

healthpoints

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COLUMBIA UNIVERSITY
MEDICAL CENTER

Department of Surgery
In affiliation with
NewYork-Presbyterian Hospital

Chronic Pancreatitis

With autologous islet cell transplantation, a diabetes-free future may be possible after total pancreatectomy.

Chronic pancreatitis is a relatively rare condition characterized by progressive, irreversible damage to the pancreas. It may be caused by gallstones, alcoholism, or hypertriglyceridemia (high concentrations of fatty molecules called triglycerides), or it may develop after an episode of acute (short-term) pancreatitis. In at least half of patients, the cause remains unknown. Over time, chronic pancreatitis leads to inability to properly digest food due to lack of digestive enzymes (pancreatic exocrine insufficiency), which can cause indigestion, bloating, diarrhea, and even malnutrition.

But the most devastating feature of chronic pancreatitis is pain, which frequently becomes severe enough to require daily narcotic medications. For those whose lives have deteriorated because of unrelenting pain, relief—and return to normal life—is possible only when the pancreas is removed.

The singular goal of total pancreatectomy (removal of the pancreas) for patients with chronic pancreatitis is to relieve pain. Because the pancreas produces digestive enzymes and hormones including insulin, this surgery is reserved only for those in whom pain is so severe and unremitting that it has led to dependence on narcotic medications. After pancreatectomy, pain is relieved in 93% of cases, but the absence of insulin production leaves patients fully diabetic.

For people whose lives had been transformed by unbearable pain and narcotic dependence, the benefits of living pain-free far outweigh the trade-off of managing surgically-induced diabetes. Diabetes is largely manageable today with advances in medications and insulin delivery devices such as continual pumps. Nevertheless, even when diabetes is well controlled, it still requires significant lifestyle changes, and it presents many risks to patients' long-term health.

At NewYork-Presbyterian/Columbia, a

new therapeutic option now enables some patients to undergo pancreatectomy without becoming diabetic. This alternative, called autologous islet transplantation, involves infusion of the patient's own pancreatic islet cells into his or her liver, where they may act like a backup pancreas, independently producing insulin.

It works like this: First, the patient's pancreas is surgically removed. Islet of Langerhans cells (the cells in the pancreas that produce insulin), are isolated from the



Beth Schrope, MD, PhD, Assistant Professor of Surgery, and Mark A. Hardy, MD, Director Emeritus and Founder, Renal & Islet Transplantation, look on as Joseph Dinorcia III, MD, Surgical Resident, uses a Ricordi chamber to harvest and purify pancreatic islet cells.

pancreas and made into a solution. The solution is then infused into the patient's liver, through the hepatic vein. Once in the liver, the islet cells may begin to produce insulin that functions just as it did when produced in the pancreas.

When autologous islet transplantation is successful, the procedure results in patients maintaining normal blood sugar levels without needing insulin. According to **Beth Schrope, MD, PhD, Assistant Professor of Surgery, Columbia University**

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Surgical Science Update

RAGE research, now in clinical trials, sheds light on mystery of diabetes-related complications.

Despite the many strides made in understanding and treating diabetes, mysteries about its course, and challenges in perfecting treatment and prevention, still remain.

Researchers at the NewYork-Presbyterian Hospital/Columbia University Medical Center (NYPH/Columbia) Division of Surgical Science are steadily unraveling one of these mysteries – the role of an important molecular component known by its acronym, RAGE. A perfect example of translational research, this work has the potential to yield therapies for preventing the most devastating complications of diabetes.

RAGE stands for Receptor for Advanced Glycation Endproducts (AGEs). AGEs form when proteins in the walls of blood vessels are exposed to excess sugar, or glucose, in the blood. The presence of excess glucose (hyperglycemia) likely activates the the AGE receptor, RAGE, in the lining of the blood vessels (the endothelium). Continued stimulation of RAGE in this way produces ongoing stress, inflammation, and cellular death in the blood vessels, including those that supply the heart.

