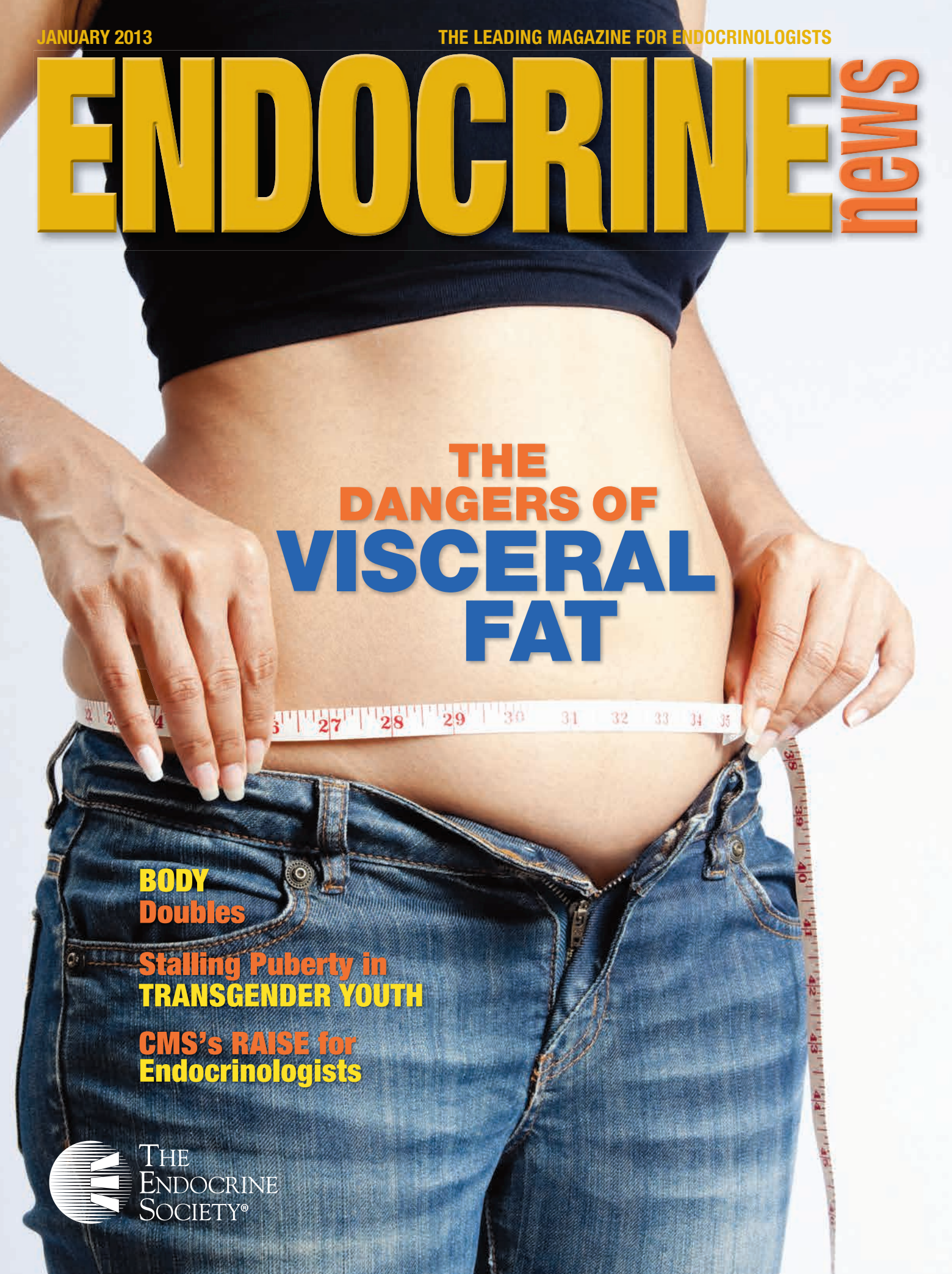
JANUARY 2013

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

ENDOCRINE news



THE DANGERS OF VISCERAL FAT

BODY Doubles

Stalling Puberty in TRANSGENDER YOUTH

CMS's RAISE for Endocrinologists

The Endocrine Society®

The Model for Clinical Excellence

Approximately 11 percent of adults in the Bronx have diabetes, one of the highest percentages in New York and in the nation. Every year, more than 4,000 people come to **Montefiore Medical Center** to visit our **Clinical Diabetes Center**.

As a New York State Department of Health Diabetes Center of Excellence, the Center was awarded a five-year grant to further the care of women with gestational diabetes.

Montefiore's diabetes self-management program, the Proactive Managed Information System for Education in Diabetes (PROMISED©), has been twice nationally recognized by the American Diabetes Association for exemplary performance and the consistent achievement of national standards.

Our patients benefit from our partnership with the Einstein Diabetes Research Center at Albert Einstein College of Medicine, which has been continually funded by the National Institutes of Health for 35 years. Through this collaboration, the Center translates scientific breakthroughs into treatments that improve health and quality of life.

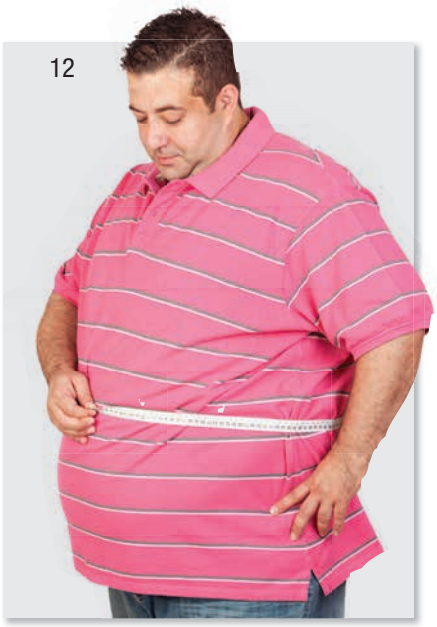
BEST HOSPITALS
U.S.News & WORLD REPORT
NATIONAL
DIABETES & ENDOCRINOLOGY
2012-13

For more information log on to **www.montefiore.org/diabetes**
or call **866-MED-TALK (633-8255)**

Montefiore
THE UNIVERSITY HOSPITAL

EINSTEIN
Albert Einstein College of Medicine
OF YESHIVA UNIVERSITY

CONTENTS



COVER Story

DEPARTMENTS

THE ENDOCRINE SOCIETY®
www.endo-society.org

Scan this QR code with your smartphone or mobile device for **Endocrine News** Online.

Building a Network for HORMONE HEALTH

William F. Young, Jr., M.D., M.Sc

In 2012, more than two million people visited the Society's patient education website, *www.hormone.org*, to learn more about hormone health, disease, and treatment—an increase of 20 percent in the number of visitors compared with the previous year. Most website visitors are patients; the rest are Society members, other healthcare providers, family members of patients, and the media. Nearly half of all visitors reside outside the United States.

The Hormone Health Network is the Society's recently rebranded and reorganized patient education resource and its direct point of contact with patient consumers. As the new name implies, this new resource seeks to unite patients, family members, the media, healthcare providers, and Society members—nationally and internationally—by providing an information network that is focused exclusively on endocrine patient education. Ultimately, the Network seeks to move patients from educated to engaged and from informed to active partners in their health care.

Since its official launch at **ENDO 2012,** the Network has laid the foundation for its new approach to patient education in an effort to raise awareness of the new brand inside and outside the Society.

Hormone Health NETWORK
www.hormone.org

The Society's recently rebranded and reorganized **PATIENT EDUCATION RESOURCE.**

The Network's signature educational product is its bilingual fact sheet series, which now includes more than 80 titles in English and Spanish covering 12 endocrine disorders and therapeutic areas. Feedback from Society members, patients, and primary care providers led to a redesign of the entire series to visually showcase the Network's patient-centered focus. The content has also been enhanced with key questions patients should ask, interesting endocrine facts, and an expanded list of resources.

Building on the fact sheets, the Hormone Health Network is expanding its education resources for patients with low literacy skills. One example of newly developed patient literature is the "What Is?" fact sheet series, which is written at a fifth-grade reading level and offers simple explanations of various endocrine glands and the functions of the hormones they produce.

A major Network goal is fostering more informed and effective patient-provider communication on hormone health, disease, and treatment. To facilitate this improved dialogue, the Network is building interactive, online tools that help educate patients and better prepare them for their next visit with their provider.

The Network's model for this type of communication tool is the Menopause Map *(www.hormone.org/MenopauseMap)*. Developed with Society menopause experts, the online, interactive Map helps women understand their hormonal and non-hormonal options for menopausal symptom relief. Nearly 10,000 women have completed the Map since its launch on May 1, 2012. The Network is developing a similar tool for men interested in testosterone therapy, and there are plans to create a third interactive tool on osteoporosis.

The Society's Strategic Plan 3 calls for us to "lead endocrine science and medicine toward the goal of improved health worldwide." To that end, the Network is pursuing deeper relationships with endocrine societies internationally. One such effort supports the Ambassador Exchange program, in which U.S. physician and trainee teams and teams in India and South Africa will visit and observe each other's endocrine practices. The Indian and South African teams have selected a number of Network fact sheets, which are being adapted for local populations and are being translated into Hindi and Zulu, respectively, to support patient education efforts in their programs.

Additionally, in response to growing global interest in its resources, the Network is working to expand the languages—such as Turkish, French, and Arabic—in which its materials are available and to build an online platform where these materials can be more easily accessed worldwide.

Throughout 2013, the Network will evaluate the success of its brand and the tactics it uses to engage an ever-larger public seeking information about endocrinology. This evaluation will enable the Network to make real-time course corrections to its outreach efforts and to provide detailed measures of the brand's strength and effectiveness. A key part of this evaluation is your feedback on the Network and its efforts. I encourage all of you to "join" the Network and become active partners in ***your*** patient education resource.

If you have any comments or questions, please contact me at *president@endo-society.org*.

William F. Young, Jr., M.D.
President, The Endocrine Society

THE ENDOCRINE SOCIETY®

JANUARY 2013

ENDOCRINE news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine News is a registered trademark owned by *The Endocrine Society*

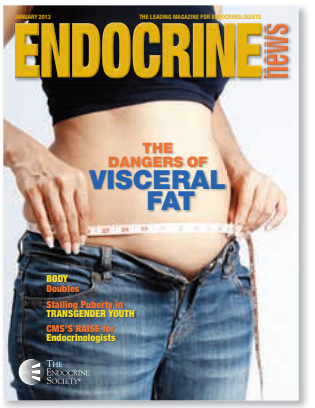
Endocrine News informs and engages the global endocrine community by delivering timely, accurate, and trusted content covering the practice, research, and profession of endocrinology.

The mission of *The Endocrine Society* is to advance excellence in endocrinology and promote its essential and integrative role in scientific discovery, medical practice, and human health.

Endocrine News® is published 12 times a year by The Endocrine Society, 8401 Connecticut Ave., Suite 900, Chevy Chase, MD 20815
Phone 301-941-0200 • Fax 301-941-0259
www.endo-society.org.

Print ISSN 2157-2089 Online ISSN 2157-2097

EDITOR'S PAGE



Welcome to the newly refurbished ***Endocrine News.*** Inside you will still find the latest in endocrinology trends and news but updated with infographics that provide further clarity on a particular topic. Also new are "OnPoint" call-out boxes detailing Society ongoings (e.g., guidelines, fact sheets, webinars, etc.) related to a particular issue covered in an article.

Speaking of coverage, this month is packed with a variety of thought-provoking articles. Our cover story by Eric Seaborg on belly fat chronicles that it's not just how much adipose tissue one has but where that might make a difference in one's health (page 12).

Puberty is rough for most kids, but for those with gender identity disorder, this period can be even tougher if the proper treatment and guidance are not provided. One suggested approach for transgender children, reported by Jacqueline Ruttimann, Ph.D., would be to use puberty-blocking drugs, essentially putting puberty on hold until the patient is of age to make an informed decision about transitioning to another gender (page 16).

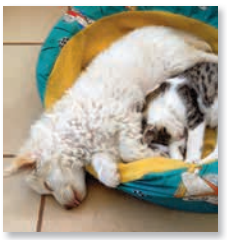
They already are the work horses of the research world, but what if mice could one day help a physician choose which treatment to give to a particular diabetes or cancer patient? Susan Perry describes how mice could one day act as "stand-ins" for real patients to avoid giving unsuccessful therapies (page 28).

We hope you enjoy this month's issue. Please let us know at *endocrinenews@endo-society.org* what you think of the changes.

Eleanore Tapscott
Senior Director of Publications

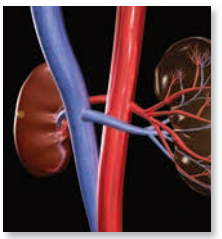
ENDOCRINE NEWS *ONLINE* EXCLUSIVES

The articles below are online only at www.endo-society.org/endo_news.
See ***Endocrine News*** Online to read them and related links.



Not-So-Strange Bedfellows

Specialized fat cells appear to foster cancer growth, opening up a new therapeutic venue.



Kidney in a Bottle

Scientists are closer to creating tissue-engineered kidneys via "organoids."

Drugs or Diet?

Cholesterol levels have improved in American adults—statins and trans fats ban may have played key roles.

Treating Alcoholism with **OXYTOCIN**

Patients seeking help for alcohol addiction are normally treated with benzodiazepines, a class of sedative-hypnotic drugs that can also be addictive. A new study finds intranasal oxytocin might be a better alternative.

"Patients who have received benzodiazepines for medical detoxification remain highly sedative-hypnotic tolerant," explained lead researcher Cort Pedersen, M.D., of the University of North Carolina at Chapel Hill. "After detox, they have symptoms related to that high tolerance, including anxiety, alcohol craving, and difficulty coping with stress as well as sleeping, all of which increase their chance of relapsing back to drinking." Oxytocin treatment may not only block withdrawal but also reverse sedative-hypnotic tolerance, thereby decreasing risk of relapse.

The study, published in *Alcoholism: Clinical and Experimental Research,* included 11 alcohol-dependent patients who had consumed alcohol heavily each day for two weeks before being admitted to a detoxification unit. They were randomly assigned to receive either 24 IU of intranasal oxytocin twice a day for three days or a placebo.

Patients' withdrawal symptoms were measured at least every four hours using the CIWA-Ar scale. If their CIWA-Ar scores rose to or above 12, they received a dose of the benzodiazepine, lorazepam, every hour until their scores fell below 10. Patients who received intranasal oxytocin required much less lorazepam to complete detoxification and had far lower CIWA scores as well as less alcohol craving than those given the placebo.

—Glenda Fauntleroy

Exposure to Light at Night Tied to **OBESITY**

Dark bedroom curtains could be the easiest weight-control option yet, according to recent findings that link light exposure during sleep to metabolic disruptions.

The research team of Kenji Obayashi, M.D., at Nara Medical University in Japan, measured light levels in the home bedrooms of more than 500 elderly volunteers. Based on the results, the participants were then divided into a dim light group and a LAN (light at night) group.

The researchers took a variety of metabolic measurements in each individual, and then compared the groups. The LAN group was associated with a host of bad metabolic indicators: significantly higher body weight, waist circumference, triglyceride levels, and low-density lipoprotein cholesterol levels, and significantly lower high-density lipoprotein levels.

One hypothesized metabolic disruption did not pan out. Light at night is known to suppress secretion of melatonin, a pineal gland hormone that is key to circadian rhythm, but is also involved in body mass regulation and lipid and glucose metabolism. The researchers measured the urinary excretion of a major melatonin metabolite as an index of melatonin secretion but found no significant difference between the groups.

In a paper awaiting publication in ***The Journal of Clinical Endocrinology & Metabolism*** [jcem.endojournals.org], the researchers say that their study supports the many epidemiological findings that associate night-shift work with obesity and dyslipidemia, but is the first to demonstrate this link in a home setting.

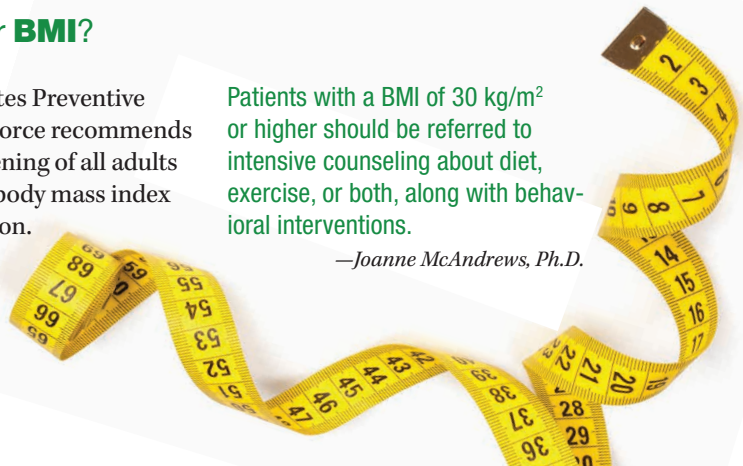
—Eric Seaborg

What's Your **BMI**?

The United States Preventive Services Task Force recommends physician screening of all adults for obesity via body mass index (BMI) calculation.

