Seizure Disorder

resource guide

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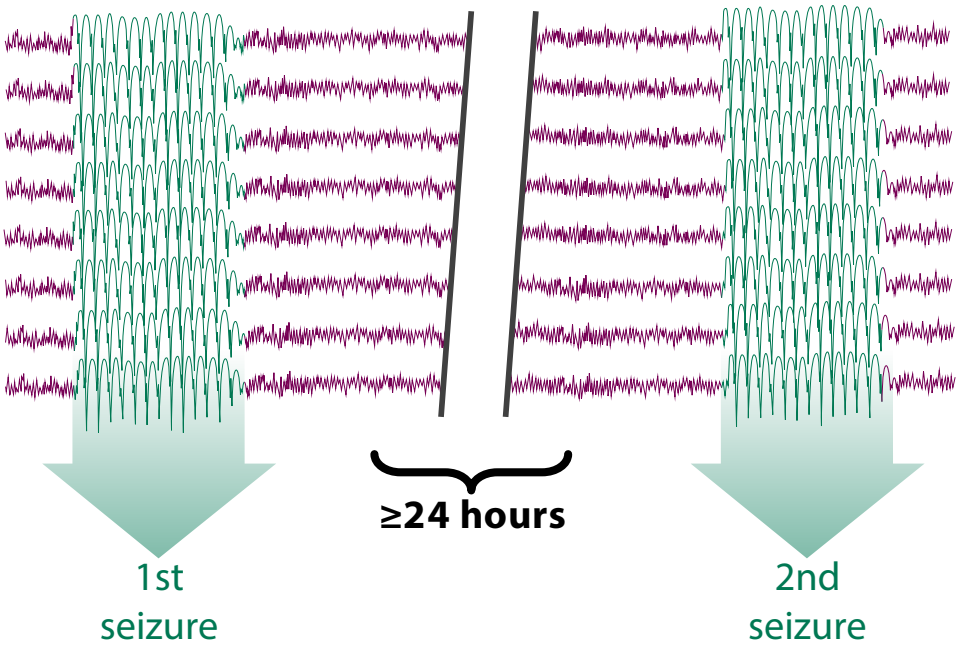
Prevalence of Epilepsy

Classification of Seizures

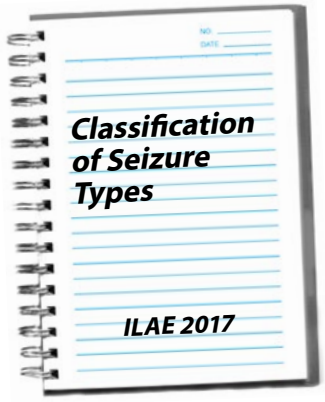
Epilepsy is characterized by recurring unprovoked seizures.[2]



A person who has had 2 or more unprovoked seizures, separated by at least 24 hours, is considered to have epilepsy (with all other possible causes of seizures being ruled out).[3]

The International League Against Epilepsy (ILAE) created a seizure classification system in 1981, which was revised in 2010.[4,5] The seizure classification system worked well for over 35 years, but did not capture many types of seizures.[6,7]

In 2017, ILAE approved a new seizure classification system: **The 2017 ILAE Classification of Seizure Types.**[6]



The 2017 classification system is designed to have some flexibility, however, it does not change the definition of epilepsy or epilepsy syndrome.[6]

The 2017 ILAE Classification of Seizure Types is summarized below and on the following pages.

The 2017 ILAE Classification of Seizure Types is based on the following 3 key features[6]:

- Localization of seizure onset
- Level of awareness during seizure
- Motor and other non-motor symptoms of seizures

In the 2017 classification system, the localization of seizure onset is determined first. Generalized seizures are presumed to affect awareness, however, focal seizures may not always affect awareness, and are now further described by the level of awareness an individual has during a seizure. Seizures are then subdivided according to the presence of either motor or non-motor symptoms during the seizure.[6]

The 2017 ILAE Classification of Seizure Types Expanded Version is presented in the table below.[6,7]

Localization at Onset	Level of Awareness	Symptoms		Other Seizure Types
		Motor	Non-Motor	
Focal Onset	Aware/ Impaired Awareness	Automatisms Atonic [6*] Clonic Epileptic spasms[6*] Hyperkinetic Myoclonic Tonic	Autonomic Behavior arrest Cognitive Emotional Sensory	**Focal to bilateral tonic-clonic**
Generalized Onset	Impaired Awareness	Tonic-clonic Clonic Tonic Myoclonic Myoclonic-tonic-clonic Myoclonic-atonic Atonic Epileptic spasms	**Absence** Typical Atypical Myoclonic Eyelid myoclonia	
Unknown Onset	Unknown	Tonic-clonic Epileptic spasms	Behavior arrest	**Unclassified[6†]**

*Degree of awareness usually is not specified.
†Due to inadequate information or inability to place in other categories.

