FAST FACTS ABOUT GLUT1 DS:[i]

Glut1 Deficiency Syndrome is a rare disorder. Fewer than 300 cases have been reported since the disorder was first identified in 1991.

Glucose transporter type 1 deficiency syndrome (Glut1-DS) is characterized by infantile seizures refractory to anticonvulsants, followed by deceleration of head growth, delays in mental and motor development, spasticity, ataxia, dysarthria, opsoclonus, and other paroxysmal neurologic phenomena, often occurring prior to meals.

Affected infants appear normal at birth following an uneventful pregnancy and delivery. Birth weight and Apgar scores are normal. Affected children then experience infantile-onset epileptic encephalopathy associated with delayed neurologic development, deceleration of head growth and resulting microcephaly,ataxia, and spasticity.

Seizures usually begin between age one and four months and are the first clinical indication of brain dysfunction.

Apneic episodes and abnormal episodic eye movements simulating opsoclonus may precede the onset of seizures by several months. Five seizure types occur: generalized tonic or clonic, myoclonic, atypical absence, atonic, and unclassified. The frequency of seizures varies among affected individuals. Some experience daily events; others have only occasional seizures separated by days, weeks, or months; two individuals have never had a clinical seizure.

Other paroxysmal events including intermittent ataxia, mental confusion, lethargy or somnolence, hemiparesis, abnormalities of movement or posture such as dystonia, total body paralysis, sleep disturbances, and recurrent headaches have also been described. It is unclear whether these events represent epileptic or non-epileptic phenomena. These neurologic symptoms generally fluctuate and may be influenced by factors such as fasting or fatigue.

Varying degrees of cognitive impairment, ranging from learning disabilities to severe mental retardation, are characteristic.

Varying degrees of speech and language impairment are observed in all affected individuals. Dysarthria is common and associates with dysfluency (i.e., excessively interrupted speech). Both receptive and expressive language abilities are affected, with expressive language skills disproportionately affected.

Social adaptive behavior is an exceptional strength. Individuals with Glut1-DS tend to be comfortable in group and school settings and interact well with others.

Paroxysmal exercise-induced dyskinesias (PED) are involuntary intermittent movements triggered by prolonged physical exertion. Autosomal dominant inheritance may occur. Recently, mutations in the glucose transporter 1 (GLUT1) gene have been identified as a cause in some patients with autosomal dominant PED.

The diagnosis of Glut1-DS is established in neurologically impaired individuals with 1) reduced cerebrospinal fluid (CSF) glucose concentration (hypoglychorrhachia) that seldom, if ever, exceeds 40 mg/dL; and 2) low ratio of CSF glucose concentration to blood glucose concentration (consistently -0.33-0.01; normal ratio: 0.65 -0.01). *SLC2A1* is the only gene known to be associated with Glut1-DS.

Pathogenesis. The disease manifestations can be explained in terms of current understanding of glucose transport in the brain. Glucose is the principal fuel source for brain metabolism; the glucose transporter Glut1 (solute carrier family 2, facilitated glucose transporter member 1), the protein product of SLC2A1, is the fundamental vehicle by which glucose enters the brain.

The cerebral metabolic rate for glucose is low during fetal development and at birth. The rate increases linearly after birth, peaks around age three years, remains high for the remainder of the first decade of life, and gradually declines during the second decade of life to the rate of glucose utilization seen in early adulthood. It thus appears that the risk for clinical manifestations during fetal development and the newborn period is low, whereas the risk is increased later in infancy and early childhood.

