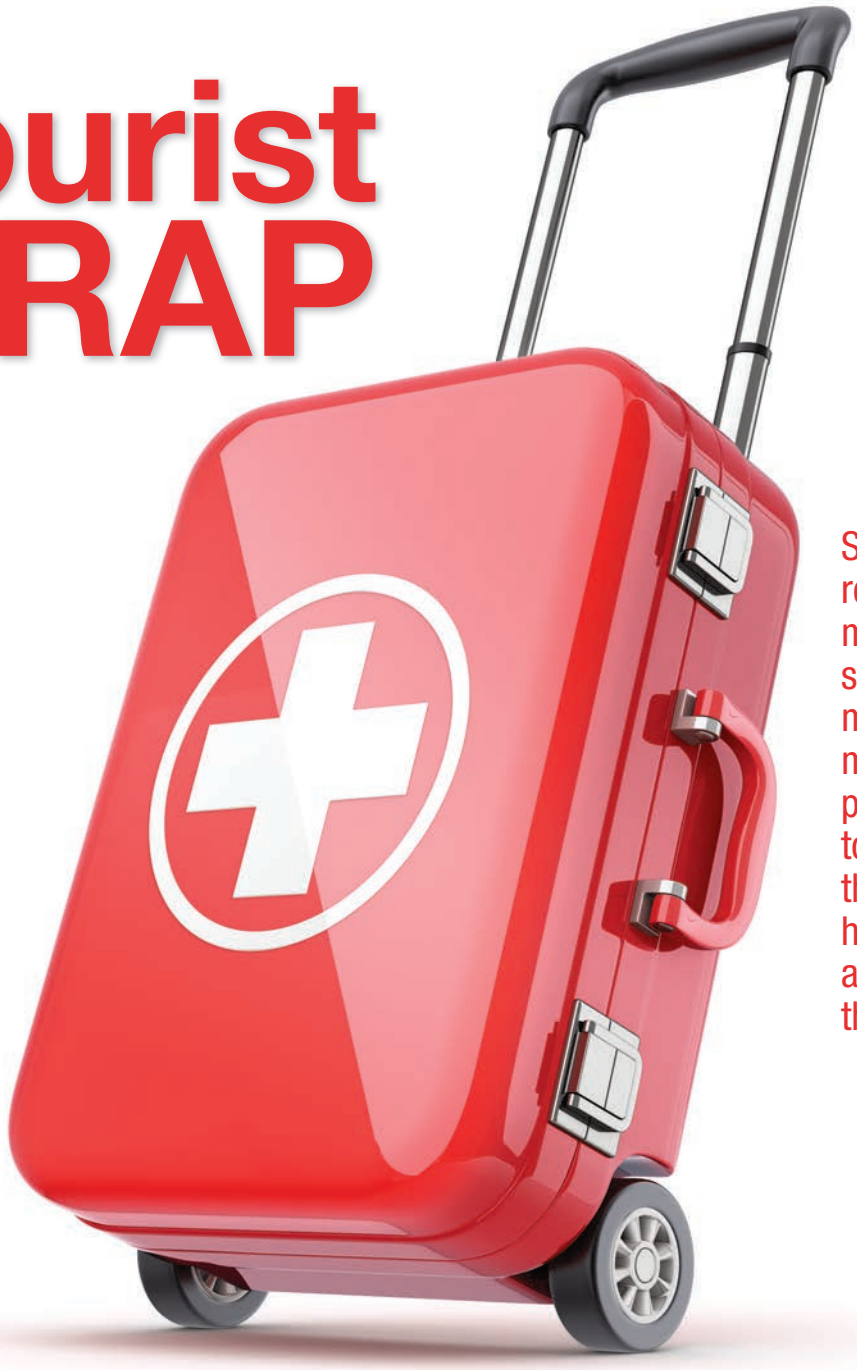
JUNE 2015

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

ENDOCRINE news™

Tourist TRAP



Sensational media reports and devious marketing have made stem cell tourism a multi-billion dollar market. Before your patients span the globe to find an elusive cure, the first step is an honest conversation about the realities of these alleged miracles.

BELLY FLOPS:
Bariatric Surgery Emergencies

FACT VS. FICTION:
The Truth About Pediatric Thyroid Cancer

ENDOCRINE SOCIETY

Wearable insulin delivery helps patients adhere to therapy and stay in control.

Type 2 can leave your patients feeling overwhelmed. But once they get their V-Go on, suddenly it clicks. V-Go provides a steady rate of insulin all day and night as well as a hassle-free and discreet way for patients to give themselves insulin at mealtimes. With just 1 application, 1 insulin, and a few simple clicks, V-Go gives your patients basal-bolus delivery they can stick with.

Find out if V-Go is right for your patients.

Call 1-855-899-4209

Visit www.vgoclickit.com

VGO®
DISPOSABLE INSULIN DELIVERY

Suddenly, it clicks

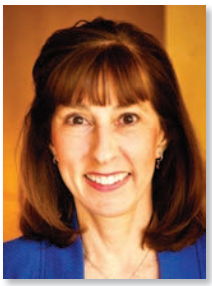
Important Risk Information: If regular adjustments or modifications to the basal rate of insulin are required in a 24-hour period, or if the amount of insulin used at meals requires adjustments of less than 2-Unit increments, use of the V-Go Disposable Insulin Delivery Device may result in hypoglycemia. The following conditions may occur during insulin therapy with 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. V-Go should be removed before any magnetic resonance imaging (MRI) testing.

valeritas

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

ENDOCRINE SOCIETY
Hormone Science to Health

Society Advocacy Makes ALL Our Voices Heard



Lisa H. Fish, MD

Many of us know the Endocrine Society best through attending meetings and reading journals, but there are other areas in which the Society works hard to meet the needs of its members. We have a very active program in advocacy, in which we reach out to policy makers to influence decisions that have relevance for our members. The Society's Advocacy and Public Outreach Core Committee (APOCC), of which I am a past member, works with our advocacy staff to set and carry out this important agenda.