The classification of an individual seizure can stop at any level.[8] The 3 key features are reviewed below and on the following pages.

The first key feature in the 2017 ILAE Classification of Seizure Types is the **localization of seizure onset**. The localization of seizure onset affects the choice of seizure medication, possibilities for epilepsy surgery, prognosis, and possible causes.[6]

2017 Terminology	Previous Terminology	Definition
Focal seizures[6]	Partial seizures	Start in an area or network of cells on 1 side of the brain
Generalized seizures[6]	Primary generalized seizures	Engage or involve networks on both sides of the brain
Focal to bilateral seizures[6]	Secondarily generalized seizures	Start on 1 side of the brain and spread to both sides
Unknown onset[6]	Not defined in 1981	The seizure onset is unknown. This seizure type can change if the seizure onset becomes clear

Focal seizure | **Generalized seizure** | **Focal to bilateral seizure** | **Unknown onset**

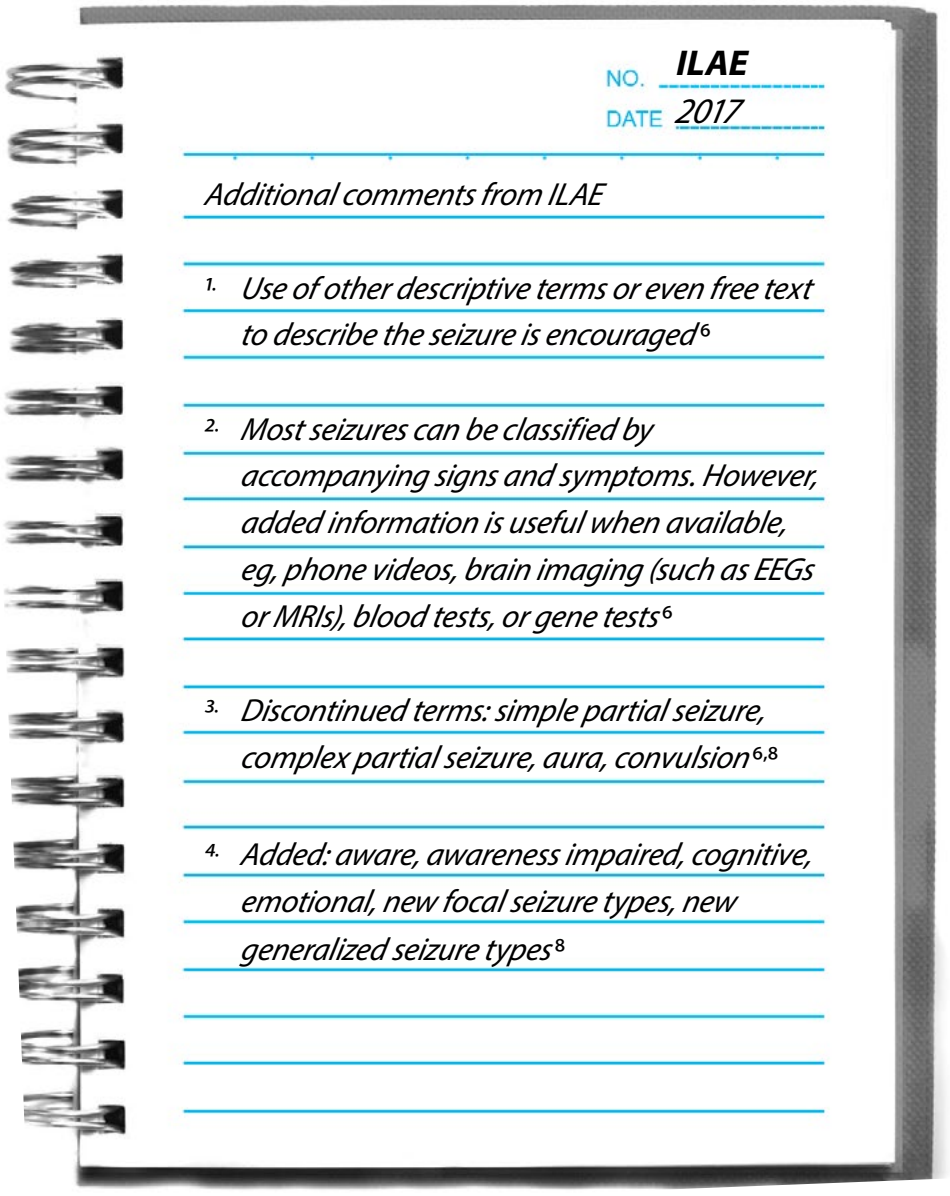
The second key feature in the 2017 ILAE Classification of Seizure Types is the **level of awareness during a seizure** as awareness is easier to evaluate than consciousness.[6]

