The early identification of metabolic and congenital disorders is the focus of this newsletter. All babies deserve the chance of a healthy future. The state of Iowa screens infants for metabolic and congenital disorders at least 24 hours after their birth, but not later than five days after the infant’s birth. The most important step in preventing adverse health consequences such as mental retardation, serious illness, and even death can be avoided with a satisfactory or valid newborn metabolic screening specimen. If you have any questions or we can be of any help to you please give us a call (515) 281-3836 or email. We would love to hear from you. Please forward any comments, questions, or suggestions for the “Heel Stick News” to:

Iowa Dept. of Public Health – Center for Genetics
Lucas State Office Building, 5th Floor
321 E. 12th Street
Des Moines, IA 50319-0075
Email: dawn.mouw@idph.state.ia.us

‘Tis the Season to Submit Your Specimens

Due to the increase in mail and packages during the holiday season, we would like you to review your submission process of your INMSP specimens. Here are some helpful hints:

1. Plan ahead for the holidays and weekends. If the holiday falls on a Thursday or Friday and the specimen is not mailed until Monday, there will be a three to four day delay in receiving the specimen for testing.
2. Fed-ex or overnight specimens around the holidays.
3. Mail the specimen from the post office rather than a neighborhood mailbox.
4. Designate a responsible party to mail the specimens and to receive and record the results.
5. Don’t “batch” specimens (waiting for two or more specimens to mail at the same time).

The hours of the Neonatal Metabolic Screening Laboratory at the University Hygienic Laboratory are 8:00 AM to 4:30 PM Monday through Friday and 8:00 AM to 12:00 PM on Saturdays. The lab is staffed on some holidays.

Mail is picked up at the main post office in Des Moines by 8:30 AM. Overnight couriers may deliver specimens to:

University Hygienic Laboratory
1521 2nd Ave.
Des Moines, IA 50314
Quality INMSP Specimens

All procedures in the newborn metabolic screening process reflect a commitment to produce accurate, clinically useful results. No procedure is more important than the first – specimen collection. Every specimen arriving at the neonatal metabolic screening laboratory is evaluated before testing. If an unacceptable specimen is submitted, a request for a new specimen will be made, which causes delays that could have serious medical consequences for an afflicted child.

Last year, specimens for 289 babies were rejected because of poor quality. The second specimen for 34 of these babies were never collected and sent in for testing. Filter paper with correctly collected blood spots contains a calculated amount of blood. The laboratory uses the blood spots to perform quantitative tests. Poor quality specimens will affect the validity of the test.

<table>
<thead>
<tr>
<th>SPECIMEN PROBLEM</th>
<th>POSSIBLE CAUSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantity Insufficient</td>
<td>• Removing the filter paper before blood has completely filled the circle.</td>
</tr>
<tr>
<td></td>
<td>• Using a blood drop that is too small.</td>
</tr>
<tr>
<td>Appears Clotted Or Layered</td>
<td>• Touching same circle to blood more than one time.</td>
</tr>
<tr>
<td></td>
<td>• Filling the circle on both sides of the filter paper.</td>
</tr>
<tr>
<td></td>
<td>• Allowing the blood in a capillary tube to coagulate before applying to filter paper.</td>
</tr>
<tr>
<td>Appears Scratched</td>
<td>• Drawing blood on the paper with a capillary tube.</td>
</tr>
<tr>
<td></td>
<td>• Touching the heel to the filter paper.</td>
</tr>
<tr>
<td>Appears Contaminated</td>
<td>• Filter paper has come into contact with hand, or substances such as alcohol, water, lotion, etc.</td>
</tr>
<tr>
<td>Shows Serum Separation</td>
<td>• Alcohol was not wiped from the puncture site before making the skin puncture.</td>
</tr>
<tr>
<td></td>
<td>• Blood in the capillary tube coagulated before applying it to filter paper.</td>
</tr>
<tr>
<td></td>
<td>• Squeezing around the puncture site.</td>
</tr>
<tr>
<td>Supersaturated</td>
<td>• Applying excess blood to filter paper.</td>
</tr>
<tr>
<td></td>
<td>• Applying blood to both sides of filter paper.</td>
</tr>
<tr>
<td></td>
<td>• Filling the capillary with too much blood before applying.</td>
</tr>
</tbody>
</table>

Did you know...
Ø Date of birth
Ø Time of birth
Ø Date of specimen collection
Ø Time of specimen collection
Ø Transfusion status
Ø Weight of infant at the time of collection

are crucial information for the interpretation of the Iowa Neonatal Metabolic Screening test results?

