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Testing Fate

A Drop of Blood Saves One Baby; Another Falls Ill

Inconsistencies in Screening Mean Rare Diseases Go Undetected and Untreated

Zach's Mysterious Headaches

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In California, it is being called the tale of the two Zacharys.

In April 2003, in a hospital northeast of Oakland, Zachary Wyvill was born with a very rare enzyme deficiency that has left him unable to eat on his own, walk or crawl. A month later, another child named Zachary was born with the same genetic disorder in a hospital 60 miles to the east. But today, this boy, Zachary Black, is a healthy 1-year-old. His disease is kept in check with a special diet and vitamins.

Zachary Black's condition was picked up during a special newborn-screening project carried out in many, but not all, California hospitals from January 2002 to July 2003. Zachary Wyvill's condition wasn't detected because his blood wasn't screened. By the time doctors recognized his problem, he was already severely disabled, probably for the rest of his life.

Zachary Black

All states require some kind of testing for newborns, but the policies are a hodgepodge. California, for example, requires that newborns be screened for only four treatable diseases. Other states, such as New Jersey and Mississippi, mandate screening at birth for 30 to 40 disorders. Some states test without parental consent; others require it.

By some government and medical estimates, the lack of standardized newborn screening is responsible for the illness and death of several thousand children every year. The cost of treating and caring for children who suffer from these rare diseases can range from $500,000 to $1 million a year, according to the U.S. Centers for Disease Control and Prevention.

"No child in America with one of these diseases should ever go undetected at birth," says Harry Hannon, director of newborn-screening services at the U.S. Centers for Disease Control and Prevention. "That some infants aren't being caught and treated when possible is a national tragedy."

Now there's pressure to revamp the testing of newborns because of new technology. A machine

first developed 15 years ago can now identify more than three dozen congenital diseases, such as the one that affects the two Zacharys, from a small spot of blood extracted from newborn babies' heels. If detected by this test -- which costs $50 to $80 -- most of these conditions can be readily treated, even cured.

Dr. Hannon says the new test should be standard care for all newborns, much as a blood-pressure test is part of every medical check-up. But many states haven't expanded newborn screening, citing costs. California's pilot program was shut down last July as "a direct result of the state's deep fiscal problems," says George Cunningham, who oversees the state program. Today few children in California are being screened for many rare diseases, including the one that affects the two Zacharys.

Georgia has three machines that can conduct the new tests, but they are sitting unused for lack of funding, says Paul Fernhoff, a genetics professor and chairman of the state's newborn-screening advisory task force. Last year, Georgia's health department decided to start using the technology after a local chapter of the March of Dimes pledged $1 million to buy the machines. But Dr. Fernhoff says the state has yet to provide funds to pay for the tests or hire staff to run the machines.

Because the diseases involved are so rare, expanded newborn screening hasn't received as much funding or attention as health-care issues which affect larger numbers of people. "The issue is still under the radar," says Mike Watson, executive director of the American College of Medical Genetics. "Ninety-nine-point-nine percent of the public can't even pronounce these diseases. Why should we expect people to be concerned about them?"

Keith Nash

Nathan and Zachary Wyvill

The two Zacharys' disorder -- glutaric acidemia type 1, or, more simply, GA1 -- results from a genetic glitch so uncommon it strikes only one in about 75,000 infants. If not caught in the first six to nine months of life, the GA1 gene mutation will kill brain cells and cripple muscles. Though Zachary Wyvill is quick to smile and respond to conversation, he can barely move his arms and legs, or even lift his head. Daily nourishment is provided by fluids fed through a thin tube into his stomach.

Zachary Black is robust. His GA1 is under control today because his mother gave her consent, as required by state law, to be part of California's short-lived screening program when he was born last May at Doctors Medical Center in Modesto.

John Muir Medical Center in Walnut Creek, where Zachary Wyvill was born last year, was also offering the test when he was born. State health officials say 75% of babies born at John Muir while the program was offered were screened with the new diagnostic test.

