

Newborn Screening for Immunodeficiency: How-to and What Is Possible

Current screening procedure. Targeted, physician-based screening

Problems with targeted screening. Requires patient presentation. Requires appropriate identification of targets. Requires manifestations of illness.

Presentation: SCID presentations: Well-appearing infant until development of symptoms. Onset of pulmonary infections, diarrhea, failure to thrive, rash, sepsis Symptoms of illness are usually symptoms of infection.

Identification of targets: Without specific training, primary care physicians may not recognize red flags. Targeted, physician-based screening works best with simple, easily recognized criteria.

Rarity of SCID: True incidence unknown. Rarity in and of itself is not a contraindication to screening.

Effectiveness of treatment: Improved survival and reduced charges in patients diagnosed due to family history.

Potential improvements. Physician and patient education (Modell criteria).

1	Eight or more new ear infections within 1 year.	Recurrent, deep skin or organ abscesses.	6
2	Two or more serious sinus infections within 1 year.	Persistent thrush in mouth or elsewhere on skin, after age 1.	7
3	Two or more months on antibiotics with little effect.	Need for intravenous antibiotics to clear infections.	8
4	Two or more pneumonias within 1 year.	Two or more deep-seated infections.	9
5	Failure of an infant to gain weight or grow normally.	A family history of Primary Immunodeficiency.	10

Mass screening. Buckley (since 1980s) – Absolute lymphocyte count. (Physician-based mass screening) State newborn screening programs. Run by state, each state establishes its own panel. HRSA recommendations of typically screened disorders. Selection of a disorder for screening is a *political* decision. Standardized criteria (used to compile the HRSA recommendations). Original HRSA recommendation was against SCID screening for want of an adequate test.

New testing methods. TREC (Douek, Puck). Episomal DNA “byproduct” of T-cell development. No TRECS = No new T cells.

Lymphopenia as a screening parameter. Not all lymphopenia is SCID (and not all SCID is lymphopenic, though most is). Further work needed on non-SCID lymphopenia.

Formal cost-effectiveness study. Standardized assessment of costs and benefits of a procedure to allow comparisons of different procedures. Does not assign a value to life or quality of life, but does report cost of the benefit obtained.

Table II. Threshold values at which screening becomes cost-effective for the given willingness-to-pay

Variable	Willingness-to-pay		
	\$50,000/ QALY	\$75,000/ QALY	\$100,000/ QALY
False negative rate	0.9%	45.0%	61.2%
False positive rate	0.4%	2.1%	3.2%
Test cost	\$4.96	\$9.80	\$14.85
Incidence	1:49,700	1:92,100	1:125,600
Treatment cost	\$59,900	\$708,600	\$1,357,300
Follow-up cost	\$280	\$1675	\$3087

Wisconsin Screening Pilot Program. 70,000 live births per year (Routes). 41,154 infants screened 8 required referral, 4 had significant PIDD (DiGeorge, Idiopathic T-cell lymphopenia, Trisomy 21 with septicemia, and RAC2 deficiency). One transplant performed. Future screening pilots planned in Massachusetts, Maryland and elsewhere.

Further improvements. Access for high incidence populations (Amish, Navajo, Apache, First Nations, Saudi Arabia, Iran).

What is expected of clinicians. Results of screening are reported to treating physician at the time of screening. Reporting usually includes a further evaluation plan. NBS program responsibility ends with reporting (though most follow-up outcomes to some extent). Screening tests do not make a diagnosis.

Suggestive findings in a patient who was screened negative should be evaluated as if no screening had occurred.

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