Medical Terminology Dictionary:[ii]

Alpa Lipoic Acid:

- It is used as a dietary supplement for its antioxidant properties.
- Lipoic acid has been the subject of numerous research studies and clinical trials: Prevent organ dysfunction, Reduce endothelial dysfunction and improve albuminuria, Treat or prevent cardiovascular disease, Accelerate chronic wound healing, Reduce levels of ADMA in diabetic end-stage renal disease patients on hemodialysis, Management of burning mouth syndrome, Reduce iron overload, Treat metabolic syndrome, Improve or prevent age-related cognitive dysfunction, Prevent or slow the progression of Alzheimer's Disease, Prevent erectile dysfunction, Prevent migraines, Treat multiple sclerosis, Treat chronic diseases associated with oxidative stress, Reduce inflammation, and Treat peripheral artery disease.

Anticonvulsant- an·ti·con·vul·sant

n. A drug that prevents or relieves convulsions.

Ataxia- a·tax·i·a

n. Loss of the ability to coordinate muscular movement

* ***The International Ataxia Awareness Day is observed on September 25 each year.***

Atkins Diet:

The Atkins diet involves a very low-carbohydrate, high protein regimen and is a form of a ketogenic diet. It emphasizes meat, poultry, fish, fowl, cheese, and eggs, while discouraging foods such as bread, pasta, fruit, and sugar.

- The four-step diet starts with a two-week induction program designed to cause the body to enter a state of ketosis or fat burning phase.
- Liberal, but not unlimited, amounts of fat and protein are allowed but carbohydrate intake is restricted to 20 net grams per day.
- The induction phase is characterized by initial rapid weight loss.
- Long-term weight loss occurs because with a low amount of carbohydrate intake, the body is forced to burn fat as a primary fuel source for energy.
- Low carbohydrate diets have been the subject of heated debate in medical circles for three decades and are still controversial.
- The ketogenic diet team at Johns Hopkins Hospital created a modified Atkins diet for epileptic patients as a method to reduce seizures.

Autosomal dominant: An **autosomal dominant** trait or disorder is one that occurs in those who have inherited one copy of a particular mutated gene in one of the 22 pairs of autosomes (non-sex chromosomes). The phenotype it gives will be expressed even though only one copy of the mutated gene is inherited. This contrasts with an autosomal recessive trait or disorder which requires the inheritance of two copies of the mutated gene for the phenotype to be expressed.

- The chances of an **autosomal dominant** disorder being inherited are 50% if only one parent has the mutant gene. This is because only one copy of the mutant gene is needed and the offspring will inherit a normal gene from the unaffected parent.
- If the parent has two of the mutant genes, the offspring produced from mating with an unaffected parent will always have the disorder.
- If the mutant gene is inherited, the offspring will have the trait or suffer from the disorder depending upon its penetrance.
- Although the mutated gene should be present in successive generations in which there are more than one or two offspring (vertical transmission), it may appear that a generation is skipped if there is reduced penetrance.

Carnitine:

- is a quaternary ammonium compound biosynthesized from the amino acids lysine and methionine.
- In living cells, it is required for the transport of fatty acids from the cytosol into the mitochondria during the breakdown of lipids (fats) for the generation of metabolic energy.
- It is widely available as a nutritional supplement.
- A substance found in skeletal and cardiac muscle and certain other tissues that functions as a carrier of fatty acids across the membranes of the mitochondria.
- It is used therapeutically in treating angina and certain deficiency diseases, particularly glucose transporter type 1 deficiency syndrome, endocardial fibroelastosis, and as an anti-thyroid agent.
- It has actions that closely resemble those of amino acids and B vitamins.
- An amino acid found in meat, dairy sources, avocados, tempeh, and wheat.

Deceleration- de·cel·er·ate

v. **de·cel·er·at·ed**, **de·cel·er·at·ing**, **de·cel·er·ates**

v.tr.

1. To decrease the velocity of.
2. To slow down the rate of advancement of.

v.intr.

To decrease in velocity.

Dysartria- dys·ar·thri·a

n. Difficulty in articulating words, caused by impairment of the muscles used in speech.

Dyskinesia: **dys·ki·ne·sia-**

A movement disorder which consists of effects including diminished voluntary movements.

