



MAY 2001

**A cop with a dying boy,
a scientist hot on the case**

Saving Ryan

By MARGERY STEIN

LATE AFTERNOON on a sunny Saturday, Mark Dant and his three-year-old son, Ryan, were playing ball in the backyard of their home in Carrollton, Texas. Crouching low, Mark, 32, wound up and lofted the soft plastic ball to his son. Ryan, toy bat at the ready, swung and connected with a thwack, sending

PHOTOGRAPHED BY WILL VAN OVERBEEK

the ball whistling over his dad's head. "Wow, great hit!" yelled Mark. "If this were a real game, you'd be on first base now."

Like millions of proud fathers, he had big dreams for his little boy. One was built on their shared passion for baseball. Mark played as often as four nights a week with his fellow officers in the Carrollton Police Department. Now his son was showing a real knack for the game. "He's a natural," Mark said to his wife, Jeanne, as the three of them headed to the dinner table. "Who knows, maybe he'll be a pro."

On that spring day in 1991, so bright and full of promise, no one could have foreseen the darkness about to fall on the Dant family.

TO HIS PARENTS, Ryan had always been the very picture of health—a ball of fire with an infectious grin and crinkly brown eyes. They'd never noticed anything unusual about him.

But at a checkup in August, the pediatrician thought Ryan's head and liver seemed unusually large. So he referred the boy to Dr. Lewis Waber, a pediatric geneticist. Waber ran some tests, then called the Dants into his office when the results came back.

"I don't have good news," said Waber. "Your son tested positive for a genetic disease called MPS I."

As Mark and Jeanne listened in stunned silence, Waber explained

that Ryan's body lacked a crucial enzyme that cells need to break down sugar. Without the enzyme, sugar molecules form thick deposits that clog the cells, stiffen joints and damage organs. Children with this disease almost never live past their teens.

Worst of all, added Waber, there was no cure. And because MPS I was so rare, affecting only a few thousand children around the world, drug companies weren't interested in funding the research.

"One thing you can do for Ryan," Waber said, "is love him for as long as he's with you."

AROUND THE TIME the Dants were learning of Ryan's disease, a brilliant young scientist named Emil Kakkis was busily scrubbing the floors and walls of his new laboratory—a cramped old Quonset hut in Torrance, Calif. A Ph.D. in biological chemistry with post-doctoral training in genetics, Kakkis had just been awarded a fellowship at Harbor-UCLA Medical Center.

But money was tight; he couldn't afford a staff or an ordinary laboratory. So with the help of a part-time assistant and his father-in-law, a contractor, Kakkis set up shop in this 300-square-foot building behind the medical center.

An intensely focused man with penetrating eyes and dark, curly hair, Kakkis had found a little-explored area of science that seemed ripe with the possibility of a breakthrough.

This, he thought, could be his chance to improve lives and strike a blow against a killing disease. He threw himself into his work. His mission: to create the missing enzyme and develop a treatment for MPS I.

ON THEIR DRIVE back home from Waber's office, Mark and Jeanne Dant felt numb and overwhelmed. For months after Ryan's diagnosis, his parents were consumed by sorrow, drifting through their daily routines like sleepwalkers. Night after night Mark lay in bed, staring at the ceiling, his mind racing as he struggled to accept the unacceptable: *my little boy is dying.*

On Waber's advice, Mark flew to Denver to attend a conference sponsored by the National MPS Society, an organization for families affected by the disease. There he saw firsthand the horrors of MPS—boys and girls with rigid joints and truncated bodies, five-year-olds with tracheotomies, 12-year-olds with the mental ability of kids half their age.

These children were doomed, and yet they gave Mark a new understanding of courage. Instead of feel-



In Stride—"We've played baseball together," says Mark, "ever since Ryan learned to walk."

ing sorry for themselves, they were warm, outgoing and high-spirited. And their parents, Mark thought, were the most loving mothers and fathers he'd ever seen. Somehow they'd come to accept the beast that was killing their sons and daughters.

Not Mark. He left Denver determined to keep his son from the same ghastly fate. But how? The odds were

stacked against him, and every minute brought Ryan closer to death.

