoked or acute symptomatic seizures is 8-10% and the chance of developing epilepsy is 2-3%.
- The incidence of epilepsy worldwide is 50.4 per 100,000 per year.
- A total of 1.6 million patients presented to the emergency department to be evaluated for seizures and nearly 400,000 patients presented to emergency department (ED) with new-onset seizure in 2011.
- Seizure is either classified as focal (involving one hemisphere) or generalized (involving both hemispheres).
- Clinicians should obtain patients' clinical history to distinguish between the seizure type and eliminate other events that mimic seizures such as migraine, transient ischemic attack, syncope, neurological disorders, sleeping disorder, psychogenic nonepileptic seizures, movement disorders, and panic attacks.

Risk factors for epilepsy

- Several factors may contribute to increased risk of epilepsy including: age at onset; family history; extreme sleep deprivation; use of alcohol/illicit drugs; medications (e.g., clozapine, cephalosporins, fluoroquinolones, bupropion, and tramadol); metabolic abnormalities; altered homeostasis; toxin contact; history of central nervous system infections or disease; head injuries; or prior neurological surgeries.

Evaluation and diagnosis

- Patients presenting with a new-onset seizure need to undergo several tests to assess potential diagnosis for epilepsy.
- Patient's history and physical exam should focus on patient's experience, recollection, and awareness of the event.
- Subjective symptoms should be obtained at the patient interview pertaining to the onset of a seizure.
- Physical evaluation and a witness are necessary for patients unable to recall the actions during a seizure.
- Brain imaging such as CT, MRI, and epilepsy protocol-specific MRT should be considered with a new-onset seizures.
- Electroencephalography is recommended within 24-48 hours of new-onset of seizures.
- Screen for hypoglycemia, uremia, drug intoxication, and hyponatremia with a new-onset seizure.

Seizure recurrence

- The chance of recurrence is 35% after new-onset seizure within 5 years, chance of recurrence increases to 75% after a second seizure, and is even higher in those with abnormal neurological exam.

Table 1: Treatment for seizures

Narrow-spectrum medications^a	Initial titration instructions	Target maintenance dose mg/d
Carbamazepine ^{b,c,d}	200 mg twice daily, increase over 1-4 week to target	800-1200
Eslicarbazepine	400 mg daily, increase by 400-600 mg each week	800-1200
Gabapentin ^e	300-900 mg/day, increase over 1-2 week	900-1800
Lacosamide ^f	100 mg twice daily, increase by 100 mg total every week	300-400
Oxcarbazepine	300 mg twice daily, increase over 1-2 weeks	1200
Phenytoin ^{b,c,d}	100 mg three times daily, increase to target every 3-5 days	300-600
Broad-spectrum medication^g		
Lamotrigine ^{c,e,h}	25 mg daily X 2 weeks, 50 mg daily x 2 weeks, 100 mg daily x 2 weeks, then can increase by 50 mg every 1-2 weeks	250-350
Levetiracetam ^{e,f}	500 mg twice daily, increase by 500 mg every 1-2 weeks to target	1000-2000
Topiramate	25 twice daily, increase by 25-50 mg every week	200-400
Valproate ^{f,b}	250 mg twice daily or three times daily, increase dose by 250-500 mg every week	500-1500
Zonisamide	100 mg daily, increase by 100 mg every 2 weeks	200-400

^a Focal seizure

^b Avoid in patients taking multiple medications or those with multiple morbidities

^c Commonly associated with rash

^d Screen for HLA-B*15:02 in Asian descent

^e Recommended in patients ≥ 65 years of age

^f Available for intravenous administration

^g Most Generalized and Focal seizures

^h Plasma concentration decreased by oral contraceptives

Adverse effects (AE)

- Approximately 7-31% experienced AE with antiepileptic medication for the first time after a new-onset seizure and 88% in those receiving multiple therapies for epilepsy.

Women receiving antiepileptic medication(s)

- Intrauterine devices contraception is recommended to avoid the drug-drug interactions observed between hormonal contraception and many antiepileptic medications.

Response rate

- Of the patients diagnosed with epilepsy after 2 or more unprovoked seizures, approximately 50% will become seizure-free after initiating the first antiepileptic medication.
- Seizure-free period declines with increased number of antiepileptic medication regimens, with 13% becoming seizure-free after a second antiepileptic medication, and 4% after a third antiepileptic medication.

Patient education

- Help patients understand the difference between new-onset seizure and new-onset epilepsy, discuss with patient the underlying etiologies of seizure, and educate patients on factors that may lower seizure threshold.

Duration of therapy

- In patients with treatable and self-limited seizures, treatment with antiepileptic medication could be 7 days.
- Seizure caused by brain injury can be prophylactically treated from 1 month to 6 months.
- Successful remission include seizure-free for >2 years while taking antiepileptic medications and a normal neurological exam.

Conclusion

- A careful patient evaluation is needed in those with a new-onset seizure to correctly diagnose and appropriately treat those presenting with epilepsy.