SCID Secondary Conditions Identified by the Texas Newborn Screening Program

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October 27, 2014

SCID NBS Screening

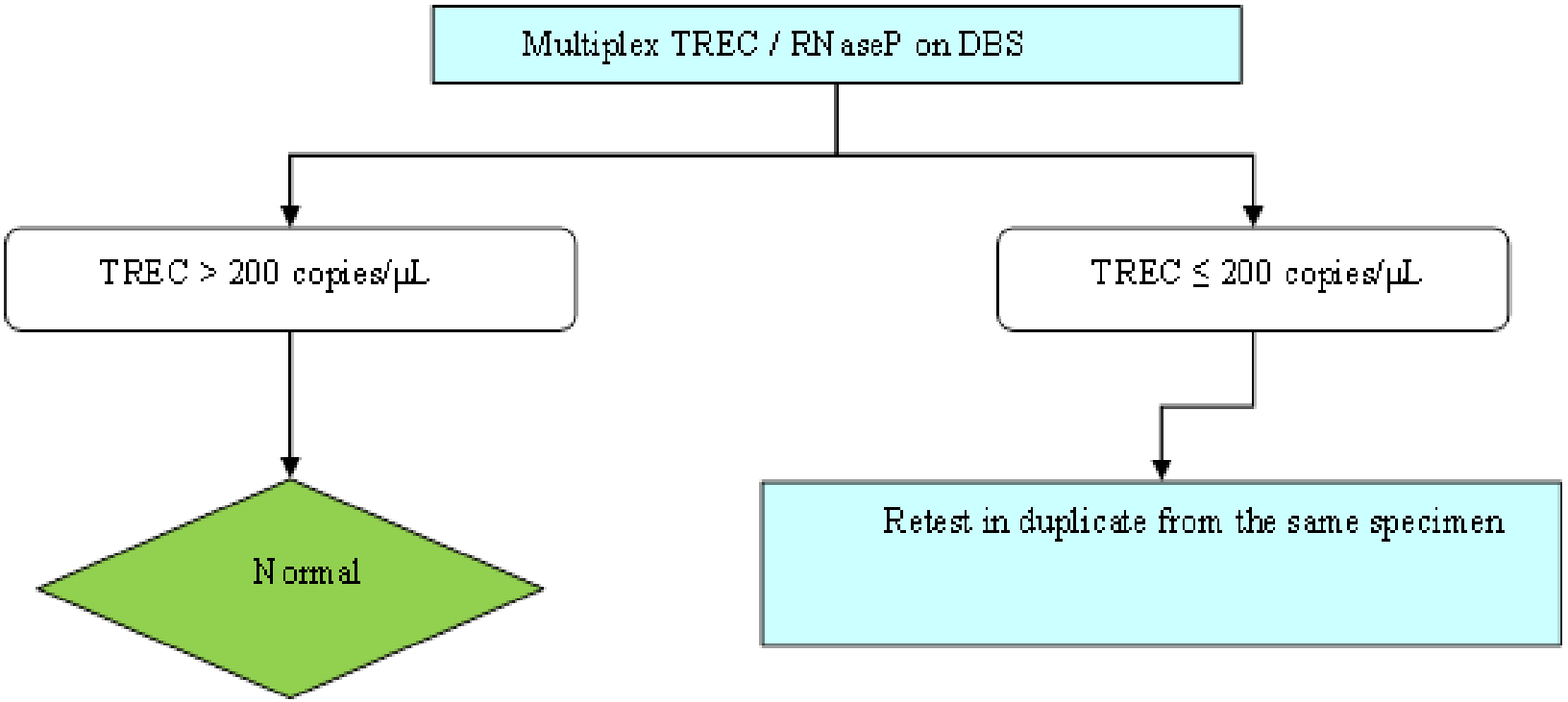
- SCID is a group of rare inherited immune disorders in which T lymphocytes fail to develop and B lymphocytes are either absent or compromised
- Incidence is ~1/58,000
- Over 15 known gene defects, most common of which is an X linked form
- Untreated babies develop recurrent bacterial viral and fungal infections and die by 1 year of age
- Early treatment by HSCT can be life saving

