



Carol Collett, Susan Wilkins and Dr. William Russell

What is Congenital Hypothyroidism?

By William E. Russell, MD and Bradley VanSickle, MD, PhD

Congenital Hypothyroidism (CH) is a group of disorders that result in deficient thyroid hormone production beginning before birth. It occurs in roughly 1 in 3500 births. The most common cause of CH is complete absence of the thyroid gland (thyroid agenesis) due to failed development *in utero*. It can also be caused by poorly functioning thyroid tissue, often misplaced at an ectopic site such as at the base of the tongue (thyroid dysgenesis); by enzyme defects resulting in impaired thyroid hormone production (thyroid hormone synthetic defects); by abnormalities of the TSH (thyroid-stimulating hormone) receptor making the thyroid insensitive to TSH regulation (TSH resistance); and by iodine deficiency. These conditions result in deficient function of the thyroid gland itself, and are termed *primary* hypothyroidism. In *secondary* forms of hypothyroidism, the thyroid gland is normal, but there is a defect in the thyroid regulating hormones from the hypothalamus or the pituitary gland.

These conditions are less common than primary hypothyroidism and can be accompanied by other pituitary hormone deficiencies (such as growth hormone deficiency, diabetes insipidus, or deficient cortisol regulation) or by brain abnormalities. Maternal thyroid disease that generates antithyroid antibodies (such as Hashimoto thyroiditis), use of antithyroid medications (PTU or methimazole) for maternal hyperthyroidism, and excessive iodine exposure (contrast agents for imaging studies, cough medicine or medications) are additional causes of hypothyroidism in newborn, albeit only transiently.

Why screen for Congenital Hypothyroidism?

Babies with CH who are not treated promptly exhibit poor growth, prolonged jaundice, coarse facial features, deafness, delayed skeletal maturation, neurological abnormalities, deafness and, most importantly, severe mental retardation because early brain development requires thyroid hormones (thyroxine, or T4, and triiodothyronine, or T3). The main reason for identifying these infants at birth is that if left untreated, CH results in irreversible mental retardation. The intellectual deficiency of late-diagnosed CH has been estimated to be 5 IQ points per month delay in treatment. Newborn screening for CH is done because affected newborns rarely show clinical features until later in the first year of life. Prompt diagnosis and treatment prevents mental retardation and the other (Continued on page 4)

First Newsletter Birthday

Celebrate the first year birthday of the newsletter with the Newborn Screening Staff! We are overjoyed that first year information served as valuable resources for pediatrician offices, health departments and hospitals. We are also excited that we were able to utilize the expertise of the GAC. We look forward to another exciting year. Happy Reading!

Abnormal Lab Follow-up

Once the lab identifies an abnormal value on any of the newborn screening tests, the information is brought to newborn screening nurses for follow-up. Recommendations for follow-up are called to the provider listed in the demographic section of the filter paper (which was completed when specimen was obtained). *We take follow-up seriously.* If abnormal labs are called to your facility and you are not the provider seeing the baby, we ask that you notify our office immediately in order for us to provide follow-up continuity.

Sickle Cell Awareness

September is Sickle Cell Awareness Month. Hemoglobinopathies is one of the categories screened for in the newborn screen panel. Remember to mark your calendar!

Warmer Weather is Approaching!

Please remember to place filter paper cards inside the post office for delivery and not outside in the post office receptacle. Heat has the potential to affect results.

NBS Video

Please be watching for the soon distribution of the NBS CD which is replacing the training video.

Farewell!

NBS bids farewell and sends many thanks to the following individuals for their dedication and contribution to NBS:

Natavut Punyasavatsut, MD who served as our endocrinologist for the upper east tertiary center at ETSU Physicians and Associates- Pediatrics.

Teresa Blake, Genetic Counselor at UT Knoxville Genetics

Melanie Rickman, RN, MSN, Case Manager at St. Jude Hematology.

