CASE STUDY

Diagnostics Newborn Screening

Customer Story

How SCID Became Part of California's Newborn Screening Program

California delivered a breakthrough for preventative public health when it became the first of the nation's most populous states to adopt newborn screening for Severe Combined Immunodeficiency (SCID). Commonly known as "bubble boy disease," SCID is a primary immunodeficiency in which infants have few or no T lymphocytes, the white blood cells that help resist infections. SCID is caused by several different genetic defects, most of which are hereditary, and is fatal. But if detected within the first few weeks of life, the disease can be cured with cord blood or bone marrow transplants. Before newborn screening, SCID and related disorders were typically not detected until a child developed symptoms, which was often too late to initiate transplant treatment because the body was already under attack by opportunistic infections.

Newborn screening can save lives or prevent debilitating outcomes, so the cause has attracted many passionate advocates whose coordinated efforts have led to better lives for children and their families. Public attention was ignited in 2003 when a case of two children born at the same time, one screened for more conditions than the other, brought home the benefits of expanded screening vs. the severe consequences of not looking for treatable conditions as early as possible. Dubbed the case of the two Zachary's, it involved two boys born in 2003 with the same rare enzyme deficiency but in two different California hospitals. Zachary Black's birth hospital was part of a pilot program to test expanded screening, while Zachary Wyvill's only screened for the four conditions mandated at that time by state law. Baby Black was diagnosed and successfully treated, but Baby Wyvill's disease was not recognized for more than half a year, leaving him disabled by the damage already done.

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"It's unworthy of who we are as a country if we allow some babies to suffer when there is a screen that could prevent it," said Vicki Modell, who with her husband Fred runs the Jeffrey Modell Foundation. The foundation, named after the son they lost to Primary Immunodeficiency (PI) disease, is dedicated to the diagnosis, treatment and ultimately cure of PI Diseases.

Since the two Zachary's made headlines in the media including *The Wall Street Journal,* the menu of newborn screens has expanded in all states, but advocates are still fighting for widespread addition of SCID. Currently, 20 U.S. states include SCID in their newborn disease panels[1]. But when California launched its pilot program in 2010, only Wisconsin and Massachusetts were also running pilots. California mandated the screen by law in 2011. California was able to successfully bring this life-saving screen to its state public health lab using a high-throughput TREC quantitative PCR assay with DNA isolated from routine dried blood spots, a test that was developed by the University of California, San Francisco, researchers and implemented in the lab by PerkinElmer. In its first two years, the program detected 15 cases of SCID and related disorders, and 14 of those lives were saved[2]. In addition, the program documented a much higher frequency of SCID than had been expected, adding urgency to calls that the assay be adopted as part of existing "heel-prick" newborn screens elsewhere.

Implementing a new public health program is never easy, especially in an era of fiscally conservative state budget policies. "It's not that anyone is actively resisting newborn screening for SCID. It's just that they think they don't have adequate funds," Vicki Modell said.

So how did it work for SCID in California? Advocates and public health experts who were involved in the achievement say it took two key proof-points to move the legislation:

- They needed credible numbers to prove that SCID screening was more cost-effective than waiting for the disease to be diagnosed based on symptoms. In particular, the numbers were needed to correct less reliable calculations from state finance officials who were less familiar with SCID diagnosis and treatment.
- They needed to show it could be carried out reliably in a public health lab alongside testing for the established 29 conditions already screened from a newborn dried blood sample.

Advocates in California were building on momentum from the federal level, after U.S. Secretary of Health and Human Services Kathleen Sebelius in May 2010 added SCID to the core national screening panel of 29 genetic disorders. But that decision was only a recommendation, and it remained up to states and territories whether to implement the screen.