All of the information on the specimen collection form must be entered and is critical to the interpretation and reporting of the results. The laboratory depends on the information submitted on the specimen collection form. It is very important that the handwriting on the specimen collection form is legible, complete, and accurate. Currently, if our laboratory receives specimen forms with inaccurate or missing information, a fax is sent to the submitting facility requesting additional information. The submitting facility contact person is asked to correct and complete the information and fax it back to the newborn screening laboratory. This often delays the time it takes to get the screening results.

Educational materials are available to assist birthing/submitting facilities with the specimen collection process. The educational materials include a video on specimen collection. Upon request, the Iowa Neonatal Metabolic Screening Program staff can provide an on-site education and training session. Contact the central lab at (515) 243-0141, ext 2.
Why does baby’s weight at the time of specimen collection matter?
* The test interpretation for CAH is weight dependent.
* The weight of a baby at the time of specimen collection is required to calculate the screening result.

Lab Quality Improvement

The following checklist is for your newborn metabolic screening program. It is an opportunity to review the collection and submission of newborn metabolic screening specimens in your laboratory.

How are your newborn screening (NBS) forms monitored?
* Are they stored in a clean dry place in a vertical position?
* Is the supply monitored to assure that the availability of forms is within the expiration date?

Who completes the Newborn Metabolic Screening Forms?
* Does the nursery or lab collect data to ensure ALL fields are completed, legible, and accurate?

Is your facility doing adequate documentation?
* Is there a log in the nursery or lab documenting each newborn’s date and time of birth and blood collection?
* Does your facility use the log to track the specimens until the results are received?
* Does your facility keep the carbon copy of the NBS form, and is it viewed for completeness and legibility?
* Is there someone at your facility to track unsatisfactory specimens?
* Does your facility have a system set up to guarantee that ALL newborns are screened prior to discharge?

Is parent education conducted?
* Is newborn screening education started during the perinatal period?
* Does the nursery or lab give parents the free NBS pamphlet provided by the program?

Are staff who perform heel sticks at your facility properly trained?
* Are they properly trained in the collection procedure on filter paper?
* Are they able to describe a satisfactory specimen?
* Are they able to describe an unsatisfactory specimen?
* Can they list the diseases for which Iowa screens?
* Do you track unsatisfactory specimens back to the individual who collected it and retrain as needed?

Are specimens handled and mailed properly?
* Are specimens dried for at least 3 hours away from heat and sunlight on a horizontal, level, non-absorbent surface, such as drying racks, prior to mailing?
* Are all specimens mailed within 24 hours of collection?
* Are steps taken to avoid subjecting the specimens to heat and humidity prior to mailing?
* Has your facility assigned someone to review each newborn screen prior to mailing to make sure the form is complete, legible and satisfactory?
Steroid Therapy Affects Neonatal Metabolic Screening Results

A patient’s medical condition and/or management can affect a newborn metabolic screening result. A false positive or false negative result must always be considered. The following case study illustrates the importance of interpreting laboratory test results within the context of each patient’s current medical situation.

Case Study
A term, 3300 gram male infant was delivered by C-section due to cephalopelvic disproportion. The pregnancy was without complications. Soon after birth, the infant was noted to be hypoglycemic and in respiratory distress. Physical examination revealed a hypospadias and associated chordee. Further urologic evaluation was postponed at this time due to the critical nature of his respiratory status. The infant’s respiratory function continued to deteriorate, which necessitated transfer to a facility with a Level 2 nursery. He was ventilated and received vasoressors and steroids for hypotension. The infant developed a course consistent with persistent fetal circulation and was then transferred to a facility with a Level 3 nursery on day of life 3. The initial newborn metabolic screen was collected at this time and was normal. As infant recovered from persistent fetal circulation, ventilatory support was weaned and a course of decadron was administered to decrease the swelling of the airways. At 13 days of life, a urologic evaluation determined that the apparent hypospadias was actually ambiguous genitalia. Diagnostic testing, including chromosome studies were performed and indicated that the infant was a female with virilized genitalia due to congenital adrenal hyperplasia. The infant's serum 17 hydroxyprogesterone became markedly elevated 48 hours after steroid therapy ended.

