Seven Additional Newborn Screening Disorders Coming to NJ: Are You Ready?

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DISCLOSURES

- Genzyme, A Sanofi Company
  - Consultant, independent research contractor, member of advisory committees, speaker, clinical trial principal investigator
- NJDOH
  - MCH Block Grant recipient
- Chair, NJ NBS Pediatric Metabolic/Genetic Specialty Group
- Co-Chair, NJ NBS LSD and ALD Working Groups
WHAT ARE LYSOSOMES?

- Membrane-limited cytoplasmic organelles
- Contain cocktail of acid hydrolytic enzymes*
- Digest extracellular lipid, protein, carbohydrate, and nucleic acid macromolecules intracellularly
- Degrade cell membranes and organelles during apoptosis

*Glycosidase, peptidase, sulfatase, lipase, phosphatase, nuclease, peroxidase, reductase, thioesterase, etc.
## LYSOSOMAL STORAGE DISORDERS

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucopolysaccharidoses (11)</td>
<td>MPS I, MPS II, MPS III-A-D, MPS IV A-B, MPS VI, MPS VII, MPS IX</td>
</tr>
<tr>
<td>Glycoproteinoses (6)</td>
<td>Aspartylglucosaminuria, Fucosidosis, α-Mannosidosis, β-Mannosidosis, Sialidosis, N-acetyl-α-glucosaminidase def.</td>
</tr>
<tr>
<td>Multiple Enzyme Deficiencies (5)</td>
<td>Mucolipidosis II, Mucolipidosis III-A, Mucolipidosis III-B, Multiple Sulfatase def., Galactosialidosis</td>
</tr>
<tr>
<td>Glycogen Storage Disease (1)</td>
<td>Pompe Disease</td>
</tr>
<tr>
<td>Lysosomal Transport Defects (3)</td>
<td>Cystinosis, Sialic Acid Storage Disease, MMA</td>
</tr>
<tr>
<td>Lysosomal/endosomal Trafficking /fusion Defects (5)</td>
<td>N-P type C1, N-P type C2, Mucolipidosis IV, Danon Disease, Chediak-Higashi</td>
</tr>
<tr>
<td>Neuronal Cereoid Lipofuscinoses (11)</td>
<td>CLN1-3, CLN4A, CLN4B, CLN5-10</td>
</tr>
</tbody>
</table>
HOW ARE LYSOSOMAL STORAGE DISORDERS INHERITED?

- LSDs are inherited in an autosomal recessive (AR) fashion EXCEPT for Fabry Disease and Hunter Syndrome (MPS II), which are X-linked (XL)
  - Increased incidence with consanguinity (AR)
  - Large family cohorts with Fabry disease (XL)
LYSOSOMAL STORAGE DISORDERS

- Underdiagnosed and misdiagnosed due to:
  - Early demise (included in differential for NIH)
  - Later onset – residual enzyme activity level
  - Non-specific findings (substantial overlap)
- Normal appearance at birth – majority
- Normal development – variable time period
- No acute metabolic crisis
- Chronic, progressive evolution of symptoms in the absence of treatment
LYSOSOMAL STORAGE DISORDERS

Manifestations

Parenchymal (Visceral)
- Pulmonary (apnea, recurrent pneumonia, obstructive airway, pulmonary htn)
- CV (cardiomyopathy, arrhythmias, CHF, vascular occlusion, valvular disease)
- GI (FTT, N/V, episodic diarrhea, bloating)
- HSM (thrombocytopenia), hernias
- Proteinuria, renal failure

CNS
- Myopathy, szs, spasticity, bulbar palsies, ataxia, depression, peripheral neuropathy, intellectual decline

Connective Tissue
- Coarse facial features (macroglossia, gingival hyperplasia)
- Dysostosis multiplex (DM)
- Cutaneous findings (angiokeratomas, ichthyosis, xanthomas)