Generalized seizures are presumed to affect awareness or consciousness in some way, therefore special terms are not needed. However, **focal seizures** can further be described by the level of awareness during a seizure.[6]

2017 Terminology	Previous Terminology	Definition
Focal aware[6]	Simple partial seizure	Awareness remains intact, even if the person is unable to talk or respond
Focal impaired awareness[6]	Complex partial seizure	Awareness is impaired or affected at any time during a seizure, even if the person has a vague idea of what happened
Awareness unknown[6]	Not defined in 1981	When awareness during a seizure is unknown because a person lives alone or has seizures only at night

The third key feature in the 2017 ILAE Classification of Seizure Types are the **motor and other non-motor symptoms of seizures**. This key feature provides a way to describe unknown onset seizures.[6]

2017 Terminology	Definition
Focal Motor Seizure[6]	Seizures that involve some type of movement, eg, twitching, jerking, or stiffening movements of a body part or automatism
Focal Non-Motor Seizure[6]	Other non-motor symptoms occur first, eg, change in sensation, emotions, thinking, or experience
Generalized Motor Seizure[6]	Seizure with stiffening (tonic) and jerking (clonic). Loosely corresponds to *grand mal*
Generalized Non-Motor Seizure[6]	Seizure involving brief changes in awareness, staring, and some may involve automatic or repeated movements, eg, lipsmacking. Primarily absence seizures, *petit mal*
Unknown Onset Motor Seizure[6]	Seizure with stiffening (tonic) and jerking (clonic), or epileptic spasms
Unknown Onset Non-Motor Seizure[6]	Seizure with behavior arrest


NO. ILAE
DATE 2017
Additional comments from ILAE
1. Use of other descriptive terms or even free text to describe the seizure is encouraged[6]
2. Most seizures can be classified by accompanying signs and symptoms. However, added information is useful when available, eg, phone videos, brain imaging (such as EEGs or MRIs), blood tests, or gene tests[6]
3. Discontinued terms: simple partial seizure, complex partial seizure, aura, convulsion[6,8]
4. Added: aware, awareness impaired, cognitive, emotional, new focal seizure types, new generalized seizure types[8]

Pharmacologic antiepileptic drugs (AEDs) are the most common approach for treating epilepsy.[3] Although the precise mechanism by which AEDs exert their anticonvulsant activity is unknown, AEDs are thought to fall into 2 general categories based on their mechanism of action.[9]

Some AEDs are thought to work via neuron inhibition:

- Sodium channel blockers[10-13]
- Calcium channel blockers[14]
- Glutamate blockers[15,16]

Other AEDs are thought to work via neuron induction:

- GABA agonist[16,17]

GABA= gamma-aminobutyric acid.

About 36% of patients were shown to have uncontrolled seizures following trials with 2 or more AEDs.[18]

