Endocrine Notes

Updates for physicians on practices, advances and research from Cleveland Clinic’s Endocrinology & Metabolism Institute

In This Issue:

2 New Entity: Primary Hypoparathyroidism with Normal PTH
4 A Rare Case of Aneurysm Diagnosed During Pregnancy
6 Robotic Approach Preferred for Adenectomy
8 STAMPEDE Substudy Asks Whether Gastric Bypass Reverses Beta Cell Dysfunction
9 STAMPEDE II Study Now Enrolling Patients
10 Bariatric Surgery Now Standard Treatment for Morbidly Obese Diabetic Patients
11 Gastric Plication Holds Promise for Extreme Weight Loss
12 Adult Growth Hormone Deficiency: Study Compares Glucagon stimulation Test to Insulin Tolerance Test
14 Publications
18 Live and Online CME
19 Current Clinical Trials
20 Staff Directory

Cleveland Clinic’s Diabetes & Endocrinology Program is ranked 5th in the nation in U.S. News & World Report’s annual America’s Best Hospitals survey.

2011
Dear Colleagues,

I am pleased to present the 2011 edition of *Endocrine Notes* from Cleveland Clinic’s Endocrinology & Metabolism Institute.

Inside, we offer highlights from our multidisciplinary team’s most recent work:

- Our report on a new parathyroid disease entity: primary hyperparathyroidism with normal PTH levels.
- A rare case of acromegaly that was diagnosed during pregnancy.
- A report on our experience with robotic adrenalectomy, which has become the preferred surgical approach.
- A STAMPEDE substudy examining the clinical and metabolic factors involved in remission and non-remission of diabetes after gastric bypass surgery.
- Information about the STAMPEDE II trial.
- The designation of bariatric surgery as a first-line treatment for type 2 diabetes in the morbidly obese and the promise that gastric plication holds for drastic weight reduction.
- A study evaluating the glucagon stimulation test as an alternative to the insulin tolerance test for determining growth hormone deficiency in adults.

The Endocrinology & Metabolism Institute is one of 26 Cleveland Clinic institutes that group related specialties together to provide integrated, patient-centered care. Collaboration among endocrinologists, endocrine surgeons, bariatricians, bariatric surgeons and a cardiologist allows us to transcend the traditional borders between disciplines to improve patient care.

Throughout our institute, our staff remains committed to Cleveland Clinic’s core ideology: “Patients First.” Our institute comprises:

- The Department of Endocrinology, Diabetes and Metabolism, which manages specialized centers of care for patients with diabetes, thyroid disorders and pituitary disorders.
- The Department of Endocrine Surgery, which performs the highest number of surgical procedures in the region.
- The Bariatric and Metabolic Institute, which has been designated a Bariatric Surgery Center of Excellence by the American Society for Metabolic and Bariatric Surgery.

I hope that you find this issue of *Endocrine Notes* useful for your practice. Your comments and questions are always welcome. Please feel free to contact me at 216.444.6568 or 800.223.2273, ext. 46568.

Sincerely,

James B. Young, MD
Chairman, Endocrinology & Metabolism Institute
Professor of Medicine and Executive Dean, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University
George and Linda Kaufman Chair
Physician Director, Institutional Relations and Development
Primary hyperparathyroidism (PHP) is not rare. One percent of the population and 2 percent of women over age 55 develop this condition. When they do, they normally manifest the classical picture of high calcium and high parathyroid hormone (PTH) measurements in the blood. But atypical presentations are becoming more appreciated; a case in point is normocalcemic PHP. Ten percent of patients will have normal calcium levels and high PTH, making PHP hard to differentiate from other causes of elevated PTH.

In Cleveland Clinic’s Department of Endocrine Surgery, we have described another entity of PHP, which we have designated normohormonal primary hyperparathyroidism (NHPHP). Patients with this entity have high calcium levels but normal-to-low PTH levels – as low as 5 pg/mL. Knowledge of this subgroup may help the diagnosis of PHP to be made earlier.

We feel it is appropriate to accept this atypical biochemistry profile in the face of an otherwise quite usual PHP presentation. These patients have clearly enlarged parathyroids, kidney stones and osteoporosis, as you would find in a classical patient. This is a real subtype of the disease.

