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Epilepsy

A new definition

Epilepsy is a disease of the nerves that lasts a long time, maybe even a lifetime. People who have epilepsy are prone to seizures. They are caused by a sudden surge in electrical signals in the brain. But not all people who have had a seizure have epilepsy. Earlier this year, the International League Against Epilepsy (ILAE) published an updated definition of epilepsy. The new definition is designed for practical use by doctors and their patients. According to this definition, a person has epilepsy if they have¹:

- ≥ 2 unprovoked seizures more than 24 hours apart
- 1 unprovoked seizure and a high risk ($\geq 60\%$) of having another one over the next 10 years
- An epilepsy syndrome

Not all seizures look the same

All of these things can be a sign of a seizure:

- Staring spell
- Temporary loss of vision
- Experiencing an unusual taste or smell
- Tingling or numb feeling
- Feeling of being electrically shocked
- Forgetful, confused, or experiencing a memory lapse
- Loss of awareness of time
- Tremors, twitching, jerking, uncontrolled shaking
- Rigid, tense muscles
- Tongue biting
- Drooling
- Loss of control over urine or stool
- Trouble breathing
- Loss of consciousness

Partial seizures affect just one part of the brain. Generalized seizures affect both sides of it.



Causes of epilepsy

These things can cause seizures:

- Alzheimer disease
- Brain tumor
- Chemical imbalance (low blood sugar, calcium, or magnesium; abnormal electrolytes)
- Problems during birth (eg, lack of oxygen)
- Certain conditions a baby is born with (eg, tuberous sclerosis, neurofibromatosis)
- Genetics (mutations, ie, changes, in a gene)
- Head trauma
- Inborn errors of metabolism
- Infections that scar the brain (eg, meningitis, encephalitis, cysticercosis, or brain abscess),
- Maternal drug use
- Stroke

Often, a cause cannot be found.

Diagnostic strategy

When a person has a seizure, doctors try to find out exactly what's going on. They start by learning everything they can about the seizure. They ask the person exactly what happened before, during, and after the seizure. Then they do a physical exam to look for conditions that might have caused the seizure. They might order blood tests to help with this. Next is a neurologic exam that may include tests for:

- The 5 senses
- Reflexes and muscle activity
- Walking and coordination
- Ability to remember words, do arithmetic, and name objects

That is followed by an electroencephalogram (EEG) to look at the brain's electrical activity. Finally, imaging studies may be done to look for too much spinal fluid, scar tissue, or tangles of blood vessels. Magnetic resonance imaging (MRI) is preferred. Computed tomography (CT) scans are also used.

The American Academy of Neurology recommends these things for every patient²:

- Determination of seizure type and frequency
- Determination of the cause
- Electroencephalogram (EEG)
- MRI or CT scan

Treatment strategy

Of course, if an underlying condition caused the seizure, it is treated. If not, the patient may be prescribed an antiepileptic. These drugs work for about 70% of patients.³ Which of the 15+ drugs is chosen depends on the type of epilepsy. These drugs don't cure the root cause of the seizures but do help prevent them. When drugs don't work, surgery or some type of nerve stimulation can be tried.

Some patients (ie, children with a mutation in the *SLC2A1* gene) can be successfully treated with a high fat, low carbohydrate diet. This diet is known as the ketogenic diet.

How the clinical laboratory can help

Some seizures are caused by conditions that can be cured. Lab tests can help find out if that is the case in an individual patient. Tests that are used for this purpose include an RBC, WBC, platelets, electrolytes (particularly sodium), glucose, spinal tap (to rule out infection in patients with a fever), and a drug screen for tricyclic antidepressants, cocaine, and other stimulants.

When to suspect genetics as the underlying cause

Here are some epilepsy diseases caused by gene mutations:

- Congenital disorders of glycosylation
- Disorders of peroxisome biogenesis
- Disorders of the RAS/MAPK pathway
- Early infantile epileptic encephalopathies
- Epilepsy in X-linked mental retardation
- Generalized/myoclonic/absence epilepsies, febrile seizures
- Holoprosencephaly
- Hyperekplexia
- Joubert syndrome and related disorders
- Leukodystrophies
- Lysosomal storage disorders
- Migraine
- Neuronal ceroid lipofuscinosis
- Neuronal migration disorders
- Selected inborn errors of metabolism
- Selected mitochondrial disorders
- Severe microcephaly/pontocerebellar hypoplasia
- Syndromic disorders

Genetic testing can detect mutations that cause epilepsy. Athena Diagnostics, a Quest Diagnostics company, offers such testing. Athena uses a next generation targeted sequencing method. This method allows many genes to be sequenced at the same time. That is very important for epilepsy, since many genes are involved. Genetic testing can help:

- Establish a specific diagnosis and save the patient from more stressful and costly testing
- Help predict what's to come for the patient
- Guide treatment strategy
- Give information that can be used when counseling relatives

Lab tests can also help with drug monitoring. They can detect or confirm certain side effects. Tests used for this purpose include RBC, WBC, platelets, electrolytes, and liver and kidney function tests. Blood levels of the specific antiepileptic drug can help⁴:

- Guide dosing decisions for drugs that have a lot of variability within and between people
- Find out if the patient is taking the drug as instructed
- Diagnose toxicity
- Assess treatment failure when it seems as if the patient is getting the right dose of the drug
- Find the blood level that corresponds to a patient's optimal drug dose; this level can be used to assess any subsequent loss of seizure control or changes in drug formulation
- Guide dosage changes when required by changes in drug formulation, patient age, or medical condition
- Determine need for dosage change in patients with known or potential drug interactions

References

1. Fisher RS, Acevedo C, Arzimnoglou A, et al. ILAE official report: a practical clinical definition of epilepsy. *Epilepsia*. 2014;55:475-482.
2. Fountain NB, Van Ness PC, Swain-Eng R et al. Quality improvement in neurology: AAN epilepsy quality measures: report of the Quality Measurement and Reporting Subcommittee of the American Academy of Neurology. *Neurology*. 2011;76:94-99.
3. Seizure and epilepsy medicines. Epilepsy Foundation Web site. <http://www.epilepsy.com/learn/treating-seizures-and-epilepsy/seizure-and-epilepsy-medicines>. Accessed June 27, 2014.
4. Patsalos PN, Berry DJ, Bourgeois BFD, et al. Antiepileptic drugs—best practice guidelines for therapeutic drug monitoring: A position paper by the subcommission on therapeutic drug monitoring, ILAE Commission on Therapeutic Strategies. *Epilepsia*. 2008;49:1239-1276.