Now as president, each weekend I receive what I fondly refer to as "my homework" of letters and positions to review and approve before they are sent. I am impressed by the breadth and depth of our efforts to encourage lawmakers and federal agencies to fund and support the work that our members do in research and clinical care. I want to highlight some of these advocacy efforts for you:

- **Research Funding** — Our Society is a strong and vocal advocate for increasing federal support for biomedical research. We recently conducted a Hill Day in which members of APOCC and the Research Affairs Core Committee came to Washington, D.C., and met with their congressional delegations. This was to support the funding of research, and the Society submitted testimony to the House and Senate Appropriations Committees urging Congress to fund the National Institutes of Health at $32 billion and to protect research from further funding cuts.
- **Research Affairs** — We regularly weigh in on the enactment of policies relevant to research. Recently, we provided comments to Congress on chemical safety, rules on government travel to scientific conferences, and the inclusion of female animals, tissues, and cell lines in basic research.
- **Global Advocacy & EDCs** — Our work on endocrine disrupting chemicals (EDCs) is providing us with the opportunity to expand our advocacy efforts beyond the U.S. and work with the European Union and global policy makers. This is particularly important, as 41% of our membership is international. In June, the Society will be participating in a meeting with the European Commission on developing criteria to define endocrine disruptors. This fall we will be participating in a global policy conference on chemical management to share the endocrine perspective.
- **Physician Payment** — We successfully advocated for passing legislation in April that finally repealed Medicare's flawed payment formula, the sustainable growth rate (SGR) formula. This was a prolonged and intransigent problem resulting in 17 temporary fixes over 12 years, and it was a relief for all to have a permanent solution to prevent a 21% cut in Medicare payments to doctors.
- **Coverage of Diabetes Technology** — We continue to engage with federal agencies, Capitol Hill, and private insurers to improve access for all patients to diabetes technologies.
- **Media Outreach** — We are working consistently with the media to share information about endocrine issues, provide experts for reports, and respond to breaking news.

For areas in which you have an interest or an important stake, it is vital for you to lend your voice and participate by contacting your elected representatives.

I cannot stress enough what a difference it makes to have constituents in the Congressional and Senate districts who weigh in on these issues.

Now that you have a sense of the different areas of involvement of the Endocrine Society, it is important to realize what a vital role each of our members plays in this process. For areas in which you have an interest or an important stake, it is vital for you to lend your voice and participate by contacting your elected representatives. I cannot stress enough what a difference it makes to have constituents in the Congressional and Senate districts who weigh in on these issues. When the Society sends out Advocacy Alerts, you can quickly and efficiently send a form letter to your representatives. You are welcome to edit the letter, but you don't need to, as the responses for and against each piece of legislation are tallied and influence the responses of your elected officials.

In addition, if you have a question or concern about an area of advocacy, or want to encourage input into a new area, please contact the Endocrine Society's government affairs team at ***govt-prof@endocrine.org***. EN

Lisa H. Fish, MD
President, Endocrine Society

ENDOCRINE SOCIETY

JUNE 2015

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, 2055 L Street, NW, Suite 600, Washington, DC 20036
Phone 202-971-3636 • Fax 202-736-9708
www.endocrine.org.

Print ISSN 2157-2089 Online ISSN 2157-2097

Mark A. Newman

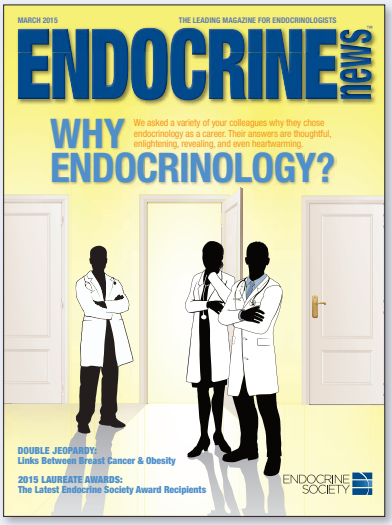
This month's cover story by associate editor Derek Bagley takes us around the world as he explores the controversial and sometimes deadly topic of stem cell tourism in "Tourist Trap" on page 12. Due to the media making such a big deal out of what seems to be "miracle cures" for certain diseases as well as a plethora of misinformation online, this phenomenon is only going to grow in popularity. According to statistics in the story, there are anywhere between 700 and 1,000 of these stem cell clinics around the world and when one gets shut down, another one opens up elsewhere. Stem cell tourism has grown from a cottage industry into a new and often nefarious niche travel market.

Kelly Horvath dives into the falsities and misinformation that are swirling around the diagnosis, treatment, and even the causes of pediatric thyroid cancer. In "Fairytales: Dispelling Pediatric Thyroid Cancer Myths" on page 20, she talks to experts who say that not only is pediatric thyroid cancer not as rare as once believed, but there are myriad opinions surrounding treatments as well. "In the pediatric population, where almost all thyroid cancers are papillary, a pediatric ENT surgeon is required because it's not a simple thyroidectomy," says James D. Sidman, MD, director, ENT and Facial Plastic Surgery, Children's Hospitals and Clinics of Minnesota, in Minneapolis. "Papillary cancer patients need to have a modified radical neck dissection to strip out all of the lymph nodes."

