**ABSTRACT**

Epilepsy affects 50 million people worldwide, with a prevalence of 4-10 per 1000 in the UK. Ten percent of people will have a seizure during their lifetime, without necessarily developing epilepsy. The risk of an individual developing epilepsy in their lifetime is 3-5%. Essentially, regardless of your chosen specialty, it is likely you will encounter patients with epilepsy, either during an acute seizure event or as a co-morbid condition. Like any chronic medical condition, the aim of management is to allow patients to live life as normally as possible; indeed, this is the case for the majority of patients, with up to 70% becoming seizure-free on monotherapy.

**KEYWORDS:** Seizures, Epilepticus, GABA, Brain.

**1. INTRODUCTION**

1.1 Definition of Epilepsy

It is a group of neurological diseases characterized by epileptic seizures. Epileptic seizures are episodes that can vary from brief and nearly undetectable to long periods of vigorous shaking. In epilepsy, seizures tend to recur, and have no immediate underlying cause while seizures that occur due to a specific cause are not deemed to represent epilepsy.

The cause of most cases of epilepsy is unknown, although some people develop epilepsy as the result of brain injury, stroke, brain tumors, and substance use disorders. Known genetic mutations are directly linked to only a small proportion of cases. Epileptic seizures are the result of excessive and abnormal cortical nerve cell activity in the brain. The diagnosis typically involves ruling out other conditions that might cause similar symptoms such as fainting. Additionally, making the diagnosis involves determining if any other cause of
seizures is present such as alcohol withdrawal or electrolyte problems. This may be done by imaging the brain and performing blood tests.

2. HISTORY$^{[2]}$
Hippocrates, 17th century engraving by Peter Paul Rubens of an antique bust. The oldest medical records show that epilepsy has been affecting people at least since the beginning of recorded history. Throughout ancient history, the disease was thought to be a spiritual condition. The world’s oldest description of an epileptic seizure comes from a text in Akkadian (a language used in ancient Mesopotamia) and was written around 2000 BC.

The oldest known detailed record of the disease itself is in the Sakikku, a Babylonian cuneiform medical text from 1067–1046 BC. This text gives signs and symptoms, details treatment and likely outcomes, and describes many features of the different seizure types. As the Babylonians had no biomedical understanding of the nature of disease, they attributed the seizures to possession by evil spirits and called for treating the condition through spiritual means. Around 900 BC, Punarvasu Atreya described epilepsy as loss of consciousness; this definition was carried forward into the Ayurvedic text of Charaka Samhita (about 400 BC).

3. SIGNS AND SYMPTOMS$^{[3]}$

3.1 Seizures
The most common type (60%) of seizures are convulsive. Of these, one-third begins as generalized seizures from the start, affecting both hemispheres of the brain. Two-thirds begin as partial seizures (which affect one hemisphere of the brain) which may then progress to generalized seizures. The remaining 40% of seizures are non-convulsive. An example of this type is the absence seizure, which presents as a decreased level of consciousness and usually lasts about 10 seconds.
4. CAUSES[^5]

See also: Causes of seizures

Epilepsy can have both genetic and acquired causes, with interaction of these factors in many cases. Established acquired causes include serious brain trauma, stroke, tumors and problems in the brain as a result of a previous infection. In about 60% of cases the cause is unknown. Epilepsies caused by genetic, congenital, or developmental conditions are more common among younger people, while brain tumors and strokes are more likely in older people.

4.1 Genetics

Genetics is believed to be involved in the majority of cases, either directly or indirectly. Some epilepsies are due to a single gene defect (1–2%); most are due to the interaction of multiple genes and environmental factors. Each of the single gene defects is rare, with more than 200 in all described. Most genes involved affect ion channels, either directly or indirectly. These include genes for ion channels themselves, enzymes, GABA, and G protein-coupled receptors.

