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healthpoints

ALL THE POSSIBILITIES OF MODERN MEDICINE

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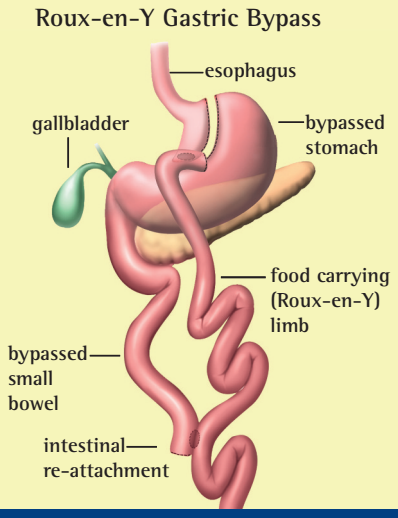

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Metabolic Surgery

Why Surgery May Be Treatment of Choice for Diabetes and Metabolic Syndrome

Melissa Bagloo, MD
Assistant Professor of Clinical Surgery, Center for Metabolic and Weight Loss Surgery

As experience with metabolic surgery has increased, it has become a very important therapeutic option for patients with morbid obesity and diabetes. New research continues to shed light on why this may be the treatment of choice for more patients with diabetes as well as those with metabolic syndrome.

For years, surgeons have observed that weight loss surgery has the additional benefit of resolving diabetes in over 80% of obese patients with diabetes. "Patients' blood sugar levels improve dramatically almost immediately after gastric bypass surgery, and far before any significant weight loss occurs," according to **Melissa Bagloo, MD**, *Assistant Professor of Clinical Surgery*. What's more, studies have found that when patients lose the same amount of weight through diet as through surgery, those who had surgery experienced significantly better improvement in their diabetes than those who lost weight non-surgically. This indicates that the surgery itself–not just losing weight–is responsible for metabolic shifts in the body.

This metabolic effect is significant for any patient who is obese, and is particularly compelling for those with metabolic syndrome. Metabolic syndrome is the combination of several medical problems associated with morbid obesity: high blood pressure, glucose intolerance/insulin resistance, excess body fat and high cholesterol.

According to Dr. Bagloo, "Patients don't necessarily have to have all of the above conditions, but when three or more occur together, the association of these problems is called metabolic syndrome." Identifying metabolic syndrome is important because the syndrome increases the risk for cardiovascular disease, stroke, type 2 diabetes, kidney disease, and other problems. People with metabolic syndrome are twice as likely to develop heart disease and five times as likely to develop diabetes as those who don't have metabolic syndrome. The primary goal of treatment is to reduce the risk of heart disease and diabetes.

"NewYork-Presbyterian/Columbia **Center for Metabolic and Weight Loss Surgery** performs all types of bariatric (weight loss) surgery, including minimally invasive laparoscopic gastric banding, Roux-en-Y gastric bypass surgery, and sleeve gastrectomy. The effects on metabolic functions are most pronounced after gastric bypass surgery," says Dr. Bagloo.

As a leader in the field of bariatric surgery, the Center for Metabolic and Weight Loss Surgery has long advanced and studied the effects of weight loss surgery among patients who have a body mass index (BMI) of 35 and above. Dr. Bagloo explains, "Although we do not yet know what the underlying mechanisms are for this effect, we know that operating on patients with these

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Breast Cancer Research

Dr. Feldman Explains New Study on Exemestane

Sheldon Feldman, MD, Chief, Breast Surgery Section

As reported in the New York Times June 5, 2011, the drug exemestane (Aromasin) was found to significantly reduce the occurrence of breast cancer in post-menopausal women at high risk of developing breast cancer. Not only was the risk of breast cancer reduced by 65% in the study, but the drug was found safe and more tolerable than other drugs in its class.

The ensuing media attention has generated a flurry of questions among patients with breast cancer, many of whom are asking whether they can take exemestane instead of tamoxifen, with the hope of avoiding the side effects associated with the latter medication.

To clear up some common misconceptions and put this study in perspective, **Sheldon Feldman, MD,** *Chief of the Breast Surgery Section* at NewYork-Presbyterian/Columbia, talked with e-healthpoints.

What did this study find?

Dr. Feldman: The study included about 4500 postmenopausal women at moderately high risk of developing breast cancer. Half the participants took exemestane and half took a placebo for three years. At that point, 11 of the women taking exemestane had developed breast cancer, and 32 taking the placebo had developed breast cancer. That translates to a 65% reduction in risk associated with this medication.

The drug also reduced the incidence of precancerous lesions including ductal carcinoma in situ, lobular carcinoma in situ, atypical ductal hyperplasia, and atypical lobular hyperplasia.

What kind of drug is exemestane?

Dr. Feldman: Exemestane is an aromatase inhibitor, which are agents that suppress estrogen production and inhibit the development of breast cancer after menopause.

After menopause, a woman's body makes very little estrogen. The little that is made is produced by the adrenal glands, which make testosterone, and then the aromatase enzyme converts the testosterone into estrogen. Aromatase inhibitors block this conversion, thereby shutting off the main source of estrogen production in postmenopausal women.

