

TN Newborn Screening Newsletter

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Galactosemia

By Dr. Jewell C. Ward

What exactly is galactosemia?

Galactosemia (elevated galactose in the blood) describes several inherited conditions that affect the body's ability to handle the sugar, *galactose*. Galactose is formed from the breakdown of the milk sugar, *lactose*; it is also found in many other foods. There are three inherited conditions that may result in elevation of galactose in the blood due to defects in the metabolism of galactose. These include: *classical* and Duarte variant galactosemia (due to transferase enzyme deficiency), galactokinase deficiency, and galactose epimerase deficiency. The transferase enzyme deficiency resulting in classical galactosemia is the defect targeted by newborn screening programs. The body

cannot metabolize the second step (*galactose-1-phosphate*, gal-1-P) in the further breakdown of galactose, regardless of source. The block exists because the enzyme that metabolizes this step (GALT, transferase, Gal-1-PUT are all names used) has decreased activity. Therefore when a baby with classical galactosemia takes breast milk or regular formula, gal-1-P and galactose increase in the blood, and may cause problems in the liver, eye, brain and can lead to severe infection, unless treated promptly.

Milder variants of this enzyme deficiency exist, such as the Duarte variant (D/g) and are more common than the classical type. These are detected by newborn screening as well. The other two types of galactosemia listed above are also detectable by newborn screening (Continued on page 4)

Effects of Heat on Newborn Screening Specimens

By Christine D. McKeever

As we transition from the cooler months into warmer weather, we want to advise you that heat and humidity can have negative impact on newborn screening specimens so much so that results can be affected. Heat can cause the blood specimen to firmly adhere to the filter paper to the extent that it becomes difficult to dissolve the blood for testing. Heat and humidity can also degrade substances or enzymes within the specimen such as Biotinidase or GALT. As a result test values can be reported abnormally.

As a reminder, once specimens are collected, air dry at least 3 hours. Do not expose specimens to direct sunlight or any heat source in an effort to speed drying. Please mail specimens within 24 hours of collection. Do not put specimens to be mailed into a metal mail receptacle as temperatures in these mailboxes are extremely hot. Also do not leave specimens in a hot car prior to delivery at the Post office.

Little control to heat or humidity exposure can be exercised once the specimen leaves your care. However each facility can examine protocols and implement practices to prevent heat and humidity exposure within your facility. Doing so may prevent false results and the need for recollection.



Filter Paper Demographic Assistance

When completing demographic information on the filter paper, please remember to complete the following information: first specimen or repeat, birth date and time, specimen collection date and time, **all information in section, “Status of infant at time of collection”** and other blank areas where information is to be checked or written in. *Appropriate demographic information in conjunction with lab values is needed for appropriate clinical decisions.* **Notices of incomplete information will be sent if birth date and time or collection date and time are omitted.**

Voice Response System Tidbit

When a specimen has been received and results are not complete for reporting, there is a chance that the voice response system will not provide any information. Please ask staff for assistance to confirm specimen has been received.

Tentative State Holiday Schedule

April 6th – Good Friday
May 28th – Memorial Day
July 4th - Independence Day
September 3rd - Labor Day
November 22nd - Thanksgiving
December 25th - Christmas

What do the Newborn Screening nurses do?

By Mitzi Lamberth

This question has been asked numerous times so I thought I would take this opportunity to answer that question. The main part of the job consists of calling all abnormal results to the PCP, Health Departments as well as to the Genetics, Endocrinology or Hematology Centers. There are three nurses who contact the healthcare provider for the infant and give recommendations for what action needs to be taken next, such as repeat filter paper, change diet or other information. The nurses continue to follow-up on these infants with abnormal results to ensure that the necessary follow-up has been done. We will follow these infants until a disposition is made. We also follow-up on all of the specimens that are unsatisfactory and specimens collected at less than 24 hours of age. The information that the nurses call to the healthcare provider has been established in conjunction with the Genetic Centers, Endocrinologists and Hematologists across the state. Most of our time is spent on the telephone with healthcare providers across the state. Letters are sent out daily to the parents and the PCP's regarding a need for repeat testing. Therefore, we receive a large number of calls from the parents regarding the results on their infant.

