

Pediatric Immunologists' Drive Efforts for SCID Screening for Newborns

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CINCINNATI – Physicians at Cincinnati Children's Hospital Medical Center helped develop follow-up guidelines for a test to screen newborns against severe combined immune deficiency disease (SCID), which the state of Ohio has added to its list of mandatory infant screenings.

Effective July 29, the new testing requirement is a critical improvement in newborn screening, according to [Kimberly A. Risma, MD, PhD](#), a physician scientist in the Division of Allergy and Immunology.

“Using this test to screen infants will allow physicians to identify patients with SCID prior to them becoming ill from exposure to infectious agents (bacterial, viral, fungal) or live vaccines such as those for rotavirus,” said Risma. “SCID occurs in about 1 per 40,000-100,000 live births, and infants with SCID commonly experience chronic diarrhea, failure to thrive and early onset of life threatening infections.”

SCID is a life-threatening, genetic disorder in which the body lacks functional T cells, leading to impairments in the immune system and extreme vulnerability to infectious diseases. The most severe form of primary immunodeficiency, SCID is more popularly known as the “bubble boy disease” because the increased susceptibility of individuals with SCID often requires them to live in sterile, germ-free environments.

The most common treatment for SCID is bone marrow transplantation (BMT), although [recent gene therapy trials](#) are showing promise.

Dr. Risma worked with members of the Ohio State Screening Laboratory and other pediatric immunologists at



Cincinnati Children's and across Ohio to develop algorithms that will guide pediatricians' response to abnormal tests. Here at Cincinnati Children's, Risma established the process for following up on abnormal screens, drawing upon a well-established clinical partnership between the Divisions of Allergy and Immunology and Bone Marrow Transplantation (BMT) and Immunodeficiency. Risma's research and clinical interests include immunodeficiency and gene therapy. She is also Director of the Allergy and Immunology Fellowship Program at Cincinnati Children's. The Allergy and Immunology fellows and faculty members and BMT faculty and staff all anticipate being called upon for expertise when abnormal lab results are “called out” to pediatricians.

Collaborating with Dr. Risma at Cincinnati Children's was Rebecca Marsh, MD, Jack Bleasing, MD, PhD, and Lisa Filipovich, MD. Around the state, the team included Ram Chandrasekar, PhD, at the Ohio Department of Health, and numerous immunologists, including physicians Rebecca Scherzer, MD, and Peter Mustillo, MD, at Nationwide Children's Hospital.

The state newborn screening for SCID uses a laboratory technique called polymerase chain reaction (PCR) to detect circular pieces of DNA (T-cell receptor excision circles [TRECs]) that are found only in healthy T cells. If a high number of cycles of PCR are required to detect a signal from the newborn dried blood spot, it suggests a low number of T cells and possible or moderate risk for SCID, prompting a request for a repeat screen.

The cutoff for an abnormal TREC test in Ohio was set at 0.05% of all screens. This means that Ohio pediatricians can anticipate approximately 60-70 abnormal tests to be reported across the state per year. The majority of these abnormal tests will be spurious, occurring most frequently in preterm babies or babies who have had a blood transfusion prior to testing, both of which may lead to an abnormal test. However, SCID can occur in a preterm or term infant, so 3 abnormal tests in a preterm infant or 2 abnormal tests in a full-term infant will prompt a request for a follow up blood test to identify healthy T cells by flow cytometry and consultation with an immunologist.

In the special circumstance of the TREC signal being *absent* in a full-term infant, the recommended follow up is a definitive blood draw for flow cytometry rather than repeating the newborn screen. Absent TRECs in a full-term infant is a very rare finding and represents the highest risk for SCID. These abnormal test results would be “called out” not only to the pediatrician but also to the closest immunology referral center to ensure prompt follow up. Once a patient suspected of having SCID is identified at Cincinnati Children’s, specific testing will be performed in the Diagnostic Immunology Laboratory, immunologists in the Primary Immunodeficiency Clinic will evaluate the patient and members of the Division of BMT and Immunodeficiency will provide treatment (BMT or gene therapy).

Pediatricians are encouraged to recommend isolation and hold live vaccines for a child with an abnormal test until the definitive testing is complete. A list of referral centers will be provided to pediatricians receiving an abnormal test result.

“As of August 2013, there are 16 states screening newborns for SCID – a monumental effort, as the PCR methodology has not been routinely utilized for other newborn tests,” says Risma. “We are fortunate at Cincinnati Children’s to have a cadre of immunologists and support staff who are ready to accommodate the children identified by an abnormal screen. Our Immunodeficiency Clinic is supported by a team of 8 immunologists working together in the Immunodeficiency Clinic and the Diagnostic Immunology Lab, where definitive testing by flow cytometry may be performed. Our center also hosts one of the largest BMT programs for children in the country. Early recognition and treatment will certainly change the outcome for these babies.”

About Cincinnati Children’s

Cincinnati Children’s Hospital Medical Center ranks third in the nation among all Honor Roll hospitals in U.S. News and World Report’s 2013 Best Children’s Hospitals ranking. It is ranked #1 for cancer and in the top 10 for nine of 10 pediatric specialties. Cincinnati Children’s is one of the top two recipients of pediatric research grants from the National Institutes of Health and a research and teaching affiliate of the University of Cincinnati College of Medicine. The medical center is internationally recognized for improving child health and transforming delivery of care through fully integrated, globally recognized research, education and innovation. Additional information can be found at www.cincinnatichildrens.org. Connect on [the Cincinnati Children’s blog](#), via [Facebook](#) and on [Twitter](#).

Learn more about the Immunodeficiency Resources and Divisions of Allergy and Immunology and Bone Marrow Transplantation and Immunodeficiency at Cincinnati Children’s

Allergy and Immunology Program

<http://www.cincinnatichildrens.org/service/a/allergy-immunology/default/>

Allergy and Immunology Fellowship Program

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Immunodeficiency Clinic

<http://www.cincinnatichildrens.org/service/i/immune-deficiency/default/>

Diagnostic Immunology Laboratory

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Bone Marrow Transplantation Program

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Gene Therapy News at Cincinnati Children’s

<http://www.cincinnatichildrens.org/professional/resources/research-horizons/archives/2013/winter/breakthrough/>