Sensorineural/mixed HL

Vision
- corneal clouding, cherry red spot, optic atrophy, glaucoma, lens opacities, ophthalmoplegia
GAUCHER DISEASE

<table>
<thead>
<tr>
<th>Gene/Enzyme</th>
<th>GBA/Acid β-glucosidase (glucocerebrosidase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td>Hepatosplenomegaly, anemia, thrombocytopenia, bone crises, Erlenmeyer flask deformities (femoral shaft), avascular necrosis and fracture (femoral/humeral head, vertebral bodies, pelvis), osteopenia, lytic lesions (humeral, tibial, fibular shaft), growth restriction, pulmonary hypertension, interstitial lung disease, cholelithiasis; strabismus, cortical thumbs, neck retroflexion with type 2</td>
</tr>
<tr>
<td>Testing</td>
<td>Enzyme level (residual activity not always reliable predictor of severity) and mutation analysis (some genotype/phenotype correlation)</td>
</tr>
<tr>
<td>Management</td>
<td>Monitor hematologic and biochemical parameters, organomegaly, quality of life, bisphosphonates</td>
</tr>
<tr>
<td>Treatment</td>
<td>Imiglucerase (Cerezyme) [1993], Velaglucerase alfa (VPRIV), Miglustat (Zavesca)<em>, Taliglucerase alfa (Elelyso), Eliglustat (Cerdelga)</em></td>
</tr>
<tr>
<td>Other</td>
<td>Avoid splenectomy; risk factor for Parkinson disease; increased incidence in individuals of Ashkenazi Jewish ancestry; continuum (3 major types, 1-3) and 2 subtypes (perinatal lethal &amp; CV)</td>
</tr>
</tbody>
</table>
# Fabry Disease

<table>
<thead>
<tr>
<th>Gene/Enzyme</th>
<th>GLA/α-Galactosidase A</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical features</strong></td>
<td>Acroparesthesias, crises, hypohidrosis, heat/cold intolerance, angiookeratomas, corneal opacities, retinal vascular lesions, episodic diarrhea, bloating, N/V, progressive renal insufficiency, ESRD, LVH, coronary and valvular disease, arrhythmias, cardiomyopathy, TIA, early stroke, depression, tinnitus, hearing loss, fatigue</td>
</tr>
<tr>
<td><strong>Testing</strong></td>
<td>Enzyme level (residual activity not always reliable predictor of severity) and mutation analysis</td>
</tr>
<tr>
<td><strong>Management</strong></td>
<td>Monitor renal, neurologic, and cardiac function, pain control, pancrelipase, aspirin, ACE inhibitors, valve replacement, dialysis, avoidance of stimuli that precipitate pain, avoidance of smoking</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Agalsidase beta (Fabrazyme) [2003]</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Most commonly reported features in women (heterozygotes) were cardiac (59%) and neurological (77%); treatment criteria and monitoring regimen should be the same in men and women; cardiac, renal, and cerebrovascular variant forms</td>
</tr>
</tbody>
</table>
# Pompe Disease

<table>
<thead>
<tr>
<th>Gene/Enzyme</th>
<th>GAA/α-1,4-Glucosidase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical features</strong></td>
<td>Cardiomegaly, hepatomegaly, hypotonia, cardiomyopathy, FTT, macroGLOSSIA, cardiorespiratory failure, ptosis, muscle weakness, exercise intolerance, sleep apnea, hearing loss, osteopenia, fx</td>
</tr>
<tr>
<td><strong>Testing</strong></td>
<td>Enzyme level (may require fibroblasts and/or muscle) and mutation analysis; mutational analysis may permit determination of CRIM status and whether immunomodulatory protocol is required</td>
</tr>
<tr>
<td><strong>Management</strong></td>
<td>Monitor cardiac, pulmonary, GI, nutrition, hearing, neurologic function, and fracture risk</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Aglucosidase alfa (Myozyme) [2006], (Lumizyme)</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Continuum (3 major types – classic infantile-onset, non-classic IO, and late-onset); high surgical/anesthesia risk; avoid certain agents (digoxin, ionotropes, diuretics); pseudodeficiency allele is common in Asian populations</td>
</tr>
</tbody>
</table>
POMPE DISEASE

