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Silent Alarm: Screening program detects rare metabolic disorders in newborns

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SONDRA AND ERIC TOMPKINS KNEW SOMETHING WAS WRONG even before they got the phone call. Their son Nathan had appeared healthy at birth. He arrived in the world with 10 fingers, 10 toes, a cherubic face and a perfect little body that weighed a normal 8 pounds 10 ounces. Yet within the first week, they realized something wasn't right.

Sondra Tompkins said Nathan started having trouble breast-feeding after about six days. When he tried to nurse, he gagged as he sucked.

And then there was the strange odor. Tompkins said her baby suddenly started to smell like burnt sugar or pancakes. She thought at first the odor was coming from her breast milk. But even after bathing Nathan and changing his clothes, the smell persisted.

"It was like walking into an International House of Pancakes," she said.

Just as she was about to pick up the phone and call her pediatrician, the doctor called them. She had bad news: in a metabolic screening, Nathan had tested positive for a rare genetic disorder. He needed to come to the hospital right away.

"I just became hysterical immediately," Tompkins said. "My first concern was, 'Is he going to die?'"

Tompkins said the next few weeks were a nightmare. At Providence Alaska Medical Center's pediatric intensive care unit, Nathan was hooked up to a ventilator and intravenous lines. He became lethargic and didn't open his eyes for a week.

The Tompkins family learned that Nathan had maple syrup urine disease, named for the distinctive smell associated with the condition. People with the disease lack enzymes to break down three of the 20 amino acids the body needs to grow. One of the acids, leucine, is highly toxic to those with the condition.

After two days, Nathan's leucine levels soared so high he had to be evacuated to Seattle's Children's Hospital, where he underwent hemodialysis to bring down the levels.

The leucine had probably started killing brain cells, Tompkins said, but doctors couldn't say then whether it would result in developmental delays. If left unchecked, the disease can cause mental retardation or death.

Nathan celebrated his first birthday Sept. 12 and seems like any other baby. Tompkins said he has been just slightly behind in learning motor skills but is otherwise meeting all

the milestones pediatricians look for to determine healthy development.

"We're very happy that he's doing as well as he is," she said.

Tompkins credits Nathan's healthy development to Alaska's newborn screening program, which allowed doctors to diagnose his problem early. Had the family lived in one of 15 states that don't screen infants for maple syrup urine disease, Nathan likely would have suffered lasting damage, she said.

"If something is wrong with your baby, days make a difference." But his life will never be simple, she added.

Many parents manage the disease through diet, but Nathan is also on a waiting list for a liver transplant. If effective, the transplanted liver would enable him to process the amino acids that are now toxic to him. In the meantime, everything he eats must be closely and constantly monitored.

Tompkins said she and her husband never imagined something like this would happen to one of their children. They are both healthy, and Sondra said she ate well, exercised and didn't drink or smoke during pregnancy. But all that didn't matter; the metabolic condition lurked in their genes.

They also have an older son, Matthew, now 2, who does not have maple syrup urine disease or any other metabolic condition.

"It's like newborn roulette," she said. "Unless you know the gene pattern of both you and your husband, you can't be guaranteed something like this won't happen to you."

METABOLIC SCREENING

Fortunately, these kinds of genetic conditions are rare. Parents can be tested to see if they are carriers for maple syrup urine disease or other afflictions before they conceive a child, but it wouldn't be practical or cost-effective to do so with every parent.

Maple syrup urine disease is so rare that it affects only one in 150,000 infants.

Other disorders are more common, but overall, the chance of getting any of the 31 screenable genetic disorders is only one in 2,200 live births. That figure is based on data collected recently in Oregon and Idaho, said Thalia Wood, Alaska's newborn metabolic screening program coordinator.

What states do instead is screen newborns for the presence of metabolic or other genetic diseases, which is easy to do and cost-effective. All states currently test for phenylketonuria, an amino acid disorder, and hypothyroidism, a disease that affects thyroid production, Wood said. But after that, every state has a different panel of disorders it tests for.

