

Edward Horton, M.D., '55: Insulin insider

By Jennifer Durgin

They met over a dead body in the early 1960s. Dr. Edward Horton, then a pathology resident at Mary Hitchcock Memorial Hospital, got a call one night to perform an emergency autopsy on the victim of an automobile accident. He phoned the on-call second-year medical student to request his assistance.

“So this young medical student shows up,” Horton remembers. “His name was Kenneth Quickel.” Thirty years later, Dr. Quickel phoned Horton with a request of his own. Quickel was by then president of the Joslin Diabetes Center in Boston, and Horton was a prominent endocrinologist at the University of Vermont (UVM). Quickel wanted to hire Horton as medical director and director of clinical research at Joslin, but Horton resisted. He was happy chairing the Department of Medicine at UVM, where he had led some of the most influential studies in the history of diabetes research.

Horton’s work centers on type II diabetes—once known as adult-onset diabetes and most commonly associated with obesity. In type II, the body stops responding correctly to insulin, a pancreatic hormone that is necessary to metabolize sugar. In type I diabetes, the pancreas produces too little insulin or sometimes none at all. Both types of diabetes result in high levels of sugar in the blood and a long list of complications—including heart disease, stroke, kidney disease, eye problems, and nerve damage.

Horton was curious, he says, about “how insulin worked on the cells in the body, how exercise worked to increase glucose uptake in skeletal muscle, and what the effect of physical training was on insulin sensitivity.” His interest in understanding the relationship between exercise and glucose metabolism is not surprising, given that he’s been an athlete and avid skier his whole life. As an undergraduate at Dartmouth College, he belonged to both the Nordic and Alpine ski teams. Even today, in his mid-seventies, he still zips down the slopes. Some of his colleagues who have skied with him question whether he knows how to turn. “He just goes straight down!” jokes Michael Hirshman, who managed Horton’s lab at UVM for many years and now works with him at Joslin.

Among Horton’s most notable research projects at UVM were the Vermont Studies on Experimental Obesity in Man. “We did studies from the late 1960s up and through the mid-1970s, taking normal lean volunteers, who had no history of obesity, no history of diabetes, overfeeding them, and having them gain 25% of their body weight,” he explains. Other researchers had recruited obese subjects, reduced their weight, and looked for changes, but no one had done the opposite. “We were the first people,” says Horton, “to show that if you overfed people, you made them insulin resistant. We fortunately didn’t

make anyone diabetic. We didn’t cause anybody to have heart attacks or anything like that.” Horton acknowledges that such a study, although acceptable at that time, probably would not be allowed today. Nevertheless, it provided important insight into diabetes.

Until Horton’s work, it was not known whether insulin resistance was exclusively a genetic problem or whether it had an environmental component, too. Physicians and researchers now know that type II diabetes depends on three factors: genetic predisposition, the development of insulin resistance, and impaired insulin secretion.

When Horton became interested in diabetes research 40 years ago, he never imagined that the disease would become as prevalent as it is today . . . “truly a worldwide epidemic.”

In addition to running a lab and chairing the Department of Medicine at UVM, Horton also served on the editorial boards of several journals and in leadership posts for a couple of national societies. He was president of the American Society for Clinical Nutrition in 1986 and headed the American Diabetes Association in 1990. But of all his activities, Horton most enjoyed mentoring young researchers. And they enjoyed working with him.

“I went to [the University of] Vermont because he was there,” says Laurie Goodyear, who worked in Horton’s lab as a Ph.D. student. “Any time there’d be visitors or people coming to work in the lab, he’d always have them to his house and really make [them] feel part of what was going on.” And, she adds, Horton “really took the time to teach and help you learn.”

For example, he taught Goodyear that “you can do good science and be a good researcher, but still be a good person,” she says. “You don’t have to be cutthroat.” Goodyear admires the way Horton combines an upbeat attitude with the passion of a hard-core scientist.

All of Horton’s accomplishments made him a top candidate for the Joslin positions. So Quickel “worked on me for about two years,” recalls Horton. But “the clincher of the deal,” he says, was when the two met in Hanover, N.H.—almost halfway between Burlington, Vt., and Boston—for lunch.

Hanover was Horton’s hometown as well as where he had begun his medical education. He’d graduated from Dartmouth College in 1954 and from DMS—then a feeder school—in 1955. After completing his M.D. at Harvard in 1957, he’d interned in surgery at Johns Hopkins and then headed to Germany, with his wife, to serve in the Army for three years. In 1961, when his military stint was up, he wasn’t sure whether he wanted to pursue general surgery or internal medicine. So he returned to Hanover to do a pathology fellowship. The year-long position, he reasoned, would give him time to settle on a career path. He eventually decided on medicine, thanks in part to the guidance of Dr. Allan Tisdale, then head of all the residency programs at Mary Hitchcock Memorial Hospital.

