(Abnormal) Newborn Screening: Promises + Pitfalls

Kristen Lee, MD
Clinical Assistant Professor of Pediatrics and Internal Medicine
Division of Pediatric Genetics, Metabolism, & Genomic Medicine
Division of Genetic Medicine
University of Michigan
lekriste@med.umich.edu

October 1, 2022
Objectives

• Review purpose of newborn screening ("Promises")
• Discuss advances in recommended uniform screening panel (RUSP) and how Michigan is implementing these additions
• Review recommendations for abnormal newborn screens
• Discuss some challenges with newborn screens ("Pitfalls")
• Identify available resources for providers and families to find information
What is Newborn Screening?

- It’s NOT the “PKU test”

But it did start out that way:

- 1958: bacterial inhibition assay for PKU (bacterial growth induced by high Phe concentrations in serum spots)
- 1961: local (NY) newborn screening for PKU started using blood collected and dried on filter paper following a heel stick
- 1962: state-wide screening for PKU began with support from the “National Association for Retarded Children” and despite the opposition by organized medical groups
What is Newborn Screening (NBS)?

• A public health system of services and activities that screens the 4 million neonates born annually in the US to identify conditions whose mortality, morbidity or disabilities can be reduced or eliminated by pre-symptomatic detection.
  – Largest and longest running population screening program
• One of 10 great public health achievements in last decade in the US – and notable around the world
• An effective newborn screening program includes: education, screening, diagnosis, follow-up, treatment and evaluation.
  – Improved outcomes, changing natural history of disease

PMID: 21597455, 29758802
Newborn Screening

**Traditional**
- One blood spot
- One test
- One marker
- One disease
  secondary disease

**Expanded+**
- One blood spot
- One test
- Many markers
  - amino acids
  - acylcarnitines
  - enzymes
  - proteins
- Many diseases
  - multiple forms, severities
NBS and Public Policy

• Federal government plays a limited role
  – SACHDNC (Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children)
    • Advises the Secretary of HHS on the most appropriate application of universal NBS tests, technologies, policies, guidelines, and standards
  – Secretary of HHS and SACHDNC work together to create **RUSP**

• Each state chooses the screening platform, panel of conditions, and pays the costs of NBS

• Each state evaluates its own program

• Information on individual state screening programs available at:
  – NNSGRC: National Newborn Screening and Genetics Resource Center
  – genes-r-us.uthsca.org
List of disorders recommended by the Secretary of the Department of Health and Human Services to be added to all states screening programs

Disorders are chosen based on evidence that supports potential net benefit of screening, the ability of states to screen for the disorder, and availability of effective treatments
  - It is recommended that every newborn be screened for all disorders on the RUSP

Most states screen for the majority of disorders on the RUSP; newer conditions are still in process of adoption
  - Some states also screen for additional disorders

Conditions must be nominated by a committee and undergo multiple phases of review before being added to RUSP
# MI NBS (as of 8/31/22)

## Amino Acid Disorders
1. Arginemia (ARG)
2. Argininosuccinic acidemia (ASA)
3. Citrullinemia Type I (CIT-I)
4. Citrullinemia Type II (CIT-II)
5. Homocystinuria (HCY)
6. Hypermetioninemia (MET)
7. Maple syrup urine disease (MSUD)
8. Phenylketonuria (PKU)
   - Benign hyperphenylalaninemia defect (H-PHE)
   - Biotinidase cofactor biosynthesis defect (BIOT-BS)
   - Biotinidase cofactor regeneration defect (BIOT-REG)
9. Tyrosinemia Type I (TYR-I)
10. Tyrosinemia Type II (TYR-II)
11. Tyrosinemia Type III (TYR-III)

## Hemoglobinopathies
12. S-beta thalassemia
13. S/C disease
14. Sickle cell anemia
15. Variant hemoglobinopathies
16. Hemoglobin H disease