Before menopause, the body is flooded with estrogen because the ovaries are still working. So if aromatase inhibitors like exemestane are given to premenopausal women, the drug won't stop the estrogen production in the ovaries.

What does this study suggest for women interested in preventing breast cancer?

Dr. Feldman: This is the question that needs to be carefully looked at, because there are some common misconceptions arising in the wake of this study.

First, women need to understand that exemestane is only effective after menopause. If women take it before menopause, they will not receive the estrogen-suppressing benefit.

Second, this study investigated using exemestane for preventing breast cancer from occurring in the first place – not treating it after it has been diagnosed. Exemestane has previously been shown to be effective in treating women with breast cancer, and like tamoxifen, exemestane is commonly used for treatment. The importance of this study is that it provides clear evidence about its value in preventing breast cancer as well.

Third, the patients in the exemestane study were at higher risk of developing breast cancer than the general population, based on a risk assessment model called *Gail*, but the study did not include women who have BRCA1 or BRCA2 gene mutations, who are at the highest risk.

Is exemestane effective in preventing all forms of breast cancer?

Dr. Feldman: In short, no. There are many different types of breast cancer. This study found exemestane was only effective in preventing estrogen receptor or progesterone receptor positive breast cancers, which are easier to treat and less dangerous than other types of breast cancer. The drug had no significant effect in preventing other types of breast cancer.

Clearly it is an important thing to prevent any type of breast cancer, but in the long term no survival benefit has been demonstrated with the use of exemestane.

If we could find ways to prevent the more aggressive forms of breast cancer with the worst prognosis, such as HER2 or triple-negative breast cancer, then we would be better able to improve survival rates associated with breast cancer. The 'home run' in breast cancer research will be to develop an agent to prevent estrogen receptive negative breast cancer and to be able to offer that prevention to younger women with many years of potential future risk.

How does exemestane compare to tamoxifen and raloxifene?

Dr. Feldman: Historically, tamoxifen was found to be effective in preventing breast cancer because women who took it for treatment of cancer in one breast were found to have a significantly reduced risk of developing cancer in the opposite breast. We know that taking tamoxifen before menopause, earlier in life, has a long-term protective effect,

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and that tamoxifen and raloxifene are effective in preventing breast cancer in both pre- and post-menopausal women. Exemestane, on the other hand, is effective only after menopause. It can't be used to protect women during the important years before menopause, but only in their later years.

The research so far indicates that exemestane appears to be safer than tamoxifen and raloxifene, which are associated with a higher risk of endometrial cancer and blood clots, as well as effects such as fatigue and depression. Because of these risks and effects, many women are reluctant to take tamoxifen and raloxifene. Although bone loss has been a concern with other aromatase inhibitors, exemestane did not produce any measurable changes in bone health. Its main side effects included aches, hot flashes, joint pain, and fatigue–but overall these effects were less problematic than those associated with tamoxifen. So overall, exemestane's safety profile appears to be very reassuring.

How do you counsel women about preventing breast cancer?

Dr. Feldman: Reducing risk for breast cancer may involve many options. Lifestyle choices, especially diet and weight management, are extremely important. I counsel women to maintain a healthy weight, because fat cells have estrogen receptors in them, and more fat cells promote breast cancer. Good nutrition and good quality food are both very important.

When we are considering methods of prevention, medications have to be nontoxic and have acceptable side effects, or women will not take them. If there were a completely nontoxic pill to prevent breast cancer, people would take it – but there isn't, so the better option is to exercise and eat well.

Beyond lifestyle measures, we can offer many options, both medical and surgical. Exemestane is one more tool we now have available, which may be a good choice for post-menopausal women at high risk based on their family history. Women at very high risk, such as those with BRCA1 or BRCA2 gene mutations, may choose surgical prevention. We have great surgical techniques including excellent reconstructive methods, and the rate of risk-reducing mastectomies has been increasing.

In short, anyone concerned about risk of breast cancer should come to NYP/Columbia for an evaluation and to learn about the options for prevention. ■

Full text of the study on exemestane is available at the *New England Journal of Medicine*, at:
www.nejm.org/doi/full/10.1056/NEJMoa1103507

For more information on breast cancer treatments, please visit: www.breastmd.org

Pancreatic Cancer Vaccine Trial Opens

New study at the Pancreas Center will test a vaccine for preventing pancreatic cancer

Unlike some other forms of cancer, pancreatic cancer is often detected only in advanced stages, making it one of the most deadly forms of cancer overall. Surgical removal of tumors is possible in only 10% to 20% of patients. Chemotherapy is not nearly as beneficial as patients and physicians would hope, and the risk of recurrence after treatment is high. Given these conditions, researchers are working hard to develop alternative therapies that extend patients' lives past the average survival time, 20 months after diagnosis.

One of the most promising areas of research entails development of vaccines to harness the immune system to fight the cancer from within. An important study at NewYork-Presbyterian/Columbia's **Pancreas Center** is now moving this concept one step closer to reality. The trial is studying whether a new vaccine, developed specifically to target pancreatic cancer cells, will help to prevent recurrences among patients who have had pancreatic tumors surgically removed.