**An unusual finding**

We conducted a review of 843 patients who had undergone initial bilateral parathyroid exploration at Cleveland Clinic between January 2005 and December 2010. Of the study population, 46 patients (5.5 percent) were found to have preoperative iPTH values within the normal reference range (10-60 mg/mL at Cleveland Clinic, or the normal range at the testing laboratory). All 46 had hypercalcemia, with values up to 12.5 mg/dL.

A review of medical histories found that PHP had been discovered incidentally in 74 percent of patients. However, 70 percent had at least one symptom of PHP, 50 percent had abnormal bone density studies, 17 percent had a history of nephrolithiasis, and 37 percent reported neuropsychiatric symptoms such as fatigue, irritability, altered mood, poor concentration or declining memory. None had a family history of PHP or hypercalcemia. Preoperative localization studies accurately detected parathyroid disease in 80 percent.

**Subgroups identified**

The study also noted three subgroups of NHPHP:

- **Subgroup I** consisted of 7 patients with preoperative iPTH values < 40 pg/mL, the lowest measuring 5 pg/mL.
- **Subgroup II** consisted of 19 patients, all having preoperative iPTH values ≤ 60 pg/mL.
- **Subgroup III** consisted of 20 patients who occasionally demonstrated iPTH values > 60 pg/mL, even though most were ≤ 60 pg/mL.
Other than the preoperative iPTH values, there were no statistically significant differences among these subgroups or classical PHP patients for any of the following features: age, gender, degree of hypercalcemia, 24-hour urinary calcium value and vitamin D levels, rate of parathyroid adenoma (74 percent) versus multi-gland disease (24 percent), and size of abnormal parathyroids. All NHPHP patients had resolution of hypercalcemia following surgery.

A few distinct subgroup differences are interesting to highlight. For example, patients in subgroups I and II were more commonly diagnosed by the endocrine surgeon after being referred for thyroid disease, as compared with patients who had higher iPTH values. Subgroup I had the lowest prevalence of bone loss and neuropsychiatric symptoms. Preoperative localization studies failed to detect abnormal parathyroid glands more often in patients with lower iPTH values, despite a similar prevalence of parathyroid adenomas and abnormal gland volumes.

A distinct phenotype
Given such differences among the subgroups, we initially wondered whether we were simply diagnosing PHP at an earlier phase of disease evolution. However, when we found similar degrees of hypercalcemia, morphology of parathyroid disease and abnormal gland volume among all subgroups, we became convinced that NHPHP is a real entity – a distinct phenotype of PHP.

In our publication, we suggest several possible explanations for the NHPHP phenomenon. One hypothesis is derived from PTH patterns before and after surgery (illustrated in the graph on page 2.) These patterns suggest that some patients may have parathyroids that simply function at a lower “set-point” for PTH.

Further tests ordered thoughtfully
At Cleveland Clinic, the usual practice is to proceed to surgery once two sets of laboratory data confirm the diagnosis of PHP. NHPHP patients had multiple additional data points of serum calcium and iPTH before proceeding to surgery. Some were given more elaborate tests, such as PTHrp measurement, SPEP, selective venous sampling or CT scanning to evaluate for malignancy. The additional testing did not elucidate other etiologies of hypercalcemia, and all patients had PHP.

Having performed this study and having this data to reference, we are comfortable recommending an imaging workup and surgery to NHPHP patients who fit the hyperparathyroid disease profile. We do not assume that other causes of hypercalcemia will be more likely so that expensive additional tests will be mandatory for all. However, we believe that additional testing should be performed selectively based on an individual patient’s medical history.

The study suggests that when patients have high calcium levels but iPTH levels < 60 pg/mL and even < 40 pg/mL, the diagnosis of primary hyperparathyroidism should be considered, particularly if no other etiology of hypercalcemia can be identified. Although a minority of patients have this profile, they are highly likely to have a parathyroid tumor, and surgery is curative.

About the authors
Dr. Milas is Director of the Thyroid Center; Dr. Wallace worked with her and other Cleveland Clinic endocrine surgeons on this study as a fellow in the Department of Endocrine Surgery.

For more information, please contact Dr. Milas at 216.444.4985 or at milasm@ccf.org.
A Rare Case of Acromegaly Diagnosed During Pregnancy

Pregnancy in patients with acromegaly is rare, with less than 150 cases reported in the literature. Currently, there are no guidelines regarding the diagnosis or management of acromegaly during pregnancy.