## Endocrine Disorders
17. Congenital adrenal hyperplasia (CAH)
18. Congenital hypothyroidism (CH)

## Fatty Acid Oxidation Disorders
19. Carnitine acylcarnitine translocase deficiency (CACT)
20. Carnitine palmitoyltransferase I deficiency (CPT-1A)
21. Carnitine palmitoyltransferase II deficiency (CPT-II)
22. Carnitine uptake defect (CUD)
23. Dienoyl-CoA reductase deficiency (DERED)
24. Glutaric acidemia type II (GA-2)
25. Long-chain L-3-hydroxy acyl-CoA dehydrogenase deficiency (LCHAD)
26. Medium/short-chain L-3-hydroxy acyl-CoA dehydrogenase deficiency (M/SCCHAD)
27. Medium-chain acyl-CoA dehydrogenase deficiency (MCAD)
28. Medium-chain ketoacyl-CoA thiolase deficiency (MCKAT)
29. Trifunctional protein deficiency (TFP)
30. Very long-chain acyl-CoA dehydrogenase deficiency (VLCHAD)

## Organic Acid Disorders
27. 2-Methyl-3-hydroxy butyric aciduria (2M3HBA)
28. 2-Methylbutyryl-CoA dehydrogenase deficiency (2MBG)
29. 3-hydroxy 3-methylglutaric aciduria (HMG)
30. 3-Methylcrotonyl-CoA carboxylase deficiency (3-MCC)
31. 3-Methylglutaconic aciduria (3MGA)
32. Beta-ketothiolase deficiency (BKT)
33. Glutaric acidemia type I (GA-I)
34. Isovaleric acidemia (IVA)
35. Malonic acidemia (MAL)
36. Methylmalonic acidemia cobalamin disorders (Cbl A,B)
37. Methylmalonic aciduria with homocystinuria (Cbl C,D)
38. Methylmalonic acidemia methylmalonyl-CoA mutase (MUT)
39. Multiple carboxylase deficiency (MCD)
40. Propionic acidemia (PROP)

## Lysosomal Storage Disorders
48. Glycogen Storage Disease Type II (Pompe)
49. Mucopolysaccharidosis Type I (MPS I)

## Disorders Coming Soon
This condition has been approved for addition to Michigan's panel but implementation is in progress and screening has not yet begun.
- Guanidinoacetate methyltransferase (GAMT) deficiency

## Other Disorders
50. Biotinidase deficiency (BIOT)
51. Galactosemia (GALT)
52. Cystic fibrosis (CF)
53. Severe combined immunodeficiency (SCID)
54. T-cell related lymphocyte deficiencies
55. X-linked Adrenoleukodystrophy (X-ALD)
56. Spinal muscular atrophy (SMA)
57. Hearing
58. Critical Congenital Heart Disease (CCHD)
### Disorders Identified in MI Newborns via NBS, 1965-2020