While it's true that bariatric surgery can be the solution to a number of problems in obese patients, it is also possible that the effects of the surgery could send the patient to the ER. In "Belly Flops: Complications of Bariatric Surgery" on page 16, Glenda Fauntleroy details these emergencies and what clinicians can do to avoid them whenever possible. Number one on that list is to make sure that the proper patients are selected for these procedures in the first place. "You can easily see that there may be patients who are not followed by physicians and who wake up one day and see themselves as being very obese and then see a magazine advertisement for some doctor who does a lot of bariatric surgery and they think it's a quick fix," says Jeffrey Mechanick, MD, clinical professor Medicine, Endocrinology, Diabetes, and Bone Disease at New York's Mount Sinai Hospital, who adds that these are the patients and the scenario at the highest risk for post-operative complications.

In case any of you are wondering when we plan the topics for 2016, the answer is: Now. So if you have any suggestions for stories you'd like to see in *Endocrine News*, I encourage you to send them my way at ***mnewman@endocrine.org***. EN

Mark A. Newman,
Editor, Endocrine News



Dear Mr. Newman,

I have read with great interest what my colleagues have written about why they chose endocrinology as a career. They basically said it all, and most of the reasons resonated well with my own take on the matter. I would like to share with you my additional personal perspective on this, if that were possible:

I was 16 years old in 1985, and I moved from Beirut, Lebanon, to Montreal, Canada, because of increasing street fighting in Beirut during the civil war.

I moved, but my menses did not move with me. I remained without a period for six months; and after an extensive work-up with an excellent endocrinologist there, her remarks were: "Eat better, and find a nice boyfriend!" In other words, she meant have a healthy lifestyle and decrease your stress level. I was fascinated that an external factor (such as moving) could affect an internal factor as intimate as my menstrual cycle. I do not think I even knew what a hormone was back then.

I later chose medical school contemplating psychiatry, but during training exposure, and being drawn to holistic approaches, I finally chose a residency in Combined Med/Peds, and Endocrinology was the natural cherry culminating it. It integrates (as my colleagues have so eloquently stated) the molecular to the clinical, and within the clinical, all body systems including behavior. External factors must also be part of history taking especially in endocrinology. Lastly, with diabetes, almost every aspect of daily life may have an impact on glycemia. As I tell medical students, in a person with diabetes, the glucose level represents an integration of all factors in their life. "Everything is blood sugar." I dare add, "Everything is endocrinology."

I thank you for the interesting topics tackled in *Endocrine News*. It is a joy to read!

Mona Nasrallah, MD, associate professor of clinical medicine, Endocrinology and Metabolism, American University of Beirut, Beirut, Lebanon

EDITOR'S RESPONSE:

Dear Dr. Nasrallah,

Thank you for sharing your story.

I must admit, I am heartened by the number of responses I've received regarding "Why Endocrinology?" in the March issue. Not only does it tell me that this type of story really speaks to the members of the Endocrine Society, it reminds me that all of us have our own stories to share about the choices we make in life.

Thanks once again for sharing your unique and heartfelt perspective.

Regards,
Mark A. Newman

By Derek Bagley

High-Altitude Residents Exhibit Lower Prevalence of **DIABETES AND OBESITY**

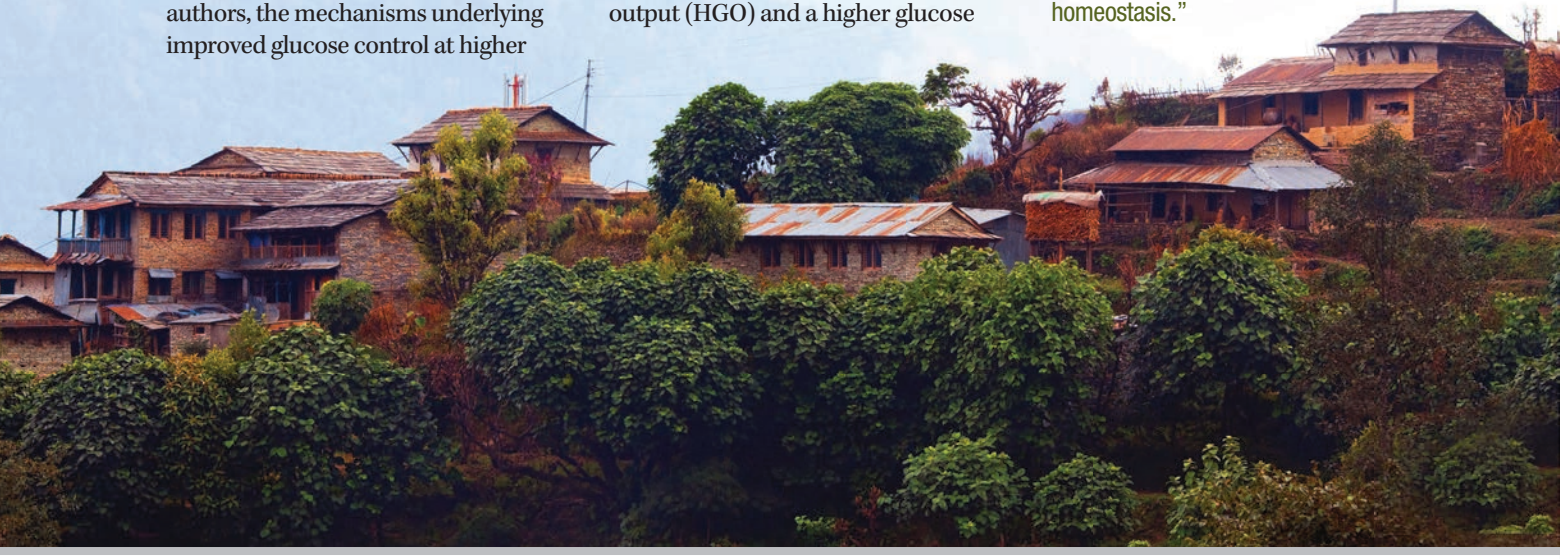
People who live at altitudes above 1,500 meters tend to have a lower fasting glycemia and better glucose tolerance compared to those who live closer to sea level, and understanding why that is could lead to new therapeutic options, according to a study recently published in *Endocrine Reviews.*

