The SCID Screening Experience in New York State

Michele Caggana, Sc.D., FACMG
New York State Department of Health
Newborn Screening Program
Automated assay developed and validated 12/2009-9/2010

Validation package submitted 9/08/2010

CLEP and emergency regulation approved 9/27/2010

SCID screening started 9/29/2010

1st “True SCID” baby detected 12/27/2010

New presumptive positive action category added 1/25/2011

Commissioner of Health officially adds SCID to NSP panel 4/12/2011
SCID SCREENING ALGORITHM

Dried Blood Spot Specimen

Multiplex PCR (TREC/RNaseP)

TREC ≥200 and RNase P WAL

SCREEN NEGATIVE

TREC values are copies/µL whole blood RNaseP values are Cq

RNase P ≥ 35

Sample is retested in duplicate

TREC <200

2 of 3 RNaseP WAL and 2 of 3 TREC < 200
OR Average of 3 TREC ≥200

SCREEN NEGATIVE

2 of 3 RNaseP WAL AND 2 of 3 TREC < 200
AND Average of 3 TREC >125<200
AND Gestational age ≥37
AND Has never been a PP before

PRESUMPTIVE POSITIVE

2 of 3 RNaseP WAL AND 2 of 3 TREC <200
AND Average of 3 TREC <200
AND Gestational age <37

REPEAT PREMATURE

2 of 3 RNaseP WAL AND 2 of 3 TREC <125
AND Gestational age ≥37
OR Average of 3 TREC <200 if a previous PP
OR Average of 3 TREC <125 if an initial specimen

REFERRAL

TREC values are copies/µL whole blood RNaseP values are Cq
In the Beginning......

- TREC $\geq 200$
- RNase P $\geq 35$ Cq

- 9/29/2010 to 1/24/2011
- No PP category
- Every baby < 200 TREC$\mathrm{s}$ referred to flow cytometry
- 166 referrals to flow cytometry
- $\sim$41 referrals per month (1 in 530)
In the Middle......

- TREC ≥ 200 and RNase P  ≥ 35 Cq
- TREC< 150

- 1/25/2011 to 7/20/2011
- PP category introduced; ≥150 ≤200 repeat sample
- Every baby < 150 TREC referred to flow
- 99 referrals to flow cytometry
- ~20 referrals per month (1 in 1,100 babies)
Current......

- TREC ≥ 200
- and
- RNase P ≥ 35 Cq

- TREC <125 (initial)

- 7/21/2011 to present
- PP category altered; >125 <200 repeat sample
- Every baby < 125 TREC referred to flow
- 28 referrals to flow cytometry
  ~9 referrals per month (1 in 2,400 babies)
SCID Testing Summary

- Number Infants Screened: 245, 631
- Non-Normal Results: 764
  - Full Term: 489
    - Flow requested: 279
    - Repeat NBS: 210
  - Premature (<37 weeks GA): 275
    - Flow requested: 6
    - Repeat NBS: 269
- Confirmed Cases: 32
  - SCID: 5
  - SCID Variant: 1
  - Other (Non-SCID): 26
### Results for Babies with Abnormal Flow Cytometry

<table>
<thead>
<tr>
<th>Count</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>SCID</td>
</tr>
<tr>
<td>1</td>
<td>T-B+NK+ SCID (congenital anomalies)</td>
</tr>
<tr>
<td>1</td>
<td>CHARGE syndrome T-B+NK+; CHD7 mutation</td>
</tr>
<tr>
<td>6</td>
<td>DiGeorge Syndrome</td>
</tr>
<tr>
<td>8</td>
<td>Idiopathic T-cell lymphopenia</td>
</tr>
<tr>
<td>1</td>
<td>Down syndrome</td>
</tr>
<tr>
<td>1</td>
<td>Chemotherapy for leukemia</td>
</tr>
<tr>
<td>1</td>
<td>Surgical thymectomy</td>
</tr>
<tr>
<td>5</td>
<td>Low CD19; unknown etiology</td>
</tr>
<tr>
<td>3</td>
<td>Abnormal CBC; 2 neutropenia; 1 low absolute lymphocyte count</td>
</tr>
</tbody>
</table>
A CLOSER LOOK

Baby Girl S.  Hispanic  Tx: 40 DOL
ADA deficiency
Prophylaxis (Bactrim and fluconzaole)
Adagen therapy
Exploring PGD for HLA match; vaccinated
“Doing very well”

Baby Boy O.  Black  Tx: 30 DOL
ADA deficiency
Prophylaxis (Bactrim, IVIG); off these 11/8/11
Adagen therapy; vaccinated
“Doing very well”
**A CLOSER LOOK**

**Baby Boy R.**  Hispanic  
X-linked SCID  
Haploidentical transplant from mom  
Known affected sibling  
“Doing very well”  

**Baby Boy S.**  Asian (Indian)  
X-linked SCID  
“Doing very well”
A CLOSER LOOK

- Baby Girl M. Caucasian  
  Tx: >1 YOL  
  30 days after "NBS"

- JAK3, trick specimen

- Hospitalized with pneumonia; IVIG infusions; PICU

- Transplanted in late May 2011

- Has some gastrointestinal malabsorption issues; otherwise doing and well

- Immunologist recognized SCID at PICU consult
<table>
<thead>
<tr>
<th>Baby Girl D.</th>
<th>Caucasian</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRECs</td>
<td>75**</td>
</tr>
<tr>
<td>T cell counts:</td>
<td>600 at 10 DOL</td>
</tr>
<tr>
<td></td>
<td>200 at 61 DOL</td>
</tr>
<tr>
<td>CD8:</td>
<td>140</td>
</tr>
<tr>
<td>Naïve T cells:</td>
<td>“Low”</td>
</tr>
<tr>
<td>Mitogen response:</td>
<td>“Normal”</td>
</tr>
<tr>
<td>Maternal engraftment?</td>
<td>“No”</td>
</tr>
<tr>
<td>IL7R defect?</td>
<td>Normal functional study</td>
</tr>
</tbody>
</table>

Baby is being monitored; T cells rebounding (11/8/11)
<table>
<thead>
<tr>
<th>Baby Girl S.</th>
<th>Caucasian</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRECs</td>
<td>143 (PP)</td>
</tr>
<tr>
<td>T cell counts:</td>
<td>741 (3944-4790)</td>
</tr>
<tr>
<td>CD4 and CD8:</td>
<td>“Low”</td>
</tr>
<tr>
<td>Naïve T cells:</td>
<td>“pending”</td>
</tr>
<tr>
<td>Mitogen response:</td>
<td>“a little low”; not &lt;10%</td>
</tr>
</tbody>
</table>

Baby is being monitored

Was vaccinated
SO WHAT’S THE INCIDENCE??

Pure SCID: 1 in 40,939

All Immunodeficiency: 1 in 7,676

Exclude:
Child on chemotherapy
8 cases of ITCL
Surgical thymectomy 1 in 11,165
ISSUES AND INSIGHTS

- PP category reduced referrals by 53%
- Zero TREC rule for premature infants
- Further adjustment of cutoff and PP category
- Minimize turnaround time – 30 DOL target
Thanks to our Immunologists Dr. V. Bonagura

Early input and enthusiasm
Quarterly phone calls
Annual in-person meetings
MORAL SUPPORT AND HELPFUL DISCUSSIONS

- Mei Baker, Ph.D
- Anne Comeau, Ph.D
- Fred Lorey, Ph.D
- Amy Brower, Ph.D and the NBSTRN
- Beth Vogel, M.S., CGC