<table>
<thead>
<tr>
<th>Type of Disorder Classification (Year Screening Began)</th>
<th>Cases in 2020 (N)</th>
<th>Cases Through 2020 (N)</th>
<th>Cumulative Detection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Galactosemia (1985)</td>
<td>3</td>
<td>222</td>
<td>1:20,620</td>
</tr>
<tr>
<td>Biotinidase Deficiencies (1987)</td>
<td>17</td>
<td>377</td>
<td>1:11,130</td>
</tr>
<tr>
<td>Amino Acid Disorders (1965)</td>
<td>11</td>
<td>803</td>
<td>1:9,253</td>
</tr>
<tr>
<td>Organic Acid Disorders (2005)</td>
<td>8</td>
<td>108</td>
<td>1:15,895</td>
</tr>
<tr>
<td>Fatty Acid Oxidation Disorders (2003)</td>
<td>7</td>
<td>294</td>
<td>1:6,725</td>
</tr>
<tr>
<td>Congenital Hypothyroidism (1977)</td>
<td>121</td>
<td>2,706</td>
<td>1:1,551</td>
</tr>
<tr>
<td>Congenital Adrenal Hyperplasia (1993)</td>
<td>9</td>
<td>184</td>
<td>1:18,052</td>
</tr>
<tr>
<td>Sickle Cell Disease (1987)</td>
<td>73</td>
<td>2,167</td>
<td>1:1,935</td>
</tr>
<tr>
<td>Hemoglobin H Disease (2012)</td>
<td>1</td>
<td>17</td>
<td>1:51,641</td>
</tr>
<tr>
<td>Cystic Fibrosis (2007)</td>
<td>26</td>
<td>348</td>
<td>1:3,843</td>
</tr>
<tr>
<td>Primary Immunodeficiencies (2011)</td>
<td>13</td>
<td>134</td>
<td>1:7,389</td>
</tr>
<tr>
<td>Lysosomal Storage Disorders (2017)</td>
<td>7</td>
<td>24</td>
<td>1:10,675</td>
</tr>
<tr>
<td>X-Linked Adrenoleukodystrophy (2019)</td>
<td>1</td>
<td>2</td>
<td>1:63,830</td>
</tr>
<tr>
<td>Spinal Muscular Atrophy* (2020)</td>
<td>10</td>
<td>12</td>
<td>1:9,898</td>
</tr>
<tr>
<td>Total</td>
<td>307</td>
<td>7,401</td>
<td>-</td>
</tr>
</tbody>
</table>

*Two cases of SMA were detected in 2019 during population studies*
Spinal Muscular Atrophy (SMA)

- Progressive disorder leading to skeletal muscle atrophy due to loss of motor neurons
- Types 0-IV (0 = most severe, IV = least severe)
- Autosomal recessive, most often due to biallelic deletion of exon 7 in \( SMN1 \)
- With only supportive treatment, affected individuals experience:
  - FTT, feeding difficulties
  - Restrictive lung disease
  - Joint contractures, scoliosis
  - Progressive muscle weakness
  - Early mortality
Why SMA for NBS?

- Huge advances in the past 5 years
  - 3 FDA approved treatments
- Early treatment is key
  - Motor neurons cannot be restored once lost
- Outcome without treatment for most individuals is early death
What’s Next?

Guanidinoacetate methyl transferase (GAMT) deficiency

GAMT deficiency is an inborn error of metabolism that affects creatine synthesis. When the guanidinoacetate methyltransferase enzyme is damaged, creatine cannot be synthesized and guanidinoacetate (GAA) accumulates. This creates a shortage of creatine in the body and excessive amounts of GAA, which is a neurotoxin. Creatine is an essential metabolite for the brain, heart and muscle. When the body does not get enough creatine and has extra GAA, it can cause developmental delay, speech problems, seizures and behavior issues such as autism and hyperactivity. Lack of early treatment can lead to lifelong cognitive impairments which may be severe. Treatment for GAMT deficiency consists of correcting the creatine deficiency and reducing GAA levels in the body and brain through dietary and medical interventions. Treatment is most effective if started early in life before symptoms arise.

Michigan plans to screen all newborns for GAMT deficiency in the second half of 2022 and will be the third state in the United States to screen for GAMT deficiency. GAMT deficiency screening will be completed using the dried filter paper blood spots collected as part of the current newborn screening process. Michigan’s Newborn Screening Laboratory will use a tandem mass spectrometry method to measure the analytes guanidinoacetate and creatine to screen for GAMT deficiency.

GAMT Deficiency Story: The Power of Newborn Screening. See the dramatic difference newborn screening can have for children with GAMT Deficiency.

This video features a Utah family’s story of two children with living with GAMT deficiency.

Watch the video here! https://youtu.be/sw0z2Rq6kZ0

Mucopolysaccharidosis Type II Recommended for the RUSP

On February 10, the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) voted to recommend the addition of mucopolysaccharidosis type II (MPS II) to the Recommended Uniform Screening Panel (RUSP). The recommendation will now be forwarded to the US Department of Health and Human Services Secretary for final approval.

