www.galactosemia.org
Understanding Galactosemia
Classic Galactosemia/Duarte Galactosemia/Galaktokinase Deficiency
What is Classic Galactosemia?
Classic Galactosemia is a rare genetic metabolic disorder. The child with classic galactosemia inherits a gene for galactosemia from both parents, who are carriers. Patients who inherit the classic galactosemia gene from each parent are sometimes described as having the genetic makeup "G/G". Normally when a person consumes a product that contains lactose (e.g., dairy products such as milk, cheese, butter), the body breaks the lactose down into galactose and glucose. Glucose is the sugar used by the body for energy. Galactosemia means too much galactose in the blood caused by the individual "missing" the enzyme (known as GALT) to convert galactose into glucose. This accumulation of galactose is a poison to the body and can cause serious complications such as the following and if untreated, as high as 75% of infants will die:

- an enlarged liver
- kidney failure
- cataract
- brain damage
Diagnosis is made usually within the first week of life by blood test from a heel prick as part of a standard newborn screening. Treatment requires the strict exclusion of lactose/galactose from the diet. Although galactosemic children are started on diet restriction at birth, there continues to be a high incidence of long-term complications involving speech and language, fine and gross motor skill delays and specific learning disabilities. Ovarian failure may occur in girls. Prenatal diagnosis by amniocentesis is also available.

What is Duarte Galactosemia?
Duarte Galactosemia is a variant of classic galactosemia. Fortunately, the complications associated with classic galactosemia have not been associated with Duarte galactosemia. The child with Duarte galactosemia inherits a gene for classic galactosemia (G) from one parent, and a Duarte variant gene (D) from the other parent. Patients with this genetic make-up are frequently referred to as D/G galactosemics.

Diagnosis of Duarte galactosemia is made usually within the first weeks of life by the same blood test used to diagnose classic galactosemia. Galactose-1-phosphate uridyltransferase (GALT) enzyme activity in D/G patients is approximately 25%-50% of that found in children born with no galactosemia gene.

There is some disagreement over the need for dietary restriction in the treatment of children with Duarte galactosemia. Consult your medical advisors (preferably a pediatric metabolic geneticist) for their advice on this topic. Dietary Options include :

- restricting lactose / galactose in the diet for a year or so then gradually introducing these items and testing for the patient's response (i.e. elevation of galactose-1-phosphate (Gal-1-P) levels in patient's blood).
- no restrictions at all, to include breastfeeding infants.
There is no research that conclusively reveals medical or other developmental complications attributable to Duarte galactosemia in D/G patients.

What is Galaktokinase Deficiency?
In humans, inherited deficiency of Galactokinase (GALK) enzyme activity caused by deleterious mutations in the human GALK1 gene can lead to a disorder called Type II
Galactosemia. If untreated, the patients will accumulate high levels of galactose and galactitol in their body tissues. But unlike the more debilitating Type I (GALTdeficiency) Galactosemia, the disease phenotypes of patients with GALK deficiency are often mild and limited to juvenile cataract formation. This clinical observation has recently been confirmed by a long-term study published by Dr. J.B. Hennermann and coworkers, where they followed the outcome of 18 newborns diagnosed with GALK deficiency through newborn screening programs between 1991 and 2010. The most effective treatment for GALK deficiency is the implementation of galactose-restricted diet.

The earliest case of Type II Galactosemia was reported by Dr. R. Gitzelmann in 1965 and the latest review for the disease was written by Dr. A.M. Bosch and coworkers in 2002. The frequency of GALK deficiency varies among different population and ranges from 1 in 200,000 to 1 in 40,000, with highest incidence reported in the Romani population where the carrier frequency is estimated to be 1 in 47. To date, more than 30 mutations in the GALK1 gene residing in chromosome 17q24 have been reported, and all of them were transmitted from parents to their children through the autosomal recessive mode of inheritance. Thanks to the efforts of Drs. D.J. Timson, R.J. Reece, H.D. Park, and H. Holden, the three-dimensional structure of the human GALK enzyme has been deciphered, and many of the mutations of the GALK1 gene have been shown to result in mutant enzymes with decreased solubility and specific activity. Among the characterized mutations, the A198V mutation appears to have the best outcome, with only moderate incidence of cataracts in later life.

Although inherited GALK deficiency can lead to cataract formation in Type II Galactosemia, pharmacological inhibition of the human GALK enzyme to create an artificial GALK-deficiency state has been suggested by Drs. A.M. Bosch, J. Fridovich-Keil, K. Lai, A. Marabotti, and D.J. Timson as a potential improved therapy for Classic Galactosemia (Type I or GALT-deficiency Galactosemia). Additionally, inhibition of GALK1 gene expression has recently been proposed.

