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Rare But Deadly
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RARE BUT DEADLY
Some simple, cheap blood tests could save thousands of kids' lives every year

By Susan Brink

Two cousins, two babies, two states. The six years between the birth of Toni Cline's daughter and Sharon Allen's son made all the difference between tragedy and joy. Kasie Cline died in Richmond, Va., in 1991 of a rare disorder called medium-chain acyl-CoA dehydrogenase, or MCAD.

Joshua Allen, born in 1997 in Wilson, N.C., with the same disorder, is today a healthy, energetic 7-year-old. What happened after Kasie's death and before Joshua's birth was the development of technology called tandem mass spectrometry, capable of screening newborn infants for MCAD as well as a variety of other rare disorders. With screening, physicians and metabolic nutritionists can develop treatment plans, often as simple as dietary changes, to save lives.

But even today, which side of a state border an infant is born on can make a life-or-death difference. Some states screen for as few as six disorders, while others screen for more than 50. That may change soon, as Secretary of Health and Human Services Michael Leavitt acts in the next few weeks on the recommendations of the American College of Medical Genetics' newborn screening expert group. The panel recommended that all 50 states screen for 29 rare disorders. All are treatable if discovered early, and none is obvious to pediatricians in the hospital nursery. Together, they affect no more than 5,000 of the 4 million infants born in the United States annually. Some are fatty-acid disorders, others involve a toxic buildup of amino or organic acids. Some hit select populations, like sickle-cell disease, which affects African-Americans.

Too late. Without screening, the disorders are discovered only when the infant becomes deathly ill. A child with undetected sickle-cell disease, for example, is vulnerable to life-threatening infections. When the disease is known, the child can be treated with antibiotics before any infection takes place. "We have preventive interventions when they're identified early," says F. Sessions Cole, newborn medicine

director at St. Louis Children's Hospital.

Consequences of delayed treatment of these hidden disorders can include seizures, retardation, and death. "We had a classic example of an infant in North Carolina who presented with glutaric acidemia [GA-1] and overwhelming brain damage," says Joseph Muenzer, associate professor of pediatrics at the University of North Carolina and chair of the state's Newborn Screening Advisory Committee. "The baby was born in Virginia, and the family moved to North Carolina. If the child had been born in North Carolina, there's a chance the problem would have been avoided." That's because testing for GA-1 is required in North Carolina. Virginia has recently added the disease to its panel of tests but has not yet implemented statewide screening.

"Parents are oblivious to this," says Dianne Frazier, professor of pediatrics and a metabolic dietitian at UNC. "They see the Band-Aid on the baby's heel, but they don't know which tests have been done." As recently as five years ago, only North Carolina and Massachusetts required that parents be offered the option of new screening tests utilizing tandem mass spectrometry to detect rare metabolic disorders. At least 35 states have increased the number of screening tests offered for infants, and more plan to do so. State movements have largely been led by parents who have lost a child; there is no uniform, national plan.

At a cost of about $70 to $120 per infant, testing all babies appears to be an obvious answer to the disasters that can befall a few. In states where advanced screening is already in effect, the cost is either folded into the hospital bill, covered by the state, or charged to parents. To hear the stories of the Allen and Cline families, universal screening of newborns seems a no-brainer.

Lethargy. Kasie Cline was born on June 6, 1990. "She was very sweet, very easygoing. She was my dream," says Toni. Perhaps too easygoing. She slept through the night almost immediately. Her parents had to wake her to feed her in the morning. "How many people wake up their infants?" she says. Now she knows that Kasie's glucose level dropped abnormally during the night, making her lethargic. It would rise with her morning feeding, setting her right for the day. One morning, when Kasie was 9 months and recently weaned, she had to be awakened. She was limp, her breathing shallow. The Clines called 911, but Kasie died of cardiac arrest in the hospital. Doctors told them it was SIDS, but the Clines were suspicious and agreed to let their pediatrician keep a frozen-tissue sample. The

doctor, long uneasy himself about the cause of death, kept searching journals and finally found a clue. He sent the tissue sample to Duke University, where it was analyzed, and the Clines were told the! ir baby had had MCAD.

"Fast forward to 1997," says Sharon Allen, Toni Cline's cousin. She vividly recalled Kasie's funeral. But when she was pregnant with her son, Joshua, she didn't give much thought to why her cousin's baby had died. Fortunately, she lived in North Carolina, and Joshua was born just a few weeks after the state began expanded screening. He was the first child identified with MCAD by the state's new screening program. "Just knowing it is 97 percent of the cure," says Sharon Allen.

Joshua cannot go too long without eating. As a baby, he had to be awakened every few hours to eat. That's because people with MCAD can't break down and store fat to turn into energy. He has to keep replenishing the energy supply, but now he's able to go up to 12 hours, or overnight, between meals. He eats a heart-healthy diet, heavy on fruits and vegetables. He's been an award-winning golfer in the 6-year-old division but will have to rule out wrestling because of its occasional demand to lose weight quickly. Knowing what might have been, his mother sees acquiescing to the quirky demands of his body as easy.

The difference that screening makes for those 5,000 infants and their families is enormous. But whatever Secretary Leavitt does in the next few months, it will be a recommendation, not a mandate, says Peter van Dyck, associate administrator of maternal and child health at the Health Resources and Services Administration, an agency of the Department of Health and Human Services. And a national recommendation doesn't translate into funds to cover the technology, the education of healthcare workers and parents, or the follow-up consultation and treatment.

Still, a recommendation from HHS will carry a lot of weight, coupled with increasing public demand as reflected in the state screening mandates. HHS has given grants to establish regional centers around the country to aid small and cash-poor states.

More tests. A greater problem is ensuring that every parent know what the Band-Aid on the heel means. Screening, after all, is not a diagnosis. It means there is reason to test further. "We'll be creating a lot of anxiety," says Lainie Ross, associate professor of pediatrics and

clinical director of the MacLean Center of Clinical Medical Ethics at the University of Chicago. "Most parents are already scared out of their minds with a newborn."

And it's possible that increased screening will find children who have less severe disease and who might have lived healthy lives never knowing anything was wrong. One 2001 Australian study, for example, concluded that screening found children with lower risk of becoming ill. "MCAD is the perfect disease we should be testing for," says Ross. "Yet the data from Australia show that they're diagnosing a lot more kids now than historically. We may be creating this whole community of people who have a diagnosis, some of whom may never get sick."

And yet, as the Clines, Allens, and countless other parents can attest, there have been tragedies that technology can help avert. "You can imagine," says R. Rodney Howell, professor of pediatrics at the University of Miami School of Medicine and chair of the newborn screening expert group, "if someone says your new baby has MCAD and we can put the baby on a special program and he or she will do fine--you'd go ballistic if you had a baby die of that condition. There are not a lot of things we do that can make this much of a difference."