MPS II, or Hunter syndrome, is an X-linked lysosomal storage disorder affecting approximately 1/100,000 to 1/170,000 male births. It is caused by a deficiency of the lysosomal enzyme iduronate-2-sulfatase, responsible for breaking down large sugar molecules called glycosaminoglycans (GAGs). The accumulation of GAGs in the cells leads to progressive organ dysfunction, skeletal deformities, cognitive impairment, neurodegenerative disease in many, and shortened life expectancy. Although there is no cure for MPS II, enzyme replacement therapy (idosulfase) is effective in improving somatic symptoms and prolonging survival. Early identification and treatment give boys with MPS II the best chance at improved outcomes.

Newborn screening for MPS II is performed by measuring iduronate-2-sulfatase activity in dried blood spots. Screening has already been successfully implemented in Illinois and Missouri, with other states expected to follow once the decision is officially added to the RUSP. The Michigan Newborn Screening Program will be initiating next steps with its advisory committees to consider the addition of MPS II to Michigan’s panel. Michigan currently screens for two other lysosomal storage disorders, Pompe disease and mucopolysaccharidosis type I, which were added in 2017.
The Communication Algorithm

1. Hospitals/Midwives
   - Specimen Submitted
   - Report sent

2. MDHHS NBS Laboratory
   - Normal screens
   - Abnormal screens

3. MDHHS NBS Follow-up
   - Early, unsatisfactory, and borderline positive screens
   - Strong positive screens

4. Primary Care Physician/Medical Home
   - Report sent
   - Diagnosis confirmed
   - NBS Follow-up Coordinating Centers

[MI NBS Program Annual Report 2020]
NBS Follow-Up Program

• Responsible for referral of positive NBS to appropriate site:
  – Medical management center (for strong positive or repeat borderline positive screens)
  – Ensure repeat NBS for borderline positive
  – Ensure repeat NBS received for unsatisfactory samples
• Responsible for education, training and QA
• Maintains short and long-term follow-up databases
• Negative results sent to birthing hospital
<table>
<thead>
<tr>
<th>Hemoglobinopathies</th>
<th>Sickle cell anemia (Hb SS), hemoglobin SC disease, sickle beta thalassemia zero (Sβ0), sickle beta thalassemia plus (Sβ+), and hemoglobin H disease.</th>
</tr>
</thead>
</table>

| Metabolic Disorders                   | Amino acid disorders, fatty acid oxidation disorders, organic acid disorders, galactosemia, biotinidase deficiency.                          |

| Sickle Cell Disease Association of America, Michigan Chapter | 18516 James Couzens Detroit, MI 48235 Telephone: 313-864-4406 Toll-free: 800-842-0973 Fax: 313-864-9980 info@scolaami.org |

| Lysosomal Storage Disorders (LSD)     | Pompe Disease & Mucopolysaccharidosis Type (MPSI)                                                                                           |

| Children’s Hospital of Michigan Metabolic Clinic | 3860 Beaubien Blvd. Detroit, MI 48201-2192 Telephone: 313-832-9330 Fax: 313-745-8030 |

| Endocrine Disorders                    | Congenital adrenal hyperplasia (CAH), Congenital hypothyroidism (CH), CF, X-ALD, SMA                                                       |

| Michigan Medicine at the University of Michigan Department of Pediatrics | 1500 E. Medical Center Dr. D1225 MPB, Box .5718 Ann Arbor, MI 48109-0718 Telephone: 734-647-8938 Fax: 734-936-7918 |

| Cystic Fibrosis (CF)                   |                                                                                                                                           |

| Spinal Muscular Atrophy (SMA)          |                                                                                                                                           |

| X-linked Adrenoleukodystrophy (X-ALD)   |                                                                                                                                           |

| Primary Immunodeficiency Disorders     | Severe combined immunodeficiency disorder (SCID) and other primary immunodeficiency disorders with T-cell lymphopenia                          |

| 3950 Beaubien St. Detroit, MI 48201 Telephone: 313-806-6571 Pager: 313-745-0203; pager number 5706 Fax: 313-966-9701 |
For all “strong positive” screening results for an IEM:

- Metabolic team charged with contacting primary medical doctor identified on NBS card with recommendations:
  - Recommend time frame for primary doctor to evaluate the neonate
  - Detailed information on laboratory investigations needed for confirmation including information on sample collection and shipment (biochemical testing)
  - Initiation of treatment/intervention as appropriate
  - Information (fact sheet) on suspected IEM
After Confirmation of an IEM

- Metabolic/ Genetics clinic visit:
  - Detailed evaluation
  - Further diagnostic testing (enzymatic/molecular confirmation) as appropriate.
  - Management (multidisciplinary approach)
  - Genetic counseling
  - Education on disorder, diet, lifestyle
  - Provision of emergency management protocol
- Children’s Special Health Care Services (CSHCS)
“When You Assume…”

- Assuming a negative screen excludes that condition (false negatives)
  - Blood specimen obtained too early (< 24 hours; hypothyroidism, FAOD)
  - Inadequate protein intake (PKU, OA, AA)
  - Patient transfused (GALT, BIOT, Hgb)
  - Dextrose (suppresses catabolism, VLCAD, etc)

- Assuming a positive test is a false positive
  - Baby looks great! (not)
  - Premature (PKU, biotin, free carnitine)
  - Hyperalimentation (PKU, AA)
  - Antibiotics (C5-acylcarnitine)
  - Improper blood collection and handling (GALT, BIOT)

- Assuming a screen is negative because you have not heard otherwise
  - PMD of record at birth assumes responsibility of following NBS results

- Assuming proper confirmatory testing was ordered
Challenges in “All” NBS

• A NBS May Be:
  – Normal
  – False negative
  – False positive
  – True positive
    • “Classic” severe
    • Asymptomatic
    • Mild disease
    • Late-onset disease (adolescence or adult)
  – Another disease
    • Secondary condition
    • Unexpected condition

• False positive screens
  – Determination of appropriate cutoff values

• Disorders with no currently effective treatment
  – Benefits from an early and accurate diagnosis
  – Immediate supportive treatment of the infant
  – Possibility of participation in research of the disorder

• Challenges
  – Rarity of disorders
  – Shortage of guidelines
  – Identifying late onset disease
  – Identifying “carriers”
Failure in Newborn Screening

• Common misunderstandings
  – “It’s not (just) a PKU test”
    • Families often confused by results and reasons
  – “It’s not genetic testing”
    • Confusion with biochemical screening

• Increased confusion of goals of NBS – and potentially impacted the future of development of NBS
  – Privacy, parental consent
  – False positive screens, over-diagnosis, over-treatment, mild and late-onset disease, “non”-disease, anxiety, “burden of knowledge”, “patient-in-waiting”
Concerns about NBS

- False-positive screening results could place families at risk for increased stress and...

- "Pat Screening Successes"

  - Late onset disease

- "Vulnerable child"

- Diagnostic odysseys – Following NBS (and also prevented by NBS...)

Waisbren SE, et al. JAMA. 2003 PMID: 14625333
https://www.newsteps.org/about/screening-successes
NBS Resources for Physicians