4.2 Acquired

Epilepsy may occur as a result of a number of other conditions including tumors, strokes, head trauma, previous infections of the central nervous system, genetic abnormalities, and as a result of brain damage around the time of birth. Of those with brain tumors, almost 30% have epilepsy, making them the cause of about 4% of cases. The risk is greatest for tumors in the temporal lobe and those that grow slowly. Other mass lesions such as cerebral cavernous malformations and arteriovenous malformations have risks as high as 40–60%. Of those who
have had a stroke, 2–4% develop epilepsy. Some evidence links epilepsy and coeliac disease and non-celiac gluten sensitivity, while other evidence does not. There appears to be a specific syndrome which includes coeliac disease, epilepsy and calcifications in the brain.

4.3 Classification

1. Barbiturate: phenobarbitone
2. Deoxybarbiturate: primidone
3. Hydantoin: phenytoin
4. Iminostilbene: carbamszepine
5. Succinimide: ethosuximide
6. Aliphatic carboxylic acid: valpric acid
7. Phenyltriazine: lamotrigine
8. Benzodiazepines: clonazepam, diazepam
9. Cyclic GABA analogue: gabapentin

Chemistry

Most of the older anticonvulsants have close structure similarity. This is depicted in fig. However, benzodiazepines, carbamazepine, valproic acid and the newer drugs are chemically diverse. Presence of a phenyl substitution confers activity against tonic-clonic seizures.

1. Phenobarbitone

Phenobarbitone was the first efficacious antiepileptic introduced in 1912. The mechanism of CNS depressant action of barbiturates is described on p. 391. The same may apply to anticonvulsant action. GABA$\alpha$A receptor mediated synaptic inhibition appears to be most important. However, phenobarbitone has specific anticonvulsant activity which is not entirely dependent on general CNS depression. Quantitative differences in the different facts of action (GABA-facilitatory, GABA-mimetic, antiglutamate, Ca$^{2+}$ entry reduction) have been noted for phenobarbitone compared to hypnotic barbiturates.
2. **Primidone**  
A deoxybarbiturate, converted by liver to phenobarbiturate and phenylethyl malonamide (PEMA). Activity is mainly due to these active metabolites because 1/2 of primidone (6-14 hr) is less than that of its active metabolites. About 1/3 primidone is excreted unchanged by kidney. Dose to dose primidone is less potent, but antiepileptic efficacy is similar to phenobarbitone. It is infrequently used now in GTCS and partial epilepsy, mainly as an adjuvant to phenytoin or carbamazepine.

3. **Phenytoin (Diphenydantoin)**  
Phenytoin is not a CNS depressant; some sedation occurs at therapeutic doses, but this does not increase further with dose; rather toxic doses produce excitement and muscular rigidity. The most outstanding action is abolition of tonic phase of maximal electroshock seizures, with no effect on or prolongation of clonic phase. It limits spread of seizure activity. Threshold for PTZ convulsions is not raised. Tonic-clonic epilepsy is suppressed but paroxysmal focal EEG discharge and ‘aura’ persist.

- **Mechanism of phenytoin**

4. **Phenytoin (Diphenylhydantoin)**  
Phenytoin has a stabilizing influence on neuronal membrane-prevents repetitive detonation of normal brain cells during depolarization shift that occurs in epileptic patient and consists of a synchronous and unusually large depolarization over which action potentials are superimposed. This is achieved by prolonging the inactivated state of voltage sensitive neuronal Na+ channel that governs the refractory period of the neurone. As a result high
frequency discharges are inhibited with little effect on normal low frequency discharges which allow Na+ channels to recover even when inactivation is prolonged. This effect has been noted at therapeutic concentration of phenytoin, while other effects like reduction in Ca2+ influx, inhibition of glutamate and facilitation of GABA responses have been demonstrated at higher/toxic concentrations.

5. **Carbamazepine**
Chemically related to imipramine, it was introduced in the 1960s for the trigeminal neuralgia; is now a first line antiepileptic drug. Its pharmacological actions resemble phenytoin, but important differences have been noted in experimental studies.

6. **Ethosuximide**
The most prominent action of ethosuximide is antagonism of PTZ induced clonic seizures at doses which produce no other discernable action. It raises seizure threshold but does not modify maximal electroshock seizures or inhibit kindling. Clinically it is effective only in absence seizures.