Newborn Screen Refusals

When parents refuse to have newborn screens obtained on their infants there is a form to be completed by the staff member and signed by the parent. Once completed in its entirety, the form is to be notarized. The form can be found at: <http://www2.state.tn.us/health/Lab/index.htm>

When To vs. When Not To

Nurses and health care staff are often faced with individual circumstances surrounding each baby that leads to the question: "When should I do the newborn screen?" These circumstances sometimes include feed status, baby transferring from the facility to another, transfusions as well as others. In best circumstances, the specimen is collected after 24 hrs, regardless of the feed status. If baby is being transferred out, condition changes, is to be transfused or have surgery, please collect the specimen prior to (even if it is less than 24 hours). The NBS specimen is our only indicator of knowing that a baby exists. If recollection is needed, the current provider will be notified.



Karla J. Matteson, PhD

Primum Non Nocere (First, do no harm)

By Karla J. Matteson, PhD and Dr. Ilse Anderson

Using the proper collection method to obtain newborn screening samples is crucial. Improperly collected specimens may cause false positive or false negative results. Either situation is problematic. False positive results lead to repeat screening/diagnostic testing, cause unnecessary stress on families, add work to an already overburdened state follow-up system and strain economic resources. False negative results are of utmost concern as a child with a treatable inborn error of metabolism may go undetected, leading to morbidity and possible mortality.

Proper technique (as described in the written and video versions of “Let’s Do It Right the First Time”) results in the collection of free flowing non-lysed whole blood. The “normal” range of each analyte for TN infants tested at the Tennessee state laboratory is based on the use of specimens collected, on average, the correct way. When a specimen is collected improperly, i.e.; from a line containing TPN, or by dropping blood collected in anticoagulant, the resulting blood spot does not contain the same volume of blood (red cells and serum) as a correctly collected specimen.

Blood spots created from blood collected in anticoagulants are diluted by the

anticoagulant, have an altered pH, and react with the collection paper in a different way than untreated blood. In addition, these specimens tend to be over saturated as “one drop” from a syringe or needle is not the same as “one drop” from a heel stick. Thus, the amount of serum actually impregnating the filter paper, and the chemical characteristics of that serum may differ from that of a free flowing sample.

Blood spot specimens produced from blood collected from a line or port will be contaminated with solutions used to flush the equipment and possibly by the pharmaceutical or nutritional solutions that are being infused through the equipment. Thus, there may be elevated amino acid results from TPN contamination, or inhibition or competition by pharmaceutical molecules. In addition, such blood spots tend to be over saturated as the blood is usually collected in another tube and transferred to the collection paper.

Using blood specimens collected for other purposes or through alternative routes, as the source for the newborn screening card preparation is undoubtedly convenient for the health care provider. However, the medical consequences of this convenience are first, the possibility of false positive results requiring a second or third test to clear up the abnormal results generated by such incorrectly collected specimens, or second and more concerning, false negative results leading to a child with delayed diagnosis and possible irreversible damage. ♦



Congenital Hypothyroidism continued

Physical changes. Neonatal screening represents one of the most successful public health initiatives of the last century as early detection and treatment of infants has eliminated CH (previously called cretinism) as a leading cause of mental retardation and institutionalization.

What test is used to screen for Congenital Hypothyroidism?

In Tennessee, a “primary TSH screening” approach is used. The only measurement made on the infant’s blood spot is of TSH. A major confounding factor in primary TSH screening is the normal surge in TSH that occurs at birth. For the first 3-6 hours of life, TSH levels dramatically rise and then decrease. Blood spot samples obtained before 24 hours of age may show TSH levels above the established cut-off values and subject the infant to potentially unnecessary repeat testing. Therefore it is important that blood spot samples are obtained after 24 hours of life for appropriate interpretation of TSH levels.