But Zachary and his fraternal twin, Nathan, apparently fell through the cracks. The boys were born seven weeks premature, and their parents, David and Cynthia, say they have no recollection of being asked during those first hectic weeks if the children could be included in the testing project.

The state's health department says its records show that blood samples taken from the twins were sent to the lab conducting the new test. But because a state-required parental consent form didn't accompany the samples, the test wasn't performed, state officials say.

A spokesperson at John Muir says because of federal patient-privacy rules, the hospital can't comment on the case.

"This should not have happened," says Mr. Wyvill. "It shouldn't happen again to somebody else's

child." He believes expanded newborn testing should be mandatory, without requiring parental consent, to avoid paperwork glitches that may mean a child doesn't get the test.

After Mr. Wyvill described his son's disabled condition at a state hearing earlier this year, a new bill making the test mandatory without parental consent was introduced in the state legislature. But given California's financial woes, it is unclear whether it will remain in the budget or if Gov. Arnold Schwarzenegger will approve it. A spokeswoman for the governor says he won't comment on the proposal until it reaches his desk.

The new test employs a technology called "tandem mass spectrometry" that was first developed in 1990 and introduced for neonatal screening in a handful of states a few years later. Often called tandem mass, it represents a significant advance as it can detect 40 different genetic or metabolic anomalies from just a tiny spot of blood. Previously, these conditions had to be looked for one at a time -- a process too expensive and time-consuming to make economic sense, since each of the diseases is rare.

The tandem mass machines cost about $300,000 each. Hospitals take a blood sample from a newborn and send it out to a lab for testing.

The largest producer of mass tandem equipment for newborn screening world-wide is PerkinElmer Inc. of Boston, which says the business provided about 9% of last year's revenue of $1.5 billion. While many state health departments conduct the tests, several nonprofit labs also provide the service. Pediatrix Medical Group Inc. of Sunrise, Fla., is the only publicly traded firm marketing newborn screening services to states and hospitals. Pediatrix has been actively lobbying for mandatory testing in California and other states.

As of two years ago, only 20 states offered tandem mass for newborn screening, according to a 2002 U.S. General Accounting Office report. Only 13 states require its use, the GAO says. Last year, Mississippi became the only state to mandate testing for all 40 of the treatable illnesses detectable by the machine.

"It's a real mess," says Nancy Green, medical director of the March of Dimes, a nonprofit organization based in White Plains, N.Y., which seeks to combat childhood disease. The group put out a report this year calling for all states to mandate the use of tandem mass to test for at least 10 diseases.

Mississippi passed its expanded screening law in 2002, after lobbying by a family whose child died from a genetic disease that could have been caught by the new test, says Jerry McClure, director of Mississippi's division of genetics services. Last year, the state's new test detected six children with genetic diseases that its previous program wouldn't have identified at birth, he says. "Just catching one baby made the program worth the cost and more," Dr. McClure says.

Mandatory newborn screening was first instituted by a handful of states in the 1960s, after research by pediatrician Robert Guthrie. Dr. Guthrie linked many cases of childhood mental retardation to an enzyme deficiency called PKU, which can be treated with a dietary change. Unable to get the federal government to authorize all hospitals to test for PKU, the doctor made his case by petitioning one state at a time. Eventually, every state passed laws requiring mandatory testing for PKU. Over time, states added a handful of other diseases for testing, some mandatory, some not.

As a result, newborn screening evolved into a public-health service overseen by states -- largely unnoticed by parents.

"It is a silent story," says Susan Winter, a genetics specialist at Children's Hospital in Madera, Calif., where Zachary Black was born. "Parents only become aware of newborn screening when their child is detected, or tragically, when they become sick."

Dave and Cindy Wyvill say their only concern at first was that their twins, Nathan and Zachary,

born prematurely, needed to stay in John Muir's neonatal intensive care unit for several weeks. Not until the boys were almost four months old did the parents notice that Zach's head looked bigger than Nathan's, says Mr. Wyvill, 32, an accountant for an engineering firm. A CT scan found some excess fluid lining Zachary's skull. Referred to a neurosurgeon at Children's Hospital and Research Center in nearby Oakland, the Wyvills say they were told the problem would likely resolve itself. A spokeswoman for Children's Hospital declined to comment on the case, citing patient-privacy laws.

