Newborn Metabolic Screening...
So Much More Than “The PKU Test”

Sarah Viall, MSN, PPCNP-BC
Newborn Screening Program Coordinator
Division of Genetics & Metabolism
Conflicts of Interest

I have no conflicts of interest to disclose.
Case 1: Katy

7 day old for one week well-child check

PMHx

• 38 weeks GA, NSVD, Apgars 8 and 9, BW 2.98 kg
• Discharged home DOL 4 with no complications, breastfeeding

Before you walk into the room...

• Weight 2.94 kg
• Breastfeeding “well”, completes ~ 20 minute feed
• Waking to feed, parents describe as “alert, healthy”
Case 1

NEWBORN SCREENING PROGRAM
VIRGINIA DEPARTMENT OF GENERAL SERVICES
DIVISION OF CONSOLIDATED LABORATORY SERVICES
600 North 5th Street, Richmond VA 23219
(804) 648-4488
Toll Free (866) 376-7740

Print Date: 01/28/2015
Print Time: 12:39 pm

Report Date: 01/28/2015

Baby’s Name/Mother’s Name

Medical ID: ____________________________
Year of Birth: ____________________________

Phone: ____________________________
Fax: ____________________________

Patient: ____________________________
Provider: ____________________________

Date of Birth: ____________________________

Physician: ____________________________

Birth Date: 01/28/2015
Birth Time: 09:51
Collection Date: 01/28/2015
Collection Time: 17:40

Receive Date: 01/28/2015

Physician: INOVA CARES CLINIC

Mother’s Address:

Tests performed

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<tr>
<th>Test performed</th>
<th>Normal Results</th>
<th>Result</th>
<th>Normal range</th>
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<tr>
<td>Bioiminidase Screen</td>
<td>Within Normal Limits</td>
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<tr>
<td>CAH</td>
<td>Within Normal Limits</td>
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<tr>
<td>FATTY ACID OXIDATION PROFI</td>
<td>Within normal limits</td>
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<td>Galactose Screen - Beutler Screen</td>
<td>Within Normal Limits</td>
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<td>Homoglobinopathy Screen</td>
<td>Normal Newborn Hemoglobin</td>
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<td>K+ - Cystic Fibrosis</td>
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<td>ORGANIC ACIDEMIA PROFILE</td>
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<td>T4 PROFILE</td>
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<td>Neonatal TSH Screen</td>
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Tests performed

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<th>Result</th>
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<td>ABNORMAL AMINO ACID PROFILE</td>
<td>Maple Syrup Urine Disease Screen</td>
<td>Above Normal Limits</td>
<td>313.03 umol/L</td>
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</table>

SEND REPEAT BLOOD SPOT TO CONSOLIDATED LABORATORY SERVICE IMMEDIATELY

* See attached document for all tests performed
Case 1: Katy

ATTENTION HEALTH CARE PROVIDER:

At the time of routine newborn screening, this baby was screened for genetic or metabolic disorders as required by the State of Virginia. A laboratory report is enclosed for your records. The results of this screening indicate:

Maple Syrup Urine Disease Screen  Above Normal Limits  313.03 umol/L

It is necessary that our laboratory confirm these findings by performing additional testing on a repeat filter paper blood spot collected by a heelstick from the infant. Please submit this sample to us AS SOON AS POSSIBLE with all pertinent requested information. The results will be forwarded to you as soon as they are available.

Clinical information concerning these results is available through the Virginia Newborn Screening Services of the Virginia Department of Health at (804) 864-7714 or (804) 864-7715. Laboratory information can be obtained by calling the Newborn Screening Laboratory at (804) 648-4480 or Toll free at (866) 378-7730 at the Department of General Services, Division of Consolidated Laboratories.
Case 1: Katy

PE: “mild odor of pancakes/maple syrup”

PNP calls Metabolic Specialist

Immediate visit

- Plasma amino acids:
  - Leucine = 2,100 umol/L (48-160)
  - Isoleucine = 560 umol/L (26-91)
  - Valine = 820 umol/L (44-190)
  - Alloisoleucine = 165 umol/L (0-5)

Diagnosis: Maple Syrup Urine Disease (MSUD)
Newborn Screen Basics
Terminology

- Newborn Screen (NBS)
- Newborn Metabolic Screen (NMS)
- Expanded Newborn Screen

***NOT the “PKU Test”***
Take Home Points

**NOT** the “PKU Test”

Anxiety reduction

Use resources and support!
Communication of Results

Every state follow-up program is different

Contact order varies

When contacting families...