Researchers led by Orison O. Woolcott, MD, of the Diabetes and Obesity Research Institute at Cedars-Sinai Medical Center in Los Angeles, noted that about 7% of the world's population (about 440 million people) live above 1,500 meters, but there hasn't been much research on the long-term effects of living at that altitude. There is emerging evidence of the lower prevalence of both obesity and diabetes at higher altitudes, but, according to the authors, the mechanisms underlying improved glucose control at higher altitudes remain unclear.

The authors looked at the most current evidence on glucose homeostasis in residents living above 1,500 meters and reached a number of hypotheses. Insulin is unlikely to play a part. The liver may be involved since "studies showing higher glucagon levels in highlanders and reduced hepatic glycogen content in rodents chronically exposed to hypoxia suggest that the liver may play a role," they write. The gut may be implicated, but that's unclear, since most studies have focused on the short-term exposure to high altitudes.

Woolcott and colleagues hypothesized that the lower fasting glycemia in individuals living at high altitudes is determined by a lower hepatic glucose output (HGO) and a higher glucose disposal in the skeletal muscle, since "in the postabsorptive state, blood glucose supply depends primarily on the liver, whereas glucose disposal occurs primarily in the brain (~50%) and to a lesser extent in the skeletal muscle (<25%)." That widely accepted concept, along with the evidence of higher glucose disposal in vivo in highlanders and increased glucose uptake in the skeletal muscle induced by anoxia and hypoxia in vivo, helped the team reach that hypothesis.

The authors pointed out that further experimental studies could have an important clinical impact, and understanding "the mechanisms that regulate and maintain the lower fasting glycemia in individuals who live at higher altitudes could lead to new therapeutics for impaired glucose homeostasis."



Metformin Rarely Prescribed to Treat Pre-Diabetes

Low-cost metformin is effective at treating pre-diabetes, but the drug is rarely prescribed for it, according to a study recently published in the *Annals of Internal Medicine*. Metformin has been shown to prevent full-blown diabetes, but researchers found that only 3.7% of patients were prescribed metformin for their pre-diabetes over the study's three-year window.

Researchers led by Tannaz Moin, MD, assistant professor of medicine in the Division of Endocrinology at the David Geffen School of Medicine at UCLA and VA Greater Los Angeles, analyzed a national sample of 17,352 adults aged 19 through 58 with pre-diabetes. They found:

- Prevalence of metformin prescriptions was 7.8% for patients with a BMI of greater than 35 kg/m2.
- Metformin prescriptions were nearly twice as high for women (4.8%) than for men (2.8%).
- Among patients with pre-diabetes, prevalence of prescriptions for obese individuals was 6.6% vs. 3.5%

for non-obese people.

- Prescription prevalence for people with pre-diabetes and two comorbidities was 4.2% vs. 2.8% with people with no comorbidities.

The reasons for this metformin underuse are not clear, the researchers write, though lack of knowledge of the 2002 Diabetes Prevention Program (DPP) Study, which showed that both lifestyle changes and metformin use can prevent or delay progression to diabetes among those with pre-diabetes, or the fact that the drug does not have FDA approval for pre-diabetes, or reluctance by both patient and physician to "medicalize" pre-diabetes, may play into it.

"Metformin or lifestyle changes can be used to prevent diabetes, but getting people to make those changes is really difficult," Moin says in a statement. "Diabetes is prevalent, but pre-diabetes is even more prevalent and we have evidence-based therapies like metformin that are very safe and work. Metformin is rarely being used for diabetes prevention among people at risk for developing it. This is something that patients and doctors need to be talking about and thinking about."

While adopting healthier life habits can definitely curb the progression of pre-diabetes, it isn't always easy to make those changes. For instance, setting aside time for weekly classes on healthy lifestyle changes and regular exercise can be particularly challenging for people with long work hours or other commitments that eat into their time. "Taking metformin in cases like these could be a viable alternative, so patients should be educated about the potential benefits of metformin as an option for preventive treatment since it is covered by most prescription drug plans, is inexpensive, and has been shown to be very safe in long-term studies," Moin says.

Cellular Defect Linked to Diabetes

A cellular defect that can impair the body's ability to handle high glucose levels and could point the way to a potential new treatment for diabetes has been identified by Columbia University Medical Center (CUMC) researchers, according to a study recently published in the *Journal of Clinical Investigation*. The CUMC team found that ryanodine receptor type 2 (RyR2) calcium channels in insulin-producing cells play an important and previously underappreciated role in glucose balance.

RyR2 channels control intracellular calcium release. When leaky, they were found to reduce insulin release from the pancreas, resulting in high blood sugar levels in a test that measures the ability to regulate glucose. The researchers also demonstrated, in a mouse model of diabetes, that these leaks can be stopped and glucose levels normalized with an experimental drug called Rycal.