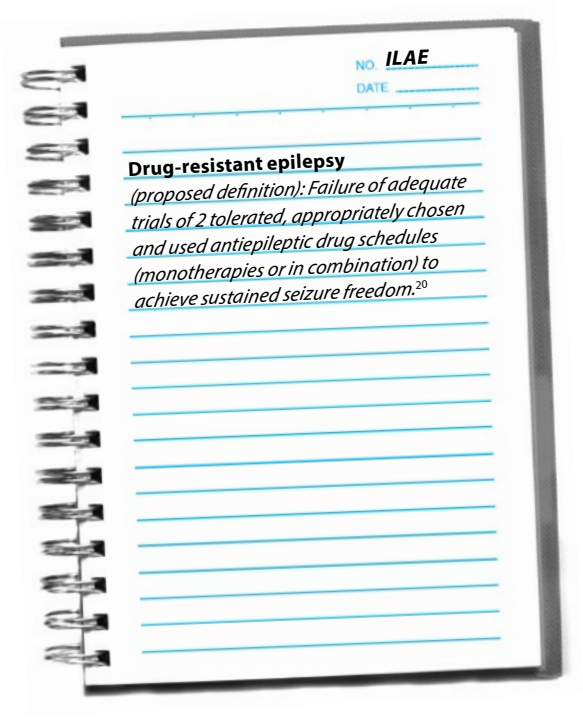
Based on the severity of symptoms, there is a range of nonpharmacologic options that can be considered for patients with refractory epilepsy[19]:

Dietary adjustments
Such as a ketogenic diet, which is high in fat and low in carbohydrates, may benefit patients with refractory seizures who have failed to respond to several AEDs and are not suitable candidates for surgery[19]

Surgical intervention
For patients with severe drug-resistant epilepsy who ideally have a single epileptogenic focus in a cortical region that is not involved in key language, memory, or motor process[19]

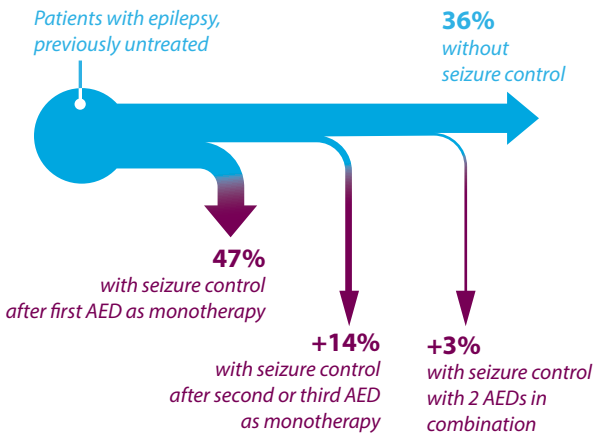
Medical device
Patients with refractory epilepsy who are not suitable for epilepsy surgery or those who continue to experience seizures post-operatively may benefit from neurostimulation. This treatment involves electrical stimulation of the nervous system using either a surgically implanted device or non-invasive stimulation[19]

In an effort to create a definition that is consistently used across the field, the ILAE has proposed the following definition of drug-resistant epilepsy[20]:



A prospective non-interventional study showed that **almost half (44%) of patients with newly diagnosed epilepsy were free of seizures for at least 1 year after trying the first AED.[18]**

Importantly, **36% of patients were left without seizure control after trying 2 or more AEDs and/or a combination AED treatment regimen.[18]**



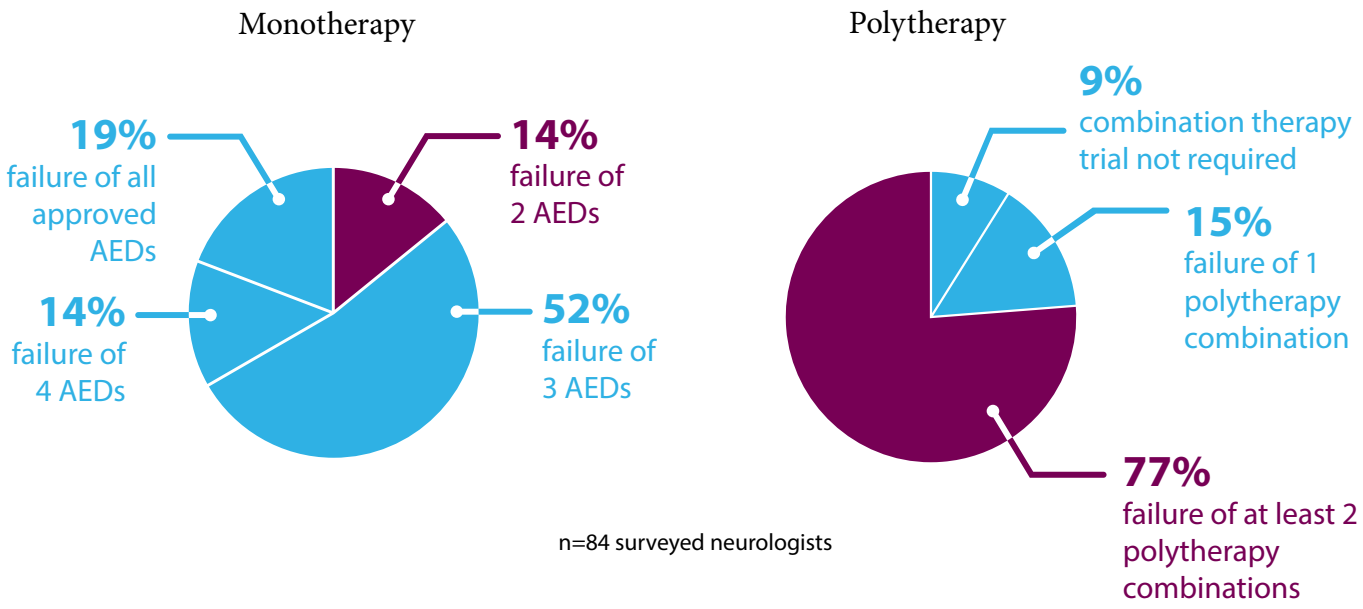
Study design: Newly diagnosed patients (n=470) with epilepsy were followed for 13 years (1984-1997) after initiating AED therapy. Seizure-free was defined as the absence of seizures for at least 1 year on current therapy or while not taking any medication; the median duration of follow-up was 5 years.[18]