• Recognized provider
• Abnormal ✗ positive
  • Screening NOT diagnostic test
• Treatable disorders
Metabolic Disorders of the Newborn Screen
Genetics

Hematology
Hemoglobinopathies

Pulmonary
Cystic Fibrosis

Endocrine
Congenital Endocrinopathies

Metabolism
Organic Acidurias
Fatty Acid Oxidation Disorders
Amino Acidopathies
Other Enzyme Deficiencies

Hearing
Congenital Hearing Loss

Immunology
Severe Combined Immunodeficiency

Cardiology
Critical Congenital Heart Disease
Recommended Uniform Screening Panel (RUSP)

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<th>Core Condition</th>
<th>Organic acid conditions</th>
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Source: [HRSA](http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/recommendedpanel/uniformscreeningpanel.pdf)

Organic Acid Conditions
Fatty Acid Oxidation Disorders
Amino Acid Disorders
Other Metabolic Disorders
General Principles: Metabolism


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General Principles: Pathophysiology

Normal:

Disease:

Excess Blue

Not Enough Orange & Yellow
General Principles: Inheritance

Source: http://www.brusselsgenetics.be/media/images/Illustraties/ill_eng/ill-12-E2_orig.jpg
General Principles: Onset

❖ Neonatal
  • Poor feeding
  • Vomiting
  • Abnormal tone
  • Odor*
  • Lethargy
  • Seizures
  • Irritability
  • Hyperammonemia
  • Can quickly progress to coma or death

❖ Childhood

❖ Adulthood
General Principles: Management

Diet changes

Avoidance of fasting

Careful intercurrent illness management

Vitamin supplementation

Medications (rarely)
Abnormal Metabolic Newborn Screen Cases
Case 2: Logan

State of Maryland
Department of Health and Mental Hygiene
Laboratories Administration
201 West Preston Street
Baltimore, Maryland 21201
Lawrence J. Hogan, Jr., Governor - Van T. Mitchell, Secretary
Robert Myers, Ph.D., Director
Maryland Newborn Screening Follow-Up Program
Telephone Number: (410) 767 - 6738
FAX Number: (410) 333 - 5018

FOR SPECIMEN COLLECTED 03/2015 SHOWING GALACTOSE WNL AND REDUCED GAL'T. THIS REPEAT SPECIMEN WAS OBTAINED 40 DAYS OF AGE FROM INFANT TWIN BORN AT 36 WEEKS GESTATION. INFANT USING LACTOSE FORMULA FOR FeEDINGS AND IS SHOWING GOOD WEIGHT GAIN. LATER FOR CLASSICAL GALACTOSEMIA OR HAS A MILD VARIANT WILL CONTACT PCP TO RECOMMEND QUANTITATIVE GAL'T LEVELS TO HELP MAKE THAT DETERMINATION.

Certified Letter Date: 03/26/2015

LLAMEREESPOKE WITH PCP OFFICE ASKING IF REPEAT NBS HAS BEEN COLLECTED. NURSE WILL NEED TO CALL BE BACK.

03/ /2015 LLAMEREES RECEIVED CALL BACK FROM NURSE CARRIE AT PCP OFFICE. SHE REPORTED INFANT IS DOING WELL AND REPEAT NBS WAS COLLECTED 03/17/2015 AND MAILED. WILL WATCH FOR REPEAT SPECIMEN.

03/ /2015 WATSONJ REPEAT SPECIMEN COLLECTED ON 03/13/2015 IS CURRENTLY PENDING.

