An Informational Guide for US Healthcare Professionals

Lennox-Gastaut syndrome

Lennox-Gastaut syndrome (LGS) is a rare, severe, and drug-resistant form of epilepsy that begins in early childhood and changes throughout life[1-3]

A high risk of mortality over time

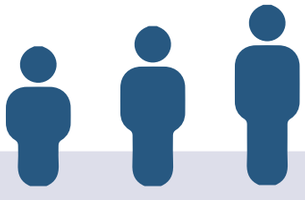
High-risk seizures in LGS predispose patients to status epilepticus, sudden unexpected death in epilepsy (SUDEP), and head injury[3,10,18]

All-cause mortality risk compared to general population[18]

3X
greater for children with epilepsy

14X
greater for children with LGS

Mortality risk persists as patients age[3]



The mortality rate for LGS is estimated to be 3% to 7%, over mean follow-up periods of 8.5 and 9.7 years, respectively[3]

The importance of timely diagnosis and effective treatment

Inadequate seizure control can lead to worsening prognosis

- There are 6 FDA-approved AEDs for the treatment of LGS, but 80% to 90% of patients continue to have seizures throughout their lives[1,9,10]
- The frequency and severity of seizures can impact the level of cognitive impairment patients experience[1,2,4,6,10]

Diagnosis and treatment are critical

- Timely diagnosis is important, as early treatment and better seizure control may be associated with better cognitive outcomes and overall improved prognosis[3,6]
- Careful selection of treatment is needed for better cognitive outcomes and overall improved prognosis[3]

If you suspect LGS, consult a specialist to confirm or rule out an LGS diagnosis

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The classic description of LGS focuses on typical clinical features[1-3]

Multiple seizure types

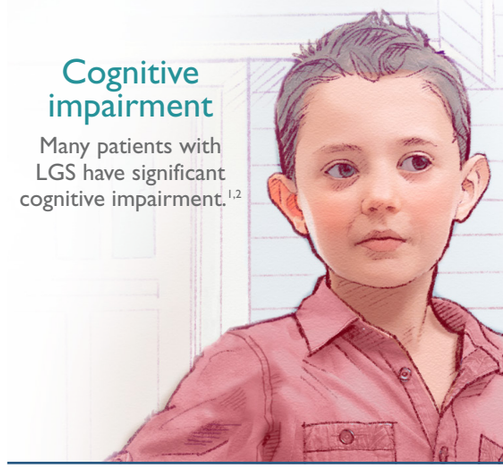
LGS involves a variety of seizure types including tonic and atypical absence; drop seizures occur in at least 50% of patients.[1,2,4,5]

Cognitive impairment

Many patients with LGS have significant cognitive impairment.[1,2]

Slow spike-wave EEG

A distinct EEG pattern is the third characteristic feature of LGS for most patients.[1-3]



LGS presentation, however, is variable and not all patients display all components of the classic triad at onset[1-3]

- Patients with LGS may present with a wide range of characteristics that mimic other epilepsies such as Dravet syndrome, Doose syndrome, and focal cryptogenic epilepsy[1,3]
- LGS signs and symptoms change over time[1-3,6]

Understanding the variability in LGS presentation, between individuals and over time, helps ensure accurate diagnosis and effective management[1,3,7]

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Signs and symptoms of LGS change as patients age

LGS background and challenges

LGS leads to cognitive and physical impairments that have a significant impact on patients and caregivers.[8] While the heterogeneous clinical presentation of LGS makes it a challenge to recognize, early diagnosis is vital, as appropriate treatment may affect disease course and improve quality of life.[1,3,6,7] It is also important to evaluate adult patients with LGS-like symptoms who may not have been accurately diagnosed earlier.

