Carpe Diem – Seize the Day Blog

Editor's Note: Content presented in the Carpe Diem – Seize the Day Blog is for awareness and ***informational purposes only, and it is not meant to be a diagnostic tool.***

Lennox-Gastaut Syndrome (LGS) is a severe and uncommon type of epilepsy that begins in early childhood and can continue into adulthood. LGS is characterized by recurrent seizures of varying types, an abnormal electroencephalogram (EEG), and mental impairments. Brain malformation, damage, and infection are linked to about 70 percent of cases of LGS, according to Frontiers in Genetics.

An estimated 3 percent to 4 percent of children with epilepsy develop LGS. The condition typically begins between ages 2 and 5, and it occurs more frequently in males. Seizures can continue into adolescence and adulthood.

LGS belongs to a group of disorders called epileptic encephalopathies, which can lead to progressive cognitive impairment, developmental delays, and behavioral problems. LGS can be difficult to treat because it is resistant (refractory) to many types of Anti-Seizure Medications (ASMs). Some people with LGS are able to live independently, but most individuals with this condition need assistance with activities of daily living. Complete recovery from LGS is rare, and there currently is no cure. People with LGS have a mortality rate fourteen times higher than those in the general population.

Lennox-Gastaut Syndrome Symptoms and Seizures
People with LGS experience multiple types of epileptic seizures, including the following types.

Tonic Seizures
The majority of individuals with LGS experience tonic seizures. Tonic seizures typically cause muscles to uncontrollably stiffen. They last around 20 seconds and occur primarily during sleep. A person who experiences this type of seizure while awake may experience sudden falls, and they may become tired or confused right afterward.

Atonic Seizures
Individuals with LGS may experience atonic seizures, also known as drop attacks. During an atonic seizure, a person loses muscle tone, causing their body to go limp and fall to the ground. Helmets or other head protection may be needed to protect from injury.

Atypical Absence Seizures
Atypical absence seizures may also affect people with LGS. Atypical absence seizures are brief (usually lasting just a few seconds) and cause a short period of "blanking out" or staring into space. Usually, the child does not remember having this type of seizure after it ends.

Focal Seizures
Focal seizures, which typically affect only one side of the brain, are another common seizure in people with LGS.

Myoclonic Seizures
Myoclonic seizures are less common but sometimes seen with LGS. These are brief, shock-like jerks of a muscle or a group of muscles.

Tonic-Clonic Seizures
These seizures combine characteristics of tonic (stiffening) and clonic (rhythmical jerking). During tonic-clonic seizures, a person can lose consciousness.

Infantile Spasms
Some children with LGS may be initially affected by infantile spasms. Also known as West syndrome, they involve sudden, involuntary contractions of the head, neck, and torso, or uncontrolled extension of legs and arms.

Status Epilepticus
Seizures that last longer than five minutes or occur too close together for a person to recover can be life-threatening. They may require emergency medical intervention. Two types of status epilepticus seizures — convulsive and nonconvulsive — can affect awareness and body movements. They also can promote or worsen cognitive decline. More than two-thirds of people with LGS experience status epilepticus.

Developmental and Behavioral Issues With Lennox-Gastaut Syndrome
Most children with LGS have intellectual disabilities or learning problems even before seizures begin. These issues may worsen over time, particularly if seizures are frequent or severe. In a 17-year assessment of children with LGS, up to 99 percent of participants exhibited mental disabilities. Many had delayed development of motor skills, such as sitting and crawling. Behavioral problems, such as hyperactivity and aggression, occurred in half of the participants.

The majority of children with LGS will continue to have seizures into adulthood. As a result of the developmental and behavioral issues common in LGS, most people with this condition require help with activities of daily living.

Diagnosing Lennox-Gastaut Syndrome
To be diagnosed with LGS, a person must exhibit the following symptoms:

Cognitive or behavioral challenges
A diagnosis is usually made — together with a multidisciplinary team — after a thorough physical exam, medical history, and neurological evaluation. You will likely undergo an EEG to analyze the brain's electrical activity and seizures. Magnetic resonance imaging (MRI) may also be ordered to help physicians examine brain structure and locate the cause of the seizure activity. It can take several years to correctly diagnose LGS because the disease has significant overlap with other types of epilepsy, and it may not show its unique features when seizures begin.

Causes of Lennox-Gastaut Syndrome
An estimated 70 percent to 80 percent of people experience symptomatic LGS — when the disease has an identifiable cause. Here are some of the causes of LGS.

Brain Injury or Developmental Problems
When part of the brain has developed abnormally (also called brain malformation) or is injured, it becomes more prone to seizures.

Genetic Disorders
In most LGS cases, there is no family history of the disorder. A family history of epilepsy has been observed in up to 30 percent of people with LGS.

Other Causes
LGS can also develop from other epilepsy syndromes, such as West syndrome or Ohtahara syndrome. When the cause is unknown, LGS is classified as cryptogenic. In 25 percent of people with LGS, no cause can be found.

Treating Lennox-Gastaut Syndrome
LGS can be difficult to treat. Treatment options are limited because of the disease's resistance to antiepileptic drugs. Typically, at least two AEDs are needed. Side effects of these medications may also affect quality of life. A combination of seizure medications and other treatments is typically used to control LGS-related seizures.

