

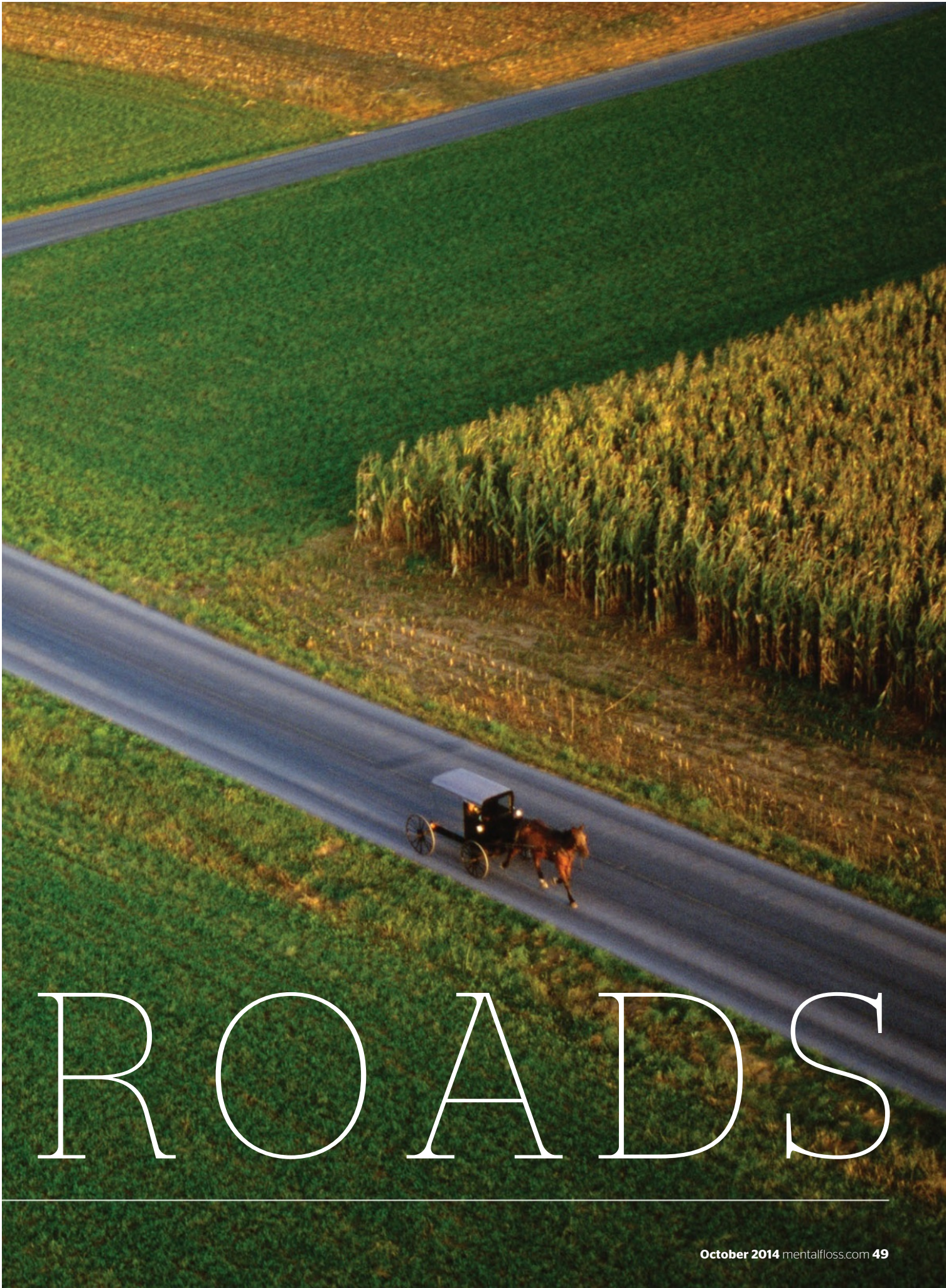
*The most high-tech advances in genetic research are happening in the most unexpected place—the heart of quiet Amish country.*

STORY BY **RENE EBERSOLE**

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CROSS



# ROADS

# HOLMES MORTON WAS WRAPPED UP IN A MEDICAL MYSTERY.

It was spring 1988, and Morton, a fellow at the Children's Hospital of Philadelphia, had recently opened the case of Danny Lapp, a 6-year-old Amish boy with a condition that baffled doctors. Danny was born healthy, but at 14 months, he caught what seemed to be a routine stomach bug. It wasn't: The illness had left him paralyzed and brain-damaged so badly that his limbs flailed uncontrollably and he could communicate only by rolling his eyes. The doctors chalked it up to cerebral palsy and moved on.