What is Congenital Adrenal Hyperplasia?
Congenital adrenal hyperplasia (CAH) is a group of inherited disorders caused by abnormalities in specific enzymes of the adrenal gland. Ninety percent of congenital adrenal hyperplasia cases are caused by the lack of the enzyme 21-hydroxylase. The enzyme deficiency prevents the body from making hormones necessary for the normal functioning of the body. Increased production of a male hormone called androgen can result in ambiguous genitalia and rapid growth and skeletal maturation in childhood. Babies with untreated congenital adrenal hyperplasia may develop vomiting and severe dehydration, which can be life threatening. Treatment requires supplying the body with cortisol and a salt-retaining hormone in amounts that adrenal gland would normally make. Hydrocortisone and Florinef are the medications most often used. Female infants may require surgical correction of ambiguous genitalia. Children with CAH should be followed regularly by a Pediatric Endocrinologist.

The infant described in the case study did not demonstrate electrolyte abnormalities often associated with congenital adrenal hyperplasia. These abnormalities may have been masked due to the administration of corticosteroids, parenteral nutrition, and frequent sodium bicarbonate infusions.

Why was the newborn metabolic screen negative for congenital adrenal hyperplasia?
The laboratory method used to screen newborns for congenital adrenal hyperplasia measures 17 hydroxyprogesterone levels. However, hormone (steroid) therapy administered to the mother during pregnancy, or to the infant immediately after birth, may suppress the 17 hydroxyprogesterone levels. The baby in the case study received several courses of steroids prior to the collection of the newborn screening specimen.
What is the screening practice for infants who have received steroids?
When an infant or his/her mother has received steroids, it should be noted on the newborn metabolic screening collection form. The laboratory will request a second specimen be collected for congenital adrenal hyperplasia. The practitioner should contact a pediatric endocrinology consultant regarding management of these situations and the appropriate time to recollect this specimen.

Other neonatal metabolic screening considerations:
There are a number of items to record on the collection form to ensure the best interpretation of newborn screening results for congenital adrenal hyperplasia: baby’s weight, gestational age, steroid therapy, transfusion, age when specimen was collected, and if infant is sick. The infant’s weight, steroid therapy, prematurity, illness, early collection, transfusion, and blood collection with preservatives can affect the results. Please see the practitioner’s manual section on congenital adrenal hyperplasia for further information on screening practice considerations. The practitioner’s manual is available electronically at www.idph.state.ia.us/genetics. For a hard copy, please contact the Center for Genetics.

Did you know...
three of our newborn metabolic screening tests are red blood cell based. They are:
- Hemoglobinopathy
- Galactosemia
- Biotinidase
Transfusions will interfere with the tests for these disorders. The lab cannot report these test results if the transfusion status is not provided on the collection form. If you know a baby is going to be transfused and is less than 24 hours of age, collect the neonatal metabolic specimen before the transfusion. The tests for these disorders can be reported on babies less than 24 hours of age. Another specimen can be collected from the baby after transfusion for the PKU, Hypothyroidism, and CAH tests.

### Current Billing Codes for Neonatal Metabolic Screening Program

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Lab Methodology</th>
<th>Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>82261</td>
<td>Assay of Biotinidase</td>
<td>Biotinidase Deficiency</td>
</tr>
<tr>
<td>82776</td>
<td>Galactose Transferase Test</td>
<td>Galactosemia</td>
</tr>
<tr>
<td>83020</td>
<td>Hemoglobin Electrophoresis</td>
<td>Hemoglobinopathies</td>
</tr>
<tr>
<td>83789</td>
<td>Tandem Mass Spectrometry, Quantitative</td>
<td>Expanded Screening Disorders</td>
</tr>
<tr>
<td>84144</td>
<td>Assay of Progesterone</td>
<td>Congenital Adrenal Hyperplasia</td>
</tr>
<tr>
<td>84443</td>
<td>Assay of Thyroid Stimulating Hormone</td>
<td>Congenital Hypothyroidism</td>
</tr>
</tbody>
</table>
Can Parents Refuse a Neonatal Metabolic Screen?