Patients with a BMI of 30 kg/m^2 or higher should be referred to intensive counseling about diet, exercise, or both, along with behavioral interventions.

—Joanne McAndrews, Ph.D.



HUMAN EGGS from Stem Cells

Scientists may be on the brink of developing a means of increasing a woman's fertility by creating a supply of reproductively viable eggs. In a study published in *Nature Medicine,* Jonathan L. Tilly, Ph.D., from Massachusetts General Hospital in Boston, led a team of researchers who devised a method to generate human oocytes from stem cells.

The researchers used a fluorescence-activated cell-sorting technique to isolate and culture egg-producing stem cells from ovaries of adult mice and found that the cells, once delivered back to the ovaries, could produce fertilization-competent eggs. They then took stem cells from women's ovaries, marked them with the fluorescent material, and injected them into human ovarian tissue grafted under the mice's skin. Human follicles containing fluorescently marked oocytes derived from the stem cells were found one to two weeks later.

This discovery "opens the door for development of unprecedented technologies to overcome infertility in women and perhaps even delay the timing of ovarian failure," wrote Tilly.

—Glenda Fauntleroy

Androgens Linked to **BABY ACNE**

Androgens cause sebaceous gland hypertrophy (SGH) and acne during puberty, but infants also often have SGH and acne-like blemishes. The goal of a study, led by Ulla Sankilampi, M.D., Ph.D., at University of Eastern Finland and Kuopio University Hospital in Finland, and to be published in an upcoming issue of *The Journal of Clinical Endocrinology & Metabolism* [jcem.endojournals.org], was to investigate in infants the association of postnatal urinary androgens with SGH.

Fifty-four full-term infants (28 girls and 26 boys) and 48 preterm infants (26 girls and 22 boys) were followed monthly starting at one week of age and continuing until six months of age. During each visit, researchers noted the occurrence of SGH and the prevalence of acne and collected the infants' urine to determine levels of dehydroepiandrosterone sulfate (DHEAS) and testosterone.

SGH was found in 89 percent of the full-term infants and 96 percent of preterm infants. Acne (defined as more than five papules) was present in 91 percent of full-term infants and in 75 percent of the preterms. SGH and acne were associated with elevated urinary DHEAS and testosterone in infants of both sexes and terms. Peak urinary androgen levels preceded the peak occurrence of acne, researchers noted.

This study is the first to link SGH and acne in infants with urinary androgen secretion, according to the authors.

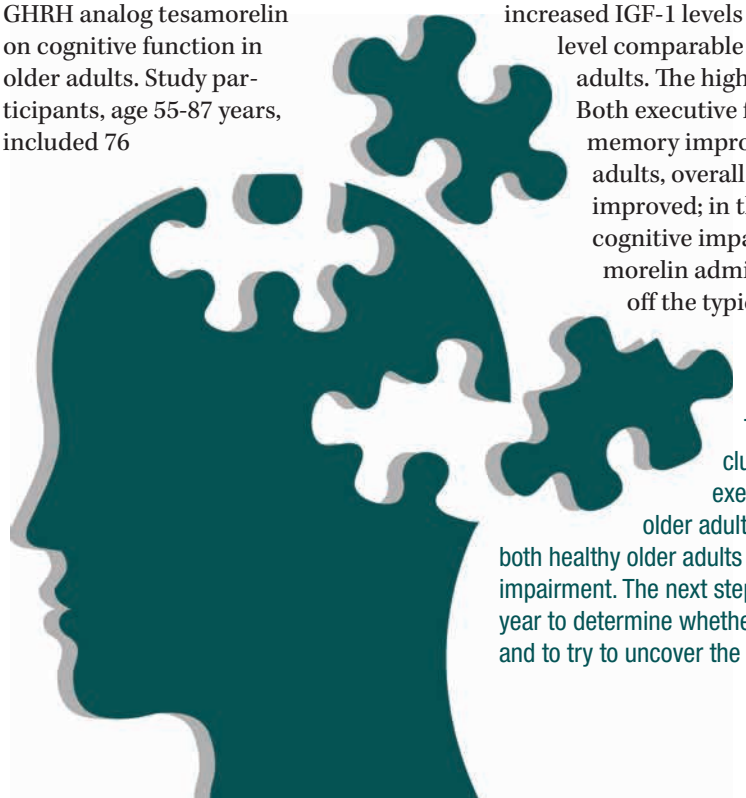
—Joanne McAndrews, Ph.D.

TESAMORELIN Improves Older Adult Cognitive Function

Because growth hormone–releasing hormone (GHRH), growth hormone, and insulin-like growth factor 1 (IGF-1) levels decrease with aging, these hormones could be implicated in the onset of age-related cognitive impairment.

Laura D. Baker, Ph.D., at the University of Washington, Seattle, led a team of scientists who studied the effects of the GHRH analog tesamorelin on cognitive function in older adults. Study participants, age 55-87 years, included 76 healthy adults and 61 adults with mild cognitive impairment. Participants injected one mg of tesamorelin daily for 20 weeks, then took a series of cognitive tests to evaluate both visual and verbal memory and executive function.

In their paper, originally published online in *Archives of Neurology,* the researchers report that tesamorelin increased IGF-1 levels 117 percent, to a level comparable to that in young adults. The high levels lasted a day. Both executive function and verbal memory improved. In healthy adults, overall cognitive function improved; in those with mild cognitive impairments, tesamorelin administration staved off the typical decline, which commonly results in Alzheimer's disease.

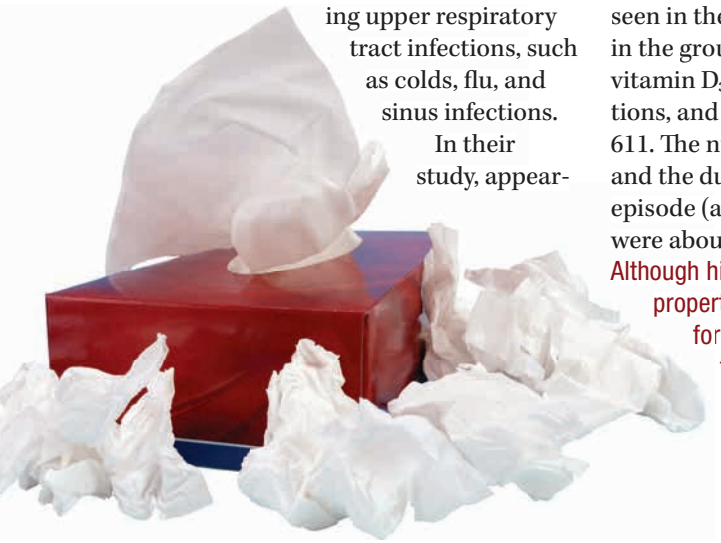


The researchers conclude that tesamorelin exerts positive effects on older adult cognitive function in both healthy older adults and those with mild impairment. The next step is a trial lasting one year to determine whether the results hold up and to try to uncover the pathways at work.

—Kelly Horvath

VITAMIN D Offers No Immunity from Colds

For those hoping to ward off a cold by taking vitamin D_3, a new study finds the supplements give no protection. Vitamin D has long been considered to play a role in immune function. Lead researcher David Murdoch, M.D., from the University of Otago, Christchurch, New Zealand, said he was anticipating there might be some benefit in preventing upper respiratory tract infections, such as colds, flu, and sinus infections. In their study, appearing in *JAMA*, the researchers randomly divided 322 healthy adults into two groups. One group received an initial dose of 200,000 IU of oral vitamin D_3, then 200,000 IU one month later, and 100,000 IU every month for 18 months. The second group was given a placebo in the same dosing increments.



No significant differences were seen in the outcomes of the adults in the groups. Participants taking vitamin D_3 had 593 respiratory infections, and those on the placebo had 611. The number of missed work days and the duration of symptoms per episode (about 12 days per episode) were about the same.

Although his team did not find immunity properties in vitamin D supplements for healthy adults, Murdoch said further research of populations with low baseline vitamin D levels or at risk for vitamin D insufficiency is justified.

—Glenda Fauntleroy

BPA EXPOSURE Lowers Thyroid Hormone in Newborns

Evidence of the endocrine-disrupting properties of the ubiquitous chemical bisphenol A (BPA) continues to mount, with the latest finding an association between exposure to BPA during pregnancy and altered thyroid function in pregnant women and their male babies.

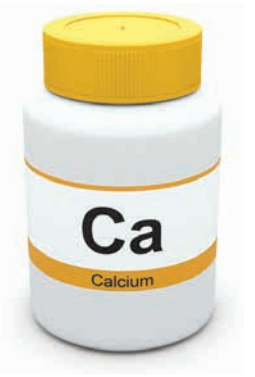
BPA has been found in placental tissue and amniotic fluid, raising the question of how it might affect the fetus.

A team led by Jonathan Chevrier, Ph.D., of the University of California, Berkeley, tested about 500 low-income pregnant women and their newborns for a relation of BPA to thyroid hormones because of the essential role these hormones play in early growth and brain development. The researchers measured BPA concentrations in two urine samples collected from the women during the first and second half of pregnancy and compared them with measurements of free thyroxine (T4), total T4, and thyroid-stimulating hormone (TSH) in the women and TSH in their newborns.

In a study published in *Environmental Health Perspectives*, they note that BPA's effects can be hard to document because the chemical's short half-life in the body—less than six hours. When the BPA measurements were made in close time proximity to the hormone measurements, BPA was associated with reduced T4 levels in the women.

Higher BPA concentrations in women during pregnancy were associated with lower TSH levels in male newborns, but not in female infants. This association was stronger when BPA was measured in the third trimester compared with earlier in the pregnancy.

— Eric Seaborg



Calcium Supplements and **HYPERPARATHYROIDISM**

Primary hyperparathyroidism affects up to 2 percent of postmenopausal women in the U.S., leaving them with fragile bones, fatigue, depression, nausea, loss of appetite, and increased risk of kidney stones. An analysis of the long-running Nurses' Health Study, however, suggests an association between increased calcium intake and a reduced risk of the condition. The analysis appeared in the *BMJ*.

The Nurses' Health Study has enrolled and tracked 121,700 female registered nurses since 1976. Every two years, the participants complete questionnaires on exercise and other lifestyle choices, as well as newly diagnosed diseases; every four years they report on their diets. Researchers at Brigham and Women's Hospital and Harvard University analyzed data amassed between 1986 and 2008 from more than 58,000 participants and learned that 277 participants were diagnosed with hyperparathyroidism in that 22-year period. The team then divided the women into five equal groups according to nutrient intake and found that women who took at least 500 mg of calcium per day had a 40 to 70 percent lower risk of developing the condition than those who didn't take calcium supplements, depending on variables such as age, body weight, smoking, alcohol use, and protein, vitamin A, and vitamin D intake.

A few caveats, however: The researchers noted that the study population included only women, and nearly all of the participants were white, so the results do not automatically apply to men or to women of other races.

—Terri D'Arrigo

Benefits of Extended Endocrine Therapy for **BREAST CANCER PATIENTS**

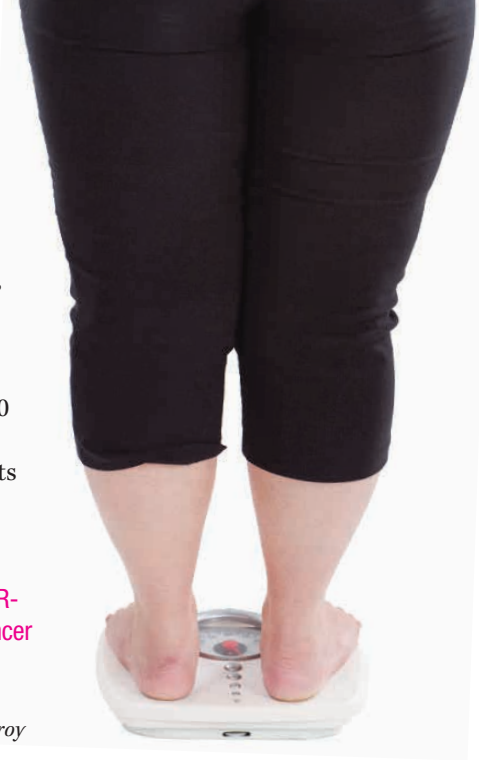
Despite treatment, women with estrogen receptor (ER)-positive breast cancer are more likely to die of the cancer 5 to 10 years after diagnosis than are ER-negative patients. A new study now offers physicians a method for determining which ER-positive patients are at highest risk.

Researchers at the Cancer Center and Cancer Institute at Fudan University in Shanghai, China, report that although the standard therapy for patients with ER-positive, early-stage breast cancer is five-year adjuvant endocrine therapy (tamoxifen and aromatase inhibitor), their study aimed to help resolve whether some patients might benefit from 5 or 10 additional years of endocrine therapy.

The study, appearing in *The Journal of Clinical Endocrinology & Metabolism* [jcem.endojournals.org], used data from the National Cancer Institute's Surveillance Epidemiology and End-Results (SEER) Cancer database and included nearly 112,000 female patients with invasive breast cancer. Researchers stratified patients by ER status, age, and lymph node status.

The researchers, led by Ke-Da Yu, M.D., concluded that some subpopulations of ER-positive patients at high risk of breast cancer death 5–10 years after diagnosis can be identified by age and lymph node status.

—Glenda Fauntleroy



Don't Just **SIT THERE**

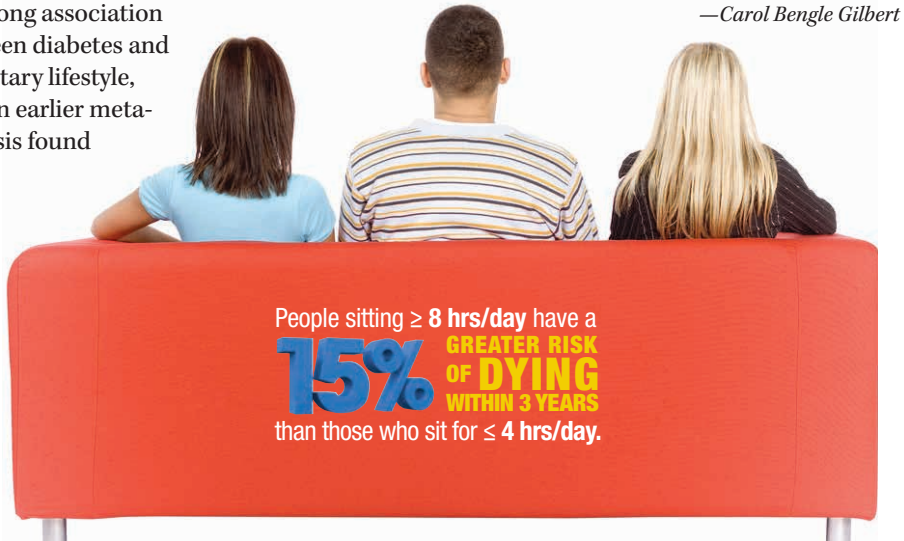
Want to avoid getting diabetes or cardiovascular disease? You might try standing up and moving around more often, a study led by E.G. Wilmot, M.B., Ch.B., research fellow in the Diabetes Research Group, University of Leicester, United Kingdom, suggests.

With the average adult spending 50 to 60 percent of the day in sedentary pursuits, the couch potato lifestyle's health effects are a growing concern among healthcare providers. Two earlier narrative reviews with small sample sizes suggested a moderate-to-strong association between diabetes and sedentary lifestyle, and an earlier meta-analysis found a link between television time and diabetes. The current meta-analysis study looked more broadly at sedentary behavior rather than time spent watching television and considered cardiovascular effects and overall mortality in addition to diabetes.

The researchers examined data on 794,577 participants in 18 studies, of which 16 were prospective. The rest were cross-sectional, and 10 of the 18 looked specifically at diabetes. Sedentary time was associated with increases in relative risk for all conditions studied, but the predictive effects and intervals were significant only for diabetes. Diabetes risk increased 112 percent for the most sedentary subjects. Researchers also noted a 147 percent increased risk of cardiovascular events and a 49 percent increased risk of death in these extreme subjects.

The study, published in *Diabetologia,* may have important implications for future research and public health policy. The researchers concluded that an urgent need for follow-up exists to determine whether reductions in sedentary time will translate into health benefits and how to best change sedentary behavior in adult populations.

—Carol Bengle Gilbert



DIABETES' OBESITY Paradox

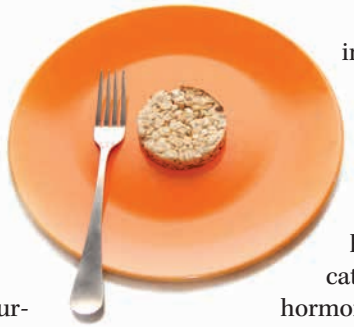
In a shocking reversal of what we have come to expect about health and weight status, scientists report that normal-weight people with diabetes, particularly older adults and nonwhites, have double the risk of death compared to overweight or obese people who have diabetes.

In their paper, published in *The Journal of the American Medical Association*, Mercedes R. Carnethon, Ph.D., at Northwestern University, Chicago, and her team of scientists suggest that the "obesity paradox" may occur because genetic factors make normal-weight people more susceptible to adverse complications of diabetes.