- The presence of involuntary movements, similar to tics or chorea. Dyskinesia can be anything from a slight tremor of the hands to uncontrollable movement of, most commonly, the upper body but can also be seen in the lower extremities. Dis-coordination can also occur internally especially with the respiratory muscles and it often goes unrecognized.
- Dyskinesia is a symptom of several medical disorders and is distinguished by the underlying cause.

Dystonia: **Dystonia** is a neurological movement disorder, in which sustained muscle-contractions cause twisting and repetitive movements or abnormal postures.

- The disorder may be hereditary or caused by other factors such as birth-related or other physical trauma, infection, poisoning or reaction to pharmaceutical drugs, particularly neuroleptics.
- Treatment is difficult and has been limited to minimizing the symptoms of the disorder, since there is no cure available.

Encephalopathy- literally means disorder or disease of the brain. In modern usage, encephalopathy does not refer to a single disease, but rather to a syndrome of global brain dysfunction. This syndrome can be caused by many different illnesses.

Epileptic Seizure Types:

Absence seizures

- These seizures are sometimes referred to as **petit mal seizures.** In absence seizures, the person may appear to be staring into space with or without jerking or twitching movements of the eye muscles. These periods last for seconds, or even tens of seconds.
- Those experiencing absence seizures sometimes move from one location to another without any purpose.

Focal seizures (also called **partial seizures**)

- Are seizures which affect only a small part of the brain and are split into two main categories; **simple partial seizures** and **complex partial seizures.**
- A simple partial seizure will often be a precursor to a larger seizure. In this case, the simple partial seizure is usually called an **aura**.
- **Focal seizures** are common in temporal lobe epilepsy.

Atonic seizures (also called **drop seizures**, **akinetic seizures** or drop attacks), are a minor type of seizure.

- They consist of a brief lapse in muscle tone that are caused by temporary alterations in brain function.
- The seizures are brief - usually less than fifteen seconds. They begin in childhood and may persist into adulthood.
- The seizure itself causes no damage, but the loss of muscle control can result in indirect damage from falling.
- Atonic seizures can occur while standing, walking or sitting and are often noticeable by a head drop (the neck muscles releasing) and damage sometimes results from hitting the face or head.
- In some cases, a person may become temporarily paralyzed in part of his or her body. This usually does not last longer than 3 minutes.

Gelastic seizure, also known as **"gelastic epilepsy"**

- is a rare type of seizure that involves a sudden burst of energy, usually in the form of laughing or crying.
- This syndrome usually occurs for no obvious reason and is uncontrollable. It is slightly more common in males than females.
- The term Gelastic originates from the Greek word "Gelos" which means laughter. This syndrome can go for very long periods of time without a diagnosis, as it may appear to be much like normal laughing or crying, if it occurs infrequently.
- It has been associated with several different conditions such as temporal and frontal lesions, tumors, dilated temporal horns, atrophy, tuberous sclerosis, hemangiomas, and post infectious foci, but mainly hypothalamic hamartomas.

Jacksonian seizure (or Jacksonian march)

- Are associated with a progression of the location of the seizure in the brain, which leads to a "march" of the motor presentation of symptoms.
- **Jacksonian seizures** are initiated with abnormal electrical activity within the primary motor cortex.
- They are unique in that they travel through the primary motor cortex in succession, affecting the corresponding muscles, often beginning with the fingers. This is felt as a tingling sensation. It then affects the hand and moves on to more proximal areas.
- Symptoms often associated with a **Jacksonian seizure** are sudden head and eye movements, tingling, numbness, smacking of the lips, and sudden muscle contractions.
- Most of the time, any one of these actions can be seen as normal movements, without being associated with the seizure occurring.
- They occur at no particular moment and last only briefly.
- They can also start at the feet, same tingling (pins and needles), there is cramping of the foot muscles which, due to the signals from the brain, causes great pain.

