Clinical Evidence Handbook
A Publication of BMJ Publishing Group

Epilepsy (Generalized and Partial)

MELISSA MAGUIRE, *Newcastle General Hospital, Newcastle upon Tyne, United Kingdom*
ANTHONY MARSON, *University of Liverpool, Liverpool, United Kingdom*
SRIDHARAN RAMARATNAM, *Apollo Hospitals, Chennai (Madras), India*

This is one in a series of chapters excerpted from the *Clinical Evidence Handbook*, published by the BMJ Publishing Group, London, U.K. The medical information contained herein is the most accurate available at the date of publication. More updated and comprehensive information on this topic may be available in future print editions of the *Clinical Evidence Handbook*, as well as online at http://www.clinicalevidence.bmj.com (subscription required). Those who receive a complimentary print copy of the *Clinical Evidence Handbook* from United Health Foundation can gain complimentary online access by registering on the Web site using the ISBN number of their book.

EB CME

This clinical content conforms to AAFP criteria for evidence-based continuing medical education (EB CME). See CME Quiz on page 389.

A collection of *Clinical Evidence Handbook* published in *AFP* is available at http://www.aafp.org/afp/bmj.

During their lifetime, about 3 percent of persons will be diagnosed with epilepsy, but about 70 percent of persons with epilepsy eventually go into remission.

After a first seizure, antiepileptic drugs may delay or prevent subsequent seizures, but they can cause adverse effects, and their long-term benefit is unknown. Antiepileptic drug treatment after a single seizure does not reduce the risk of drug-resistant epilepsy in the long term.

Carbamazepine, gabapentin, lamotrigine, levetiracetam, phenobarbital, phenytoin, sodium valproate, and topiramate are widely considered effective in controlling seizures in newly diagnosed generalized (tonic-clonic) or partial epilepsy, but we found no randomized controlled trials comparing them with placebo, and a placebo-controlled trial would now be considered unethical.

• Systematic reviews found no reliable evidence on which to base a choice among antiepileptic drugs.

• Adding second-line drugs to usual treatment reduces seizure frequency in persons with drug-resistant generalized or partial epilepsy, but it increases adverse effects such as dizziness and somnolence. We do not know if any one antiepileptic drug is more likely to reduce seizures compared with the others.

CAUTION: Vigabatrin, which may be used as second-line treatment, causes concentric visual field abnormalities in about 40 percent of persons, and these abnormalities are probably irreversible.

In persons with partial or generalized epilepsy who have been seizure-free for at least two years on treatment, almost 60 percent of those who withdraw from antiepileptic treatment will remain seizure-free, compared with almost 80 percent who continue treatment.

Educational programs may reduce seizure frequency and improve psychosocial functioning in persons with partial or generalized epilepsy, but we do not know whether relaxation, yoga, biofeedback, cognitive behavior therapy, relaxation plus behavior modification, or family counseling are beneficial.

There is consensus that temporal lobectomy or amygdalohippocampectomy can improve seizure control and quality of life in persons with drug-resistant temporal lobe epilepsy, but they can cause neurologic adverse effects.

High-level vagus nerve stimulation may reduce seizure frequency in persons with drug-resistant partial seizures, but it may

Clinical Questions: Generalized Epilepsy

What are the effects of monotherapy in generalized epilepsy (tonic-clonic type)?

Likely to be beneficial	Carbamazepine*
	Gabapentin*
	Lamotrigine*
	Levetiracetam*
	Phenobarbital*
	Phenytoin*
	Sodium valproate*
	Topiramate*

What are the effects of additional treatments in persons with drug-resistant generalized epilepsy?

Beneficial	Addition of second-line antiepileptics

What are the effects of surgery in persons with drug-resistant generalized epilepsy?

Unknown effectiveness	Hemispherectomy

**—Categorization based on consensus.*

cause hoarseness and dyspnea, and long-term effects are unknown. We do not know whether different stimulation cycles are more effective at reducing seizure frequency or at increasing the proportion of responders.

We do not know whether hemispherectomy improves seizure control in persons with drug-resistant generalized epilepsy.

We do not know whether lesionectomy improves seizure control in persons with drug-resistant temporal lobe epilepsy.

Definition

Epilepsy is a group of disorders rather than a single disease. Seizures can be classified by type as partial or focal (categorized as simple partial, complex partial, and secondary generalized tonic-clonic seizures) or generalized (categorized as generalized tonic-clonic, absence, myoclonic, tonic, and atonic seizures). Temporal lobe epilepsy is a form of partial or focal epilepsy. A person is considered to have epilepsy if they have