“Newborn Screening, Diagnosis, and Treatment for Pompe Disease Guidance Supplement”

Kishnani, Priya; Hwu, Wuh-Liang; Atherton, Andrea; Bodamer, Olaf; Burton, Barbara; Day-Salvatore, Debra; Giugliani, Roberto; Jones, Simon; Kronn, David; Nakamura, Kimitoshi; Okuyama, Torayuki; Scott, C.; Swoboda, Kathryn

Supplement is scheduled to appear as a print-and-online companion to the July 2017 issue of Pediatrics. All supplements are published in the online edition at www.pediatrics.org and will be released online on the 1st of the publication month.
### MPS I

<table>
<thead>
<tr>
<th>Gene/Enzyme</th>
<th>Clinical features</th>
<th>Testing</th>
<th>Management</th>
<th>Treatment</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td>Umbilical/inguinal hernias, frequent URIs, facial coarsening, hepatosplenomegaly, macroglossia, hearing loss, corneal clouding, mitral/aortic valve regurgitation, gibbus deformity, joint ROM limitation, recurrent rhinitis, carpal tunnel syndrome, hydrocephalus, ID possible</td>
<td>Enzyme level (residual activity not always reliable predictor of severity) and mutation analysis (some genotype/phenotype correlation); pseudodeficiency alleles complicate diagnosis</td>
<td>Intervention for developmental delays; hats with visors/sunglasses to reduce glare; cardiac valve replacement prn; physical therapy, orthopedic surgery prn (joint replacement, atlanto-occipital stabilization, early median nerve decompression for carpal tunnel syndrome); shunting for hydrocephalus; tonsillectomy and adenoidectomy for eustachian tube dysfunction and/or upper airway obstruction; tracheostomy for sleep apnea, pulmonary hypertension, right heart failure; PE tubes; surgical intervention for cervical myelopathy.</td>
<td>Hematopoietic stem cell transplant (HSCT), ERT (Aldurazyme® [2003]), intrathecal ERT in clinical trials</td>
<td>Continuum (severe to attenuated)</td>
</tr>
</tbody>
</table>
**Mucopolysaccharidosis Type I Newborn Screening: Best Practices for Diagnosis and Management**

Lorne A. Clarke, MD, CM, FRCP, FCCMG1, Andrea M. Atherton, MS, CGC2,*, Barbara K. Burton, MD, FAAP, FACMG3, Debra L. Day-Salvatore, MD, PhD, FAAP, FACMG4, Paige Kaplan, MB, BCH, FRCP, FCCMG, FAAP, FACMG5, Nancy D. Leslie, MD6, C. Ronald Scott, MD7, David W. Stockton, MD, FACMG8, Janet A. Thomas, MD, FAAP, FACMG9, and Joseph Munzner, MD, PhD10

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**Table II. Challenges in predicting disease severity following positive NBS for MPS I**

- No biochemical criteria reliably distinguish MPS I subtypes
- Many signs and symptoms that establish an MPS I diagnosis in older patients do not differentiate between attenuated and severe phenotypes, or are not present in newborns
- In the absence of 2 pathogenic *IDUA* variants previously reported to be associated with defined disease severity, genotype/phenotype correlation is complicated by the existence of private (reported only in single individuals with MPS I) missense mutations that can not be used to predict the phenotype
- *IDUA* enzyme analysis is complicated by pseudo-deficiency because of:
  - Benign variants
  - Reduced in vitro enzyme activity in clinically unaffected individuals
  - Prevalence in African American population
Figure. Proposed decision making algorithm for positive MPS I newborn screen. VUS, variant of unknown significance (ie, non-recurrent missense variant).
### 17.1 Recommended Schedule of Assessments

