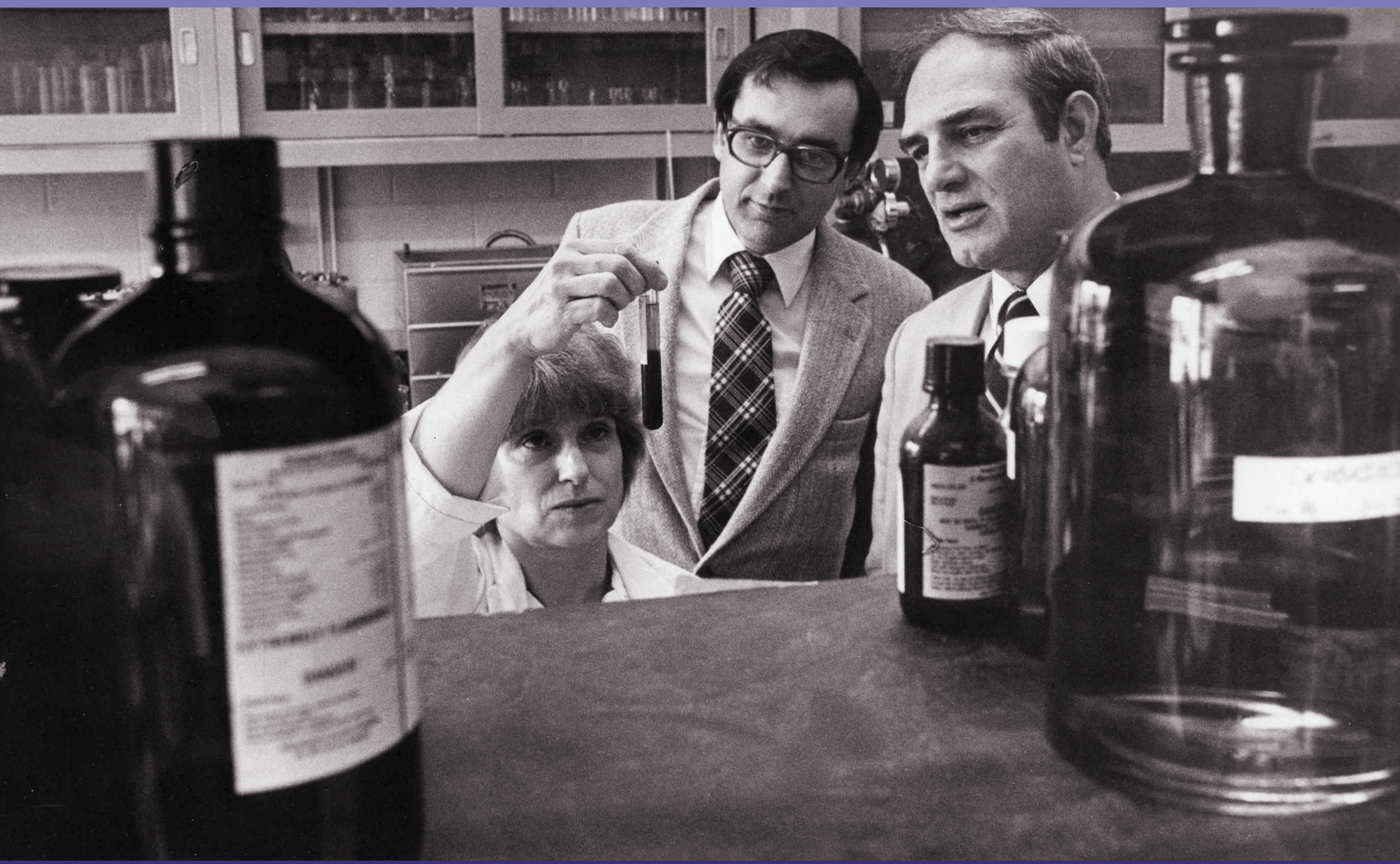


Children in Western Pennsylvania and around the world benefited from the diabetes treatment advances that started here and spread. Allan Drash led much of that work. He's shown here (right) in 1985 with colleagues Trevor Orchard and Eileen LaRocca.