ONE DAY Ryan came home from kindergarten in tears. He'd argued with another child, he told his parents, but it wasn't the disagreement that upset him. It was the other boy's remarks afterward.

"He said it doesn't matter what I think, because I'm going to die soon anyway. Is that true?"

Mark and Jeanne knelt and put their arms around him. "No, it's not true," Jeanne said softly. "Everybody gets sick with things called diseases. You have a special disease called MPS I. There's no medicine for it yet, but we're sure scientists are going to figure it out very soon." After giving it some thought, Ryan looked up at her and smiled.

But the disease was already beginning to tighten its grip. In the first grade, Ryan developed piercing headaches accompanied by waves of nausea. A couple of times a month, his father had to rush to his school to take the sick boy home, where Ryan would throw up until he was exhausted, and then sleep until morning. He missed so many days he had to repeat the first grade.

AFTER A YEAR OF RESEARCH, growing cells in flasks and purifying their protein secretions through a maze of glass tubing, Kakkis had managed to create cells that could produce the enzyme missing in patients with MPS I. He tested the enzyme

on dogs with the disease, and within weeks he had compelling results: harmful deposits in the animals' organs began to break down.

Kakkis felt certain that in time, he could develop a purer form of the enzyme for treating children with MPS I. It probably wouldn't cure them, but it might keep the illness at bay until a better treatment could be developed.

As the months slipped by, his goal drifted further from reach. On his bare-bones budget, he couldn't buy the proper materials or hire a scientist experienced in enzyme production. In fact, unless he could come up with more funding, he'd never be able to take the next crucial step.

IN THE FALL OF 1992, Mark and Jeanne set up the non-profit Ryan Foundation for MPS Children to raise money for MPS I research. Learning as they went, they built a grass-roots organization of volunteers who fanned out around Texas and beyond, signing up corporate sponsors, holding fishing competitions and placing jars for donations at gas stations. Their first fund-raiser, a bake sale, netted only \$342. Eventually, though, they hit on the idea of weekend golf tournaments. The first one raised \$25,000, and subsequent tournaments brought in even more. Mark sent the money to the MPS Society, hoping they'd put it to good use.

But money alone could do nothing for Ryan, whose condition steadily

worsened. One afternoon he collapsed on the soccer field during a game. Doctors discovered that his liver and spleen had ballooned to twice their normal size, a typical symptom of MPS I. The swelling revealed a hernia that required immediate surgery. Not long afterward Ryan developed severe pain in his neck and back, and a spinal tap showed his spinal-fluid pressure was alarmingly high.

His body was battered, but not his spirit. At Ryan's school, the boys' exercise routine included running three laps around the football field. Ryan, struggling to breathe, couldn't keep up—yet when his teacher cut him back to two laps, he protested.

"I don't want to be different," he said.

BY DECEMBER OF 1994, Emil Kakkis was desperate. None of the drug companies he'd approached wanted to invest in his research. Now it was clear: without more money, his work could proceed no further.

As it happened, Mark and Jeanne were in Orlando, Fla., that month, attending an MPS conference. One day while mingling with the crowd, they met Elizabeth Neufeld, a lead-



Mission Possible—"I wanted people to see that this drug was going to work," says Kakkis.

ing MPS researcher. Neufeld told them about a scientist in California who had made remarkable progress on MPS I. Unfortunately, she said, a lack of funding had brought his research to a standstill.

Smiles broke out on Mark's and Jeanne's faces as the same question shot through their minds: *could this be the answer to our prayers?*

After a sleepless night, Mark phoned Kakkis and told him about the Ryan Foundation. "Starting to

day," he said, "every penny I raise will go to your research on MPS I."

Kakkis couldn't believe his ears. "I'm at the end of my rope," he said, "but I know I'm on the right track. I'd be profoundly grateful for any help you can give me."

"For the work you're doing," Mark replied, "I'm the one who's profoundly grateful."