<table>
<thead>
<tr>
<th></th>
<th>Initial Assessments</th>
<th>Every 6 Months</th>
<th>Every 12 Months</th>
<th>Every Other Year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General</strong></td>
<td></td>
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<tr>
<td>Demographics</td>
<td>X</td>
<td></td>
<td></td>
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<tr>
<td>Patient Diagnosis</td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Medical History</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td>Physical Examination</td>
<td>X</td>
<td>X</td>
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<tr>
<td>General Appearance</td>
<td></td>
<td></td>
<td>X</td>
<td>X</td>
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<tr>
<td><strong>MPS I Disease Clinical Assessments</strong></td>
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<tr>
<td>Neurologic/CNS</td>
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<tr>
<td>MRI of Brain</td>
<td>X</td>
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<tr>
<td>MRI of Spine</td>
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<tr>
<td>Median Nerve Conduction Velocity</td>
<td>X</td>
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<td>X</td>
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<tr>
<td>Cognitive Testing (EQ/IQ)</td>
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<tr>
<td><strong>Ophthalmologic</strong></td>
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<tr>
<td>Visual Acuity</td>
<td>X</td>
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<td></td>
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<tr>
<td>Retinal Examination</td>
<td></td>
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<tr>
<td>Corneal Examination</td>
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<tr>
<td><strong>Auditory</strong></td>
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<tr>
<td>Audiology</td>
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<tr>
<td>Cardiac</td>
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<tr>
<td>Echocardiogram</td>
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<td>EKG</td>
<td>X</td>
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<tr>
<td><strong>Respiratory</strong></td>
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<tr>
<td>FVC/FEV1</td>
<td></td>
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<td>X</td>
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<tr>
<td><strong>Gastrointestinal</strong></td>
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<tr>
<td>Spleen Volume</td>
<td>X</td>
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<tr>
<td>Liver Volume</td>
<td>X</td>
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<tr>
<td><strong>Musculoskeletal</strong></td>
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<tr>
<td>Skeletal Survey by X-ray</td>
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<tr>
<td><strong>Vitals and Laboratory Tests</strong></td>
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<tr>
<td>Height/Weight</td>
<td></td>
<td>X</td>
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<td>X</td>
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<tr>
<td>Head Circumference</td>
<td></td>
<td>X</td>
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<tr>
<td>Blood Pressure</td>
<td>X</td>
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<tr>
<td>Enzyme Activity Level</td>
<td></td>
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<tr>
<td>Urinary GAG Level</td>
<td>X</td>
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<tr>
<td>Uric Acid</td>
<td>X</td>
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<tr>
<td><strong>Antibody testing</strong></td>
<td></td>
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<tr>
<td>MPS I Health Assessment Questionnaire, or other tools exploring functional ability and quality of life</td>
<td>X</td>
<td>X</td>
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</table>
## MPS II

<table>
<thead>
<tr>
<th>Gene/Enzyme</th>
<th>Clinical features</th>
<th>Testing</th>
<th>Management</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Short stature, macrocephaly w/wo hydrocephalus, macroglossia, hoarse voice, hearing loss, hepatosplenomegaly, progressive airway disease, spinal stenosis, cardiac (valvular) disease, carpal tunnel syndrome, joint contractures, chronic diarrhea, delayed milestones, cognitive impairment may be severe, normal-near/normal intelligence possible</td>
<td>Enzyme level (residual activity not always reliable predictor of severity) and mutation analysis (some genotype/phenotype correlation)</td>
<td>Developmental, occupational, and physical therapy; shunting for hydrocephalus; tonsillectomy and adenoidectomy; positive pressure ventilation (CPAP or tracheostomy); carpal tunnel release; cardiac valve replacement; inguinal hernia repair; and hip replacement</td>
<td>Elaprase® [2006]</td>
</tr>
</tbody>
</table>
ENZYME REPLACEMENT THERAPY (ERT)