"We've known that calcium in the pancreatic beta cells plays a significant role in regulating insulin secretion, but calcium levels were thought to be controlled largely by the entry of calcium into the cell," says senior author Andrew R. Marks, MD, professor and chair of Physiology and Cellular Biophysics at CUMC. "It turns out that there's another mechanism in pancreatic beta cells that also controls calcium. This mechanism involves RyR2 channels, and leaks in these channels can lead to impaired glucose tolerance. These findings open up a whole new area of research into the molecular underpinnings of prediabetes and diabetes and point to potential therapeutic targets."

The CUMC researchers were initially studying a rare form of exercise-induced arrhythmia called catecholaminergic polymorphic ventricular tachycardia (CPVT), which can be caused by mutations in the RyR2 gene. "When we generated murine models of CPVT that harbor mutations in the RyR2 channels that make them leaky, we observed that they weren't secreting enough insulin in response to glucose," says lead author Gaetano Santulli, MD, PhD, a cardiologist at CUMC. "Since RyR2 channels are also expressed in pancreatic cells, we wondered whether they were mechanistically contributing to the glucose imbalance."

The investigators performed glucose tolerance tests on 27 CPVT patients with known mutations that make the RyR2 channels leaky. Many of these individuals exhibited reduced serum insulin levels and higher-than-normal blood sugar following a glucose challenge — a novel finding in this type of patient. "This was completely unexpected, and it suggested we were on to something important in terms of understanding diabetes," says Marks.

The researchers then turned back to the mouse models of CPVT, in an effort to determine what role, if any, RyR2s might play in impaired glucose tolerance. "Pancreatic beta cells were found to have leaky RyR2s, which were disrupting the function of mitochondria that provide cells with energy required for insulin release. The dysfunction was consistent with mitochondrial alterations that have been described in pancreatic beta cells from patients with type 2 diabetes," says Santulli.

Finally, the scientists tested the effects of Rycal (an experimental drug that Marks' team has shown can stop RyR2 leak) on CPVT mice with RyR2 mutations and on type 2 diabetic mice. The drug improved insulin secretion and glucose tolerance in both mouse models. "The advantage of Rycal is that many drugs now used to treat type 2 diabetes increase the risk for low blood sugar and for heart disease," says Marks. "Based on the mechanism of action of Rycal, we would not expect this drug to cause either of these. Also, Rycals are currently being tested in patients with heart disease and muscle disorders and have a good safety record so far."

EDCS, ALONG WITH OBESITY, Increase CVD Risk in Younger Women

Pesticide exposure has been implicated along with obesity in increased cardiovascular disease risk and inflammation in premenopausal women, according to a new study in the *Journal of Clinical Endocrinology & Metabolism.*

Researchers looked at the effects of exposure to polychlorinated pesticides such as DDT. "After the body breaks down DDT along with similar pesticides, chemical remnants called metabolites accumulate in women's fat tissue," says one of the study's authors, Diana Teixeira, a PhD student at the University of Porto in Porto, Portugal. "When higher amounts of these environmental estrogens collect in the fat tissue, it can compromise the protective effect the body's natural estrogen has on a premenopausal woman's heart health. This leaves women at increased risk of developing cardiovascular disease and inflammation."

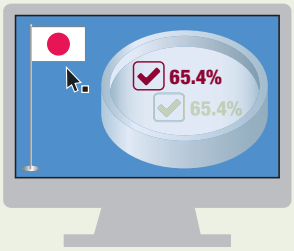
Investigators analyzed the amount of endocrine-disrupting chemicals in fat tissue and blood samples from 121 obese women who underwent bariatric surgery at S. João Hospital in Porto. Among the participants, 73 were classified as premenopausal and 48 were postmenopausal. The researchers tested the participants' fasting blood glucose and cholesterol. Using the Framingham risk score, the researchers assessed the women's 10-year risk of developing cardiovascular disease.

They found that among premenopausal women, women with higher concentrations of environmental estrogens in their visceral fat tissue from the belly were more likely to have higher average blood sugar levels. Among premenopausal women, those with higher levels of environmental estrogens in their blood tended to have more inflammation and faced a greater risk of cardiovascular disease on the Framingham scale. "Our findings show that endocrine-disrupting chemicals tend to aggravate complications of obesity, including inflammation and cardiovascular disease risk, in premenopausal women," Teixeira says. "Measuring environmental estrogen levels may help physicians identify women who are at risk of developing cardiovascular and metabolic disease so they can take preventative action."

Fast FACTS About Stem Cell Tourism

The global stem cell market is projected to reach $120 billion by 2018.

There are an estimated 700 clinics around the world offering stem cell therapies.

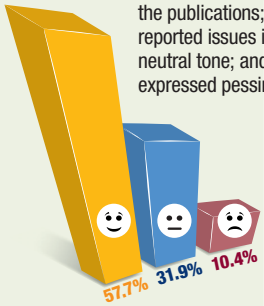


A recent online survey conducted in Japan revealed that 65.4% of the respondents believed regenerative medicine would become a reality within the next 10 years.

In 2013 alone, around 900,000 Americans traveled abroad for medical treatments.

Stem cell therapies average around $30,000 per treatment.

69% of all news reports that indicated timelines predicted that stem cell therapies will be available within 5 to 10 years or sooner, just around the corner, or in the near future.