Other possible explanations are that diabetes is undiagnosed by physicians not expecting it in normal-weight patients, or that obesity itself protects against disease progression by providing greater fuel reserves for those in chronic illness–induced catabolic states.

—Kelly Horvath

STARVATION HORMONE Increases Life Span



Eat hearty, live long? UT Southwestern Medical Center researchers say a recent study shows that transgenic mice with higher-than-normal fibroblast growth factor-21 (FGF21) levels were able to achieve the longevity gains typically associated with calorie restriction.

Cornell University researchers demonstrated in 1934 that a low-calorie diet containing sufficient nutrients to avoid malnutrition could increase life spans in laboratory mice. It wasn't until 2007, however, that scientists identified the starvation-averting effects of FGF21. FGF21 promotes survival during prolonged fasting by facilitating the burning of fatty acids, suppressing growth, and inducing hibernation-like behavior. Although extra FGF21 can extend life, too little may cause insulin resistance, cancer, and other diseases.

A recent study showed that the hormone can reduce obesity in mice. The current research is the first to explore its effects on longevity in non-obese mice. Without decreasing food intake, male mice chronically exposed to FGF21 experienced longevity gains of about 30 percent, whereas female mice lived 40 percent longer, equivalent to human life span increases observed in calorie restriction research.

The mechanism for FGF21's life-extending effects seems to be an increase in insulin sensitivity and blocking of the growth hormone/insulin-like growth factor-1 signaling pathway.

The researchers say these findings, published in *eLIFE* [www.elifesciences.org], could have important implications for investigating hormone therapies to increase human life spans.

Although FGF21 offered longevity benefits, its drawbacks include infertility in female mice, and smaller size and bone density loss in both sexes. Researcher Steven Kliewer, Ph.D., professor of molecular biology and pharmacology, described the experimental mice as "spry" despite their reduced bone density and suggested it didn't impair their quality of life. He said future studies are needed to try to separate the bone density and infertility effects of FGF21 from the life-extending qualities.

—Carol Bengle Gilbert

Obesity During Pregnancy May Increase **INSULIN IN OFFSPRING**

A mother's obesity during pregnancy and lactation may increase insulin levels in her baby's blood—a condition known as hyperinsulinemia—and change the baby's heart structure and function.

In the past, the mechanisms underlying the relationship between maternal obesity and offspring cardiac function have eluded researchers. It is not known if detrimental effects on the heart were simply a consequence of increased weight and adiposity in the offspring that leads to cardiac hypertrophy. A new study, pending publication in *Endocrinology* [endo.endojournals.org], using a mouse model, sheds light on this question.

An earlier investigation noted heavier and fatter mouse offspring at 3 and 6 months when their mothers consumed an obesity-promoting diet. This current study refined those results. Comparing heart structure in mouse pups at 8 weeks, before overt signs of obesity developed in the experimental (Mat-Ob) group, researchers identified cardiac changes.

The pups in both Mat-Ob and control groups had similar body weights up to 8 weeks. Despite their similar weights, the Mat-Ob pups had higher heart weight and greater absolute cardiac mass. Their hearts displayed physical changes consistent with cardiac hypertrophy. Researchers also observed several molecular markers of hypertrophy. Left ventricular hypertrophy is a predictor of heart disease and mortality.

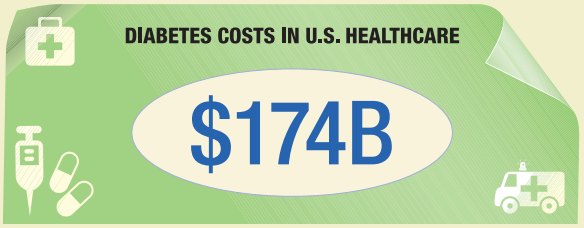
By focusing on their hearts' condition before the Mat-Ob pups showed overt signs of obesity, researchers answered the chicken-and-egg question, eliminating increased weight and adiposity as causes of the hypertrophy. The Mat-Ob pups, however, were hyperinsulinemic at 8 weeks of age. The presence of hyperinsulinemia arising in the absence of adiposity implicates primary insulin resistance in tissues, such as the skeletal muscle, involved in regulating glycemia. Because the heart tissue remains insulin responsive, it becomes over-stimulated by insulin, leading to cardiac hypertrophy.

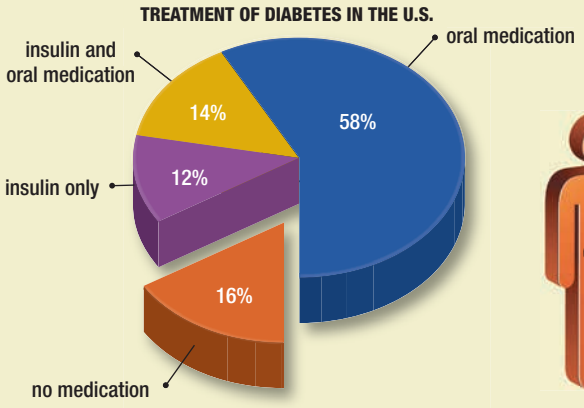
With the rising incidence of pregnant obese women and an accompanying surge in gestational diabetes, more babies are born at risk for insulin resistance, myocardial hypertrophy (increased heart cell size and thickening of the heart muscle), and cardiovascular disease. The researchers propose that increased plasma insulin resulting from maternal obesity affects the development of the heart and, therefore, has potential as a possible treatment target.

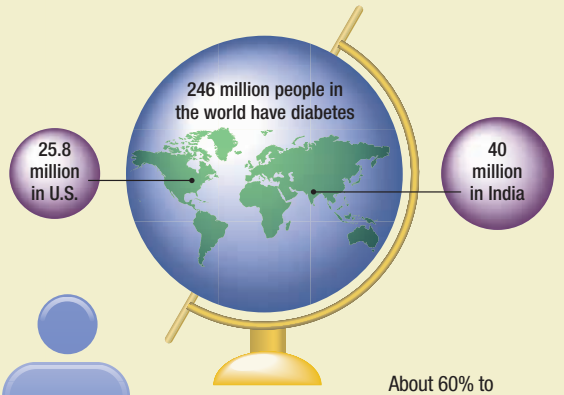
—Carol Bengle Gilbert

Fast**FACTS** about Diabetes

When people think of diabetes, it usually is type 2 diabetes. Here's how this disease takes its toll on the health of individuals and the nation.







60% of non-tramatic lower-limb amputations in the U.S. occur in people with diabetes.

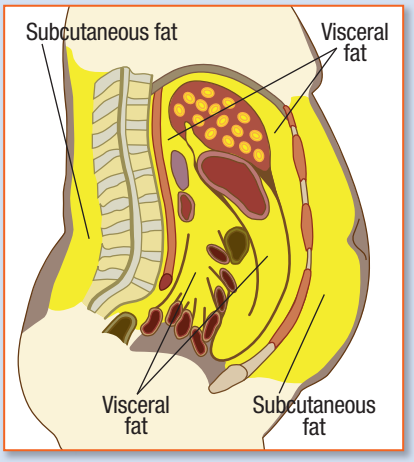
About 60% to 70% of people with diabetes have mild to severe forms of nervous system damage.

Diabetes accounts for 44% of all new cases of kidney failure.

Adults with diabetes die from heart disease 2 to 4 times more often than adults without diabetes.

Sources: CDC, NIDDK, and JAPI

VISCERAL FAT vs. SUBCUTANEOUS FAT
Visceral fat lies beneath the abdominal muscle surrounding the vital organs where it releases various hormones. It is not visible. On the other hand, subcutaneous fat is right underneath the skin and can be seen.



THE DANGERS OF VISCERAL FAT

Viseral fat better predictor of metabolic risk, researchers find

By Eric Seaborg

AT-A-GLANCE:

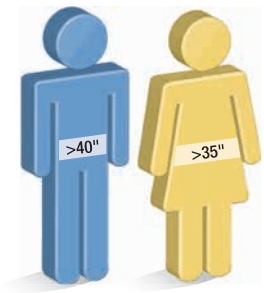
- **Waist circumference poses a risk for metabolic syndrome.**
- **Visceral fat increases risk more than subcutaneous fat.**
- **Diet and exercise can directly target visceral fat.**

Most physicians have experienced this apparent contradiction: Jane Doe carries so much weight on her hips and thighs that it pushes her body mass index (BMI) into the obese range. Yet her blood sugar, lipids, and other metabolic tests remain normal. John Doe's BMI classifies him as overweight but not obese, perhaps thanks to his thin arms and thin legs. All his fat is around his middle. And it is the non-obese John Doe who develops diabetes.

The key difference could lie in whether they carry their extra weight in the body types called "apples" or "pears." Apples are big in the abdomen, with visceral fat wrapped around their vital organs. Pears expand out farther down, their extra calories taking the form of less metabolically active subcutaneous fat.

DIFFERENCE IN BODY TYPES
Apples are big in the abdomen, with visceral fat wrapped around vital organs. Pears expand out farther down, with less metabolically active subcutaneous fat.

The risks of overweight and obesity—diabetes, heart disease, stroke, and metabolic syndrome—are well-known, but researchers are making progress in understanding why these risks increase greatly when fat is added inside the peritoneal cavity as visceral fat. The easiest and most accepted indicator of visceral fat is waist circumference, and although many studies have shown that it is no better than BMI in predicting problems such as cardiovascular risk, many experts see it as a better measure of metabolic risk, especially in women.



WAIST WATCHERS
A waist circumference at or above 102 cm (40 inches) for men and 88 cm (35 inches) for women is considered a risk factor.

Latest Guideline

That belief is reflected in guidelines that have adopted waist circumference over BMI, including the National Cholesterol Education Program Adult Treatment Panel III guideline for identifying metabolic syndrome, which recommends that a waist circumference at or above 102 cm (40 inches) for men and 88 cm (35 inches) for women be considered a risk factor. The Endocrine Society Guideline on Metabolic Risk recommends these cutoffs for most patients, but drops them in East Asian and South Asian patients to 90 cm (35.5 inches) for men and 80 cm (31.5 inches) for women.

Waist circumference measurement is not difficult, but because it is not as routine as height and weight, both nurses and patients can be resistant or at least unaccustomed to it, said Daniel Bessesen, M.D., chief of endocrinology at Denver Health Medical Center. The proper procedure is to measure at the top of the hip bone with the tape measure parallel to the floor at the end of a relaxed expiration.

The waist-to-hip ratio has been proposed as another abdominal alternative, but there is no evidence that is better than waist circumference or BMI, and it is a more complicated measurement and calculation.

None of these anthropometric measures can distinguish between subcutaneous fat located around the waist and visceral, also known as intra-abdominal, fat. Only an expensive procedure like magnetic resonance spectroscopy or imaging can visualize the fat in its specific depots.

Visceral fat is associated with a constellation of metabolic abnormalities, including insulin resistance, hyperinsulinemia, glucose intolerance, type 2 diabetes, high triglycerides, dyslipidemia, inflammation, and altered cytokine profile. (Its relationships with other obesity-related problems like arthritis and cancer are not well known.) To investigate whether central adiposity is a root cause of these problems or is simply a marker of deeper abnormalities, researchers tested the effects of removing the fat surgically.

MEASURING WAIST CIRCUMFERENCE
The proper procedure is to measure at the top of the hip bone with the tape measure parallel to the floor at the end of a relaxed expiration.

Liposuction Outcomes

Samuel Klein, M.D., professor of medicine and nutritional science and director of the Center for Human Nutrition at Washington University School of Medicine in St. Louis, and his colleagues used liposuction to remove large amounts of abdominal subcutaneous adipose tissue, corresponding to a 10 percent reduction in total body fat and a 7 percent reduction in weight. In contrast to what would be expected from a similar weight loss by dieting, the fat reduction did not improve metabolic outcomes such as insulin sensitivity, blood pressure, plasma triglycerides, and cholesterol.

But that was subcutaneous fat, so Klein worked with another group that did a more invasive procedure to remove visceral adipose tissue by surgically removing the omentum. The surgery did not improve insulin sensitivity or other measures of metabolic function in patients who also had Roux-en-Y gastric bypass surgery or on its own in obese subjects with type 2 diabetes.

"It is not the loss of fat that's important, but how you lose the fat that's important," Klein told *Endocrine News*. "When you remove fat by eating less and being more physically active, you shrink your fat cells to a smaller size and you eliminate fat in other organs like muscle tissue [and] liver tissue, as well as reducing visceral fat. When you remove fat by liposuction, you remove billions of subcutaneous fat cells without changing any of the other parameters, and some of those other parameters are probably important to improve metabolic function."

OnPOINT from The Endocrine Society

The Endocrine Society's patient education resource, the Hormone Health Network, has published a fact sheet titled "Hormones and Obesity" that details the guidelines for body mass index and the steps one can take to lose the excess weight. See *http://www.hormone.org/Other/upload/FS_CMD_Obesity_EN-web.pdf*.

Energy Balance

Gastric bypass patients' diabetes can go into remission after surgery but before they have lost much weight, providing more evidence that the fat itself may not be the issue. The highly cited recent studies of Roy Taylor, M.D., of Newcastle University in the United Kingdom showed that obese patients who restrict their intake to 600 calories a day can resolve their type 2 diabetes within weeks. Magnetic resonance imaging scans revealed that fat levels in these patients' pancreases and livers declined to normal levels, and their pancreases regained their ability to make insulin. "We believe this shows that type 2 diabetes is all about energy balance in the body," Taylor said. "If you are eating more than you burn, then the excess is stored in the liver and pancreas as fat, which can lead to type 2 diabetes in some people."

Klein said his studies have also showed that fat in the liver is very sensitive to small changes in energy balance, and "within 48 hours we found that you can reduce fat in the liver by 25 percent by just calorie restriction." But he cautioned that whether liver fat is a marker or a cause is not known.

Another line of inquiry proposes that the excess visceral adiposity is caused by an overactivated hypothalamic-pituitary-adrenal axis leading to increased control of carbohydrate and lipid metabolism by glucocorticoids. Because visceral adipocytes have more glucocorticoid receptors than subcutaneous adipose cells, the activated axis could promote visceral fat deposition while inducing insulin resistance in the liver and skeletal muscle.

Visceral fat cells differ from subcutaneous fat cells in other ways with negative metabolic consequences—they secrete less leptin and are associated with higher levels of cortisol.

Weight Redistribution

Why some fat cells go to the thighs and some go to the belly is not known, but part of the reason may be hormonal—when women go through menopause, some of their weight redistributes to the abdomen, with accompanying adverse changes in metabolic tests. And there is undoubtedly a genetic

LIPOSUCTION FAIL
When you remove fat by liposuction, you remove billions of subcutaneous fat cells without changing any of the other parameters, and some of those other parameters are probably important to improve metabolic function.

component, said Naveed Sattar, M.D., Ph.D., professor of metabolic medicine at the University of Glasgow in the United Kingdom. People vary in the amounts that their subcutaneous fat depots can hold, and evidently once that capacity is exhausted "you start to put fat centrally, and your visceral fat accumulation, and that of associated organs such as liver, goes up," he said.

Although Sattar notes that waist circumference is the "best anthropometric predictor of visceral fat," and might be better in terms of predicting metabolic risks such as diabetes, he was part of a group that published a study last year in the *Lancet* that found that measures such as BMI and waist circumference do not significantly improve assessment of cardiovascular risk when metabolic information is already available on "downstream" measures such blood pressure, diabetes status, and lipid levels.

MODERATE EXERCISE HELPS
The U.S. Department of Health and Human Services suggests a minimum of 2.5 hours per week of moderate exercise. Activities may include jogging, swimming, brisk walking, and cycling.

A rather simple measure of the risk has been proposed by one of the leaders in the field, Jean-Pierre Després, Ph.D., of the Université Laval in Quebec City, Canada. His studies show that an elevated fasting triglyceride level and enlarged waistline are "predictive of excess visceral adiposity, a clinical phenotype that we first described as 'hypertriglyceridemic waist'." These simple markers could allow cardiologists and primary-care physicians to identify patients with excess visceral fat putting them at increased cardiovascular risk, he concluded in a recent issue of *Circulation.*

Another reason for relying on indicators such as insulin sensitivity and lipids is that they reveal what is happening in the body, which can vary greatly at the same levels of fat. For example, some normal weight people are "metabolically obese" in these measures, and conversely, the tests of patients who are "fat and fit" can remain in the normal range despite their weight, evidently because they are active and in good aerobic condition.

More fat means more insulin; more insulin means more counter-regulatory hormones, which means more **FAT IN THE BELLY.**

Simple Treatment

Researchers can debate ultimate causes, but there is no doubt that a major underlying driver is too many calories. And that means that whether an overweight patient has visceral or subcutaneous fat, the frontline treatment is the same: The patient should eat less, exercise more, and adopt a healthier lifestyle. The value of waist circumference may be that it provides one more argument to convince a patient of this necessity—or, in extreme cases, of the need for bariatric surgery or weight-loss drugs.

"Numbers do have power for a patient," Bessesen told *Endocrine News.* "I often have a patient who says, 'I just cannot weigh 200 pounds. My weight is 201 pounds, and that's unacceptable', as though 198 is OK, but 201 is not. It ultimately comes down to somebody deciding to take action. The factor that ultimately tips somebody over is often a number."