The diagnosis and monitoring of acromegaly during pregnancy are complicated by the presence of a placental growth hormone (GH) source, resulting in physiologic changes in pituitary GH secretion and insulin-like growth factor-1 (IGF-1) production. Commercial assays cannot distinguish between pituitary GH and placental GH.

Fertility is decreased in women with acromegaly due to altered gonadotropin secretion, but the following case illustrates that when pregnancy does occur, its outcome is usually favorable. Metabolic complications are uncommon, and most patients do not experience an increase in the size of their pituitary adenomas.

Case history and presentation
A 30-year old woman, G2P1, 13 weeks' gestation, was referred to specialists in Cleveland Clinic’s Endocrinology & Metabolism Institute and Ob/Gyn & Women’s Health Institute. She presented with clinical features suggestive of acromegaly, including worsening headache, coarse facial features, acne, increased jawline, and enlargement of the hands and feet over two years. The IGF-1 level of 816 ng/mL was elevated (nonpregnant reference range: 138-410). A pregnancy two years earlier was uneventful.

The labs revealed a prolactin of 99 ng/mL (2.0-17.4); a repeat IGF-1 of 1,085 ng/mL; and basal and nadir GH of 13.9 and 12.8 ng/mL, respectively, during oral glucose tolerance testing. Glucose levels, blood pressure and visual field tests were normal. Pituitary MRI without contrast revealed a 1.5 cm macroadenoma with no impingement on the optic chiasm.

Managing symptoms during pregnancy
Severe headache prompted therapy, but the patient was unable to tolerate the dopamine receptor agonist bromocriptine. She was then started on 50 μg of the
somatostatin analog octreotide every eight hours at 19 weeks’ gestation, which resulted in significant headache relief and clinical improvement. The IGF-1 level decreased to 671 ng/mL and remained relatively stable during the rest of the pregnancy, while the GH level progressively increased, peaking at 43.9 ng/mL at 33 weeks’ gestation.

At 38 ½ weeks’ gestation, the patient delivered a healthy baby girl (3355 g). Breastfeeding was unsuccessful due to lack of milk production. At one week postpartum, while the patient remained on octreotide, the GH level declined inexplicably to 1.13 ng/mL. At four weeks postpartum, the GH and IGF-1 levels were 15.2 ng/mL and 1090 ng/mL, respectively.

Scheduling surgery after delivery

Pituitary MRI at four weeks postpartum showed that the patient’s adenoma was stable. She underwent transsphenoidal resection of the adenoma, which immunostained positively for GH, but surgery failed to achieve a biochemical cure. Postoperatively, the GH level was 7.5 ng/mL, and the IGF-1 level was 892 ng/mL. She was started on a long-acting somatostatin analog.

Treatment considerations during pregnancy

As was true for this patient, the majority of pregnancies in patients with acromegaly are uneventful, and newborns are unaffected. Even without treatment, research to date shows that little change in the size of pituitary adenomas and no worsening of visual fields during pregnancy are to be expected.

Dopamine agonists and somatostatin analogs appear to be safe during pregnancy, but because safety data are sparse, their usage is generally reserved for symptomatic patients. The use of the GH receptor antagonist pegvisomant seems promising during pregnancy when somatostatin analogs and surgery fail to control tumor growth. However, experience with pegvisomant is extremely limited, so its use will require further study.

Surgery can be safely postponed until after delivery for most patients except when it is needed in an emergency for acute visual loss or pituitary apoplexy.

About the authors

Dr. Cheng worked on this case as a fellow in the Department of Endocrinology, Diabetes and Metabolism with Laurence Kennedy, MD, Chair, and endocrinologists Amir Hamrahian, MD, Charles Faiman, MD, and Betul Hatipoglu, MD; and with obstetrician Fadi Khoury, MD.

For further information, contact Dr. Hamrahian at 216.445.8538 or hamraha@ccf.org, or Dr. Kennedy at 216.445.8645 or kennedi4@ccf.org.

Based on poster presentation at American Association of Clinical Endocrinologists (AACE) 20th Annual Meeting and Clinical Congress, San Diego, Calif., April 13-17, 2011.

### Table: Anterior pituitary function tests at 13 weeks’ gestation

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<th>Level</th>
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*Cross-reactivity with placental GH in our assay is not known.
After several years’ experience in performing robotic adrenalectomies, Cleveland Clinic endocrine surgeons have found that robotic surgery provides significant advantages over conventional laparoscopy. To date, they have performed more than 71 robotic adrenalectomies with no complications and no mortality.