03/ /2015 LLAMEREES RECEIVED REPORT FOR SPECIMEN COLLECTED 03/2015 SHOWING GALACTOSE WNL AND REDUCED GAL'T. THIS REPEAT SPECIMEN WAS OBTAINED AT APPROXIMATELY 40 DAYS OF AGE FROM INFANT TWIN BORN AT 36 WEEKS GESTATION. INFANT USING LACTOSE FORMULA FOR FEEDINGS AND IS SHOWING GOOD WEIGHT GAIN. LATER FOR CLASSICAL GALACTOSEMIA OR HAS A MILD VARIANT WILL CONTACT PCP TO RECOMMEND QUANTITATIVE GAL'T LEVELS TO HELP MAKE THAT DETERMINATION.

03/ /2015 LLAMEREES UM FOR CARRIE, NURSE TO CALL BE BACK.

03/ /2015 LLAMEREES RECEIVED CALL BACK FROM CARRIE, RN AT PCP OFFICE. REPORTED THAT REPEAT NBS IS SHOWING GAL'T ENZYME IS REDUCED AND GALACTOSE WNL. IT IS POSSIBLE INFANT IS A CARRIER FOR GALACTOSEMIA OR MAY HAVE A MILD VARIANT CALLED DUARTE. RECOMMENDED QUANTITATIVE GAL'T (GALACTOSE 1 PHOSPHATE URIDYL TRANSFERASE) LEVEL TO HELP DETERMINE IF A CARRIER OR DUARTE. IF PCP PREFERS, WE CAN FACILITATE REFERRAL TO GENETICS FOR THIS FOLLOW UP TESTING. CARRIE REPORTED INFANT IS DOING WELL. FAXED QUANTITATIVE GAL'T ORDERING INFO TO PCP OFFICE ALONG WITH WORKSHEET.
Case 2: Logan

You call Logan’s parents who confirm he’s well; no vomiting, fever or changes in behavior. 2-3 oz. breast milk or regular formula q 2-3 hours. After explaining NBS result, what do you tell them to do next?

A. You will no longer be able to breastfeed because your child has galactosemia.
B. Switch to soy formula immediately until we can collect further testing.
C. Return immediately for a repeat further testing.
## Case 2: Logan

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<th>Birth Date</th>
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<th>Weight</th>
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**CAPITOL MEDICAL GROUP**
8401 Connecticut Avenue
Chevy Chase, MD 20827
1-301-907

**Genetic Evaluation:** Childrens National Medical Center

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<tr>
<th>Mother</th>
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**Notes:**
- LLAMMEMEE SPOKE WITH PCP OFFICE ASKING IF REPEAT NBS HAS BEEN COLLECTED. NURSE WILL NEED TO CALL BACK.
- LLAMMEMEE RECEIVED CALL BACK FROM NURSE CARRIE AT PCP OFFICE. SHE REPORTED INFANT IS DOING WELL AND REPEAT NBS WAS COLLECTED 03/17/2015 AND MAILED. WILL WATCH FOR REPEAT SPECIMEN.
- LLAMMEMEE RECEIVED REPORT FOR SPECIMEN COLLECTED 03/2015 SHOWING GALACTOSE WNL AND REDUCED GALT. THIS REPEAT SPECIMEN WAS OBTAINED AT APPOXIMATELY 40 DAYS OF AGE FROM INFANT TWIN BORN AT 36 WEEKS GESTATION. INFANT USING LACTOSE FORMULA FOR FEEDINGS AND IS SHOWING GOOD WEIGHT GAIN. LIKELY INFANT IS A CARRIER FOR CLASSICAL GALACTOSEmia OR HAS A MILD VARIANT. WILL CONTACT PCP TO RECOMMEND QUANTITATIVE GALT LEVELS TO HELP MAKE THAT DETERMINATION.
- LLAMMEMEE LM FOR CARRIE, NURSE TO CALL BACK.
- LLAMMEMEE RECEIVED CALL BACK FROM CARRIE, RN AT PCP OFFICE. REPORTED THAT REPEAT NBS IS SHOWING GALT ENZYME IS REDUCED AND GALACTOSE WNL. IT IS POSSIBLE INFANT IS A CARRIER FOR GALACTOSEmia OR MAY HAVE A MILD VARIANT CALLED DUARTE. RECOMMENDED QUANTITATIVE GALT (GALACTOSE 1 PHOSPHATE URIDYLYL TRANSFERASE) LEVEL TO HELP DETERMINE IF A CARRIER OR DUARTE. IF PCP PREFERENCES, WE CAN FACILITATE REFERRAL TO GENETICS FOR THIS FOLLOW UP TESTING. CARRIE REPORTED INFANT IS DOING WELL. FAXED QUANTITATIVE GALT ORDERING IN TO PCP OFFICE ALONG WITH WORKSHEET 240-482.
Case 2: Logan