Yes, a parent/guardian may refuse a neonatal metabolic screen for their infant. It is the responsibility of the healthcare provider to inform the parent/guardian of the consequences of treatment and nontreatment. If a parent/guardian refuses the screen, it must be documented in writing.

“Iowa Neonatal Metabolic Screening Program Waiver for Newborn Screening Refusal” forms are available. The Iowa Department of Public Health (IDPH) and the University Hygienic Laboratory (UHL) designed a three-ply colored form to aid healthcare providers in obtaining the appropriately signed waiver as legal documentation from parents/guardians who refuse to participate in the neonatal metabolic screening program. The original form should be placed in the infant’s medical record. The yellow copy should be forwarded to the Newborn Screening Laboratory/IDPH, and the pink copy is for the parent/guardian to keep for their records. Copies of the form may be ordered from UHL through the hospital’s contact person.

Iowa Expanded Screening Panel

Tandem mass spectrometry (MS/MS) technology can potentially screen for up to 30 additional disorders simultaneously from a single blood spot specimen. The detectable disorders fall into three categories of inheritable metabolic disorders: amino acid disorders, fatty acid oxidation disorders, and organic acid disorders.

Individuals with amino acid disorders have a deficiency in one of several pathways or cycles involved in protein metabolism. For the amino acid disorders detectable by MS/MS, early treatment allows for the prevention of brain damage, mental retardation, coma, seizures, autistic-like disorders, and even death.

Individuals with fatty acid oxidation disorders are unable to break down fats into energy because of specific enzyme deficiencies essential in the fatty acid metabolic pathway. Normally, fat is broken down into energy by enzymes. This energy keeps the body running whenever it runs out of its main source of energy, glucose. It is crucial that individuals with these disorders avoid prolonged fasting. Prolonged fasting can lead to severe, life threatening hypoglycemia, vomiting, lethargy, coma, cardiopulmonary arrest or sudden unexplained death. It is estimated that 1 to 2 out of 100 “SIDS” cases are the result of an undiagnosed fatty acid oxidation disorder.

The last group of disorders screened by MS/MS are organic acid disorders. These disorders occur because of alterations in pathways of intermediary metabolism for amino acids, carbohydrates, and fatty acids. Newborn detection of the disorders and early treatment allows for prevention of symptoms, which include neonatal hypotonia, respiratory acidosis, muscle atrophy, seizures, developmental delays, and death.

It is estimated that screening for MS/MS detectable disorders will identify three to eight additional newborns each year. Information about the specific disorders screened for by MS/MS can be found in the INMSP practitioner manual and will be downloadable at www.idph.state.ia.us/genetics in the near future.

Routine reporting of disorders detectable by MS/MS began on specimens received on or after August 1, 2003. This process occurs exactly as it has for the other disorders for which INMSP screens. Specimen collection has not changed—nothing different needs to be done. An example of the MS/MS detectable disorder results on the INMSP report can be found at www.idph.state.ia.us/genetics.
Disorders Detectable by MS/MS

The following is a list of the disorders currently detectable by the MS/MS screening:

**Amino Acid disorders:**

(ARG) Argininemia
(ASA) Argininosuccinic Aciduria
(ASS) Citrullinemia or ASA Synthetase Deficiency
(HCU) Homocystinuria or Cystathione Synthetase Deficiency
(HHH) Hyperornithinemia, Hyperammonemia, Homocitrullinuria Syndrome
(HORN) Hyperornithinemia or Ornithine Oxo-Acid Aminotransferase Deficiency
(MSUD) Maple Syrup Urine Disease
(NKH) Non-ketotic Hyperglycinemia

