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SPECIALTY REPORT | WINTER 2016

Hilda and J. Lester Gabrilove
Division of Endocrinology, Diabetes and Bone Disease

Mount Sinai Advances Artificial Pancreas Research

Research under way at the Icahn School of Medicine at Mount Sinai (ISMMS) has the potential to revolutionize the management of type 1 diabetes (T1D), freeing patients from repeatedly testing their sugar with finger sticks and having to adjust their insulin regimens.

The clinical research study, funded by JDRF, is the first outpatient study of artificial pancreas (AP) systems in New York State. A joint effort among ISMMS, the University of Virginia (UVA), and the Mayo Clinic, the study followed 10 patients with T1D for five days, during which the UVA-developed AP system provided them with continuous glucose monitoring and insulin pump therapy at night. The AP system runs a software algorithm on a smartphone that communicates with a standard insulin pump and glucose sensor to maintain each participant’s sugar levels within a designated range to avert nighttime hypoglycemia and ensure a goal glucose level in the morning (see photo at left).

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New Approaches to Care In the Adrenal Center

The Adrenal Center at Mount Sinai, under the co-direction of William B. Inabnet III, MD, Chair of Surgery at Mount Sinai Beth Israel and the Eugene W. Friedman Professor of Surgical Oncology at the Icahn School of Medicine at Mount Sinai, and Alice C. Levine, MD, Professor of Medicine (Endocrinology, Diabetes and Bone Disease) at the Icahn School of Medicine, has become one of the leading centers for adrenal referrals on the East Coast in only five years. Here are updates from the Center.

360-Degree Treatment of Pheos

The results of an international retreat of 15 experts held at Mount Sinai to improve the diagnosis and management of phaeochromocytomas (pheos) were published in the November 2014 issue of Endocrine Practice. This was the first publication aimed at developing a comprehensive clinical pathway for the management of pheos. The outcome of the retreat was a consensus for the diagnosis, periphereve management, and postoperative management of pheos, with specific recommendations from our team of adrenal experts, which includes adrenal surgeons, endocrinologists, nuclear medicine doctors, radiologists, clinical laboratory experts, anesthesiologists, and genetic counselors. Our clinical pathway model can be applied by other institutions, with many medical centers already expressing interest in using it.

Using Mifepristone in a New Way

A poster presented at the Endocrine Society annual meeting in San Diego in March 2015 showed that the drug mifepristone, which blocks the action of the hormone cortisol, produces positive effects on glucose parameters and insulin sensitivity as well as beneficial effects on depression scores and quality of life in patients with mild overproduction of cortisol due to adrenal incidentalomas. This was the first time the drug had been studied in patients with this type of adrenal tumor.

Top Recruits

This year we welcomed two impressive fellowship-trained endocrine surgeons to the Adrenal Center:

• Gustavo Fernandez-Ranvier, MD, Assistant Professor of Surgery (Metabolic, Endocrine, and Minimally Invasive) at the Icahn School of Medicine at Mount Sinai
• Hyunsook Shuh, MD, Assistant Professor of Surgery at the Icahn School of Medicine at Mount Sinai

NEUPLY PUBLISHED

Alice C. Levine, MD, Co-Director of the Adrenal Center, was editor of a recent book, Adrenal Cortical Neoplasia, Endocrine Clinics of North America Series, Volume 44, Number 2, June 2015.

One Insulinoma Cure Begets Another

Many physicians spend their entire careers without finding a true case of insulinoma. Ronald Tamler, MD, PhD, MBA, Director of the Mount Sinai Clinical Diabetes Institute and Associate Professor of Medicine (Endocrinology, Diabetes and Bone Disease) at the Icahn School of Medicine at Mount Sinai, cured two separate insulinoma cases in just one year.

In 2014, a 53-year-old woman from Rockland County, New York, had been experiencing sudden drops in blood sugar (down to a disconcerting 14 mg/dl) that left her incoherent and with gaps in memory. The patient’s endocrinologist was stumped by the normal lab workup and CT, so he referred her to Dr. Tamler at The Mount Sinai Hospital.