In healthy individuals, inflammation leads to tissue repair, and after repair is achieved, the inflammatory process stops. In people with diabetes, however, inflammation leads to injury of the blood vessels because the hyperglycemic-RAGE axis causes the inflammatory process to run rampant – it does not stop. Continued inflammation likely accelerates the formation of atherosclerotic plaque (hardening of the arteries), eye and kidney disease, and

problems with blood flow to the extremities — some of the most serious complications in diabetes.

Ann Marie Schmidt, MD, Chief, Division of Surgical Science, explains, “In order to stay healthy, all organisms need a healthy cellular repair process. Diabetes causes vascular problems in two important ways – it not only damages the blood vessels, but it impairs the body's natural ability to repair itself, in part by mobilizing ‘stem’ or ‘progenitor’ cells from the peripheral blood or bone marrow. The inability to repair itself then leads to further damage.” By the time symptoms of diabetes complications appear, a person's blood vessels are extensively damaged.

Damage to the endothelium is what leads to the development of black toes and feet, the potential for gangrene, and loss of toes in patients with diabetes. Signs of such injury also include nerve damage (neuropathy), impaired wound healing, and vulnerability to infection. The abnormal inflammatory process is also responsible for degeneration of nerve cells, which leads to Alzheimer's disease – another area of Dr. Schmidt's research that could benefit from RAGE-based therapies.

Under her leadership, the Surgical Science Division has shown that removing the effect of RAGE from mice with diabetes restores their natural repair mechanisms. According to Dr. Schmidt, “The results suggest that blocking RAGE (with medication) might help replenish and revive the vasculature in people with diabetes.” There were no observable negative effects from

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Dr. Oz Show



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(Rockefeller Plaza in New York, NY)

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(Phone lines are open 9:00 am – 5:00 pm Mon. – Fri.)



**Annual Pancreatic Cancer Awareness Day
and 2010 Purple Stride Walk**

November 2010, New York, NY
Details to come in the next issue
of *Healthpoints*.

**Gala Dinner to
Benefit Pulmonary Services at
NewYork-Presbyterian Hospital**

Proceeds from the Gala will be used to support
clinical research and treatment of pulmonary disease at the
Weill Cornell and Columbia campuses.

Date: Thursday, April 15, 2010

Time: 6:30 pm cocktails; 7:30 pm dinner

**Entertainment: Lionel Richie at 9:30 pm
(30 minute show)**

Venue: Grand Ballroom, the Waldorf Astoria, New York

**Individual ticket prices begin at \$1000,
and tables at \$10,000.**

**To request information or purchase tickets,
please call (212) 972-2268**

blocking RAGE in the mouse studies.

