

Galactosemia

An Exploration of the Metabolic Effects, Genetics, Affected Homeostatic Systems, and
the Mechanism of Treatment

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Metabolic Effects of Galactosemia

Galactose (GAL) is a sugar found mainly in milk products as well as many other food products. Galactosemia is a genetic and metabolic disorder that prevents individuals from using GAL in the body in a normal way (Bame, 2001).

In a normal body, GAL is converted into glucose (GLU) by an enzyme. First, the enzyme splits the lactose into GAL and GLU. Once split, GAL is changed into GLU by a different enzyme called *galactose-1-phosphate uridylyl transferase* (GALT) (Bame, 2001).

In a case of galactosemia, the GALT enzyme is missing and GAL can not be broken down and used and GAL products such as *galactitol*, *galactose-1-phosphate* (gal-p-1), and *galactose* build up in the body. The problem lies in the phosphate not being released from GAL, as it has many functions in the body and with galactosemia these functions slow or stop all together.

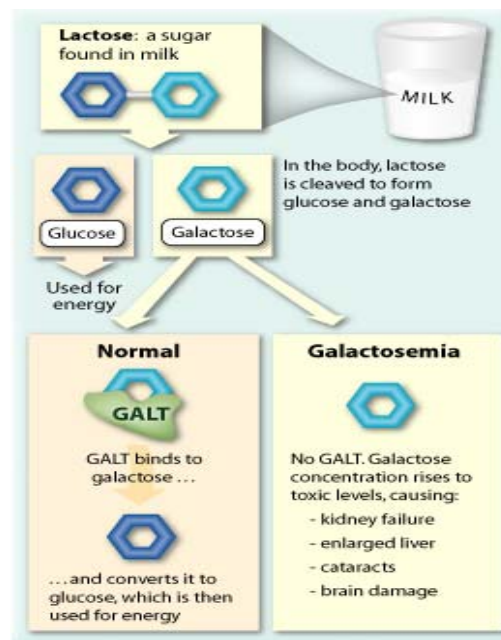


Figure 1: Metabolism of galactose in normal bodies vs. galactosemic bodies

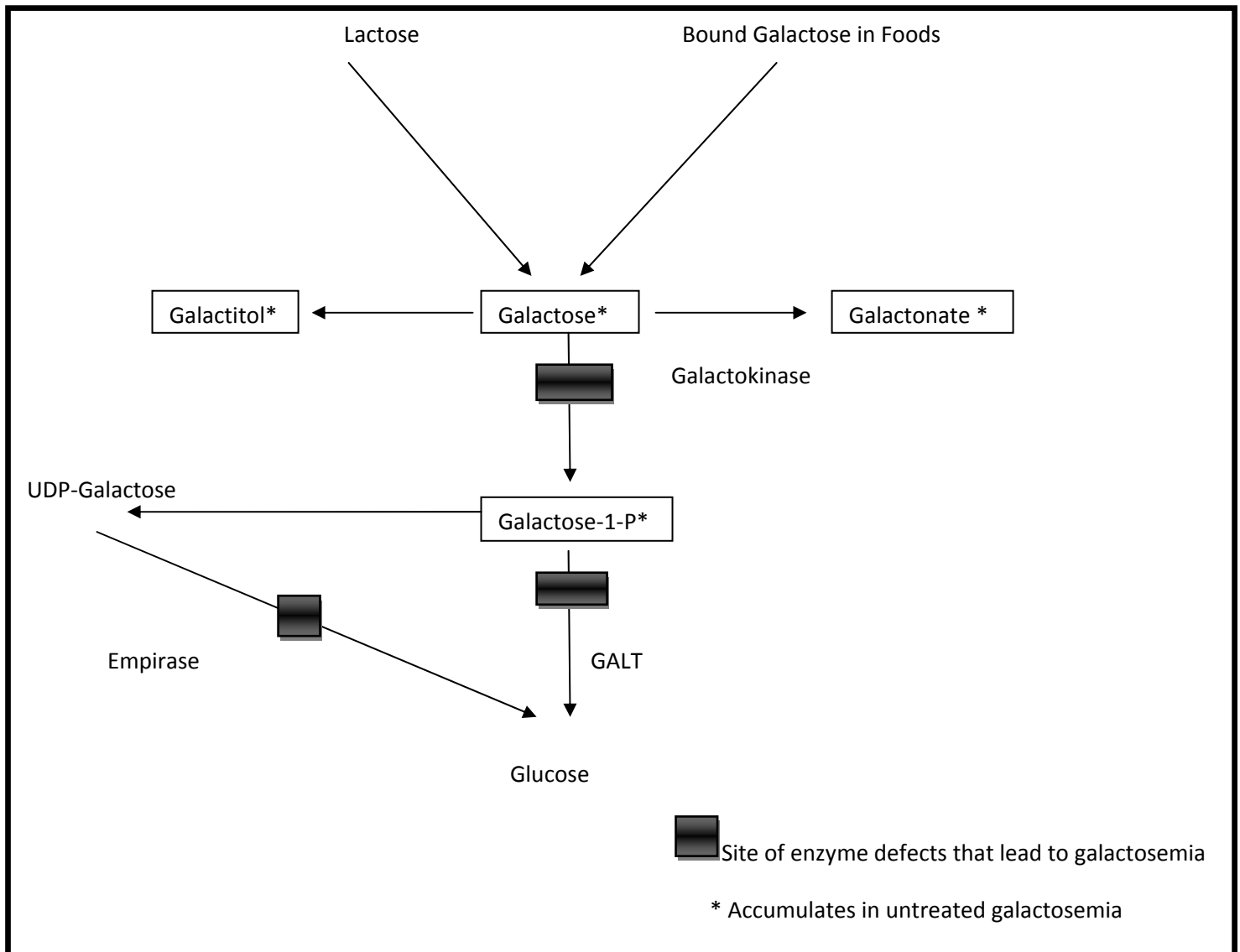
Also, the disorder can be caused by a deficiency of the GALT enzyme which helps in catalyzing the production of uridylylphosphate (UDP)-galactose from galactose-1-phosphate and UDP-glucose. When GALT enzyme activity is deficient, Gal-1-P and galactose accumulate. GAL-1-P competes with the UTP-dependant glucose-1-P to reduce UDP production. The galactose is then converted into galactitol in cells and produces cataracts due to a swelling (Elsas, 2005).

