Lennox Gastaut Syndrome
Diagnostic evaluation and the global approach

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LGS: Diagnosis

Given poor prognosis for seizure control and cognitive outcome

The term LGS should be applied with caution

Arzimanoglou et al 2009

LGS: Diagnosis

- Classic triad: many seizure types, slow spike and wave, mental retardation

- Some consider the presence of fast 10 Hz rhythms associated with tonic seizure or that occur with minimal clinical manifestation esp. during non-REM sleep essential for diagnosis

LGS: Diagnosis

- Diagnosis difficult especially at onset
- Cause, history, seizure types and EEG are not pathognomonic for LGS
- Core seizure types may not be present at onset, may have focal or myoclonic seizures initially
- May have different EEG features
- Have to occasionally rely on quantitative

LGS: Investigations

EEG:

- Sleep recording is almost a must *(more likely to capture tonic seizures and fast activity)*
- EEG abnormal at onset: slow, poorly organized background
- Bursts of diffuse slow spike and wave 2-2.5 Hz esp. while awake*: ictal vs interictal*
- Bursts of fast rhythms, polyspikes,10 Hz esp. when asleep: *may have subtle apnea or brief axial contraction.* Important pattern in distinguishing

LGS: Investigations

MRI

- Inconsistent findings since etiology is variable
  - Focal or multifocal malformations of cortical development
  - Tuberous sclerosis
  - Metabolic diseases
  - Ischemic injury

LGS: Investigations

- **Blood tests**
  - Genetic studies: chromosomal microarray, high resolution chromosomes
  - Metabolic evaluation
  - Specific mutations: DCX, ARX, Rett, Angelman

- **CSF studies:**
  - Neurotransmitters
  - Vitamin deficiencies

LGS: Differential diagnosis

- Doose Syndrome: *younger child, myoclonic-astatic, slow spike and wave and fast spike and wave, background normal for age, no multifocal discharges, children normal at onset, less tonic seizures*
- Dravet Syndrome
- Early- onset childhood absence epilepsy
- Secondarily generalized seizures can have tonic features (esp. frontal lobe epilepsy, usually asymmetric)

LGS: Neuropsychological features

- Mental and behavioral disorders maybe early manifestations of the syndrome
- Most impaired: cognitive function is reaction time and information processing
- Mental retardation present from onset in 20-60%
- Becomes more prominent over time. Within 5 years 75-95% have mental retardation
- Oguni et al: full scale IQ decreased by 15 points over 10 years in 82% of patients

LGS: Neuropsychological features

- Cognitive deterioration:
  - Patients with frequent seizures or frequent episodes of status epilepticus
  - Worse the earlier the onset of the seizures
- *Cognitive deterioration can occur even if seizures are well controlled*

Filippini et al 2006

LGS: Neuropsychological features

- Not clear whether there progressive damage or failure of brain development
- Some of the cognitive skills may fluctuate with seizure control

LGS: Neuropsychological features

Boel et al 2004 reported behavioral problems in all of their LGS patients

- Attention problems
- Aggression
- Autistic features
- Psychosis

LGS: Global approach

Seizures

- Agreement on treatment goals should be reached with parents or caregivers
- Assessment of quality of life is more important than measurement of seizure outcome

LGS: Global approach

- The aims might be different depending on stage of disease and particular child : newly diagnosed previously healthy child with developmental deterioration vs known epilepsy patient with progression

LGS: Global approach

- Because seizures are very resistant to treatment, seizure reduction may not be the ultimate goal

- Quality of life maybe more impaired by the side effects of medications or other treatments than the seizures themselves

LGS: Global approach

Impact on health related quality of life:

- Social impact: Patients and their families have to deal with stigma of mental illness and epilepsy
- Sleep difficulties:
  - Related to several factors
  - Higher frequency of sleep problems in children with refractory epilepsy
  - Nocturnal seizures interrupt sleep
  - Poor sleep habits in children with developmental

Gallop et al 2009

LGS: Global approach

Impact on health related quality of life:

- **Physical impact:**
  - Injuries related to seizures: mostly face and mouth
  - Gait disturbances occur, some patients become wheel chair bound
  - Maybe wheel chair bound to limit injuries
  - Helmet