Despite the patient’s completely normal lab workup, Dr. Tamler began to suspect an insulin-producing tumor. He noticed that glucose-level and C-peptide tests had never been conducted at the same time, so he ordered a repeat fasting test that showed a blood glucose level of 51 mg/dl with a C-peptide of 2.5. The case was closed: the patient had an insulin-secreting tumor. Once blood glucose drops below 60 mg/dl, insulin production should shut off. An endoscopic ultrasound located a one-centimeter tumor in the pancreas. Shortly thereafter, the patient underwent successful laparoscopic removal of the tumor by William B. Inabnet III, MD, Chair of Surgery at Mount Sinai Beth Israel and the Eugene W. Friedman Professor of Surgical Oncology at the Icahn School of Medicine at Mount Sinai.

A few months later, The New York Times Magazine featured the case in its column “Think Like a Doctor,” in which the magazine challenges its readers to solve a diagnostic mystery.

Hundreds of miles away in Florida, a teacher read the article and felt as though she were reading about her own case. Told by her endocrinologist that she did not have an insulinoma and that she was imagining things, she caught a plane to New York City to see Dr. Tamler. After reading her original workup, Dr. Tamler cut the visit short. “I recognized the same constellation as in my prior insulinoma patient, remembering that ‘normal’ is sometimes abnormal. Her insulin output during hypoglycemia should have been zero. We immediately sent her for an endoscopic ultrasound, which revealed a 12-millimeter insulinoma in the head of the pancreas,” Dr. Tamler recalls.

What should have been a quick referral for timely surgery touched off a three-month battle with the patient’s insurance company, which endorsed the care of a Florida surgeon who recommended an open laparotomy with a Whipple procedure. During this period, the teacher experienced near-daily hypoglycemia and had to begin taking dextrose.

“Insulinoma enucleation (or removal) is always preferred unless malignancy is suspected. More invasive procedures such as the Whipple procedure are pursued if enucleation is not feasible or safe,” says Dr. Inabnet. “In most cases, insulinomas are benign and ideally suited for laparoscopic and minimally invasive approaches, as was the case here.”

Finally, the patient won her fight with the insurance company and proceeded to have surgery with Dr. Inabnet. She left The Mount Sinai Hospital two days after the surgery, cured.

Many doctors never see a true case of insulinoma in their entire careers. One Mount Sinai physician saw two in just one year.
Solving an Undiagnosed Case Of Acromegaly

V. Brown, a retired nurse, age 59, went to a New York City hospital in 2014, complaining of chest pain. A sufferer of lifelong medical problems, she was diagnosed with hypertrophic cardiomyopathy. After alerting her cardiologist to recent weight gain, she was referred to an endocrinologist.

In November 2014, Ms. Brown developed a sudden, severe headache, which prompted her to revisit her primary hospital. Along with the headache, she was experiencing nausea and double vision. Her blood pressure was found to be elevated, so her doctor increased her prescription dosage of Isotaran—an one of five medications she was taking.

Due to her multitude of serious ailments, she was forced to retire early on disability.

After seeing a news program that featured Donald Smith, MD, Associate Professor of Medicine (Cardiology) and Preventive Medicine at the Icahn School of Medicine at Mount Sinai, she made an appointment to discuss whether she qualified for bariatric surgery.

Dr. Smith, an endocrinologist who sees cardiac patients, suspected acromegaly after reviewing Ms. Brown’s history of spinal stenosis, sciatica, carpal tunnel, and sleep apnea, and hearing her concerns about recent weight gain and swelling in her face, hands, and feet. She also reported the appearance of widely spaced teeth, an enlarged jaw, and a shoe size that had increased from 8.5 to 13. Dr. Smith ordered labs, which came back showing an elevated insulin-like growth factor-1, or IGF-1. He immediately referred Ms. Brown to Eliza Geer, MD, Medical Director of the Pituitary Care and Research Center and Associate Professor in Endocrinology and Neurosurgery.

Dr. Geer confirmed that Ms. Brown’s IGF-1 level was elevated, at 566 ng/ml, with a growth-hormone level of 5.36 ng/ml, confirming Dr. Smith’s suspicion: the patient had been battling undiagnosed acromegaly, missed by her original physicians, for many years.