The trial includes two arms: 350 patients will receive chemotherapy alone or with radiation therapy, and 350 will receive chemotherapy alone or with radiation, plus the new pancreatic cancer vaccine. Those receiving the vaccine will receive a series of injections, administered one month apart, beginning 8 to 10 weeks after surgery. Patients will be monitored every 3 months for the first 36 months, every 6 months for 2 years, and then annually to determine whether the vaccine helps to reduce the rate of recurrence.

The vaccine in this phase III trial was developed on the basis of a hypothesis called hyperacute immunotherapy. According to **M. Wasif Saif, MD, MBBS**, *Medical Director, Pancreas Center and Director, GI Oncology Section, Division*

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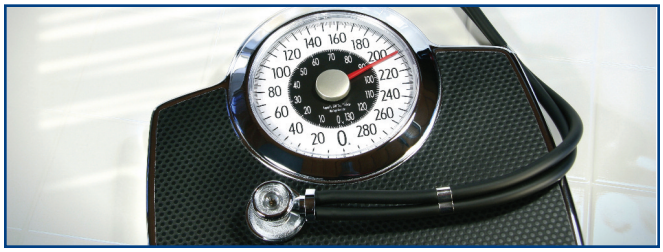
diseases causes a significant improvement in metabolic problems. We believe gut hormones play an integral role in this process and that a change in this milieu accounts for the results that are seen clinically."

Based on those observations, the Center is now studying the effect of weight loss surgery among patients with diabetes and BMI between 30-35. "By performing metabolic surgery, we hope to reverse these conditions to improve quality of life and decrease long-term effects and complications," says Dr. Bagloo. Because it is not known how surgery might affect patients at lower body weight in the long term, or what other complications might occur, this is being carefully studied in the setting of a trial. At this time, select patients with BMI between 30-35 may be eligible for participation in the Diabetes Surgery Study, which is currently underway at three sites in the U.S. and in Taiwan. ■

For more information about weight loss surgery, diabetes, and metabolic syndrome, please visit: www.obesitymd.org



Gastric Bypass Study

A recent study in *Science Translational Medicine*, "Differential Metabolic Impact of Gastric Bypass Surgery Versus Dietary Intervention in Obese Diabetic Subjects Despite Identical Weight Loss," found an important clue as to why surgery dramatically improves or resolves diabetes. The researchers found that after gastric bypass surgery, the levels of a certain type of amino acids (branched-chain amino acids) circulating in the blood were significantly reduced. This reduction in amino acids improved patients' sensitivity to insulin, having the effect of normalizing their blood sugar levels.

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of Hematology/Oncology, immunotherapy works by causing "hyperacute rejection." In the way that other vaccines cause the body to develop an immune response against measles, polio or another disease, the pancreatic cancer vaccine triggers an immune reaction that leads to immunity against specific pancreatic cancer cells. In this case, the pancreatic cancer vaccine is produced using alpha-GT epitopes from mouse cells, which are not found on human cells. These epitopes cause a reaction that leads human cells to attack pancreatic cancer cells from within (called cell mediated immunity).

Data from a multicenter phase II study (preceding the current phase) showed encouraging results for this therapy. At 12 and 24 months after surgery, survival rates were 91% and 54% respectively, which is a significant improvement upon the median survival rate of 16 months. Patients are still being followed up to determine long-term survival benefits.

The phase III trial opened at NewYork-Presbyterian/Columbia in late April, 2011. Dr. Saif strongly encourages eligible patients to consider enrolling in this trial. As he explains, "This is an important study for every patient and family member with pancreatic cancer. It is very important to come to centers that offer this study, and to understand that we now have more therapies to offer to patients with pancreatic cancer." ■

To read about hyperacute immunotherapy for pancreatic cancer, see Dr. Saif's March, 2011 article in the *Journal of the Pancreas*, "Adjuvant therapy of pancreatic cancer: beyond gemcitabine: Highlights from the 2011 ASCO Gastrointestinal Cancers Symposium." San Francisco, CA. January 20-22, 2011.

For information about pancreatic cancer, treatments at the Pancreas Center, and other clinical studies, please visit the Pancreas Center's web site at: www.columbiasurgery.org/pancreas

Division of Cardiothoracic Surgery: New Leadership

NewYork-Presbyterian Hospital/Columbia University Medical Center has appointed **Emile Bacha, MD** *Chief of the Division of Cardiothoracic Surgery.* In addition to his new leadership role, Dr. Bacha is Director of Congenital and Pediatric Cardiac Surgery at NewYork-Presbyterian Morgan Stanley Children's Hospital/Columbia.

NewYork-Presbyterian Hospital/Columbia University Medical Center has appointed **Michael Argenziano, MD** *Chief of the Section of Adult Cardiac Surgery* within the division. In addition to his new appointment, Dr. Argenziano is Director of Minimally Invasive Cardiac Surgery, Director of the Surgical Arrhythmia Program, and Director of the Thoracic surgery residency at NewYork-Presbyterian/Columbia. ■

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