Newborn Screening:
Because you touch the future everyday

January 2007
Purpose of Newborn Screening

• Program to screen for congenital and heritable disorders
• These disorders may cause severe mental retardation, illness, or death if not treated early in life
• If treated, infants may live relatively normal lives
• Results in savings in medical costs over time
If Untreated, Disorders

• Can result in:
  – Growth problems
  – Developmental delays
  – Behavioral/emotional problems
  – Deafness or blindness
  – Retardation
  – Seizures
  – Coma, sometimes leading to death
NBS Screening

- Identification is a multi-step process
  - Blood specimens from infants are analyzed by the laboratory
  - If a result is abnormal, laboratory staff notifies case management staff
  - Case management provides follow-up to assist linking families with appropriate providers to
    - Confirm the test results and
    - Ensure the infant has the disorder prior to treatment
    - Ensure the infant receives appropriate treatment
Results from Lab

• Normal Screen Results
  – Results are sent to submitter when all test are final

• Abnormal results
  – Results are reported to Case Management as soon as available for that disorder
Abnormal Results for each disorder

• High Panic Codes
  – are reported to RN in NBS Case Management
  – RN will notify MD ASAP. If MD unavailable RN will notify mother

• Low Panic Codes
  – Health Tech will notify MD or facility
  – Mother notified by letter
NORMAL SCREEN

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Screening Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amine Academia</td>
<td>Normal</td>
</tr>
<tr>
<td>Fatty Acid Oxidation Disorders</td>
<td>Normal</td>
</tr>
<tr>
<td>Organic Acidemia</td>
<td>Normal</td>
</tr>
<tr>
<td>Galactosemia</td>
<td>Normal</td>
</tr>
<tr>
<td>Biotinidase Deficiency</td>
<td>Normal</td>
</tr>
<tr>
<td>Endocrine Disorders</td>
<td>Normal</td>
</tr>
<tr>
<td>Hemoglobinopathies</td>
<td>Normal</td>
</tr>
</tbody>
</table>

[Global Message Text - to be editable by DSFS]

ATTENTION: The Texas Department of State Health Services has completed implementation of the expanded screening panel. This is the new mailing format.
Abnormal Specimen

• Case Management will send:
  – Lab results for that disorder
  – ACT sheet specific to that disorder
  – FACT sheet for families
  – List of Metabolic Specialists
CHANDRAMA KHUMCHAROEN - ####
ST. VINCENT'S MEDICAL CENTER
10812 SPRINGHILL JUNCTION
AUSTIN, TX 78756

Newborn Screening Report - ####

Patient Name: First Last
Mother's Name: First Last
Date of Birth: MM/DD/YYYY
Medical Record: XXXXXXXXXXX
Birth Weight: ### grams
Race/Ethnicity: Am. Indian
Sex: Female
Birth Order: x
Feed: Mother's SSN:
Status: [May require up to 3 lines or one long line]
Mother's Address: Street
City, State, Zip
Mother's Phone: (xxx) xxx-xxxx
Physician: JANET McINTYRE-JOHNSON, MD
Physician Phone: (xxx) xxx-xxxx

ABNORMAL SCREEN

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Screening Result</th>
<th>Analyte</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amino Acidemias</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Fatty Acid Oxidation Disorders</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Organic Aciocemias:</td>
<td>Abnormal Result: See Note 1</td>
<td>Elevated</td>
</tr>
<tr>
<td></td>
<td>CSDFC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>C2</td>
<td>Elevated</td>
</tr>
<tr>
<td></td>
<td>All other analyses</td>
<td>Normal</td>
</tr>
<tr>
<td>Galactosemia:</td>
<td>Abnormal Result: See Note 4</td>
<td>GALT</td>
</tr>
<tr>
<td>Biotinidase Deficiency:</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Endocrine Disorders:</td>
<td>Unsatisfactory: See Note 1</td>
<td>CAH - 17 OH progesterone</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>All other analyses</td>
</tr>
<tr>
<td>Hemoglobinopathies:</td>
<td>Normal</td>
<td></td>
</tr>
</tbody>
</table>

Screening Result Notes:
1. (DSHS Abnormal Result Maller Description from library Ex: This result is suggestive of Glutaric Acidemia Type 2. An immediate recollection is necessary to further evaluate this infant.

2. [Global Message Text - To be editable by DSHE]

ATTENTION: The Texas Department of State Health Services has completed implementation of the expanded screening panel. This is the new maller format.