And one advantage that waist circumference offers over weight is that a patient who exercises can lose fat but gain muscle to weigh about the same. But bringing the belt in a notch is unequivocal evidence of progress. EN

—Seaborg is a freelance writer in Charlotteville, VA

ENO LINKS For additional links related to this feature, please visit Endocrine News Online at www.endo-society.org/endo_news.

METABOLICALLY OBESE
The tests of patients who are "fat and fit" can remain in the normal range despite their weight, evidently because they are active and in good aerobic condition.

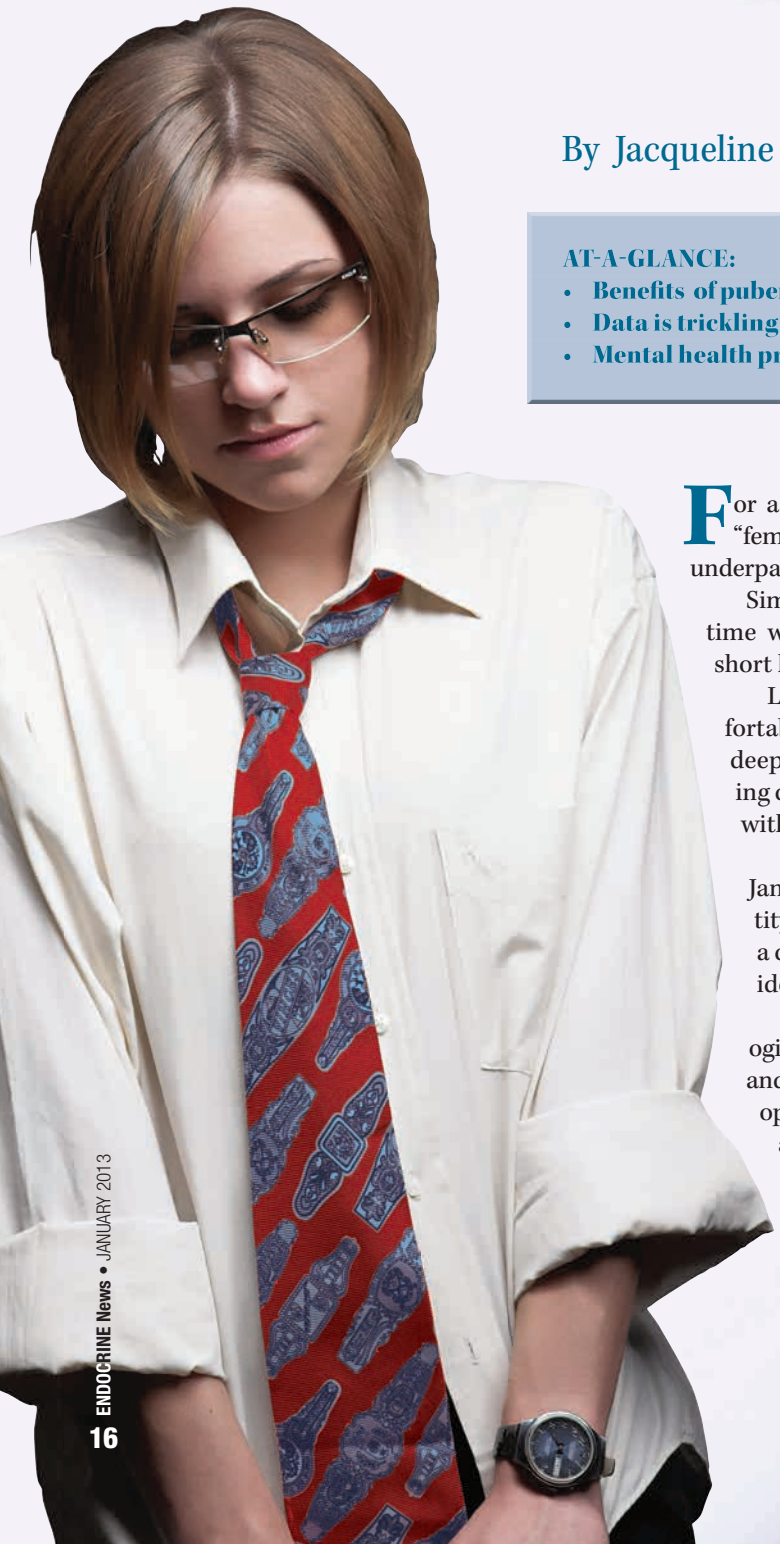
DIET DOs & DON'Ts

While there's no single culprit, there are food ingredients that can make it harder to lose weight around your waist. Trans fats seem to promote abdominal fat deposition and the apple body shape, says Lawrence Rudel, professor of pathology and biochemistry at the Wake Forest University School of Medicine. (Trans fats are in some margarines, crackers, cookies, and other foods made with partially hydrogenated oils.) In a study, Rudel found that trans-fat fed monkeys deposited 30 percent more fat in their abdomens than monounsaturated-fat fed monkeys.

Foods that help battle belly fat more efficiently include:

- Nuts (walnuts, almonds, pistachios, and macadamias)
- Dark chocolate
- Seeds (sunflower and flaxseeds)
- Avocados
- Olive oil (use to cook lean meats and vegetables)

BLOCKING PUBERTY in



By Jacqueline Ruttimann, Ph.D.

AT-A-GLANCE:
- **Benefits of puberty blockers outweigh the risks, say some.**
- **Data is trickling in as to the benefits and risks of drugs.**
- **Mental health professionals help with diagnoses.**

For as long as his parents could remember, 12-year-old Jack acted "female." He favored Barbies over Transformers, often wore his sister's underpants, and refused to use urinals.

Similarly, the mother of 14-year-old Janice cannot remember a time when her daughter did not dress androgynously—preferring short haircuts, boxer shorts, and extra-tight sports bras.

Like many young adolescents, Jack and Janice are uncomfortable with their bodies. However, their anguish runs a lot deeper. At 10, Jack attempted to leap out of a rapidly moving car. Janice has had repeated episodes of cutting herself with a razor blade.

Separate psychologists working with Jack and Janice confirmed that the teens have gender identity disorder (GID) and are possibly transgender, a catch-all phrase for individuals whose gender identity is different from their biological sex.

Increasingly, pediatricians and psychologists are challenged by cases like Jack's and Janice's in which kids want to be the opposite gender. It is an emotional and confusing time for the family and the children, who often are on the cusp of puberty at the very time they are reject-

TRANSGENDER YOUTH

Drugs delay puberty onset, giving children time to sort out gender identity

ing their biological gender. One solution specialists recommend is puberty blockers, drugs that delay the onset of puberty and give the children time to sort out their gender identity.

"Pediatric endocrinologists are the only specialists who see children and adolescents who require pubertal blocking drugs in the course of regular practice," said Norman Spack, a pediatric endocrinologist at Boston Children's Hospital whose practice mainly focuses on transgender youth. "If they do not get involved in cases where they can be helpful, it is unlikely anyone else will."

In the course of their practices, pediatric endocrinologists typically use drugs that delay puberty, such as gonadotropin-releasing hormone (GnRH) analogues, to treat conditions such as central precocious puberty and congenital adrenal hyperplasia. The drugs have a good track record, with 30 years of follow-up data showing them to be safe and effective. For transgender patients, the verdict is still out; as transgender patients enter adulthood, data are trickling in as to the benefits and risks of these drugs.

Deciding to treat with such drugs may not be an easy choice, Spack admitted. "It is difficult for pediatric endocrinologists to grasp the idea of treating a child who otherwise seems perfectly normal and may not reveal his/her mental suffering and risk of self-harm. It is all too easy to turn away referred patients with whom the physician has no prior relationship and whose condition may be considered psychiatric."

Gender fluidity is common among children, but it typically crystallizes during the teenage years. Among preadolescents who

Gender fluidity is common among children but typically it crystalizes around the teenage years.

manifest GID traits, 80 percent will "desist" from being transgender before entering adolescence, according to Kenneth Zucker, Ph.D., of the University of Toronto. Half or more of the youths will go on to identify themselves as gay or lesbian.

Despite increased coverage in the popular press, the prevalence of transgenderism is quite low—about one in 10,000–30,000, according to the fourth edition of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM IV).

In a recent commentary in *Pediatrics,* Walter J. Meyer III, a psychiatrist at the University of Texas Medical Branch in Galveston, Texas, whose practice includes young patients with gender identity issues, cautioned pediatricians not to be so quick to diagnose transgender conditions.

"Many of the presentations in the public media concerning childhood GID give the impression that a child with cross-gender behavior needs to change to the new gender or at least should be evaluated for such a change," he wrote. "Very little information in the public domain talks about the normality of gender questioning and gender role exploration and the rarity of an actual change. The burden of that education is going to fall on the pediatrician."

"It's becoming clear that **the most desirable physical result with the least physical intervention** is to prevent pubertal progression in the first place."

—Norman Spack, Boston Children's Hospital

Once the pediatrician verifies GID, other specialists need to weigh in.

"Pediatric endocrinologists should work with a mental health professional who will support this diagnosis or who can vet the patient for this diagnosis," Meyer said in an interview with *Endocrine News.*

Transgender is not a mindset, it is a condition that is most likely hardwired into a person from the onset.

"A transgender patient says 'change my body, not my mind,'" explained Milton Diamond, a sexologist with a research focus on transitional and intersex conditions. "A therapist tries to get them to think they're delusional and they don't think they are." Diamond says transgenderism is in a person's genes. In his research on transexuality in twins, he has found that among identical twins, if one transitions, the other does also in about 40 percent of the cases. With fraternal twins, this usually does not happen—only 4 percent of these twins do.

MALE-TO-FEMALE ADULT PATIENTS OFTEN SUFFER PHYSICALLY AND PSYCHOLOGICALLY:

- battling male pattern hair loss
- undergoing voice training
- having their thyroid cartilage shaved to remove their Adam's apples
- feeling stuck in a body that's too big for a typical female

His studies have also shown that transgenders' brains are more similar to the gender they want to be than to their biological gender.

"Experiments show that just the way people are right- or left-handed, individuals that are transgender are shown to hear and smell like their preferred gender," added Diamond. (Except for taste and touch, men generally underperform in the sensory department compared with women.)

Spack, who co-directs the Gender Management Service, or GeMS, at Boston Children's Hospital, one of the United States' first gender identity pediatric clinics, champions early treatment before patients reach adulthood.

During his 40-year career, he says he has treated some 200 adult transgender patients who would have benefited from biological clock-stopping drugs. Male-to-female adult patients often suffer physically and psychologically—battling male pattern hair loss, undergoing voice training, having their thyroid cartilage shaved to remove their Adam's apples, and feeling stuck in a body that's too big for a typical female. The late transformation can also be expensive. Patients spend thousands of dollars on hair removal, breast augmentation surgery, and facial feminization surgery.

When American women transition to men at an adult age, their height is typically 5 feet 4 inches, considerably below the mean of 5 feet 10 inches for men. Such patients would have menstruated monthly for years and would face complicated breast reduction to attain a flat chest with an appropriately located areola and nipple.

WHEN TO BEGIN PUBERTY BLOCKERS

The lack of availability of medical services for transgenders 20 years ago was "a wasteland," Spack told a packed audience at ENDO 2012 in Houston. In 2009 he co-authored The Endocrine Society Guideline that recommended the use of GnRH analogues in prepubertal, Tanner Stage 2 children and

lifetime use of sex-changing hormones with monitoring for potential health risks.

"There was an attitudinal shift to be able to say that The Endocrine Society supports this," said Spack. Today a dozen pediatric endocrinology transgender programs exist in the United States compared with two or three a few years ago.

Although attitudes about treatment are changing, Spack said transgender kids are not being treated soon enough. In his own practice, he advocates starting puberty blockers earlier than in the Society guidelines of under the age of 16. The best age for boys, he says, is 12–14 years, while they are at Tanner Stage 2, and have a testicular volume of 4–6 cc; girls should come in younger, at age 10–12 years, with Tanner Stage 2 breast development.

"If a biological female comes in at 15, she's physically a woman and may have been menstruating for three years," he said. She would have already reached her peak height, which might have been augmented with earlier GnRH analogues. If she starts blockers at ages 10-13, she would not need a mastectomy because Tanner 2/3 breasts recede with treatment.

"It's becoming clear that the most desirable physical result with the least physical intervention is to prevent pubertal progression in the first place," Spack said.

Adult transgender genotypic males outnumber genotypic females by a three-to-one ratio while in cohorts under age 21, the sex ratios are equal, he said. The reason for the disparity among transgender adults is mostly cultural; most Westernized countries accept women who are "masculine" in looks and behavior, so a girl may have more difficulty in identifying the depth of her feelings or convincing family and doctors of them.

Spack's GeMS program is modeled after the Dutch program that was created by Peggy Cohen-Kettenis, Ph.D., in Amsterdam. The premise of both programs is to treat the patient's natural puberty like an unintended precocity. Dutch physicians administer GnRH analogues to patients at Tanner Stages 2–3, in an attempt to buy more diagnostic time and ensure that patients really want to transition to the other gender.

If at age 16, patients decide to proceed with the transition, they are put on cross-sex steroids such as testosterone and estradiol. The next step is gonadectomies (e.g., oophorectomy, hysterectomy, feminizing genitoplasty with orchiectomies), surgeries that cannot be lawfully performed in the Netherlands and North America until patients are 18. Mental health counseling is continuous and formal evaluations take place at each major decision point in the process.

Before entering Spack's program, patients must be between Tanner Stages 2and 5 (10 years or above for boys and 9 years or above for girls) and have been in counseling with a gender therapist for six months. The therapist is required to write a referral letter recommending pharmacologic endocrine intervention and stating that other than depression and anxiety associated with gender nonconformity, the patient has no severe psychopathology. Patients must also have the support of both custodial parents.

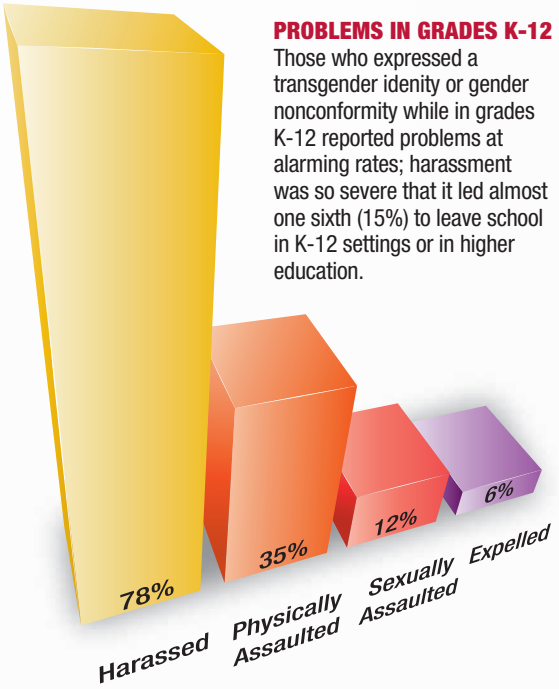
Once these requirements are established, Spack and his interdisciplinary staff of endocrinologists, urologists, gynecologists, geneticists, psychologists, medical ethicists, and social workers are called into action. Candidates for medication undergo a rigorous five-hour battery of psychological tests and a physical examination to determine pubertal stage.

In his ENDO 2012 lecture, Spack explained that before Tanner 2, most patients are willing to live in both genders. "It's hard to distinguish whether they will desist or persist in becoming transgender and there is no litmus test before Tanner 2 puberty," said Spack. Very few of his patients or those in the Dutch program decide to stay their biological gender after beginning pubertal blockers. The Dutch have treated more than 100 patients with GnRH who have reached over 18 years of age. Spack has seen 105 new patients ages 10-19 since 2007; more than a third of his patients (40) have been Tanner Stage 2–3 and have received GnRH treatment.

Along with buying more diagnostic time, using pubertal blockade drugs **enables physicians to use fewer cross-sex hormones when the time comes.**

OnPOINT from The Endocrine Society

The Endocrine Society published its paradigm-changing clinical practice guideline "Endocrine Treatment of Transsexual Persons" in 2009, which recommended the use of GnRH analogues at Tanner 2 and cross-sex steroids around age 16, with monitoring for potential health risks (www.endo-society.org/guidelines/final/upload/Endocrine-Treatment-of-Transsexual-Persons.pdf).



PROBLEMS IN GRADES K-12
Those who expressed a transgender idenity or gender nonconformity while in grades K-12 reported problems at alarming rates; harassment was so severe that it led almost one sixth (15%) to leave school in K-12 settings or in higher education.

Once the psychiatrist and endocrinologist have given the greenlight, the patient begins with one of several GnRH analogues, either a depo injection of Leuprolide that lasts one to three months or an inch-long implant of Histerlin that lasts two years. The latter shuts down gonadotrophic secretion very quickly—within a couple of weeks. The patient undergoes a state of biologic limbo, in which secondary sexual characteristics such as breast budding, testicular enlargement, and axillary and torso hair growth are halted. Height and bone mass, however, still proceed at a pre-pubertal rate.

Usually between ages 14 and 16, patients still look prepubertal compared with the maturity of their peers. Although the delay can be psychologically challenging for the patients who may desire to look like their preferred genders, the slowdown gives them an opportunity to reconsider the transition. GnRH analogues are reversible. Cessation of them usually results in patients restarting their genetically intended puberty within six months.