<table>
<thead>
<tr>
<th>BENEFITS</th>
<th>CHALLENGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safe and effective in reversing visceral manifestations</td>
<td>Does not cross the blood-brain barrier</td>
</tr>
<tr>
<td>Appears to retard and prevent progression of connective tissue manifestations</td>
<td>Does not penetrate well into skeletal muscle</td>
</tr>
<tr>
<td>No known teratogenicity to date</td>
<td>Does not reverse major structural damage (e.g. bone)</td>
</tr>
</tbody>
</table>
<pre><code>                                                                               | Antibody development; infusion-related reactions                                                |
                                                                               | Cost; need for regular infusions                                                               |
                                                                               | When to treat? Optimal dose and frequency                                                      |
</code></pre>
ERT

Infusion-Related
- Seen in 8.5%
- Discomfort, pruritis, burning, swelling at venipuncture site

Additional Reactions
- Seen in 4.5%
- Nausea, abdominal pain, diarrhea, rash, fatigue, headache, fever, dizziness, chills, tachycardia

Hypersensitivity
- Seen in 4.0%
- Pruritis, flushing, angioedema, urticaria, chest discomfort, back spasms, respiratory symptoms, hypotension
NIEMANN-PICK A/B DISEASE

<table>
<thead>
<tr>
<th>Gene/Enzyme</th>
<th>SMPD1/Acid Sphingomyelinase (A &amp; B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td>Jaundice, HSM, FTT, cherry red spot, irritability, sleep disturbance, progressive neurological deterioration</td>
</tr>
<tr>
<td>Testing</td>
<td>Enzyme level and mutation analysis</td>
</tr>
<tr>
<td>Management</td>
<td>Supportive</td>
</tr>
<tr>
<td>Treatment</td>
<td>Hematopoietic stem cell transplant</td>
</tr>
<tr>
<td>Other</td>
<td>Increased incidence in individuals of Ashkenazi Jewish ancestry; type B is allelic characterized primarily by visceral involvement and survival into adulthood</td>
</tr>
</tbody>
</table>
## KRABBE DISEASE

<table>
<thead>
<tr>
<th>Gene/Enzyme</th>
<th>GALC/Galactosylceramidase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical features</td>
<td>Extreme irritability, spasticity, and developmental delay; vision loss, walking difficulties, delayed milestones, regression</td>
</tr>
<tr>
<td>Testing</td>
<td>Enzyme activity and mutation analysis</td>
</tr>
<tr>
<td>Management</td>
<td>Supportive</td>
</tr>
<tr>
<td>Treatment</td>
<td>Hematopoietic stem cell transplant (HSCT) within first 3-4 weeks of life for presymptomatic individuals attenuates clinical course and improves survival, but is not curative</td>
</tr>
<tr>
<td>Other</td>
<td>30-Kb deletion associated with infantile form when homozygous; c.857G&gt;A found in late-onset</td>
</tr>
</tbody>
</table>
PEROXISISOME

- Organelle present in all human cells except mature erythrocytes
- Metabolic functions include $\beta$-oxidation of VLCFA, $\alpha$-oxidation of phytanic acid, and biosynthesis of plasmalogen and bile acids
- Two major subgroups of disorders
  - Biogenesis defects (e.g. Zellweger spectrum)
  - Single enzyme/transporter defects (e.g. X-linked adrenoleukodystrophy)
X-LINKED ADRENOLEUKODYSTROPHY

- Affects ~1 in 20,000 males
- At least 20% of heterozygote females are symptomatic
- Affects nervous system white matter and adrenal cortex – 3 main phenotypes in males
  - Childhood cerebral form (35%) manifesting between 4-8 years – ADHD, progressive impairment of cognition, behavior, vision, hearing, & motor function – total disability within 2 years
  - Adrenomyeloneuropathy (AMN) (~45%) – manifests in late 20s as progressive paraparesis, sphincter disturbance, sexual dysfunction, and often impaired adrenocortical function and is progressive
  - Addison only disease (10%) – primary adrenocortical insufficiency (average age of 7 years); AMN may develop later
X-ALD CONFIRMATORY TESTING