“Increased dexterity from articulating instruments and 3-D vision makes dissection faster and easier. As a result, we are able to remove larger tumors minimally invasively that would have otherwise required an open operation,” says Cleveland Clinic endocrine surgeon Eren Berber, MD, below, who spearheads the technology and is training other Endocrinology & Metabolism Institute surgeons.

“Moreover, when we compared the robotic series with past laparoscopies, it became clear that the duration of the surgery was similar, if not shorter, despite removing larger tumors.

“We also noticed a trend toward a shorter hospital stay. Overall, both immediate postoperative pain and length of stay were slightly less with the robotic approach.”

Robot ideal for posterior approach

Additionally, robotic technology has enabled the surgeons to refine the posterior approach, which Dr. Berber and his colleagues were first in the world to describe.

“Rigid laparoscopic instruments made the procedure cumbersome, but the articulated instrumentation provided by the robot makes the operation more ergonomic,” he explains.

“With the robot, we have fewer instrument collisions and can reach difficult angles more easily.

“Although the posterior approach is technically more demanding, we prefer it over the lateral transabdominal approach. Because we do not enter the intra-abdominal cavity, patients have less postoperative pain and may recover faster.”

The surgeons especially favor the posterior approach in certain patients with bilateral tumors or significant abdominal scarring. However, they prefer the lateral transabdominal approach for patients with thicker back tissue or with tumors larger than 6 cm.

The robotic approach also compares favorably to the laparoscopic approach in posterior procedures. “Posterior
Robotic adrenalectomy is about 30 minutes faster than posterior laparoscopic adrenalectomy,” notes Dr. Berber.

**Large volume of adrenal procedures**
Cleveland Clinic’s volume of adrenal operations is one of the largest in the world, notes Dr. Berber, who believes that a comprehensive adrenal surgery program should offer a variety of surgical options.

Open adrenalectomy is available for tumors that have invaded surrounding structures. Dr. Berber and colleagues also offer radiofrequency ablation, a technique they pioneered in the treatment of adrenal tumors. Patients with unresectable tumors and patients too sick for surgery are ideal candidates for radiofrequency ablation.

**Other robotic procedures offered**
Cleveland Clinic endocrine surgeons offer a comprehensive spectrum of surgical procedures, including robotic alternatives. For example, besides robotic adrenalectomy, Cleveland Clinic endocrine surgeons have amassed one of the largest experiences with robotic thyroidectomy and robotic parathyroidectomy in the United States.

These procedures are performed through axillary incisions to eliminate visible scarring on the neck.

**Tracking adrenal tumor patients’ outcomes**
Data from all adrenal tumor patients is entered into an IRB-approved registry that is used to evaluate outcomes and compare surgical options. The registry, started in 2000, now contains information on 300 cases.

Dr. Berber directs a weekly multidisciplinary adrenal diseases clinic with Cleveland Clinic endocrinologists and radiologists.

To refer patients for evaluation or for further information, please contact Dr. Berber at 216.445.0555 or at berbere@ccf.org.
“Weight loss is a key component in the resolution of type 2 DM, and bariatric surgery can be highly effective in inducing weight loss,” says Cleveland Clinic endocrinologist Sangeeta Kashyap, MD. “However, DM does not always resolve with bariatric surgery, even with optimal weight loss.”

A Cleveland Clinic study, Surgical Therapy and Medications Potentially Eradicate Diabetes Efficiently (STAMPEDE), is comparing the efficacy and safety of Roux-en-Y gastric bypass surgery, sleeve gastrectomy and advanced medical therapy in restoring normal blood glucose levels (HbA1c ≤ 6 percent) among diabetic patients who are moderately obese (BMI 27-43 Kg/m2). Philip Schauer, MD, Director of the Bariatric and Metabolic Institute (pictured above), is principal investigator.

Looking for underlying factors

STAMPEDE is reaffirming the value of bariatric procedures in helping many patients achieve glycemic control, yet a number of patients have been unable to achieve or maintain DM remission despite dramatic weight loss. This prompted Dr. Kashyap to launch a substudy of STAMPEDE, funded by the American Diabetes Association, to examine the clinical and metabolic factors determining DM non-remission after either Roux-en-Y gastric bypass or sleeve gastrectomy.

