Happy New Year! Several changes in the Iowa Neonatal Metabolic Screening Program have occurred within the past year. This issue of the Heel Stick News will focus on congenital hypothyroidism. We are trying to provide both practical and medical information for professionals to use. Please let us know what you think about our newsletter and its content, what you like, what you want to see more of, and what you don’t like in the Heel Stick News.

Family Benefits from Newborn Screening Program

Macy Schanbacher is a lively, cheerful 15 month old girl who loves Cookie Monster and looking at all of the animals on her family’s farm. Her bright demeanor gives no indication that she has congenital hypothyroidism. For Macy, the serious complications of untreated congenital hypothyroidism were avoided because treatment was started soon after the disorder was identified through the Iowa Newborn Metabolic Screen.

Congenital hypothyroidism is the most common disorder detected by newborn screening. In Iowa, approximately ten to fifteen babies are born with congenital hypothyroidism every year. This disorder results from the loss of thyroid function because the thyroid gland did not develop properly, is absent, or is in the wrong location. Because of this, the thyroid gland will not produce enough thyroid hormone. Thyroid hormone is essential for normal body growth and brain development. If the congenital hypothyroidism is not treated soon after birth, profound mental retardation as well as growth retardation, will occur by 2 to 3 months of age.

Infants with congenital hypothyroidism may demonstrate few or no signs of the disorder at birth. This was true for Macy. “I was surprised,” Barb Schanbacher, said of her reaction to learning that her daughter Macy’s newborn screen was abnormal, “but we were also relieved that this was found early, and felt reassured that this is a fixable problem.” Treatment for congenital hypothyroidism consists of taking a daily thyroid hormone supplement. Thyroid hormone replacement will be required for the rest of Macy’s life, but this has easily become part of her daily morning routine. Because of early identification, as well as early and continued treatment, Macy is growing and meeting her developmental milestones just as any other child her age.
The Iowa Neonatal Metabolic Screening Program

Congenital Hypothyroidism

By Marcia Valbracht, MHA

Introduction

This article describes the discovery and early treatments for Congenital, or Primary Hypothyroidism (CH).

What is Congenital Hypothyroidism (CH)?

The term “Congenital” refers to the presence of a condition at birth, whether inherited or caused by the environment.

In normal infants, the endocrine feedback system regulates thyroid hormone secretion. Thyroid hormone is important for the normal functioning of all the body’s organs and is essential in normal brain development. According to a policy statement by the American Academy of Pediatrics (AAP) in their recommended guidelines, “CH represents the most common preventable cause of mental retardation.” It is caused by inadequate production of thyroid hormone. In congenital, also known as primary, hypothyroidism, this may be due to a total or partial failure of the thyroid gland to develop, or its development may occur in an abnormal location.

An infant with an untreated deficiency of thyroid hormone will experience debilitating effects on the central nervous system and the skeleton. By the time clinical symptoms have developed, at approximately three months of age, mental and growth retardation has already occurred. Infants that go untreated into adulthood suffer from deafness, motor defects (muscle spasms and crossed eyes), short stature, and mental retardation (once known as cretinism).

Some of the clinical symptoms in an untreated newborn with hypothyroidism include long lasting neonatal jaundice, constipation, lethargy and poor muscle tone, feeding problems, a large tongue, puffy face, large fontanel (soft spot on baby’s head), distended abdomen, and umbilical hernia. However these symptoms are only found in one-third of babies with CH and may be present in infants without the condition. Symptoms are not a reliable indicator of CH and should never be relied on as a diagnostic tool.

Why do some newborns with CH appear healthy at birth? Data collected in the 1990’s suggests that hypothyroid babies in the womb develop an increase in an enzyme that converts maternal thyroid hormone that crosses the placenta to their own use. The fetus may be able to produce near normal fetal brain triiodothyronine (T3) concentrations if the mother has normal thyroid functions; therefore, the baby is born showing no symptoms of CH. Early detection through newborn screening and proper treatment can reverse any effects of fetal hypothyroidism in all but the most severe cases (babies born to mothers with thyroid problems). (AAP Policy Statement, 1993.)