Onset

Peak onset of LGS is between 3 and 5 years of age, with symptoms typically emerging between 2 and 8 years of age.[1,2,9]

LGS symptoms persist into adulthood, with 80% to 90% of patients continuing to have seizures.[1,9,10]

Prevalence

Up to 4% of children with epilepsy are diagnosed with LGS.[11]

Etiology

70% to 80% of LGS patients have an identifiable cause for their syndrome.[1,3,12,13]

- Brain abnormalities play a major role in precipitating LGS[2]
- LGS may be preceded by infantile epilepsy conditions, such as West syndrome[1-3]

Research is currently being done to identify genes associated with LGS.[14]

Currently no biomarker

LGS has no consistent genetic variant or biomarker that confirms a diagnosis.[1,3]

LGS changes over time and continued evaluation of patients and their symptoms is important to optimize diagnosis[1,3,7,15]

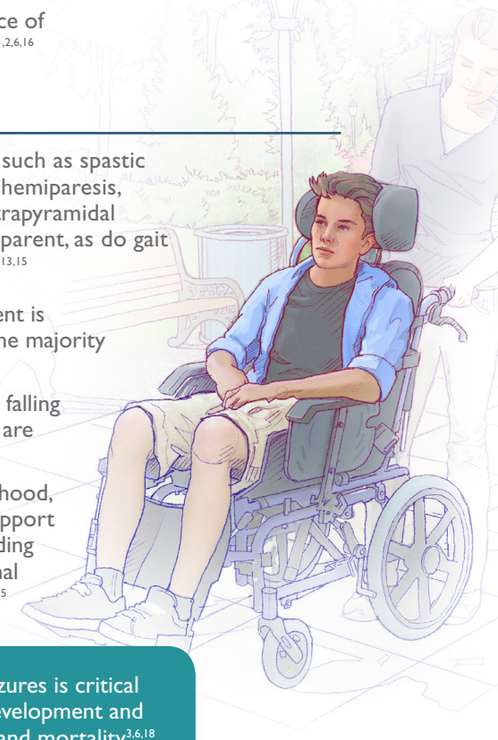
	Young children/Onset	Adolescents/Adults
Seizures	• Most commonly generalized tonic, atonic, and atypical absence*[2,3,5,10] • Tonic seizures during sleep[1-3] • Seizures occur several times per week with most patients experiencing daily seizures[6,9,10,12,15]	• Generalized tonic-clonic, atonic, and atypical absence seizures continue[3,9,15] • Tonic seizures may or may not be seen during wakefulness[16] • Tonic seizures are present during sleep and may become the most distinctive seizure type[1,16] • Change in seizure frequency and fewer daytime seizures in some patients[16] • Increase in drop attacks leading to injuries in some patients[6,15]
Cognitive Impairment	• Most patients exhibit cognitive impairment in early childhood, but up to 1/3 of children with LGS may show normal functioning prior to or at the time of seizure onset[1,2] • Behavioral problems are also often present[1,3,9]	• Cognitive impairments may become more noticeable at later ages[1,2] • Significantly impaired IQ relative to peers: 75% to 95% have cognitive impairments 5 years from onset[2,4,17] • Behavioral problems such as hyperactivity, aggression, and autistic traits are seen in 50% of patients with LGS[1,9,16] • Some patients begin exhibiting symptoms of psychosis[2,15]
EEG	• EEG pattern of slow spike-wave complexes[1-3]	• Decrease in or disappearance of slow spike-wave complexes[1,2,6,16]

*Generalized tonic-clonic and focal seizures may also occur.

- Cognitive functioning over time correlates with the severity and frequency of seizures[1,2,4,6,10]
- The changing presentation of LGS in adulthood may reflect a combination of factors, including:
  - Long-term effects of antiepileptic drugs (AEDs)[6,7]
  - Long-term effects of recurrent seizures on brain function[7]
  - Neurologic maturation[6,7,15]
  - Impact of puberty and physical maturation[6,15]

Over time, neurologic deficits such as spastic paraparesis and quadriparesis, hemiparesis, generalized hypotonia, and extrapyramidal features may become more apparent, as do gait deterioration and dysphagia.[5-7,13,15]

- Lifelong functional impairment is seen in patients with LGS; the majority rely on caregivers[8,15]
- Social and language features falling within the autism spectrum are commonly seen[1]
- As patients move into adulthood, management may involve support from other disciplines including physiotherapists, occupational therapists, and psychiatrists[15]



Timely management of seizures is critical to a patient's neurologic development and long-term risk for disability and mortality[3,6,18]