In practice, though, doctors have varying opinions about what it means to be resistant to an AED.

When a group of surveyed neurologists, all practicing in Michigan (n=84), were asked how they define drug-resistant epilepsy, 14% answered with failure of 2 AED monotherapy trials and 52% answered with failure of 3 AED monotherapy trials.[21]

With respect to polytherapy regimens, 77% of respondents stated that patients had to fail a minimum of 2 polytherapy combinations before being considered medically refractory.[21]

Q: When do you consider your epilepsy patients to have failed drug therapy and become "medically refractory"?[21]



n=84 surveyed neurologists

There are 2 life-threatening conditions associated with epilepsy that doctors and patients need to be aware of: *status epilepticus* and *sudden unexpected death in epilepsy (SUDEP)*.[22,23]

- Status epilepticus[22]
- Sudden unexpected death in epilepsy (SUDEP)[23]

Status epilepticus is continuous seizure activity that is caused by the failure of mechanisms responsible for seizure termination or by the initiation of mechanisms that lead to abnormally prolonged seizures.[24]

Status epilepticus can cause neuronal death and injury that depend on the type and duration of seizures.[24]

Status epilepticus can be distinguished with the use of 2 "operational dimensions," or time points.[24]

t_1	t_2
The time point which a seizure is regarded as abnormally prolonged	The time of ongoing seizure activity beyond which there is risk of long-term consequences
For example:	**For example:**
Tonic-clonic 5 min.	Tonic-clonic 30 min.
Focal* 10 min.	Focal* >60 min.

*With impaired consciousness.