THE DOC WHO BUILT A DIABETES TREATMENT AND RESEARCH CENTER WITHOUT PEER | BY CHUCK STARESINIC

"WE HAD DR. DRASH"

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A slight 6-year-old girl from Pittsburgh's North Side became ill with a virus one day. Her sickness was not all that unusual—she developed a fever and was vomiting. But when she failed to bounce back after several days, her parents took her to the pediatrician, who said, "She has a virus," and sent her home with instructions to rest and wait it out.

This was in the early 1970s. She may have had a run-of-the-mill viral infection initially, but something else was happening now. She lost weight. She urinated a lot, and she was always thirsty. The parents bypassed their pediatrician and brought her straight to Children's Hospital of Pittsburgh. It seemed like they had been in the hospital only moments when someone said, "This looks like diabetes."

Those were scary words. Diabetes may be manageable, but much less was known about how to manage it back then. All the parents knew was that their child was no longer just sick; she had an incurable disease. Some children entered the hospital in her state, continued to deteriorate, and died. Some came home less than whole. They were frail or had damaged minds. Others survived but lost something of their childhood.

At Children's, the physicians and nurses saw it a bit differently. There was an acute crisis to overcome in that the girl's blood was becoming increasingly acidic. This was life-threatening, but if she overcame it, the family could manage her disease.

Ketoacidosis, as the condition is called, is the most common, acute, and serious complication resulting from diabetes in childhood. The crisis often leads to the initial diagnosis. The problem begins, many experts believe, when the immune system reacts to a common virus in an uncommon way. Rather than fighting off the virus, then ramping down the attack, the immune system continues its assault, attacking cells in the pancreas.

Tucked into pearly clusters in the pancreas called islets of Langerhans, these cells produce insulin, a hormone that metabolizes glucose to fuel the body. When the body experiences a glucose shortage, it begins to metabolize fat instead, causing sudden weight loss and a buildup of acidic byproducts in the blood called ketones. Uncontrolled, it can lead to swelling in the brain, kidney failure, death of bowel tissue, and heart attack.

Through happenstance, the girl's family had arrived at what was arguably the best place in the world for a diabetic child to go. What is now Children's Hospital of Pittsburgh of UPMC and the University of Pittsburgh were building a diabetes research center without peer. Children in Western Pennsylvania benefited from the treatment advances that started here and spread around the world.

The physician who walked into the room that day and talked with the family about their daughter's diagnosis was the one most responsible for the bustling hive of diabetes-related research in Pittsburgh: Allan Drash, a pediatric endocrinologist and professor of pediatrics in the University of Pittsburgh School of Medicine. He and others had created a multifaceted center that simultaneously advanced the treatment of diabetic patients and probed the underlying epidemiology—who gets the disease, and why?

The girl in our story not only recovered from her bout with ketoacidosis, but she also went on to become a nurse and a diabetes educator. For decades afterward, she and her parents remembered the words of Dr. Drash.

He told them the disease could be managed. "Diabetes will become a part of your life," he said, "but do not give up on your dreams for your child. She can achieve anything she puts her mind to."

Allan Drash was a Tennessee native who stayed close to home for college (Vanderbilt University), then went to medical school at the University of Virginia, trained at Johns Hopkins Hospital, and later accepted a position with Children's Hospital of Pittsburgh. He was a pediatric endocrinologist who set about perfecting a clinic to treat children suffering from diabetes.

The year was 1966, and, compared to what we know now, physicians had an incomplete understanding of the disease. They knew that many people experienced adult-onset diabetes in their 40s or later. These people showed insulin resistance, meaning their insulin didn't process glucose as well as it should have. Other people developed diabetes in childhood or early adulthood. Both of these groups experienced hyperglycemia—excess sugar in the blood. But it wasn't clear whether there were major differences between the two types of diabetes aside from the age of onset.

"Diabetes will become part of your life," he said, "but do not give up on your dreams for your child."