Early Descriptions

Goiter is an ancient affliction recorded as early as 3000 BC in China. The term originated from the French word, “gutter,” meaning throat. The thyroid gland swells and can be seen as an enlargement on the front of the neck. It occurs as a possible symptom of hypothyroidism.

Hypothyroidism may also have been one of the main causes of a condition referred to as cretinism. One of the earliest references to cretinism was recorded in 1754 in Diderot’s encyclopedia as “an imbecile who was deaf and dumb and had a goiter hanging to the...” continued on page 3
The wide variety of symptoms for cretinism arose because it was a catchall term for many different disorders. A maternal deficiency in iodine or congenital errors in thyroid synthesis resulted in mental retardation and a short, grotesque appearance. For many centuries the Alpine villages of Europe had recognized this condition. In 1810, Napoleon ordered a survey in what is now the Swiss canton of Valais that counted 4,000 cretins among 70,000 inhabitants. In the first half of the 19th century more surveys followed in all of the cantons, which found that deaf-mutism and goiter often were concurrent and used to define cretinism. (Wolff, J., 2001.) Other symptoms of cretinism include severe mental deficiency, squint and motor spasticity of the arms and legs. The symptoms may vary widely within an affected group of people. Sir Robert McCarrison described two forms of cretinism he found in northwestern India during the early 1900’s. One form included the neuromotor defects mentioned earlier; the other, severe hypothyroidism, short stature, delayed bone and sexual growth, puffy features, thickened and dry skin, and hair loss. (Tonglet, R., et al. 1992.)

**Early Treatments**

In the 1800’s it became known that the defective development of the thyroid was involved in mental retardation in infants without thyroid glands. Some early treatments at this time consisted of frying sheep’s thyroid glands and eating them with currant jelly. (Surks, M.I., 1991.) A form of dried animal thyroid gland would also be placed or injected under the skin of thyroid patients. (Murray, G., 1891.)

In 1891, a 46-year-old woman in the UK consented to thyroid extract treatment. Her symptoms improved and she remained in good health until her death at age 74. (Murray, G., 1920.) This same method was used successfully in the US in 1896. A 39-year-old woman began treatment and continued until she died at age 91. (Burgess, A., 1946.)

**Scientific Research and Newborn Screening**

Though beneficial treatment was known as early as the 1930’s, not much was known about the metabolic pathway of hypothyroidism. Treatment was not always begun early enough to ward off mental retardation. As radioactive iodine became more available after World War II, it was used as a research tool that led to important advances in the diagnosis and treatment of hypothyroidism. By 1953, many scientists understood the causes and effects of congenital hypothyroidism in infants, particularly those with goiter. When the thyroid gland is absent or fails to operate, as in primary hypothyroidism, there is a reduction in free thyroxine (T4) and triiodothyronine (T3) to the pituitary gland. This stimulates the increase of thyroid stimulating hormone (TSH), which in turn is trying to increase (without success) the T4 output. Scientists investigated methods to detect and measure these hormones in the blood to diagnose and treat affected individuals.

In 1972, Klein, Meltzer, and Kenny documented that treatment initiated before three months of age leads to an improved prognosis for mental development.

In 1974, pilot studies in Quebec and Pittsburgh paved the way for routine newborn screening in essentially all developed countries of the world. With the availability of increasingly sensitive radioimmunoassay methods for the measurement of thyroxine and thyroid stimulating hormone and the development of methods using filter paper blood spots as a testing medium, mass screening spread throughout North America and Europe. The Iowa newborn screening program began screening Iowa’s newborns for CH in 1980 with a radioimmunoassay that calculated T4 and TSH levels. By 1982, 25 million infants had been screened worldwide. Eastern Europe, South America, Asia and Africa are only now beginning to develop programs to screen for CH.
“The Iowa Neonatal Metabolic Screening Program Congenital Hypothyroidism” continued from page 3

Newer assay techniques such as enzyme linked immunoassay (ELISA), chemiluminescent, and fluorometric assays have a greater sensitivity for thyroid stimulating hormone and have been incorporated into the Iowa newborn screening program.