You call Logan’s parents who confirm he’s well; no vomiting, fever or changes in behavior. 2-3 oz. breast milk or regular formula q 2-3 hours. After explaining NBS result, what do you tell them to do next?

A. You will no longer be able to breastfeed because your child has galactosemia.

B. Switch to soy formula immediately until we can collect further testing.

C. Return immediately for a repeat further testing.
Galactosemia

Deficiency of Galactose-1-Phosphate Uridylyltransferase (GALT) Enzyme
  • Responsible for processing galactose
  • → Build-up of toxic galactose compounds

Symptoms
  • Poor feeding
  • Jaundice
  • Vomiting/diarrhea
  • Lethargy
  • Fever

Typical Onset: DOL 3 or 4
Galactosemia Screening

TWO Analytes (typically):

• Galactose-1-Phosphate-Uridyltransferase (GALT)
• Galactose and/or galactose-1-phosphate (*Toxic*)

Abnormal GALT↓

• Classic galactosemia
• Duarte variant galactosemia
• Classic galactosemia carrier
• False positive (heat!)

Abnormal galactose/galactose-1-phosphate↑

• Classic galactosemia
• Other variant galactosemia
Galactosemia Screening

Abnormal GALT + galactose = CRITICAL

• Classic galactosemia
• Duarte variant galactosemia

IMMEDIATE galactose-restriction

• NO breast feeding
• NO regular formula
• Soy or hydrolyzed formula only
Galactosemia Screening

Confirmatory Testing

• Galactose-1-Phosphate
  • Toxic metabolite!

• GALT Enzyme
  • 0% = Classic galactosemia
  • 25% of normal = Duarte variant galactosemia
  • 50% of normal = likely carrier of galactosemia

• GALT Gene Sequencing
Case 3: Garth

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Propionylcarnitine (C3) = 12.05 µmol/L (Normal < 4.00 µmol/L)
Propionylcarnitine/Palmitoylcarnitine (C3/C16) ratio = 4.05 (Normal < 2.20)

Acylcarnitine Profile
Camitine Uptake Deficiency

RESULT: PRESUMPTIVE POSITIVE

Propionylcarnitine (C3) = 12.05 µmol/L (Normal < 4.00 µmol/L)
Propionylcarnitine/Palmitoylcarnitine (C3/C16) ratio = 4.05 (Normal < 2.20)

The concentration of Propionylcarnitine (C3) and other indices such as the relative ratios of C3 to Acetylcarmitine (C2) or C3 to Palmitoylcarnitine (C16) were substantially above normal. The possible causes are Propionic Acidemia, Methylymalonic Acidemia, Cobaamin Defects, or Vitamin B12 Deficiency. We urgently recommend an organic acid analysis of urine and another dried filter paper blood specimen as well as a referral to a metabolic specialist.

DNA analysis detected no copies of the common Propionic Acidemia alleles E168K, 1218del 14/ins 12, 1170 ins T, or Methylymalonic Acidemia alleles N219Y, G717V. Depending on population, these Propionic Acidemia mutations can account for up to 50% of the mutations that cause disease, while most Methylymalonic Acidemia mutations are private and family specific.