7. **Valproic Acid (Sodium Valproate)**
It is a branched chain aliphatic carboxylic acid with a broad spectrum anticonvulsant action. It is more potent in blocking PTZ seizures than in modifying maximal electroshock. Establishment of chronic experimental seizure foci and kindling are also prevented. Remarkably, at anticonvulsant doses, valproate produces little sedation or other central effects. Likewise, it is effective in partial seizures and GTCS as well as absence seizures.

8. **Clonazepam**
It is a benzodiazepine with prominent anticonvulsant properties: blocks PTZ seizures at doses which produce mild sedation. Efficacy in modifying maximal electroshock seizures is low. Though in experimental models of chronic epilepsy in inhibits spread rather than the focus itself, it is singularly ineffective in GTCS. Production of generalized seizures by kindling is suppressed, but local after-discharges persist.

9. **Diazepam**
It has anticonvulsant activity in a variety of models but is not used for long term therapy of epilepsy because of prominent sedative action and rapid development of tolerance to the
antiepileptic effect. However, it is the drug of choice for emergency control of convulsions, e.g. status epilepticus, tetanus, ecampsia, convulsant drug poisoning, etc.

5. MECHANISM OF ACTION OF EPILEPTIC DRUG \[6\]

Symptomatic Partial Epilepsy

5.1 Major Types of Epilepsy

<table>
<thead>
<tr>
<th>Types of Epilepsy</th>
<th>Generalized Epilepsy</th>
<th>Partial Epilepsy</th>
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<tr>
<td>Idiopathic (genetic causes)</td>
<td>- Childhood absence epilepsy</td>
<td>- Benign focal epilepsy of childhood</td>
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<td></td>
<td>- Juvenile myoclonic epilepsy</td>
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5.2 Idiopathic Generalized Epilepsy

In idiopathic generalized epilepsy, there is often, but not always, a family history of epilepsy. Idiopathic generalized epilepsy tends to appear during childhood or adolescence, although it may not be diagnosed until adulthood. In this type of epilepsy, no nervous system (brain or spinal cord) abnormalities, other than the seizures, can be identified on either an EEG or imaging studies (MRI).

The types of seizures affecting patients with idiopathic generalized epilepsy may include:

- Myoclonic seizures (sudden and very short duration jerking of the extremities)
- Absence seizures (staring spells)
- Generalized tonic-clonic seizures (grand mal seizures)

Idiopathic generalized epilepsy is usually treated with medications. Some people outgrow this condition and stop having seizures, as is the case with childhood absence epilepsy and a large number of patients with juvenile myoclonic epilepsy.

- **Classification**

The International League Against Epilepsy (ILAE) provided a classification of the epilepsies and epileptic syndromes in 1989 as follows:

1. Localization-related epilepsies and syndromes
   1. Unknown cause (e.g. benign childhood epilepsy with centrotemporal spikes)
   2. Symptomatic/cryptogenic (e.g. temporal lobe epilepsy)
2. Generalized
   1. Unknown cause (e.g. childhood absence epilepsy)
   2. Cryptogenic or symptomatic (e.g. Lennox-Gastaut syndrome)
   3. Symptomatic (e.g. early infantile epileptic encephalopathy with suppression burst)
   3. Epilepsies and syndromes undetermined whether partial or generalized
   1. With both generalized and partial seizures (e.g. epilepsy with continuous spike-waves during slow wave sleep)
   4. Special syndromes (with situation-related seiz.)
5.2 Pathophysiology Of Epileps

![Pathophysiology of Epilepsy](image)

6. DIAGNOSIS[7]

An EEG can aid in locating the focus of the epileptic seizure.

The diagnosis of epilepsy is typically made based on observation of the seizure onset and the underlying cause. An electroencephalogram (EEG) to look for abnormal patterns of brain waves and neuroimaging (CT scan or MRI) to look at the structure of the brain are also usually part of the workup. While figuring out a specific epileptic syndrome is often attempted, it is not always possible. Video and EEG monitoring may be useful in difficult cases.