Clinical Questions: Partial Epilepsy

What are the effects of starting antiepileptic drug treatment after a single seizure?	
Trade-off between benefits and harms	Antiepileptic drugs
What are the effects of monotherapy in partial epilepsy?	
Likely to be beneficial	Carbamazepine*
	Gabapentin*
	Lamotrigine*
	Levetiracetam*
	Phenobarbital*
	Phenytoin*
	Sodium valproate*
	Topiramate*
What are the effects of additional treatments in persons with drug-resistant partial epilepsy?	
Beneficial	Addition of second-line drugs (allopurinol, eslicarbazepine, gabapentin, lacosamide, lamotrigine, levetiracetam, losigamone, oxcarbazepine, retigabine, tiagabine, topiramate, vigabatrin, or zonisamide)
What is the risk of relapse in persons in remission when withdrawing antiepileptic drugs?	
Trade-off between benefits and harms	Antiepileptic drug withdrawal for persons with partial or generalized epilepsy in remission
What are the effects of behavioral and psychological treatments in persons with generalized or partial epilepsy?	
Likely to be beneficial	Educational programs
Unknown effectiveness	Biofeedback
	Cognitive behavior therapy
	Family counseling
	Relaxation plus behavior modification
	Relaxation therapy
	Yoga
What are the effects of surgery in persons with drug-resistant temporal lobe epilepsy?	
Likely to be beneficial	Amygdalohippocampectomy*
	Temporal lobectomy*
	Vagus nerve stimulation as adjunctive therapy for drug-resistant partial seizures
Unknown effectiveness	Lesionectomy

**—Categorization based on consensus.*

had two or more unprovoked seizures. This review focuses on pharmacologic treatment of single seizure that may progress to epilepsy, and with pharmacologic and surgical treatments of generalized and partial epilepsy. This review also covers behavioral and psychological treatments of epilepsy (generalized or partial) and the risk of relapse in persons with epilepsy (generalized or partial) on withdrawing antiepileptic drugs. Status epilepticus is not covered in this review.

Incidence and Prevalence

Epilepsy (generalized or partial) is common, with an estimated average prevalence of 5.5 out of 1,000 persons in Europe, 6.8 out of 1,000 persons in the United States, and 7.5 out of 1,000 persons in Australia. Prevalence rates in developing countries vary widely, with studies in sub-Saharan Africa reporting rates of 5.2 to 74.4 out of 1,000 persons, studies in Asia reporting rates of 1.5 to 14.0 out of 1,000 persons, and studies in Latin America reporting rates of 17 to 22 out of 1,000 persons. The annual incidence of epilepsy is 24 to 56 out of 100,000 persons in Europe, 44 out of 100,000 persons in the United States, 63 to 158 out of 100,000 persons in sub-Saharan Africa, 113 to 190 out of 100,000 persons in Latin America, and 28 to 60 out of 100,000 persons in Asia. The worldwide incidence of single unprovoked seizures is 23 to 61 out of 100,000 person-years. About 3 percent of persons will be diagnosed with epilepsy at some time in their lives.

Etiology and Risk Factors

Epilepsy is a symptom rather than a disease, and it may be caused by various disorders involving the brain. The causes and risk factors include birth or neonatal injuries, congenital or metabolic disorders, head injuries, tumors, infections of the brain or meninges, genetic defects, degenerative disease of the brain, cerebrovascular disease, or demyelinating disease. Epilepsy can be classified by cause. Idiopathic generalized epilepsies (e.g., juvenile myoclonic epilepsy, childhood absence epilepsy) are largely genetic. Symptomatic epilepsies result from a known cerebral abnormality; for example, temporal lobe epilepsy may result from a congenital defect, mesial temporal sclerosis, or a tumor. Symptomatic generalized epilepsies (e.g., West syndrome, Lennox-Gastaut syndrome) are associated with diffuse cerebral dysfunction and may be caused by anoxic brain injury or metabolic defect. Cryptogenic epilepsies are those that cannot be classified as idiopathic or symptomatic.

Prognosis

About 60 percent of untreated persons have no further seizures during the two years after their first seizure. Prognosis is good for most persons with epilepsy. About 70 percent of persons with epilepsy go into remission, defined as being seizure-free for five years on or off treatment. This leaves 20 to 30 percent of persons who will develop chronic epilepsy, which is often treated with multiple antiepileptic drugs.

EDITOR'S NOTE: Eslicarbazepine, losigamone, and retigabine are not available in the United States.

SEARCH DATE: July 2009.

Author disclosure: Anthony Marson has been paid for speaking at meetings by Johnson and Johnson, Janssen Cilag, Sanofi, and UCB SA, and by Glaxo Wellcome and UCB SA for attending conferences. Sridharan Ramaratnam has received hospitality from the following pharmaceutical companies: Sun Pharmaceuticals (India), Novartis (India), and by Sanofi Aventis for attending conferences. Sridharan Ramaratnam is involved in ongoing clinical trials for UCB Pharma, Pfizer, and Johnson and Johnson.

Adapted with permission from Maguire M, Marson A, Ramaratnam S. Epilepsy (generalised). *Clin Evid Handbook.* December 2010:437-438; and Maguire M, Marson A, Ramaratnam S. Epilepsy (partial). *Clin Evid Handbook.* December 2010:439-441. Please visit http://www.clinicalevidence.bmj.com for full text and references. ■