

SYMPTOMS:

seizures

(seen in 90% of patients)

multiple types of seizures
broad range of seizure frequency
onset before age 2 in 90% of patients
but can be much later
generally refractory to anticonvulsants

movement disorders

(seen in the majority of patients and can be complex)

- dystonia • ataxia • chorea • ballismus
- paroxysmal exercise induced dyskinesias (PED)
- tremor • dyspraxia • athetosis • spasticity
- myoclonus

developmental delays

cognitive:

range from mild learning difficulties
to severe intellectual disability

speech and language:

delayed development *(more severely in expressive
language than receptive)*, dysarthria, dysfluency

motor:

gross and fine motor development delay

more possible symptoms

episodic confusion
headaches
alternating hemiplegia of childhood
hemolytic anemia
opsoclonus
microcephaly

RESOURCES:

- GeneReviews®
- Genetics Home Reference
- The Child Brain Foundation
- Ketogenic Diet Resources
www.charliefoundation.org
- www.matthewsfriends.org

REGISTRY:

- Patient Registry
www.G1DRegistry.org

CITATIONS:

- 1 Arsov T, Mullen SA, Damiano JA, Lawrence KM, Huh LL, Nolan M, Young H, Thouin A, Dahl HH, Berkovic SF, Crompton DE, Sadleir LG, Scheffer IE. Early onset absence epilepsy: 1 in 10 cases is caused by GLUT1 deficiency. *Epilepsia*. 2012 Dec; 53(12):e204-7
- 2 Mullen SA, Marini C, Suls A, Mei D, Della Giustina E, Buti D, Arsov T, Damiano J, Lawrence K, De Jonghe P, Berkovic SF, Scheffer IE, Guerrini R. Glucose transporter 1 deficiency as a treatable cause of myoclonic astatic epilepsy. *Arch Neurol*. 2011 Sep; 68(9):1152-5
- 3 Arsov T, Mullen SA, Rogers S, Phillips AM, Lawrence KM, Damiano JA, Goldberg-Stern H, Afawi Z, Kivity S, Trager C, Petrou S, Berkovic SF, Scheffer IE. Glucose transporter 1 deficiency in the idiopathic generalized epilepsies. *Ann Neurol*. 2012 Nov;72(5): 807-15

For more information:

Visit us online at www.G1DFoundation.org.



www.G1DFoundation.org

PROFESSIONAL GUIDE



www.G1DFoundation.org

Glut1 Deficiency (G1D) is a rarely diagnosed neurological condition that results from insufficient brain glucose supply. Mutations in the SLC2A1 gene impair the function of the facilitated glucose transporter protein type 1 (Glut1), which is the principal transporter responsible for moving glucose across the blood-brain barrier. Since glucose is the primary fuel source for the brain, this deficiency results in an energy crisis that causes an array of signs and symptoms across a broad spectrum of severity.

Glut1 Deficiency should be considered in any pediatric or adult patient with refractory epilepsy and/or movement disorders. Proper and early diagnosis and treatment can lead to profound improvements in symptoms and in quality of life.

Who has Glut1 Deficiency?

- G1D cases worldwide currently number in the hundreds, although experts believe there are many more undiagnosed patients. Exact prevalence is unknown.
- There is no known susceptibility for gender, race, or ethnicity.
- The average age of diagnosis is between 5 and 6 years old.
- Clinical phenotype can vary between affected individuals, even within the same family pedigree.
- Mutations in the SLC2A1 gene have been found in 10% of early onset absence seizures¹, 5% of Myoclonic Astatic Epilepsy (Doose Syndrome)², and are estimated to be found in 1% of the idiopathic generalized epilepsy population³.

CAUSE:

G1D is caused by a mutation of the gene SLC2A1 located on the short arm of chromosome 1.

- There are more than 100 different types of mutations and deletions reported in patients, which include missense, nonsense, oligonucleotide deletion, large intragenic deletion, complete gene deletion, contiguous gene deletion, insertion, and splice site.
- De novo mutations cause G1D in more than 90% of patients currently identified, although several patients with inherited G1D have been found.
- G1D is inherited most commonly through an autosomal dominant pattern, although more rare cases of autosomal recessive inheritance have been reported.

DID YOU KNOW?

The condition is also known as **Glucose Transporter Type1 Deficiency Syndrome, G1D, Glut1, Glut1 DS, and De Vivo Disease.**

DID YOU KNOW?

Symptoms, especially in the movement domain, can be continuous or intermittent. Fasting, hunger (especially prior to breakfast), fatigue, excitement, anxiety, heat, exertion, and illness can cause temporary symptom worsening.

DID YOU KNOW?

Most patients appear healthy at birth following uneventful pregnancies and delivery. Apgar scores are generally normal.

TREATMENT:

A ketogenic diet is the standard of care for Glut1 Deficiency.

- Ketones represent an alternate fuel for the brain. The ketogenic diet is high in fats and low in protein and carbohydrates, which supports the production of ketones.
- The diet effectively reduces the severity of many symptoms in most patients.
- The classical ketogenic diet is recommended for patients in childhood to ensure the highest level of ketone energy for the developing brain. Older patients have used alternative ketogenic diets such as the Modified Atkins diet, which is less restrictive and can help improve palatability and compliance.
- Standard anticonvulsants are generally ineffective, as they do not address the underlying energy issues. Some patients may benefit from a single medication in addition to the diet for enhanced seizure control.
- Acetazolamide, triheptanoin (C7 oil), and alpha lipoic acid have been reported to help with some symptoms, although more research is needed.
- Phenobarbital, diazepam, sodium valproate, and caffeine can impede glucose transport and should be avoided.
- Patients benefit from a multi-disciplinary team approach to care, incorporating metabolic and neurology specialists, dietitians, and various rehabilitative therapists.

DIAGNOSIS:

1. Glucose tests in cerebro-spinal fluid and in blood:

- single most important laboratory observation
- performed after a four hour fast
- normal blood glucose, low CSF glucose (below 60mg/dL, most below 40 mg/dL)
- CSF/blood glucose ratio is usually less than 0.4
- CSF lactate is low-normal or low

2. Genetic testing (SLC2A1) 85-90% accuracy

- recommended second step after low CSF glucose results
- begin with sequence analysis, single gene preferred
- if sequencing is inconclusive, proceed to deletion/duplication or SOMA
- if deletion/duplication is negative, proceed to MLPA

3. Red blood cell uptake assay

- functional measure of glucose transport across the cell membrane
- currently available only in research setting