With primary TSH screening, it is important to note that many infants with secondary hypothyroidism may not be identified, as TSH levels are not usually elevated above established cut-off values. **It is essential that any infant who manifests symptoms of hypothyroidism be re-tested by the primary care physician, regardless of the newborn screening results.** These symptoms include: gestation > 42 weeks, large fontanel, especially the presence of a posterior fontanel > 1 cm², hypothermia, cold extremities, prolonged jaundice, poor feeding,

lethargy, hoarse cry, hypotonia, constipation or umbilical hernia. While children with primary hypothyroidism have an elevated TSH, children with secondary hypothyroidism can have a normal, low, or minimally elevated TSH, but, invariably, a low free T4. Additional clinical findings in children with secondary hypothyroidism include midline brain and facial abnormalities, including optic nerve hypoplasia.

What happens when a baby with an elevated TSH is identified?

When the TSH exceeds the cut-off values, the primary care provider is contacted by the Newborn Screening Program to initiate follow-up studies. These may include: a) repeat filter paper testing for intermediate TSH elevations, or b) confirmatory serum studies (TSH, T4, or free T4) when TSH elevations are above the critical cut-off value. It is important to note that cut-off values for TSH by filter paper blood spot methodology are different from the normal range established for serum samples. Also, normal TSH and thyroxine (T4) values are higher in the first week of life compared to adults and older children. Other blood measurements or diagnostic studies may also be warranted. These include tests of pituitary and adrenal function, imaging studies such as thyroid ultrasounds, radioiodine or technetium scans to locate ectopic thyroid tissue, or X-rays of the knee or ankle to establish the skeletal maturity. **It is the goal of the Newborn Screening Program to identify and begin treatment of all children with congenital hypothyroidism within the first 10 days of life.** It is critical that follow-up information regarding the results of testing and treatment be reported to the TN Department of Health

promptly on the case report form provided with the initial notification. A network of pediatric endocrinologists has been established in each region of the state to assist in evaluation and treatment of infants with positive screening results.

How is an infant with CH treated?

The goal of treatment is to reduce the TSH to normal, and to bring the total or free T4 concentration in the blood to the upper quartile of the normal range for age as rapidly as possible. Levothyroxine is prescribed at a dose of 10-15 mcg/kg given as a single daily dose from a crushed tablet. Liquid suspensions of l-thyroxine have unpredictable bioavailability and stability, and should not be used. Infants with CH are followed very closely for the first 2 years of life with frequent blood testing of TSH and free T4 levels and office visits to monitor growth and development. The frequency of lab testing and office visits decreases during the late toddler years but continues at least every 6 months until adulthood. When the diagnosis or the cause of the hypothyroidism is in doubt, it is always prudent to begin treatment early and consider discontinuation of treatment and retesting after age 3 years, when the critical influence of thyroid hormones on brain development has passed.

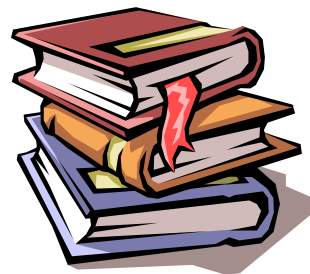
What is the outcome of infants with CH?

With prompt diagnosis, appropriate therapy and monitoring, and parental compliance, the outcomes of CH screening have been overwhelmingly positive, and the long-term developmental and intellectual deficits

of CH largely, if not totally, prevented. However, it should be noted that rarely an infant could be so severely affected before birth that some intellectual deficits may result despite timely diagnosis and treatment. Through early identification of CH by newborn screening programs, more than 1500 infants annually in the US are given the opportunity to lead healthy, normal lives.

The special case of premature infants.

All premature infants should have filter paper samples obtained after 24 hours of life. However, because of immaturity of the hypothalamic-pituitary-thyroid axis, very premature infants with CH may not show an elevation of the TSH for several weeks, and can be missed at initial screening. **The TN Genetic Advisory Committee strongly recommends that all infants with a birth weight of less than 1000 grams have repeat filter paper screening at one month of age, regardless of initial screening results.** Physicians caring for premature infants should maintain a high clinical suspicion for thyroid hormone abnormalities and a low threshold for checking TSH and free T4 levels. ♦



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