Genetics of Galactosemia

A person unaffected by galactosemia (neither carrier nor galactosemic) inherits two 'normal' genes for the production of the GALT enzyme (the enzyme needed to convert galactose into a form useable by the body). This person's genotype would be N/N and their enzyme activity would be normal.

A person who is a carrier of classic galactosemia inherits one normal gene from one parent and one gene containing the error that leads to classic galactosemia from the other parent. This person's genotype would be G/N and their enzyme activity would be less than normal, but not so much so as to cause medical complications or require dietary management.

A person who is classic galactosemic inherits two genes with the error, one from each of his/her parents. This person's genotype would be G/G and their enzyme activity would be essentially zero.

Genotypes involving the Duarte variant gene include:

D/N = carrier of Duarte galactosemia (about 75% enzyme activity)
D/D = homozygous carrier of Duarte galactosemia (about 50% enzyme activity)
D/G = Duarte galactosemia (about 25 - 50% enzyme activity ??)

History of Galactosemia

Galactosemia was first "discovered" in 1908. Von Ruess, in a 1908 publication entitled, "Sugar Excretion in Infancy," reported on a breast-fed infant with failure to thrive, enlargement of the
liver and spleen, and "galactosuria". This infant ceased to excrete galactose through the urine when milk products were removed from the diet. The infant, however, later died because of other complications (the baby had been given tea laced with cognac as treatment as well). An autopsy revealed cirrhosis of the liver, which they thought was due to the infant's alcohol ingestion. Though confirmation of the diagnosis was not possible at that time, it has been generally accepted that Von Ruess was the first to report on a patient with galactosemia.

By 1917, "galactosuria" was a broadly recognized inherited disorder and was treated by removal of milk products from the diet.

The disease was first recognized and described in detail (ie published work) in 1935 by Mason and Turner. Leloir worked out the metabolic pathway and the process of sugar-nucleotides and won the Nobel prize in Chemistry in 1970 for his work. He and coworkers elucidated the pathway for converting galactose to glucose in the early 50's.

Although, the clinicians recognized galactosemia very early in the century, the defective gene that caused it wasn't found until 1956. Another major break-through was when it was first found to be detectable through a newborn screening method in 1963. This method was developed by Guthrie and Paigen. Galactosemia was the second disorder found to be detectable through newborn screening methods by Robert Guthrie.

Diet Resources
Sources of Diet Guidelines
Unfortunately, the classic galactosemic diet is a controversial one. Different clinics, doctors, and parents follow different rules. Below is a list of diet guides that some parents follow. You can get these guides from your doctor/clinic/nutritionist. Please check with your own clinic for diet advice. It is important to follow your own doctor’s advice, because what one clinic recommends for diet may not be what another recommends. We understand the frustration this brings and this is why we encourage all parents to gather as much information as they can, work with their clinic, so that they can make the best possible decision they can for their own child.

1) Understanding Galactosemia A Diet Guide
Linda Gleason, MS, RD
Matthew Rasberry, RD
Sandy van Calcar, PhD, RD
    Download "Understanding Galactosemia A Diet Guide" (PDF)

2) A Guide for the Family of the Child With Galactosemia
The Ross Metabolic Formula System, Ross Laboratories
Medical Editor: Phyllis B. Acosta, Dr. PH, RD

Galactosemia Food Information Cooperative Web Site
A web site created and maintained by parents of children with galactosemia for parents of children with galactosemia. This site contains information contributed by many parents who deal with the galactosemic diet on a daily basis. It is not a replacement for label reading, but it can certainly reduce the amount of time hunting for products in the grocery store aisles. Includes sections on acceptable manufactured foods, menus, recipes, manufacturer contact information, and even a section on suggestions for various holidays. Check it out, then send in YOUR contributions !!
Note - the material on the Galactosemia Food Information Cooperative Website was not created by Galactosemia Foundation.

Other Diet Links
To view the Other Diet Links please review and accept our disclaimer agreement.

Unacceptable Ingredients
Since actual products change on a regular basis it is imperative that you re-read every label every time you buy. Various parents and dietitians have put together this list of unacceptable ingredients in an attempt to simplify the ingredient dilemma.

Please, remember to always check with your clinic and dietitian. Gather all information available and then make your own decision.