But another doctor Danny saw had been skeptical. Something about that diagnosis didn't fit, so he sent a urine sample to Morton, a specialist in pediatrics and biochemical genetics. Now the results were in, and Morton drove through the quilted patchwork of farmland surrounding Lancaster, Pennsylvania, to meet with Danny's parents.

The Lapps suspected their son's condition might be permanent, but they were glad to hear what Morton had to say. They were relieved to have a real diagnosis. But as they talked, the Lapps revealed something shocking, something that would shed light on a rare disease and change the course of genetic research for years to come. Danny, they said, wasn't the only one.

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he son of a West Virginia coal mine engineer, Morton was a high school dropout working on a Great Lakes freighter when he first became intrigued by genetic disorders after reading an article in a scientific journal. Before long, he'd move from working in a boiler room to an independent study program at Trinity College and then on to Harvard Medical School.

Morton's specialty included genetic conditions caused by dangerous enzyme deficiencies, so when he tested Danny's urine, he looked for enzyme irregularities. What he found was so unusual that, at first, he didn't believe it. But the results did not lie: Danny's urine was laced with glutaric acid.

Everyone's body produces glutaric acid, but in healthy people's urine, it's undetectable. The fact that it showed up in Danny's sample indicated that he didn't have cerebral palsy at all: He had a gene mutation called glutaric aciduria type 1 (GA1), a disorder that prevented his body from properly processing certain organic acids.

While healthy kidneys can flush glutaric acid from the brain and other organs, routine illnesses—like chicken pox, the flu, or, in Danny's case, a simple bout of diarrhea—can interfere with this process. In children, it triggers stroke-like episodes that irreparably damage the brain. "I was hopeful that by discovering his problem and treating him we would see some improvement," Morton remembers. But Danny's brain damage was too severe. "Once the damage is done, you lose the opportunity to change the outcome."

Morton had solved the mystery: Danny was a textbook case of GA1. But the thing was, there was no textbook. At the time, the scientific literature noted only eight known cases of GA1. Doctors, even those dealing with the rarest diseases, barely knew about the condition. No one at Children's Hospital had ever seen it.

The fact that there were other Amish children like Danny was alarming. Morton's mind raced. Was it possible that this disease—a condition so rare it existed only in the margins of medical literature—was rampant among the Amish?



Morton spent that summer driving around Lancaster County, knocking on farmhouse doors, asking about the health of each household's children. By the end of August 1989, he had identified more than 20 Amish children with what appeared to be GA1—all of them disabled like Danny.

While GA1 is incredibly rare, it fits a pattern. GA1 reminded Morton of another inherited disease, phenylketonuria, or PKU, a disorder that prevents children's bodies from breaking down an amino acid. Much like GA1, the accumulating chemicals can cause brain damage. And although the effects can be devastating, very few children actually suffer from it. Newborns are routinely screened for enzyme deficiencies at birth: If they have it, they're put on a low-protein diet that keeps their amino acid lev-

els in check and prevents PKU from ever becoming a problem. Morton wondered whether he could develop a similar protocol for treating children afflicted with GA1. If he could just test babies for glutaric acid at birth, he might have a shot at preventing more children from ending up like Danny. "I became convinced it could be treatable," he says.

Morton's first instinct was to apply for a grant to test his theory. Medical research was already happening in Lancaster County, and researchers have long known that inherited disorders are common in Amish and Mennonite communities. The populations there stemmed from a small group of Swiss and German Anabaptists who settled down in the area in the early 1700s. Generation after generation had intermarried, protecting their culture but also increasing the odds of passing down hereditary illnesses. Researchers had been swarming Lancaster

The Clinic for Special Children provides state-of-the-art care for young Amish afflicted with rare genetic illnesses.



Holmes Morton worked in the Merchant Marine before attending Harvard Medical School and becoming a specialist in metabolic illnesses.

County to collect blood samples for decades, hoping to better understand the disorders. Their studies helped pinpoint gene mutations responsible for dozens of diseases.

But Morton couldn't find funding—there wasn't much support for rare diseases. What's more, little of the research done around Lancaster actually went to helping locals. Researchers would come in, draw blood, and leave. To Morton, it amounted to "medical tourism." "That's when we decided to do this on our own," he says.

**T**he Plain People, the collective term for the Mennonites and Amish, have a complicated relationship with technology. Both groups cautiously debate the effect a new technology may have on the community before accepting it or rejecting it. The Mennonites are more lax, while the stricter Amish don't own cars, computers, or cell phones.

But both groups accept modern medicine. It's just sometimes hard for them to access. They pay for health care themselves. Hospital care is expensive, and the Amish can only travel short distances by horse and buggy. But because some Amish children are dreadfully sick, those families have no other choice but to give modern hospitals a shot, a situation that puts families in a tough financial position.