6.1 Tests

An electroencephalogram (EEG) can assist in showing brain activity suggestive of an increased risk of seizures. It is only recommended for those who are likely to have had an epileptic seizure on the basis of symptoms. In the diagnosis of epilepsy, electroencephalography may help distinguish the type of seizure or syndrome present. In children it is typically only needed after a second seizure. It cannot be used to rule out the diagnosis, and may be falsely positive in those without the disease. In certain situations it may be useful to perform the EEG while the affected individual is sleeping or sleep deprived.
Diagnostic imaging by CT scan and MRI is recommended after a first non-febrile seizure to detect structural problems in and around the brain.

6.3 Treatment of Epilepsies
Antiepileptic drugs suppress seizures, but do not cure the disorder; the disease may fadeout though after years of successful control. The aim of drugs is to control and totally prevent all seizure activity at an acceptable level of side effects. With the currently available drugs, this can be achieved in about half of the patients. Another 20-30% attain partial control, while the rest remain resistant. The cause of epilepsy should be searched in the patient; if found and treatable, an attempt to remove it should be made.

6.4 Side Effect of Epilepsy Drug
Before any epilepsy drug is prescribed, your health care provider will discuss with you the potential benefits, side effect, and risk.

a. Common or predictable side effect: these are generic, non specific, and dose related side effect which occur with any epilepsy drug because it affect the central nervous system. These side effect include blurry or double vision, fatigue, sleepiness, unsteadiness, as well as stomach upset.

b. Idiosyncratic side effects: these are rare and unpredictable reaction which are not dose related. Most often, these side effect are skin rashes, low blood cell counts, and liver problem.

7. PREVENTION
Epilepsy—a disorder in which person recurring unprompted seizures due to abnormal electrical activity in the brain—affect an estimated 50 million people worldwide. In above half those people, the cause of the epilepsy unknown. Among the other 25 million individual, the cause may be a defect in the structure of the brain, a tumor or stroke, or a severe head injury—the most common known cause in young adult, according to the epilepsy therapy project. Their for, its important to protect your head with a helmet any time you are engaged in and activity in which your head could be damaged, such as playing contact sport like football or riding bicycle all-terrain vehicle or motorcycle.
8. MANAGEMENT\textsuperscript{[9]}

Epilepsy is usually treated with daily medication once a second seizure has occurred, but for those at high risk, medication may be started after the first seizure. In some cases, a special diet, the implantation of a neurostimulator, or neurosurgery may be required.

8.1 First Aid

Rolling a person with an active tonic-clonic seizure onto their side and into the recovery position helps prevent fluids from getting into the lungs. Putting fingers, a bite block or tongue depressor in the mouth is not recommended as it might make the person vomit or result in the rescuer being bitten. Efforts should be taken to prevent further self-injury. Spinal precautions are generally not needed.

If a seizure lasts longer than 5 minutes or if there are more than two seizures in an hour without a return to a normal level of consciousness between them, it is considered a medical emergency known as status epilepticus. This may require medical help to keep the airway open and protected; a nasopharyngeal airway may be useful for this. At home the recommended initial medication for seizure of a long duration is midazolam placed in the mouth. Diazepam may also be used rectally.

8.2 Medications

Anticonvulsants

The mainstay treatment of epilepsy is anticonvulsant medications, possibly for the person's entire life. The choice of anticonvulsant is based on seizure type, epilepsy syndrome, other medications used, other health problems, and the person's age and lifestyle. A single medication is recommended initially; if this is not effective, switching to a single other medication is recommended. Two medications at once is recommended only if a single medication does not work.