FOOD INGREDIENTS WHICH ARE UNACCEPTABLE IN THE DIET FOR GALACTOSEMIA:

Butter
Nonfat Milk
Milk
Nonfat Dry Milk
Buttermilk
Cream
Milk Chocolate
Cheese
Buttermilk Solids
Nonfat Dry Milk Solids
Milk Derivatives
Dried Cheese
Milk Solids
Lactose
Casein
Sour Cream
Dry Milk
Whey and Whey Solids
Dry Milk Protein
Yogurt
Organ Meats (liver, heart, kidney brains, sweetbreads, pancreas)
Sodium Caseinate
Calcium Caseinate
Tragacanth Gum
Lactostearin
Lactalbumin
Dough Conditioners*
Hydrolyzed Protein**
Margarine***
MSG (Monosodium Glutamate)****
Soy Sauce*****
NOTE: Lactate, Lactic acid and Lactylate do not contain lactose and are acceptable ingredients.

* Dough Conditioners may include caseinates which are UNACCEPTABLE. Most labels specify the name of the conditioner which is added to the product. If not, contact the company to make sure that all are acceptable.
** Hydrolyzed protein is UNACCEPTABLE and is commonly found in canned meats, like tuna. Hydrolyzed vegetable protein, however, is acceptable.

*** A few diet margarine’s do not contain milk. Check labels before using any brand. If "margarine" is listed as an ingredient in any processed food, consider the product UNACCEPTABLE.

**** MSG or Monosodium Glutamate itself is acceptable; however, some MSG’s contain lactose extenders. It is best to avoid MSG whenever possible.

***** Soy sauce is UNACCEPTABLE if it is fermented. Brands must be checked before including this in the galactosemic diet.

**Calcium Supplementation/Recommendations**

Given the necessary restriction on dairy items in the galactosemic diet, parents sometimes wonder whether their galactosemic child is getting sufficient calcium.

Ask your doctor or clinic what the recommended calcium intake is for your child. If your child sees a nutritionist, you may ask him/her to perform a three-day diet analysis to determine if your child is getting enough calcium (as well as other nutrients).

There are a number of natural food sources of calcium among the foods acceptable for a galactosemic diet. If you are advised to increase your child’s daily intake of calcium, it may be best to try to increase these natural sources in your child’s diet before turning to supplements.

Advice on calcium supplements varies from clinic to clinic. Below is a list of calcium supplements that some parents are using. Keep in mind that this list just represents some of the types of calcium supplements given to children with galactosemia and is NOT an endorsement for any of the products. As with anything, check labels carefully (for restricted ingredients) and always check with your own doctor/clinic before giving any supplement to your child. Keep in mind companies frequently change ingredients in their products.

- **Tums** - some are still using, although there has been talk about Tums being bad for tooth enamel among other things
- **Centrum Vitamins** - "Bone Health" - suppose to be lactose and dairy-free (It is like a regular vitamin)
- **CalQuick (Twin Labs)** - liquid calcium supplement (600 mg/tablespoon)
- **Liquid Cal Mag+ (KAL)** (600 mg/tablespoon)
- **Multi-vitamins with extra calcium**

Keep in mind that there are different forms of calcium used in supplements (e.g. calcium carbonate, calcium phosphate, calcium citrate, calcium gluconate, etc.). Some forms of calcium are thought to be more easily absorbed into the body than others. Another factor to consider is that levels of calcium in the blood may not always indicate the actual calcium used by the body to increase bone density. Ask your nutritionist for advice on this matter.

Calcium recommendations vary depending on age and special needs. In addition, levels of estrogen can affect calcium needs in women. Note: Calcium requires adequate Vitamin D to be absorbed into the body.
Potential Complications

Cataracts

A cataract is a clouding of the lens of the eye. The lens is a crystal-clear, flexible structure near the front of the eyeball. It helps to keep vision in focus, and screens and refracts light rays. The lens has no blood supply. It is nourished by the vitreous (the watery substance that surrounds it). Cataracts may form in one or both eyes. If they form in both eyes, their growth rate may be very different. Cataracts are not cancerous.

Appropriate health care includes treatment by an ophthalmologist or surgery to remove the lens.

Cataracts are one of the possible complications of classic galactosemia. Cataracts are mostly observed in newborns but can also occur in adults. It is thought that 10-30% of newborns with classic galactosemia develop cataracts in the first few days or weeks of life. Once a newborn is put on a galactose-restricted diet, cataracts usually clear up on their own. Surgery is sometimes necessary in rarer cases.

It is believed that if the galactose restricted diet is followed, cataracts do not develop in galactosemic children.