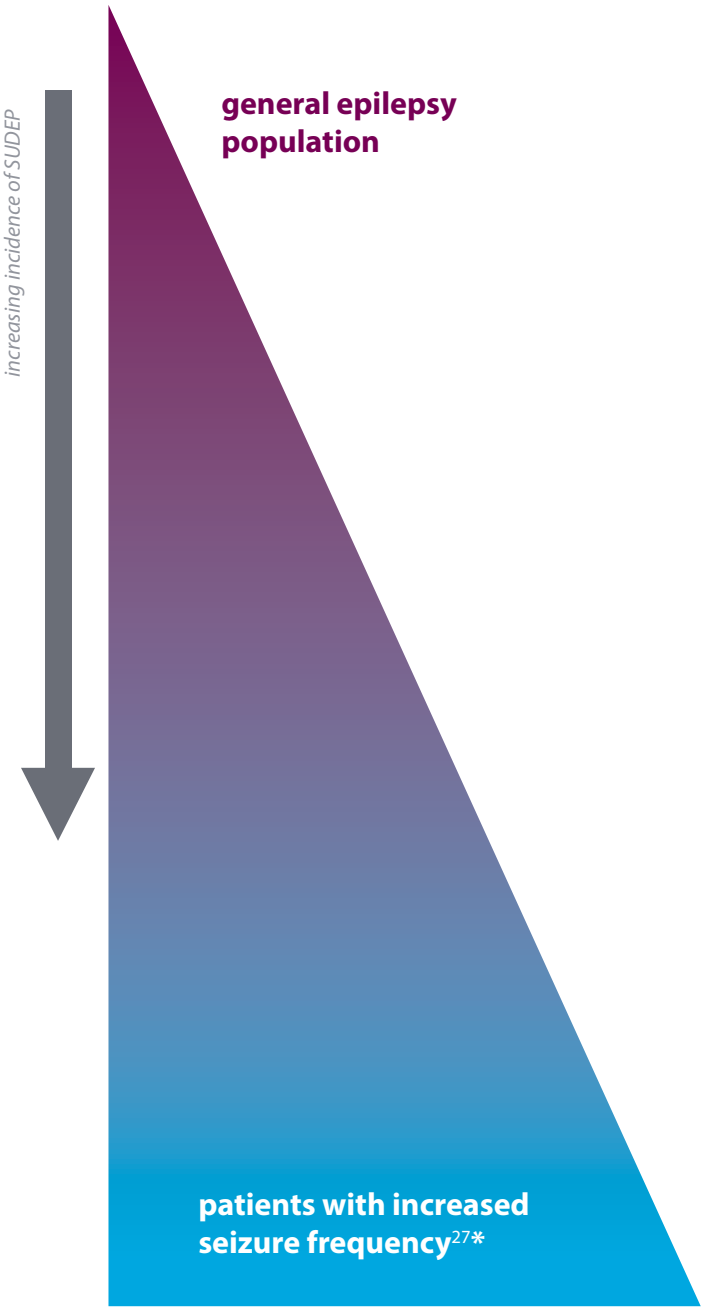
t_1 indicates the time that emergency treatment of status epilepticus should be started. t_2 indicates the time at which long-term consequences may be expected.[24]

The mortality rate for patients who experience status epilepticus in the US has been shown to be as high as 20%.[25] The treatment for status epilepticus needs to be initiated immediately because the prognosis worsens with increasing duration of the seizure.[26]

SUDEP, or sudden unexpected death in epilepsy, may occur without obvious reason and is not usually a direct result of an epileptic seizure.[23]

The incidence of SUDEP has been shown to vary across study populations. One prospective study conducted at 3 epilepsy centers, which enrolled 4578 patients, found the overall incidence of SUDEP was approximately 1.2 per 1000 patient-years in epilepsy. This same cohort study found that a progressive increase in the risk of SUDEP was correlated with increased seizure frequency.[27]

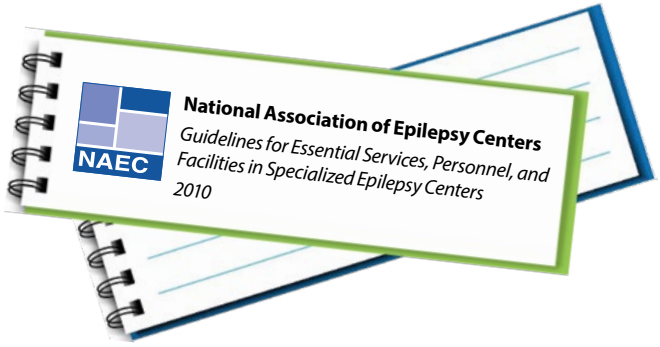
The specific causes of SUDEP are not well understood, but multiple clinical risk factors have been uncovered, including high frequency of any type of seizure in the past year, 1-3 tonic-clonic seizures in the past year, and longer duration of epilepsy (≥30 years).[27]



*More than 50 seizures of any type per month or 1-3 tonic-clonic seizures per year.[27]

Referral to a Specialist

The National Association of Epilepsy Centers (NAEC) has evidence-based referral guidelines for physicians who are managing patients with refractory epilepsy.[28]



If a patient's seizures have not been brought under control after 3 months of care by a primary care physician, referral to a neurologist, or an epilepsy center with an epileptologist (if locally available), may be appropriate.[28]