SCID Secondary Conditions Identified by Texas NBS Program

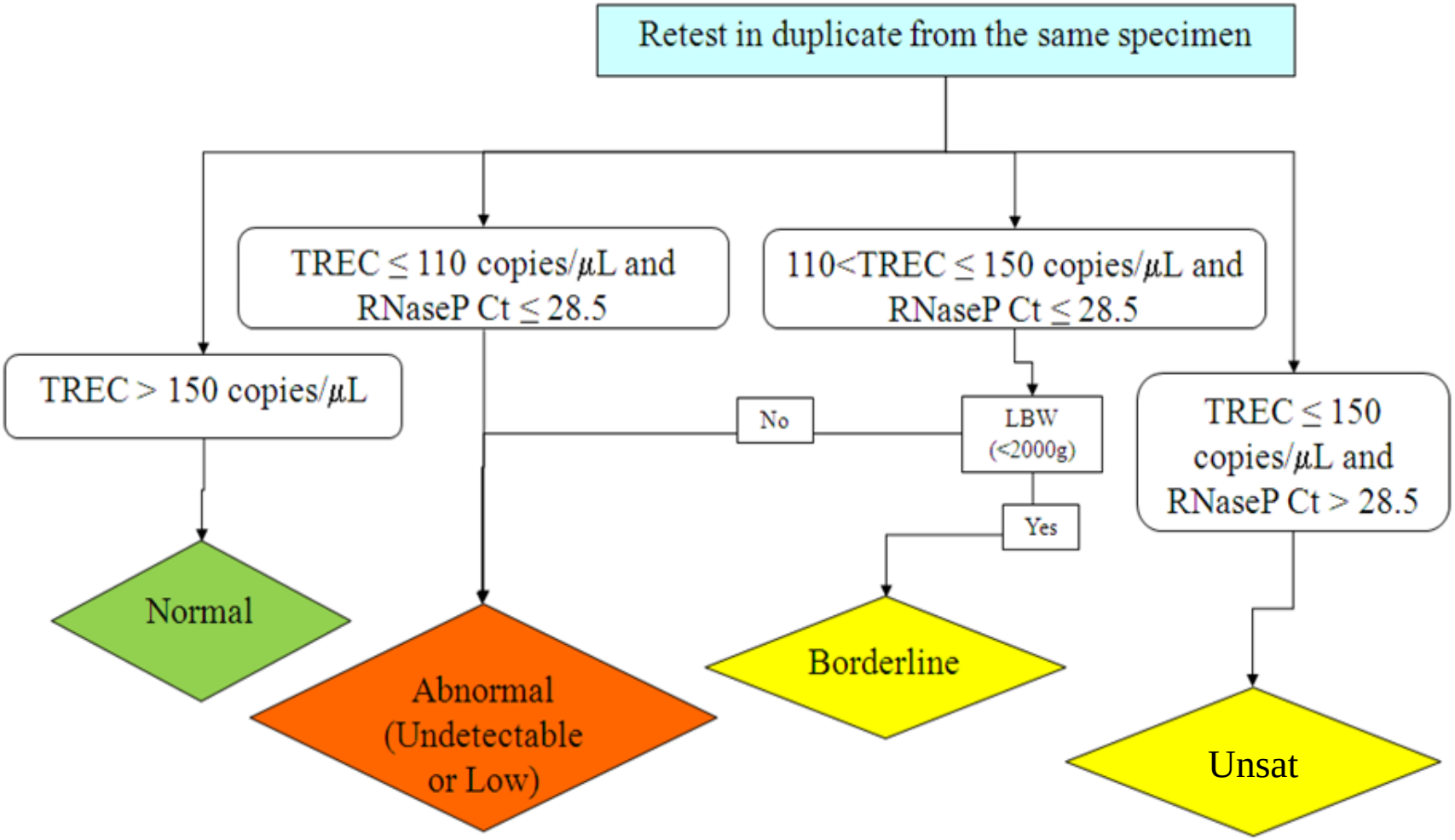
- The Texas NBS Program implemented statewide SCID screening on 12/1/2012.
- Texas requires two newborn screens with SCID screening on both screens.
- Approximately 731,312 births* since implementation (12/01/2012-10/01/2014)
- Testing was accomplished utilizing T cell receptor excision circle (TREC) assays.
- A statewide ad hoc pediatric immunologist work group was engaged to assist with designing laboratory algorithm and follow up protocols prior to implementation

*preliminary data

Initial Screening Algorithm



Retest SCID Algorithm



Follow Up Actions

Result of 1st Screen	Result of 2nd Screen	Result of 3rd Screen	Action
Undetectable	All (Abnormal Low or Borderline or Unsat or Normal)		Referral
Abnormal Low	Abnormal Low		Referral
Abnormal Low	Unsat		Repeat
All	Undetectable		Referral
Abnormal Low or Borderline or Unsat	Normal		No further follow up - Cleared
Normal	Abnormal Low or unsat		Repeat
Normal	Borderline		Repeat at 37wk CGA
Normal	Abnormal Low	Unsat	Repeat
Normal	Unsat	Abnormal Low	Repeat if normal BW. Repeat at 37 wks CGA if LBW.
Normal	Normal	Abnormal Low	Normal BW – Referral if baby is sick. Repeat at 37 wks CGA if LBW.
Low birth weight < 2 kg Normal, Unsat, Borderline, Abnormal Low	< 2 kg Unsat, Borderline, Abnormal Low	@37 weeks CGA Abnormal low, borderline, Undetectable	Referral
> 2 kg Unsat	> 2 kg Unsat or Undetectable		Referral