Genetic analysis for the Propionic Acidemia alleles E168K, 1218del 14/ins 12, 1170 ins T, and the Methylymalonic Acidemia alleles N219Y, G717V are performed using polymerase chain reaction and melting curve analysis to detect the mutant and wild type forms of the genes. These disorders are inherited as autosomal recessive traits.
Case 3: Garth

6 day old male

PMHx

• Born at 39 weeks GA, C-section
• ABO incompatibility, history of jaundice with phototherapy x 48 hours
• Discharged DOL 4, breast and formula feeding

In the office

• Well appearing, jaundiced to the nipples
• Mom describes “maybe he’s been eating a little less”
Case 3: Garth

After attempting to contact the metabolic specialist for several hours you have not heard back. It’s nearing the end of the day, what do you do next?

A. Send this child to the emergency room.
B. Send the family home with careful instructions to go to the ER for any concerning signs/symptoms. Try the specialist again tomorrow.
C. Send the family home. Tell them to contact the metabolic specialist to schedule an appointment as soon as possible.
Newborn Screening ACT Sheet
[Elevated C3 Acylcarnitine]
Propionic Acidemia and Methylmalonic Acidemia

**Differential Diagnosis:** Propionic acidemia (PA): Methylmalonic acidemias (MMA) including defects in B12 synthesis and transport; maternal severe B12 deficiency.

**Condition Description:** PA is caused by a defect in propionyl-CoA carboxylase which converts propionyl-CoA to methylmalonyl-CoA; MMA results from a defect in methylmalonyl-CoA mutase which converts methylmalonyl-CoA to succinyl-CoA or from lack of the required B12 cofactor for methylmalonyl-CoA mutase (cobalamin A, B, C, D, and F).

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**YOU SHOULD TAKE THE FOLLOWING ACTIONS IMMEDIATELY:**

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Consult with pediatric metabolic specialist.
- Evaluate the newborn; check urine for ketones and, if elevated or infant is ill, initiate emergency treatment as indicated by metabolic specialist and transport immediately to tertiary center with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Educate family about signs, symptoms and need for urgent treatment of hyperammonemia and metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea).
- Report findings to newborn screening program.

---

**Diagnostic Evaluation:** Plasma acylcarnitine confirms the increased C3. Blood amino acid analysis may show increased glycine. Urine organic acid analysis will demonstrate increased metabolites characteristic of propionic acidemia or increased methylmalonic acid characteristic of methylmalonic acidemia. Plasma total homocysteine will be elevated in the cobalamin C, D and F deficiencies. Serum vitamin B12 may be elevated in the cobalamin disorders.

**Clinical Considerations:** Patients with PA and severe cases of MMA typically present in the neonate with metabolic ketoacidosis, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Long-term complications are common, early treatment may be lifesaving and continued treatment may be beneficial.
Case 3: Garth

After attempting to contact the metabolic specialist for several hours you have not heard back. It’s nearing the end of the day, what do you do?

⭐ A. Send this child to the emergency room.

B. Send the family home with careful instructions to go to the ER for any concerning signs/symptoms. Try the specialist again tomorrow.

C. Send the family home. Tell them to contact the metabolic specialist to schedule an appointment as soon as possible.
Organic Acid (OA) Conditions

Disorders of metabolism identifiable by specific urine metabolites
  - Typically disordered amino acid (protein) metabolism

Symptoms
  - Lethargy
  - Feeding problems
  - Ketonuria
  - Can quickly progress to cerebral edema, coma, death

Onset: Variable
  - Birth – early childhood
OA Screening

Analytes

• Acylcarnitines (denoted as C#)
  • Odd # chains (i.e. C₃, C₅DC)

Confirmatory Testing

• Urine organic acids
• +/- Acylcarnitines
• +/- Genetic testing
## Case 4: Amanda