“As endocrinologists, we need to understand which patients will benefit most from bariatric surgery in order to optimize patient selection and determine the point at which surgery should be recommended,” says Dr. Kashyap.

“Data from this study, in conjunction with clinical trial data, will allow us to define metabolic adaptations with respect to changes in intestinal hormones and fat-generated hormones following various bariatric procedures.”

This will help to further understanding of the potential bariatric surgery holds for the treatment of DM in moderate obesity. The study may also be useful in establishing appropriate expectations, because patients with DM expect their disease to resolve following bariatric surgery.

Zeroing in on incretin biology

After surgery, not all patients are likely to achieve complete remission. Dr. Kashyap believes this may be due to poor baseline residual B-cell function and a lack of incretin stimulation induced by either procedure. It is currently unclear whether weight loss alone or incretin-related effects on B-cell function is the dominant mechanism related to long-term DM remission.

“Given their potential to enhance insulin secretion, promote B-cell growth and induce weight loss, understanding the differential response of incretin hormones to the various bariatric procedures in patients who achieve DM remission versus non-remission is critical,” she says.

The ability of bariatric surgery to reverse DM may depend on disease duration and severity. Patients with recent-onset DM and mild hyperglycemia who do not require insulin are likely to have the greatest baseline B-cell function. Those with poor...
residual B-cell function at baseline may not experience the full benefit of incretin stimulation and weight-loss-related improvements in insulin sensitivity and thus achieve only partial remission or nonremission.

Weight regain also considered

A second issue to evaluate is the effect of weight regain on DM. Although most patients experience substantial weight loss in the 12 months following bariatric surgery, weight regain beginning in year two does occur in some patients. Dr. Kashyap hopes to determine how weight regain leads to non-response by establishing the weight-related effects on lipotoxicity-mediated insulin resistance 12 and 24 months following bariatric surgery.

Lipotoxicity plays a central role in inducing B-cell dysfunction and insulin resistance, which lead to the development of DM. Therefore, “the impact of bariatric surgery on the weight-related and non-weight-related effects of lipotoxicity must be determined in patients achieving longer-term, complete DM remission versus non-remission,” she says. “Since weight regain is associated with an increase in fat mass, we expect to see a direct impact of weight regain on impairing insulin sensitivity and glucose tolerance.”

One-year outcomes for the study will be available in 2012, and two-year outcomes will be available in 2013.

For more information, please contact Dr. Kashyap (above) at 216.445.2679 or at kashyas@ccf.org.

Cleveland Clinic is currently enrolling patients for the STAMPEDE II (Surgical Therapy and Medications Potentially Eradicate Diabetes Efficiently) study. The randomized, controlled trial will examine short- and long-term outcomes of advanced medical therapy versus advanced medical therapy combined with Roux-en-Y gastric bypass.

The effect of each approach on disease progression, complications and organ damage will be evaluated. Sixty men and women with type 2 diabetes are sought for the study. Candidates must be between 20 and 60 years of age and have a body mass index between 27 and 43 kg/m2.

Co-investigators for STAMPEDE II are Philip Schauer, MD, Director of the Cleveland Clinic Bariatric and Metabolic Institute; Sangeeta Kashyap, MD, of the Department of Endocrinology, Diabetes and Metabolism; and John Kirwan, PhD, of the departments of Gastroenterology and Hepatology, and Pathobiology.

For more information about STAMPEDE II, call 800.223.2273, ext. 53983, or visit clinicaltrials.gov.
Endocrine Notes | 10 | 2011

Bariatric Surgery Now Standard Treatment for Morbidly Obese Diabetic Patients

In March 2011, the International Diabetes Federation (IDF) issued a position statement upgrading bariatric surgery from an option to a priority for morbidly obese patients (BMI > 35 kg/m²) with type 2 diabetes mellitus (DM).

“The value of bariatric procedures in helping morbidly obese patients achieve glycemic control has been confirmed. It is time for metabolic surgery to be an accepted option, because diabetes in severely obese patients is often refractory to conventional therapy with insulin and oral agents, due to severe insulin resistance,” explains Philip Schauer, MD, Director of the Cleveland Clinic Bariatric and Metabolic Institute and a member of the IDF expert panel that authored the position statement.

The IDF statement also says that patients with a BMI of 30–35 kg/m² should be considered for surgery when hemoglobin A1c is > 7.5 percent despite optimal therapy, and particularly if weight is increasing or in the presence of other weight-responsive co-morbidities that are not achieving targets using conventional therapies, including hypertension, dyslipidemia and obstructive sleep apnea.