For more information, please refer to http://www.dshs.state.tx.us/newborn
The specimen received was Unsatisfactory for testing Congenital Adrenal Hyperplasia. An immediate recollection is necessary to further evaluate this infant.
Newborn Screening ACT Sheet
[Absent/Reduced biotinidase activity]

Biotinidase Deficiency

**Differential Diagnosis:** Biotinidase deficiency; see C5-OH for non-biotinidase associated conditions.

**Metabolic Description:** Biotinidase deficiency results from defective activity of the biotinidase enzyme. When identified (possibly) through elevated C5-OH, 3-hydroxyisovaleric acid and 3-methylcrotonylglycine are elevated and holocarboxylase synthase deficiency must be considered.

**You Should Take the Following IMMEDIATE Actions:**

1. Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, lethargy, hypotonia).
2. See and evaluate infant.
3. If infant cannot be seen immediately at metabolic specialist, undertake confirmatory testing in consultation with a metabolic specialist.
4. Initial testing: enzyme assay for biotinidase
5. Repeat newborn screen if second screen has not been done.
7. Report findings to newborn screening program.

**Confirmation of Diagnosis:** Enzyme assay for biotinidase reveals low activity. Plasma acylcarnitine analysis may show normal or increased 3-hydroxyisovaleric acid and 3-methylcrotonylglycine. C5-OH acylcarnitine may be high but lack of an abnormal acylcarnitine profile does not rule out biotinidase deficiency.

**Clinical Expectations:** The neonate is usually asymptomatic but episodic hypoglycemia, lethargy, hypotonia, and mild developmental delay can occur at any time from the neonatal period through childhood. Untreated biotinidase deficiency leads to developmental delay, seizures, alopecia, and hearing deficits. Biotin treatment is available and highly effective.

**Reporting:** Report diagnostic result to family and NBS program.

**Additional Information:**

**Gene Tests**

**OMIM**

**Genetics Home Reference**
Medium Chain Acyl-CoA Dehydrogenase Deficiency (MCAD)

What is MCAD?
MCAD is a type of fatty acid oxidation disorder. People with MCAD have problems breaking down fat into energy for the body.

What Causes MCAD?
Enzymes help start chemical reactions in the body. MCAD happens when an enzyme called “medium chain acyl-CoA dehydrogenase” is either missing or not working. This enzyme breaks down certain fats in the food we eat into energy. It also breaks down fat already stored in the body.

What Symptoms or Problems Occur with MCAD?
(Symptoms are something out of the ordinary that a parent notices.)
MCAD can cause hours or days called Metabolic Crises. Children with MCAD often show symptoms for the first time between 3 months and 2 years of age. Some of the first signs of a Metabolic Crisis are:
- too much sleepiness
- behavior changes (such as crying for no reason)
- irritable mood
- poor appetite

If a Metabolic Crisis is not treated, a child with MCAD can develop:
- breathing problems
- seizures
- mental retardation
- cerebral palsy
- coma, sometimes leading to death

What is the Treatment for MCAD?
The following treatments are often used for children with MCAD:

1. Do not go a long time without food – Babies and young children with MCAD need to eat often to avoid low blood sugar or a Metabolic Crisis. They should not go without food for more than 4 to 6 hours. Some babies need to eat even more often. It is important that babies be fed during the night. They need to be woken to eat if they do not wake up on their own. Young children with MCAD may need to have a starchy snack (such as bread, cereal, rice) before bed and another during the night. They may need another snack first thing in the morning. Your dietitian can give you ideas for good night-time snacks. Dietitians know what are the correct foods to eat. Most teens and adults with MCAD can go without food for up to 12 hours without problems when they are well. They need to continue the other treatments for life.

2. Diet – Sometimes a low-fat, high carbohydrate diet (such as vegetables, fruits, grains) is advised. Your dietitian can create a food plan with the right type and amount of fat your child needs. Ask your doctor whether or not your child needs to have any changes in his or her diet.

3. Leucine – Leucine (Carnitine) may be prescribed for some children. This is safe and natural and helps body cells make energy. It also helps the body get rid of harmful wastes.

