

The SCID Screening Experience in New York State



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**New York State Department of Health
Newborn Screening Program**





COUNTDOWN TO SCID

- 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 values are copies/ μ L whole blood RNaseP values are Cq

TREC ≥ 200
and
RNase P WAL

SCREEN NEGATIVE

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

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

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

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

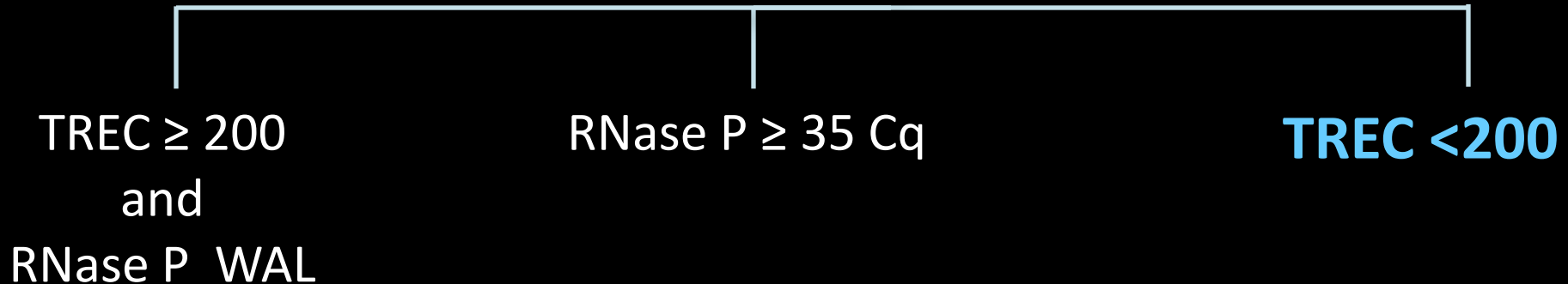
SCREEN NEGATIVE

PRESUMPTIVE POSITIVE

REPEAT PREMATURE

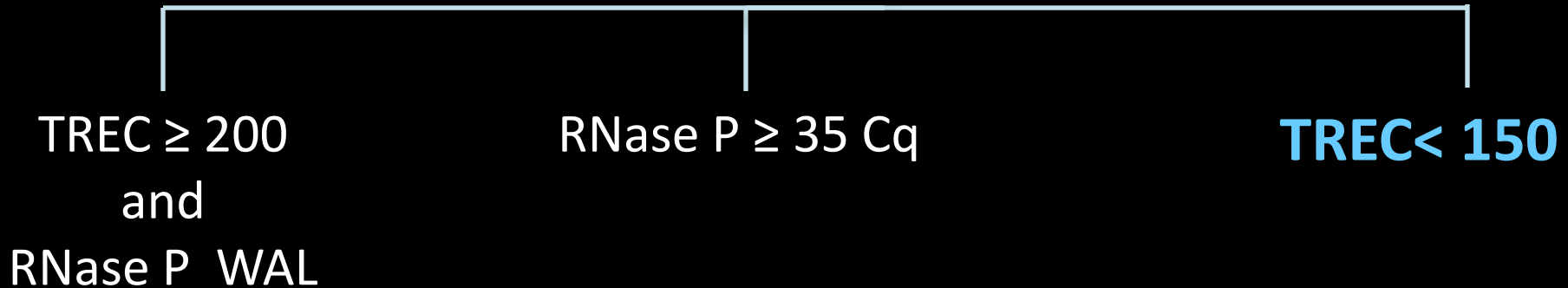
REFERRAL

In the Beginning.....



- **9/29/2010 to 1/24/2011**
- **No PP category**
- **Every baby $<$ 200 TRECs referred to flow**
- **166 referrals to flow cytometry**
~41 referrals per month (1 in 530)

In the Middle.....



- 1/25/2011 to 7/20/2011
- PP category introduced; $\geq 150 \leq 200$ repeat sample
- Every baby < 150 TRECs referred to flow
- 99 referrals to flow cytometry
~20 referrals per month (1 in 1,100 babies)

Current.....



TREC \geq 200
and
RNase P WAL

RNase P \geq 35 Cq

**TREC $<$ 125
(initial)**

- 7/21/2011 to present
- PP category altered; $\geq 125 \leq 200$ repeat sample
- Every baby $<$ 125 TRECs 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	285
• 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

5 SCID (2 ADA, 2 IL2RG, 1 JAK3)

- 1 T-B+NK+ SCID (congenital anomalies)
- 1 CHARGE syndrome T-B+NK+; CHD7 mutation
- 6 DiGeorge Syndrome
- 8 Idiopathic T-cell lymphopenia
- 1 Down syndrome
- 1 Chemotherapy for leukemia
- 1 Surgical thymectomy
- 5 Low CD19; unknown etiology
- 3 Abnormal CBC; 2 neutropenia; 1 low absolute lymphocyte count

A CLOSER LOOK



Baby Girl S. **Hispanic** **Tx: 40 DOL**

ADA deficiency

Prophylaxis (Bactrim and fluconazole)

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

Tx: 59 DOL / BMT

X-linked SCID

Haploidentical transplant from mom

Known affected sibling

“Doing very well”

Baby Boy S.

