EPILEPSY

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Abstract: Epilepsy is a group of neurological disorders characterized by epileptic seizures. The cause of most cases of epilepsy is unknown, although some people develop epilepsy as the result of brain injury, stroke, brain tumor, and drug and alcohol misuse. Diagnostic imaging by CT scan and MRI is recommended after a first non-febrile seizure to detect structural problems in and around the brain. 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.

Key words: Epilepsy, ECG, Seizures tenicclonic, Phenytonic.

EPILEPSY

Epilepsy (from the Ancient Greek word meaning "to seize,") [1] is a group of neurological disorders characterized by epileptic seizures. [3] Epileptic seizures are episodes that can vary from brief and nearly undetectable to long periods of vigorous shaking.[4] In epilepsy, seizures tend to recur, and have no immediate underlying cause [2] while seizures that occur due to a specific cause are not deemed to represent epilepsy. [5]

The cause of most cases of epilepsy is unknown, although some people develop epilepsy as the result of brain injury, stroke, brain tumor, and drug and alcohol misuse. Genetic mutations are linked to a small proportion of the disease.[6] Epileptic seizures are the result of abnormal and excessive cortical nerve cell activity in the brain.[5] The diagnosis typically involves ruling out other conditions that might cause similar symptoms such as syncope.

Additionally it involves determining if any other causes of seizures are present such as alcohol withdrawal or electrolyte problems. This may be done by doing imaging of the brain and blood tests. Epilepsy can often be confirmed with an electroencephalogram(EEG) but a normal test does not rule out the disease.[6]

About 1% of people worldwide (65 million) have epilepsy and nearly 80% of cases occur in developing countries. Epilepsy becomes more common as people age. In the developed world, onset of new cases occurs most frequently in infants and the elderly; in the developing world this is in older children and young adults due to differences in the frequency of the underlying causes [7].

Signs and symptoms

Epilepsy is characterized by a long-term risk

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of recurrent seizures. These seizures may present in several ways depending on the part of the brain involved and the person's age.

Seizures

The most common type (60%) of seizures are convulsive. Of these, two-thirds begin as focal seizures (which may then become generalized) while one-third begin as 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.

Focal seizures are often preceded by certain experiences, known as an aura. These may include sensory (visual, hearing or smell), psychic, autonomic, or motor phenomena. Automatisms may occur; these are non-consciously generated activities and mostly simple repetitive movements like smacking of the lips.[8]

There are six main types of generalized seizures: tonic- clonic, tonic, clonic, myoclonic, absence, and atonic seizures. They all involve loss of consciousness and typically happen without warning.

Tonic-clonic seizures present with a contraction of the limbs followed by their extension along with arching of the back which lasts 10–30 seconds (the tonic phase). A cry may be heard due to contraction of the chest muscles. This is then followed by a shaking of the limbs in unison (clonic phase). Tonic seizures produce constant contractions of the muscles. A person often turns blue as breathing is stopped. In clonic seizures there is shaking of the limbs in unison. After the shaking has stopped it may take 10–30 minutes for the person to return to normal; this period is called the "postictal phase". Loss of bowel or bladder control may occur during a seizure. The tongue may be bitten at either the tip or on the sides during a seizure. In tonic-clonic seizure, bites to the sides are more common.[9]

Myoclonic seizures involve spasms of muscles in either a few areas or all over. Absence seizures can be subtle with only a slight turn of the head or eye blinking. The person does not fall over and returns to normal right after it ends. Atonic seizures involve the loss of muscle activity for greater than one second. This typically occurs on both sides of the body[10]

Postictal

After the active portion of a seizure, there is typically a period of confusion referred to as the postictal period before a normal level of consciousness returns. This usually lasts 3 to 15 minutes but may last for hours. Other common symptoms include feeling tired, headache, difficulty speaking, and abnormal behavior. Psychosis after a seizure is relatively common, occurring in 6–10% of people. Often people do not remember what happened during this time.[11]

Psychosocial

Epilepsy can have adverse effects on social and psychological well-being. These effects may include social isolation, stigmatization, or disability. They may result in lower educational achievement and worse employment outcomes. Learning difficulties are common in those with the condition, and

especially among children with epilepsy.[12]

Definition

1. At least two unprovoked (or reflex) seizures occurring greater than 24 hours apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome

Diagnosis of epilepsy

The diagnosis of epilepsy is typically made based on the description of the seizure and the underlying cause. An electro encephalogram and neuroimaging are also usually part of the workup. Video and EEG monitoring may be useful in difficult cases[12].