Although the treatments are considered safe, they are not risk-free. Most transgenders become infertile as a result of the hormonal switching medications. Estrogens diminish sperm production in males, and testosterone's cessation of menses can cause polycystic ovaries in women; these changes usually lead to infertility. Some late-pubertal male patients have opted for sperm banking, but equivalent options for women are limited. Egg freezing is an arduous and expensive procedure requiring ovarian hyperstimulation with HCG, akin to women undergoing in vitro fertilization, and not as likely to be successful, especially if the ovaries are immature when GnRH-suppressed.

"It's hard to have a conversation about fertility when the patient is 12 or 14 years old," said Spack. "It's important for patients to continue to be in psychotherapy during this long diagnostic phase so they can fully understand the implication of taking cross-steroids, even though they are waiting anxiously to get them."

Another risk is cancer. Girls who have breasts and undergo testosterone treatment need regular mammogram screening as adult men; those who have their uteruses while on testosterone may develop endometrial cancer. Both risks can be mitigated by surgical removal of the organs.

Among the arguments for using pubertal blockers to gain more diagnostic time is that patients will not need as many cross-sex hormones later in the transition process. Fewer estrogens in patients means a decreased risk of blood clotting and pulmonary embolism; fewer androgens reduces the likelihood of hypertension. Another plus, Spack said, is that most male-to-female adult patients who took GnRH analogues end up with appropriate size breasts for their frame and never feel the need to have further reconstructive surgery.

For Jack and Janice, not having options may be a case of life and death. According to Youth Pride Inc., a U.S. advocacy group for lesbian, gay, bisexual, transgender, and questioning youth, about two thirds of transgender youth have reported being verbally, physically, and sexually attacked by either their peers or an adult family member, and one third have attempted suicide.

"A lot of people are concerned that delaying puberty may cause some harm," said Meyer. "On a whole, much less harm is done by giving blockers than by not giving blockers." EN

—Ruttimann is Associate Editor of Endocrine News

On a whole, **much less harm is done by giving blockers** than by not giving blockers. But they aren't without risk, especially in terms of fertility.

BARRIERS TO MEDICAL CARE

The most common barriers to accessing regular medical care reported include:

- 64% - lack of insurance
- 46% - inability to pay
- 32% - provider insensitivity or hostility to transgendered people
- 32% - fear of transgender status being revealed

Transgender people struggle with accessing medical care:

- 39% - do not have a physician for routine health care
- 52% - had taken hormones at some point in their lives
- 37% - did not know where to obtain trans-related services

Source: Washington Transgender Needs Assessment Survey (WTNAS)

ENO LINKS For additional links related to this feature, please visit Endocrine News Online at www.endo-society.org/endo_news.

CELEBRATING SCIENCE AT ENDO 2013


The Endocrine Society's 95th Annual Meeting & Expo to be held in San Francisco June 15–18 will showcase a century of scientific breakthroughs in four days. Set against the backdrop of San Francisco's iconic Golden Gate Bridge, **ENDO 2013** is the perfect venue for great feats in endocrinology.

Experts Abound

A number of notable experts will speak at **ENDO 2013.** The Clinical Investigator Award Lecture will be presented by Steven Kahn, M.B., Ch.B., who will highlight the roles of beta-cells in type 2 diabetes pathogenesis. In the Gerald D. Aurbach Award Lecture, Mitchell Lazar, M.D., Ph.D., will explore the influence of circadian epigenomic regulation on metabolism. Donald McDonnell, Ph.D., will examine the estrogen receptor's mediation of bone and breast pathologies in the Roy O. Greep Award Lecture. Gary Hammer, M.D., Ph.D., will present the Edwin B. Astwood Award Lecture on the implications of adrenal stem cells for human disease.

The popular Master Clinician and Clinical Practice Guideline sessions will continue at **ENDO 2013.** Three Master Clinician sessions will provide in-depth examinations of complex adrenal, type 2 diabetes, and osteoporosis cases. Best treatment practices for diabetes and pregnancy, hypertriglyceridemia, and polycystic ovarian syndrome will be presented during three Clinical Practice Guideline sessions.

Endocrinology took the spotlight in 2012 with the awarding of the Nobel Prize in Chemistry to Brian Kobilka, M.D., and Robert Lefkowitz, M.D., for their studies on G protein–coupled receptors (GPCRs). To celebrate this achievement, **ENDO 2013** is offering a forum entitled "New Light on GPCRs," which brings together global experts to present insights into GPCR structure/function and roles in metabolic regulation. For the "Year in GPCRs," Graeme Milligan, Ph.D., F.R.S.E., will review developments in GPCR research made over the past year. The Clark T. Sawin Memorial Lecture, presented by Delbert A. Fisher awardee Jesse Roth, M.D., F.A.C.P., will delve into more than a century of advances in signaling.

A new and provocative feature is "Endocrinology and the News." This special session will focus on interactions between scientists and the media with two researchers who have received increased scrutiny because of the controversial nature of their findings. Tyrone Hayes, Ph.D., well-known for his work in endocrine disruptors, and Robert Lustig, M.D., a pediatric endocrinologist critical of high-fructose corn syrup, will discuss their experiences and strategies for media relations.

The new Featured Poster Presentations is one of the highlights at **ENDO 2013.** These presentations will give select authors of high-scoring abstracts the opportunity to take the podium and present a preview of their posters. Those interested may submit their abstracts during the regular Call for Abstracts period that closes Jan. 30, 2013, at noon ET.

Downtown Excursions

The diversity of topics planned for **ENDO 2013** complements the many communities and attractions within San Francisco's 49 square miles. As the financial and cultural heart of northern California, San Francisco offers visitors world-class museums, music, and food among the varying neighborhoods. The Mission District is the city's oldest neighborhood, founded in 1776, and has grown into a hotspot of galleries and ethnic restaurants. The Italian North Beach area is famous for its numerous jazz bars and gelato parlors, and San Francisco's Chinatown remains the oldest and one of the largest such neighborhoods in the country. Top-notch dim sum restaurants speckle the streets, but cuisines of all kinds can be found within walking distance, or even by cable car. After a meal accompanied by a local craft beer, attendees may stroll across the Golden Gate Bridge or take a ferry across the foggy waters to Alcatraz. San Francisco's accessible tourism sights provide plenty to do between **ENDO 2013's** events.

"Endocrinology and the News" and the new Featured Poster Presentations comprise two of the biggest highlights at this year's meeting.

More information for attendees can be found at *www.endo-society.org/Endo2013*. Conference registration opened on Dec. 5, 2012, for members, and will open Jan. 3, 2013, for non-members. EN

— Melissa Mapes is a freelance writer in Washington, D.C.

The Endocrine Society AMBASSADOR EXCHANGE PROGRAM Takes Flight

Gary Hammer, M.D., Ph.D. (top) and his postdoctoral fellow, Tobias Else, M.D. (right) from the University of Michigan Medical School in Ann Arbor.

Two U.S. Endocrine Society members will embark this month on a trip halfway across the globe to India. Gary Hammer, M.D., Ph.D., and his postdoctoral fellow, Tobias Else, M.D., from the University of Michigan Medical School in Ann Arbor, will launch The Endocrine Society's Ambassador Exchange Program, in which mentors and their trainees observe how national, ethnic, economic, and cultural factors shape endocrine care.

Life Changing

In this pilot program funded by The Endocrine Society, an endocrinologist and a trainee from an established U.S. center will visit an international center where resources are limited and indigent populations are served. In turn, an endocrinologist and trainee from the host international center will then visit the U.S. center to complete the exchange. All four participants will attend and present their experiences at ENDO 2013, The Endocrine Society's 95th Annual Meeting & Expo.

The idea is the brain child of Society President William Young, Jr., M.D. "Throughout my professional career, I have been fortunate to participate in such exchanges, which I consider life-changing experiences," he said.

Medical institutions individually sponsor their own medical student and scientific exchange programs among successful institutions in developed nations. What makes the Society's program different is that it focuses on practicing clinicians and trainees at the bedside and links resource-rich developed nations with resource-poor developing nations.

President Young and a Working group, which included representatives from the Society's Council, trainee constituency, and Society staff, chose the participants and institutions for this pilot program. By traveling to hospitals and clinics in low- and middle-income countries (LMIC, as defined by the World Bank), U.S.-based clinicians gain additional insight into the natural progression of endocrine disorders not frequently observed in the U.S. In turn, LMIC-based clinicians will learn about new technologies and best practices in U.S. institutions.

Eye Opening

King Edward Memorial Hospital (KEM) in Mumbai, India, will be the first host site. Serving the indigent population of Mumbai, KEM services close to 2 million patients a year. Although the hospital staffs a sizable number of doctors (390 staff M.D.s and 550 residents in training), it has no nursing staff. Patients are cared for by the family, who at times sleep there for months, along with their pets and farm animals.

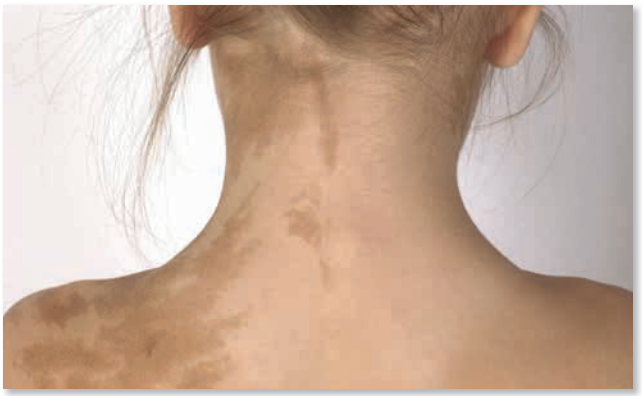
"Like many developing countries, the healthcare disparities are profound in terms of limited resources and people. We will see things we don't see any more, such as patients in end-stage diseases. It will be a real eye-opening experience," said Hammer.

King Edward Memorial Hospital (KEM) in Mumbai, India, is the first host site. Serving the indigent population of Mumbai, KEM sees close to 2 million patients a year.

Nalini S. Shah, M.D., chair of Endocrinology, and her fellow Shruthi Kare, M.D., will then visit the University of Michigan two weeks before ENDO 2013. The University of Michigan's Comprehensive Cancer Center is one of the world's only comprehensive adrenal cancer clinics. This premier research and academic institution was initially funded by a foundational gift by the UM football

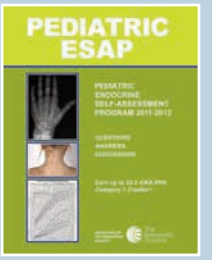
continued on page 23

PRECOCIOUS PUBERTY: A Case Study From PEDIATRIC ESAP



QUESTION

Pediatric ESAP is a great tool for board exam preparation and offers learners CME credits and MOC points upon completion. Test yourself with this case from Pediatric ESAP™, brought to you by The Endocrine Society's Pediatric Self-Assessment Committee. For the answer to this case, go to page 30.



A 5-year-old girl presents to your office with a history of breast buds and vaginal bleeding. Laboratory studies done by her pediatrician show an elevated estradiol concentration with LH and FSH levels below the detection limit of the assays. Her medical history is notable for several long bone fractures associated with minimal trauma. Radiographs from her orthopedist reveal a progressive shepherd's crook deformity of the left proximal femur with areas of "ground glass"–appearing bone. When you examine her head, you detect several areas of asymmetry in her skull. On skin examination, you observe the following (see photograph):

This patient is at increased risk for which one of the following?

A Hypophosphatemia
B Hypothyroidism
C Malignant melanoma
D GH deficiency
E Optic glioma

continued on page 30

continued from page 22

coach, Bo Schembechler, in memory of his wife, Millie, who died from adrenal cancer. The National Cancer Institute of the National Institutes of Health also provides funding and resources to the center.

While at KEM, Hammer and Else will deliver medical and endocrine lectures, attend patient-based education rounds in hospitals, and provide case-based conferences. They will also demonstrate use of patient education and materials by going over fact sheets from the Hormone Health Network that have been translated to Hindi.

For Else, this opportunity does more than satisfy his wanderlust. Before joining Hammer's lab, Else was a medical student in Germany and spent some time observing clinics in England and Austria. "I'm excited to go," he said. "I am eager to see it from my professional vision and learn something that you wouldn't normally do if you were traveling."

Not only are the program's participants going to personally and professionally benefit, but so will The Endocrine Society. The Society's third Strategic Plan (SP3) emphasizes its commitment to "the goal of improved human health worldwide." The program would position the organization as a global health leader among professional societies and extend its impact and influence into the world arena.

Although the Ambassador program is a pilot study, the goal would be to create a sustaining model funded by external funding. The Endocrine Society will seek external funding from two sources: pharmaceutical and biotechnology companies (and their respective foundations) with an interest in developing nations (e.g., Eli Lilly and Company and its Lilly Foundation, Medtronic and its Medtronic Foundation), and independent foundations with global health funding programs (e.g., Josiah Macy, Jr. Foundation, Bill & Melinda Gates Foundation).

Although the Ambassador program is a pilot study, the goal would be to create **A SUSTAINING MODEL FUNDED BY EXTERNAL FUNDING FROM PHARMACEUTICAL AND BIOTECHNOLOGY COMPANIES.**

In the Spring, Susan Madel, M.D., M.P.H., and Ilona Lorcinz from the University of Pennsylvania (UPenn) in Philadelphia will visit Chris Hani Baragwanath (Bara) Hospital in Soweto, South Africa, an institution in which more than 50 percent of the patients admitted have HIV. Roy Shires, FCP(SA), Ph.D., and Kershlin Naidoo, M.D., from Bara will then repay the visit and go to UPenn. EN

—Jaqueline Ruttimann, Ph.D., Associate Editor of Endocrine News

ENO LINKS For additional links related to this feature, please visit Endocrine News Online at www.endo-society.org/endo_news.

VOTE

2013 ELECTION FOR OFFICERS AND COUNCILS

The polls are now open for the 2013 Election and you are encouraged to vote. All members with voting privileges were sent an electronic ballot in early January. You can access online voting instructions by visiting **www.endo-society.org/membership/election.cfm**.

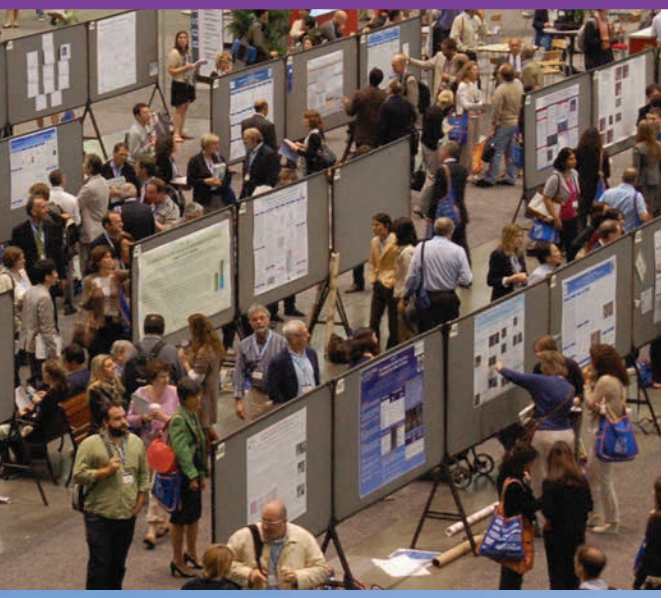
Questions should be directed to Elizabeth Kan at 301.941.0206 or ekan@endo-society.org.

BALLOTS WILL BE ACCEPTED THROUGH MARCH 3, 2013.

Look for the electronic ballots in your e-mail.

The Endocrine Society®

ENDO 2013 Abstract Submission is Now Open



Submit your best science for oral, poster, and poster preview presentations for The Endocrine Society's 95th Annual Meeting & Expo, June 15–18, 2013, San Francisco, CA.

NEW THIS YEAR! **"Featured Poster Presenters"** A small number of poster presenters with high-scoring abstracts will be invited to give a brief podium presentation as a preview of their poster.

ENDO is the **premier event to showcase your research.** In 2012, more than 2,600 abstract presenters chose ENDO as the venue to share their research, exchange ideas, and network with nearly 8,000 endocrine researchers and practitioners.

Abstract Submission Deadline:
January 30, 2013, 12:00 PM (noon) ET

To submit an abstract, register, or see an expanded list of over 120 categories visit www.endo-society.org/endo2013

THE ENDOCRINE SOCIETY®

Victoza® vs sitagliptin—dig deeper into the differences.

Victoza® works like natural GLP-1 to treat type 2 diabetes.[1]

After 52 weeks—

Greater HbA_{1c} reductions vs sitagliptin
1.3% with Victoza® 1.2 mg to 1.5% with Victoza® 1.8 mg vs 0.9% with sitagliptin 100 mg[2]*

Greater weight reductions vs sitagliptin
2.8 kg with Victoza® 1.2 mg to 3.7 kg with Victoza® 1.8 mg vs 1.2 kg with sitagliptin 100 mg[2†]

More than 600,000 patients worldwide have been prescribed Victoza®.[3]

VICTOZA® ▼
liraglutide

*Victoza 1.2 mg + metformin (n=155); Victoza 1.8 mg + metformin (n=176); vs sitagliptin 100 mg + metformin (n=166) over 52 weeks.
†Victoza 1.2 mg + metformin (n=155); Victoza 1.8 mg + metformin (n=176); vs sitagliptin 100 mg + metformin (n=166) over 52 weeks.

