



HEEL STICK NEWS

RAISING AWARENESS OF IOWA NEONATAL METABOLIC SCREENING PROGRAM (INMSP)

July 2005

Issue 6

"We act as though comfort and luxury were the chief requirements of life, when all that we need to make us happy is something to be enthusiastic about."

- Albert Einstein



Applause! Applause!

Ryan's initial newborn screen, collected at three days of age, was presumptive positive for phenylketonuria (PKU). The diagnosis of classic PKU was confirmed and he was started on a phenylalanine-restricted diet at 9 days of age. That was in 1986.

Forward to 2005 – Ryan remains on the phenylalanine restricted diet and has been followed in the Metabolic Management Clinic at the University of Iowa Hospitals and Clinics since the time of diagnosis. He will remain on the PKU diet for life.

Ryan graduated from Clinton High School this May. His cumulative grade point average was above 4.0, and he was in the top five percent of his graduating class. He participated in band, choir, cross country, swimming, track, tennis, Students Against Drunk Driving (SADD), Drug Abuse Resistance Education (DARE), foreign language club, math club, history club and student council.

Ryan has been on the Mayor's Youth Commission for five years and a volunteer counselor at the Muscular Dystrophy Camp for three years. His list of achievements and awards goes on and on. He has received scholarship offers from many prestigious colleges from across the nation. He will be attending Drake University this fall.

Most recently, it was announced that Ryan was one of four winners, nationwide, to receive a Guthrie Scholarship. In memory of Dr. Robert Guthrie, the National PKU News started this higher education scholarship program after his death in 1995. Dr. Guthrie developed the newborn screening test for PKU in 1961 and then worked tirelessly for more than 30 years to establish newborn screening programs in the U.S. and many other countries. Like thousands of others, Ryan was saved from devastating mental retardation caused by untreated PKU. Over the past 17 years, Ryan has followed the phenylalanine-restricted diet without complaint and even during his teenage years, maintained excellent metabolic control. Ryan's future is bright; he is a true Iowa Neonatal Screening Success Story.



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People take different roads seeking fulfillment and happiness. Just because they're not on your road doesn't mean they've gotten lost.

- H. Jackson Brown, Jr.

Cystic Fibrosis Contact:

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Applause! Applause! continued from page 1....

Zachariah (DOB: 11/2000) was the first baby to be diagnosed with medium chain acyl coA dehydrogenase deficiency (MCAD) through the Iowa Neonatal Metabolic Screening Program (INMSP). He was born just a few weeks after the INMSP began a pilot to screen for MCAD deficiency. Without early identification through newborn screening, 30 percent of these babies will die or have significant morbidity secondary to significant hypoglycemia. With early identification, monitoring, education and early medical

care during times of illness, the prognosis is excellent.

Today, Zachariah is a healthy, happy four year old. His growth and development are completely normal and his prognosis is excellent. He also happens to be the poster boy for the INMSP pamphlet (http://www.idph.state.ia.us/genetics/common/pdf/INMSP_brochureBW.pdf). Since Iowa started screening for MCAD deficiency, 11 other newborns have been identified, confirmed and receive follow-up. To date, all are doing just as well as Zachariah.



Newborn Screening for Cystic Fibrosis - Its Time Has Come

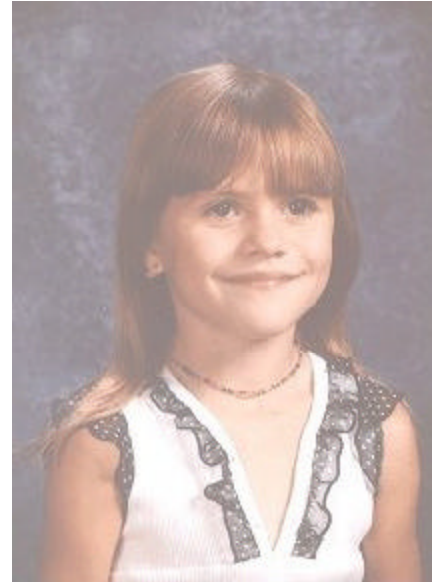
Cystic fibrosis is the most common fatal genetic disorder among Caucasians, with a carrier rate of about one in 25. This results in about one child with cystic fibrosis born among 2,500 births. Iowa is joining nine other states in universal newborn screening for cystic fibrosis. Begun as pilot programs in 1982 in Colorado and 1985 in Wisconsin, population-based screening in those states has been in place since 1987 and 1994, respectively. Data from those initial programs and experience from other countries combined with increasingly aggressive early intervention in the treatment of cystic fibrosis have now convincingly demonstrated the advantages of diagnosing cystic fibrosis at birth without waiting for them to develop the usual symptoms associated with this disease.