Classification of epilepsy causes

A. Unknown cause (mostly genetic or presumed genetic origin)
1. Pure epilepsies due to single gene disorders
2. Pure epilepsies with complex inheritance

B. Symptomatic (associated with gross anatomic or pathologic abnormalities)
a. Mostly genetic or developmental causation
1. Childhood epilepsy syndromes
2. Progressive myoclonic epilepsies
3. Neurocutaneous syndromes
4. Other neurologic single gene disorders
5. Disorders of chromosome function
6. Developmental anomalies of cerebral structure

b.Mostly acquired causes
1. Hippocampal sclerosis
2. Perinatal and infantile causes
3. Cerebral trauma, tumor or infection
4. Cerebrovascular disorders
5. Cerebral immunologic disorders
6. Degenerative and other neurologic conditions

C. Provoked (a specific systemic or environmental factor is the predominant cause of the seizures)
1. Provoking factors
2. Reflex epilepsies

D. Crytogenic (presumed symptomatic nature in which the cause has not been identified[13]

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. MRI is generally a better imaging test except when bleeding is suspected, for which CT is more sensitive and more easily available.[13] If someone attends the emergency room with a seizure but returns to normal quickly, imaging tests may be done at a later point. If a person has a previous diagnosis of epilepsy with previous imaging, repeating the imaging is usually not needed

even if there are subsequent seizures.[14]

For adults, the testing of electrolyte, blood glucose and calcium levels is important to rule out problems with these as causes. An EEG can rule out problems with the rhythm of the heart. A lumbar puncture may be useful to diagnose a central nervous system infection but is not routinely needed. In children additional tests may be required such as urine biochemistry and blood testing looking for metabolic disorders. [15]

A high blood prolactin level within the first 20 minutes following a seizure may be useful to confirm an epileptic seizure as opposed to psychogenic non-epileptic seizure.[16]

Prevention

While many cases are not preventable, efforts to reduce head injuries, provide good care around the time of birth, and reduce environmental parasites such as the pork tapeworm may be effective. Efforts in one part of Central America to decrease rates of pork tapeworm resulted in a 50% decrease in new cases of epilepsy.[17]

Management

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[14].

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.

If a seizure lasts longer than 5 minutes or if there are more than two seizures in an hour without a return to normal 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. [18] In hospital, intravenous lorazepam is preferred. If two doses of benzodiazepines are not effective,other medications such as phenytoin are recommended. Convulsive status epilepticus that does not respond to initial treatment typically requires admission to the intensive care unit and treatment with stronger agents such as thiopentone or propofol.[14]

A step-wise treatment strategy

(1) Any precipitating factors for seizures, such as fever in young children, excessive fatigue, alcohol and drug abuse, and photo-sensitivity should be identified and the patient and relatives counselled about their avoidance.
(2) The reasons for, goals and limitations of antiepileptic drug treatment, the likely duration of therapy and the need for regular tablet taking should be explained.
(3) A patient should be commenced on a small dose of one of the first line antiepileptic drugs for their type of seizure and dose increments made if seizures continue and side-effects do

not occur, with increments being guided by the measurement of serum drug concentrations.

(4) If seizures continue despite a maximally tolerated dose of a first line antiepileptic drug, the diagnosis of epilepsy and its putative aetiology should be reconsidered, and compliance checked with counselling, tablet counts and measurement of the serum drug concentration.

(5) Another first line drug should then be commenced, built up to an optimal dose and the initial agent then withdrawn. The ideal rate of drug withdrawal in this situation is controversial; phenytoin and sodium valproate probably may be safely withdrawn over a few days, but carbamazepine, barbiturate and benzodiazepine withdrawal should be over a period of weeks [19].

(6) The dose of the second drug, taken alone, should then be adjusted to optimum, as was the initial agent.

