

LGS FOUNDATION

LENNOX-GASTAUT SYNDROME



GET THE FACTS



DEFINITION & NATURAL HISTORY

- Lennox-Gastaut Syndrome (LGS) is a rare and severe form of childhood-onset epilepsy.¹
- LGS is commonly characterized by a triad of features including multiple seizure types, intellectual disability or regression, and an abnormal EEG with general slow spike-and-wave discharges.^{2,3}
- However, the definition of LGS has varied over time resulting in misclassification and over-diagnosis in the past.⁴
- LGS typically occurs between two and eight years of age with peak onset at 3-5 years.⁵
- Lennox-Gastaut Syndrome is named after Drs. William Lennox and Henri Gastaut. Lennox (1945) along with his colleague Davis (1950) described the triad of cognitive impairment, multiple seizures and slow spike and wave discharges in the EEG; Dr. Gastaut described the syndrome in 1966.
- Margaret Buchtal-Lennox proposed the name LGS in tribute to the work of Lennox and the Marseille School headed by Dr. Gastaut.⁶

MORTALITY

- The mortality rate associated with Lennox-Gastaut Syndrome ranges from 3 to 7%, with many deaths related to accidents.⁷
- People with Lennox-Gastaut Syndrome have an increased risk of death compared to their peers of the same age. Although the risk is not fully understood, it is partly due to poorly controlled seizures and injuries from falls.⁸
- 25% of deaths are due to underlying neurological conditions.⁹
- SUDEP is defined as a sudden and unexpected non-traumatic or non-drowning-related death in a patient with epilepsy that may or may not be due to a recent seizure.¹⁰
- Risk factors most consistently associated with SUDEP are: seizures that can't be controlled, treatment with multiple anticonvulsant drugs, having long standing chronic epilepsy. Other factors include generalized tonic-clonic seizures, nocturnal seizures, developmental delays, stopping the use of anticonvulsant medicine abruptly, and onset of epilepsy at a young age.¹¹
- The incidence of SUDEP is higher in patients with LGS.¹²
- People with epilepsy have a two-to-threefold increased mortality¹³ and are 24 times more likely to die of sudden death compared with the general population.¹⁴

EPIDEMIOLOGY

- The prevalence of LGS has been estimated at 1-4 percent of all childhood epilepsies¹⁵ and about 3 – 10% of childhood epilepsies¹⁶
- Incidence = 2 / 100,000 or .6% of all new onset epilepsies
- Lennox-Gastaut Syndrome affects between 14,500 – 18,500 children under the age of 18 in the United States and over 30,000 children and adults in the U.S.¹⁷

ETIOLOGIES

- Etiologies can include meningitis/encephalitis, encephalopathy, structural abnormalities, pre/perinatal, genetic, metabolic disorders, and other.
- Infantile Spasms precede LGS in about 30% of cases¹⁸, although figures as high of 54% have been reported.¹⁹
- LGS does not usually run in families but genetic factors may play a role in the etiology.^{20 21}

COGNITIVE DYSFUNCTION / INTELLECTUAL IMPAIRMENT

- LGS has a profound deleterious effect on intellectual and psychosocial function.²²
- Cognitive impairments are clinically apparent in 20 – 60% of patients at time of diagnosis²³
- The cognitive impairment becomes more apparent over time, and within 5 years of onset, serious intellectual problems are noted in 75 – 95% of patients²⁴
- Those with cryptogenic have a better cognitive outcome than symptomatic; those with symptomatic have higher percentage of moderate to severe MR
- The progression of LGS after seizure onset is often associated with slowing and/or arrest of cognitive development, and, in 50 percent of cases, behavioral problems including hyperactivity and aggressiveness.²⁵

BEHAVIORAL DISTURBANCES

- Many patients with LGS develop behavioral and psychiatric disorders²⁶
- Attention problems, aggression and autistic features can be very prominent in LGS and represent enormous challenges for the family²⁷
- Those with cryptogenic have a better cognitive outcome than symptomatic; those with symptomatic have higher percentage of moderate to severe MR
- Cognitive problems are greatest with earlier onset suggesting a profound effect on brain maturation at a critical stage of development
- Older children with LGS experience character problems, acute or chronic psychosis with aggressiveness, irritability or social isolation.²⁸

DIFFERENTIAL DIAGNOSIS

- One study reported misdiagnosis in 38/103 patients referred with a diagnosis of LGS²⁹
- Distinguishing LGS syndrome from other epilepsy syndromes has been challenging as it is characterized by plethora of underlying causes, multiple types of seizures, and cognitive impairment. Seizures are classified according to the International League Against Epilepsy (ILAE) classification, and specific epilepsy syndromes of childhood are recorded when their essential diagnostic elements are fulfilled. It is now agreed that a number of individual syndromes, including LGS, form a spectrum of childhood epilepsies, each with differentiating criteria.