In 1967, one year after arriving in Pittsburgh, Drash published a study confirming that most children with diabetes were not insulin resistant like most adults with diabetes. The children were insulin deficient. They had no insulin, or they had not nearly enough. The study contributed to a new understanding that there were two types of diabetes: Type 1 usually came to light in childhood and was marked by a deficiency of insulin. Type 2 usually appeared in adulthood and was marked by the body's resistance to the insulin it produced.

Drash's motivation was to find the best treatment for diabetic children. Aggressive treatment with insulin injections eventually became the unquestioned standard of care for type 1—hence the moniker insulin-dependent diabetes. Drash was instrumental in pushing for federal funding of the Diabetes Control and Complication Trial, which eventually grew to 29 sites. It demonstrated that metabolic control was critically important in the development and rate of progression of vascular complications in people with diabetes. And it showed that an aggressive regimen that included multiple daily injections of insulin was the most important element of treatment.

He quietly fomented a revolution in endocrinology at a time when pediatric endocrinology was a rather neglected field. At professional conferences, he and other endocrinologists who treated children typically had a session or two devoted to their interests. His work on diabetes illustrated his point that children were not just smaller in size than adult patients: Diabetes, like many other endocrine disorders, was fundamentally different in children than it was in adults. Drash lobbied for pediatric endocrinology to be taken more seriously. And, over the course of his career, it was.

In Pittsburgh, Drash employed a unique team approach to treating diabetes. He believed in treating the family, not just the child. He enlisted nutritionists, nurses, social workers, educators, and psychologists. Physicians in his clinic were just one part of a team that strived to educate the family and manage the disease with aggressive monitoring and intervention.

With philanthropic help, Children's Hospital provided funding so that families who could not otherwise afford care could receive the same treatment.

The epidemiology of diabetes intrigued Drash. There were hints that genetics played a role—siblings and other relatives of diabetic children seemed to be at higher risk of developing the disease. Because early diagnosis and intervention were important elements of successful treatment, Drash believed that epidemiology was a natural extension of the clinic. In the early 1970s, Drash and epidemiologist Lewis Kuller developed a registry that aimed to include every child in Allegheny County diagnosed with type 1 diabetes.

"Allan focused very much on developing an unusual, multidisciplinary clinic that gave quality care for children," says Kuller, who is now a Distinguished Professor of Public Health at Pitt. "And that helped in developing the registry and getting families and patients into research programs. The research program just blossomed dramatically."

Epidemiologists who trained in Pittsburgh include Ronald LaPorte, a Pitt professor of epidemiology who led the diabetes project for years, and Trevor Orchard, currently the interim chair of epidemiology at Pitt.

The diabetes epidemiology group in Pittsburgh exported the model worldwide, with Drash as its principal ambassador. In 1990, Drash calculated that he had averaged 100 days of travel per year for the preceding eight years. "We were married 38 years," says Diane Drash. "There were no real holidays.

We would travel for meetings, or when he would lecture or give a keynote address at a conference."

She recalls her husband, who died on August 3, 2009, visiting clinics around the world: "I loved to watch him interact with parents and children. His whole life was built around trying to help children with diabetes and to reassure parents."

His travel and years of professional duties led to one memorable argument with his then-teenage daughter, one of two Drash children. A few days later, Drash wrote a long, thoughtful letter to his daughter about his reasons for being dedicated to his profession and his love for her.

He wrote, "There is nothing more important than to be consumed by a sense of dedication and responsibility to a profession, a calling, that takes one out of one's own self and into the service of others. It is not the job of medicine that is demanding, but that we are demanding of ourselves."

About his dreams for her, he wrote, "Despite what the U.S. Constitution says… Happiness should not be pursued. It is the byproduct of a meaningful, contributing life. I hope for you such a life."

At Children's Hospital of Pittsburgh, Drash trained a long line of stellar pediatric endocrinologists. Dorothy Becker is a Pitt professor of pediatrics who now occupies Drash's former position as chief of pediatric endocrinology and diabetes. She also is the director of the diabetes program at Children's and is principal investigator on a multicenter trial funded by the NIH to determine whether a cow's-milk infant formula can keep children from later developing type 2 diabetes. She "continues to carry forward [Drash's] investigative prowess," notes Orchard. Ingrid Libman is another Drash trainee, an MD/PhD assistant professor of pediatrics who works in prevention and treatment of type 2 diabetes in children. Silva Arslanian, the Richard L. Day Professor of Pediatrics, is an internationally recognized endocrinologist and authority on the long-term consequences of type 2 diabetes and racial disparities in its prevalence.