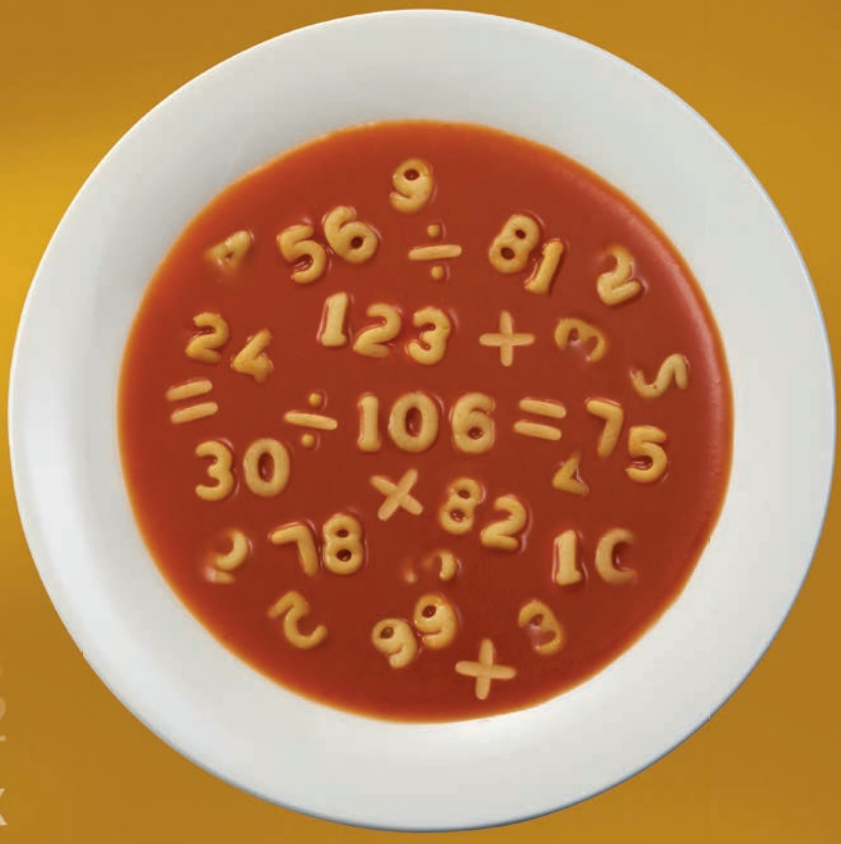
In a study of 307 newspaper articles, the overall perspective on the future of stem cell research was optimistic in 57.7% of the publications; 31.9% reported issues in a neutral tone; and 10.4% expressed pessimism.

Sources: *CellR4*, National Center for Biotechnology Information, *Canada Family Physician*, *Science Translational Medicine*

ACCU-CHEK® Aviva Expert

Roche

Now patients can enjoy the meal without worrying about the math.



Introducing the first blood glucose meter with a built-in insulin calculator.[1] The ACCU-CHEK® Aviva Expert.

- Optimized glycemic control
- Advanced accuracy
- Personalized dosing advice based on blood glucose reading, number of carbs entered, on-board insulin, and health factors like stress, illness, or exercise

Learn more by talking to your ACCU-CHEK representative or by visiting **accu-chek.com/expertEN**

Rx only

Small change. Big difference.

[1] **It's the first and only meter not part of an insulin pump system to feature an insulin calculator.**

ACCU-CHEK®

Tourist TRAP

Sensational media reports and devious marketing have made stem cell tourism a multi-billion dollar industry. Before your patients span the globe to find an elusive cure, the first step is an honest conversation about the realities of these alleged miracles.

By Derek Bagley

Cheri Deal, PhD, MD, chief of Pediatric Endocrinology at the University Teaching Hospital Ste-Justine, in Montreal, first encountered stem cell tourism when one of her patient's families wanted to seek treatment for their baby's blindness associated with septo-optic dysplasia, one of the causes of congenital hypopituitarism. In the family's desperation, they hoped to travel to Asia to "cure" the girl's blindness with stem cell treatments, and were told that this must be done as soon as possible if the therapy is to work. Deal began reaching out to other pediatric endocrinologists and to pediatric ophthalmologists to see whether others had similar requests.

"They were all Internet consumers of health information," Deal says, "and saw claims on the web that this would restore the sight of their child. When I queried other pediatric endocrinologist colleagues, many had anecdotal tales of patients elsewhere in Canada and in the U.S. doing the same."

Stem cell tourism is, unfortunately, a growing industry, with a market estimated to be in the billions, and between 700 and 1,000 clinics worldwide. The numbers are hard to pin down because these clinics are difficult to track and regulate, because it's largely an Internet-based industry. If one clinic gets shut down by a government agency that takes notice, another one will pop up to replace it, and business will continue as usual.

Last, Best Hope?

Clinics promising stem cell therapies prey on the desperate, either crippling a patient's family with an enormous financial burden (treatments cost an average of $30,000), or sometimes actually crippling the patient. The clinics providing these procedures use web advertising that does not adhere to the same ethical framework as in North America. Deal says that leads to "at the very least, thousands of dollars spent for nothing, and at the worst, complications that could culminate in prolonged hospitalizations, permanent handicaps, or death."

But patients continue to seek these treatments, because they fall victim to "scienceploitation," a term coined by Timothy Caulfield, LLM, FRSC, FCAHS, a professor and research director at the University of Alberta and a lawyer who specializes in medical ethics. According to Caulfield, it's the idea of taking genuinely exciting science and exploiting it to sell products. "It's an area that has received a huge amount of coverage in popular culture," Caulfield says. "The idea of stem cells and stem cell research — the phrase evokes 'cutting edge.' It's almost a marker of hope for the future."