**Fatty Acid Oxidation disorders:**

(24DR) 2,4-Dienoyl-CoA Reductase Deficiency
(CACT) Carnitine/Acylcarnitine Translocase Deficiency
(CPT1) Carnitine Palmitoyltransferase Deficiency-Type I
(CPT2) Carnitine Palmitoyltransferase Deficiency-Type II
(CTD) Carnitine Transport Defect
(GA2) Multiple Acyl-CoA Dehydrogenase Deficiency or Glutaric Acidemia Type II
(LCHAD) Long-chain Hydroxyacyl-CoA Dehydrogenase Deficiency
(MCAD) Medium-chain Acyl-CoA Dehydrogenase Deficiency
(SCAD) Short-chain Acyl-CoA Dehydrogenase Deficiency
(TFP) Trifunctional Protein Deficiency
(VLCAD) Very Long-Chain Acyl-CoA Dehydrogenase Deficiency

**Organic Acid disorders:**

(2MBCD) 2-Methylbutyryl-CoA Dehydrogenase Deficiency
(3MCC) 3-Methylcrotonyl-CoA Carboxylase Deficiency
(3 MGH) 3-Methylglutaconyl-CoA Hydratase Deficiency
(5OP) Glutathione Synthase Deficiency or 5-Oxoprolinuria
(BKT) Mitochondrial Acetoacetyl-CoA Thiolase Deficiency or 3-Ketothiolase Deficiency
(GA1) Glutaric Acidemia
(HMG) 3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency
(IBD) Isobutyryl-CoA Dehydrogenase Deficiency
(IVA) Isovaleric Acidemia
(MCD) Multiple CoA Carboxylase Deficiency
(MMA) Methymalonic Acidemia
(PPA) Propionic Acidemia
(TYR) Tyrosinemia I, II, III

Administrative Rule Changes

The Department of Public Health has submitted rule changes for Chapter 4 Birth Defects Institute. The rules changes provide clarification of Chapter 4 through additional definitions, add tandem mass spectrometry detectable disorders to the newborn metabolic screening panel, and provide surveillance of individuals identified by the newborn metabolic screening of selected neuromuscular disorders.

The revisions were adopted by the Board of Health on September 10, 2003. They are scheduled to be effective November 5, 2003.
Resource Page

This is an opportunity for you to learn about services available in Iowa. The children diagnosed with a metabolic and congenital disorder through newborn metabolic screening will often be eligible for these services. This will be an ongoing opportunity for you to learn about and provide referrals to those services.

**Early ACCESS** is a partnership between families with young children, birth to age three, and providers from the Departments of Education, Public Health, Human Services, and the Child Health Specialty Clinics. The purpose of Early ACCESS is for families and staff to work together in identifying, coordinating and providing needed services and resources to help the family assist their infant or toddler to grow and develop.

With Early ACCESS, the family and providers work together to identify and address specific family concerns and priorities as they relate to the child’s overall growth and development. In addition, broader family needs and concerns can be addressed by locating additional supports and resources in the local community for the family and/or child. All services to the child are provided in the child’s home and community settings where children of the same age without disabilities participate.

**Eligibility and Age Requirements** An infant or toddler under the age of three (birth to age three) who,

- has a condition or disability that is known to have a high probability of later delays if early intervention services were not provided, or
- is already experiencing a 25% delay in one or more areas of growth or development.

**Cost** There are no costs to families for service coordination activities; evaluation/assessment activities to determine eligibility or identify concerns, priorities and resources of the family; and development and reviews of the Individualized Family Service Plan. The service coordinator works with the family to determine costs and payment arrangements of other needed services. Some services may have charges or sliding fee scales or may be provided at no cost to families. Costs are determined by a variety of factors that are individualized to each child and family.

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Save the Dates

**January 21-23, 2004**
NBDPN 2004 Annual Meeting: Advances and Opportunities for Birth Defects Surveillance, Research, and Prevention will be held at the Marriott City Center in Salt Lake City, Utah. Additional information is available at:

**May 3-6, 2004**
The Newborn Screening and Genetic Testing Symposium will be held at the Crowne Plaza Ravinia in Atlanta, Georgia. It will consist of 2 ½ days of sessions, presentations, and exhibits on the latest information on newborn screening and genetic testing. Pre-conference workshops on QA/QC and Follow-up are also planned. Visit the website at www.aphl.org for up-to-the-minute information.

**July 26-28, 2004**
The National Center on Birth Defects and Developmental Disabilities (NCBDDD) conference will be held at the Omni Shoreham Hotel in Washington, DC. Visit this website for additional information as it becomes available.

Here’s the web address: http://www.cdc.gov/ncbddd/default.htm