Jill P. Crandall, M.D., is all too familiar with diabetes. “My mother had type 1 diabetes, and I saw her testing her blood sugar, taking shots, dealing with the day-to-day intrusions,” she says. “I saw the effect the disease has on people’s lives.”

Today Dr. Crandall, at right, is a professor of clinical medicine (endocrinology) and director of the Diabetes Clinical Trials Unit at Albert Einstein College of Medicine. As an attending physician in endocrinology, she sees patients in the diabetes clinic at Montefiore, the University Hospital and academic medical center for Einstein. Every day, she confronts diabetes and its serious complications, including cardiovascular, nerve, kidney, eye and foot damage.

Her mission is prevention.

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Preventing Diabetes
Dr. Crandall is Einstein’s principal investigator (PI) for the multicenter Diabetes Prevention Program Outcomes Study, supported by the National Institutes of Health (NIH). People enrolled in this study started out with prediabetes—blood sugar that’s elevated but not quite at the diabetes level. “This study was designed to show how well diet and exercise, or the oral drug metformin, prevent or delay type 2 diabetes in people at high risk,” says Dr. Crandall. The research program showed that type 2 diabetes can indeed be prevented or delayed. Follow-up will tell whether these treatments will prevent diabetes complications.

Dr. Crandall is also investigating whether the red wine extract resveratrol can prevent diabetes. In a pilot study involving 10 patients with prediabetes, she found that resveratrol improved insulin sensitivity and blood sugar levels following meals. A $600,000 grant from the American Diabetes Association has allowed her to conduct a larger study. Participants receive resveratrol capsules rather than red wine, since it would take hundreds of bottles daily to reach therapeutic levels. “There have been a lot of health claims made for resveratrol based on relatively little evidence,” she says. “Our goal is to find out if these assertions are true.”

Preventing Complications
A challenge for diabetes researchers is preventing diabetes’ dangerous complications (including cardiovascular, nerve, kidney, eye and foot damage). Such complications afflict people with both type 1 and type 2 diabetes and result from abnormally high blood levels of sugar, which damage tissues throughout the body. The landmark Diabetes Control and Complications Trial, conducted at Einstein and 28 other sites in the United States and Canada during the 1980s and 1990s, provided clear and convincing evidence that controlling blood sugar is the key to preventing these complications.

An Einstein-Montefiore team is taking part in a major NIH-supported effort to prevent diabetes complications, called the Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study (GRADE). “This nationwide clinical trial is looking for the most effective combination of glucose-lowering medications,” says Dr. Crandall. She and Diane McKee, M.D., associate professor and co-director of the research division in the department of family and social medicine, are spearheading GRADE at Einstein. Why here? “Unfortunately, our diverse Bronx population has a high rate of type 2 diabetes,” says Dr. Crandall. “With our clinical research center and Montefiore as our clinical partner, we’re well positioned to carry out this important trial.”

Dr. Crandall is also the Einstein PI for Preventing Early Renal Loss. This study, sponsored by the NIH and the Juvenile Diabetes Research Foundation, is testing an old drug (allopurinol) for a new purpose: protecting kidney function in people with type 1 diabetes. Controlling blood sugar and blood pressure and using blood pressure medications called RAS blockers doesn’t prevent kidney disease in everyone at risk. “This study has the potential to change the way diabetic kidney disease is treated and improve the outlook for many patients with diabetes,” says Dr. Crandall.

Q: What are some of the lesser-known complications of diabetes?
A: Diabetes can affect the skin, mouth, bones and hearing. And new findings point to a possible association between insulin resistance and Alzheimer’s disease. Researchers found that type 2 diabetes patients with higher insulin resistance had greater damage to the brain’s gray matter than type 2 individuals with lower insulin resistance.
Managing Type 2 Diabetes

Joel Zonszein, M.D.
Professor of Clinical Medicine
Department of Medicine (Endocrinology)
Albert Einstein College of Medicine
Director, Clinical Diabetes Center
Attending Physician, Medicine
Montefiore

For patients with type 2 diabetes, glycemic control—maintaining blood sugar at normal levels—is crucial for good health. Taking the right prescription drug can be important in this effort, and the right treatment can help enormously.

Dr. Zonszein led a study that looked at factors associated with successful, long-term glycemic control in patients who had both type 2 diabetes and cardiovascular disease. These patients had received either insulin or drugs that make people more sensitive to insulin’s effects. Certain patients were more likely to maintain long-term glycemic control if they took insulin-sensitizing drugs rather than insulin. These patients generally were younger, had had the disease for a shorter time, were physically active, had lower blood sugar levels and were not on insulin when they began treatment. The study appeared in the Journal of Diabetes and Its Complications.