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The situation can be seen as a traffic light. Green light means that the body has normal levels of GALT and GAL will be used normally. With a red light, the body has no GALT, or not enough of it. This prevents GAL from being used properly. Galactitol, GAL, gal-1-P, and galactonate build up in the blood and tissues causing spillage into the urine, and cause the symptoms of galactosemia to appear (Bame, 2001).

There are two types of galactosemia – classic galactosemia (G/G) and Duarte variant galactosemia (D/G). G/G is far more serious and affected individuals only have GALT enzyme activity of approximately 5% and do not have the ability to oxidize galactose to CO₂. D/G individuals have GALT enzyme activity that is between 5% and 20% (Elsas, 2005).

Figure 2: galactose metabolism (Bame, 2001).



Genetic Transmission:

In each person's body, there are two copies of each gene. Galactosemia is inherited in a recessive trait, meaning that affected individuals must have two copies of a mutated gene. If only one mutated gene is inherited, the person is considered a carrier and will most likely never know that they have the mutation without a genetic test.

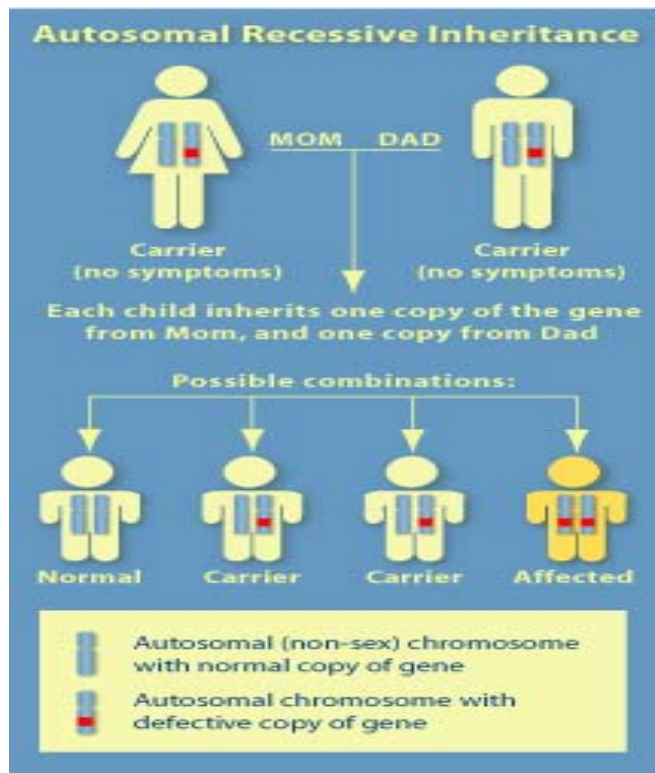


Figure 3: Autosomal Recessive Inheritance

In galactosemia, both copies of the gene coding for one of the enzymes that is required to convert galactose into glucose does not work and the pathway becomes blocked. But, with a carrier, that enzyme production can go on normally due to the regular gene compensating for the mutated one.

If two carriers with the same mutated gene have children, there is a 25% chance that their child will end up with both the mutated genes and develop galactosemia (Health A-Z, 2008).

This mutation is found on the gene that codes for galactose-1-phosphate uridyl transferase (GALT) is located on chromosome 9 (The Adult Metabolic Transition Project 2008). There are many known mutations of this gene, but the most common one is "Q188R." This is the mutation that causes galactosemia. A milder form of galactosemia known as the "Duarte variant" is also caused by a mutation within the GALT gene. It is the

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changes to the GALT gene that cause different levels of enzyme production and function. In galactosemia, the GALT gene's mutation often times leads to the enzymes not working at all (The Adult Metabolic Transition Project, 2008).

Each parent with a galactosemic child has one normal (□) and one altered galactosemia (■) gene. Each of their four children will have one of the following sets of genes (Bame, 2001):

Gene set A: (□□). This body will make enough enzyme to use GALT normally. This will be passed onto any children created from this body.

Gene set B: (□■) or Gene set C: (■□). These bodies will make enough GALT to use GAL normally, but may pass on the galactosemia gene on to any children she has. A person with this gene set is called a *carrier*. Being a carrier does not affect one's health at all. Any parents with a galactosemic child are carriers, as their other children may also be.

Gene Set D: (■■). This person will have galactosemia as they have received one altered gene from each of their parents (one from mother, one from father). The body will not be able to use the GAL in food. The galactosemia gene will also be passed onto any offspring from this person (Bame, 2001).