PROGNOSIS

- The long-term prognosis for LGS is generally poor due to uncontrolled seizures with only 10 percent of cases (mostly cryptogenic) experiencing full seizure remission. ³⁰
- No significant difference in seizure frequency between the cryptogenic (54%) and symptomatic (63%) subgroups, although patients in the symptomatic subgroup had more types of seizures
- Idiopathic and symptomatic LGS are similar in terms of final seizure and intellectual outcome
- Due to the refractory nature of LGS and multiple seizure types, only a minority achieve satisfactory control of seizures. ³¹

ADULTHOOD

- 80% of children with LGS continue to experience seizures, psychiatric, and behavioral deficits in adulthood. ³²
- A defined strategy for transitioning patients from pediatric to adult care should be an essential component of the long-term management plan ³³
- Because EEG readings and seizure types may evolve and change as the patient grows older, it may be difficult to identify a history of LGS in adult patients.³⁴

OTHER

- LGS has a devastating impact on patients' quality of life and inflicts a considerable burden on their caregivers ³⁵
- There is no cure for LGS.³⁶ Management options include antiepileptic drugs (AEDs), ketogenic diet, brain surgery (e.g. corpus callosotomy) and vagus nerve stimulation (VNS)³⁷
- Only 6 randomized double blind controlled trials have been conducted
- The LGS Foundation was the first patient advocacy / non-profit organization formed dedicated to this syndrome in 2008 by Christina SanInocencio, the sibling of an adult man with LGS.
- Lennox- Gastaut Syndrome awareness day is November 1st, annually.
- The awareness color for LGS is sage green.

FOR MORE INFORMATION

Visit our website at www.lgsfoundation.org

CONTACT US:

192 LEXINGTON AVE SUITE 212
NEW YORK, NY 10016

Phone: 718-374-3800
info@lgsfoundation.org

REFERENCES

- 1 Glauser, Tracey. Lennox-Gastaut Syndrome. Medscape. 2011. <http://emedicine.medscape.com/article/1176735-overview>. Accessed 8/20/2012
- 2 Glauser, Tracey. Lennox-Gastaut Syndrome. Medscape. 2011. <http://emedicine.medscape.com/article/1176735-overview>. Accessed 8/20/2012
- 3 Arzimanoglou, Alexis et al. Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. *The Lancet*. 2009; 8(1) 82-93.
- 4 Prama Krishnian, Definition and Natural History of Lennox Gastaut Syndrome. Slide Share. Accessed 5/15/2014
- 5 Lundbeck, https://www.lundbeck.com/upload/us/files/pdf/Fact_Sheets/PR104_FS_LGS_ATD_10.20.11.pdf
- 6 By Mary C Spiciarich MD and Solomon L Moshe MD;
http://www.medmerits.com/index.php/article/lennox_gastaut_syndrome/PL. Accessed 2/15/2015
- 7 Glauser TA, Morita DA. Lennox-Gastaut syndrome. eMedicine web site. Available at: <http://www.emedicine.com/neuro/topic186.htm>. Accessed November 7, 2003.
- 8 Genetics Home Reference Page, National Institutes of Health. <http://ghr.nlm.nih.gov/condition/lennox-gastaut-syndrome>. Accessed 5/15/2014
- 9 Camfield P, Camfield C. Long-term prognosis for symptomatic (secondarily) generalized epilepsies: a population-based study. *Epilepsia*. 2007;48:1128-32.
- 10 Friedman, D, Hirsch, D. Sudden Unexpected Death in Epilepsy- An Overview of Current Understanding and Future Perspectives. *European Neurological Review*, 2012 7(1):67-71
- 11 CURE Epilepsy Website. <http://www.cureepilepsy.org/research/sudep-faq.asp>. Accessed 3.1.15
- 12 Pramod, K. Definition and Natural History of Lennox-Gastaut Syndrome. Slideshare.Net;
<http://www.slideshare.net/drpramodkrishnan/definition-and-natural-history-of-lennox-gastaut-syndrome>. Accessed 3.1.15
- 13 Hauser W, Annerggers J, Elveback L, Mortality in patients with epilepsy, *Epilepsia*, 1980;21:399-412
- 14 Hauser W, Annerggers J, Elveback L, Mortality in patients with epilepsy, *Epilepsia*, 1980;21:399-412
- 15 Glauser, Tracey. Lennox-Gastaut Syndrome. Medscape. 2011. <http://emedicine.medscape.com/article/1176735-overview>. Accessed 8/20/2012
- 16 Sidenvall R, Forsgren L, Heijbel J. Prevalence and characteristics of epilepsy in children in northern Sweden. *Seizure* 1996;5:139- 46
- 17 Trevathan E, Murphy CC, Yeargin-Allsopp M. Prevalence and descriptive epidemiology of Lennox-Gastaut syndrome among Atlanta children. *Epilepsia*. 1997 Dec;38(12):1283-8
- 18 Albert P. Aldenkamp, Fritz E. Dreifuss, W. Renier, T.P.B.M. Suurmeijer, *Epilepsy in Children and Adolescents*. Pg. 51
- 19 Ohtahara S, Yamatogi Y, Ohtsuka Y, Oka E, Ishida T. Prognosis of West syndrome with special reference to Lennox syndrome: a developmental study. In: Wada JA, Penry JK, eds. *Advances in epileptology: The Xth Epilepsy International Symposium*. New York: Raven Press, 1980: 149-54.
- 20 Crumrine PK: Lennox-Gastaut syndrome. *J Child Neurol* 2002, (Suppl 1):70-75.
- 21 Chevrie JJ, Aicardi J: Childhood epileptic encephalopathy with slow spike-wave: a statistical study of 80 cases. *Epilepsia* 1972, 13:259-271
- 22 Camfield C, Camfield P. (2008) Twenty years after childhood-onset symptomatic generalized epilepsy the social outcome is usually dependency or death: a population-based study. *Dev Med Child Neurol* 50:859-863.
- 23 Arzimanoglou A, French J, Blume WT, Cross JH, Ernst J-P, Feucht M, Genton P, Guerrini R, Kluger G, Pellock JM, Perucca E, Wheless JM. (2009) Lennox-Gastaut syndrome: a consensus approach on diagnosis, assessment, management, and trial methodology. *Lancet Neurol* 8:82-93
- 24 Beaumanoir A. (1982) The Lennox-Gastaut syndrome: a personal study. *Electroencephalogr Clin Neurophysiol Suppl* 35:85-99
- 25 Van Rijckevorsel, Kenou et al. Treatment of Lennox-Gastaut syndrome: overview and recent findings. *Neuropsychiatric Disease and Treatment*. 2008; 4(6)1001-1019.
- 26 Glauser TA. (2004) Following catastrophic epilepsy patients from childhood to adulthood. *Epilepsia* 45(Suppl. 5):23-26.
- 27 Glauser TA. (2004) Following catastrophic epilepsy patients from childhood to adulthood. *Epilepsia* 45(Suppl. 5):23-26.
- 28 Glauser, Tracey. Lennox-Gastaut Syndrome Clinical Presentation. Medscape, 2011
<http://emedicine.medscape.com/article/1176735-clinical>. Last accessed 8/20/2012
- 29 Beaumanoir A. (1982) The Lennox-Gastaut syndrome: a personal study. *Electroencephalogr Clin Neurophysiol Suppl* 35:85-99.
- 30 Markand ON. Lennox-Gastaut syndrome (childhood epileptic encephalopathy). *J Clin Neurophysiol*. 2003; 20: 426-441.
- 31 Crumrine PK. Management of Seizures in Lennox-Gastaut Syndrome. *Pediatric Drugs*. 2011;13 (2): 107-118.
- 32 Camfield and Camfield, 2008; van Rijckevorsel, 2008
- 33 Jurasek L, Ray L, Quigley D. (2010) Development and implementation of an adolescent epilepsy transition clinic. *J Neurosci Nurs* 42:181-189.
- 34 Ferlazzo E, et al. Lennox-Gastaut syndrome in adulthood: Clinical and EEG features. *Epilepsy Res*. 2010; 89 (2-3): 271-277.
- 35 Gallop, et al. Impact of Lennox Gastaut Syndrome on HRQL of patients and caregivers: Literature review. *Seizure*. October 2009. V 18 | 8 P554-558

36 NINDS. Lennox-Gastaut Syndrome Information Page.

<http://www.ninds.nih.gov/disorders/lennoxgastautsyndrome/lennoxgastautsyndrome.htm>. Accessed 8/21/2012.

37 Borggraefe I, Noachtar S. Pharmacotherapy of Seizures Associated with Lennox-Gastaut Syndrome. *Clinical Medicine Insights: Therapeutics*. 2010;2:15-24.