Many patients have eye examinations to check for the presence of cataracts on a regular basis. More frequent during the first year of life (e.g every 3-4 months), such exams can be reduced in frequency (e.g. 1 or 2 times a year) in older children. It is a good idea to have an eye exam if for some reason Gal-1-P levels are observed to rise above a ‘target’ range.

Learning Disabilities

A learning disability is a disorder that interferes with a person's ability to master a skill (such as reading, writing, arithmetic concepts, etc.). Learning disabilities can show up in many ways such as, specific difficulties with spoken and written language, coordination, self-control, or attention.

Learning disabilities can be lifelong conditions that, in some cases, affect many parts of a person’s life: school or work, daily routines, family and social life. Some people, may have overlapping learning disabilities. Other people may have a single, isolated learning problem that has little or no impact on other areas of their lives. Also, some individuals can manage, or even overcome, learning disabilities with focused therapy or specialized instruction, and/or medication.
It is important to know that not all learning problems are necessarily learning disabilities. Many children are simply slower in developing certain skills. Because children show natural differences in their rate of development, sometimes what seems to be a learning disability may simply be a delay in maturation. By law, learning disability is defined as a significant gap between a person’s intelligence and the skills the person has achieved at each age.

(Source: NIMH - National Institute of Mental Health - for more information see their web page at www.nimh.nih.gov)

Learning Disabilities and Galactosemia:
Although know one really knows exactly why, there have been some specific learning disabilities associated with classic galactosemia. (note - there have been no learning disabilities positively associated with Duarte Galactosemia). Even some children who were diagnosed relatively quickly after birth and who are following the "restricted diet" have developed learning disabilities. Some of the learning disabilities associated with galactosemia include: speech and language difficulties, fine and/or gross motor difficulties, and difficulty with math or reading in school. Unfortunately, there are no firm numbers to quantify the percentage of galactosemics who experience learning disabilities.

It is important to know that not all children with galactosemia have learning disabilities. Because many galactosemic children do have problems, it is something very important to be aware of in observing a child's development.

One aspect of learning disabilities and galactosemia that is important for parents to keep in mind is that neurological impairments (e.g. fine motor difficulties) can sometimes present themselves "disguised" as a learning disability. For example, a child with trouble writing numerals or pointing may appear to have a learning disability with regard to arithmetic concepts, when the case may well be that the child understands the math concept just fine, but simply cannot control his/her writing sufficiently well enough to demonstrate mastery of the concept. It is important to note that a child may in fact have both problems.

Questions:
How do I know if my child has a learning disability? (Ages 0 - 3)
Because every child develops differently, this can be a difficult question to answer. Your child's pediatrician should be your first source of information. He or she should be able to, with your input, notice any signs of problems in your child's development. Be sure to inform your doctor of the types of problems that have been associated with galactosemia. (Because galactosemia is very rare, your doctor may know very little, if anything, about galactosemia). If he/she knows what to "look for", it can be very helpful to him/her. Also, sometimes parents know best, so if you suspect a problem, and your doctor does not agree with you, get a second opinion. Research shows that the earlier a problem is treated, the better it is for the child. Remember to keep in mind that children develop at different rates - learning disability is defined as a significant gap between a person’s intelligence and the skills the person has achieved at each age.

What kind of services should I get for my child if I suspect a developmental problem or learning disability?
Many local school systems offer free programs for young children (infants and toddlers) as well as for older children. You can call your local school system to ask for an evaluation for your child and/or to ask that your child be put into a program that would be appropriate for him. If you are unable to get services form you local school system, try a private
therapist/teacher or institution. Some medical insurance companies may pay for all or part of these services. Check with your own policy.

Some helpful WWW resources:
National Institute of Mental Health - NIMH
(This site contains a great deal of information about learning disabilities.)

www.ldonline.org
(This site contains an interactive guide to learning disabilities for parents, teachers, and children.)

National Center for Learning Disabilities
"The National Center for Learning Disabilities provides national leadership in support of children and adults with learning disabilities by providing information, resources, and referral services; developing and supporting innovative educational programs, seminars, and workshops; conducting a public awareness campaign; and advocating for more effective policies and legislation to help individuals with learning disabilities"

Learning Disabilities Association
"Our purpose is to advance the education and general welfare of children and adults of normal or potentially normal intelligence who manifest disabilities of a perceptual, conceptual or coordinative nature".