There are a number of medications available. Phenytoin, carbamazepine and valproate appear to be equally effective in both partial and generalized seizures.\textsuperscript{[89]} Controlled release carbamazepine appears to work as well as immediate release carbamazepine, and may have fewer side effects. In the United Kingdom, carbamazepine or lamotrigine are recommended as first-line treatment for partial seizures, with levetiracetam and valproate as second-line due to issues of cost and side effects.
8.3 Surgery
Epilepsy surgery may be an option for people with partial seizures that remain a problem despite other treatments. These other treatments include at least a trial of two or three medications. The goal of surgery is total control of seizures and this may be achieved in 60–70% of cases. Common procedures include cutting out the hippocampus via an anterior temporal lobe resection, removal of tumors, and removing parts of the neocortex. Some procedures such as a corpus callosotomy are attempted in an effort to decrease the number of seizures rather than cure the condition. Following surgery, medications may be slowly withdrawn in many cases.\[98\]

Neurostimulation may be another option in those who are not candidates for surgery. Three types have been shown to be effective in those who do not respond to medications: vagus nerve stimulation, anterior thalamic stimulation, and closed-loop responsive stimulation.

8.4 Alternative Medicine
Alternative medicine, including acupuncture, psychological interventions, routine vitamins, and yoga, have no reliable evidence to support their use in epilepsy. There is not enough evidence to support the use of cannabis. Melatonin is insufficiently supported by evidence.

9. PROGNOSIS\[10\]
Epilepsy cannot usually be cured, but medication can control seizures effectively in about 70% of cases. Of those with generalized seizures, more than 80% can be well controlled with medications while this is true in only 50% of people with partial seizures. One predictor of long-term outcome is the number of seizures that occur in the first six months. Other factors increasing the risk of a poor outcome include little response to the initial treatment, generalized seizures, a family history of epilepsy, psychiatric problems, and waves on the EEG representing generalized epileptiform activity. In the developing world, 75% of people are either untreated or not appropriately treated. In Africa, 90% do not get treatment. This is partly related to appropriate medications not being available or being too expensive.

9.1 Mortality
People with epilepsy are at an increased risk of death. This increase is between 1.6 and 4.1 fold greater than that of the general population and is often related to: the underlying cause of the seizures, status epilepticus, suicide, trauma, and sudden unexpected death in epilepsy (SUDEP). Death from status epilepticus is primarily due to an underlying problem rather than
missing doses of medications. The risk of suicide is increased between two and six times in those with epilepsy. The cause of this is unclear. SUDEP appears to be partly related to the frequency of generalized tonic-clonic seizures and accounts for about 15% of epilepsy related deaths. It is unclear how to decrease its risk. The greatest increase in mortality from epilepsy is among the elderly. Those with epilepsy due to an unknown cause have little increased risk. In the United Kingdom, it is estimated that 40–60% of deaths are possibly preventable. In the developing world, many deaths are due to untreated epilepsy leading to falls or status epilepticus.

10. EPIDEMIOLOGY\(^{[12]}\)

Epilepsy is one of the most common serious neurological disorders affecting about 65 million people globally. It affects 1% of the population by age 20 and 3% of the population by age 75. It is more common in males than females with the overall difference being small. Most of those with the disorder (80%) are in the developing world.

The number of people who currently have active epilepsy is in the range 5–10 per 1,000, with active epilepsy defined as someone with epilepsy who has had at least one seizure in the last five years. Epilepsy begins each year in 40–70 per 100,000 in developed countries and 80–140 per 100,000 in developing countries. Poverty is a risk and includes both being from a poor country and being poor relative to others within one's country. In the developed world epilepsy most commonly starts either in the young or in the old. In the developing world its onset is more common in older children and young adults due to the higher rates of trauma and infectious diseases. In developed countries the number of cases a year has decreased in children and increased among the elderly between the 1970s and 2003. This has been attributed partly to better survival following strokes in the elderly.

11. SOCIETY AND CULTURE\(^{[13]}\)

11.1 Stigma

Stigma is commonly experienced, around the world, by those with epilepsy. It can affect people economically, socially and culturally. In India and China, epilepsy may be used as justification to deny marriage. People in some areas still believe those with epilepsy to be cursed. In Tanzania, as in other parts of Africa, epilepsy is associated with possession by evil spirits, witchcraft, or poisoning and is believed by many to be contagious, for which there is no evidence. Before 1970 the United Kingdom had laws which prevented people with
epilepsy from marrying. The stigma may result in some people with epilepsy denying that they have ever had seizures.

