Taking the Sting Out of Diabetes

The long hallway that stretches the length of the Division of Surgical Research, situated on the ninth floor of the Montreal General Hospital site of the McGill University Health Centre (MUHC), is nondescript except for a collection of portraits of surgical residents and faculty. The portraits, which are black-and-white or colour, with some framed and others laminated, neatly encapsulate the history of the division. Many of the smiling faces in these images appear only once. There are a few individuals, however, who can be seen again and again, with various tie widths and hairstyles, depending on the year. Dr. Lawrence Rosenberg is one of these recurring figures, and this photographic record charting his progress from surgical resident to Director of the Division of Surgical Research documents one of the most remarkable careers in the MUHC's recent history.

When confronted with this evidence, Rosenberg says with a smile, "I've been here forever." Forever, in this case, means almost 30 years. He obtained his MD from McGill University in 1979 and then did his specialty training in General Surgery at the Montreal General Hospital. Not content with the "relaxed" schedule of a full-time surgical resident, Rosenberg completed a PhD in Experimental Surgery during his residency. He then left Montreal briefly, "to see how things were done elsewhere and learn new techniques," completing post-doctoral studies, including a transplant surgery fellowship, at the University of Michigan. This would turn out to be Rosenberg's only professional foray outside of his alma mater.

Upon Rosenberg's return to Montreal in 1987, he was appointed Assistant Professor of Surgery and Medicine at McGill. His return was motivated by a combination of exigency and emotion. "I came back to Montreal to meet both legal and moral obligations," he says, explaining that his American work visa had expired and that he had made a commitment to the chairman of the McGill Surgical Department to return to the Montreal General Hospital after his post-doctoral training. Since then, Rosenberg hasn't looked back, using the resources of the MUHC to find success and professional satisfaction through the creation of a practice that marries laboratory research, teaching and clinical work. He is now a Professor of Surgery and Medicine and also holds the A.G. Thompson Chair of Surgical Research at the MUHC.

Rosenberg's career has focused on the pancreas, the elongated organ in the abdomen that has two distinct functions, one classified as endocrine, the other, as exocrine. Endocrine refers to the pancreatic secretion of key hormones such as insulin, and exocrine concerns the organ's production and secretion of digestive enzymes. Rosenberg explains that as a clinician he is mostly concerned with the exocrine function, while as a researcher he is dedicated to studying the endocrine role.

The humble pancreas may seem like an unusual organ to which a physician would dedicate an entire career, but for Rosenberg the choice was easy. "For some reason I was always interested in pancreatic diseases, and I had a close uncle who died of pancreatic cancer," he says. Rosenberg's singular focus paid incredible dividends 25 years ago when he and several colleagues made a discovery that one day might make daily insulin injections a thing of the past for the millions of people worldwide who suffer from insulin-dependant diabetes. Diabetes occurs when the pancreas fails to produce enough insulin to regulate blood glucose levels. Nearly two million Canadians are affected by the condition, which can result in blindness, kidney failure and amputations.

It all began in 1981, when Rosenberg and the late William Duguid, who at the time was pathologist-in-chief at the Montreal General Hospital, made a remarkable discovery: the adult pancreas is capable of growing new insulin-producing cells. By surgically manipulating the pancreas, Rosenberg and Duguid were able to stimulate the growth of a molecule called islet neogenesis associated protein (INGAP), which is a key factor in the production of insulin. In 1986, Rosenberg and Duguid showed that injecting a crude extract made from pancreatic

tissue into animals resulted in the formation of new insulin-producing cells and the reversal of diabetic symptoms. Ten years later, Rosenberg and an American colleague, Aaron Vinik from the Strelitz Diabetes Research Institute, identified that the active ingredient in the crude extract was their earlier discovery, INGAP.

Today, INGAP and a smaller derivative of the protein, INGAP peptide, are undergoing human clinical trials in the United States. Anticipating a breakthrough, a group of private biotech companies is working with McGill to bring a commercially marketable version of the protein to market. "The trials are ongoing, and the INGAP peptide is showing great promise," says Rosenberg. "Out of all the treatments currently available for diabetes, I believe INGAP will be the most useful." If no hiccups disrupt the process, the treatment might be available to patients in as little as five years.

Leaving the business of monitoring the INGAP trials to others, Rosenberg switched his research priority to growing new pancreatic islet cells – the cells that produce insulin – for transplantation. "The major limitation to using islet transplantation for the treatment of diabetes on a large scale," he says, "is that we simply don't have enough donor-derived tissue."

Inspired by the regenerative properties of stem cells, Rosenberg and his colleagues discovered that cells from adult islets themselves have stem-cell-like properties and can be induced to create new cells. Using this technique, many new insulin-producing cells can be created from one pancreas. "If we can grow more tissue from one organ, many more patients will be able to benefit from islet cell transplantation. This project offers the greatest chance of successfully developing a renewable source of cells for islet replacement through transplantation," he says.

The MUHC's Islet Transplant Program will open its doors next summer. "We have the technique down pat," Rosenberg says. "We're just waiting for the completion of lab renovations to accommodate the procedure." By next fall, he and his colleagues will perform transplants on candidates whose diabetes is difficult to control. The hope is that following the transplant the recipients will no longer require synthetic insulin.

Although it is his diabetes research that has earned Rosenberg his international reputation, he remains a dedicated clinician, treating a steady stream of patients at the MUHC's Pancreatic Diseases Clinic. Here, patients are mostly treated for pancreatic cancer or pancreatitis, a severe inflammation of the pancreas often caused by gallstones or the excessive consumption of alcohol. In his role as overseer of the MUHC's Graduate Surgery Research Program, Rosenberg is also much in demand as a teacher. More than 55 students – a mix of medical residents and graduate students in the biological sciences – are enrolled in this innovative research training program. In addition, he mentors several graduate students and two research assistants who work in his lab. "Like most physician-scientists at the MUHC, I take great pride not just in my research but in the care I give to patients and in my work as a teacher," Rosenberg says. "All three of these things are what make an academic health centre like the MUHC tick."

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> Dr. Lawrence Rosenberg, Director of the Division of Surgical Research, MUHC

Listening to Rosenberg describe his rich and varied career at the MUHC, it is easy to imagine what future photos in the busy hallway of the Division of Surgical Research will show. Amongst the rows of new faces, one familiar smile will continue to appear. "My work is appreciated here. The MUHC continues to be extremely supportive, giving me every opportunity to pursue my scientific and medical interests," Rosenberg says. "I've spent my entire career here. It's my home." ❇

Equipping Excellence

Cardiovascular diseases are the number one cause of death in Canada. This deadly family of conditions includes high blood pressure (hypertension), coronary heart disease, heart attack (myocardial infarction), Sudden Cardiac Arrest (SCA), heart muscle disorders (cardiomyopathy) and stroke. For patients who are undergoing treatment for a cardiovascular condition, accurate monitoring is key given that even a tiny change to the heart's rhythm can spell disaster.

When patients are hospitalized at the MUHC, **cardiac monitors** are used to continuously track and record the electrical activity of their heart. Electrodes are attached to the patient's body and a bedside monitor provides a visual display of his or her vital signs. Any change is immediately visible to nurses and doctors, and at the first sign of a potentially dangerous rhythm, the monitor sounds an alarm.

The cardiac care specialists at the MUHC have a number of cardiac monitors in constant use, but more are needed to meet the growing demand for specialized cardiovascular care. These simple but critical tools, which cost around $25,000 each, can make the difference between life and death for the more than 20,000 cardiac patients who pass through the MUHC's doors every year. ❇

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