- Follow-up Coordinating Centers and their Teams
- State provided provider fact sheets
- American College of Medical Genetics
  - Algorithms
  - ACT Sheet
- New England Acute Illness Protocols
  - UCD, FAOD, OA
  - http://newenglandconsortium.org/for-professionals/acute-illness-protocols/
- British Inherited Metabolic Disease Group
- Other websites
  - https://www.newbornscreening.info/
  - https://newsteps.org
<table>
<thead>
<tr>
<th>Newborn Screening Links</th>
<th>Website URL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Michigan Newborn Screening</td>
<td>Michigan.gov/newbornscreening</td>
</tr>
<tr>
<td><strong>Michigan Newborn Screening Online</strong> (Order placement website)</td>
<td>Michigan.gov/nbsorders</td>
</tr>
<tr>
<td>Michigan Critical Congenital Heart Disease Newborn Screening Program</td>
<td>Michigan.gov/cchd</td>
</tr>
<tr>
<td>Michigan BioTrust for Health Parental Consent Process Training</td>
<td>Michigan.gov/biotrust</td>
</tr>
<tr>
<td>Genetics Home Reference</td>
<td>medlineplus.gov/genetics</td>
</tr>
<tr>
<td><strong>Centers for Disease Control and Prevention Genomics Resources</strong></td>
<td>cdc.gov/genomics/resources</td>
</tr>
<tr>
<td>Newborn Screening Course</td>
<td><a href="https://courses.mihealth.org/PUBLIC/home.html">https://courses.mihealth.org/PUBLIC/home.html</a></td>
</tr>
<tr>
<td>American Academy of Pediatrics</td>
<td>aap.org</td>
</tr>
<tr>
<td><strong>Sickle Cell Disease Association of America – Michigan Chapter, Inc.</strong></td>
<td>scdaami.org</td>
</tr>
</tbody>
</table>
Hypothetical Case Presentation

- It’s Friday afternoon, 4:30pm
- Admin knocks on your door, brings you a fax that was just seen, apologizes, and asks how they can help
• 6 do female presenting to clinic following an abnormal newborn screen

- Born at 39 weeks' gestation, uncomplicated C-section, uncomplicated newborn course
- No concerns per parents since hospital discharge
- Breastfeeding well, + Vit D supplementation

Hypothetical Case Presentation
LYSosomal STORAGE DISORDER

STRONG POSITIVE TEST - NEEDS PHYSICIAN REVIEW

Dear Doctor,

The infant identified below as your patient has a strong positive result for Pompe Disease. Refer to the table below for action needed.

<table>
<thead>
<tr>
<th>Baby:</th>
<th>(MAIN)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accession #:</td>
<td>Kit Number:</td>
</tr>
<tr>
<td>Birth Date:</td>
<td>Specimen Type: Initial</td>
</tr>
<tr>
<td>Collection Date:</td>
<td>Medical Record:</td>
</tr>
<tr>
<td>Collection Age: 24 hours</td>
<td>Gestation: 39 wks</td>
</tr>
<tr>
<td>Birth Order: Single</td>
<td>Weight: 3682 grams</td>
</tr>
<tr>
<td>Birth Facility:</td>
<td>NICU:</td>
</tr>
</tbody>
</table>

Disorder: Possible Pompe Disease (Glycogen Storage Disease II)

<table>
<thead>
<tr>
<th>Lysosomal Storage Disorder</th>
<th>Patient Screening Result</th>
<th>Expected Screening Result</th>
<th>Determination</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-glucosidase (GAA)</td>
<td>0.99 μmol/L/hr</td>
<td>&gt; 2.00 μmol/L/hr</td>
<td>Abnormal</td>
</tr>
</tbody>
</table>

Interpretation: Possible Medical Emergency

Action Required:
- Possible
- Lysosomal Storage Disorder

*Please call the designated follow-up coordinating center immediately should clinical symptoms (e.g., hypotonia, cardiac hypertrophy, poor suck, macroglycemia, decreased feeding, tachypnea, lethargy) present.

Infant has been referred to designated follow-up coordinating center* for confirmatory testing and follow-up instructions.

Do not send diagnostic labs or initiate treatment before contacting the designated follow-up coordinating center*.

*The Michigan Department of Health & Human Services designated follow-up coordinating center is:

- Lysosomal Storage Diseases Clinic, Children's Hospital of Michigan. Phone: 313-832-9330.
After hours information, contact the metabolic consultant on call at 313-745-0203, page #96025.

