RESOURCES

The Glut1 Deficiency Foundation is a non-profit family organization dedicated to improving the lives of those in the Glut1 Deficiency community through its mission of:

- increased awareness
- improved education
- advocacy for patients and families
- support and funding for research

Additional Ketogenic Diet Resources:
- www.charliefoundation.org
- www.matthewsfriends.org

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Glucose Transporter Type 1 Deficiency Syndrome (Glut1 Deficiency, G1D, Glut1D, De Vivo Disease, or Glut1 DS) is a genetic disorder affecting brain metabolism. Glut1 (a protein) is responsible for transporting glucose (a sugar) across the blood brain barrier and also may act independently as a regulator of certain brain functions. The Glut1 protein is made by the SLC2A1 gene located on chromosome 1. If this gene is damaged by a mutation, the protein is not made in sufficient quantity, and glucose transport into the brain is impaired. Glucose is the primary source of fuel for the brain and is important for other aspects of brain metabolism and neural function. The brains of Glut1 Deficiency patients are therefore missing critical metabolic components necessary for normal brain growth and functioning.

think of it this way...

the Glut1 Deficiency brain is always being starved and cannot perform its normal functions adequately. What are these brain functions? They include the ability to think, learn, control body movements, and to communicate. Disturbances in these functions represent the outward symptoms and signs of Glut1 Deficiency.
Glut1 Deficiency results in numerous signs and symptoms, which vary from one patient to another. Some symptoms may be present all the time such as cognitive and motor difficulties, while other signs may come and go like seizures or headaches. Symptoms fall into four categories – seizures, cognition, behavior, and movement. Not all patients experience all symptoms or have the same severity or frequency.

**Behavioral**

Behavioral symptoms affect relations with other people and may include short attention span, intractability, and delays in achieving age-appropriate behaviors. Sociability with peers, however, is a strength in Glut1 Deficiency patients.

**Movement**

Movement symptoms relate to the quality of motor functions. Walking may be delayed or difficult because legs are stiff (spasticity), balance is poor (ataxia), or posture is twisted (dystonia). Fine motor deficits may affect speech quality and manipulative skills, such as writing. These abnormalities may be constant or intermittent (paroxysmal).

**Intermittent**

Other intermittent symptoms may include headaches, confusion, and loss of energy. Some young patients may experience occasional abnormal eye-head movements which may resemble opsoconlus or nystagmus but are distinct enough to have been recently assigned a new term — aberrant gaze saccades.

Another characteristic of Glut1 Deficiency is that symptoms may fluctuate around food intake. Worsening may occur with hunger, especially just before meals, during periods of fasting, and upon and just after waking in the morning. Temporary symptom improvements may be noted after eating.

All symptoms may be aggravated or triggered by other factors such as fatigue, heat, anxiety, and sickness. The symptom picture for each patient may evolve and change over time as children with Glut1 Deficiency progress through adolescence and into adulthood.

**Seizures**

Patients typically begin to experience seizures between 3-6 months of age, but some occur much later. Absence seizures (staring spells), jerky movements, or head drops are most common, although other seizure types may occur and include generalized tonic clonic, focal, myoclonic, atypical absence, atonic, or unclassified. The frequency, severity, and types of seizures may vary considerably among Glut1 Deficiency patients and do not necessarily correspond to the severity of other symptoms. Most seizures in Glut1 Deficiency patients are not easily treated with anti-seizure medications. Approximately 10 percent of patients do not experience seizures.

**Cognitive**

As developmental milestones are delayed, cognitive symptoms often become apparent. Cognitive deficits range from subtle learning difficulties to severe intellectual disabilities. Often speech and language are impaired.
Early diagnosis is critical in order to initiate treatment during the important early stages of brain development. To make a proper diagnosis, it is important to know the symptoms of Glut1 Deficiency. However, other diseases also may share some of these signs and symptoms.

When Glut1 Deficiency is suspected, a fasting lumbar puncture (spinal tap) should be performed. If spinal fluid concentrations of glucose (and sometimes lactate) are lower than normal, these results support the clinical suspicion and justify the diagnosis of Glut1 Deficiency. Gene-sequencing analysis to look for a genetic mutation in the SLC2A1 gene also confirms the diagnosis if positive, although mutations have not been identified in approximately 15 percent of Glut1 Deficiency patients. A highly specialized lab test called the red blood cell uptake assay also may confirm Glut1 Deficiency but is not commercially available.