Studies from the Wisconsin program, in addition to experience from Australia and the Netherlands, have suggested better growth and weight gain and less lung disease when the diagnosis of cystic fibrosis was made by newborn screening. An analysis on a larger scale recently came from the Cystic Fibrosis Foundation Registry. The outcome of 245 children diagnosed with cystic fibrosis by newborn screening in previous years compared with 819 not identified until the onset of symptoms eventually resulted in appropriate diagnostic testing. Growth and weight gain were substantially greater in those diagnosed by newborn screening and fewer lung infections were seen. Sixty-four percent of those diagnosed following onset of symptoms were hospitalized during the first year of life, whereas only 22 percent of those diagnosed by newborn screening were hospitalized during infancy. With some patients followed for over 10 years beyond initial diagnosis, the advantage for those diagnosed by newborn screening persisted.

What can this mean in Iowa for children with cystic fibrosis and families? Shannon Hildenbrand, mother of Devann Hildenbrand, now seven years old, can tell you what it would have meant to her. Although Devann had a history of chronic cough and poor growth since her first year of life, the diagnosis of cystic fibrosis was not made until she was admitted to the University of Iowa Hospital with respiratory distress at age three. Expressing the frustration of her early experience, Devann's mother comments, *continued on page three...*

Newborn Screening for Cystic Fibrosis continued from page 2....

“Being a new parent, you don’t know what to expect. It was frustrating when no one seemed to know what was wrong with Devann. The news of newborn screening in Iowa means that others won’t be in the position we were of watching a child progressively getting worse with the fear of her dying.” Devann now appears healthy and is thriving, but her lungs are now chronically infected with *Pseudomonas* at an earlier age than would likely have occurred had she been diagnosed by newborn screening. This places her at greater risk for future progressive lung damage.



How will this addition to the Iowa Neonatal Metabolic Screening Program be done?

Using blood from the same card now collected for the other components of newborn screening, immunoreactive trypsinogen will be assayed, and the top five percent of levels will be subjected to DNA analysis, examining for the 25 most common genetic mutations for cystic fibrosis. Infants positive for this two-step procedure will be referred to one of the cystic fibrosis centers serving Iowa residents for the diagnostic measurement of chloride content in sweat. The centers include the University of Iowa Hospital and Clinics at Iowa City and its affiliate program at the McFarland Clinic in Ames, Blank Children’s Hospital in Des Moines, University of Nebraska Medical Center in Omaha, and the Sioux Valley Hospital in Sioux Falls, South Dakota. Since only 15 percent of those positively screened will have cystic fibrosis, with most of the others being asymptomatic carriers, those centers will provide genetic counseling for all families with positive screens. Those determined to have cystic fibrosis will then be advised to be followed at regular three-month intervals at a cystic fibrosis center. Cystic fibrosis centers are certified by the Cystic Fibrosis Foundation using annual evaluations that include regular on-site inspections for adequacy of multidisciplinary health care personnel, quality of care, quality control for diagnostic testing, facilities, teaching of physicians-in-training and research.

Things to Ponder

Can you cry under water?

Why are you IN a movie , but ON TV?

If raising children was going to be easy, it never would have started with something called labor!

Wouldn't it be nice if whenever we messed up our life we could simply press 'Ctrl Alt Delete' and start all over?

Two-tiered Screening Strategy for Cystic Fibrosis

The INMSP laboratory will be using a two-tiered screening strategy for detecting individuals with cystic fibrosis (CF). A measurement of the immunoreactive trypsinogen (IRT) level from the standard dried blood spot specimen will be used as an initial screen test for cystic fibrosis. Specimens with an IRT level in the top five percent will have a DNA mutation test performed on the same dried blood spot to analyze for the 25 most common CF-causing mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene. This strategy is expected to identify 99 percent of the babies affected with cystic fibrosis.