- Pediatric Genetics, University of Michigan. Phone: 734-764-0579.
After hours information, page the on-call pediatric geneticist at 734-936-6267.
### NEWBORN SCREENING CONFIDENTIAL LABORATORY REPORT

**Final Report**

**Michigan Dept. of Health and Human Services**

**Bureau of Laboratories**

**3350 N Martin Luther King Jr Blvd**

**Lansing, MI 48906**

---

#### Baby's Name:

**Gender:**

**Weight:** 3,050 gms

**Accession #:**

**Kit #:**

**Med. Record #:**

**Specimen Type:**

---

#### Mother's Name:

**Disorder/Analyte(s)**

<table>
<thead>
<tr>
<th>Disorder/Analyte(s)</th>
<th>Patient Screening Results</th>
<th>Expected Screening Results</th>
<th>Determination</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amino Acid Disorders</td>
<td>Within Normal Limits</td>
<td>Within Normal Limits</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Fatty Acid Oxid. Disorders</td>
<td>Within Normal Limits</td>
<td>Within Normal Limits</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Organic Acid Disorders</td>
<td>Within Normal Limits</td>
<td>Within Normal Limits</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Endocrine Disorders</td>
<td>Within Normal Limits</td>
<td>Within Normal Limits</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Enzyme Disorders</td>
<td>Within Normal Limits</td>
<td>Within Normal Limits</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Hemoglobinopathy</td>
<td>Within Normal Limits</td>
<td>Within Normal Limits</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>Within Normal Limits</td>
<td>Within Normal Limits</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>SCID</td>
<td>Within Normal Limits</td>
<td>Within Normal Limits</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>ADA SCID</td>
<td>Within Normal Limits</td>
<td>Within Normal Limits</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>SMA</td>
<td>Within Normal Limits</td>
<td>Within Normal Limits</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>XLD C28:0-LPC</td>
<td>0.53 µmol/L</td>
<td>&lt; 0.24 µmol/L</td>
<td>Abnormal</td>
<td>1</td>
</tr>
</tbody>
</table>

**COMMENTS:** For questions regarding reported results please call 517-335-4181.

1. XLD Strong Positive. This infant has been referred to the newborn screening and coordinating program for XLD (734) 647-8938.
• Positive screen not as urgent for XALD
• Positive fact sheet sent to PCP from NBS state coordinating center, PCP faxes referral to choose follow-up center
• Patient seen by genetics for confirmatory testing/genetic counseling depending on sex of infant
• If positive, will be seen by Endocrinology & Neurology by 3-4 months of age, Hematology for discussion of BMT at follow-up positive counseling appointment
- Positive screen = urgent
- Positive fact sheet sent to PCP from NBS state coordinating center; coordinating center reaches out to PCP (or NICU/SCN if patient still admitted for newborn hospitalization)
- Patient evaluated same day (either in genetics clinic or inpatient/ED) for confirmatory testing
- If positive for IOPD, goal to start ERT by DOL 14
Take Aways

- Newborn screen abnormalities ≠ universal same acuity
- Time to appropriate follow-up is individual disorder dependent
- Lean on your NBS Follow-up Coordinating Centers to help assist appropriate evaluation
• NBS may not identify every affected individual with a disorder
• May not identify milder forms or variations of some conditions
• NBS is not meant to identify carrier status
• Will not identify disorders not on the MI NBS panel (even though they may be related to those disorders on the panel)
• Overall goal of NBS is to improve quality of life for babies through early diagnosis and treatment
• Time is very important in this process
• We don’t always have all the answers, but we’re here to be a resource for providers and for families
References

- MDHHS NBS Program. https://www.michigan.gov/mdhhs/0,5885,7-339-73971_4911_4916-64851--00.html
- ACMG ACT Sheets. https://www.acmg.net/ACMG/Medical-Genetics-Practice-Resources/ACT_Sheets_and_Algorithms.aspx
- Koppaka R. MMWR 2011. PMID: 21597455
Thank You!

• Special Acknowledgements
  – Adelyn Beil, MS MPH LCGC
  – Rachel Fisher, MS LCGC

• Michigan Medicine Pediatric Genetics Division
• NBS Lab Staff and Follow-up Center Staff