11.2 Economics
Seizures result in direct economic costs of about one billion dollars in the United States. Epilepsy resulted in economic costs in Europe of around 15.5 billion Euros in 2004. In India epilepsy is estimated to result in costs of 1.7 billion USD or 0.5% of the GDP. It is the cause of about 1% of emergency department visits (2% for emergency departments for children) in the United States.

11.3 Vehicles
See also: Epilepsy and driving
Those with epilepsy are at about twice the risk of being involved in a motor vehicular collision and thus in many areas of the world are not allowed to drive or only able to drive if certain conditions are met. In some places physicians are required by law to report if a person has had a seizure to the licensing body while in others the requirement is only that they encourage the person in question to report it themselves. Countries that require physician reporting include Sweden, Austria, Denmark and Spain. Countries that require the individual to report include the UK, and New Zealand and the physician may report if they believe the individual has not already. In Canada, the United States and Australia the requirements around reporting vary by province or state. If seizures are well controlled most feel allowing driving is reasonable.

11.4 Support Organizations
There are organizations that provide support for people and families affected by epilepsy. The Out of the Shadows campaign, a joint effort by the World Health Organization, the International League Against Epilepsy and the International Bureau for Epilepsy, provides help internationally. The Joint Epilepsy Council serves the UK and Ireland. In the United States, the Epilepsy Foundation is a national organization that works to increase the acceptance of those with the disease, their ability to function in society and to promote research for a cure. The Epilepsy Foundation, some hospitals, and some individuals also run support groups in the United States.
12. RESEARCH[14]
Seizure prediction refers to attempts to forecast epileptic seizures based on the EEG before they occur. As of 2011, no effective mechanism to predict seizures has been developed. Kindling, where repeated exposures to events that could cause seizures eventually causes seizures more easily, has been used to create animal models of epilepsy.

Gene therapy is being studied in some types of epilepsy. Medications that alter immune function, such as intravenous immunoglobulins, are poorly supported by evidence. Noninvasive stereotactic radio surgery is, as of 2012, being compared to standard surgery for certain types of epilepsy.

Common locations for the start of seizures and neural networks have been found to be affected in the majority of epilepsy. Efforts to figure out how epilepsy occurs are working to take into account the different regions of the brain and the timing of their activity.

13. OTHER ANIMALS[15]
Epilepsy occurs in a number of other animals including dogs and cats and is the most common brain disorder in dogs. It is typically treated with anticonvulsants such as phenobarbital or bromide in dogs and phenobarbital in cats. Imepitoin is also used in dogs. While generalized seizures in horses are fairly easy to diagnose, it may be more difficult in non-generalized seizures and EEGs may be useful.

14. COMPLICATIONS OF EPILEPSY[16]
Complications of complex partial seizures are easily triggered by emotional stress. The limbic seizures (i.e., hypothalamus, hippocampus, amygdale) of the brain may be damaged by seizures activity. The limbic system is concerned with emotion and motivation.

This patient may develop cognitive and behavioral difficulties, such as the following:

- Interictal personality: humorlessness, dependence, obsessions, anger, hypo-or hypersexuality, emotionality.
- Memory loss: short term memory loss attributable to dysfunction in the hippocampus, anoma
- Poriomania: prolonged aimless wandering followed by amnesia Complication associated with tonic-clonic seizures may involve injury, such as the following.
- Aspiration (inhalation into the lung) of secretion or vomited stomach content.
15. CONCLUSION[17]

Neurobehavioral disorder can profoundly affect the lives of people with epilepsy.

- In general, the more frequent and more severe the seizures, the more likely that neurobehavioral disorder will develop.
- These disorders should be actively considered in evaluating patient with epilepsy-both at the first visit and follow up.
- Many of these disorders such as anxiety, depression and psychosis can be treated with medication.
- There are other disorder may also response to behavioral and other non pharmacologic therapies.
- Identification and treatment of cognitive and behavioral disorder can leads to significant improvement in quality of life.

16. REFERENCES

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