“The IDF writing group reviewed the data related to other conventional, standard bariatric operations and novel interventional procedures and considered gastric banding (above left), sleeve gastrectomy (above middle), gastric bypass (Roux-en-Y, above right), biliopancreatic diversion and duodenal switch in its clinical recommendations.
Gastric Plication Holds Promise for Extreme Weight Loss

Gastric plication, called laparoscopic greater curvature plication (LGCP) when performed laparoscopically, is a promising investigational bariatric procedure that may be useful in achieving weight loss and metabolic goals with very low morbidity.

Neither the stomach nor intestines are removed, enabling the plication to be reversed or converted to another procedure at a later time, if desired. The entire procedure can be completed in less than one hour. Most patients leave the hospital after a few hours in recovery and can return to work within seven to 10 days. Problems are rare, and major complications occur in fewer than 1 percent of cases.

LGCP is considered investigational as a primary procedure for weight loss and is being offered to patients at Cleveland Clinic as part of a clinical trial that will better define short- and long-term benefits.

Philip Schauer, MD, Director of the Cleveland Clinic Bariatric and Metabolic Institute, and colleagues have helped pioneer the procedure and have published initial results showing significant weight loss.

"Depending on their preoperative weight, patients can expect to lose 40 to 70 percent of their excess body weight in the first year after surgery. Although long-term studies are not yet available, this weight loss results in significant improvement in diabetes as well as hypertension, obstructive sleep apnea and hypercholesterolemia in the postoperative period," he says.

In LGCP, the surgeon makes several incisions (< 1 cm) in the abdomen as portals for the video camera and instrumentation. One or more folds are made in the stomach, reducing volume to approximately 75 percent to enhance satiety and reduce appetite. No stapling or cutting is involved; the folds are sutured in place.

For more information about gastric plication, contact Dr. Schauer at 216.444.4794 or at schauerp@ccf.org.
Study Compares Glucagon Stimulation Test to Insulin Tolerance Test in Evaluating Adult Growth Hormone Deficiency

With current availability of GHRH limited to research use only, there is no satisfactory alternative to the insulin tolerance test (ITT) for evaluation of growth hormone deficiency (GHD) in adults. The glucagon stimulation test (GST) has been recommended as an alternative. Cleveland Clinic is one of four institutions participating in a study comparing the GST to the ITT for this purpose.

“Our hypothesis is that the GST can accurately and safely diagnose GHD in patients with hypothalamic-pituitary disorders. It is readily available, relatively inexpensive and well-tolerated,” says Cleveland Clinic endocrinologist Amir Hamrahian, MD. “Unlike the ITT, it is not labor-intensive, and there are few contraindications to its use. This is particularly important for clinical endocrinologists who are not comfortable with the ITT or do not have the necessary staff or logistical support to conduct ITTs in their office.”

**Three study arms**

In order to determine the cutoff point with the highest sensitivity and specificity to differentiate between GHD and normal growth hormone levels, the study has been designed with one ITT and two glucagon arms. One glucagon arm evaluates the standard GST; the other evaluates glucagon dosage based on weight.

The GST may also be used to evaluate the integrity of the hypothalamic-pituitary-adrenal axis by provoking ACTH and cortisol secretion. “Cortisol release in response to glucagon seems to be ACTH-dependent. Similar to the ITT, the GST examines the entire HPA axis. Whether the test can accurately evaluate the integrity of the hypothalamic-pituitary-adrenal axis and use the same cutoff values for cortisol as the ITT and ACTH stimulation tests is unknown,” says Dr. Hamrahian.

It is normal to give 1 or 1.5 mg glucagon if the patient’s weight is greater than 90 kg. In this study, participants are given 0.03 mg/kg, up to a maximum of 3 mg, to determine whether increasing the dose improves the ability of the test to use the same cutoff values as the ITT and ACTH stimulation tests. “This would assure us that the GST will provide results closer to the current gold standard,” he explains.