- MRI abnormal in males with neurologic symptoms (symmetric enhanced T2 signal in parieto-occipital region)
- 99% of males & ~80% of heterozygote females have elevated plasma VLCFA concentrations (C26:0; C24:0/C22:0; C26:00/C22:0)
- Mutation and deletion/duplication (~6%) analysis of the \( ABCD1 \) gene – 7% \( de \) \( novo \) alterations
X-ALD TREATMENT

- BMT – option for males with evidence of brain involvement by MRI but minimal neurologic or neuropsychologic dysfunction
- Corticosteroid replacement therapy for adrenal insufficiency – no effect on nervous system
- Physical therapy, support, and counseling
- MRI surveillance
## NBS for LSDs by MS/MS

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Prevalence</th>
<th>Referrals</th>
<th>Confirmations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabry disease</td>
<td>1/3,860 males</td>
<td>28</td>
<td>9</td>
</tr>
<tr>
<td>Pompe disease</td>
<td>1/8,684</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Gaucher disease</td>
<td>1/17,368</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Niemann-Pick A/B</td>
<td></td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Combined prevalence of 3 alone: 1/2,316

Referred for evaluation: 1/914

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<table>
<thead>
<tr>
<th>Disorder</th>
<th>Prevalence</th>
<th>Referrals</th>
<th>Confirmations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabry disease</td>
<td>1/13,341 males</td>
<td>34</td>
<td>3</td>
</tr>
<tr>
<td>Pompe disease</td>
<td>1/4,447</td>
<td>64</td>
<td>9</td>
</tr>
<tr>
<td>Gaucher disease</td>
<td>1/13,341</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>Niemann-Pick A/B</td>
<td></td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

Combined prevalence of 4: 1/2,354

Referred for evaluation: 1/333

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*Mechtler et al.: 2012 – 34,736 participants in Austria*

*Wittmann et al.: 2012 – 40,024 participants in Hungary*
NBS for LSDs by MS/MS
New Estimated Prevalence

- Fabry disease – 1/7,800 males
- Pompe disease – 1/27,500
- MPS I – 1/35,500
- Combined prevalence of the 3 alone – 1/7,500
  - Combined incidence of all LSDs previously estimated to be 1/6,000
- Estimates based on NBS are 2 to 4 times greater than that estimated by clinical diagnosis

- Pompe disease – 1/11,300
  - 4 infantile,
  - 41 possible late-onset
  - 47 carriers
  - 29 pseudodeficiency
  - 63% of those tested were unaffected
- X-ALD – 1/11,800
  - 46 mutations (28M:18F)
  - 80% of positive screens confirmed to have pathogenic variant


NY STATE NBS RESULTS AS OF 2/7/2017 (NBSTRN) – 543,00 screens
NJ NBS FOLLOW-UP for LSDs/X-ALD

• All infants with a positive NBS in NJ for a lysosomal or peroxisomal disorder will need to be evaluated by a consultant
• Long-term management and follow-up will be critical
• Detailed prospective data collection needs to be a priority
Newborn Screening
It’s more than PKU

Scott Shone, PhD
April 25, 2017

Learning Objectives

- Understand the importance of newborn screening and the impact of early intervention.

- Explain the difference between screening and diagnostic laboratory tests.
Screening Tests vs. Diagnostic Tests

**Screening Tests**
- Detects potential disease indicators
- Testing for large numbers of asymptomatic people
- Less expensive
- Done quickly
- Minimize false negatives [missed cases]

**Diagnostic Tests**
- Establishes disease presence/absence
- Testing for small numbers of symptomatic people or those with positive screening tests
- More expensive
- Can take longer
- Minimize false positives [unnecessary treatments]

Different Models for Screening Newborns
In the beginning there was only PKU

Dr. Robert Guthrie

PKU test on blood spots developed in 1961
Federal Mandates
Why these disorders?