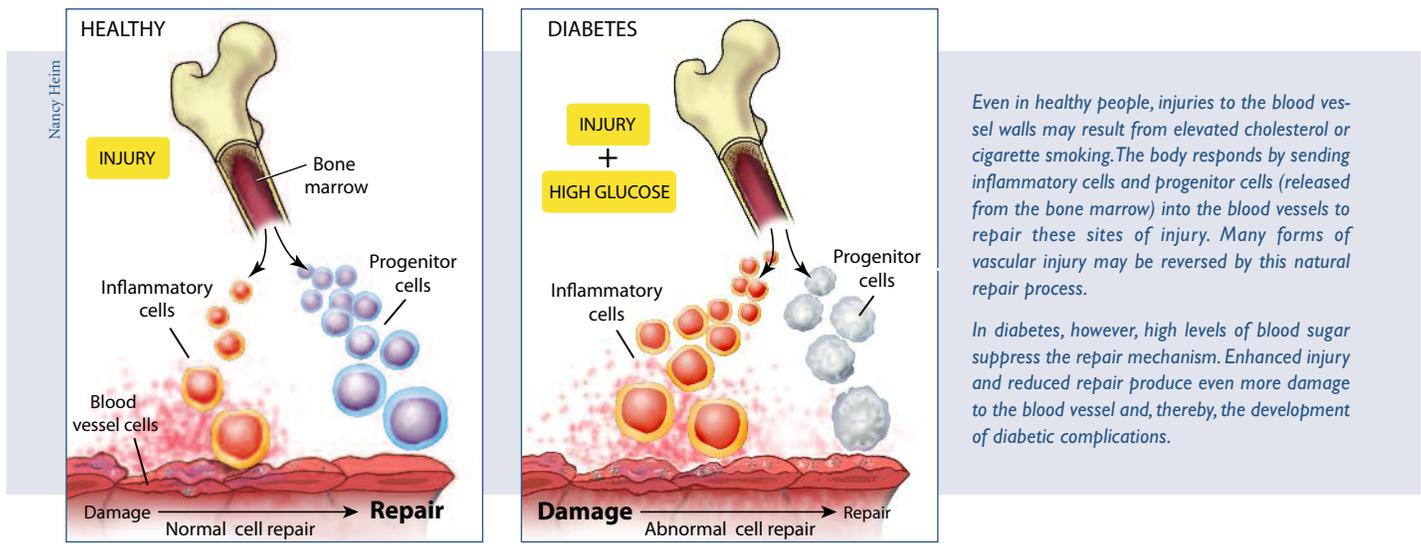
The division's study of RAGE is not new. Since 1992, Dr. Schmidt's team has been steadfast in its work on the RAGE axis, observing its mechanisms in test tubes and in mice. What is new is that the team's 'bench' work has moved one step closer to 'bedside' application.

The question now under consideration is whether blocking RAGE in humans will be beneficial as in mice, and, importantly, if it will have any harmful effects. That is the focus of the current clinical trial, which is using a drug to block RAGE in two groups: patients with Alzheimer's disease and patients with diabetic kidney disease. If blocking RAGE in these patients is effective and

safe, it will advance the researchers one step closer towards development of a new therapy. "Blocking RAGE does not seem to block the positive inflammatory actions, but this is not fully proven yet," says Dr. Schmidt. The trial, which is taking place at several institutions in addition to NYPH/Columbia, is expected to last several more years, although initial results are expected later in 2010.

"Moving studies 'from mouse to man' takes great amounts of time and effort, but the hope of alleviating human suffering makes the work a labor of love," says Dr. Schmidt. ♦

For more information, visit Surgical Science in the Research section of www.columbiasurgery.org



Renal 3000

Circle for Life: Renal 3000

Date: Wednesday, April 21, 2010

Time: 11:00 am – 1:00 pm

Location: The Armory,

168th Street & Fort Washington Avenue, New York, NY

New York-Presbyterian Hospital/Columbia University

Medical Center will host *Circle for Life: Renal 3000*

to celebrate the hospital's 3000 kidney transplants

and honor transplant recipients and donors. This event

is for renal transplant patients, donors, their guests,

and invited faculty.

Registration and entry by invitation only.

For more information, contact Stephanie Scheeler at

201.346.7003 or sas2258@columbia.edu



Annual Breast Cancer in Women of Color Breast Cancer 101



FREE and open to everyone, but registration is required.

Date: September 25, 2010

Time: 8:30 am – 1:00 pm

Location: Club 101, 101 Park Avenue (At East 40th Street)

New York, NY

www.club101ny.com

This year's program, *Breast Cancer 101*, will provide in-depth information about the latest research, surgical options, clinical trials, holistic health, support groups, survivor testimonials, and more.

Come, or tell your friends and family about our day of learning for women of color and those who treat them.

For information, contact Christine Rein at

201.346.7014 or cmr2146@columbia.edu



Chronic Pancreatitis ~ continued from page 1

College of Physicians and Surgeons, the procedure is fully successful in one third of patients. "In this group, the cells maintain their natural function, insulin continues to be produced, and patients live both pain-free and diabetes-free." The durability of success varies, with patients remaining insulin-independent for as little as one year up to 11 years.