Pitt's diabetes epidemiology project was probably the largest such project in the world, Kuller says. "In our international project, we had 155 centers in 70 countries across the world. For a while, we were publishing 35 to 40 papers a year at a time when we were probably responsible for 20 to 30 percent of the world's literature in that area." To offer evidence, Kuller walks to a bookshelf across the hall from his office. He pulls down a few bound sets of scientific papers, each roughly as thick as the Pittsburgh telephone book.

"This is [from] the early days," he says, paging through the bibliography in the front of one volume. "It's almost all Drash. It's Drash and epidemiology group. It was a broad project, from the basic immunology all the way up to the global work."

Pitt's reputation has attracted expertise throughout the health sciences schools. Linda Siminerio—a diabetes educator, faculty member in the schools of medicine and nursing, and executive director of the University of Pittsburgh Diabetes Institute—was the national spokesperson for World Diabetes Day in 2009.

Andrew Stewart, Pitt professor of medicine and chief of the Division of Endocrinology and Metabolism, left Yale University to join the Pitt faculty in 1997. Stewart's lab has identified the genes and proteins involved in the creation of new insulin-producing cells. Stewart is exploring the possibility that we might stimulate the production of new cells in patients with diabetes, restoring their ability to manufacture insulin.

In the mid-'80s, Drash and his colleagues recruited Massimo Trucco, an MD immunologist and geneticist who was prepared to take the expertise in Pittsburgh and build on it to create a new understanding of the basic immunology and genetics behind type 1 diabetes. Today, Pitt's Trucco is the Hillman Professor of Pediatric Immunology, a professor of pathology, human genetics, and epidemiology, as well as director of the Division of Immunogenetics.

Simply put, Trucco is on the trail of a cure for diabetes. He has uncovered genes that confer susceptibility to type 1 diabetes and described some of the molecular activities in the immune system that cause the destruction of insulin-producing cells. Trucco and his colleagues—notably Nick Giannoukakis, an associate professor of pathology and immunology—have developed cell and microparticle vaccines that reverse or prevent type 1 diabetes in mice. The group is wrapping up a safety trial of a vaccine in recently diagnosed children.

"Allan had this phenomenal commitment to taking care of the people," says Kuller. "It wasn't just screening these kids to do an interesting genetic study. He was actually saying, 'Hey, what are we going to do about it?'"

For much of four decades, until his death last year, Drash was the doctor leading the way for families in Pittsburgh with diabetic children. One former patient says it's impossible to overstate the significance of his words and actions on her family. Drash told her parents not to let their child be defined by a diagnosis:

"We all know what that diagnosis means. It's this overwhelming shadow of darkness. But we never had that. We had Dr. Drash." ■

Children's Hospital is establishing the Allan Drash Diabetes Scholarship to further the careers of pediatric diabetes trainees and perpetuate Dr. Drash's work. To contribute contact Chip Eagle, 412-586-6317 chip.eagle@chp.edu

To protect patient privacy, some details were changed in this story.

DIABETES INVESTMENTS

When he was 35 years old, Allan Drash received an offer to relocate from Johns Hopkins University to Children's Hospital of Pittsburgh and the University of Pittsburgh. One of the attractions for Drash was that, at Children's, the diabetes clinic had long been a priority. A $1 million fund had been established in 1937 by Emilie Renziehausen to support the care of diabetic children and honor the memory of her two brothers, one of whom had diabetes. The interest from that fund has contributed to clinical care at Children's for more than 70 years. The fund allows for aggressive outreach to families coping with diabetes, regardless of the family's financial situation. Additional gifts from the Renziehausen family through the years have created an additional trust fund at Children's to support laboratory research and education. These deep roots have nourished an extraordinary breadth and depth of diabetes research at Pitt. ***—CS***