Whereas a two-tiered test of low T4 and elevated TSH was used in the past, now only an elevated TSH screen is the screen of choice. Foley and Torresani found in 1996 that an increase in thyroid stimulating hormone to levels indicative of primary CH might occur before comparable decreases in the levels of free T4 and free T3.

What happens then?
When a baby’s test results show that he or she may have primary hypothyroidism, the laboratory staff calls the consulting physicians located in the Department of Pediatrics at the University of Iowa Hospital and Clinic. They immediately contact the baby’s physician and coordinate the follow-up testing, diagnosis and treatment. Studies released in 1986 showed that when treatment is initiated within 45 days of birth, the treated infants have normal IQ values (Fisher, 1986.) Babies can be easily treated with synthetic hormones.

Incidence
The incidence of congenital primary hypothyroidism is estimated at 1 in 4,000 live births.

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Info from the Center

Kimberly Piper has accepted the position of State Genetics Coordinator for with the Iowa Department of Public Health, Center for Congenital and Inherited Disorders.

Kim brings considerable experience to this position. As a management employee at one of Iowa’s largest maternity centers, Kim managed a multi-million dollar budget and over 30 FTEs and provided oversight for the hospital-based Maternal Serum Alpha-fetoprotein and Neonatal Metabolic Screening programs. More recently, Kim has been employed with the Iowa Department of Public Health as a Perinatal Health Consultant. In this role, she worked closely with multiple programs within the department that addressed services for children and families. In each of her previous positions, Kim saw first-hand the impact of congenital and inherited disorders on families and will bring that knowledge and understanding to her new position. Kim has also worked with a number of external partners including Iowa maternity hospitals, the March of Dimes Folic Acid Campaign and the Iowa March of Dimes Prematurity Prevention Campaign.

Kim is committed to building on the strengths of Iowa’s current genetics program and shares with you a commitment to making the program even stronger!

Visit our website www.idph.state.ia.us/genetics
Notes from Endocrine

The recommended treatment for congenital hypothyroidism is daily replacement therapy with synthetic thyroid hormone tablets called levothyroxine. Levothyroxine has a narrow therapeutic index and careful dosage titration is necessary to avoid the consequences of over- or under- treatment. For babies and children, these consequences include adverse effects on intellectual and physical growth and development. Last June, the Food and Drug Administration (FDA) approved for the first time the generic form of levothyroxine preparations as equivalent to branded preparations such as Synthroid. In response to the FDA’s decision, the American Association of Clinical Endocrinologists (AACE), The American Thyroid Association (ATA), and The Endocrine Society (TES) issued a joint statement regarding the FDA’s decision to allow generic thyroid substitution. In this statement, the primary concern voiced was that the FDA made this decision without adequate input from the clinical endocrinology community, the recognized experts who care for patients with thyroid disease. For this reason, the AACE, ATA, TES, provide the following recommendations:

Health care practitioners and patients should be aware that the levothyroxine preparation might be switched at the pharmacy. Adverse events may occur before the patient or clinician realizes that a change in thyroid preparation was made.

Patients should request to remain on their current levothyroxine preparation until they have consulted with their healthcare practitioner.

Patients should be aware that if they receive a new levothyroxine preparation, they would need to have their thyroid level retested to determine if they need a dose adjustment.

