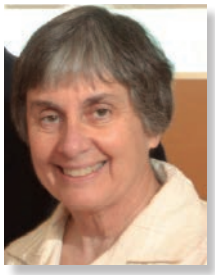
Proof Positive: Study Confirms the Need for Early Screening and Intervention for SCID


Jennifer M. Puck, MD

The publishing of a landmark study in *The Journal of the American Medical Association* highlights findings of a large group of contributors* led by Jennifer M. Puck, MD, senior author of the study and a renowned Severe Combined Immune Deficiency (SCID) expert who is also a member of the IDF Medical Advisory Committee. The study, "Newborn Screening for Severe Combined Immunodeficiency in 11 Screening Programs in the U.S.," published August 20, 2014, presented data from a wide range of screening programs, established an incidence rate based on populations, and discussed the significance of early intervention.

Success of SCID Newborn Screening

This retrospective study of more than 3 million infants from 11 newborn screening programs confirms the undeniable value of early detection and treatment of SCID. When diagnosed early following screening, 92% of infants with SCID received early intervention, such as bone marrow transplants, and survived. The study also found an incidence of one case of SCID per 58,000, nearly twice the previously estimated rate of one in 100,000. Newborn screening for SCID is performed using measurement of T cell receptor excision circles (TRECs). Absent or low TREC levels can indicate insufficient T cell production characteristic of SCID, but can also flag infants with non-SCID conditions in which T lymphocytes may be dangerously low.

Dr. Puck remarked on the unique size and comprehensiveness of the study, "Assembling data from over 3 million infants screened has not only given the most accurate estimate of the true frequency of SCID (1/58,000 births), but has proven that early treatment optimizes survival." Further, she added, "What's also interesting is that although the individual states each developed an independent approach to TREC testing and follow-up, all approaches successfully identified SCID."

One factor that hinders early detection of SCID without newborn screening is frequent absence of any family history. Previous studies indicated that fewer than 20% of infants with SCID have had known affected relatives. "Although it's always important to ask about a family history, most SCID patients are sporadic," says Dr. Puck.

Genetic Types of SCID

There are at least 13 different genetic defects that can cause SCID. Experts previously believed that nearly half of infants with SCID had the X chromosome-linked variety caused by a mutation in the common gamma chain of lymphocyte receptors. However, according to the article, newborn screening data found only 19% with this genetic form. Dr. Puck points out, "Our understanding has changed due to having higher patient numbers and unbiased, population-based ascertainment. Data from universal screening is more accurate than previous assessments, which were derived only from infants who were treated at specialized transplant centers." It will be interesting to see whether other countries have similar results from SCID newborn screening. Unquestionably, there are population subgroups where a specific gene and a particular mutation causes SCID at more frequent rate, for instance within the Navajo nation and in Amish communities in the U.S.

Non-SCID Conditions

The breadth of this study has also allowed for the identification of non-SCID conditions marked by low T lymphocytes at birth; some of these also require early intervention. According to Dr. Puck, "The infants with non-SCID conditions in whom TREC testing led to diagnosis of low T cells represent a spectrum of disorders. Some had congenital syndromes, such as DiGeorge/chromosome 22q deletion, trisomy-21, cartilage hair hypoplasia, CHARGE syndrome, ataxia telangiectasia or other multisystem disorders in which the immune problems are accompanied by problems in other organ systems." If these conditions are very severe and discernable with low T cell counts and low T cell function, they should be followed by pediatric immunologists. Avoidance of live vaccinations such as the rotavirus vaccine may be prudent, and other interventions may be required.

This study by Dr. Puck and colleagues adds weight to the IDF SCID Newborn Screening Campaign to see universal newborn screening for SCID implemented across the nation and provides proof positive that the TREC test is an effective instrument to identify SCID early enough to deliver life-saving intervention. As more and more states are following the 2010 U.S. Department of Health and Human Services recommendation that every state include this vital screening, this new study has the strength to answer lingering questions and provide an added push for states that have been slow to implement the practice. Newborn screening for SCID saves lives.

For the latest information, visit the IDF SCID Newborn Screening Campaign Blog: www.idfscidnewbornscreening.org.

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