What is Glut1 Deficiency?

Glucose Transporter Type 1 Deficiency Syndrome is a rarely diagnosed metabolic condition where glucose isn’t transported properly across the blood brain barrier, starving the brain of energy it needs to grow and function as it should.

The energy crisis causes an array of signs and symptoms across a broad spectrum of severity.

also known as: Glut1 Deficiency, G1D, Glut1, Glut1 DS, De Vivo Disease
What causes Glut1 Deficiency?

G1D is caused by a mutation on the first chromosome of the SLC2A1 gene.

- There are approximately 100 different types of mutations and deletions identified in patients.

- De novo mutations cause Glut1 Deficiency in 90% of patients currently identified, although several cases of inherited G1D have been found.

- It is inherited most commonly through an autosomal dominant pattern, although rare cases of autosomal recessive inheritance have been identified from asymptomatic parents.
Who has Glut1 Deficiency?

- G1D cases worldwide currently number around 500, although experts believe there are many more. It affects both genders and all ethnic groups equally.

- The average age of diagnosis is between 5 and 6 years old.

- Several families have been discovered with multiple relatives affected in different ways and to varying degrees.

- G1D is found in 10% of early onset absence seizures, 5% of Myoclonic Astatic Epilepsy (Doose Syndrome), and in an estimated 1% of the idiopathic generalized epilepsy population.

[www.G1Dregistry.org](http://www.G1Dregistry.org)
What are the symptoms?

More common symptoms may include:
- seizures
- movement disorders
- speech and language disorders
- developmental delays

Less common symptoms may include:
- episodes of confusion
- headaches
- alternating hemiplegia of childhood
- hemolytic anemia
- opsoclonus
- microcephaly

Patients appear normal at birth following uneventful pregnancies and delivery.

Apgar scores are normal.
Seizures

• 90% of Glut1 Deficiency patients have seizures (multiple types).

• 90% of patients have seizure onset before age 2, although some have presented much later.

• Seizures associated with Glut1 Deficiency in early childhood can initially be diagnosed as focal and evolve to generalized EEG patterns over time.

• AEDs are usually of limited or no benefit.

• Recent research shows seizures generally improve to some degree as patients enter adulthood. Puberty can be challenging.

• Seizure frequency does not correlate with phenotypic severity.
Movement Disorders

- The majority of patients experience some type of complex movement disorder: dystonia, ataxia, chorea, spasticity, tremor, dyspraxia.

- Symptoms may be continuous or intermittent.
  - can be influenced by fasting, fever, sickness, heat, exertion.

- PED: paroxysmal dyskinesias
  - exercise/exertion induced

- Recent research shows movement disorders generally worsen to some degree as patients enter adolescence and early adulthood.
Most patients experience some degree of cognitive delay ranging from mild to moderate learning disabilities to severe intellectual disability.

Most patients require special assistance in school and structured supports as adults.

Speech and language development can be affected. Receptive and more severely expressive language, dysarthria, dysfluency.

Gross and fine motor development can be affected.
How is Glut1 Deficiency diagnosed?

**Lumbar Puncture - most important laboratory observation**
- four hour fast
- normal blood glucose, low CSF glucose (below 60mg/dL)
- CSF/blood glucose ratio usually less than .4
- CSF lactate is low-normal or low

**Gene Test (SLC2A1) 85-90% accuracy**
- recommended second step after low CSF glucose results
- begin with sequence analysis
- proceed to duplication/deletion if sequencing is inconclusive

**Red Blood Cell Uptake Assay**
- functional measure of glucose transport across the cell membrane
- available in the research setting, not clinically
How is Glut1 Deficiency treated?

A ketogenic diet is the standard of care

- By restricting carbs and ingesting high levels of fat, a ketogenic diet leads to the production of ketones, which the body uses as an alternative energy source in the absence of glucose.

- The diet is effective against many symptoms in most patients.

- Anticonvulsants or AED’s are generally ineffective, although some patients may benefit from a single medication in addition to the diet.
• Historically the classical version has been preferred, especially in younger children to make sure ketone levels are high enough to provide the energy needed for the developing brain.

• There is growing evidence of the effectiveness of alternative forms of ketogenic diets, especially in older patients where they can be less restrictive, more palatable, and lead to better compliance.
  • MCT version
  • Modified Atkins
Potential new therapies?

• There has been recent research involving human patients indicating that triheptanoin (an odd-carbon chain fatty acid also known as C7) can be beneficial in treating Glut1 Deficiency.
  • medical food research - Dr. Juan Pascual UTSW
  • clinical trials for pharmaceutical grade with orphan drug designation - Ultragenyx Pharmaceuticals
    www.clinicaltrials.gov

• Ketone esters are under investigation as a potential treatment and studies are getting underway in the animal model at the University of South Florida.