As the weeks went by, "we could tell something was wrong with Zach," says Mrs. Wyvill, also 32. "We had a comparison right in front of us." Nathan was standing up in his mother's lap, but Zachary couldn't.

In early October, Mr. Wyvill came down with the flu, and the whole family got sick. After a few days of throwing up and diarrhea, "Nathan got better, but I couldn't get Zachary to take his bottle," Mrs. Wyvill recalls.

Worried Zach might be dehydrated, the Wyvills took him to the emergency room at John Muir where he was given fluids through an intravenous line. The next day, Tuesday, Oct. 14, they went back to Children's Hospital in Oakland where they say doctors told them Zach likely was still suffering effects of the stomach flu. Back home on Wednesday, Zach still was unable to eat. By that evening, Zach was referred again to Children's Hospital.

"We were terrified," says Mrs. Wyvill. "He was screaming all night." Doctors guessed that the excess fluid lining his skull might be causing a severe headache and gave him Tylenol and Benadryl, she says. Zach slept most of Thursday. Over the next few days, as doctors debated what might be wrong, Zach was inconsolable. "I was convinced he was going to die," Mrs. Wyvill says.

After Zach had spent almost a week in Children's Hospital, doctors placed a shunt under his skull to drain off the fluid. But it provided no relief and a day later, several perplexed specialists huddled together. Finally, one of the many blood and urine tests taken over the previous few days pinpointed the problem. Zachary had a disease none of the doctors had seen before: glutaric acidemia type 1.

GA1 seemingly strikes out of nowhere. The deficiency occurs when a child inherits two malformed copies of the enzyme's gene, one from each parent. Parents who pass along the gene rarely know they are carriers. But without even one working copy of the gene, a child is unable to digest two amino acids found in most food proteins. Over time, the undigested acids form a poison that destroys brain cells.

About 20 years ago, doctors in Pennsylvania recognized the disorder as the cause of a spate of cerebral palsy-like illnesses among Amish families. The doctors developed a diet low in protein and high in certain vitamins that blocked the nerve destruction. That's the diet that helped Zachary Black.

But Zachary Wyvill never went on the diet. After his diagnosis with GA1, his parents took him to Greg Enns, a metabolic and genetics disease specialist at Stanford University Medical Center in Palo Alto, and learned some terrible news. "Zach suffered extensive damage" during the weeks in October when doctors were stumped by the boy's condition, Dr. Enns says.

Dr. Enns also asked the couple why Zachary's GA1 hadn't been caught during California's tandem-mass screening program, as it was still running in April 2003 when Zach was born. If Zach had been put on the diet at that point, he'd likely be fine, Dr. Enns told them. By then, Zach's care had cost more than $300,000, most of it covered by insurance.

The boy's future is uncertain. He will surely be in a wheelchair, doctors say. It isn't clear whether he will be able to talk or feed himself when he grows up.

As the most-populous state in the country, with more than a half-million babies born each year, California was being targeted by parent groups lobbying for greater use of tandem mass. Even though the individual diseases detected by tandem mass are rare, taken together, the 40 or so diseases arise in about 1 in 1,000 babies. A study by California's health department found 53 infants referred for treatment because of the expanded screening who would not have been otherwise detected at birth.

In March, state Sen. Dede Alpert, a Democrat from San Diego, held a hearing on the screening-project results. Mr. Wyvill heard about the inquiry and decided to testify during a public-comment period. Meanwhile, a March of Dimes lobbyist asked several families whose children's illnesses had been discovered during the test program to testify, including Chad Black and Bridget Campbell, Zachary Black's parents.

Unknown to each other, the two families sat side by side in the audience. When his turn came, Mr. Black stood up with his son in his arms and said, "If not diagnosed, we don't know where Zachary would be today."

"All I could think," says Mrs. Wyvill, "is 'I can tell you exactly where your Zachary would be. He would be where my Zachary is.' " A few minutes later she stood up and said it.

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