Things to Remember
Always call your doctor when your child has any of the following:
- poor appetite
- low energy or too much sleepiness
- vomiting
- diarrhea
- an infection
- a fever

People with MCAD need to eat extra starchy foods and drink more fluids during any illness – even if they don’t feel hungry – or they could develop low blood sugar or a Metabolic Crisis. Children who are sick often don’t want to eat. If they won’t or can’t eat, they may need to be treated in the hospital to prevent problems.
Estimated Expansion Statistics

- Approximately 400,000 births a year
- Approximately 800,000 specimens a year collected
- Follow-up on approximately 15,000 abnormal screens a year
- Approximately 600 diagnosed cases per year
Current Legislation & Rules

Requires newborn screening on 27 disorders

- 6 Amino acid disorders including PKU
- 5 Fatty acid oxidation disorders
- 9 Organic acid disorders
- Galactosemia-1-phosphate uridyltransferase deficiency
- Biotinidase deficiency
- 3 Sickling hemoglobinopathies, including sickle cell disease
- 2 Endocrine disorders
Texas babies are mandated to have 2 newborn screens

- The first screen at 24-48 hours or before leaving hospital, whichever is first
- The second screen at 1-2 weeks of age
NICU Babies

First screen must be taken 24-48 hours of life regardless of feeding status or weight
Tandem Mass Spectrometer (MS/MS)

- Molecules are sorted & weighed by mass
- Compounds analyzed are amino acids & acylcarnitines
  - Amino acids: building blocks for proteins
  - Acylcarnitine = Carnitine (vehicle) + fatty acid
    - Identified by size of fatty acid: short, medium, long and designated by initials & numbers
Expanded Newborn Screening

In 2005 HB790 was passed requiring expansion of the newborn screening program using the ACMG (American College of Medical Genetics) recommended panel as funds allowed
Criteria for screened disorders

- Disorder occurs with significant frequency
- Test are inexpensive and reliable
- Effective treatment/intervention exists
- If untreated, baby may die or develop severe retardation
- Affected baby may appear normal at birth
Organic Acid Metabolism Disorders

- IVA - Isovaleric acidemia
- GA I – Glutaric acidemia type I
- HMG – 3-OH 3-CH3 glutaric aciduria
- MCD – Multiple carboxylase deficiency
- MUT – Methylmalonic acidemia (mutase def)
- 3MCC – 3-Methylcrotonyl-CoA carboxylase deficiency
- Cbl A,B – Methylmalonic acidemia
- PROP – Propionic acidemia
- BKT – Beta-ketothiolase deficiency
Fatty Acid Oxidation Disorders

- MCAD – Medium-chain acyl-CoA dehydrogenase deficiency
- VLCAD – Very long-chain acyl-CoA dehydrogenase deficiency
- LCHAD – Long-chain L-3-OH acyl-CoA dehydrogenase deficiency
- TFP – Trifunctional protein deficiency
- CUD – Carnitine uptake defect
Amino Acid Metabolism Disorders

- PKU – Phenylketonuria
- MSUD – Maple syrup urine disease
- HCY – Homocystinuria
- CIT – Citrullinemia
- ASA – Argininosuccinic acidemia
- TYR I – Tyrosinemia type I
Hemoglobinopathies

- **SCA** – Sickle cell anemia
- **Hb S/Th** – Hb S/ Beta-thalassemia
- **Hb S/C** – Hb S/C disease
Others

- HYPOTH – Congenital hypothyroidism
- BIOT – Biotinidase deficiency
- CAH – Congenital adrenal hyperplasia
- GALT – Galactosemia
- HEAR – Hearing deficiency
This tear off sheet goes to parent:
To remind them to get #2 screen
To give to pediatrician
Doctor will be able to call into Lab’s Voice Response System to access results of 1st screen.
New forms will ask for (in military time):

- Time of birth
- Time of collection
New Screen will not require additional blood spots
“UNSAT”: THE TOP 5
• Do not use Expired Forms
  – Check Form Serial #
  – Rotate your stock
  – Celebrate the New Year by sending back expired forms
• Avoid Contaminants
• Do not touch filter paper
  – EDTA
    • Do not use purple capped tubes
    • Be careful of hand lotion
• Dry flat 3-4 hours
• Do not put in plastic bag
#3

- Mail specimen within 24 hours
  - Do Not Batch
  - Eliminate unnecessary Stops
  - If someone is on vacation- assign to someone else
#2

- **Date of Collection**
  - Specimen cannot be processed without date of collection
- **Date of Birth**
  - New forms will also ask for time of birth
- **Other Demographic are Important**
  - Get mother’s name, address
  - Get a good phone # for someone to call if abnormal
  - Get MD’s name if possible
#1

• Get a good Blood Spot!
  – Must soak through to other side of filter paper
  – Do not scratch or abrade paper