Stem cell therapies have indeed permeated popular culture, with clinics marketing their product through direct-to-consumer Internet campaigns, social media, patient "testimonials" on blogs, and even through

reputable news outlets. A Google search for "stem cell treatment" turns up a number of sleek websites, all promising stem cell therapies to help with everything from cancer and diabetes to autism and aging. "Clinics can leverage that kind of popular culture coverage in order to market unproven therapies," Caulfield says.

Compounding the problem is the fact that this is a hotly contested issue, with passionate people involved, especially those desperate patients willing to travel halfway around the world in a last-ditch effort for their health or, more and more often, their child's health.

Caulfield and Amy Zarzeczny, a health law scholar at the University of Regina, wrote in a 2012 article in *Canada Family Physician* that it is "essential that physicians be sensitive to the motivations underlying the interest in stem cell tourism." So here we'll take a look at the motivations and the mindsets of patients who are ready and willing to leave it all behind, the best approach for handling these kinds of questions when they come up in your office, and what the future holds for stem cell research.

Human Interest

In 2006, Peyton Manning, then quarterback for the Indianapolis Colts, injured his neck in a game against the Washington Redskins. He continued to play without much complaint or incident until 2010 when he reinjured his neck, leaving him in pain and unable to throw the ball with as much strength and accuracy as he — and his fans — were used to. So in 2011, before undergoing neck surgery, Manning reportedly traveled to Europe for a stem cell procedure, in which a clinic took fat cells from Manning's own body and used them to regenerate nerves in his neck.

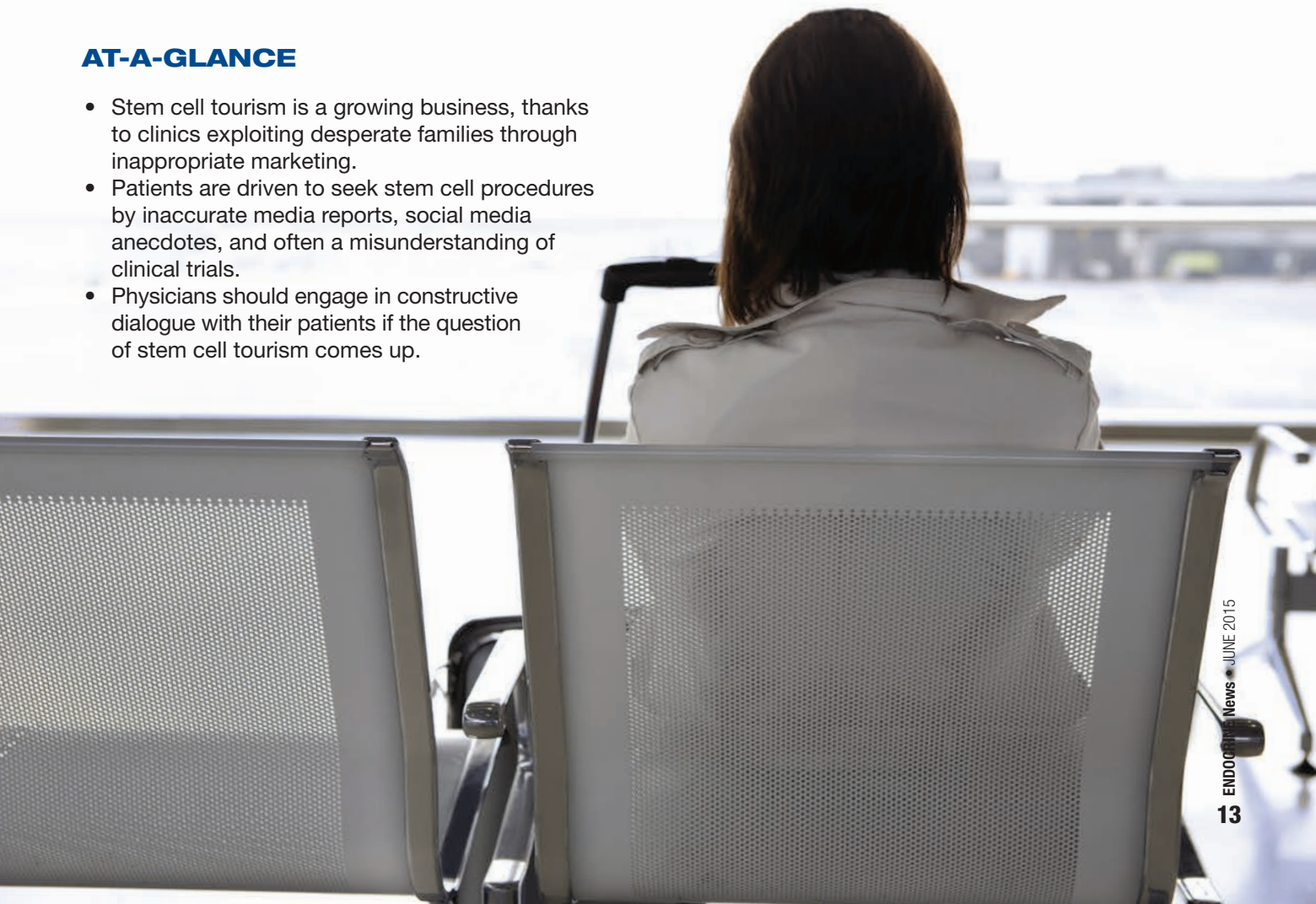
The news, of course, made headlines, and while there were a few physicians and researchers criticizing Manning's treatment, many news outlets uncritically reported the news, with some even going so far as to say the stem cell treatment saved Manning's career.