Screening for cystic fibrosis using this two-tiered IRT / DNA approach cannot always distinguish babies who are CF carriers from babies who are affected; therefore, sweat chloride testing by the Cystic Fibrosis Foundation (CFF) approved quantitative pilocarpine

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Two-tiered Screening Strategy continued from page three...

iontophoresis method is recommended for all babies with either one or two identified mutations. In addition, because over 1000 mutations have been identified in the CF gene there is the possibility that a baby could have two rare mutations not included in our 25 mutation panel. Therefore, babies who have an extremely elevated IRT > 170 ng/mL, without identifiable mutations, will also be recommended for sweat chloride testing.

During the pilot study, normal CF screening results will not be reported out by the laboratory. Only those babies with one or two identified mutations or with an IRT > 170ng/mL will be reported to the INMSP CF follow-up coordinator and/or CF consulting physician. The laboratory will not report pilot screening results to the birthing facility or to the attending physician.

All abnormal results will be called to the primary care provider by the CF follow-up coordinator and recommendations regarding sweat chloride testing at a certified CF center to confirm or rule out the diagnosis of CF will be provided. A follow-up letter with the results, recommendations, the contact information for the nearest certified CF center and a letter for the parents describing the results will be faxed to the primary care provider by the CF follow-up coordinator.

The Laboratory Log

2004 INMSP University Hygienic Laboratory Report

| | |
|----------------------------------|--------|
| Total number of infants screened | 39,571 |
| Initial screens | 38,233 |
| Repeat screens | 1,338 |
| Rejected screens | 297 |
| Waived screens | 16 |

Why do we have repeat screens? Repeat screens may be required for a number of reasons. It does NOT mean there is anything wrong with the baby. The reasons for additional specimens include:

- 1) *Unsatisfactory specimens:* There was something wrong with the sample and it needs to be recollected.
- 2) *Early collection:* The sample was drawn before the baby was 24 hours old. A second specimen must be collected as soon as possible to avoid missing a disorder.
- 3) *Abnormal test result:* An abnormal test result means there may be a disorder present. Our follow-up consultants will work with you to determine if further evaluation is needed.

When the first test indicates a possible problem, a new specimen is requested, and the tests are repeated. Due to the potential severity of a particular disorder, the doctor may treat the infant immediately while waiting for the results of a second series of tests. ***If you are asked to retest an infant, please act quickly, as many of these disorders do irreversible damage in a short period of time.***

Iowa Neonatal Metabolic Screening Program (INMSP) Per legislated mandate, the INMSP provides early identification of genetic and metabolic disorders by screening all newborns in the state of Iowa. The program also provides comprehensive follow up, treatment and education to individuals and their families affected with genetic and metabolic conditions in order to avoid adverse health consequences such as mental retardation and death.

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See our laboratory
address updates on
page 8!

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Notes from Endocrine

The endocrine follow up component consists of three physician consultants and one nurse coordinator specializing in pediatric endocrinology at The Children's Hospital of Iowa located at the University of Iowa Hospital. The primary responsibility of the endocrine follow-up staff is to provide consultation and case management for abnormal congenital adrenal hyperplasia (CAH) and congenital hypothyroidism (CH) results identified through the newborn screen. The chart below identifies the year's 2004 endocrine summary report.

| Disorder | Presumptive Positive | Borderline Abnormal | Confirmed |
|--------------------------------------|----------------------|---------------------|---------------------|
| Congenital Adrenal Hyperplasia (CAH) | 6 | 73 | 3 (Salt wasting) |
| Congenital Hypothyroidism (CH) | 13 | 250 | 18 |

Currently, 45 patients with Congenital Adrenal Hyperplasia (CAH) and 80 patients with Congenital Hypothyroidism (CH) are followed in the Pediatric Endocrinology Clinic at the Children's Hospital of Iowa.

**Center for
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Info from the Center

The 2005 legislative session has brought a lot of activity for the Center and the INMSP staff. House File 176 was introduced by Representatives Petersen, Kressig, and Maddox. This bill would require insurance companies to provide coverage for metabolic formula and special medical foods for persons with inborn errors of metabolism with dietary restrictions.

After much work and negotiations by the March of Dimes, the Center and the INMSP staff, the bill passed out of the House Commerce Subcommittee to the House for consideration (as HF765). The insurance company lobby did not favor the bill, and many legislators were hesitant to support an insurance mandate. House Majority Leader Gipp declined to bring the Bill to the House Floor for debate, and the bill died in the funnel deadline.