**Recruitment ongoing**

The study is recruiting 30 patients with adult-onset hypothalamic-pituitary disorders: 15 with one pituitary hormone deficiency (PHD) other than GHD, and 15 with two or more PHDs. Twenty healthy controls matched for age, sex and body mass index are also being recruited. The ITT and two GSTs will be done at intervals of five to 28 days. During the GST, blood glucose, cortisol and serum GH levels will be measured at baseline and every 30 minutes, up to 240 minutes.
“Our hypothesis is that the GST can accurately and safely diagnose growth hormone deficiency in patients with hypothalamic-pituitary disorders...Whether the test can accurately evaluate the integrity of the hypothalamic-pituitary-adrenal axis and use the same cutoff values for cortisol as the ITT and ACTH stimulation tests is unknown.”

Other centers participating in this study are Massachusetts General Hospital, the University of Oregon and Allegheny Hospital.

All patients will receive a small stipend for travel expenses. To refer candidates to Cleveland Clinic or to obtain further information about inclusion and exclusion criteria, please contact Dr. Hamrahian at 216.445.8538 or at hamraha@ccf.org.
Below are peer-reviewed journal articles and book chapters published within the past year by Endocrinology & Metabolism Institute staff.

**Journals**

**Am J Clin Nutr**

**Am J Transplant**

**Ann Intern Med**

**Ann Surg**


**Can J Anaesth**


**Cleve Clin J Med**


**Diabetes**

**Diabetes Care**

Diabetes Obes Metab


Endocr Pract


Expert Rev Endocrinol Metab

Gastrointest Endosc Clin N Am

HPB (Oxford)

Int J Endocrinol
Yusupov E, Li-Ng M, Pollack S, Yeh JK, Mikhail M, Aloia JF. Vitamin D and serum cytokines in a randomized clinical trial. *Int J Endocrinol.* 2010;2010:305054.

J Am Coll Surg

J Clin Endocrinol Metab

J Endourol

J Hepatol

J Long Term Eff Med Implants

Metab Syndr Relat Disord

Minerva Endocrinol

continued on next page
Endocrine Notes | 16 | 2011

Nature

Pituitary

Surg Endosc

Surg Laparosc Endosc Percutan Tech

Surg Laparosc Endosc Percutan Tech

Surg Obes Relat Dis

Surg Obes Relat Dis

Surg Obes Relat Dis

Surg Obes Relat Dis

Surg Obes Relat Dis

Surg Obes Relat Dis

Surg Obes Relat Dis

Surgery

Thyroid


Thyroid

Ulusal Cerrahi Dergisi

Book Chapters


The 9th Annual Dr. Roizen’s Preventive Care and Integrative Medicine Conference

Focus: Reversing Metabolic and Endocrine Disorders, including Metabolic Syndrome, Type 2 Diabetes and Thyroid Disorders, and Increasing Sexual Enjoyment

December 9-11, 2011

Mirage Hotel and Resort, Las Vegas, Nev.

This activity has been approved for AMA PRA Category 1 Credits.

To register, please call 216.448.0777, email cmeregistration@ccf.org or visit www.ccfcme.org/wellness11.

Online CME

Online webcasts of interest to endocrinologists and approved for AMA PRA Category 1 Credits™ include:

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<tr>
<td></td>
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For a full list of all Cleveland Clinic CME opportunities, please visit ccfcme.org; to manage your CME credits, use the myCME.com Web portal, available 24/7.
## Current Clinical Trials

