Study finds SCID previously underdiagnosed in infants with fatal infections

August 19 2014

In this image, blood is collected from a newborn for screening. Credit: Credit: U.S. Air Force photo/Staff Sgt. Eric T. Sheler

Severe combined immunodeficiency (SCID), a potentially life-threatening, but treatable, disorder affecting infants, is twice as common as previously believed, according to a new study that is the first to examine the national impact of this newborn screening test.

The study is the first combined analysis of more than 3 million infants screened for SCID in 10 states and the Navajo Nation. Infants from participating programs born from the start of the first pilot program in

January 2008 through July 2013 were included.

In May, 2010, SCID was the 29th condition added to the national recommended uniform panel for newborn screened disorders, and California began screening newborns statewide on August 15, 2010, just four years ago. Currently, 23 states conduct newborn screening for SCID, and the test is performed for nearly two-thirds of infants born across the country.

"Now that infants with SCID are being detected at a very young age, we can tailor protection and early treatment for them while they are still healthy, without having to also treat the complications from infections that result from the disease. This leads to the best outcomes in terms of survival and immune reconstitution," said senior author Jennifer Puck, MD, a pediatric immunologist at UCSF Benioff Children's Hospital San Francisco, who developed the dried blood spot test to screen newborns for SCID.

The study will appear in the August 19 issue of *JAMA*.

SCID is a group of rare disorders caused by defects in genes involved in the development and function of T and B lymphocytes, immune cells critical for fighting infections. All babies are protected from infections during the first months of life by antibodies transferred from their mothers. However, as this early protection wanes at around two months of age, babies born with SCID are at risk for life-threatening infections. SCID is fatal, usually within the first year of life, unless treated with immune-restoring treatments such as transplantation of blood-forming cells from the bone marrow of a healthy donor or gene therapy. Over 80 percent of affected infants do not have a family history of the condition to alert their doctors of the condition before serious infections develop.

Co-first authors Antonia Kwan, PhD, a postdoctoral scholar at UCSF

and Roshini Abraham, PhD of the Mayo Clinic, gathered data from screening programs and immunologists who followed up with infants in the participating states. "Although each public health program was designed a bit differently, all were successful at detecting SCID, and no cases of SCID were missed," said Kwan.

The researchers found the screening detected 52 SCID cases, affecting 1 in 58,000 infants. Previous estimates, based on limited data, had suggested that SCID was more rare, affecting only 1 in 100,000 babies. The incidence of SCID was not significantly different in any state program but was higher in the Navajo Nation, where an ancestral trait is known to confer a higher risk of being born with the disease.

The ability to diagnose infants early allows physicians to immediately set up infection precautions to protect the baby, and start treatment while the baby is healthy. Of the 52 babies found in the study to have SCID, 49 received immune-repairing therapies such as transplants of blood-forming stem cells, enzyme replacement therapy and/or gene therapy. Three infants died before treatment was given. Four died after receiving transplants, while the other 45 treated infants survived.

Of those 52 cases of SCID identified by newborn screening, nine were considered "leaky SCID." These infants had an incomplete mutation in a typical SCID gene, retaining small amounts of immune function that can actually be detrimental because the poorly regulated cells can attack the baby's own tissues. "We're finding that leaky SCID is more common than previously thought," said Puck. "Before screening we'd typically not make the diagnosis for several months or even years, but because of newborn screening they are being treated before they get into any trouble."

The screening test detects more than a dozen genetic causes of SCID, in addition to other conditions with significantly low T cells. The

researchers discovered that population-based testing uncovers a broader range of the underlying genetic causes for SCID than previously known. For example, X-linked SCID, a form of the disorder caused by mutations in a gene on the X chromosome and affecting only males, previously had been thought to account for half of the cases of the condition, but this study found only 19 percent of newborn screened SCID infants had X-linked disease with a corresponding increase in other gene defects. Moreover, the proportion of SCID infants without a known genetic defect (15 percent) was higher than anticipated, indicating that widespread screening presents opportunities to discover previously unknown genes implicated in SCID.

"The whole point of newborn screening is to identify conditions that are treatable, and for which early treatment saves lives," said Puck. "The excellent outcomes of SCID infants across the country reported in this study prove that SCID is such a condition."

More information: Paper: DOI: 10.1001/jama.2014.9132
Editorial: DOI: 10.1001/jama.2014.9133

Provided by University of California, San Francisco