Implementation of Newborn Screening for Severe Combined Immune Deficiency

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NBSTRN-CC
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American College of Medical Genetics ACT SHEET

**Combined Immunodeficiency (SCID) and Conditions on T Cell Lymphopenia**

Combined Immunodeficiency (SCID) includes a group of rare but serious, and potentially fatal, diseases in which T lymphocytes fail to develop and B lymphocytes are either absent or compromised. This leads to the term “combined.” Untreated patients develop life-threatening infections due to the screening test for T cell receptor antigen molecules (TRAC), a byproduct of normal T cell activation. In certain related conditions with low T cells, for example Deficiency Syndromes with may cause low T cells and low TRAC.

**FOLLOWING ACTIONS:**
Inform them of the newborn screening results. Point out that additional tests are required to...
Implementation Status

Selected Populations

No Screening

Screening

Pilots/Screening in 2013

Newborn Screening Translational Research Network
Estimated Newborns Screened Through December 31st 2012

*Based on annual birthrate
**3 week total
***NICHD Pilot

Newborn Screening Translational Research Network
### Selected Stats

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
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<tbody>
<tr>
<td>Total Number of Newborns Screened by 12/31/12</td>
<td>2.85 M</td>
</tr>
<tr>
<td>Percentage of Births Screened</td>
<td>45%</td>
</tr>
<tr>
<td>States Planning Pilots or Screening in 2013</td>
<td>12</td>
</tr>
<tr>
<td>Estimated Percentage of Births Screened by 2014</td>
<td>62%</td>
</tr>
<tr>
<td>Clinically Diagnosed Cases Since RUSP Addition in Non-screening States</td>
<td>15</td>
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Resources for NBS Laboratories

- **CDC**
  - Conduct Individualized Laboratory Training
  - Support Laboratory Test Development
  - Supply Quality Control Reference Materials
  - Provide Proficiency Testing through NSQAP

- **NICHD**
  - National Pilot Protocols and Algorithms
  - R4S SCID Data Portal through NBSTRN
  - Monthly Stakeholder Calls through NBSTRN
  - Information Resource through NBSTRN
Clinical Laboratory and Standards Institute (CLSI) Guideline ILA-36

- "Newborn Blood Spot Screening for SCID by Measurement of T-cell Receptor Excision Circles"
- Approved Dec 2012; Publication scheduled for May 2013
- Addresses laboratory operations, instrumentation, TREC assay protocols, automated methodologies, diagnostic tests, short-term and long-term follow-up.

CDC Cooperative Agreements

- Oct 2011-Sep 2013
- Michigan: More than 150,000 screened; 4 SCID found
- Minnesota: Completed method development; began screening Jan 2013
**R4S SCID Module**

- **NBSTRN funded the SCID module for R4S**
- **Facilitates analytical validation of screening assay**
- **Collects clinical information**
- **Tutorials can be arranged at any time**
- **Co-curators**
  - Roshini Abraham, PhD
  - Fred Lorey, PhD

**Condition Types**

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>SCID</td>
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<tr>
<td>Leaky SCID/Omenn Syndrome</td>
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<tr>
<td>Variant SCID</td>
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<tr>
<td>Syndromes with T cell impairment</td>
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<tr>
<td>Secondary T cell lymphopenia other than preterm alone</td>
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<tr>
<td>Preterm alone</td>
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**Conditions by Flow Phenotyping**

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<tr>
<td>T-B+NK-</td>
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<tr>
<td>T-B-NK-</td>
</tr>
<tr>
<td>T-B-NK+</td>
</tr>
<tr>
<td>T-B+NK+</td>
</tr>
<tr>
<td>Other</td>
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Resources for Health Care Providers

HRSA, ACMG
- Clinical Decision Support Materials
- ACT Sheets
- Available online

Immune Deficiency Foundation
- SCID Newborn Screening Toolkit for Advocates
- Rotavirus Vaccine Pamphlet
- Parent Education Materials

CDC, APHL, and Jeffrey Modell Foundation
- Two-year fellowship for post-doctoral candidates
- Newborn screening research including immune deficiencies
IDF offers educational resources to families and state

- IDF SCID Newborn Screening Campaign website and blog
- Educational guides to be of use to the states in their follow up protocols for SCID screening
- Two educational guides for parents have been developed by IDF and experts in SCID with the help of the New York-Mid-Atlantic Consortium for Genetic and Newborn Screening Services (NYMAC).

- Targeted advocacy actions

- IDF will be holding the IDF 2013 National Conference in Baltimore, MD June 27-29, 2013
Resources for NBS Researchers

https://www.nbstrn.org/resources/scid-resources
Expansion of SCID Newborn Screening Pilots

- NIH initiated project to enable additional states to pilot screening – Dr. Michele Caggana, PI

- Key Features
  - Initiates pilots in high number birth states (New York, California)
  - High capacity assay development (New York, California)
  - Regionalization model
    - Puerto Rico → Massachusetts
    - Louisiana → Wisconsin
  - CDC quality assurance program
  - Utilize NBSTRN
  - SCID data portal
  - Monthly conference calls to share expertise
Characteristics of SCID Cases
Race or Ethnicity

New York and California Pilots
N = 9

- Asian

Duke Retrospective Study
N = 111

- African American
- Hispanic
- American Indian
- Caucasian
- Arabic
### SCID

**ID**  
Source of information  
State

**Birth weight**  
Neonatal complications  
Type of neonatal complications

**Type of neonatal complications-other, spec**  
Sex  
Race

- Unknown  
- Yes  
- No

- Infection/sepsis  
- Antibiotics  
- Hypoglycemia  
- IV fluids  
- Jaundice  
- Premature (< 37 weeks gestation)  
- Transfused  
- Respiratory distress  
- APGAR < 5  
- Seizures  
- Other
California Cases to Flow Cytometry in First 18 Months

- 10 Typical SCID
- 1 Leaky SCID (Ommen Syndrome)
- 4 Variant SCID
- 8 Syndromes with low T cells
- 7 Secondary low T cells
- 5 Preterm births

Normal (81)
99.91% specificity; missed cases partial ADA, MHC-II.

- Of infants called for confirmatory flow cytometry, 30% had clinically significant T cell lymphopenia.

- Centralized flow cytometry as a 2nd tier test within the screening program permits timely and consistent diagnosis.

- All 11 infants with SCID received definitive treatments, with >90% survival at 6-21 months, superior to outcomes reported for SCID without newborn screening.

- Newborn screening offers the opportunity to study and treat pre-symptomatic immunodeficient infants with a wide spectrum of T lymphopenic disorders.
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Discussion

❖ Thank you!