Under care of primary care physician

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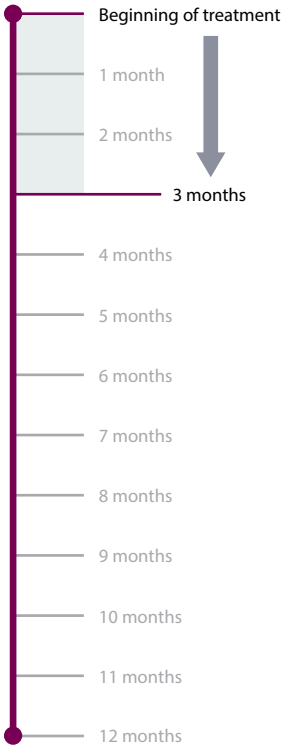
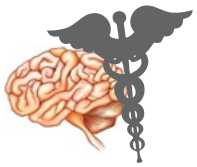
No seizure control after **3 months**

Referral to neurologist or epileptologist may be appropriate



If a patient's seizures have not been brought under control after 9-12 months of care by a neurologist, the patient may be referred to an epilepsy center with an epileptologist.[28]



Under care of neurologist

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No seizure control after **9-12 months**

Refer to epileptologist

The majority of people with epilepsy can have successful and productive lives.

Many states will issue a **driver's license** to a patient with epilepsy after the patient has shown evidence of seizure control for a pre-specified amount of time (different in each state).[3]

There are a few seizure types that occur only during sleep or that do not involve loss of consciousness. Some states may allow driving exceptions in these cases.[3]

Patients with epilepsy should use caution when engaged in inherently risky recreational activities, such as climbing, swimming, or sailing.[3]

Patients with epilepsy:

Take PRECAUTIONS when engaging in activities that involve risk

Patients with epilepsy can have a healthy **pregnancy and birth.[3]**

A woman with epilepsy who plans to become pregnant should meet with her health care team to reassess the current need for antiseizure medication. The health care team will also determine the optimal medication to balance seizure control and avoid birth defects, and the lowest dose for going into planned pregnancy. Any change in medication should occur prior to the pregnancy, if possible.[3]

Some recommendations for patients with epilepsy who are pregnant or planning to become pregnant may include[3]:

- Using prenatal vitamins, including supplemental folic acid
- Maintaining healthy sleep patterns
- Adhering to an agreed-upon antiepileptic treatment regimen
- Avoiding stimuli known to trigger or worsen seizures

Section 7:
Advocacy Resources for Patients With Epilepsy*

National Association of Epilepsy Centers (NAEC)

The NAEC is a non-profit trade association that strives to make high quality health care available and affordable for epilepsy patients across the country. The primary objectives of NAEC are to connect people with epilepsy to specialized epilepsy care and to support epileptologists and administrators in the operations of their epilepsy centers.

Web: www.naec-epilepsy.org
Email: info@naec-epilepsy.org
Phone: 202-800-7074

Purple Day

Purple Day is an an annual international grassroots effort, observed on March 26, which is dedicated to increasing awareness about epilepsy worldwide.

Web: www.purpleday.org
Email: usa@purpleday.org

Citizens United for Research in Epilepsy (CURE)

CURE is a non-profit organization that raises funds for epilepsy research, founded by families of patients with epilepsy.

Web: www.CUREepilepsy.org
Email: info@CUREepilepsy.org
Phone: 312-255-1801

Talk About It!

The mission of the "Talk About It!" Foundation is to lead the fight to overcome the challenges of living with epilepsy and to accelerate therapies to stop seizures, find cures, and save lives.

Web: www.talkaboutit.org

Epilepsy Foundation

The Epilepsy Foundation is a national non-profit organization with nearly 50 local affiliates throughout the United States. The mission of the Epilepsy Foundation is to prevent, control, and cure epilepsy through community services, enhance public education about epilepsy, lead federal and local advocacy efforts, and support research into new treatments and therapies.

Web: www.epilepsy.com
Email: ContactUs@efa.org

24/7 Helpline:
800-EFA-1000 (800-332-1000)

Living Well With Epilepsy

Living Well With Epilepsy is a publication dedicated to inspiring people with epilepsy, increasing epilepsy awareness, and promoting channels of communication with organizations that further epilepsy research.

Web: www.livingwellwithepilepsy.com
Email: info@livingwellwithepilepsy.com

PatientsLikeMe

PatientsLikeMe is committed to putting patients first by providing a better and more effective way to share their real-world health experience.

Web: www.patientslikeme.com
Email: support@patientslikeme.com

*Sunovion Pharmaceuticals Inc. does not endorse any specific resource mentioned in this section.

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