The nurses also send out quarterly reports to all hospitals across the state. These reports provide the hospitals with the number of specimens collected and the unsatisfactory specimen rate for the hospital. We contact the health departments across the state to assist

when an infant has not been located in a timely manner, to get the additional testing.

Now that we are testing for over 40 analytes which are related to over 60 diseases, there is a much greater volume of abnormal results that must be followed. We were receiving so many calls for newborn screening results that we added the Voice Response System (VRS) so that healthcare providers could access the results without having to call the nurses. VRS will also fax the results to the PCP. Anyone who has not signed up for the Voice Response System is encouraged to do so. Just fax your name and phone number to 615-262-6458 and we will be in contact with you to get you signed on to the system. We have found this to be incredibly helpful.

There are many other responsibilities for the nurses but by far the most important is getting the abnormal results called so that the infant can received the necessary follow-up and treatment. Our goal is to prevent death and decrease negative outcomes for infants with certain types of diseases.



Galactosemia con't

How serious is this condition?

Classical galactosemia(g/g), Type II can be lethal if not recognized early by Newborn Screening and/or clinical symptoms. Typically an infant may develop poor feeding, vomiting, jaundice, lethargy and bleeding. Hypoglycemia and a blood infection (E. coli) may cause shock and can develop within the first weeks of life and can be fatal if untreated. Cataracts (clouding of the lens) may be detected early if not treated in about 10% of cases. Type II occurs in about 1/50,000 births in the US.

Variant galactosemia forms of Type II are more frequent than classical galactosemia. The most common is the Duarte variant (D/g). Generally there are no clinical symptoms in the neonate of this type. Detection and treatment is usually recommended as a precautionary measure.

Two other genetic conditions include: rare galactokinase deficiency, galactosemia type I, which results in increased total galactose due to a block in the first step in metabolism of galactose, usually leading to cataract formation if not treated; and a galactose epimerase deficiency, galactosemia type III, leading to variable metabolism of UDP-galactose.

How is newborn screening for galactosemia affected by the infant's diet?

Breast milk is the recommended diet for all infants. Breast milk contains lactose. Proprietary formulas contain lactose

(unless labeled 'lacto-free'). Soy based and many other non-lactose formulas contain other types of sugar as energy sources.

Newborn screening in TN (and many other states) presume the infant has had exposure to lactose, and screen, *total galactose* (detects multiple forms of galactose, including gal-1-P and galactose). If an infant has a problem handling gal-1-P, the screen would detect this if the child has had *lactose in the diet prior to screening*. As a precaution, the state Newborn Screening Program screens the enzyme deficiency in classical galactosemia (GALT) on all infants with modest elevations of total galactose, thereby reducing the chance that a truly affected child will be missed because of diet differences. However for standard detection, lactose feeding is recommended prior to the newborn screen, and certainly by breast when possible. If indicated by the primary care provider, dietary source can be changed after newborn screening is performed.

Certain infants (such as premature and sick infants on IV nutrition and not on full feeds) can be screened, upon request, to have the enzyme test ('transferase') done in addition to the standard newborn screening for total galactose. There is a 'check-off' box on each newborn screening card. Since the total galactose and transferase are red-blood cell based tests, transfusion may affect these results.

Some state newborn screening programs rely on the enzyme test as the first screening test, but there are problems with that screening, particularly in the states with warmer climates.

What happens when an elevation of total galactose is found?