Morton realized he had to provide home visits. But what the area really needed, he thought, was a clinic that could both study and identify diseases and provide on-the-ground services. Morton and his wife,

Caroline, began planning to move their three kids near Lancaster. They wanted to be in Amish country, where they would apply for a second mortgage and get a nonprofit off the ground.

In 1989, *The Wall Street Journal* reported on the Mortons' dream of opening a clinic. Donations flooded in, including a large check and a generous equipment donation from Hewlett-Packard. Support came from the Amish too. A local farmer donated some land for the clinic. Some of his grandchildren were afflicted with GA1.

A year later, a team of Amish carpenters and farmers raised the roof on the medical center—a post-and-beam structure joined in traditional barn style, with pegs and no nails. There, two worlds merged: horse-hitching posts lined the plain exterior while state-of-the-art research equipment was housed inside. The community embraced the clinic, auctioning off quilts and handicrafts to raise hundreds of thousands of dollars for the cause. The Clinic for Special Children was born: one of the world's few free-standing health facilities specializing in treating kids with genetic diseases.

Before the clinic doors even opened, Morton began collecting urine samples, screening newborn babies for GA1 and a similar mutation that causes Maple Syrup Urine Disease, another serious metabolic disorder, in Mennonites. If the babies had either mutation, he put them on a low-protein diet—limiting their intake of breast milk or formula and supplementing it with a protein-free formula that could pack on calories.

The precaution was somewhat effective. The early intervention and low cost made the treatment straightforward, but it wasn't perfect. When Kevin

Strauss, a young Harvard-trained pediatrician, joined the clinic in 2001, two-thirds of the children with GA1 were being protected. But a good number were still suffering. Strauss was on the job no more than five months when he witnessed the disease first-hand. "It was one of the most horrible experiences of my life," he says. "A child who was getting ready to walk, doing really well, and then became absolutely devastated over the course of about an hour."

The doctors were stumped. "Even with all the research we had done, we were just missing something with this disease," Strauss says. The preventive diet wasn't enough. Could there be a way to halt glutaric acid from building up in the brain altogether?

**M**orton and Strauss doubled down and synthesized a formula that provided the ideal balance of amino acids. In 2006, they launched a clinical trial, treating 10 babies from the time they were born until they reached 18 months. The results seemed too good to be true. During the two-year trial, none of the children suffered catastrophic injuries. The formula did more than just help: "It was a 100 percent success rate," Strauss says.

Today, they have successfully treated all 22 patients in the study. GA1 has become "almost a perfectly treatable disease," says Strauss. Now testing for it is routine in hospitals across the country. Of the roughly four million babies born each year in the U.S., approximately 1 in every 30,000 to 40,000 newborns—and one in every 300 Amish babies—tests positive. But with proper treatment, they can all avoid brain injury.

Of course, GA1 is just one disease among many. To date, Morton's clinic has identified roughly 150 rare illnesses in Plain People—all caused by a single gene mutation. About half of the disorders affect the nervous system; the others cause things like kidney disease, heart disease, limb malformations, and immune system disorders. Newborn testing and therapy has made it possible to cure about 40 percent of these conditions. Another 40 percent are treatable but not curable. The rest are a mystery.

Unique genetic diseases are not exclusive to the Plain People. They're found all over the world—India, Saudi Arabia, Brazil, Italy, Israel—wherever a small population grows and expands but essentially stays in place. But outside Lancaster County, there are few facilities specializing in treating such diseases. "These are the things that mainstream medicine doesn't care about, because they're rare," Strauss says. "But if it's the child sitting right in front of you, it's not rare. It's in the room."

Morton is determined to build more clinics in places where rare diseases occur, particularly where more Amish and Mennonites live. So far, five other clinics have been built, and although the diseases each clinic specializes in are rare, the impact of their

research is far-reaching. In July, the clinic Morton founded, along with a number of academic partners, published a paper examining genes possibly associated with bipolar disorder in the Amish. The study size was small, but the clues written in the DNA may help researchers understand a mysterious mental illness that afflicts millions.

Strauss envisions a day when pinpointing these kinds of gene mutations will be as easy as taking someone's temperature. "Imagine if you could actually know that a person's going to get bipolar disorder and prevent it. That's an idea that will make most psychologists fall over in their chairs. Well, why

isn't it possible? Bipolar's a genetic disease." It's the same with other inherited illnesses, he says—heart disease, diabetes, Alzheimer's.

It may not be a long way off. After all, only a couple of decades have passed since Morton first drove through the rolling farmland of Amish country to meet a boy with a rare hereditary illness. And now there's a cure. Sometimes, real progress happens in places where time seems to stand still. ☺

**THE RESULTS  
SEEMED TOO GOOD  
TO BE TRUE.  
"IT WAS A  
100 PERCENT  
SUCCESS RATE,"  
STRAUSS SAYS.**

The clinic was built in the traditional barn-raising style on donated farmland.