MARK and Jeanne clung to the belief that Kakkis would find success, even as they worried it would come too late for Ryan. Simply pulling on a T-shirt had become almost impossible for the boy, since he couldn't raise his hands over his head. At school, children made fun of his curled fingers. When he could no longer grip a baseball bat, his dad attached Velcro fasteners to the bat handle and his batting gloves.

For Mark, saving his son and other victims of MPS I became an obsession. He devoted every spare moment to the Ryan Foundation, giving up vacations, weekends, softball with his fellow officers, and even abandoning his longtime ambition of becoming chief of police. The lives of these kids, he decided, were more important than any job.

For three years, hundreds of thousands of dollars in donations to the Ryan Foundation kept Kakkis afloat. Arriving at the lab early and staying past midnight, he eventually managed to purify the enzyme.

He'd cleared a major hurdle, but the race was far from won. So Kakkis labored on, even though he knew it would take still larger sums of money to produce the amount of enzyme needed for tests on human patients. He'd seen one miracle already. Maybe another would come along.

Eventually word of his success with the MPS I enzyme made its way to Grant Denison, CEO of a biotechnology startup called BioMarin Pharmaceutical in Novato, Calif. BioMarin had begun exploring ways to treat MPS I, and Denison hoped to find someone who'd already gotten a jump on the research. It took a while, but at last he found exactly what he was looking for.

One day in late 1996, Kakkis answered the phone and listened in astonished disbelief as Denison explained: BioMarin wanted to help the scientist complete his work and, if possible, bring a treatment to market. Ultimately, the company agreed to give him the money he would need—\$5 million.

STARING UP FROM THE PILLOW, Ryan Dant looked small and vulnerable in his adult-size hospital bed. His face was pale. His swollen belly pushed out the front of his T-shirt, which was covered with the scrawled good wishes of his classmates.

It was February 13, 1998, and Ryan was in the pediatric intensive care unit at Harbor-UCLA Medical Center. He'd been chosen to be the third of ten children to receive the

experimental treatment developed by Emil Kakkis. Now, as he lay in a large room amid other patients and the loud beeping of heart monitors, he was awaiting his first infusion.

Sitting beside him on the bed were his father and mother. A few feet away, examining the device that would deliver the solution into Ryan's body, stood Kakkis.

"Okay, we're ready," said the researcher. Then he smiled and motioned for Mark and Jeanne to come near. "We're going to do this together," he said. So the three of them each put a finger on the machine's start button and pushed.

No one spoke as the clear fluid slowly began making its way through the tube. After a moment, Kakkis said in a soft voice, "That's it. We're on our way." Mark and Jeanne sank back on their son's bed, draped their arms around each other and cried.

A week later Ryan stood in front of a mirror with his shirt pulled up and mouth agape. "Wow! Mom, Dad!" he shouted, staring at his belly. "Look at how much smaller it is." Within six months his liver and spleen had shrunk, his limbs had loosened up and his energy had skyrocketed.

Ryan now gets a four-hour infusion of the enzyme every Monday at

the University of Texas Southwestern Medical Center in Dallas. In the years since he began the treatment, he's gained 35 pounds and grown nearly five inches. His headaches have subsided and his fingers have straightened considerably. Other kids have stopped staring at him, and much to his relief, he's no longer the shortest kid in his class.

Best of all, baseball is back at the center of Ryan's life. His cap and glove have come out of retirement, and he has joined a city baseball league. His dad, not one to break up a good partnership, also signed up. For two years now, father and son have gone to every game together—Ryan, the player, and Mark, his very devoted coach.

Ryan's family and Emil Kakkis hope that before long, the FDA will approve the drug for general use. Meanwhile the Ryan Foundation, which paid the hotel bills for the families of all the children during the clinical trials, is raising money for research in gene-replacement therapy—what Mark says could be "the final step in the cure" for MPS I.

For more information, visit the Internet sites for the Ryan Foundation (ryanfoundation.org) and the MPS Society (mpsociety.org).

CARTOON QUIP

Budding wine connoisseur to sommelier: "Hmmm, yes ... the bottle is shiny and green. The wine smells not at all like a wet dog, and there are no bugs in it. This will do nicely."

— DAN PIRARO, Universal Press Syndicate