Screening Can Diagnose Severe T-Cell Lymphopenia in Newborns

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December 8, 2009 — DNA testing on newborns can identify T-cell lymphopenia, a blood disorder that compromises the immune system, the effect of which can be lessened with early diagnosis, according to a study published online December 9 in the *Journal of the American Medical Association.*

"Infants with severe T-cell lymphopenia, including severe combined immunodeficiency (SCID), often appear normal at birth and have no family history of immunodeficiency. Consequently, many infants with severe T-cell deficiencies are not identified until life-threatening infections occur," write John M. Routes, MD, from the Medical College of Wisconsin and the Children's Research Institute, Milwaukee, and colleagues.

In the study, the Wisconsin State Laboratory of Hygiene screened all 71,000 infants born in Wisconsin during a 1-year period beginning January 2008. Testing for SCID and severe T-cell lymphopenia was conducted using the T-cell receptor excision circle (TREC) assay, quantitating the number of TRECs contained in a 3.2-mm disk (about 3 μL) punched from a dried blood spot of the NBS card.

NBS cards with TREC values of less than 25 μL underwent a second analysis for TRECs and β-actin, carried out with 2 new 3.2-mm punches, to guarantee the presence and integrity of the DNA. Those that again came back with abnormalities were validated for T-cell lymphopenia by flow cytometry or a repeat TREC assay using a new NBS card. Numbers for infants of less than 37 weeks' gestation whose TREC assays were abnormal or inconclusive were reevaluated when they reached the equivalent of 37 weeks.

In 17 infants of a minimum of 37 weeks' gestation, at least 1 atypical TREC assay was discovered (TREC values < 25/μL). Samples from 11 of those newborns were analyzed to enumerate T cells. Eight newborns were found to have T-cell lymphopenia, all of whom were then assessed by a clinical immunologist.

That finding demonstrates that the incidence of primary and secondary immunodeficiencies found by the TREC assay (8:100,000) is greater than that required for inclusion in state NBS programs. Diagnosing T-cell lymphopenia in newborns is important because it allows for the avoidance of certain infection triggers and permits prompt treatment.

"For example, hematopoietic stem cell transplantation is more successful when performed in the first 3 months of life. Administration of attenuated vaccines that are recommended in early infancy and which can cause serious infection in infants with T-cell lymphopenia can also be avoided," the authors write.
A limitation of the study, according to researchers, was their inability to evaluate the total number of Wisconsin newborns with clinically significant T-cell lymphopenia, which hampered their capacity to accurately assess the true sensitivity and specificity of the TREC assay to detect severe T-cell lymphopenia.

An important implication of the study, researchers said, is the low cost of T-cell lymphopenia screening, which runs $5.50 per assay. Although a formal examination is needed, the cost-effectiveness of newborn screening for SCID, a relatively high incidence of T-cell lymphopenia, and the TREC assay's affordability suggest that NBS may be cost-effective.

"In conclusion, the Wisconsin screening program demonstrates the feasibility of the TREC assay performed on NBS cards to identify infants with primary and secondary forms of T-cell lymphopenia," the authors write.

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