- **Cognitive and behavioral impact:**
  - Cognitive delay

LGS: Global approach

Impact on health related quality of life:

- Impact on the caregiver:
  - Seizures unpredictable, cannot prevent injuries -> parental anxiety
  - Hard to have people care for child->identify community/state respite resources
  - Marital problems, job stress
  - Most caregivers indicate physical and emotional health being negatively impacted
  - Chronic fatigue and sleep deprivation
  - Limited leisure activities and social interaction

LGS: Global approach

- Neurologist/epileptologist: treatment plan, goal, quality of life
- Physiatry
- Mental health (psychiatry/psychology)
- Sleep Medicine
- Developmental pediatrics
- Social work
- Dietician
- Anticipate need to transition to adult care!

LGS: The Transition

- 75 % of children with symptomatic generalized epilepsy will survive for at least 20 years after initial diagnosis
- Most will have poor social outcome and are dependent for nearly all activities of daily living
- > 80% of children with LGS will continue to experience seizures as adults
- Patients who are able to control and direct certain aspects of their life have better quality of life

LGS: The Transition

- Most families are very hesitant to leave the pediatric practice
- Most pediatric neurologists are hesitant to let patients transition

(attachment, concern less time will be spent with patient, lack of willing adult neurologists, difficulties coordinating transition, insurance)

LGS: The Transition

- Transition clinic: attended by adult and pediatric neurologists or adult and pediatric nurses before handing care
- Advise families as to how to organize medical records, medications
- Referral to supportive agencies for disability
- Education about possible change in health insurance
- Establish guardianship before age 18

Camfield et al 2011

LGS: The Transition

- Reproductive care
- Bone health
- Safety at home and in the community: medical and personal identification, alarms, risk of abuse
- Options for living environments
- Vocational training and life skills