Diabetes and Kidney Disease

Michael A. Brownlee, M.D.
Anita and Jack Saltz Chair in Diabetes Research
Professor of Medicine (Endocrinology)
Professor of Pathology
Associate Director for Biomedical Sciences
Einstein Diabetes Research Center
Albert Einstein College of Medicine
Attending Physician, Medicine (Endocrinology)
Montefiore

Diabetes is the leading cause of kidney failure worldwide, yet not all patients with high blood sugar develop kidney disease (also known as diabetic nephropathy). Researchers have begun to identify the genes that determine whether diabetic nephropathy will occur.

Dr. Brownlee and colleagues reported in the journal Diabetes that the gene Glo1 controls the likelihood that someone will develop diabetic nephropathy in response to high blood sugar levels. Glo1 encodes glyoxalase 1, an enzyme that detoxifies a by-product of glucose metabolism. The group found that glyoxalase 1 helps prevent oxidative stress that can damage the kidneys. When the Glo1 gene was turned off in nondiabetic mice, they experienced kidney damage identical to that caused by diabetes. These findings may lead to new therapeutic approaches for treating diabetic nephropathy.

ON THE WEB
To learn more about the Diabetes Research Center, please visit:
www.einstein.yu.edu/diabetes

DRC Initiates Regional Diabetes Center

For the last several years, Einstein has hosted a diabetes conference that brings together leading diabetes researchers from New York–area medical centers. Out of these interactions have come various partnerships—most recently a regional diabetes research center that will combine the strengths of Mount Sinai and Einstein. Mount Sinai will bring its expertise in beta cells and in community outreach; Einstein offers strong basic research in the molecular mechanisms of diabetes and clinical research studies.

Einstein DRC director Jeffrey E. Pessin, Ph.D., was the driving force behind the initiative. “We want to keep the conversation among diabetes researchers going all year long,” says Dr. Pessin. Individual researchers from Columbia and New York University will also participate. Dr. Pessin will serve as director of the new center; Einstein’s Meredith A. Hawkins, M.D., and Mount Sinai’s Andrew Stewart, M.D., will be associate directors.
Notable Gift

For more than two decades, the Einstein DRC has hosted “Friday morning rounds” throughout the academic year. Held in the Ethel and Samuel J. LeFrak Auditorium, these events feature presentations by diabetes experts from Einstein and other leading academic institutions in the United States and abroad.

The rounds are open to basic scientists, clinical researchers and healthcare providers from Einstein and collaborating medical institutions such as Mount Sinai and Columbia. Einstein postdoctoral fellows, M.D. trainees and other researchers and clinicians are also invited to participate.

The talks typically draw between 80 and 110 attendees. “We almost always have a full house,” says Meredith A. Hawkins, M.D., an associate director of the DRC, who organizes the program and who joined the DRC as a postdoctoral fellow 20 years ago.

The meetings begin with breakfast, allowing speakers and attendees a chance to mingle informally. The breakfast hour “stimulates great questions and discussions,” notes Dr. Hawkins. “It’s also very helpful for younger investigators, who can meet leaders in the field.”

Thanks to a recent donation to the DRC from an anonymous supporter, the rounds will continue to bring together the best and brightest in the diabetes research community. “We are extremely grateful for this generous gift,” says Dr. Hawkins. “It will allow us to continue our search for better ways to treat and prevent type 1 and type 2 diabetes and to stem the global diabetes epidemic.”

Speakers and Topics

In addition to our own Dr. Pessin (“An Unexpected Molecular Crosstalk Between Metabolism and NF-kB Signaling”) and Dean Allen M. Spiegel, M.D. (“Hyper and Hypoparathyroidism: New Molecular Genetic and Clinical Studies”), recent presenters at the DRC’s Friday morning rounds have included:

- Blandine LaFerrere, M.D., Columbia University College of Physicians and Surgeons (“Remission of Diabetes After Bariatric Surgery: Beyond Incretins”)
- Yaron Tomer, M.D., Mount Sinai Hospital (“Type 1 Diabetes and Autoimmune Thyroiditis: The Genetic Connection”)
- Rebecca Simmons, M.D., University of Pennsylvania (“The Epigenetic Landscape of the Beta Cell in Type 2 Diabetes”)
- Adolfo Garcia-Ocana, Ph.D., Mount Sinai Hospital (“Recent Advances in the Regulation of Pancreatic Beta Cell Replication”)

To learn more about supporting the work of the DRC, please contact:
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