Jacksonian seizures are extremely varied and may involve, for example, apparently purposeful movements such as turning the head, eye movements, smacking the lips, mouth movements, drooling, and rhythmic muscle contractions in a part of the body, abnormal numbness, tingling, and a crawling sensation over the skin.

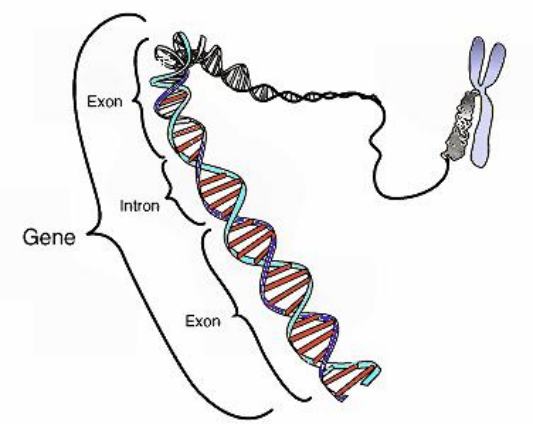
***Subclinical Seizure*:** is a type of seizure often experienced by people with epilepsy in which an EEG trace will show abnormal brain activity, usually for a short duration of time but which does not present any noticeable clinical signs or symptoms.

- This often manifests as a single spike on the EEG trace or a slowing of brain activity not correlating to their level of consciousness or awareness.
- **Subclinical seizures** can be useful to a neurologist when displayed on an EEG in the diagnosis of epilepsy.

Tonic-clonic seizures are a type of generalized seizure affecting the entire brain. Formerly known as **grand mal seizures** or **gran mal seizures**, these terms are now discouraged and are rarely used in a clinical setting.

- **Tonic-clonic seizures** are the seizure type most commonly associated with epilepsy and seizures in general, though it is a misconception that they are the only type.
- **Tonic-clonic seizures** are induced deliberately in Electroconvulsive Therapy.

Gene:



This stylistic diagram shows a gene in relation to the double helix structure of DNA and to a Chromosome (right). The chromosome is X-shaped because it is dividing. Introns are regions often found in eukaryote genes that are removed in the splicing process (after the DNA is transcribed into RNA): Only the exons encode the protein. This diagram labels a region of only 50 or so bases as a gene. In reality, most genes are hundreds of times larger.

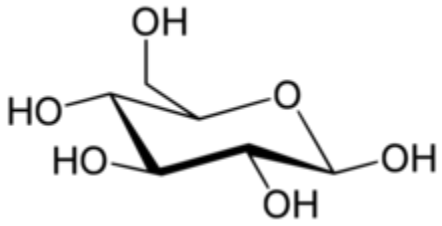
- A **gene** is a unit of heredity in a living organism. It normally resides on a stretch of DNA that codes for a type of protein or for an RNA chain that has a function in the organism.
- All living things depend on genes, as they specify all proteins and functional RNA chains.
- Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring, although some organelles (e.g. mitochondria) are self-replicating and are not coded for by the organism's DNA.
- All organisms have many genes corresponding to many different biological traits, some of which are immediately visible, such as eye color or number of limbs, and some of which are not, such as blood type or increased risk for specific diseases, or the thousands of basic biochemical processes that comprise life.

Glucose Transporter: **Glucose transporters** (GLUT or SLC2A family) are a family of membrane proteins found in most mammalian cells.

- Glucose is an essential substrate for the metabolism of most cells. Because glucose is a polar molecule, transport through biological membranes requires specific transport proteins.
- Each **glucose transporter** isoform plays a specific role in glucose metabolism determined by its pattern of tissue expression, substrate specificity, transport kinetics, and regulated expression in different physiological conditions.
- To date, 13 members of the GLUT/SLC2 have been identified.
- On the basis of sequence similarities, the GLUT family has been divided into three subclasses.
- GLUTs are integral membrane proteins that contain 12 membrane-spanning helices with both the amino and carboxyl termini exposed on the cytoplasmic side of the plasma membrane.
- GLUT proteins transport glucose and related hexoses according to a model of alternate conformation which predicts that the transporter exposes a single substrate binding site toward either the outside or the inside of the cell.
- Binding of glucose to one site provokes a conformational change associated with transport, and releases glucose to the other side of the membrane.

