

## WISCONSIN NEWBORN SCREENING LABORATORY NEWSLETTER

Newborn Screening Newsletter  
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SCID Testing

This newsletter is to announce that on February 18, 2008, the Wisconsin Newborn Screening Program will begin reporting test results for the disorder, **Severe Combined Immune Deficiency (SCID)**. This test has been added to the panel of 48 other disorders, including the hearing test. SCID is a genetic disorder that causes death, usually in the first few months of life due to common childhood infections because affected babies do not have a functional cellular or humoral immune system. You may remember the 1976 TV movie and story, *The Boy in the Plastic Bubble*, starring John Travolta, where a Texas boy was kept in a sterile plastic “bubble” to keep him from acquiring even the simplest infection that could kill him. That boy had SCID. If SCID is diagnosed early in life, before the onset of infections, bone marrow can be curative. In fact, recent advances in bone marrow transplantation have led to long-term success rates of up to 95%, when transplants are done before 2 months of age. With the emergence of an effective treatment, researchers including the NBS team at the State Laboratory of Hygiene with colleagues at the Medical College of Wisconsin, have been investigating methods designed to detect SCID babies through newborn screening. Although several approaches exist, the most promising is based on the measurement of small DNA fragments called T-Cell Excision Circles (TRECs), which are a by-product of the production of normally functioning T-cells. A SCID baby does not produce normal T-cells, hence does not develop an immune system and will not have detectable TRECs. Because TRECs are essentially a strand of DNA, TRECs are detectable in the whole blood specimen spotted on the NBS filter paper.

During the past year, our research team at the WSLH has developed a DNA based procedure that quantitate the number of TRECs in the dried blood spot specimens using a real-time polymerase chain reaction technology. We have tested the procedure on more than 10,000 de-identified specimens simulating routine newborn screening and are now ready to test all babies born in Wisconsin for SCID. An extensive review by the Newborn Screening Umbrella Committee and the Wisconsin Department of Health and Family Services determined that SCID met the Wisconsin criteria for inclusion in the NBS program.

- Criteria 1: Prevalence: Prevalence of the disorder must warrant screening.  
**It is estimated that the prevalence of SCID is about 1:65,000 births. This may be low due to the fact that many babies may be dying before a diagnosis is made.**
- Criteria 2: Morbidity and Mortality: Early detection benefits outweigh adverse consequences of false positives, cost to screen, etc.

**Without early detection and treatment there is significant morbidity and mortality in babies born with SCID. Our preliminary studies indicate that the false positive rate will be very low.**

- Criteria 3: Potential for successful treatment: effective management can be implemented to benefit infants.  
**Successful bone marrow transplants can actually cure SCID.**
- Criteria 4: Laboratory feasibility: Methodology must be adaptable to mass screening.  
**The Wisconsin State Laboratory of Hygiene methodology will handle the 300 to 400 specimens we receive daily on a cost-effective basis.**
- Criteria 5: Costs: Cost of test must be comparable to that of other established tests.  
**The cost of the TREC assay (~\$6.00) is about the same as some of the other disorders on the screening panel (e.g., congenital adrenal hyperplasia, hypothyroidism). It should be noted that the newborn screening fee will NOT be increased to pay for the SCID test at this time. We are seeking outside funding for the initial 3-4 year assessment period.**

### **Issues relating to routine screening and reporting of SCID**

The written reports from the newborn screening program will include SCID test results beginning February 18th, 2008. The current amount of blood collected for newborn screening is sufficient to perform the SCID testing. No additional blood will be needed or requested. **SCID Immunodeficiencies**, will be listed on “normal” reports along with the analyte measured (TREC), units (*TRECs/μL*), and the cut-off value ( $\geq 25$ ). Since there is no conventional unit for TRECs (i.e.  $\mu\text{mol/L}$ ,  $\text{mg/dL}$ , etc.) we chose TREC/uL. “Normal” SCID results will be reported on the comprehensive “normal” newborn screening report which is printed on *white* paper and sent to the specimen submitter (hospital, midwife, etc). “Abnormal” ( $< 25$  TREC/ $\mu\text{L}$ ) results will be reported directly to the baby’s physician by telephone. At that time one of our four designated immunodeficiency clinical consultants, who are pediatric immunologists, will be available by phone to discuss appropriate follow-up for the baby. The phone call from the State Laboratory will be followed by an “abnormal” written report on *blue* paper which is sent to the physician and to the specimen collection site, most often the hospital of birth. As with “abnormal” reports for other tests, the *SCID Immunodeficiency* reports will include test results (Number of TREC’s), interpretation, and recommended course of action for follow up. Examples of both the **Normal** and **Possible Abnormal** reports are attached to this newsletter.

The addition of SCID testing to Wisconsin’s NBS program is another example of public health working to improve the health and well being of Wisconsin citizens. Any success, as always, depends upon the collaboration and cooperation of all the partners involved: Wisconsin Department of Health and Family Services, State Laboratory of Hygiene, Children’s Hospital of Wisconsin, Medical College of Wisconsin, University of Wisconsin School of Medicine and Public Health, local health departments, volunteer medical specialists (our clinical consultants), primary health care providers, hospital staff, and the families. Being the first screening program anywhere in the world to implement

population-wide testing for SCID is an outstanding accomplishment for Wisconsin's statewide newborn screening partnership.

Thanks to all of you who continue to support newborn screening in Wisconsin. SCID testing offers Wisconsin newborns and their families an improved chance at a healthy life. It is exciting, and our success will depend on all our collective efforts.

Please forward this newsletter to members of the medical staff in your institution.

Sincerely yours,

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Attachments (2)