Camfield et al 2011

Therapeutic Management of Lennox-Gastaut Syndrome

Blanca Vazquez,MD

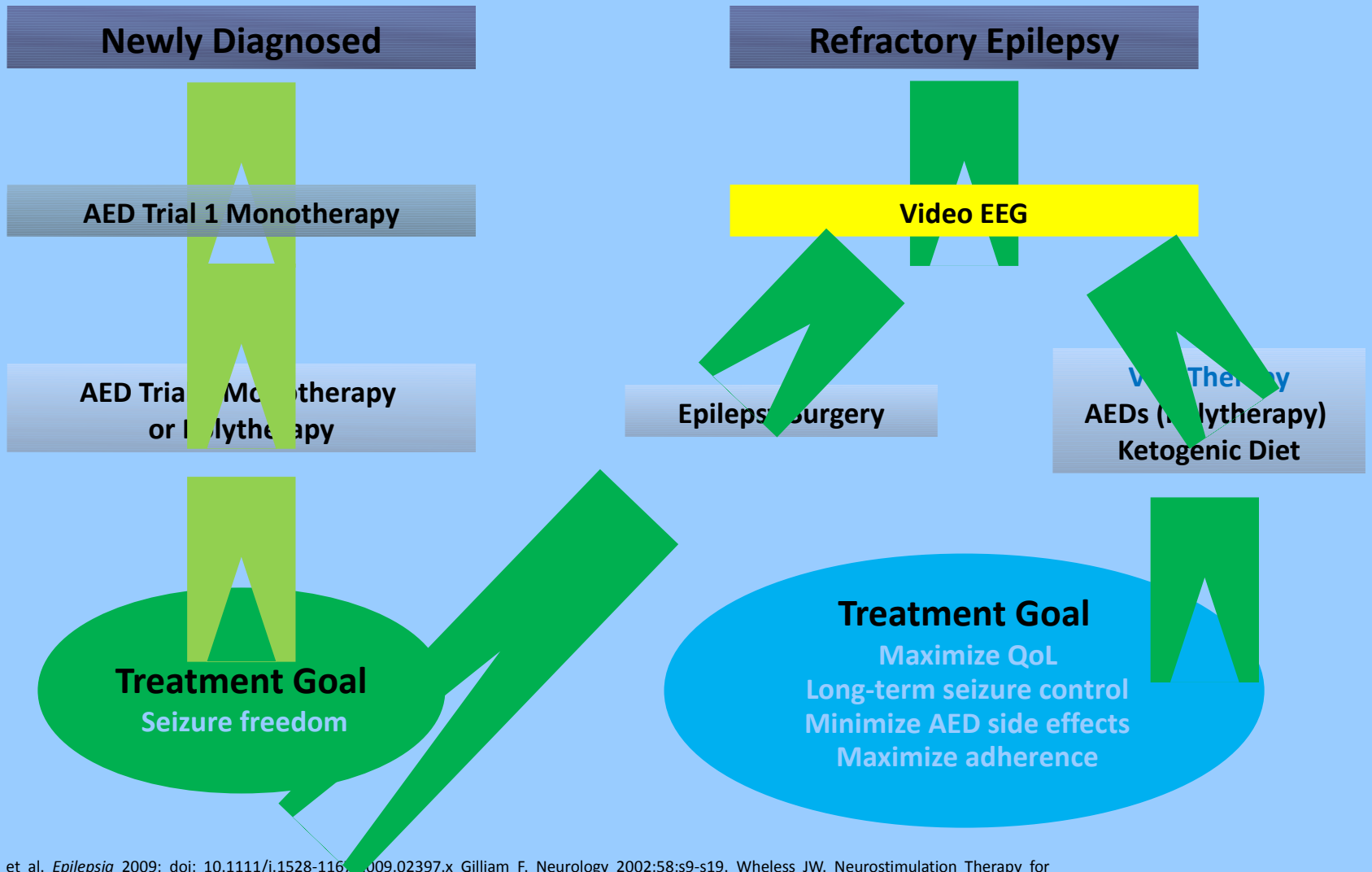
Challenges in Managing LGS

- Polymorphic Intractable seizure Types
- Different Etiologies
- Cognitive and Behavioral Abnormalities
- High Incidence of Status Epilepticus
- Broad range of Comorbid Conditions

Principle of Antiepilpetic treatment LGS

- Seizures associated with LGS are highly resistant to AED treatment
- Often needs Polypharmacy
- Overtreatment with antiepileptic drugs is common
- Tonic seizures are the most difficult to treat
- Transient beneficial Effects