I guess this is a "bad news-good news" report. Since HF 765 did not come to fruition, Representative Janet Petersen, Representative Ralph Watts and Senator Pat Ward worked to get a state appropriation for the metabolic formula program in House File 882 – the so-called "Christmas Bill" that provides appropriations and policy effective dates for various programs. They were successful in getting an appropriation (state money) of \$160,000 for the metabolic ~~formula program included in the bill.~~ ----Kim Piper, State Genetics Coordinator

For more information on our Special Medical Formula Program access the following website:
http://www.idph.state.ia.us/genetics/practitioner_page.asp.

Visit our website
www.idph.state.ia.us/genetics

Metabolic Matters.....

2004 INMSP Metabolic Report

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One man has enthusiasm for 30 minutes, another for 30 days, but it is the man who has it for 30 years who makes a success of his life.

- Edward B. Butler

| Infant's Diagnosis | Presumptive Positive | Confirmed |
|--|----------------------|-----------|
| Presumptive Positive Galactosemia | 14 | 3 Classic |
| Borderline Galactosemia | 21 | 17 DG |
| Biotinidase Deficiency | 23 | 4 Partial |
| (PKU) Phenylketonuria | 41 | 4 Mild |
| (CTD) Carnitine Transport Defect | 17 | 1 |
| (TPN) Total Parental Nutrition | 64 | |
| (CPT1) Carnitine Palmitoyltransferase Deficiency-Type I | 22 | |
| (MAC) Multiple Acylcarnitines | 12 | 1 (MCAD) |
| Mixed Presumptive Positive | 18 | |
| (PPA) Propionic Acidemia (MMA) Methylmalonic Acidemia | 15 | |
| (IVA) Isovaleric Acidemia (2MBCD) 2-Methylbutyryl-CoA Dehydrogenase Deficiency | 7 | |
| (HMET) Hypermethioninemia/(HCU) Homocystinuria | 26 | 1 |
| (MSUD) Maple Syrup Urine Disease | 16 | |
| (SCAD) Short Chain Acyl-CoA Dehydrogenase Deficiency (IBD) Isobutyryl-CoA Dehydrogenase Deficiency | 4 | 1 |
| (VLCAD) Very-Long-Chain Acyl-CoA Dehydrogenase Deficiency | 7 | |
| (GA1) Glutaric Acidemia Type I | 7 | |
| (TYR) Tyrosinemia | 8 | |
| (3MCC) 3-Methylcrotonyl-CoA Carboxylase Deficiency (3MGH) 3-Methylglutaconyl-CoA Hydratase Deficiency | 10 | 1 |
| (NKH) Nonketotic Hyperglycinemia | 3 | |
| (MCAD) Medium Chain Acyl-CoA Dehydrogenase Deficiency | 13 | 4 |
| (MA) Malonic Aciduria | 3 | |
| (24DR) 2,4 Dienoyl-CoA Reductase Deficiency | 1 | |

Metabolic Follow-up Program practices:

The Central Laboratory calls the follow-up staff to report all abnormal metabolic results. If the results reviewed are related to the expanded panel (MS/MS) newborn screening, Dr. Copeland, the metabolic consultant, is contacted. She reviews the spectra numbers and determines if further testing is recommended. If results are related to biotinidase or galactosemia testing, the confirmatory process is determined by the follow-up procedure protocol.

Follow-up staff will call the submitting physician listed on the newborn screening form to report the results. Follow-up recommendations are given to the physician or nurse. A faxed letter that also includes information on the possible metabolic disorder suspected follows the phone call. The follow-up staff continue to follow-up on the abnormal screen until the abnormal screen is confirmed normal or true disease.

What would you do if ...

the lottery said that you have a 1 in 1,500 chance of winning the jackpot? Would you buy a ticket? One of every 1,500 babies born in the United States will have a disorder that is detectable through newborn screening.

Frequently Asked Questions

If newborn metabolic screening is not done for some reason in the first week of life, is it worthwhile to still screen the baby later?

Yes. While some disorders may begin to be expressed and some damage may have already occurred, treatment begun at any time will always be beneficial to the infant. Additionally, the family should be made aware of the infant's metabolic disorder, its genetic implications, and given appropriate counseling. Ideally, all babies should be screened in the first week of life, but screening a baby later is better than never screening at all.

Is there an age limit for newborn metabolic screening?

Infants can be screened for all disorders up to one year of age. CH and CAH ranges apply to the newborn period, and interpretation of results from specimens collected after the newborn period should be performed in consultation with the appropriate specialist. A specimen received on a child greater than one year of age will not have CH and CAH reported.