First-Line Treatment
The Anti-Seizure Medication Valproic Acid (Depakene) is considered the first-line monotherapy for LGS in children and adults because it is effective against a wide spectrum of seizures. Clonazepam (Klonopin) is another effective first-line ASM, but side effects can limit its usefulness over time.

Second-Line Treatment
If Valproic Acid fails to control seizures, other drugs — such as clobazam (Onfi), lamotrigine (Lamictal), topiramate (Topamax), and rufinamide (Banzel) — may be prescribed. These AEDs are approved by the U.S. Food and Drug Administration (FDA) as add-on therapies to treat seizures associated with Lennox-Gastaut syndrome. Levetiracetam (Keppra), which is approved for partial seizures, may also be used as an add-on therapy for LGS.

Third-Line Treatment
The anticonvulsant drug felbamate (Felbatol) is also approved for treating seizures in children with LGS. Felbamate has been found to be safe and effective, but rare, serious side effects make it a third- or fourth line LGS medication.

Anti-Seizure Medications (ASMs) may be associated with significant side effects, especially for people on multidrug, high-dose regimens. These drugs can also become less effective over time and can cause sedation. Taking multiple medications can sometimes worsen seizure control.

Treatment regimens will change throughout a person's life — as types and frequency of seizures change and the effectiveness of a particular therapy decreases. It is important for family members and caretakers to work closely with doctors to manage prescribed medications and to keep a list of drugs that may worsen seizures or have other serious side effects.

Cannabidiol
An oral form of cannabidiol (CBD, a chemical found in marijuana), Epidiolex is the first FDA-approved drug to control LGS-related seizures. In a phase 3 clinical trial published in The Lancet in 2018, monthly drop-seizure frequency dropped by a median of 44 percent among those treated with prescribed medications and CBD from baseline. This is compared to 22 percent with the placebo.

Fenfluramine
In March 2022, the FDA approved fenfluramine (Fintepla) for the treatment of Lennox-Gastaut syndrome in people ages two and over. In a phase 3 clinical trial, fenfluramine was shown to reduce the frequency of drop seizures in people with treatment resistant LGS. Additionally, it was well tolerated and found to be safe for trial participants.

Dietary Therapies for Lennox-Gastaut Syndrome
Some research indicates that dietary changes can be effective in controlling seizures brought on by LGS.

Ketogenic Diet
A ketogenic diet and its variations, including a modified Atkins diet, are often used to treat children with LGS who have not responded well to AEDs. In one study, the high-fat, low-carb diet — in combination with at least one epilepsy medication — helped more than 50 percent of children with epilepsy reduce seizures by half. In addition, 15 percent of study participants became seizure-free on the ketogenic diet.

Low Glycemic Index Diet
The low glycemic index treatment (LGIT) is a less-restrictive alternative for people with drug-resistant LGS. Lower in fat than the ketogenic diet, LGIT includes carbohydrates that are low-glycemic (a measurement of how much a food raises your blood sugar level after eating). Some became seizure-free, and others were able to reduce use of anticonvulsant medications.

Before starting any of these specific diets, be sure to consult your doctor about whether it is right for you, as other medical problems may need to be considered.

Other Therapies for Lennox-Gastaut Syndrome
There are several additional therapies for LGS beyond medications.

Vagus Nerve Stimulation
Vagus nerve stimulation (VNS) is an effective treatment for people with LGS who do not respond to medication. A device surgically implanted in the chest sends mild electrical signals to

the brain, via the vagus nerve, to treat seizures. A VNS study of fifty people with LGS found a 58 percent reduction in seizures within six months. The study concluded that VNS is well-tolerated and safe, and that it may improve quality of life.

Corpus Callosotomy
In some people with LGS, a bundle of nerves in the brain can be surgically addressed via a procedure called corpus callosotomy to help control seizures. Corpus callosotomy does not require any brain tissue to be cut.

Resective Surgery
This type of epilepsy surgery removes areas of the brain that cause seizures, with the goal of stopping them altogether. In a 2018 study of long-term outcomes of resective surgery for refractory LGS, 50 percent of people were seizure-free after six years. This also led to improved behavior and social competence.

Rescue Medications for Lennox-Gastaut Syndrome
Rescue medicines can prevent and treat life-threatening seizures. The most commonly prescribed rescue medicines are fast-acting benzodiazepines: diazepam (Valium), lorazepam (Ativan), and midazolam (Versed). These rescue medications are given orally, under the tongue (sublingual), between the cheek and gum (buccally), or sprayed into a nostril (nasal spray). Diastat, the rectal form of diazepam, is most often prescribed for children.

Developing a seizure response plan is important in helping prevent or manage emergency situations. Keeping a seizure diary is a self-tracking tool that can help you be proactive about seizure type and frequency — and allow your doctor to detect interactions between seizures and medications.

Editor's Note: The Carpe Diem – Seize the Day Blog will be distributed and posted weekly.
Always remember – **CARPE DIEM – SEIZE THE DAY!**

Steve.Hutton@epilepsy-ohio.org