References: 1. Victoza® [summary of product characteristics]. Bagsværd, Denmark: Novo Nordisk A/S; 2012. **2.** Pratley R, Nauck M, Bailey T, et al; for the 1860-LIRA-DPP-4 Study Group. One year of liraglutide treatment offers sustained and more effective glycaemic control and weight reduction compared with sitagliptin, both in combination with metformin, in patients with type 2 diabetes: a randomised, parallel-group, open-label trial. *Int J Clin Pract.* 2011;65(4):397-407. doi:10.1111/j.1742-1241.2011.02656.x. **3.** Internal calculations based on IMS Midas Quantum data, May 2012.

Prescribing information

Victoza® ▼ (liraglutide) 6 mg/ml solution for injection in pre-filled pen
Victoza® 3 ml pen
1 ml of solution contains 6 mg of liraglutide.
Indication: Treatment of adults with type 2 diabetes mellitus in combination with metformin or a sulphonylurea, in patients with insufficient glycaemic control despite maximal tolerated dose of metformin or sulphonylurea monotherapy; or in combination with metformin and a sulphonylurea, or metformin and a thiazolidinedione in patients with insufficient glycaemic control despite dual therapy. **Dosage:** Victoza® is administered once daily by subcutaneous injection and at any time independent of meals however it is preferable to inject around the same time of day. Victoza® should not be administered intravenously or intramuscularly. Recommended starting dose is 0.6 mg daily, after at least one week, the dose should be increased to a maintenance dose of 1.2 mg. Based on clinical response, after at least one week the dose can be increased to 1.8 mg. Daily doses higher than 1.8 mg are not recommended. When added to existing sulphonylureas or in combination with metformin and sulphonylureas, a reduction in the dose of sulphonylurea may be necessary to reduce the risk of hypoglycaemia. Victoza® can be used in the elderly (>65 years) without dose adjustment but therapeutic experience in patients ≥75 years is limited. No dose adjustment for patients with mild renal impairment (creatinine clearance (CrCl) 60-90 ml/min). Due to lack of therapeutic experience Victoza® is not to be recommended for use in patients with moderate (CrCl of 30-59 ml/min), severe (CrCl < 30 ml/min) and end-stage renal disease or patients with hepatic impairment or children <18 years. **Contraindications:** Hypersensitivity to the active substance or any of the excipients. **Warnings and Precautions for use:** Victoza® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Victoza® is not a substitute for insulin. The addition of Victoza® in patients already treated with insulin has not been evaluated and is therefore not recommended. Limited experience in patients with congestive heart failure New York Heart Association (NYHA) class I-II and no experience in patients with NYHA class III-IV. Due to limited experience Victoza® is not recommended for patients with inflammatory bowel disease and diabetic gastroparesis. Victoza® is associated with transient gastrointestinal (GI) adverse reactions. GLP-1 analogues have been associated with pancreatitis; patients should be informed of symptoms of acute pancreatitis if pancreatitis suspected, Victoza® and other suspect medicinal products should be discontinued. Thyroid adverse events, including increased blood calcitonin, goitre and thyroid neoplasm reported in clinical trials particularly in patients with pre-existing thyroid disease. Risk of dehydration in relation to GI side effects; take precautions to avoid fluid depletion. No studies on effects on ability to drive and use machinery. Patients advised to take precautions to avoid hypoglycaemia while driving and using machines, in particular when Victoza® is used in combination with sulphonylureas. In the absence of compatibility studies Victoza® must not be mixed with other medicinal products. **Fertility, pregnancy and lactation:** If a patient wishes to become pregnant, pregnancy occurs or is breast feeding, treatment with Victoza® should be discontinued; use of insulin is recommended instead. Apart from a slight decrease in number of live implants in animal studies no harmful effects on fertility observed. **Undesirable effects:** The most frequently observed adverse reactions which varied according to the combination used (sulphonylurea, metformin or a thiazolidinedione) were: Very common (≥ 1/10): nausea, diarrhoea, hypoglycaemia when used in combination with sulphonylureas, headache when used in combination with metformin and vomiting when used in combination with metformin and rosiglitazone; Common (≥1/100 to <1/10): vomiting, constipation, abdominal pain, discomfort and distension, dyspepsia, gastritis, flatulence, gastroesophageal reflux disease, gastroenteritis viral, toothache, headache, dizziness, nasopharyngitis, bronchitis, hypoglycaemia, anorexia, appetite decreased, fatigue and pyrexia. GI adverse reactions are more frequent at start of therapy but are usually transient. Patients >70 years or with mild renal impairment (CrCl 60-90 ml/min) may experience more GI effects. Consistent with medicinal products containing proteins/peptides, patients may develop anti-liraglutide antibodies following treatment but this has not been associated with reduced efficacy of Victoza®. Few cases of; angioedema (0.05%), acute pancreatitis (<0.2%), injection site reactions (usually mild, approx. 2%). Rates of thyroid adverse events - 33.5, 30.0 and 21.7 events/1000 subject years of exposure for liraglutide, placebo and total comparators; Thyroid neoplasms, increased blood calcitonin and goitres are the most frequently reported thyroid adverse events/1000 subject years of exposure were 6.8, 10.9 and 5.4 of liraglutide treated patients in comparison with 6.4, 10.7 and 2.1 of placebo treated and 2.4, 6.0 and 1.8 of total comparator treated. The Summary of Product Characteristics should be consulted for a full list of side effects. **MA numbers:** Victoza® 2 x 3ml pre-filled pensEU/1/09/529/002. Victoza® 3 x 3ml pre-filled pensEU/1/09/529/003. **Legal Category:** POM. **Basic NHS Price:** Victoza® 2 x 3ml pre-filled pens: £ 78.48. Victoza® 3 x 3ml pre-filled pens: £117.72. **Further prescribing information can be obtained from:** Novo Nordisk Limited, Broadfield Park, Brighton Road, Crawley, West Sussex, RH11 9RT. **Date created:** March 2012.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novo Nordisk Limited (Telephone Novo Nordisk Customer Care Centre 0845 6005055). Calls may be monitored for training purposes.

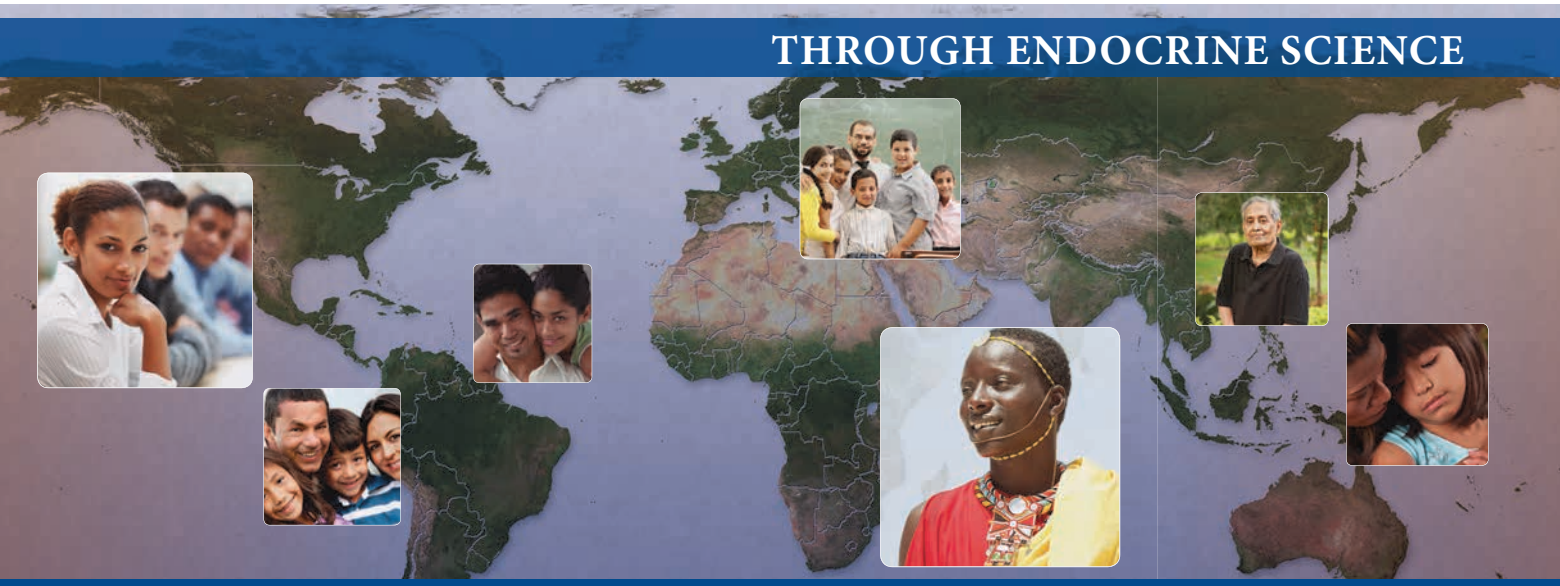
changing diabetes®

Novo Nordisk is changing diabetes. We provide innovative treatment solutions that empower people to achieve and maintain good control of their diabetes.

novo nordisk®

REGISTER NOW!

REDUCING HEALTH DISPARITIES AND IMPROVING CARE THROUGH ENDOCRINE SCIENCE



2013 Reducing Health Disparities in Type 2 Diabetes Mellitus Summit

MARCH 22 – 23, 2013 | SHERATON INNER HARBOR HOTEL

As a recognized leader in this important field, The Endocrine Society is hosting its inaugural *Reducing Health Disparities Summit* in March 2013. This conference is designed to bring together researchers, clinicians, health educators, and public and community health leaders working to build partnerships to reduce health disparities.

CONFIRMED SPEAKERS:

Griffin Rodgers, MD, *Director of NIDDK*

Louis Sullivan, MD, *former U.S. Health and Human Services Secretary*

Sherita Golden, MD, *Chair of the Society's Health Disparities Scientific Statement*

Samuel Dagogo-Jack, MD, *Vice-President of Science and Medicine for the American Diabetes Association*

Rahn K. Bailey, MD, *President, National Medical Association*

Pam Allweiss, *Centers for Disease Control and Prevention*

Patrice Harris, MD, *Board Member, American Medical Association*

Abstracts that focus on health disparities in type 2 diabetes (T2D) from various perspectives will be considered for oral or poster presentation.

Key Dates: Registration Closes March 18 | Onsite Registration March 22 | Registration Fee: $125

Visit www.endo-society.org/disparities to register!

THE ENDOCRINE SOCIETY®

MOUSE "AVATARS" Advance Personalized Medicine

Dr. Megan Sykes, director of Columbia University's Center for Translational Immnology, uses mouse avatars to study type 1 diabetes.

Research into personalized medicine has taken a new turn with the development of a type of mouse model known informally as an "avatar."

Like avatars in movies and online games, mouse avatars act as stand-ins for real people, enabling scientists to study exactly how and why the cells and tissues of individual patients react to medications. By testing the drugs first on the avatars, physicians may be able to avoid subjecting patients unnecessarily to toxic therapies.

Human cells have been experimentally implanted into mice for many years, of course. But the first mouse avatar—when drugs tested on the implanted tissue of a specific patient were then used to treat the patient—occurred only about a decade ago. The first researcher to use the technique was Dr. Manuel Hidalgo, director of the Centro Integral Oncologico Clara Campal in Madrid and an associate professor of oncology at Johns Hopkins University in Baltimore.

Much of the early work has involved cancer patients, but a few years ago, Dr. Megan Sykes, director of Columbia University's Center for Translational Immunology, began using mouse avatars to study autoimmune diseases like type 1 diabetes, in which T cells attack and destroy insulin-producing beta cells in the pancreas. Sykes and her colleagues transplanted human bone marrow stem cells from type 1 diabetes patients and healthy individuals into mice with genetically deficient immune systems. Each mouse received cells from either an individual diabetes patient or from a healthy control. Sykes donated her own cells to create the first avatar control, which she dubbed "Mini-Me." A paper on the study was published in 2012 in the journal *Science Translational Medicine*.

"This is the first time that a humanized mouse has been created with adult bone marrow stem cells from volunteers," Sykes said.

Within eight weeks, the mice had a diversity of newly created human immune cells, including T cells, B cells, and myeloid cells (non-lymphocyte cells that generate immune cells). These young cells did not attack healthy tissues.

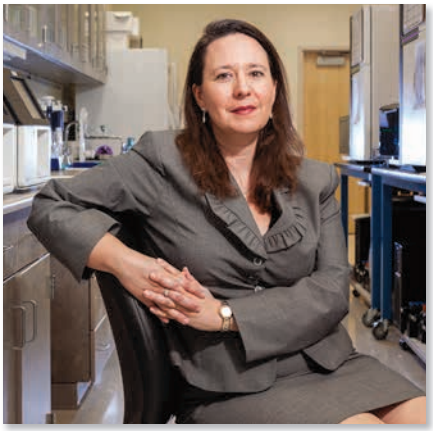
Sykes and her colleagues are currently studying the mice to determine what occurs differently in the immune systems of people with type 1 diabetes, before the disease develops. They are also beginning to test immunotherapies in these mice. In addition, Sykes hopes to learn more about the genetics of type 1 diabetes. "There are lot of genes that have been identified as predisposed to type 1 diabetes, and a lot of those genes are in the immune system," she says, "but no one knows how they drive the immune system to create diabetes."

Sykes and her colleagues are also interested in developing and using mouse avatars to study other autoimmune diseases, such as lupus and rheumatoid arthritis.

"The idea is that you could actually make [human] immune cells in the mice and give them back to the patients," said Sykes. Immune cells generated in the mice avatars might also be used in other contexts, "such as treating infections in immunosuppressed patients," she added.

The idea is that you could actually **MAKE [HUMAN] IMMUNE CELLS IN MICE** and give them back to the patients.

This personalized animal-model technique is in its early stages, and the models are being used primarily for research. Experts caution that the technique still poses many practical problems and that randomized clinical trials will be needed to prove that mouse avatars produce better outcomes for patients.



Mayo Clinic's Dr. Judy Boughey is one of the lead investigators in a mouse-avatar trial called the Breast Cancer Genome Guided Therapy Study (BEAUTY).

Avatars for Cancer Patients

Scientists are further along in developing avatars for cancer patients. Earlier this year, Hidalgo and his colleagues reported on 14 patients with refractory advanced cancers who were treated with drugs first tested on mice that had been implanted with the patients' individual tumors. The study found a strong predictivity, both positive and negative, between the drug's activity in the mouse avatars and clinical outcomes. The researchers also reported that the "treatments selected for each individual patient were not obvious and would not have been the first choice for a conventional second- or third-line treatment."

It's more likely that the results of the **RESEARCH USING AVATARS WILL DRIVE AND ELEVATE THE CARE** of all clinical patients across the country.

"Most of our patients have advanced refractory disease and have an expected survival of six to 12 months, so when patients have responded to our drug combinations and lived for two to three years, we feel that it is likely to add important survival time," said study co-author Dr. David Sidransky, a professor of oncology and otolaryngology at Johns Hopkins University. "But these results have to be confirmed in a more controlled study."

A team of Australian researchers, led by molecular geneticist Sean Grimmond of the University of Queensland, reported the results of a similar experiment in which personalized models of a patient's pancreatic cancer were created by xenografting a piece of the patient's tumor onto an immune-compromised mouse. They then tested the tumor's response to a cancer drug that gene sequencing of the tumor suggested could work. The tumors in the mice shrank, although, sadly, the patient died before the drugs could be given to him.

Pharmaceutical companies are also working with personalized animal models. Scientists at Bayer Schering Pharma in Berlin, Germany, for example, have reported using xenograft mouse models derived from the cancer cell lines of 22 patients with non-small cell lung cancer to test and improve the effectiveness of a new anticancer drug.

Mayo Clinic's Center for Individualized Medicine in Rochester, Minnesota, has launched what may be the largest mouse-avatar project to date: the Breast Cancer Genome Guided Therapy Study (BEAUTY). Its aim is to determine if personalized animal models can help with the development of more effective neoadjuvant chemotherapy for high-risk breast cancer patients.

For the study, the Mayo researchers are obtaining tumor tissue samples from 200 women with early-stage invasive breast cancer who are scheduled to receive standard chemotherapy treatment. These samples are taken twice: before chemotherapy, which shrinks the tumor, and afterward (from any residual cells removed during surgery). Both samples are genetically sequenced, as are the patient's healthy cells. The researchers then study the pre- and post-chemotherapy sequencing to determine how the patient's tumor cells have mutated in response to the drugs.

Cells from the tissue samples are also being implanted into the flanks of immune-compromised mice. The Mayo researchers will be able to use these xenograft mice to test the effects of various anti-cancer drugs or combinations of drugs on the tumors—without exposing the patient unnecessarily to those drugs.