Asian (Indian)

Tx: 102nd DOL / BMT

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**

TWO MORE



Baby Girl D.

Caucasian

TRECs

75**

T cell counts:

600 at 10 DOL

200 at 61 DOL

CD8:

140

Naïve T cells:

“Low”

Mitogen response:

“Normal”

Maternal engraftment?

“No”

IL7R defect?

Normal functional study

Baby is being monitored; T cells rebounding (11/8/11)

TWO MORE



Baby Girl S.

Caucasian

TRECs

143 (PP)

T cell counts:

741 (3944-4790)

200 at 61 DOL

CD4 and CD8:

“Low”

Naïve T cells:

“pending”

Mitogen response:

“a little low”; not <10%

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

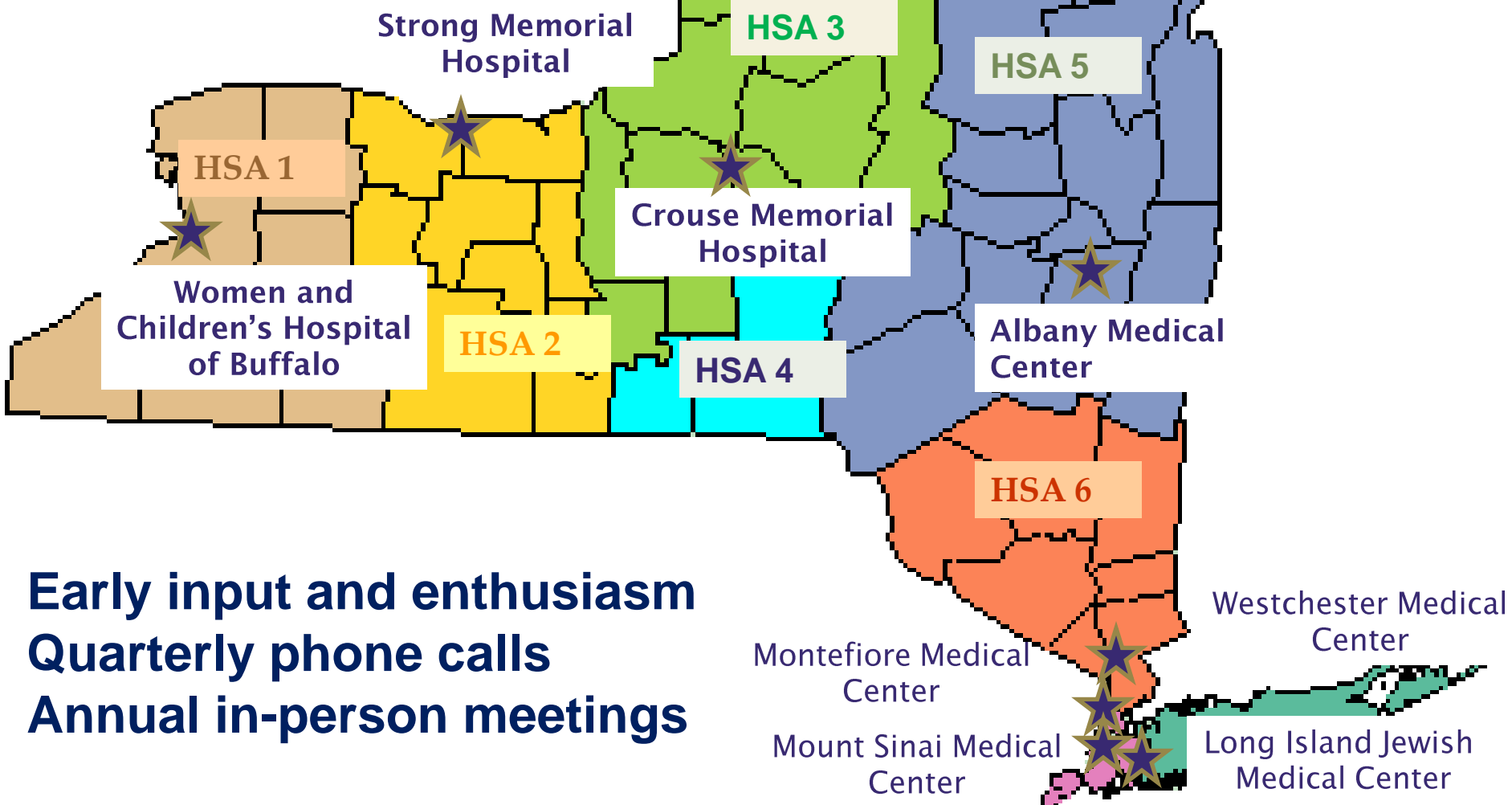
8 cases of ITCL

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

SCID Newborn Screening Staff



MORAL SUPPORT AND HELPFUL DISCUSSIONS

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