The state Newborn Screening Follow-up professionals and the state Genetics Advisory Committee determine what levels of total galactose require immediate notification. The Genetic Metabolic Centers (Memphis, Nashville, Knoxville) are on call 24/7/365 to be notified by the state immediately in the event of a 'critically abnormal' value. In addition, the primary care provider (if known) is notified. The Genetic metabolic specialist and the primary care provider then work together to get the child evaluated and further confirmatory testing and treatment begun as soon as possible. This may include hospital admission for immediate evaluation and treatment because of the serious implications in classical galactosemia.

Other elevations of total galactose not requiring immediate evaluation of the child may be seen for confirmatory testing or repeat newborn screening prior to changing the diet to a non-lactose formula while awaiting results.

If an infant is found to have classical galactosemia, or a variant that requires monitoring, who helps coordinate the diet?

The three Genetic Metabolic Centers listed above are notified of the elevations by the state and will have been involved or already have seen the infant prior to confirmatory testing. Each center has metabolic nutrition services in addition to the geneticist/specialists that are required for the periodic monitoring and guidance in the dietary restrictions for treatment in forms of galactosemia. Typically more frequent monitoring by

the centers (clinic visits with the geneticist/nutritionist/lab monitoring) occurs in infancy, and less frequent monitoring at later ages. All visits and recommendations are communicated to the primary care provider, and the clinic is available to the provider for continuing questions throughout the care. The primary care provider monitors the other health care needs of the infant/child.

Genetic counseling of the parents and extended family members is available at these centers and is part of the ongoing care for the condition.

Are there other conditions that can cause total galactose to elevate in the infant?

Yes, there are other conditions that may cause elevations. Prematurity (enzyme levels not at mature levels), liver dysfunction of other origin such as obstructive biliary disease, infections, and some metabolic storage disorders may result in secondary galactosemia.

Is classical galactosemia inherited and if so, what are the chances of it happening again in future pregnancies?

Galactosemia due to problems in the GALT gene is inherited in an autosomal recessive manner. Autosomal means the condition can occur in either males or females. Recessive means that the infant must have inherited two(2) faulty versions of the GALT gene: one from the mother and one from the father. When a child is diagnosed, the biologic parents are therefore carriers of a GALT gene mutant version. The biologic parents have a 1 in 4 or 25% chance of

having another child with a similar type of galactosemia with each pregnancy. If another pregnancy is anticipated further genetic counseling to discuss reproductive choices is recommended. The other genetic forms of galactosemia are inherited in the same manner.

What is the outcome of infants treated with classical galactosemia?

Generally most patients detected by prompt newborn screening do well, and avoid the severe consequences described above if metabolic and dietary surveillance is followed. However, in treated patients learning disabilities and speech articulation problems occur, as do ovarian problems in females.

Resources:

- GeneReviews (www.genetests.org) and search on *Galactosemia*

This site has consumer support group information under “Resources” section

- American College of Medical Genetics – ACT sheets – (www.acmg.net/resources/policies/ACT/condition-analyte-links.htm)

- Tennessee Newborn Screening web site (www2.state.tn.us/health/womenshealth/NBS/Professionals.htm#Summaries) for Guide for Providers, condition summaries, etc.

NBS Educational CD

The CD is in its final preparation stages. When complete, it will serve as a valuable resource for all steps of collecting and forwarding NBS samples. It will also have answers to frequently asked questions. Release date TBA.

NBS Demographic Tidbit

Did you know that inaccurate date of birth and collection information can alter the results of the newborn screening test results? Since specimen are to be collected after 24 hours of birth, test results are based on that standard. Remember that birth date and time as well as collection date and time are important. Please help us to “Get it Right the First Time.”

Newborn Hearing

Newborn Hearing is an intricate sector of the Newborn Screening Department. It is our valuable resource to screen newborn hearing acuity and to assist with meeting the hearing needs of newborns. Their office is located in the state lab with the newborn screening office. Their staff includes a Registered Nurse, an administrative service assistant and a clerk. Please remember to include the staff as one of newborn resources. If you have questions or needs concerning hearing services please call (615) 262-6160.



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