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<tr>
<td>International Metabolic Study (KIMS®)</td>
<td>Amir Hamrahian, MD</td>
<td>Melanie Williams 216.444.5410</td>
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<tr>
<td>A Proof of Concept, Open-Label, Forced Titration, Multicenter Study to Assess the Safety/Tolerability and Efficacy of a 10-Week Treatment of LCI699 in Patients with Cushing’s Disease</td>
<td>Amir Hamrahian, MD</td>
<td>Melanie Williams 216.444.5410</td>
</tr>
<tr>
<td>A Blinded, Placebo-Controlled, Single Ascending Dose, Phase 1 Trial for Safety, Tolerability, Pharmacokinetics and Pharmacodynamics after Subcutaneous Administration of VRS-317 in Adults with Growth Hormone Deficiency</td>
<td>Amir Hamrahian, MD</td>
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</tr>
<tr>
<td>A Phase III, Multinational, Randomized, Double-Blind, Placebo-Controlled Parallel-Group Study to Investigate the Clinical Efficacy and Safety of DiaPep277(R) in Newly Diagnosed Type 1 Diabetes Subjects</td>
<td>Leann Olansky, MD</td>
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</tr>
<tr>
<td>A Randomized, Double-Masked, Placebo-Controlled, Multicenter, Phase 2 Study to Evaluate the Safety and Renal Efficacy of LYY2382770 in Patients with Diabetic Kidney Disease Due to Type 1 or Type 2 Diabetes</td>
<td>Leann Olansky, MD</td>
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</tr>
<tr>
<td>TECOS: A Randomized, Placebo-Controlled Clinical Trial to Evaluate Cardiovascular Outcomes after Treatment with Sitagliptin in Patients with Type 2 Diabetes Mellitus and Inadequate Glycemic Control or Mono- or Dual-Combination Oral Antihyperglycemic Therapy</td>
<td>Robert Zimmerman, MD</td>
<td>Melanie Williams 216.444.5410</td>
</tr>
<tr>
<td>The Global Hypopituitary Control and Complications Study (HypoCCS)</td>
<td>Amir Hamrahian, MD</td>
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</tr>
<tr>
<td>The Diagnostic Accuracy of the Glucagon Stimulation Test for Evaluation of Adult Growth Hormone Deficiency and Hypothalamic-Pituitary-Adrenal Axis</td>
<td>Amir Hamrahian, MD</td>
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</tr>
<tr>
<td>ACROSSSTUDY - A Multicenter, Post-Marketing Surveillance Study of Somavert Therapy in Patients with Acromegaly in the USA and Europe</td>
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</tr>
<tr>
<td>Pelvic Floor Disorders in Bariatric Surgery Patients</td>
<td>Stacy Brethauer, MD</td>
<td>Sharon O'Keefe 216.445.8461</td>
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<td>A Prospective, Randomized, Controlled Trial Comparing Advanced Practice Medical Management vs. Advanced Practice Medical Management Plus Bariatric Surgery in The Treatment of Type 2 Diabetes Mellitus</td>
<td>Philip Shauer, MD</td>
<td>Chytaine Hall 216.445.3983</td>
</tr>
<tr>
<td>Prospective Randomized Comparison of Bilateral vs. Focal Neck Exploration for Sporadic Hyperparathyroidism</td>
<td>Allan Siperstein, MD</td>
<td>Linda Heil 216.444.2262</td>
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<td>Effect of Parathyroidectomy in Reducing Coronary Artery Calcification and Improving Vascular Compliance in Patients with Primary and Secondary Hyperparathyroidism</td>
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<td>T1D Exchange Type 1 Diabetes Network</td>
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<td>Gastric Plication for the Treatment of Obesity and Related Conditions</td>
<td>Philip Schauer, MD</td>
<td>Sharon O’Keefe, 216.445.8461</td>
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<td>Effect of a Portion-Controlled, Commercially Available Diet on Pre-Surgical Weight Loss and Metabolic Outcomes in Patients Undergoing Laparoscopic Bariatric Surgery</td>
<td>Leslie Heinberg, MD</td>
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</tr>
<tr>
<td>Is Nipple Stimulation by a Piercing Capable of Increasing Serum Prolactin Concentrations?</td>
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</tr>
<tr>
<td>ACCORDION: Action to Control Cardiovascular Risk in Diabetes Trial</td>
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<tr>
<td>Exenatide Study of Cardiovascular Event Lowering (EXSCEL)</td>
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<td>Name</td>
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</tr>
</tbody>
</table>

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In This Issue:

2 New Entity: Primary Hypoparathyroidism with Normal PTH
   A Rare Case of Acromegaly Diagnosed During Pregnancy
   4 Robotic Approach Preferred for Adrenalectathy
   8 STAMPEDE Substudy Asks Whether Gastric Bypa
   s Reverses Beta Cell Dysfunction
   9 STAMPEDE II Study Now Enrolling Patients
   10 Bariatric Surgery Now Standard Treatment for Morbidly Obese Diabetic Patients
   11 Gastric Mucosa Holds Promise for Extreme Weight Loss
   12 Adult Growth Hormone Deficiency Study Compares Growth Hormone Stimulation Test to Insulin Tolerance Test
   14 Publications
   18 Live and Online CME
   19 Current Clinical Trials
   20 Staff Directory

Cleveland Clinic’s Diabetes & Endocrinology Program is ranked 5th in the nation in U.S. News & World Report’s annual America’s Best Hospitals survey.

ENDOCRINE NOTES

Updates for physicians on practices, advances and research from Cleveland Clinic’s Endocrinology & Metabolism Institute

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