<table>
<thead>
<tr>
<th>Tests performed</th>
<th>Normal Results</th>
<th>Result</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMINO ACID PROFILE</td>
<td>Within normal limits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biotinidase Screen</td>
<td>Within Normal Limits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAH</td>
<td>Within Normal Limits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Galactose Screen - Beutler Screen</td>
<td>Within Normal Limits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobinopathy Screen</td>
<td>Normal Newborn Hemoglobin</td>
<td></td>
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</tr>
<tr>
<td>IRT- Cystic Fibrosis</td>
<td>Within Normal Limits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ORGANIC ACIDEA PROLIFER</td>
<td>Within normal limits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4 PROFILE</td>
<td>Within normal limits</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tests performed</th>
<th>Abnormal Results</th>
<th>Result</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABNORMAL FATTY ACID OXIDATION</td>
<td>Above Normal Limits</td>
<td>.87</td>
<td>&lt; 0.66 umol/L</td>
</tr>
<tr>
<td>C14:1</td>
<td>Above Normal Limits</td>
<td>.85</td>
<td>&lt; 0.70 umol/L</td>
</tr>
</tbody>
</table>

Interpretation: The above results for fatty acid profile are suggestive of possible VLCAD.
Case 4: Amanda

5 day old female

PMHx

- 37 weeks GA, C-section
- One episode of hypoglycemia in the nursery, resolved with oral feed

In the Office

- Well appearing
- Exclusive breastfeeding, 1-2 oz. q 3 hours
Case 4: Amanda

This is a trustworthy family and well-appearing child, is an immediate repeat newborn screen to rule out an FAOD appropriate in this case?

A. Yes
B. No
**RESOURCE: NYMAC Diagnostic Guidelines**

### Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)  
**Fatty Acid Oxidation Disorder**

<table>
<thead>
<tr>
<th>Disease (common abbreviation)</th>
<th>Very Long-chain Acyl-CoA Dehydrogenase Deficiency (VLCAD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIM #</td>
<td>201475</td>
</tr>
<tr>
<td>SNOMED Code / ICD-10-CM Code</td>
<td>237997005 / E71.310</td>
</tr>
<tr>
<td>Enzyme or other abnormality</td>
<td>Very long-chain acyl-CoA dehydrogenase 609575 / 1.3.99.13</td>
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<tr>
<td>MIM # / Enzyme Commission #</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abnormal Newborn Screening Metabolite(s)</th>
<th>Elevated C14 53192-1 Elevated C14:1 53191-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOINC Number(s)</td>
<td></td>
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</tbody>
</table>

| Initial Diagnostics at Referral Center  | Plasma acylcarnitine profile  
Mutation analysis, as negative metabolites do not rule out the disorder |
|----------------------------------------|------------------------------------------------------------------------|

| Recommended additional testing to consider at time of initial consultation | Blood glucose  
Plasma Carnitine, total and free  
Creatinine phosphokinase (CPK)  
Urine organic acids  
Liver function tests |
|--------------------------------------------------------------------------|---------------------------------------------------------------------|

| Abnormal Metabolites Expected | Elevated C14, C14:1  
Detection of known pathological mutations in trans  
Blood glucose depends on fed status of patient  
Normal/low carnitine levels  
CPK may be elevated in sick patients  
Urine organic acids are usually normal  
Liver function tests may be abnormal in sick patients |
|-----------------------------|---------------------------------------------------------------------|
Case 4: Amanda

This is a trustworthy family and well-appearing child, is an immediate repeat newborn screen to rule out an FAOD appropriate in this case?