Key Components of Newborn Screening

- Education (throughout the process)
- Screening, including specimen collection and testing
- Follow-up and result reporting
- Diagnostic confirmation
- Management
- Program evaluation and Continuous Quality Improvement
Why these disorders?

“10” Wilson-Jungner Criteria

- Important public health concern
- Diagnosis and treatment are available
- Has a latent stage; natural history understood
- Testable in an acceptable way
- Agreed policy on whom to treat
- Economic cost per case “balanced”
- Case finding should be continuous

NBS in NJ: Not just PKU anymore!

**Why these disorders?**

- PKU
- +CH
- +GALT
- +HGB
- +BD + CAH + CF + MSUD
- + 4 FAO + 6 OA + 2 UC
- + 10 FAO + 9 OA + 5 AA/UC + 2 Metabolic
- + SCID

Number of Disorders per Year:

- 1964: 1 PKU
- 1978: 2 +CH
- 1982: 3 +GALT
- 1990: 4 +HGB
- 2001: 8 +BD + CAH + CF + MSUD
- 2002: 21 + 4 FAO + 6 OA + 2 UC
- 2009: 54 + 10 FAO + 9 OA + 5 AA/UC + 2 Metabolic
- 2014: 55 + SCID

- NJ NSARC

[Diagram showing the process from PKU to SCID and the role of various committees and organizations like HRSA, SACHD, and NJ Health.]
NBS in NJ: Not just PKU anymore!

NJ Newborn Screening Program

- Single screen collected at 24 to 48 hrs of age
- ~99,500 births
  - ~118,000 specimens
- 55 disorders
  - SCID – 6/30/2014
- $150 / initial specimen
NBS System Process

ANALYTICAL

Continuous Quality Improvement

PRE ANALYTICAL
- Specimen Received
- Specimen Transported
- Specimen Collection
- Infant Born
- Parent & Provider Education

TESTING
- Specimen Punched
- Testing Performed
- Results Verified

RESULTS
- Results Reported

POST ANALYTICAL
- Physician and Parent Notified of Presumptive Positive Result
- Diagnostic Testing
- Diagnosis
- Treatment
- Long-term Follow-up And Management

Continuous Quality Improvement:

- Initial Newborn Screening Request
- Specimen Submitted By
- Baby's Physician
- Hospital Name and Address
- Baby's Medical Record No.
- Baby's Last Name (Print)
- Baby's First Name (Print)
- Mother's Name (Last Name, First Name)
- Cl. State (2)
- Phone No.
- City, State, Zip
- Hospital Name and Address
- Baby's Physician Name and Address

New Jersey Department of Health

Infant Born Specimen Collection Specimen Transported Specimen Received Results Reported Results Verified Testing Performed Specimen Punched Continuous Quality Improvement

Parent & Provider Education
Recommended Timeline

Day 1  Day 2  Day 3  Day 4  Day 5  Day 6  Day 7

Birth  Collection  Receipt in NBS Lab  Report PP Critical Results  Report All PP Results  Complete testing
What happens to the results?

- Normal Results
- Abnormal Results
  - Borderline
  - Repeat in 2 days
  - Presumptive
    - Fax results to Follow-up
    - Call results to Follow-up
    - Immediate referral to appropriate consultant
- Unsatisfactory Specimens
  - Call submitter to submit repeat

Initial Normal Results
- Submitter

All Abnormal Results
- Submitter
- Doctor of Record

All Repeat Results
- Submitter
- Doctor of Record

How to get results

1. Voice Response System
2. Call NBS Laboratory
How to get results

1. Voice Response System
2. Call NBS Laboratory
3. Fax Release Form
New Jersey NBS Program

- 1964 through 2016

- 4,016 confirmed classic cases
  - From 45 of the 55 disorders on our panel

- 3,250 cases of variant forms and carriers
Illness, irreversible damage, death

Early intervention, no/reduced damage, longer and healthier life