(7) If seizures continue despite a maximally tolerated dose of all the individual first line drugs, the next step is to try a combination of two first line drugs for that seizure type (e.g., ethosuximide and sodium valproate for Generalized, absences or phenytoin and carbamazepine for partial seizures). The chances of duotherapy controlling seizures when monotherapy has been unsuccessful is of the order of 10-15% [20].

(8) Should a combination of two first line agents be unhelpful, the drug which appears to have the most effect, and least side-effects, should be continued and the other antiepileptic drug replaced by a second line drug

(9) If the second line drug is effective, withdrawal of the initial agent should be considered. If prescription of a second line agent is unhelpful, it should not be continued.

(10) The use of a novel antiepileptic drug may be considered. As a general rule, the use of such drugs should only be as part of a formal organized trial, with very accurate documentation of seizures and side-effects.

(11) The above scheme will generally take a number of months or even years to work through. If satisfactory control cannot be obtained with drugs and the patient has partial seizures, consideration should be given to surgical treatment of the epilepsy.

Seizure type First-line drugs	
Generalized	
Tonic-clonic, tonic & clonic	Phenytoin Carbamazepine Sodium valproate
Simple absences	Ethosuximide Sodium valproate
Complex absences	Sodium valproate
Atonic)	Clonazepam/Clobazam
Infantile spasms	ACTH/steroids Clonazepam
Myoclonic	Sodium valproate Clonazepam
Partial	
Simple, complex & secondarily generalized	Phenytoin Carbamazepine Sodium valproate

Second-line drugs:

Phenobarbitone Clonazepam
Primnidone Clobazam
Acetazolamide Vigabatrin

Newer drugs for epilepsy

The number of antiepileptic drugs (AEDs) approved for use in the United States alone has more than doubled in the past 15 years (Table 1). Currently, 24 AEDs and 1 device are marketed in the United States, and additional agents are available worldwide[21].

TABLE 1. Antiepileptic Drugs and Devices Currently Approved by the Food and Drug Administration

Before 1993	1993-2005	2009-2011
Carbamazepine	Felbamate	Vigabatrin
Clonazepam	Felbamate	Rufinamide
Diazepam	Lamotrigine	Lacosamide
Ethosuccimide	Levetiracetam	Clobazam
Lorazepam	Oxcarbazepine	Ezogabine
Phenobarbital	Pregabalin	
Primidone	Topiramate	
Valproic acid	Vagus nerve stimulation	
Zonismide		

TABLE 2. AEDs Approved in 2009-2011

AED	FDA indication	Putative mechanism
Vigabatrin	Infantile spasms/add-on for partial epilepsy	Irreversible inhibition of GABA trans-minase
Rufinamide	Atonic seizures	Sodium channel modulation
Lacosamide	Add-on for partial epilepsy	Sodium channel modulation
Clobazam	Lennox-Gastaut syndrome	$GABA_A$ binding
Ezogbine	Add-on for partial epilepsy	Potassium channel modulation

AED = antiepileptic drug, FDA = Food and Drug Administration; GABA = y-aminobutyric acid.

TABLE 3. Summary of characteristics of Recently Approved AEDs in the US

Dug	Available doses	Age group	Initial dose	Tiration	Maintenance dose	Durg interactions
Ezogabine	50-,200-,300-, and 400-mg tablets	Adults	100 gm 3 time daily (300 mg/d)	Increase by no more than 50mg 3 time daily, no more than 150mg/d weekly	200-400 mg 3 time daily (600-1200 mg/d)	Carbamazepine and phenytion may reduce ezogabine levels; ezogabine can inhibit dearance of digoxin
Vigabatrin	500-mg tables; 500-mg oral powder for solution	Adults and children	500 mg twice daily; 50mg/kh daily divided twice daily	500 mg/wk; 25-50 mg/kg daily every 3 d	1500 mg twice daily (maximum); 150mg/d (maximum)	Vigabatrin may reduce phenytion levels
Rufinamide	40-mg/ml. oral solution; 200-and 400-mg tablets	Adults and children	200-400 mg twice daily; 10mg/kg daily divided twice daily	400-800 mg every other day; 10 mg/kg every other day	1600 mg twice daily (maximum); 45 mg/kg daily divided twice daily (maximum, 3200 mg/d)	Rufinamide may decrease carbamazepine and lamotringine levels; rufinamide may increase phenobarbital, phenytion, and valproic acid levels
Lacosamide	10-mg/ml. intravenous solution; 10-mg/ml. oral solution; 50-, 100-, 150-, and 200- mg tablets	Adults	50 mg twice daily	50 mg twice daily every wk	200 mg twice daily (maximum)	None
Clobazam	5-, 10-, and 20-mg tablets	Adults and children > 2y wity weight > 30 kg	5 mg twice daily; 25 mg twice daily	10 mg twice daily at 7 d; 20 mg twice daily at 14 d; 5 mg twice daily at 7 d; 10 mg twice daily at 14 d	20 mg twice daily; 10 mg twice daily	Hormonal contraceptives metabolized by CYP3A4 may have diminished efficacy when given with dobazam; fluconazole, fluvoxamine, ticlopidine, and omeprazole may increase serum levels of dobazam