"We can analyze the output from the genetic sequencing, identify what pathways are changed in the tumor compared to the host, identify potential drug targets for those pathways, and try those drugs in the xenograft mice," explained Dr. Judy Boughey, one of the lead investigators with the BEAUTY study. "That will then give us the data to go forward to consider if a drug can be used as a potential therapy for patients with that specific genetic alteration."

Clearing Obstacles

Using mice stand-ins is not without its technical challenges. The tumors often fail to grow in the mice. (The "take" rate in the BEAUTY study is about 40 to 50 percent, according to Boughey.) In addition, it can take several months to produce enough mice to test a sufficient number of drugs. As illustrated by the Grimmond case study, a patient could die waiting for the results. Boughey and her colleagues are confident, however, that these practical obstacles can be overcome.

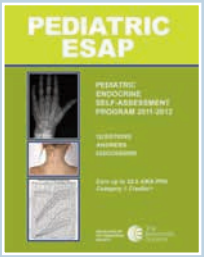
Although the research to date with mouse avatars has been promising, both Sykes and Boughey stress that it's still too soon to know what its clinical applications will be.

"We're at the beginning of exploring this field," said Boughey. "In the next five years we're going to see a lot more growth. But will it become part of the standard clinical care that every patient has their own mouse avatar running around? Probably not. It's more likely that the results of the research using avatars will drive and elevate the care of all clinical patients across the country." EN

—Susan Perry is a freelance writer in Minneapolis, MN

ENO LINKS For additional links related to this feature, please visit Endocrine News Online at www.endo-society.org/endo_news.

Precocious Puberty: A Case Study From PEDIATRIC ESAP

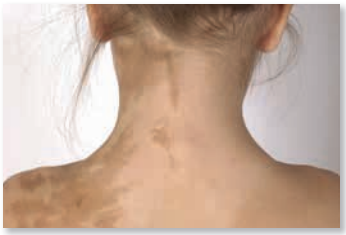


ANSWER

Pediatric ESAP™ is a self-assessment tool that includes 100 clinical case-vignettes and extensive answer discussions in all areas of pediatric endocrinology. Pediatric ESAP is a great tool for board exam preparation and offers learners CME credits and MOC points upon completion. For more information, visit *endoselfassessment.org.*

continued from page 23

The answer is:
A. Hypophosphatemia



This child has the classic triad of McCune-Albright syndrome (MAS): gonadotropin-independent precocious puberty, polyostotic fibrous dysplasia, and irregular café-au-lait spots with the typical "coast of Maine" border. This disorder is due to a sporadic postzygotic mutation in the GNAS gene, which leads to constitutive activation of Gsα. One of the more serious and disabling aspects of MAS is the polyostotic fibrous dysplasia; any bone can be affected, with the proximal femur and the craniofacial bones most commonly involved.

In addition to the bone fragility and deformity associated with fibrous dysplasia, the dysplastic bone lesions have the ability to overproduce fibroblast growth factor 23 (FGF23), a phosphaturic hormone normally produced by osteocytes. The development of hypophosphatemia in MAS is related to the skeletal disease burden. Periodic monitoring for hypophosphatemia is important in patients with MAS who have substantial fibrous dysplasia because untreated hypophosphatemia can result in rickets, muscle weakness, and further increased bone fragility. Patients with MAS who develop hypophosphatemia require treatment with phosphate and calcitriol, similar to other forms of FGF23-mediated hypophosphatemia, such as X-linked hypophosphatemic rickets.

MAS is associated with several other hyperfunctioning endocrinopathies, including Cushing syndrome, hyperthyroidism, and GH excess. GNAS mutations have not been identified in the parathyroids of patients with MAS; thus, hyperparathyroidism does not appear to be a component of this syndrome and would not be a cause of hypophosphatemia. Hormone deficiencies such as hypothyroidism (Answer B) and GH deficiency (Answer D) only occur, as expected, following surgical or ablative treatment for hormone excess conditions. Patients with fibrous dysplasia are at increased risk for sarcomatous transformation, but malignant endocrine tumors are rare.

MAS is often initially misdiagnosed as neurofibromatosis type 1, a disorder caused by inactivation of the tumor suppressor neurofibromin. Neurofibromatosis type 1 is characterized by café-au-lait spots with smooth borders ("coast of California") and neurofibromas. Neurofibromatosis type 1 can be associated with mild skeletal abnormalities, fractures, scoliosis, and osteoporosis; however, affected patients do not develop the classic proximal femur deformities seen in MAS. Melanoma (Answer C) has not been reported in MAS, but can be seen in neurofibromatosis. Patients with neurofibromatosis type 1 may develop precocious puberty; however, unlike precocious puberty associated with MAS, it is gonadotropin dependent and is often associated with intracranial lesions, such as optic and hypothalamic gliomas (Answer E). EN

CMS TO INCREASE PAYMENTS TO ENDOCRINOLOGISTS

On Nov. 1, 2012, the Centers for Medicare and Medicaid Services (CMS) released the 2013 Medicare Physician Fee Schedule final rule. The fee schedule sets the rates at which healthcare professionals are reimbursed for services provided to Medicare beneficiaries for the upcoming year. While the fee schedule reflects a 26.5 percent payment reduction caused by the flawed sustainable growth rate formula, it is expected that Congress will pass a short-term patch to prevent the cuts from taking effect. In the absence of the overall reduction, payments to endocrinologists are projected to increase by one percent.

In September 2012, The Endocrine Society submitted comments to CMS that advocated streamlined requirements for quality improvement programs and that supported payments for care coordination services. In the final rule, CMS addressed the numerous and often overlapping requirements of the various quality improvement programs and approved payment for transitional care management services.

PQRS and EHR

In the proposed rule, CMS recommended the inclusion of 264 individual measures and 26 measure groups in the 2013 Physician Quality Reporting System (PQRS) and the alignment of PQRS electronic health record (EHR)-based reporting measures with measures under the EHR incentive program. The Society supported alignment of the PQRS and EHR incentive programs, which would reduce the administrative burden that physicians and staff face in reporting quality measures to multiple programs. CMS finalized the proposed individual measures and measures groups for PQRS, along with proposals to reduce the administrative burdens of meeting the PQRS and EHR program requirements by aligning the reporting criteria for the programs. Eligible professionals who meet the program requirements will receive a 0.5 percent incentive payment in 2013 and avoid a 1.5 percent penalty in 2015.

e-Prescribing

CMS proposed to expand the e-prescribing group reporting option to include practices with 2-24 eligible professionals. To meet the e-prescribing requirements, practices would need to report 225 electronic prescriptions. The Society argued that this requirement was too arduous for smaller practices and recommended a tiered approach. In the final rule, CMS instead reduced the reporting threshold from 225 electronic prescriptions to 75, stating that a tiered approach would add unnecessary complexity to the program. The Society supports this compromise measure.

Transitional Care

In the proposed rule, CMS recommended coverage for transitional care management services for the coordination of a patient's care in the 30 days post-discharge from a hospital or nursing facility. Over the last year, the Society worked with 15 other specialty societies to develop, define, and value the transitional care management codes (99495 and 99496) and met with the CMS Deputy Administrator and Director of Medicare to advocate for coverage. In the final rule, CMS supported the societies' proposal, which was also recommended by the American Medical Association's Resource-based Relative Value Scale Update Committee, and agreed to cover these services under Medicare.

In order to bill the transitional care management codes, physicians or staff must contact the patient within two days post-discharge and a face-to-face visit must occur within seven days for highly complex patients (99496) or within 14 days for moderately complex patients (99495). The initial face-to-face visit is included in the payment for the codes, provided the visit includes certain specified care coordination services, such as medication reconciliation and coordination of physician referrals.

The Society supports payment for transitional care management services and is pleased that CMS has taken steps to reimburse appropriately for such services. The Society encourages CMS to consider additional coverage for care coordination, like chronic care management and inter-professional telephone consultations. EN

— *Meredith Dyer*

ENO LINKS For additional links related to this feature, please visit Endocrine News Online at www.endo-society.org/endo_news.

EndoCareers®

Endless Possibilities through SOCIETY AWARDS

Kristen Vella, Ph.D.
Co-Chair, Trainee and Career Development Core Committee

As a fellow early career member of The Endocrine Society, I understand the career advancement challenges that undergraduate, medical and graduate students, postdoctoral and medical, fellows, junior faculty, and early career investigators face as we consider a future in endocrinology. Whether your future is in basic or clinical research or clinical practice, publishing, funding, and recognition are critical to reaching your goals. I would like to highlight a few of the many fellowships and awards offered by The Endocrine Society for those contemplating the possibilities in endocrinology.

If you are considering submitting an abstract for **ENDO 2013, The Endocrine Society's 95th Annual Meeting & Expo,** or attending our Early Career Forum or the June workshop in San Francisco on "How to Secure Promotion and Tenure," check out the travel awards offered by The Endocrine Society. In particular, the abstract awards offer an opportunity to present your research at a national meeting and receive recognition for your outstanding work. The Early Career Forum and Promotion and Tenure travel awards provide funding to attend these highly successful sessions.

If you are an undergraduate student, medical student, or first-year graduate student, then the Summer Research Fellowship program is for you. This program provides a stipend to participate in an endocrine research project with a mentor from The Endocrine Society and to attend **ENDO 2013.** The annual meeting offers symposia and plenary lectures on basic, clinical, and translational research topics in endocrinology, and opportunities to network with peers and members of the Society.

The Society offers many awards and research fellowships. Here's a list of the Society awards available for early career professionals. (For more information see *www.endo-society.org/awards.*)

ENDO Awards and Travel Grants

The Endocrine Society Outstanding Abstract Awards: presented to authors of the best abstracts submitted for ENDO.

Eugenia Rosemberg Abstract Award: given to junior faculty/early career professionals who are within three years of completing a training program. Open to any abstract submitted in the basic science categories.

Clinical Fellows Abstract Awards/Travel Grants in Women's Health: awarded to top-scoring abstracts from clinical endocrine fellows for research in clinically relevant aspects of women's health. *Supported by Pfizer, Inc.*

Mara E. Lieberman Memorial Awards: presented to the top-scoring abstracts submitted by women. Award winners must be a graduate student, postdoctoral fellow, or junior faculty.

The Clinical Research Fellowship and Mentor Awards in Women's Health: provided to fellows who have submitted abstracts on research in clinically relevant aspects of women's health. Award winners will be required to present their projects during an oral session competition at ENDO. The mentor of the winning presentation will receive the mentor award. *Supported by Pfizer, Inc.*

Research Fellowship Awards

The Endocrine Summer Research Fellowships: awarded to undergraduate students enrolled in the third year or beyond at the time of applying or to first-year medical or graduate students.

Clinical Research Fellowship Award: given to clinical endocrine fellows conducting research in clinically relevant aspects of women's health. *Supported by Pfizer, Inc.*

Acromegaly Clinical Research Fellowship Award: provided to clinical endocrine fellows conducting research in acromegaly. *Supported by Pfizer, Inc.*

Conference Travel Grants and Other Society Awards

Early Investigators Award: provided to early career investigators within 10 years of their terminal degree date in recognition of outstanding achievements in endocrine research.

Early Investigators Workshop: given to 50 postdoctoral and clinical fellows for participation in a unique two-day workshop focused on

2013 AWARDS & ABSTRACTS DEADLINES

FUTURE LEADERS ADVANCING RESEARCH IN ENDOCRINOLOGY (FLARE)
- FLARE Workshop – January 25-26, 2013

ENDO 2013 ABSTRACT SUBMISSIONS
- Abstract Submission Deadline – January 30, 2013
- Abstract Disposition Notification – March 15, 2013
- Abstract Awards Notification – March 19, 2013

EARLY CAREER FORUM
- Travel Award Application Deadline – January 30, 2013
- Travel Award Notification Date – February 28, 2013
- Early Career Forum Open Registration – March 1, 2013
- Early Career Forum – June 14, 2013

HOW TO SECURE PROMOTION AND TENURE WORKSHOP
- Travel Award Application Deadline – January 30, 2013
- Travel Award Notification Date – February 28, 2013
- How to Secure Promotion and Tenure Workshop Open Registration – Available Now (Members); January 3, 2013 (Non-members)
- How to Secure Promotion and Tenure Workshop – June 14, 2013

RESEARCH FELLOWSHIP AWARDS
- Summer Research Fellowships Deadline – January 30, 2013
- Acromegaly Clinical Research Fellowship Award Deadline - January 30, 2013 *Supported by Pfizer, Inc.*
- Clinical Research Fellowship Award in Women's Health Deadline – January 30, 2013 *Supported by Pfizer, Inc.*
- Research Fellowship Award Notifications – March 20, 2013

EARLY INVESTIGATORS AWARDS
Supported by Pfizer, Inc.
- Application Deadline – January 30, 2013
- Award Notification Date – March 20, 2013

ENDOCRINE SELF-ASSESSMENT PROGRAM IN-TRAINING EXAM
- 2013 ESAP-ITE™ available online – April 1-30, 2013
- Registration will be available beginning January 7, 2013.

ENDO 2013
- Meeting Dates – June 15-18, 2013

research training and career development.

Future Leaders Advancing Research in Endocrinology (FLARE) Awards: provided to graduate students and postdoctoral fellows from underrepresented minority communities in the biomedical sciences to foster participation in leadership and professional development.

International Endocrine Scholars Program: presented to international scholars for participation in research training in labs of Endocrine Society members.

Medical Student Achievement Awards: presented to outstanding M.D. or D.O. students who exhibit a strong interest in endocrinology.

Minority Access Program (MAP) Summer Research and Career Development: given to undergraduates from groups underrepresented in the biomedical sciences for participation in summer research internships and career development opportunities at ENDO.

I highly encourage every early career member to look at the travel awards and fellowship opportunities available through The Endocrine Society. The spectrum of possibilities is as diverse as our membership. EN

— Kristen Vella, Ph.D.

NEWS & EVENTS

LAUREATE AWARDS – APPLY NOW

Margaret E. Wierman, M.D.
Chair, Laureate Awards Committee

As Chair of and on behalf of The Endocrine Society's Laureate Awards Committee, I am pleased to announce the launch of the Call for Nominations for the 2014 Laureate Awards. The committee will accept nominations through April 12, 2013 EST.

Each year, the Society honors endocrinologists around the world for their outstanding achievements, dedication, leadership, ground-breaking discoveries, international initiatives, and clinical care to the community. Recognition is not limited to those with established careers. These awards also recognize promising young investigators. Please join me in congratulating the 2013 Laureate Award recipients. I will have the distinct honor to present these awards at **ENDO 2013,** including the inaugural awards—International Excellence in Endocrinology and the Outstanding Clinical Practitioner Awards. Visit the Society's Web site for a list of the 2013 Laureate Award recipients.

I am delighted to announce that for the second time in two years, The Endocrine Society has developed a new Laureate Award, the Outstanding Scientific Achievement Award. This award honors members of the Society for extraordinary recent scientific accomplishments that have advanced the field of endocrinology. Nominations will be accepted for this new award beginning with this nomination cycle and will be awarded at ENDO 2014.

Our careers in the field of endocrinology are driven by our passion for science, discovery, education, and improving health worldwide. Partaking in the nomination process is among your member benefits and each of us has a responsibility to be an active participant.

When was the last time you submitted a nomination? The Laureate Awards Committee has streamlined the nomination process with an online nomination form. Resources are available on the Society's website with award criteria, answers to frequently asked questions, and a checklist for documentation. Plans are in place to further streamline the user experience.

Each of us knows someone who has advanced the field of endocrinology through their tireless research, dedication to teaching, and service. Nominations from across the Society's membership will assure that the Laureate Awards Committee will have a broad and diverse pool of candidates from which to select awardees. I hope you will join me by nominating one or more individuals for a Laureate Award. If you have questions about the Awards after reviewing the information forthcoming on the Society website, please do not hesitate to contact me. Award winners will be honored at ENDO 2014, the 96th Annual Meeting & Expo in Chicago, Illinois.

GOITER FACT SHEET AVAILABLE FROM THE HORMONE HEALTH NETWORK

While iodine deficiency is the most common cause of goiter worldwide, it is no longer commonly observed in the United States since the advent of iodized salt. More often, goiter is due to Graves' disease, Hashimoto's disease, or thyroid nodules. The Hormone Health Network's latest patient fact sheet, *Goiter,* defines this condition and describes risk factors for and potential causes of thyroid gland enlargement. While goiters are typically found during a physical exam, the fact sheet outlines other tests that may be used to confirm diagnosis, as well as available treatment options. Brief definitions and a list of suggested questions help patients have more informed conversations with their doctors. Visit *www.hormone.org* to read and download the fact sheet.

NOMINATE AN OUTSTANDING JOURNALIST

The Society is seeking nominations for the sixth-annual Award for Excellence in Science and Medical Journalism. The award recognizes reporting that is outstanding and enhances public understanding of health areas covered by the field of endocrinology.

The award is open to all credentialed print, online, and broadcast journalists. Think you or one of your colleagues qualify? Candidates may be self-nominated, or may be nominated by another person. Only one nomination is permitted for each journalist. Submissions may include any work first published between March 5, 2012, and Feb. 29, 2013.

