

LENNOX-GASTAUT SYNDROME

Lennox-Gastaut syndrome (LGS) is a rare and severe form of childhood-onset epilepsy that is one of the most difficult seizure disorders to treat due to its complex symptoms.¹ The first signs of the condition, which present between two and eight years of age, include generalized seizures, drop seizures (which can lead to abrupt and dangerous falls), and delayed mental development.² Approximately 50 percent of patients experience drop seizures.³ The prognosis for patients with LGS is poor, as up to 10 percent of children die before the age of 11.⁴

There are several known causes of LGS, including brain injury associated with pregnancy or birth, severe brain infections, developmental malformations of the brain or metabolic conditions.² It is also common among patients with infantile spasms to develop LGS.⁵ LGS accounts for approximately one to four percent of all cases of childhood epilepsy, and affects an estimated 30,000 children and adults in the United States.⁶ For unknown reasons, LGS is more common in males than in females.⁷

DISEASE IMPACT

Children with LGS experience a multitude of issues from physical impairments to emotional and intellectual disabilities. These issues include behavioral and personality disturbances, such as poor social skills, inability to solve problems, mood instability and attention-seeking behavior.¹ In about 50 percent of cases, these behavioral problems may present as hyperactivity, aggressiveness and autistic traits.² Patients may also have difficulty interpreting information or experience delays in motor skills,⁸ such as sitting, walking, talking, and controlling bladder and bowel functions. Older children with LGS can experience acute psychotic episodes, aggressiveness and irritability.¹ Some children may experience a prolonged seizure event, known as status epilepticus, that often requires medical intervention to bring the

seizure to an end.¹ These long seizures are very dangerous and increase the chance of death.⁹

In 80 to 90 percent of cases, LGS continues through adolescence into adulthood.³ Although there may be changes to seizure type, impaired mental function and behavioral issues remain, resulting in the need for lifelong care.¹ The constant supervision required for many of these patients can be emotionally draining, highly stressful and financially overwhelming for families.

TREATMENT OPTIONS

Unfortunately, there is no cure for LGS. Treatment is often difficult because patients do not respond well to currently-approved seizure medications and there are limited options to help with intellectual changes.¹⁰ As a result, there is a dire need for new therapies to reduce the frequency and impact of seizures, minimize medication side effects and help improve the quality of life.¹¹

Families often work with a multidisciplinary team of neurologists, dieticians and pediatricians to help find partial relief from seizures and disease symptoms. Treatment may include anti-seizure medications,¹⁰ intravenous blood products and corticosteroids,¹² and dietary changes, such as the high-fat, low-carb ketogenic diet.¹³ Patients often require multiple anti-seizure medications (AEDs) to find relief. The U.S. Food and Drug Administration recently approved the first in a new class of AEDs and the first plant-derived cannabinoid product for the treatment of LGS. Surgery may be an option for patients who do not respond well to medication or other therapies. Two common surgical procedures include the insertion of a vagus nerve stimulator device to help control seizures through electrical impulses and a corpus callosotomy, a more invasive procedure that severs the membrane that divides the right and left halves of the brain.¹⁰

Greenwich Biosciences, Inc. is the U.S. subsidiary of GW Pharmaceuticals plc.

¹ LGS Foundation. About Lennox-Gastaut Syndrome. Available at <http://www.lgsfoundation.org/aboutlgs>. Accessed May 15, 2018.

² van Rijkevorsel, K. Treatment of Lennox-Gastaut syndrome: overview and recent findings. *Neuropsychiatric disease and treatment* 4, 1001–1019 (2008).

³ Bourgeois, B.F., Douglass, L.M. & Sankar, R. Lennox-Gastaut syndrome: a consensus approach to differential diagnosis. *Epilepsia* 55 Suppl 4, 4–9 (2014).

⁴ Trevathan, E. Infantile Spasms and Lennox-Gastaut Syndrome. *Journal of child neurology* 17, 2S9–2S22 (2002).

⁵ Arzimanoglou, A., et al. Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. *Lancet Neurol.* 8, 82–93 (2009).

⁶ Dixon-Salazar LGS Prevalence Email 2018

⁷ National Institute of Health. Lennox-Gastaut syndrome. Available at <https://ghr.nlm.nih.gov/condition/lennox-gastaut-syndrome#definition>. Accessed May 15, 2018.

⁸ Trevathan, E., Murphy, C.C. & Yeargin-Allsopp, M. Prevalence and descriptive epidemiology of Lennox-Gastaut syndrome among Atlanta children. *Epilepsia* 38, 1283–1288 (1997).

⁹ Epilepsy Foundation. What is Status Epilepticus? Available at <http://www.epilepsy.com/learn/impact/seizure-emergencies/status-epilepticus>. Accessed May 15, 2018.

¹⁰ Epilepsy Foundation. Lennox-Gastaut Syndrome. Available at <http://www.epilepsy.com/learn/types-epilepsy-syndromes/lennox-gastaut-syndrome-lgs>. Accessed May 15, 2018.

¹¹ LGS Foundation. Treatments for Lennox-Gastaut Syndrome. Available at <http://www.lgsfoundation.org/treatments>. Accessed May 15, 2018.

¹² LGS Foundation. Non-pharmacological Treatment Options. Available at <http://www.lgsfoundation.org/nonpharmacological>. Accessed May 15, 2018.

¹³ LGS Foundation. Dietary Therapy for Lennox-Gastaut Syndrome. Available at <http://www.lgsfoundation.org/dietary>. Accessed May 15, 2018.