SCID Secondary Conditions

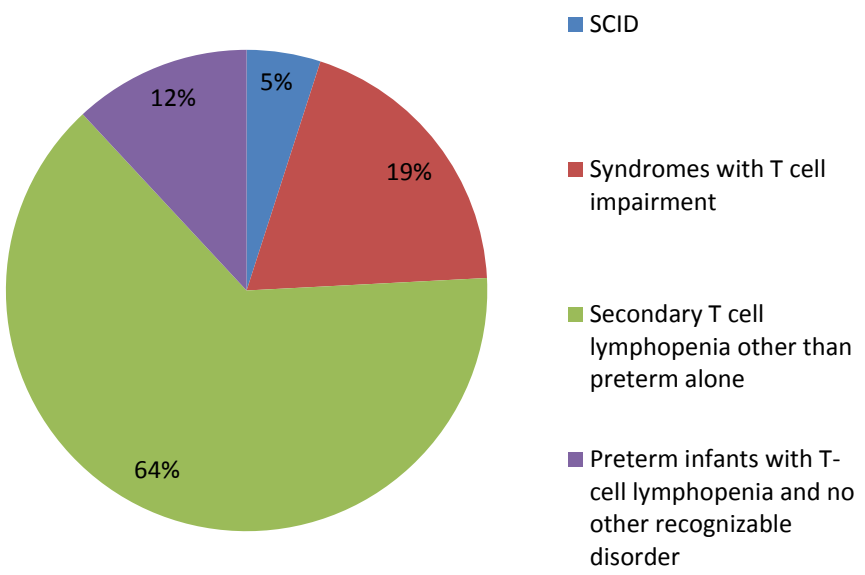
- 301 (0.04%) babies were referred for clinical evaluation and were identified with medical conditions
- Utilized the NBSTRN R4S categorization
- Diagnostic category based on information/labs received from a clinician

SCID Secondary Conditions

- Categories of secondary conditions were
  - Syndromes with T cell impairment(T-B+NK+)
    - DiGeorge Syndrome
    - Charge Syndrome
    - Ataxia Telangiectasia
  - Secondary T cell lymphopenia or T cell impairment other than preterm alone (CD3 <1500)
  - Preterm infants with no other recognizable disorder
    - Preterm babies
    - Preterm babies with prematurity related complications

	Normal 1st Screen					Abnormal Low 1st Screen					Grand Total
Count of 2nd Screen Results	Abnormal Low	Borderline Low	Unsat	Normal	Undete-ctable	Abnormal Low	Borderline Low	Unsat	Normal	Undete-ctable	
Syndromes with T cell impairment	9	1	2	3	1	30	0	1	8	4	59
Secondary T cell lymphopenia	48	1	5	15	10	48	1	3	24	7	162
Preterm infants with T-cell lymphopenia and no other recognizable disorder	2	0	1	6	1	14	0	0	3	2	29
Grand Total	59	2	8	24	12	92	1	4	35	13	250

Diagnosis Category	Count
SCID	15
SCID	15
Syndromes with T cell impairment	**58**
Chromosomal Defects	2
DiGeorge Spectrum	39
Neutropenias	1
T-Cell Syndromes	16
Secondary T cell lymphopenia other than preterm alone	**193**
Chromosomal Defects	21
Congenital Heart Defects	43
Endocrine	1
Gastrointestional Disorders/Defects	14
Hematology/Oncology Defects	6
Hepatic	4
Infectious Disease	10
Lymphatic/Fluid Imbalance	25
Multiple Congenital Anomalies with T-Cell Defect	24
Musculoskeletal Disorders	1
Nephrology/Renal	3
Neurological	3
Neutropenias	2
Pulmonary Disorders	7
T-Cell Syndromes	29
Preterm infants with T-cell lymphopenia and no other recognizable disorder	**35**
Prematurity with complications	7
Preterm	28
Grand Total	**301**



Secondary Conditions Continued

- To date all children with confirmed SCID had an abnormal first screen (either undetectable or low TREC values)
- 6 (22%) children with DiGeorge syndrome had abnormal TREC values on the second screen only
- 16 (84%) of children with congenital heart disease and an abnormal TREC value had an abnormal second screen only

Lessons Learned

- Start up period had more presumptive positives than anticipated
  - Protocols required re-evaluation and adjustment
- Most non-SCID children who met criteria for referral to an immunologist had significant health issues which spanned the gamut of congenital malformations.
- Few preterm babies required immune evaluation when rescreened at 37 weeks of gestation.
  - Preterm babies who had undetectable TRECS were referred

Lessons Learned Continued

- It is very difficult to categorize the secondary conditions detected by SCID newborn screening.
  - DiGeorge spectrum- chromosomal, MCA, cardiac
- Immunologists have as much difficulty agreeing on a diagnosis as geneticists!

TEXAS Department of State Health Services

Questions?