Kidshealth.org
A link to web articles about IEP's

Wrightslaw
You'll find hundreds of articles, cases, newsletters, and other information about special education law and advocacy in the Wrightslaw Libraries. Parents, advocates, educators, and attorneys come to Wrightslaw for accurate, up-to-date information about advocacy for children with disabilities.

Neurological Impairments
Along with well documented speech and language disorders, neurodevelopmental delays are also sometimes observed in galactosemic patients. By some estimates, galactosemics experience trouble with gait, balance, and fine motor tremors in anywhere from 13 to 20%.

In one study, 45 individuals with galactosemia were examined. In that study, 12 individuals were observed to have neurological symptoms that included ataxia, tremors, and dysmetria.

Ataxia is a total or partial inability to coordinate voluntary bodily movements (as in walking, etc.).

Tremors are rhythmic, involuntary muscular contractions characterized by oscillations (to-and-fro movements) of a part of the body. The most common of all involuntary movements, tremor can affect various body parts such as the hands, head, facial structures, vocal cords, trunk, and legs; most tremors, however, occur in the hands. Although the disorder is not life-threatening, it can be responsible for functional disability and social embarrassment. There are different types of tremors. One type is Kinetic or Intention tremor which occurs during purposeful goal-oriented tasks, for example finger-to-nose testing.

Dysmetria is improper estimation of distance during muscular activity. Dysmetria includes both hypo- and hypermetria. With hypermetria, voluntary muscular movement overreaches the
intended goal; with hypometria, voluntary movement falls short of the intended goal. Hypermetria is more commonly recognized than hypometria.

If you suspect that your child may be exhibiting symptoms of any of these conditions, consult your child's medical professional and alert them to the possibility that such a condition may be related to galactosemia. Treatment for these conditions include various types of physical therapy and/or medications.

Primary Ovarian Insufficiency (POI)
A majority of girls/women who have classic galactosemia experience Primary Ovarian Insufficiency. However, there are women with classic galactosemia who have successfully conceived and given birth. To date, the reason for the high rate of ovarian failure is not known. Talk with your child's geneticist to get the latest information about this issue. There are some tests (hormone level testing) which may be performed to check the condition of the ovaries.

(Note: There is no evidence that galactosemia has any negative effect on the reproductive health of boys.)

The Premature Ovarian Failure Support Group
The goal of this group is to offer support and information to women who have been diagnosed with Premature Ovarian Failure.

Ovarian Disorder
Places Women At Risk for Bone Loss: "Premature ovarian failure (formerly known as premature menopause), increases a woman's risk of bone loss, according to a study by researchers at the National Institute of Child Health and Human Development (NICHD)."

Oocyte Donation
The first successful pregnancy using donated eggs was reported in 1984 in Australia. Eggs were taken from a fertile donor, and replaced into the uterus of a woman with ovarian failure, after being fertilized ...

Speech Disorders
It is believed that approximately, 60% of classic galactosemic children have speech problems. Problems range from mild to moderate or severe. One type of speech disorder that has been associated with classic galactosemia is apraxia of speech, often referred to as dyspraxia. Dyspraxia is not a developmental delay of speech. It is considered a "motor speech disorder".

Verbal dyspraxia is defined below:
Verbal Dyspraxia: A sensory motor disorder of articulation characterized by impaired capacity to plan the positioning of speech musculature and muscle movements for the production of speech sounds.

While it is primarily an articulation disorder, there are a number of other related communication problems associated with dyspraxia, such as: problems of syntax (word order), language organization, and pragmatics (set of rules governing conversation). (note-Reading, writing, spelling, and spatial awareness can also be affected.)

If you suspect that your child has this disorder, or some other speech problem, have your child evaluated as soon as possible. The sooner speech therapy is started for a child who needs it, the better. Hearing tests are usually performed first to rule out any kind of hearing impairment. If your child's hearing has been checked, and a hearing problem has been ruled out as a cause for speech problems, have your child evaluated by a qualified speech
You may be able to find a qualified speech pathologist through your local school system (early intervention program.) If you suspect dyspraxia, be sure to find a speech language pathologist who is qualified, and has experience with diagnosing and treating a motor speech disorder (or oral motor function disorder). To find out more about dyspraxia and what things to consider in getting a speech evaluation, the following web sites describes much more in detail.

Speech Disorder Web Links

- Developmental Verbal Apraxia
- Apraxia-Kids (A comprehensive information site about childhood apraxia of speech.)

Physicians Directory
Download Our Physicians Directory PDF

Newly Diagnosed
As a resource for those newly diagnosed with Galactosemia we have an outreach team. Please contact them to learn more about how we can help.