The inner and outer glucose-binding sites are, it seems, located in transmembrane segments 9, 10, 11; also, the QLS motif located in the seventh transmembrane segment could be involved in the selection and affinity of transported substrate.

Glucose transporter



Class 1 Types of Glucose Transporters:

Name	Distribution	Notes
GLUT1	Is widely distributed in fetal tissues. In the adult, it is expressed at highest levels in erythrocytes and also in the endothelial cells of barrier tissues such as the blood-brain barrier. However, it is responsible for the low-level of basal glucose uptake required to sustain respiration in all cells.	Levels in cell membranes are increased by reduced glucose levels and decreased by increased glucose levels.
GLUT2	Is expressed by renal tubular cells and small intestinal epithelial cells that transport glucose, liver cells and pancreatic â cells. All three monosaccharides are transported from the intestinal mucosal cell into the portal circulation by GLUT2.	Is a high-capacity and low-affinity isoform
GLUT3	Expressed mostly in neurons (where it is believed to be the main glucose transporter isoform), and in the placenta.	Is a high-affinity isoform
GLUT4	Found in adipose tissues and striated muscle (skeletal muscle and cardiac muscle).	Is the insulin-regulated glucose transporter. Responsible for insulin-regulated glucose storage.

Hemiparesis: **Hemiparesis** is weakness on one side of the body. It is less severe than hemeplegia, the total paralysis of the arm, leg, and trunk on one side of the body.

Ketoacidosis: is a dangerous complication in which the chemical balance of the body becomes far too acidic.

- **Ketoacidosis** is most commonly seen in individuals with type I diabetes, under 19 years of age and is usually caused by the interruption of their insulin treatment or by acute infection or trauma.
- A small number of people with type II diabetes also experience ketoacidosis, but this is rare given the fact that type II diabetics still produce some insulin naturally.
- **Ketoacidosis** may also be seen in patients following a ketogenic or modified Atkins Diet when high levels of ketone bodies are present.

Common Symptoms of Ketoacidosis:

- high blood sugar levels
- frequent urination (polyuria) and thirst
- fatigue and lethargy
- nausea
- vomiting
- abdominal pain
- fruity odor to breath
- rapid, deep breathing
- muscle stiffness or aching
- coma

Common Terms Associated With Ketoacidosis:

- **Acidosis** — is an increased acidity in the blood and other body
- **Diabetes mellitus** — referred to as diabetes, is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin, or because cells do not respond to the insulin that is produced.
- **Edema** — is an abnormal accumulation of fluid beneath the skin or in one or more cavities of the body that produces swelling
- **Glucose** —is a simple sugar (monosaccharide) and an important carbohydrate in biology. Cells use it as the primary source of energy
- **Hyperglycemia** is a condition in which an excessive amount of glucose circulates in the blood plasma.
- **Hyperketonemia** — A condition characterized by an overproduction of ketones.
- **Hypoglycemia** — is an abnormally diminished content of glucose in the blood
- **Hypokalemia** — A potassium deficiency in the blood.
- **Insulin** — is a hormone produced by the pancreas which is central to regulating carbohydrate and fat metabolism in the body. Insulin causes cells in the liver, muscle, and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle.
- **Lactic acidosis** — is a physiological condition characterized by low pH in body tissues and blood (acidosis) accompanied by the buildup of lactate especially D-lactate and is considered a distinct form of metabolic acidosis
- **Metabolism** — The sum of all chemical reactions that occur in the body resulting in growth, transformation of foodstuffs into energy, waste elimination, and other bodily functions.
- **Polyuria** — is a condition usually defined as excessive or abnormally large production or passage of urine.