Dr. Geer again tested Ms. Brown’s growth-hormone levels after an oral glucose tolerance test: the paradoxical increase in growth hormone from 4.3 to 5.6 ng/ml confirmed the diagnosis of acromegaly. Dr. Geer then viewed her MRI and saw a pituitary tumor, which, based on the previous test results, she knew was a growth-hormone-secreting tumor and the cause of the acromegaly.

She referred Ms. Brown to Kalomon Post, MD, Surgical Co-Director of the Pituitary Care and Research Center and the Leonard I. Malis, MD/Corinne and Joseph Graber Professor of Medicine and Professor of Neurosurgery, who in July 2015 performed transsphenoidal surgery to remove the pituitary tumor. Immediately after surgery, Ms. Brown’s growth-hormone level dropped to approximately 1.5 ng/ml with an IGF-1 level of 348 ng/ml.

After three months, her IGF-1 had decreased to 500 ng/ml, and her growth-hormone level was 1.53 ng/ml.

Ms. Brown continues to improve today through a multimodal course of care at Mount Sinai. If needed in the future, she has access to new medications that can aid in lowering her IGF-1 and growth-hormone levels through ongoing clinical trials at the Mount Sinai Pituitary Care and Research Center. She will be attending a monthly support group offered at Mount Sinai for patients with Cushing’s disease and acromegaly. The group—the only one of its kind in New York City—provides emotional support, education, and stress-relief techniques to patients with these rare conditions.

A Nurse Practitioner Solves a $72,000 Mystery

Cynthia Esrig, a nurse practitioner who is brought in to consult on cases in which a patient is experiencing high blood glucose levels. The patient had maintained his health through restrictive diets that lasted two years but never helped his high sugar levels. Over time, his endocrinologist reached the point of prescribing 250 units of insulin. After receiving proper injection training from Ms. Esrig, the patient’s A1C test measured nearly 12 percent—almost double the target recommended by the American Diabetes Association for people with diabetes.

Ms. Esrig and the patient discussed his daily habits surrounding his diabetes care, focusing on his nutrition and insulin routines. She asked him to show her how he injected insulin. Observing him, Ms. Esrig discovered the root cause of the patient’s problem: he wasn’t removing one of the caps on the two-cap needle, therefore never inserting any insulin whatsoever into his bloodstream.

The insulin would move through the first cap but not the second. The patient had never been shown how to use the pen properly before he met Ms. Esrig at Mount Sinai.

On his second visit to Mount Sinai, the patient met with Cynthia Esrig, a nurse practitioner who is brought in to consult on cases in which a patient is experiencing high blood glucose levels. The time Ms. Esrig met with the patient, his A1C test measured nearly 12 percent—almost double the target recommended by the American Diabetes Association for people with diabetes.

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The insulin would move through the first cap but not the second. The patient had never been shown how to use the pen properly before he met Ms. Esrig at Mount Sinai.

After receiving proper injection training from Ms. Esrig, the patient’s A1C levels normalized. Today he is meeting his A1C goal of around 7 percent and injects only 20 units of insulin per day—a 92 percent reduction in insulin from what had been prescribed before he came to Mount Sinai.

“Cynthia’s discovery is a perfect example of Mount Sinai’s practice of truly listening to a patient—a lost art in some medical centers,” says Dr. Lam.

Cynthia Esrig, NP, holds the double-cap insulin pen while David W. Lam, MD, looks on. Inset: A close-up showing the first (blue) and second (clear) caps. If a patient fails to remove the second cap, no insulin will be injected.

“Our aim is to empower our patients to take control of their health care, not solely to rely on test results and medications to lead us to a cure.”
—David W. Lam, MD
Yiannis Ioannou, PhD, has developed a series of small molecules that can penetrate the blood-brain barrier and correct lipid-metabolism dysfunction in patient cells for at least eight lysosomal storage disorders. Yiannis Ioannou, PhD, Professor of Genetics and Genomic Sciences at the Icahn School of Medicine at Mount Sinai, has developed a series of small molecules that can penetrate the blood-brain barrier and correct lipid-metabolism dysfunction in patient cells for at least eight LSDs. “We’re very excited by the results of animal studies for Fabry disease, and by an 85 percent decline in cholesteryl accumulation for Niemann-Pick Type C,” two types of LSDs, he notes.