Cystic Fibrosis Pilot Project
Iowa Neonatal Metabolic Screening Program

The pilot project of newborn screening for Cystic Fibrosis (CF) has been approved by the Iowa Department of Public Health. The project began on November 1, 2004. CF is the most common fatal genetic disease of Caucasians. Delayed diagnosis of CF has been a major impediment to beginning aggressive treatment prior to the development of poor growth and permanent changes in the lung. The average age of diagnosis is greater than 2 years old, and data from Wisconsin indicate that 20 percent of those not diagnosed by neonatal screening were not diagnosed until age 4. Although a specific cure is still wanting, aggressive treatment at specialized cystic fibrosis centers has increased the average survival from less than 10 years when the disease was first identified (40 years ago), to 16 years (25 years ago), to its current mean approaching the mid-thirties. A CF newborn screening program provides the potential for a cost-saving alternative to the traditional method of diagnosing CF only after symptoms are readily apparent.

Estimates of CF identified by newborn screening in Caucasian populations have ranged from about 1 in 2,500 to almost 1 in 4,000. About 1 in 29 will be a carrier of a CF mutation. Identification of most patients with cystic fibrosis will be accomplished prior to the development of pulmonary disease and malnutrition. Early identification allows for early referral to a certified CF Foundation Center where aggressive early intervention will permit normal growth and delay the onset of lung damage from infection and inflammation.
Hello there, this is my first chance to write for the “Heel Stick News” but I feel like I’ve been a part of newborn screening in Iowa forever. Although it’s only been about six months everyone has been very helpful, and I have learned more in this short time than in all my years of training combined! When I was asked to write this article I wasn’t sure what to say. To be honest, I’m still not sure what to say. As you may know, I moved here from Portland, Oregon. I have just finished my training in Metabolic Genetics, so I’m still trying to find my style. I’m stepping into some big shoes as the medical director for the Iowa Metabolic Newborn Screening Program (INMSP) and trying hard to live up to the great reputation Iowa has already established.

That brings me to the point of this article, what do I want and foresee for the future of newborn screening in Iowa? We have the basics down great! The quality of the program and the science is top-notch with built-in room for growth. The March of Dimes recently came out with recommendations for expanded newborn screening (http://www.marchofdimes.com/aboutus/10651_13507.asp) and the American College of Medical Genetics will soon have official recommendations to make to the Secretary of Health about what newborn screening tests should be performed. We already have those covered as we prepare to add cystic fibrosis to our testing. Once again, Iowa is ahead of the curve in the development and implementation of screening technology.

Now, is the time to address some of the infrastructure issues that have arisen with our rapid growth. I want to have all the branches involved in newborn screening and the INMSP talking more to each other. Just like any growing family, we have some fragmentation that needs to be addressed. We need to strengthen communication between branches; such as between program follow-up staff and hospitals. We need to develop additional measurement and quality assurance tools. The educational program also needs to be fleshed out a bit as well. We are building on a very strong foundation so I know that these goals can be accomplished without a problem.

Like any healthy growing program we are in a time of change. The basics are in place and we are ready for the enrichment of all our programs. This will help us keep our sights on what is important, - the babies! No matter how many new tests we add or the number of new physicians added to the roll call, the babies are what this is all about and we need to do our best for them.

Did you know....

~ A filter paper blood specimen shall be collected from the infant at least 24 hours after the infant’s birth, but not later than five days after the infant’s birth.

~ All specimens shall be forwarded by first-class mail or other appropriate means within 24 hours after collection to the University Hygienic Laboratory, the center’s designated central laboratory. (See page 7 for laboratory address information.)

~ A presumptive positive test result shall be reported within 24 hours to the consulting physician, or the physician’s designee, who shall then notify the attending health care provider and the birthing hospital, birth center, or drawing laboratory.

*Taken from 641-4 Iowa Administrative Rules*
The Laboratory Log

The newborn screening lab is on the move! In April 2005 the INMSP laboratory will move to the new state laboratory complex on Ankeny’s Des Moines Area Community College (DMACC) Campus. The four laboratory buildings at DMACC will house the State Hygienic Laboratory, Iowa Division of Criminal Investigation Laboratory, State Medical Examiner’s office, and State Agriculture Laboratory.