AED = antiepileptic drug,

References

1. Magiorkinis E, Kalliopi S, Diamantis A (January 2010). "Hallmarks in the history of epilepsy: epilepsy in antiquity". Epilepsy & behavior : E&B 17 (1): 103–108.

2. Chang BS, Lowenstein DH (2003). "Epilepsy". N. Engl. J. Med. 349 (13): 1257–66.

3. Fisher, Robert S; Acevedo, C; Arzimanoglou, A; Bogacz, A; Cross, JH; Elger, CE; Engel J, Jr; Forsgren, L; French, JA; Glynn, M; Hesdorffer, DC; Lee, BI; Mathern, GW; Moshé, SL; Perucca, E; Scheffer, IE; Tomson, T; Watanabe, M; Wiebe,

S (April 2014). "ILAE Official Report: A practical clinical definition of epilepsy". Epilepsia 55 (4): 475–82. .

4. "Epilepsy". Fact Sheets. World Health Organization. October 2012. Retrieved January 24, 2013.

5. Fisher R, van Emde Boas W, Blume W, Elger C, Genton P, Lee P, Engel J (2005). "Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE)". Epilepsia 46 (4): 470–2.

6. Longo, Dan L (2012). Harrison's principles of internal medicine (18th ed.). McGraw-Hill. p. 3258.

7. Wilden, JA; Cohen-Gadol, AA (15 August 2012). "Evaluation of first nonfebrile seizures." American family physician 86 (4): 334–40.

8. Bradley, Walter G. (2012). "67". Bradley's neurology in clinical practice. (6th ed.). Philadelphia, PA: Elsevier/Saunders

9. Engel, Jerome (2008). Epilepsy :a comprehensive textbook (2nd ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins. p. 2797.

10. Simon, David A. Greenberg, Michael J. Aminoff, Roger P. (2012). "12". Clinical neurology (8th ed.). New York: McGraw-Hill Medical.

11. Panayiotopoulos, CP (2010). A clinical guide to epileptic syndromes and their treatment based on the ILAE classifications and practice parameter guidelines (Rev. 2nd ed. ed.). [London]: Springer. p. 445.

12. National Clinical Guideline Centre (2012), p. 21–28

13. Robert S. Fisher, Walter van Emde Boas, Warren Blume, Christian Elger, Pierre Genton, Phillip Lee & Jerome Jr Engel (April 2005). "Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE)". Epilepsia 46 (4): 470–472.

14. National Clinical Guideline Centre (2012), p. 57–83

15. Wallace, ed. by Sheila J.; Farrell, Kevin (2004). Epilepsy in children (2nd ed.). London: Arnold. p. 354

16. Luef, G (October 2010). "Hormonal alterations following seizures." Epilepsy & behavior: E&B 19 (2): 131–3

17. Newton, CR (29 September 2012). "Epilepsy in poor regions of the world."Lancet 380 (9848): 1193–201.

18. National Clinical Guideline Centre (2012), pp. 55–56.

19. Duncan JS, Shorvon SD, Trimble MR. The withdrawal of phenytoin, carbamazepine and sodium valproate in patients with active epilepsy. Epilepsia 1990;31:324-33

20. Reynolds EH, Shorvon SD. Monotherapy or polytherapy for epilepsy? Epilepsia 1981;22:1-10

21. Bialer M, White HS. Key factors in the discovery and development of new antiepileptic drugs. Nat Rev Drug Discov. 2010; 9(1):68-82.