From 1962 to 1967, Horton trained at Duke University Medical

Jennifer Durgin is DARTMOUTH MEDICINE magazine’s senior writer.

Center, first as a resident in internal medicine and then as a fellow in endocrinology. In 1967, he was recruited to UVM by Tisdale, who had by then become chair of medicine there. Horton's career flourished at UVM. He moved steadily up the academic ranks, becoming a full professor in 1976 and chair of medicine in 1987. He'd intended to stay at UVM—until Quickel approached him in the early 1990s.

Horton did feel drawn to the Joslin posts. Much of his time at UVM was consumed with chairing the department, and he wasn't spending as much time on research as he wanted to. Also on his mind was a close family member who had been diagnosed with type I diabetes a few years earlier. Joslin would give Horton a chance to focus all of his attention on diabetes care and research.

After that Hanover lunch, Quickel and Horton wandered over to a wooded area of the Dartmouth campus known as the Bema—a term that alludes to the Greek word for sanctuary and also stands for “big, empty meeting area.” As Horton strolled through the Bema, pondering his future, he recalled going there as a child after the Hurricane of 1938. There had been so many downed trees then that he'd been able to walk the entire length of the Bema on trunks and branches without ever touching the ground. Growing up in Hanover—near Mary Hitchcock, where his mother had worked as the head of volunteer services—had certainly influenced Horton's choice of careers. And considering that Hanover was where he had begun his medical education, it was fitting that Hanover was also the place where he made one of the biggest career decisions of his life—to leave UVM and join Joslin.

Since 1993, Horton has been the director of clinical research at Joslin and has helped to build it into a diabetes research powerhouse, with research funding that now totals some \$50 million a year. He gave up the position of medical director in 1997 to focus almost exclusively on research. Today, he is the principal investigator for two major National Institutes of Health-funded research projects.

One, called the Diabetes Prevention Program Outcomes Study (DPPOS), is a multicenter clinical trial that is trying to determine if lifestyle changes and a blood-glucose-lowering medication can stave off the development of cardiovascular disease in diabetics. “About 75% of the death rate for people with diabetes is heart disease and stroke,” explains Horton. “So all of the current interest now is on how does obesity not only cause insulin resistance, but how does



Horton, pictured here at Boston's Joslin Diabetes Center, was on the team that confirmed 30 years ago that obesity is not only strongly correlated with diabetes, but that it can actually trigger insulin resistance and lead to the onset of type II diabetes.

it cause atherosclerosis and cardiovascular disease.”

The second study, called Look AHEAD (which stands for Action for Health in Diabetes), evaluates two different interventions: trying to lose weight and exercise versus participating in a diabetes support and education program.

When Horton became interested in diabetes research more than 40 years ago, he never imagined that the disease would become as prevalent as it is today. “We're undergoing truly a worldwide epidemic of obesity and di-

abetes,” he says. “And it's really all being driven by changes in lifestyle, economic growth, and development—more food, less exercise.” More than 194 million people worldwide have the disease, according to the International Diabetes Federation (IDF). Countries with the largest numbers of diabetics in 2003 were India (35.5 million), China (23.8 million), and the United States (16 million). And the IDF estimates that about 85% to 95% of the people living with diabetes have type II, which is largely preventable.

The fundamental question facing the world, says Horton, “is how are we going to deal with this epidemic? We're understanding more about it. We're learning the links between obesity, diabetes, cardiovascular disease, and so forth. But it's much more than a medical problem. It's really a societal problem. What we have to focus on, if we are going to actually have an impact on reducing this epidemic, [is] public education—education of the policy-makers, dealing with things like city planning . . . [and] making it possible and safe for people to go out and walk, for example. There's a whole lot of issues that come into play.” This is why studies like the DPPOS and Look AHEAD are so important, he believes.

“I'm encouraged on the one hand,” Horton continues, “in terms of the new knowledge and the new medications that are being developed. . . . But I'm a little bit daunted by how we are going to deal with this epidemic on a worldwide basis, because we're not having a huge impact. Every time I see the numbers that come out from the [Centers for Disease Control and Prevention], they're worse.” But neither Horton's dismay, nor the fact that he turns 74 in September, means he'll be stepping down any time soon. His two big studies are funded for several more years, and he just took on a new research fellow.

“I'm currently full steam ahead,” he declares. “As long as you are having fun, there is no sense in retiring.” ■