Ketogenic Diet:

- is a high-fat, adequate-protein, low-carbohydrate diet that in medicine is used primarily to treat difficult-to-control (refractory) epilepsy in children.
- The diet mimics aspects of starvation by forcing the body to burn fats rather than carbohydrates. Normally, the carbohydrates contained in food are converted into glucose, which is then transported around the body and is particularly important in fuelling brain function. However, if there is very little carbohydrate in the diet, the liver converts fat into fatty acids and ketone bodies.
- The ketone bodies pass into the brain and replace glucose as an energy source. An elevated level of ketone bodies in the blood, a state known as ketosis, leads to a reduction in the frequency of epileptic seizures.
- The original therapeutic diet for pediatric epilepsy provides just enough protein for body growth and repair, and sufficient calories to maintain the correct weight for age and height.
- This classic ketogenic diet contains a 4:1 ratio by weight of fat to combined protein and carbohydrate.
- Most dietary fat is made of molecules called long-chain triglycerides (LCTs). However, medium-chain triglycerides (MCTs)—made from fatty acids with shorter carbon chains than LCTs—are more ketogenic.

Ketones:

- Are an organic compound
- Are produced by the body when fat is used instead of glucose for energy such as with the Ketogenic Diet.

Learning Disabilities: Learning disability (sometimes called a learning disorder or learning difficulty), is a classification including several disorders in which a person has difficulty learning in a typical manner, usually caused by an unknown factor or factors.

- The unknown factor is the disorder that affects the brain's ability to receive and process information.
- This disorder can make it problematic for a person to learn as quickly or in the same way as someone who isn't affected by a learning disability.
- People with a learning disability have trouble performing specific types of skills or completing tasks if left to figure things out by themselves or if taught in conventional ways.

Mental Retardation (Intellectual Disability): Mental retardation is a developmental disability that first appears in children under the age of 18. It is defined as an intellectual functioning level (as measured by standard tests for intelligence quotient) that is well below average and significant limitations in daily living skills (adaptive functioning).

Metabolic Rate: met·a·bol·ic

Basal Metabolic Rate (BMR), and the closely related resting metabolic rate (RMR), is the amount of daily energy expended by humans and other animals at rest.

Microcephaly- is a neurodevelopmental disorder in which the circumference of the head is more than two standard deviations smaller than average for the person's age and sex.

- **Microcephaly** may be congenital or it may develop in the first few years of life. The disorder may stem from a wide variety of conditions that cause abnormal growth of the brain, or from syndromes associated with chromosomal abnormalities.

Non-epileptic Seizure Types:

Non-epileptic seizures are paroxysmal events that mimic an epileptic seizure but do not involve abnormal, rhythmic discharges of cortical neurons.

- They are caused by either physiological or psychological conditions.
- A wide spectrum of phenomena may resemble epileptic seizures, which may lead to people who do not have epilepsy being misdiagnosed.

Febrile seizure- is a convulsion that is associated with a significant rise in body temperature in children ages of six months to five years.

- Febrile seizure is also known as fever fit or febrile convulsion. A fever itself is not an illness but is associated with respiratory illness.
- During simple febrile seizures, the body will become stiff and the arms and legs will begin twitching. Also, the eyes roll back. The patient loses consciousness, although their eyes remain open. Breathing can be irregular. They may become incontinent (wet or soil themselves); they may also vomit or have increased secretions (foam at the mouth). The skin may appear to be darker than normal during an episode. The seizure normally lasts for less than one minute, but uncommonly can last up to fifteen minutes.

Neuroglycopenia:

- Neuroglycopenia is a medical term that refers to a shortage of glucose in the brain, usually due to hypoglycemia.
- Glycopenia affects the function of neurons and alters brain function and behavior.
- Prolonged neuroglycopenia can result in permanent damage to the brain.