A. Yes

★ B. No

Repeat newborn screens are often NOT appropriate for fatty acid oxidation rule-out!
Fatty Acid Oxidation Disorders (FAODs)

Deficiency of enzymes required to break down fat, leading to:

- Energy deficit
- Build-up of fatty acids

Symptoms

- Variable
- Sudden death*

Onset: variable

- Birth– adulthood
## Fatty Acid Oxidation Disorders (FAODs)

<table>
<thead>
<tr>
<th>FAO Disorder</th>
<th>Sudden death</th>
<th>Fasting Intolerance</th>
<th>Skeletal Myopathy</th>
<th>Cardiomyopathy</th>
<th>Liver Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carnitine uptake defect</td>
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<tr>
<td>LCFA transport/binding defect</td>
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<tr>
<td>FA translocase deficiency</td>
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<tr>
<td>CPT-I deficiency</td>
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<tr>
<td>CACT deficiency</td>
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<tr>
<td>CPT-II deficiency (neonatal)</td>
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<tr>
<td>CPT-II deficiency (late onset)</td>
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<tr>
<td>VLCAD deficiency</td>
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<tr>
<td>ETF-QO deficiency (GA2)</td>
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<tr>
<td>LCHAD deficiency</td>
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<td>TFP deficiency</td>
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<tr>
<td>MCAD deficiency</td>
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<tr>
<td>SCAD deficiency</td>
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<tr>
<td>ETF deficiency</td>
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<tr>
<td>Riboflavin responsive GA2</td>
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<tr>
<td>M/SCHAD deficiency (SCHAD)</td>
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<tr>
<td>MCKAT deficiency</td>
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<tr>
<td>2,4-Dienoyl-CoA reductase deficiency</td>
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<tr>
<td>HMG-CoA synthase deficiency</td>
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<tr>
<td>HMG-CoA lyase deficiency</td>
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</table>

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FAOD Screening

Analytes

- Acylcarnitines (denoted as C#)
  - Even # chains (i.e. C8, C14:1)

Confirmatory Testing

- Plasma acylcarnitines
- Urine organic acids
- Free and total carnitine
- Genetic testing
Amino Acid Disorders (From Case 1, the smelly baby)

Disorders of specific amino acid metabolism

Symptoms: variable on metabolite

• MSUD: decreased feeding, lethargy progressing to encephalopathy, coma and death
• Phenylketonuria (PKU): intellectual disability

Onset: variable

• Birth– adulthood
Amino Acid Disorder Screening

Analytes

• Amino acids (i.e. phenylalanine, tyrosine)
• Not always primary markers
  • Methionine = Homocystinuria screen
  • Citrulline = Arginosuccinic aciduria screen

Confirmatory Testing

• Plasma amino acids
Case 5: Emily

New patient

• 6 month old female

PMHx

• Born in Central America, moved to U.S. one month ago
• Mom reports:
  • Birth history “normal”, term, NSVD
  • Spitting up and reflux, resolved
  • No fevers, infections, major illnesses described

In the Office

• Well-appearing
• Developmental milestones appropriate for age
Case 5: Emily

There seems to be no record of this child ever having a newborn screen. With no specific concerns, what do you do next?

A. Continue to monitor for signs/symptoms of disease, but with no specific concerns do not order any further testing.
B. Collect and send a dried blood spot to your state newborn screening program.
C. Contact your state newborn screening program for assistance.
Case 5: Emily

There seems to be no record of this child ever having a newborn screen. With no specific concerns, what do you do next?

A. Continue to monitor for signs/symptoms of disease, but with no specific concerns do not order any further testing.

B. Collect and send a dried blood spot to your state newborn screening program.

C. Contact your state newborn screening program for assistance.
RESOURCE: babysfirsttest.org

Virginia

Virginia currently screens for 29 conditions. Each state runs its program differently, for more detailed information please visit their website at http://www.vdh.virginia.gov/offhs/childandfamily/childhealth/gns/ynsp/.

DOWNLOAD BROCHURE
The state of Virginia does not have a brochure available. You can find more state specific information at their website.

What Conditions are Screened For in Virginia?