Weight will be given to entries that contribute to the public understanding of endocrinology and reflect accurate research and

EventCALENDAR

MAR 22–23: BALTIMORE
Health Disparities Summit.
www.endo-society.org/minorityactivities/conferences.cfm

APR 10–13: INDIANAPOLIS
Association of College & Research Libraries Conference.
http://conference.acrl.org/

APR 11–13: SAN FRANCISCO
Internal Medicine 2013 (American College of Physicians).
http://im2013.acponline.org/

APR 20–24: BOSTON
Experimental Biology (FASEB).
http://experimentalbiology.org/EB/pages/default.aspx?splashpage=1

APR 27–MAY 1: COPENHAGEN
15th European Congress of Endocrinology (European Society of Endocrinology)
www.ece2013.org/

The above events are sponsored by The Endocrine Society. See more events at www.endo-society.org, on the Worldwide Endocrine Events Calendar.

reporting, and originality.

The honor includes an award to be presented at **ENDO 2013: The 95th Annual Meeting & Expo,** June 15-18, in San Francisco. The recipient will also receive complimentary travel to the meeting and hotel accommodation.

Apply at *www.endo-society.org/media/Journalism-Award.cfm.* Submissions must be received by March 2.

NEW QUARTERLY JOURNAL SERIES LAUNCHES

Translational Endocrinology & Metabolism (TEAM) is a quarterly journal series that provides an integrated and new approach to endocrinology via updates and interrelation of clinical and basic information regarding specific endocrine disorders. *TEAM* represents the collective expertise of The Endocrine Society, delivering the latest "bench to bedside" information. The newly released ***TEAM: Metabolic Surgery Update*** provides current knowledge in metabolic surgery and its impact on the treatment of severe endocrine diseases. Other topics included in the subscription include Breast Cancer, Posterior Pituitary, and coming soon, Hypoglycemia.

Subscribe now and stay on the cutting edge of this exciting intersection of basic science, clinical research, and patient care. Subscriptions include a total of four issues.

For more information on *TEAM* visit *www.endojournals.org/site/translational.*

MASTER THE BOARD CERTIFICATION PROCESS AND EVALUATE YOUR PROGRESS

Managing the Maintenance of Certification (MOC) process can be complicated. That's why The Endocrine Society created a dedicated website to address the MOC needs of endocrinologists and pediatric endocrinologists. *Endoselfassessment.org* answers questions about MOC and centralizes the Society's broad range of self-assessments designed to meet MOC Part 2 and Part 4 requirements. The site houses more than a dozen MOC Part 2 products, the new practice improvement modules (PIMs) for MOC Part 4 and ESAP™ In-Training Exam (ESAP-ITE), used by fellowship programs throughout the U.S. In addition, the site hosts a number of free self-assessment modules related to a variety of endocrine practice areas.

The website *endoselfassessment.org* has proven to be a valuable resource for learners, allowing them to quickly compare products such as ESAP™, Pediatric ESAP, and the new *Evaluation of Thyroid Nodules PIM.* The site helps users manage their engagement in the modules, tracking progress in an individualized learner dashboard. Another key feature to the site is the ability for learners to report earned MOC points directly to the ABIM and ABP, helping to reduce administrative work for busy physicians and their staff. Keep pace with the latest in MOC information and learn more about the Society's numerous MOC products by visiting *endoselfassessment.org* today.

SAVE UP TO $625 OFF ENDO 2013

Endocrine Society members: Save up to $600 off the non-member rate for **ENDO 2013** in San Francisco. If you haven't renewed your membership, or are thinking about joining the Society, be sure to do so before you register for the annual meeting to take advantage of the great savings. The early registration deadline is April 24. *www.endo-society.org/save600.* EN

In **MEMORIAM**
George S. Eisenbarth, M.D., Ph.D.; Denver; 1947–2012

JOURNALS ROUNDUP

The following studies will be published in Endocrine Society journals. Before print, they are edited and posted online, in each journal's Early Release section. You can access the journals via www.endo-society.org.

Corticotropin-releasing hormone inhibits in vitro oocyte maturation in mice; modifying patient stress levels could optimize oocyte quality for in vitro fertilization techniques.
Dinopoulou V, Partsinevelos GA, Mavrogianni D, et al. *The effect of CRH and its inhibitor, antalarmin, on in vitro growth of preantral mouse follicles, early embryo development, and steroidogenesis.*

Classical nuclear ERs and mERs play a role in hypophagia and anti-dipsia.
Santollo J, Marshall A, Daniels D. *Activation of membrane-associated estrogen receptors decreases food and water intake in ovariectomized rats.*

Insulin may prevent γ-amyloid formation and accumulation.
Pandini G, Pace V, Copani A, Squatrito S, Milardi D, Vigneri R. *Insulin has multiple anti-amyloidogenic effects on human neuronal cells.*

In postpartum PAH mice, lactation does not affect cardiac remodeling but does contribute to cardiac contractile dysfunction.
Murata K, Saito C, Ishida J, et al. *Effects of lactation on postpartum cardiac function of pregnancy-associated hypertensive mice.*

SUMO-1 both activates and suppresses PPARγ functions in adipocytes.
Mikkonen L, Hirvonen J, Jänne OA. *SUMO-1 regulates body weight and adipogenesis via PPARγ in male and female mice.*

Thyroid nodule size greater than 2 cm is associated with an increased risk of well-differentiated thyroid cancer.
Kamran SC, Marqusee E, Kim MI, et al. *Thyroid nodule size and prediction of cancer.*

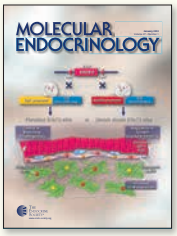
GH treatment in childhood and adolescence not only changes phenotype in youth, but also contributes to decreased comorbitites in adults in PWS.
Coupaye M, Lorenzini F, Linares CL, et al. *Growth hormone therapy for children and adolescents with Prader-Willi syndrome is associated with improved body composition and metabolic status in adulthood.*

Investigating genes involved in gonadotrope or ovarian development and function that are also expressed in the hypothalamus might help identify genes that contribute to IHH.
Abel BS, Shaw ND, Brown JM, et al. *Responsiveness to a physiologic regimen of GnRH therapy and relation to genotype in women with isolated hypogonadotropic hypogonadism.*

Induction of insulin resistance by FFAs suppresses insulin inhibition of visfatin secretion and results in the increase of visfatin, a harbinger of metabolic diseases such as type 2 diabetes, obesity, polycystic ovary syndrome, and non-alcoholic fatty liver disease.
Kowalska I, Karczewska-Kupczewska M, Adamska A, Nikolajuk A, Otziomek E, Straczkowski M. *Serum visfatin is differentially regulated by insulin and free fatty acids in healthy men.*

Depending on body type, low muscle mass is linked to different obesity-associated metabolic disorders.
Kim TN, Park MS, Yang SJ, et al. *Body size phenotypes and low muscle mass: The Korean Sarcopenic Obesity Study (KSOS).*

Older adults with persistent subclinical hypothyroidism do not have an increased risk of coronary heart disease, heart failure, or cardiovascular death.
Hyland KA, Arnold AM, Lee JS, Cappola AR. *Persistent subclinical hypothyroidism and cardiovascular risk in the elderly: The Cardiovascular Health Study.*



Autophagy may offer a new therapeutic target for AR-driven prostatic diseases.
Shi Y, Han JJ, Tennakoon JB, et al. *Androgens promote prostate cancer cell growth through the induction of autophagy.*

Another rationale for the use of mitogen-activated protein kinase inhibitors in diabetes control is provided.
Nishiki Y, Adewola A, Hatanaka M, Templin AT, Maier B, Mirmira RG. *Translational control of inducible nitric oxide synthase by p38 MAP kinase in islet β-cells.*

The histone deacetylase family may have varied functions in skeletal physiology.
Jin Z, Wei W, Dechow PC, Wan Y. *HDAC7 inhibits osteoclastogenesis by reversing RANKL-triggered β-catenin switch.*

Atypical Sertoli cell AR expression induces precocious testicular development and results in reduced adult testis size and decreased postmeiotic development.
Hazra R, Corcoran L, Robson M, et al. *Temporal role of Sertoli cell androgen receptor expression in spermatogenic development.*

CLASSIFIEDS

If you are interested in submitting classified advertising to ***Endocrine News,***
please contact Christine Whorton at endocareers@endo-society.org or 800-361-3906.

Washington Endocrinologist

Group Health Permanente, the Pacific Northwest's top-rated multi-specialty group, is currently seeking a BC/BE Endocrinologist to join our Group Practice. Group Health is dedicated to providing comprehensive, innovative, and patient-centered care to our patients. We lead the nation in EMR integration. We are looking for an additional provider to join our Endocrinologists in a stimulating setting. This provider will help to expand our Endocrinology services in the Tacoma area. The practice is exclusively outpatient consulting Endocrinology with no disabilities or hospital responsibilities. We offer generous benefits, competitive salaries, and the ability to become a shareholder in our Group Practice. Tacoma is located 20 miles south of Seattle. It is ideally situated along the saltwater banks of Puget Sound. Boasting stunning natural surroundings, you don't need to pack hiking boots to enjoy the mesmerizing outdoors. Explore the parks, gardens, and wildlife that make Tacoma a nature wonderland. The nature in Tacoma extends beyond just land. Comb the beaches of the water's edge and test the open waters in a kayak or boat. For additional information regarding this position or to submit your CV, please visit our website at *www.grouphealthphysicians.org* or contact Cayley Crotty at *crotty.c@ghc.org.*

Tennessee Endocrinologist

The Division of Endocrinology and Metabolism, Department of Medicine at the The University of Tennessee Health Science Center, Memphis, has faculty openings, academic rank based on qualification, preferred BC/BE in Endocrinology; U.S. citizenship or permanent residency; clinical experience in diabetes and metabolism research. Send letter and CV to Samuel Dagogo-Jack, MD, Chief of Endocrinology, by email at *SDJ@uthsc.edu.* The University of Tennessee is an EEO/AA Title VI/Title IX/Section 504/ADA/ADEA institution in the provision of its education and employment programs and services.

New York

Applications are invited for faculty positions in the Division of Endocrinology, Diabetes and Metabolism at SUNY Upstate Medical University in Syracuse, New York. One position will be focused primarily on patient care and teaching at our faculty group practice site (Joslin Diabetes Center, University Endocrinologists and Osteoporosis Center). We also seek physicians whose primary focus is clinical and translational research in diabetes and/or osteoporosis. Academic rank and competitive salary dependent on qualifications. Excellent benefits. The beautiful Central New York Fingerlakes region offers excellent schools, affordable housing, numerous recreational and social activities and gorgeous seasonal weather. MD/MBBS/DO, BC/BE in Endocrinology and New York State license or eligible. Please reply to: Dr. Ruth Weinstock, SUNY Upstate Medical University, Department of Medicine, Room 353 CWB, 750 East Adams Street, Syracuse, NY 13210. SUNY Upstate Medical University is an AA/EEO/ADA employer committed to excellence through diversity. Applications from women and minorities strongly encouraged.

Pennsylvania

PinnacleHealth, a multiple award winning health system located in Harrisburg, PA, capital city of the state of Pennsylvania, seeks endocrinologist to join their well respected practice consisting of two endocrinologists and four nurse practitioners. PinnacleHealth is the only hospital in Pennsylvania which has Joint Commission Gold Seal of Approval for Center of Excellence in Diabetes Care. Another outstanding component of endocrinology services is the PinnacleHealth Osteoporosis Clinic. Qualified candidates should have excellent interpersonal skills, ultrasound and biopsy expertise (can be trained with biopsy). Weekend coverage for inpatient will be I:5/6 weekends, telephone call primarily providing backup for NP. Primary goal is to increase outpatient practice. Resident rotation through the practice is possible if physician elects to participate, but not a requirement. Very competitive compensation and all pertinent benefits available to appropriate candidates as an employee of the health system. PinnacleHealth has over 600 beds in three hospitals and has the expertise of more than 800 active and courtesy physicians. It has fellowship and residency programs along with academic teaching opportunities. It has been recognized for its heart, neurosurgery, and orthopedic surgery programs and received Magnet Status for nursing excellence by the American Nurses Credentialing Center. It has many advanced technologies such as da Vinci Stm Surgical System, Aquilion ONE Computed Tomography (CGT) Scanner, Cyberknife, 3T MRI, PET CT, etc. It has experienced exceptional success with physician recruitment and retention. For additional information, interested endocrinologists should contact Malinda D. Hale, CMSR, President, Physician Options, Inc., 800-208-6088, email:*malinda@VONL.com*

INTEGRIS Health Endocrinology is Growing

We're excited about our expansion and all of the accomplishments we have achieved along the way. Join our team and become a part of the **#1 Hospital in OKC** according to U.S. News & World Report. Additionally, INTEGRIS Baptist Medical Center was the first facility in Oklahoma to achieve certification in inpatient diabetes, and the first in the nation to accomplish certification in hyperglycemic care.

Making the move to Oklahoma City means you'll enjoy a city that is truly experiencing a **renaissance** – and one that offers a low cost of living, prosperous local economy and outstanding public schools. Check out the full details on our practice and investigate what's in it for you. If it sounds like a good fit – and we're confident it will be – give us a call. We're looking forward to showing you around.

No J1 Visas Accepted • Currently Accepting Applications from H1B Visa Candidates

Practice Details:

Inpatient & outpatient consultative service

- Electronic medical record & computer order entry – clinic & hospital
- Mid-level provider support – clinic & hospital
- Diverse patient population with a plethora of endocrine pathology
- NEW state-of-the-art office/clinic with procedure & education room
- MYLab40 ultrasound machine with specialized thyroid-enhanced imaging & Power Doppler
- IV insulin & personal insulin pumps can be used on all hospital floors
- Joint Commissions certified in both inpatient diabetes & glycemic management
- Basal-bolus insulin in the hospital – no sliding scales
- Centralized education forum—referring physicians and patients throughout the community – preventative practices

Compensation Package Includes:

- Competitive salary
- Employed position
- Employment bonus
- 5 days/$5,000 CME
- Comprehensive health plan
- Excellent retirement programs
- Moving/relocation assistance
- Malpractice with tail coverage

INTEGRIS Health

For more information, contact:
Aaron Fleck • Manager, Physician Recruitment
405-945-4881 • integrisok.com/recruitment

ENDOCRINOLOGIST

Ochsner Health System

OCHSNER HEALTH SYSTEM in New Orleans is searching for a **BC/BE ENDOCRINOLOGIST to join our staff at Ochsner Baptist Medical Center**. Candidates with experience or directly from training are welcomed to apply. Areas of interest should include general endocrine disorders, diabetes, and endocrine disorders as related to pregnancy. This position is mainly outpatient based, but will serve a large Ob/Gyn group with significant inpatient consultation. Salary is competitive and commensurate with experience and training.

Ochsner Baptist Medical Center, with a deep-rooted history in Uptown New Orleans, is a fully accredited, full-service hospital staffed by more than 390 physicians. We have all private rooms, an ICU, 13 operating rooms, and a state-of-the art imaging center. We are proud to be distinguished by our excellence in specialty care and high patient satisfaction scores. Our newly renovated 24-hour full-service emergency department is staffed by a team of board-certified ER physicians.

The Ochsner Health System comprises 8 hospitals and more than 38 clinics across southeast Louisiana with over 1.5 million clinic patient visits annually. Ochsner is a major provider of graduate medical education with 23 ACGME-accredited residency and fellowship programs, including our Endocrinology Fellowship Program. Please visit our Web site at *www.ochsner.org*.

New Orleans is a cosmopolitan, historic city with a pleasant climate, unique architecture, multiple medical schools and academic centers, professional sports teams, world-class dining and cultural interests, and world-renowned live entertainment and music.

Please email CV to: *profrecruiting@ochsner.org*, Ref. # ABENDO1 or call 800-488-2240 for more information. EOE.

Sorry, no J-1 visa opportunities available.

NOW AVAILABLE FOR ADULTS WITH TYPE 2 DIABETES WHO REQUIRE INSULIN

WITH THE V-Go™, SHE'S ON THE GO

Actual size

Introducing the V-Go, an easy-to-use device providing insulin delivery that mimics the physiologic pattern found in people without diabetes.*[1]

- Simple basal-bolus insulin delivery to help control blood glucose
- No electronics, batteries, infusion sets, or programming
- Comprehensive training materials and product support

For more information, speak live 24/7 to a Valeritas Customer Care Representative at 1-866-881-1209 or visit www.go-vgo.com.

Important Risk Information: If regular adjustments or modifications to the basal rate of insulin are required in a 24-hour period, or if the amount of insulin used at meals requires adjustments of less than 2-Unit increments, use of the V-Go Disposable Insulin Delivery Device may result in hypoglycemia. The following conditions may occur during insulin therapy with the V-Go: hypoglycemia (low blood glucose) or hyperglycemia (high blood glucose). Other adverse reactions associated with V-Go use include skin irritation from the adhesive pad or infections at the infusion site. The V-Go should be removed before any magnetic resonance imaging (MRI) testing.

*If you follow the V-Go *Instructions for Patient Use*.

Reference: 1. Polonsky KS, et al. *N Engl J Med*. 1988;318:1231-1239.

valeritas

VGO™ DISPOSABLE INSULIN DELIVERY

FREEDOM TO GO

ART-288 Rev: A 7/2012