Treatment Goals for Epilepsy

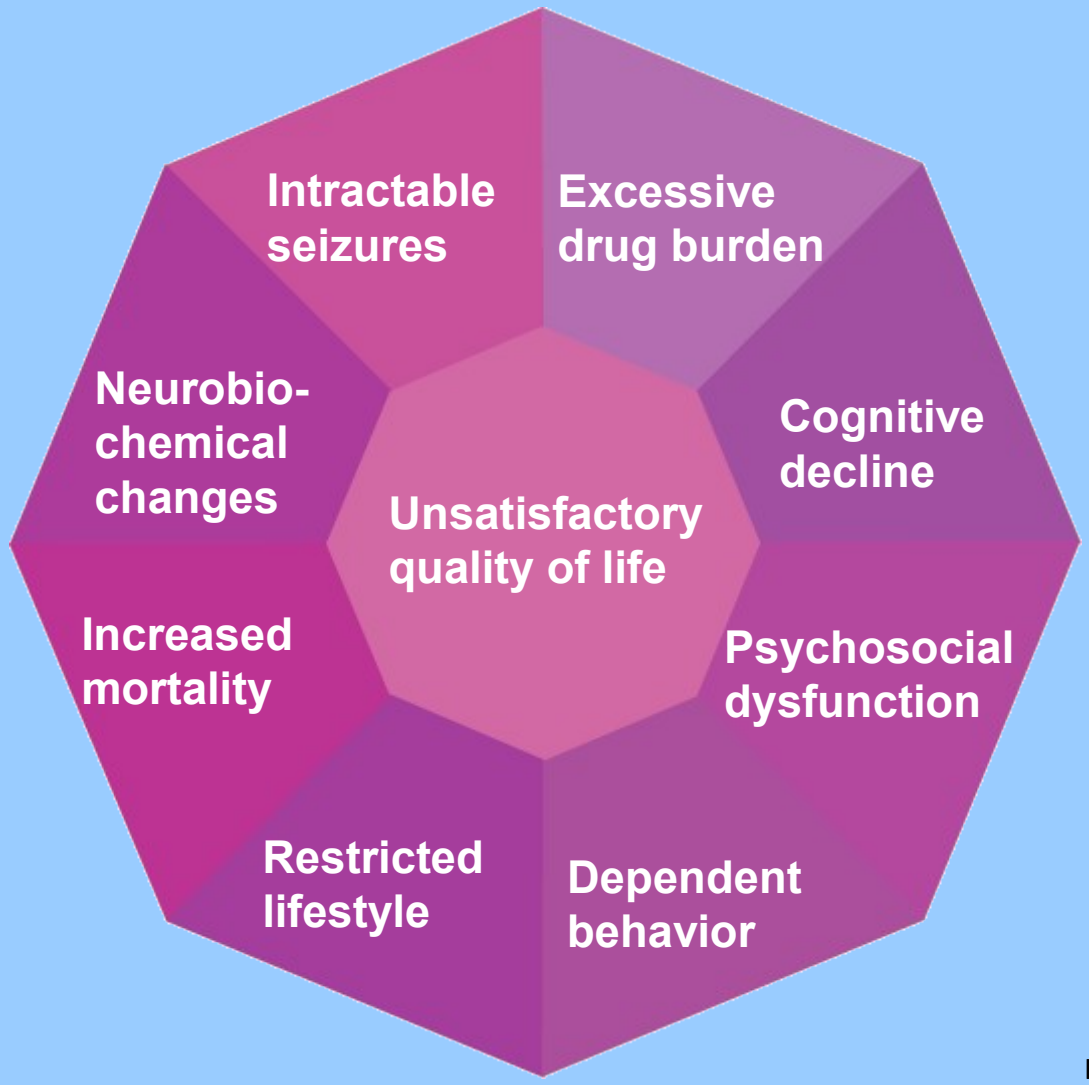


* Kwan P, et al. *Epilepsia* 2009; doi: 10.1111/j.1528-116 009.02397.x Gilliam F. Neurology 2002;58:s9-s19. Wheless JW. Neurostimulation Therapy for Epilepsy. In: Wheless JW, Willmore LJ, Brumback RA, eds. Advanced Therapy in Epilepsy. Hamilton, Ontario: BC Decker, Inc. 2008. Faught E, et al. Epilepsia 2009;50(3):501-509.

Drug Development in LGS

- A few randomized, double blind, placebo-controlled trials of single agents have been performed in LGS.
- Studies varied Considerably in their experimental design and patient selection criteria.
- No head-to-head trial comparing more than one drug have been published.

Dimensions of Treatment in LGS



Overall quality of life is a fundamental measure of successful treatment in patients with epilepsy

Kwan P and Brodie MJ. *Seizure.* 2002;11:78.

Valproic Acid

- Valproic acid is considered the most useful initial medication of choice for drop attacks, atypical absences and myoclonic seizures in LGS
- There are no controlled studies for valproic acid
- Caution must be exercised in using valproic acid in children under the age of 2 years to prevent hepatotoxicity.

New Generation of Treatments for LGS

- felbamate, lamotrigine, topiramate, rufinamide and Clobosam are the antiepileptic medications with an indication to treat seizures associated with LGS.

Benzodiazepines

- The effects of benzodiazepines are variable. A recent study showed that clobazam significantly reduced both drop and non-drop seizures in a dose-dependent manner in patients with LGS.
- Clobazam reportedly has less sedative effects than other benzodiazepines, making it an attractive potential adjunctive treatment for LGS

Felbamate

- Felbamate could also be considered as an alternative to valproic acid, because felbamate lacks the sedative side effect seen with other anticonvulsants.
- Caretakers must be provided detailed information about the potential risks of felbamate. They need to understand the risk of aplastic anemia and hepatoxicity with felbamate use, this medication must be used with caution and appropriate patient

Thank you