In kidney-transplant patients, physicians currently use measures of creatinine in the blood to monitor the transplanted organ’s status. But this method has a critical flaw: by the time increased levels of creatinine are detected, fibrosis has already developed and the kidney has been irreversibly damaged. Indeed, chronic fibrosis is the primary reason that 17 percent of kidney transplants fail by the third year, and fewer than half still function by the tenth year.

Barbara Murphy, MD, the Murray M. Rosenberg Professor of Medicine, System Chair of the Department of Medicine, and Dean for Clinical Integration and Population Health, is developing a portfolio of assays to monitor kidney function before and after transplantation. These noninvasive assessments, known as FractalDx assays, identify genetic signatures from simple blood tests to predict the likelihood that transplant recipients will develop fibrosis and graft loss. “Instead of being reactive and limiting the damage,” Dr. Murphy explains, “we’re developing a monitoring tool that can identify problems before damage occurs.”

Brain tumors, among the most aggressive cancers, consign roughly half of patients to an average life expectancy of 16 months following surgery. By the end of 2016, Isabelle Germano, MD, Director of the Comprehensive Brain Tumor Program and Professor of Neurosurgery, Neurology, and Oncological Sciences, expects to start clinical trials on a breakthrough stem-cell therapy she has developed, which, if proven successful, could prolong the lives of people with glioblastoma by several years. The approach delivers to the disease site autologous stem cells engineered to express a tumor-cell-killer gene that is activated once the tumor returns, which is 95 percent of the time.

Although some technical issues in cell manipulation remain, lab results have validated Dr. Germano’s work with induced pluripotent stem cells. “The future for treating brain tumors is in making the body’s own cells ‘smarter’ so they can fight the disease,” she says.

Cutting-edge research by Mount Sinai Health System physician-scientists in a wide range of fields is helping the Health System uncover bold new therapies to meet the urgent needs of patients and society. The Health System, one of the largest in the nation, includes the Icahn School of Medicine at Mount Sinai, with 34 departments and more than 23 multidisciplinary institutes that are designed to facilitate breakthrough science. Scientists and researchers benefit not only from extensive resources and talent inside the laboratory but also from the expertise of Mount Sinai Innovation Partners, a group that works across the entire system to attract critical funding and shape the newly developed technologies for application and commercialization.

In the field of lysosomal storage diseases (LSDs), for example, the development of small molecules—a proven effective in early trials to reverse the toxic buildup of lipids in patients’ cells—holds promise for a new treatment paradigm for these disorders. Collectively, LSDs comprise the most common genetic disorder in humans. Although enzyme replacement therapy has been the standard of care for some LSDs, the inability of proteins to cross the blood-brain barrier renders this approach ineffective for about 90 percent of the 60 known lysosomal storage disorders.
Mount Sinai Health System

Extraordinary Education
At the Icahn School of Medicine at Mount Sinai, innovative programs encourage students to pursue their passions. We admit half our class through FlexMed, our early assurance program, which accepts students during their sophomore year of college and waives their traditional premed course requirements.

1,800
Students enrolled in MD, PhD, and master’s programs and post-doctoral fellowships

$267M
Annual funding from the National Institutes of Health

#2
Nationwide in funding per principal investigator

7,000+
Physicians provide outstanding care

4.6M
Annual patient visits

Groundbreaking Research
Pioneering translational research is at the heart of our programs. Renowned scientists and physicians throughout the Health System team up in their common commitment to improving human health.

Exceptional Clinical Care
Mount Sinai is known nationally and internationally for the excellence of our clinical services.

6,000
House calls per year to the homebound elderly

10,000
Youths receiving health care and education

Community Commitment
The richest and poorest areas in New York City meet at the Mount Sinai campus. We are committed to serving the health care needs of all of our diverse communities.

Hilda and J. Lester Gabrilove
Division of Endocrinology, Diabetes and Bone Disease
Yaron Tomer, MD, Chief

Division of Endocrinology, Diabetes and Bone Disease website
www.mssm.edu/endo

Diabetes Center website
www.mssm.edu/diabetes

Pituitary Center website
www.mountsinai.org/pituitary

Adrenal Center website
http://adrenal.surgerymountsinai.org

Visiting Doctors Program
Adolescent Health Center

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