• More research is needed.
Resources

www.G1DFoundation.org

GeneReviews®
Genetics Home Reference
Child Brain Foundation
www.G1DRegistry.org

Ketogenic Diet Resources:
www.charliefoundation.org
www.matthewsfriends.org
Our Mission

The Glut1 Deficiency Foundation is a volunteer, non-profit family organization dedicated to:

- Educating others about Glut1 Deficiency by creating a forum for sharing support, experiences, resources, and information between patients, families, and healthcare professionals.
- Increasing awareness of and advocacy for Glut1 Deficiency.
- Supporting and funding researchers as they work for better treatments and an ultimate cure.

mission drives all foundation activities
Foundation History

- Initial Meeting Place: Yahoo Groups – Founded June 2004
- Initial Family Conference: Chicago July 2009
- Initial Organization Discussion: Louisville Conference July 2010
- Glut1 Deficiency Foundation: 501(c)3 Status July 2011
- Medical Advisory Board: seated January 2013
- Leadership Team Meeting: July 2014
  new positions, expanded board, new officers, new committees
Board of Directors
all are parents of Glut1 Deficiency patients

President: Jason Meyers (Louisiana)
Vice President: Greg Stoddard (Indiana)
Secretary: Rob Rapaport (Ohio)
Treasurer: Jen Lazar (Texas)
Advocacy Director: Janet Parkhurst (New Jersey)
Education Director: Glenna Steele (Kentucky)
Fundraising Director: April Breen (New York)

along with several committees and volunteers
Special Projects Director: Mike Proett (Colorado)
Medical Advisory Board

Darryl De Vivo, MD
Columbia University Medical Center
New York, New York

Kris Engelstad
Columbia University Medical Center
New York, New York

Prof. Dr. med. Jörg Klepper
Children’s Hospital Aschaffenburg
Aschaffenburg, Germany

Juan Pascual, MD, PhD
University of Texas Southwestern Medical Center
Dallas, Texas

Eric Kossoff, MD
Johns Hopkins Hospital
Baltimore, Maryland
Key Mission Projects

education    awareness    advocacy

Chicago 2009
Key Mission Projects

education    awareness    advocacy

Louisville 2010
Key Mission Projects

- education
- awareness
- advocacy

New Orleans 2011

Sunday, December 28, 14
Key Mission Projects

education  awareness  advocacy

Houston 2013
Key Mission Projects

education  awareness  advocacy
Key Mission Projects

- education
- awareness
- advocacy
Key Mission Projects

- brochure program, translations
- website enhancements, translations
- Yahoo, Rare Connect online communities
- professional conference exhibits
- congressional meetings
- family conferences
- collaborations with other international groups
- Grand Rounds
- quarterly newsletters
- family recommended specialist list
- sponsoring global ketogenic diet symposium sessions
Key Mission Projects

supporting and funding researchers

$233,000 since 2010

- C7 oil studies - mouse and human
- natural history study
- patient registry G1Dregistry.org
- research personnel
- ketone esters - mouse and rat studies
- data gathering

University of Texas Southwestern
University of South Florida

Columbia University
University of Salerno (Italy)
Fundraising Efforts

- annual online campaign kicks off on Valentine’s Day and runs through Rare Disease Day
  last year 44 families - 8 countries

- individual family fundraising events to benefit the Foundation
  varied concepts and locations

- individual donations and corporate matches

- GoodSearch/GoodShop/GoodDining

- all volunteer, so all funds go directly to our mission

thank you!
Upcoming Projects

- create a simple screening tool for practitioners
- launch a targeted diagnostic awareness campaign
- facilitate a Standard of Care with professionals
- plans for next family conference - 2015 Orlando
- host first professional conference with poster sessions - 2015 Orlando
- fund new research projects and sustain established ones
Upcoming Projects
supporting and funding researchers

- create a Scientific Advisory Board to advise research grant awards
- solicit innovative, “outside the box” proposals
- focus on building block research with specific G1D implications
  seed money to lead to larger projects and opportunities
- search out foundation grant opportunities
- continue to fund maintenance and upkeep of G1D patient registry
- fund new projects and sustain established ones
please help us

as we reach for a brighter future for all our children and all those still waiting on a life-changing diagnosis

thank you!
please join us!

Glut1 Deficiency Foundation

2015 Conference ORLANDO

meet • share • learn

Family Program July 6-7 | Professional Program July 8