In another third of patients, success is moderate. These patients require small amounts of insulin to maintain relatively normal glucose management.

In the last third of patients, the islet cells do not function as hoped, and patients become fully diabetic. In some cases, failure may occur if the pancreas was so diseased at the time of surgery that the islets are just too unhealthy. In other patients, the islet cells may be destroyed by high blood sugar from inadequately controlled diabetes.

"It is important to remember that most patients are pain-free after pancreatectomy, which is the primary goal of surgery," says Dr. Schrope. "Patients may become partially or fully diabetic, but they have their lives back. They can return to work and normal life, which is tremendous. If islet cell transplantation is successful, the ability to avoid diabetes is an added bonus."

The Department of Surgery at Columbia is one of only a few U.S. centers to offer autologous cell transplantation, which is a highly specialized and complex procedure. It has been made possible by years of groundwork laid by **Mark Hardy, MD**, *Director Emeritus and Founder, Renal & Islet Transplantation*, a pioneer of

the development of allogeneic islet cell transplantation and transplant immunology (involving transplantation from a separate donor to a recipient). During his 40-year career in kidney and pancreas transplantation at NewYork-Presbyterian/Columbia, Dr. Hardy's team had amassed not only a laboratory full of specialized equipment, but years of invaluable expertise. His research led to the first successful transplant of islet cells from pancreatic donors to recipients in 2004.

When Dr. Schrope realized that the unique needs of patients with chronic pancreatitis could potentially be met by the resources already in place from Dr. Hardy's work, she introduced the concept of doing autologous procedures (use of the patient's own cells) in this population. Because autologous transplants do not involve transplantation from one person to another, they do not pose the risk of rejection or require that patients take immunosuppressant medication after transplantation.

"Patients with chronic pancreatitis have no good treatments for their pain other than narcotics. We are very pleased that we can offer autologous islet transplantation so that they can be free from pain, while having a chance at retaining the endocrine function of the pancreas," says Dr. Schrope. ♦

For more information on islet cell transplantation at NewYork-Presbyterian/Columbia, see The Search for a Cure: Islet columbiasurgery.org/news/research/2004_islettx.html

Department of Surgery Faculty Announcements



Craig R. Smith, MD, is named Chairman of the Department of Surgery

Craig R. Smith, MD, has been appointed Chairman of the Department of Surgery at Columbia University College of Physicians and Surgeons and Surgeon-in-Chief at NewYork-Presbyterian Hospital/Columbia University Medical Center (NYPH/Columbia) and its Vivian and Seymour Milstein Family Heart Hospital.

Dr. Smith came to NYPH/Columbia as a fellow in cardiothoracic surgery in 1982, and in 1984 was appointed Associate Director of the medical center's heart transplant program. He was appointed Chief of the Division of Cardiothoracic Surgery and Chief of the Section of Cardiac Surgery in 1996. Under his direction, NYPH/Columbia's cardiac surgery programs have flourished, embracing the latest advances in cardiac surgery, valve surgery, and valve sparing aortic procedures.

Dr. Smith is co-principal investigator for the multicenter PARTNER trial, which is investigating a catheter-based approach to aortic valve surgery. ♦



Emile Bacha, MD, Joins Columbia as Director of Congenital and Pediatric Cardiac Surgery

Dr. Bacha comes to NewYork-Presbyterian Morgan Stanley Children's Hospital/Columbia University Medical Center from Harvard Medical School/Children's Hospital, Boston, where he was Associate Professor of Surgery and Senior Associate, Department of Cardiac Surgery. During 2000-2005, he was Director of Pediatric and Congenital Heart Surgery and Pediatrics at the University of Chicago/University of Chicago Hospitals, where he established a successful pediatric cardiac surgery program, including a minimally invasive surgery program.

Dr. Bacha, who specializes in minimally invasive approaches to pediatric heart surgery, has developed novel techniques to perform hybrid surgical-interventional procedures for children with complex congenital heart defects, including hypoplastic left heart syndrome. ♦

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