Since 1992, Iowa’s newborn screening laboratory (INSMP) has been located at 1521 2nd Avenue in Des Moines. They are looking forward to moving to the new laboratory facilities to rejoin the Des Moines branch of the University Hygienic Laboratory. To ensure a smooth transition, INMSP is planning the move carefully, to decrease the likelihood of delays in sample handling or turn-around times. Submitting facilities will be notified by letter of the final moving date. At that time, we will request that you dispose of all the old envelopes that have our current PO Box (1803) on them, and use ONLY the new envelopes that we will provide.

For mailing specimens via first-class mail, the new mailing address will be:
Iowa Neonatal Metabolic Screening Program (INMSP)
University Hygienic Laboratory
PO Box 249
Ankeny, IA 50021

For overnight delivery (UPS, FEDEX, etc.), the new street address will be:
Iowa Neonatal Metabolic Screening Program (INMSP)
University Hygienic Laboratory
2220 South Ankeny Boulevard
Ankeny, IA 50021

IMPORTANT! Remember, you will be contacted regarding the move date, so please continue to use the current address in Des Moines until you hear from us!

For 1st class mail delivery:
Iowa Neonatal Metabolic Screening Program (INMSP)
PO Box 1803
Des Moines, IA 50319

For overnight delivery:
Iowa Neonatal Metabolic Screening Program (INMSP)
1521 2nd Avenue
Des Moines, IA 50319-1803

Hemoglobinopathy Highlights

The Hemoglobinopathy Program at the Children’s Hospital of Iowa held their annual Hemoglobinopathy Camp in August. The camp is held at the Howard H. Cherry Boy Scout Reservation Camp in Wakonda. This camp is available for children and adolescents age 6 to 17 years old with hemoglobinopathies.

We had 14 kids that participated in activities such as archery, fishing, hiking, swimming, crafts, rock climbing, and BB gun shooting. They also took field trips to the Kernels game and attended a movie at the I-Max Theatre in Cedar Rapids. The Children’s Miracle Network, Dance Marathon, and private donations fund this program.
WIC Works for Healthy Families

The Special Supplemental Nutrition Program for Women, Infants, and Children (commonly known as WIC) is a public health program that can be helpful for many obstetric and pediatric patients even those who don’t qualify for Medicaid. The income guidelines for WIC are much higher than for Medicaid, but anyone who shows a current Medicaid card is automatically income-eligible for WIC.

Over 70 studies have demonstrated WIC’s effectiveness in producing positive prenatal and birth outcomes and improvement in children’s health. WIC provides those who participate with nutrition education, referrals for other community services and checks for specific nutritious foods. Every WIC agency in Iowa employs registered dietitians who assess the nutrition needs of each WIC participant.

WIC promotes breastfeeding as the best way to feed infants. Breastfeeding mothers who receive no infant formula receive more food than other WIC participants.

Infant formula is an option for those who choose not to breastfeed. Currently, Enfamil, Enfamil Lipil, Prosobee, Prosobee Lipil, and Lactofree Lipil are provided routinely by WIC in Iowa because of a cost-containment contract mandated by the USDA. Other formulas, including metabolic formulas can be provided if there is a medical diagnosis and prescription from the health care provider. Medicaid requires families with children under 5 years who require special formulas to apply for WIC.

You can support participation in WIC by:
- Mentioning the benefits of WIC to families
- Displaying posters and brochures in your office
- Providing medical information (height, weight, and hemoglobin or hematocrit) for families to take to WIC appointments.

Call 1(800) 532-1579 for more information.

Congenital Hypothyroidism Resources

The Magic Foundation for Children’s Growth (MAGIC)
1327 North Harlem Avenue
Oak Park, IL 60302
www.magicfoundation.org/
Phone: 1-800-362-4423

American Thyroid Association
www.Thyroid.org
Phone: 703-998-8890

American Academy of Pediatrics’ Policy Statement-Newborn Screening for Congenital Hypothyroidism: Recommended Guidelines (RE9316)
www.aap.org/policy/04407.html