What do I do if a baby has moved here from out of state?

Collect another specimen if you don't have documentation that the infant had a newborn metabolic screen prior to the move.

"The biggest mistake people make in life is not making a living at doing what they most enjoy."

- Malcolm S. Forbes

Did You Know...

There are six Hemoglobinopathy Comprehensive Care Outreach Clinics per year located in Davenport, Iowa City, and Waterloo.

Hemoglobinopathy Contact:

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Hemoglobinopathy Highlights

2004 INMSP HEMOGLOBINOPATHY REPORT

Diseases found through newborn screening:

| DIAGNOSIS | CONFIRMED |
|----------------------------|-----------|
| Hgb EE Disease | 1 |
| Hgb SC Disease | 1 |
| Hgb SS Disease | 5 |
| SE heterozygote | 1 |
| Hgb D Beta-Thalassemia | 1 |
| Bart's, possible H Disease | 2 |

Traits found through newborn screening:

| TRAIT | CONFIRMED |
|-------------------|-----------|
| FA + Bart's | 41 |
| FF only | 1 |
| AE Trait + Bart's | 5 |
| AS Trait + Bart's | 2 |
| AC Trait | 58 |
| AD Trait | 11 |
| AE Trait | 51 |
| AS Trait | 182 |
| AV Trait | 51 |

The submitting physician, listed on the INMSP form, will receive a call from follow-up staff for an abnormal hemoglobinopathy **disease**. Follow-up instructions are given to the submitting physician or nurse. The phone call is followed with a letter to the physician with the specific instructions given over the phone. Brochures of the disease are included with the letter for the physician and family.

A hemoglobinopathy **trait** is followed-up with a letter and brochures are mailed to the sub-mitting physician. Family screening and genetic counseling are recommended in this letter. The 800 number for the Regional Genetic Consultation Services is given to the families so they may utilize the services.

At this time, every baby identified through neonatal metabolic screening and confirmed with a hemoglobinopathy disease has begun treatment by their local physician or a hematologist at the Children's Hospital of Iowa in Iowa City or Blank Children's Hospital in Des Moines.

Resource Page

2005 Newborn Screening and Genetic Testing Symposium

The 2005 Newborn Screening and Genetic Testing Symposium will be held at the Hilton Portland and Executive Towers in Portland, Oregon from October 24-27, 2005. It will consist of a keynote session, general sessions, posters and an exhibit hall over the course of 2 1/2 days. The symposium will be preceded by half-day programs on Quality Assurance/Quality Control and Follow-Up and followed by a half-day program on Congenital Adrenal Hyperplasia.

Governor's Conference on Public Health: Building Iowa as a Healthy Community

Mark your calendars for the Governor's Conference on Public Health: Building Iowa as a Healthy Community, also known as Barn Raising V, on July 28 and 29, 2005, at Drake University in Des Moines.

Over the course of the two-day conference, there will be 40 workshops that will cover a variety of topics. The workshops will be divided into four tracks, "New Forces Shaping Healthy Communities," "Telling the Story of Public Health and Tools to Get the Job Done," "Public Health Administrators and Board of Health Members," and "Change Models."

The biennial conference brings together cutting-edge experts from several health care arenas. The purpose is to expand participants' knowledge, introduce new tools and resources and share successful program models through workshops and networking. The registration fee of \$50 covers CEUs, conference materials and meals, and a smoke-free reception. For more information on the Governor's Conference on Public Health: Building Iowa as a Healthy Community go to www.idph.state.ia.us.

New INMSP Laboratory Address

The newborn screening laboratory has moved to its new location within the brand new Iowa Laboratories Facility on the Des Moines Area Community College Campus in Ankeny. The phone number is (515) 725-1630 and the fax number is (515) 725-1650. The address is as follows:

| To mail specimens: | For courier or overnight delivery: |
|--------------------------------|------------------------------------|
| INMSP | INMSP |
| University Hygienic Laboratory | University Hygienic Laboratory |
| P.O. Box 249 | 2220 South Ankeny Blvd. |
| Ankeny, Iowa 50021 | Ankeny, Iowa 50021 |

With the new address, the specimen collection forms have been revised. The new forms are now also asking for mother's phone number to help our follow-up staff in tracking the babies for confirmatory testing. Please contact the INMSP laboratory for new collection forms and envelopes.

"Whatever you are, be a good one"

- Abraham Lincoln.