On This Page:
- WHAT CONDITIONS ARE SCREENED FOR IN VIRGINIA?
- ABOUT NEWBORN SCREENING IN VIRGINIA
- POLICIES AND RESOURCES
- CONTACTS

Contacts
Virginia Newborn Screening Program
Jennifer O. Macdonald, RN, BSN, MPH
Acting Newborn Screening Program Manager
jennifer.macdonald@vdh.virginia.gov
109 Governor Street, 8th Floor; Richmond, Virginia 23219
Phone: (804) 864-7729
FAX: (804) 864-7807
NBS Resources
Websites

**ACT Sheets**
http://www.ncbi.nlm.nih.gov/books/NBK55827/

**Baby’s First Test**
Babysfirsttest.org

**NYMAC**
http://www.wadsworth.org/newborn/nymac/NYMAC_Products.html

  **Diagnostic Guidelines:**
# ACT Sheets

## Newborn Screening ACT Sheets and Confirmatory Algorithms

**NEWBORN SCREENING CONDITION-ANALYTE TABLE**

<table>
<thead>
<tr>
<th>Condition Group</th>
<th>Condition</th>
<th>Analyte</th>
<th>Links</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GENETIC DISORDERS</strong></td>
<td>Biotinidase deficiency</td>
<td>Biotinidase</td>
<td>![ACT Sheet](PDF, 274K) ![Algorithm](PDF, 32K)</td>
</tr>
<tr>
<td></td>
<td>Cystic Fibrosis</td>
<td>Immunoreactive trypsinogen (IRT) + IRT or DNA</td>
<td>![ACT Sheet](PDF, 275K) ![Algorithm](PDF, 31K)</td>
</tr>
<tr>
<td></td>
<td>Hearing Loss</td>
<td>Hearing loss</td>
<td>![ACT Sheet](PDF, 276K) ![Algorithm](PDF, 39K)</td>
</tr>
<tr>
<td><strong>GALACTOSEMIAS</strong></td>
<td>Classical galactosemia</td>
<td>GALT</td>
<td>![ACT Sheet](PDF, 274K) ![Algorithm](PDF, 34K)</td>
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<tr>
<td></td>
<td>Galactokinase deficiency</td>
<td>Elevated galactose deficient GALT</td>
<td>![ACT Sheet](PDF, 271K) ![Algorithm](PDF, 37K)</td>
</tr>
</tbody>
</table>
Baby’s First Test

Newborn Screening?

Many parents are unaware of the conditions included in screening, or that it varies from state to state. Baby's First Test brings together resources to help guide parents and health professionals alike.
NYMAC

NYMAC
(New York-Mid-Atlantic Consortium for Genetics and Newborn Screening Services)

NYMAC Products
- General Information
  - NYMAC Brochure
  - NYMAC Needs Assessment and Plan
  - NYMAC Directory of Genetic and Specialty Care Services
- Distance Strategies
  Distance infants and their families must travel to a treatment center for appropriate care with the following conditions:
  - Sickle Cell Disease (SCD)
  - Congenital Primary Hypothyroidism (CH)
  - Phenylketonuria (PKU)
- Newborn Screening Standardization
  Guidelines for the clinical evaluation of infants who screen positive by newborn screening:
  - NYMAC Diagnostic Guidelines
  - State Newborn Screening Program Notification Protocols
- Consumer Education
  - Genetics and Your Health Brochures
    - Prepregnancy (English) (Spanish)
    - Prenatal (English) (Spanish)
    - Pediatrics (English) (Spanish)
    - Adolescence 11-21 (English) (Spanish)
    - Adulthood (English) (Spanish)
  - Genetic Alliance Understanding Genetics:
    A NYMAC Guide for Patients and Health Professionals
Last but not least...

Sarah Viall, MSN, PPCNP-BC
Newborn Screening Program Coordinator
Division of Genetics & Metabolism
Children’s National Health System
sviall@cnmc.org
202.476.4388
Take Home Points

**NOT** the “PKU Test”

Anxiety reduction

Use resources and support!
References

CDC Grand Rounds: Newborn Screening and Improved Outcomes
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6121a2.htm

National Newborn Screening and Global Resource Center
http://genes-r-us.uthscsa.edu/

Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children Committee Report

Star-G: Screening, Technology and Research in Genetics
http://www.newbornscreening.info/index.html
Questions?

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