One of the driving forces behind SCID screening as a public health policy was the Jeffery Modell Foundation. Fred and Vicki Modell had worked with other advocates to lobby for adding SCID to the nationally recommended panel and knew the next step was to focus on developing a pilot program in a large-population state. They had already helped Wisconsin kick off a pilot program in 2008 that detected the first classic SCID case in a newborn, but more data was needed on the frequency of the disease and the reliability and practicality of screening for it in the context of a high-volume public health laboratory. "There are now 2.2 million babies being screened. We want all the other ones," said Fred Modell. "This should be a national priority, and it is for us."

Another active voice in the discussion was Dr. Jennifer Puck, Professor of Immunology and Medical Director of the Pediatric Clinical Research Center at the University of California, San Francisco. Dr. Puck developed the test while at the NIH that became part of the standard newborn screen, an assay based on detecting T cell receptor excision circles (TRECs)[3]. The Modells and Dr. Puck worked together to engage the California Department of Public Health in a pilot effort.

"Without Dr. Puck driving this it probably wouldn't have happened as quickly or have been nearly as successful," said Dr. Fred Lorey, who at the time was acting Chief of the Genetic Disease Screening Program at the state Department of Public Health and has since retired. Dr. Puck contributed not only the underlying test but also drove development of the overall testing protocol in a way that helped ensure reliability and brought in expertise from clinicians outside the department. Under the concept, a screen that came back positive would prompt two confirmatory tests at a single lab to ensure consistency, and results would be analyzed by Dr. Puck or another clinical immunologist whose expertise complemented the knowledge of the public health lab. Dr. Puck had also worked since the early 2000s to reduce the incidence of false positives to make the screen compatible with public health program standards.

The remaining obstacles involved integrating the screen into the existing workflow and facilities of the public health lab. Without a commercial kit available, each lab that wanted to handle SCID screens would have to develop and implement its own process in-house, a potentially time-consuming solution. PerkinElmer stepped in with an offer to move its own equipment and staff into the California public health lab and run the SCID screen, contributing part of the cost as in-kind services. Also helping to off-set the screening costs were donations of $1 per screen, up to $800,000, from the Jeffrey Modell Foundation and 50 cents per screen from the Eunice Kennedy Shriver National Institute for Child Health and Human Development.

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Vicki Modell

"It worked so well," Dr. Lorey said about PerkinElmer's "lab-in-a-lab" solution for automating the screen and making it work in a big public health program. "PerkinElmer brought the equipment into our lab and we were able to have our chemists be trained at the same time. PerkinElmer provided staff as well on site. It was a new concept."

The pilot began in August 2010 and was quickly a success. "In a few short months, we had more data on newborn SCIDS than the whole world did," Lorey said. One of the key findings: The incidence of SCID and related disorders was much higher than expected. Where previous estimates had ranged from 1-in-100,000 and 1 in 150,000 the first months of the pilot project yielded a rate of 1-in-32,000. That was one of the factors that helped advocates win support for a bill authored by California Assembly member and pediatrician Dr. Richard Pan.

The bill aimed to adopt the pilot program as a permanent part of the state's required newborn screening program. At a time when state government was very focused on budget savings, supporters of SCID screening used the higher incidence numbers to help underscore the cost-effectiveness argument. Detecting the disease in time for effective transplantation treatment would be a major savings over long-term inpatient care for severe bacterial, viral and fungal infections, especially given a success rate of 95 percent for transplants in cases diagnosed in the first 3.5 months of life. "The cost to treat a baby with SCID or a SCID-related condition can cost upwards of $2 million dollars per case if not detected in a timely manner," the March of Dimes wrote in a letter supporting the bill, which passed in June 2011[4].

Since then, the number of U.S. states with standard SCID newborn screening has continued to increase as the growing amount of data show a clear cost-effectiveness benefit for public health and public budgets. The U.S. example is also attracting attention abroad, and 212 global immunology experts from 78 countries signed a "Berlin Declaration" in November 2013 calling for global implementation of newborn SCID screening. The statement at a Berlin summit organized by the Jeffrey Modell Foundation ended with a resolution "for the immediate implementation of TRECs screening in order to identify, treat and cure newborn babies born with SCID and related T cell Lymphopenia."

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Fred Modell

References

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