Currently, there is no cure for Glut1 Deficiency, however there are effective treatment methods that help nourish the growing brain and may prevent and control many symptoms. The ketogenic diet is the current standard of care, effectively controlling most seizures and improving some movement disorders in approximately two-thirds of Glut1 Deficiency patients. There also is evidence of cognitive benefits for Glut1 Deficiency patients on a ketogenic diet, and most parents report improved energy, alertness, balance, coordination, and concentration.

Variations on the ketogenic diet, including the Modified Atkins Diet and diets based on MCT oil, also have been shown to be beneficial for some patients. Other potential treatments that are the subject of current research include dietary therapy with triheptanoin (C7 oil) and exogenous ketones. There is also some anecdotal evidence for benefits derived from alpha lipoic acid supplementation and acetazolamide (Diamox) administration, although there is little formal research supporting these therapies.

Anti-seizure medications often are not effective, since they do not provide nourishment to the glucose-starved brain, although some patients do experience improved seizure control on a single anti-seizure medication.
ketogenic diet

The ketogenic diet was created in 1921 to control seizures. It is a high fat, adequate protein, and low carbohydrate diet that favors the burning of fat for energy in place of glucose. Ketone bodies are formed when fat is metabolized. The human body only has two choices for metabolic fuel: glucose is the preferred fuel and ketones are the alternative fuel. When sufficient carbohydrates are not available to make glucose (a fasting state), the body attempts to produce ketones from fat as an alternative source of energy. The ketogenic diet, by restricting carbohydrates, mimics the metabolic state of fasting and creates an elevated level of ketone bodies in the blood, also known as ketosis. Ketones cross the blood-brain barrier independent of the Glut1 protein and replace glucose as a source of energy for the brain.

The ketogenic diet must be carefully crafted and tailored to meet the individual nutritional needs of each patient and reduce the risk of side effects. It should only be used under the care of medical professionals and dietitians, and it may take some time to establish the ideal ratio and other diet variables for each patient to experience optimal tolerance and benefits.

While ketogenic diets are effective at improving symptoms in most Glut1 Deficiency patients, some do not respond as well as others. In addition, certain symptoms tend to persist in patients treated by a ketogenic diet. This raises the question whether Glut1 Deficiency is caused simply by a lack of proper brain energy or if there are more complicated and widespread systems and processes affected that need treatment options and benefits beyond what the diet can provide.

other dietary therapies

Although the ketogenic diet is the standard of care for Glut1 Deficiency, not all patients tolerate the classical version. While it is commonly used for younger patients, compliance may be more difficult as age increases. Less strict variations to the classical ketogenic diet, including Modified Atkins and MCT oil versions, may provide some of the same benefits and are gaining acceptance as alternatives.

Other dietary therapies are in the investigative stages and may prove beneficial. Triheptanoin (C7 oil), a medium chain triglyceride oil synthesized from castor beans, is a medical food that is the subject of several current and planned future studies. Exogenous ketones, which are synthetic ketones that break down into natural versions when metabolized, are another dietary treatment under investigation.

The role of these alternative treatments and their effectiveness in treating Glut1 Deficiency patients remains to be fully understood.
Rehabilitative services are beneficial since most Glut1 Deficiency patients experience movement disturbances as well as speech and language disorders. Occupational, physical, and speech/language therapies are standard for most patients, especially in childhood. Many families also report additional benefits from lesser known variations of aquatic therapy, hippotherapy, specific learning strategies, and behavioral therapy.

Learning & School

Although the cognitive ability levels among Glut1 Deficiency patients vary greatly, studies have proven that the following clinical features are common in the majority of cases.

Weak areas include:
- lowered IQ and adaptive-behavior scores
- impaired executive functions
- expressive-language and verbal memory deficits
- weaknesses in fine-motor skills and coordination
- limited visual attention to details
- weaknesses in abstract analytical skills
- difficulty with transfer of learning to new contexts

Strong areas include:
- receptive language or understanding
- social skills
- fun-loving and empathetic personalities
- perseverance

When planning instructional programs for Glut1 Deficiency patients, it is important to build upon strengths as weaknesses are remediated. The most appropriate school setting and support services vary based on individual needs and available resources. Some patients do well in a regular education program with supports and some need a more specialized setting.

A variety of both instructional and non-instructional accommodations and services can be beneficial to the academic success of Glut1 Deficiency patients and help ensure that special medical needs are met. It is important for family members to be active and vocal participants in developing and implementing school-based plans and to educate, collaborate, and form partnerships with school personnel in order to best meet the unique and individual needs of Glut1 Deficiency patients.