Lysosomal Storage Diseases: A Pilot NBS and Examination of the Associated Ethical, Legal and Social Issues

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# Financial Disclosures

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<th>Type of Affiliation/Financial Interest</th>
<th>Name of Corporate Organization</th>
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<tr>
<td>Grants/Research Support</td>
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Pilot NBS

Goal

– To conduct a pilot NBS for Fabry, Gaucher, Pompe, and Niemann Pick A/B

Approach

– Study subjects:
  • All infants born at 4 high birth rate, ethnically diverse hospitals are eligible
  • Expected enrollment: 75K-80K infants over four years
– Consent Procedure:
  • Multistep process to educate families about the study
  • Waiver of written consent with documentation of verbal consent and/or
  • Locked box to drop labeled study brochures at nursing stations
– Enzyme activities will be measured at NYS NSP using multiplexed MS-MS
– Positive samples will be shared with NBSTRN VRDBS

Starting April 2013 at Mount Sinai, other sites will start May-July 2013
After Screening...

• Notification and confirmatory testing
  – All babies with abnormal NBS for LSDs will be referred to Mount Sinai
  – Initial exam and disease-specific confirmatory testing will be performed for free
    • Enzyme assay on WBC
    • Genotyping

• True and questionable positives will be followed/treated at Mount Sinai
  – Extensive LSD experience and infrastructure
    • International Center for Fabry Disease
    • Comprehensive Gaucher Disease Treatment Center
    • International Center for Types A and B Niemann Pick Disease
    • Pompe patients will be reviewed with Co-Investigator Dr. Priya Kishnani
  – Benefit of uniform data collection/entry by committed study team
Natural History Studies

Goals:

• To describe the natural history of disease in presymptomatic patients
• To define the optimal time to initiate treatment for each disorder
• To develop evidence-based evaluation and treatment algorithms for each disorder prior to the initiation of mass newborn screening

Approach:

• Retrospective:
  Chart review of hundreds of existing diagnosed patients focused on historical earliest signs/symptoms of disease

• Prospective:
  To develop long-term follow up registries of infants identified at birth through this pilot study in collaboration with the NBSTRN
• Study Population:
  – Initial enrollment will be limited to infants identified through pilot NBS and enrolled in a natural history study

• Development of Databases
  – Reviewed NBSTRN and Illinois LSD datasets and commercial disease registries
  – Consultation with disease experts to define relevant datapoints
• Disease-Specific Data Elements
  – Medical History (initial and interval) data elements were developed to capture earliest onset signs/symptoms
    • Specific questions to capture predicted earliest s/s
    • General questions to capture unexpected earliest s/s
    • All questions include dropdown menu to capture age of onset
  – Family history
  – Physical examination
  – Laboratory /Radiographic /Consultative
Common data elements
- NBSTRN data elements were used as a general template
  - Demographics
  - NBS results
  - General neonatal history
  - Developmental assessment
  - Medications

EMR templates will “mimic” RedCap datapoints
- Ensure complete data collection
- Simplify RedCap data entry
Part 1: ETHICAL

Goal:
To define ethical concerns related to newborn screening for LSDs in general and later onset disorders in particular

Approach:
• Qualitative interviews and quantitative, validated questionnaires to evaluate the parental impact of a positive NBS for LSDs
• Results of interviews, questionnaires, and pilot NBS will be discussed in a formal Ethics panel in Year 5.
Part 2: FINANCIAL

Goal:
To evaluate the financial impact of NBS for LSDs on affected families after diagnosis

Approach:
• Medical billing and insurance information related to the LSD diagnosis will be analyzed to assess annual cost of care and treatment.

• Guided, open ended interviews to assess how the cost of their child’s treatment financially impacts daily living.
Part 3: MEDICOLEGAL

Goals:
To discuss the unique “duty to re-contact” issues associated with diagnosing newborns for disorders that might not manifest for decades

Approach:
• A panel of experts in medical professional liability and minor trust law as well as the medical and bioethics teams will be assembled in year 5 to develop, publish, and present opinion statements
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