Opsoclonus- refers to uncontrolled eye movement.

- Consists of rapid, involuntary, multivectorial (horizontal and vertical), unpredictable, conjugate fast eye movements without intersaccadic intervals.
- It is also referred to as **saccadomania** or reflexive saccade. The movements of **opsoclonus** may have a very small amplitude, appearing as tiny deviations from primary position.
- Possible etiologies of **opsoclonus** include neuroblastoma and encephalitis in children, and breast, lung, or ovarian cancer in adults. Other considerations include multiple sclerosis, toxins, or medication effects.
- It can also be caused by a lesion in the omnipause neurons which tonically inhibit initiation of saccadic eye movement (until signaled by the superior colliculus) by blocking paramedian pontine reticular formation (PPRF) burst neurons in the midbrain.

  It frequently occurs along with myoclonus in opsolclonus myoclonus syndrome.

Pathogenisis: path·o·gen·e·sis

The mechanism by which the disease is caused.

- The term can also be used to describe the origin and development of the disease and whether it is acute, chronic or recurrent.

Paroxysmal- Paroxysm

- A sudden outburst of a violent emotion or action
- A seizure, spasm, cramp, sudden attack of pain
- An increase of symptoms attacks of a disease

Phenomenon: A **phenomenon** (from Greek *φαινόμενον*), plural **phenomena**, is any observable occurrence

Psychogenic non-epileptic seizures (PNES), also known as Non-Epileptic Attack. Disorders are events superficially resembling an epileptic seizure.

- Without the characteristic electrical discharges associated with epilespsy.
- Instead, PNES are psychological in origin, and may be thought of as similar to conversion disorder.
- It is estimated that 20% of seizure patients seen at specialist epilepsy clinics have PNES.

Refractory- re·frac·to·ry

adj. Resistant to treatment

Spasticity- spas·tic

adj.

1. Of, relating to, or characterized by spasms
2. Affected by spastic paralysis.

n. A person affected with spastic paralysis.

Seizure- A **seizure**, also known as a *convulsion* or *fit*, is a sudden loss of consciousness, a change in one's state of consciousness, or a loss of control over one's body.

Speech disorder - a disorder of oral speech.

- **Defect of speech, speech defect disorder, upset** – a communication disorder where typical speech is disrupted.
- **Anarthria** – a speech disorder resulting from lesions of the central nervous system.
- **Dysarthria** – is a motor speech disorder resulting from neurological injury of the motor component of the motor-speech system
- **Dyslogia** – a speech order caused by a mental illness; lack of clarity and in verbal expression
- **Dysphonia** – is the medical term for disorders of the voice: an impairment in the ability to produce voice sounds using the vocal organs
- **Lallation** – is an imperfect enunciation of the letter "R", in which it sounds like "L", as frequently found in infantile speech
- **Lisp** – is a speech impediment
- **Stammer, Stutter** – a speech disorder involving involuntary repetitions or sounds

Somnolence: som·no·lence/ (som´no-lens)

- A state of near-sleep, a strong desire for sleep, or sleeping for unusually long periods.
- It has two distinct meanings, referring both to the usual state preceding falling asleep and the chronic condition referring to being in that state independent of a circadian rhythm.

REFERENCES:

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[i] Fast Facts About Glut1 DS summarizes information from Gene Reviews - *Glucose Transporter Type 1 Deficiency Syndrome* (Dong Wang, MD; Juan M Pascual, MD, PhD; Darryl De Vivo, MD)(Initial Posting: July 30, 2002; Last Update: July 7, 2009) which is copyrighted by the University of Washington, Seattle, 1993-2012. The source for Gene Reviews is www.genetests.org. Readers are cautioned to read the entire review which can be found at http://www.ncbi.nlm.nih.gov/books/NBK1430/ . All of this information is subject to the Gene Tests disclaimers and terms of use.

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