In 2002, newborn screening in Alaska found a total of 18 disorders among 9,830 births, according to Wood.

The state now requires that a small amount of blood be drawn from each infant's heel twice so it can be tested for six metabolic conditions, including maple syrup urine disease. Infants can also be tested for abnormal hemoglobins, which includes sickle-cell anemia, but only at the request of parents and physicians.

After Wednesday, blood will still be drawn in the same manner, but the test will screen for an additional 24 metabolic conditions, including a host of amino acid, fatty acid and organic acidemia disorders. The hemoglobin test will also become part of the regular panel. The reason for the expansion is that the Oregon State Health Laboratory, which contracts with Alaska to run the tests, recently acquired a machine called a tandem mass spectrometer, which can utilize the same sample in testing for additional conditions.

The two blood draws used to cost \$24. The new cost will be \$55, but most insurance companies should pay for the tests, Wood said.

The first draw is typically done while the mother and baby are still in the hospital or birthing center, within the first 12 to 48 hours after childbirth. The second test should be done in five to 10 days after birth, Wood said.

Most people know it as the PKU test. That's short for phenylketonuria, a disease in which carriers lack the liver enzyme to digest phenylalanine, an amino acid. Babies appear normal at birth, but if unchecked, the disease can lead to mental retardation, cerebral palsy or seizures.

Another disease detected by newborn screening is congenital adrenal hyperplasia. Infants with the disease produce too many male hormones. Yup'ik Eskimos are particularly susceptible to the disease because of their relatively small gene pool. According to Wood, the incidence among that group is one in 300. In the general population, it is one in 12,000.

Hypothyroidism is the most common condition that newborns are currently screened for in Alaska. It is marked by underactivity in the thyroid gland, and can cause mental retardation, growth failure and deafness. It is usually not fatal, Wood said.

Wood said the new screening technique could turn up an even more prevalent condition: a fatty acid oxidation disorder known as MCAD, or medium chain acyl-CoA dehydrogenase deficiency. Wood said some studies are finding a link between infants with this disorder and sudden infant death syndrome (SIDS).

MONITORING DIET

Statistically speaking, Alaska should rarely, if ever, see cases of maple syrup urine

disease. Yet there have been two cases in just two years in Anchorage. Nathan was the second. The first was Marlon Falconer.

Marlon's mom, Monica, said she and her husband, Navid, had noticed no unusual symptoms before the doctor called to tell them the bad news. Marlon was just 3 days old. He was also evacuated to Seattle, where he underwent hemodialysis.

Now Marlon is also doing well and shows no significant developmental delays, though he has been hospitalized several times for illnesses. Even common colds can aggravate the condition. Because of that, both moms say they avoid having their children near people who are sick.

Falconer and Tompkins said they want their children to live as normally as possible. They manage the boys' disease by carefully controlling every morsel they eat. Nathan drinks a special formula designed for infants with the disease. Marlon still takes the formula but also eats regular food. People with the disease continue with an adult version of the formula for the rest of their life, Tompkins said.

Both children must strictly avoid foods that contain the three amino acids they cannot process, particularly leucine. Their parents must look up everything they eat in nutritional books and carefully weigh and monitor everything that goes into their mouths. Even a single piece of fish, which contains leucine, could make them so sick they would have to go to the hospital.

Tompkins said she and her husband have chosen to get a liver transplant for Nathan, hoping it will offer him a better quality of life. But the surgery poses risks and is not for everyone, she said.

Both mothers said they strongly encourage other parents to have newborns tested. Wood said screening is mandatory for all newborns, but people can refuse it on religious grounds. About 99 percent of Alaska babies currently get the tests.

"I'm not trying to scare anybody, but you never really think you're walking around with bad genes," Tompkins said. "What you don't know can hurt you."

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