Last December, Gordie Howe, the 86-year-old hockey legend, underwent a stem cell procedure in Tijuana to treat a serious stroke. Howe was injected with neural stem cells and stem cells from bone marrow to repair brain damage and improve blood circulation. Like Manning's, Howe's alleged stem cell procedure made headlines, and again, many news outlets used words like "miracle" to describe Howe's apparent progress, with almost no negative commentary about the treatment.

These world-famous athletes then become almost spokespeople by proxy, and the efficacy of stem cell treatments becomes assumed. Caulfield says that these

AT-A-GLANCE

- Stem cell tourism is a growing business, thanks to clinics exploiting desperate families through inappropriate marketing.
- Patients are driven to seek stem cell procedures by inaccurate media reports, social media anecdotes, and often a misunderstanding of clinical trials.
- Physicians should engage in constructive dialogue with their patients if the question of stem cell tourism comes up.



kinds of stories are often reported in science-free spaces. "There's almost no critical analysis of the science or the risks or the phenomenon of stem cell tourism more broadly," he says. "They're just presented as a sports story, and the efficacy of the treatment is taken for granted.

All of these kinds of portrayals help facilitate the broader industry," Caulfield continues. "It creates this perception in popular culture, that these treatments are efficacious."

Stories like these, then, are intriguing to patients who may be considering stem cell therapies, and they give rise to other stories in newspapers and on daytime talk shows — human interest pieces on families desperate to save their child or themselves. And yet again, these stories usually are presented uncritically, out of the realm of actual science. Some newspapers even tell readers where to send money to help their stories' subjects afford their procedures. "[The stories] are often in a section of the paper — maybe even the lifestyle section — that perhaps doesn't have a tendency to be as critical or scientifically focused," Caulfield says.

Caulfield and his colleagues are now studying new media, where patient anecdotes touting stem cell treatments' efficacy appear on Twitter accounts and blogs. Research has shown that Twitter does shape public opinion, and stem cell clinics have taken notice, using Twitter to market their product. Of course, there is very little representation of risk — it's hard to fit that in 140 characters — and the Twitter feeds rely mainly on patient anecdotes to shape the narrative.

However, these patient anecdotes provide some insight into why people go to stem cell therapy clinics. These patients believe there are no side effects, or they believe it's their only and final choice, and since they're going to die anyway, they're going to die trying everything they can. These are people who think they have nothing to lose, or have lost faith in their own medical systems. Caulfield says they feel as though they're pioneers and they're being forced to seek treatment in other countries because their own has abandoned them. They also tend to believe that some kind of FDA bureaucracy or Big Pharma conspiracy is what's keeping stem cell treatments out of countries like Canada, the U.S., and the United Kingdom.

"The potential could transform modern medicine as we now know it. **Right now there appears every chance of successfully developing techniques to allow repair/replacement of human tissues and organs beyond our imagination just a few years ago."**

— Terry Davies, MD, Icahn School of Medicine, Mount Sinai Hospital, New York, N.Y.

Clinical Trial and Error

Desperation plus the media's promise of a "stem cell revolution" can certainly drive a person to seek out these therapies in faraway places. Patients also tend to view clinical trials as a regulatory necessity to get these treatments approved, as opposed to an important clinical translation step to make sure these treatments actually work. "So often when you do a good clinical trial it turns out it doesn't work," Caulfield says. "And that's almost, in fact, the norm."

Terry Davies, MD, of the Icahn School of Medicine at Mount Sinai in New York, who is currently studying human thyroid stem cell replacement, agrees. "The concept of a clinical trial is vague in the public mind," he says. "The idea that such a study *might* work is enough to propel the desperate. The fact that most such trials actually fail is not always discussed. In addition, the fact that such a trial may have worked in animals does not mean it will work in humans."

Deal says that stem cell researchers are in a difficult position, because they have to "hype" their work in order to draw public interest to continue research support. "The down side, however," she says, "is sometimes an unwarranted optimism that the patients interpret to mean that doctors can now cure anything with stem cells."

Davies says another problem when researchers "hype" their work is that private wealthy entrepreneurial donors descend, hoping that their money will influence the work and buy some sort of cure. "I don't believe that hyping research is good for anyone," he says. "Certainly we have seen the hype with islet stem cells for use in diabetes patients for quite some years but clinical trials are still far off. Of course, the more common the disease under discussion the more likely the media will be interested and allow the researchers to stretch their observations. Such talk can attract nontraditional research funding and has been seen over and over again to often be misguided."

However, Davies points out that going through the proper channels tends to produce good results. "There is good evidence that awards made on the basis of peer review (such as NIH grants and VA grants) correlate well with productivity, publications, and patent applications, and I doubt that peers are susceptible to such hype," he says.

Of course, the *potential* for stem cell therapies remains huge. "The potential could transform modern medicine as we now know it," Davies says. "Right now there appears every chance of successfully developing techniques to allow repair/replacement of human tissues and organs which was beyond our imagination just a few years ago."

He points to the fact that physicians already use bone marrow stem cell transplantation routinely in their medical practice, saying that it is "highly likely that stem cell biology will also become an important part of medical practice allowing recovery from trauma and diseases of the nervous system, the liver, the pancreas, and the thyroid to name just a few."

But the progress made in these areas will be slow. And until valid data — controlled trials with full data transparency — showing the efficacy of stem cell procedures is presented, Davies says there is "no place for stem cell tourism in the real world."

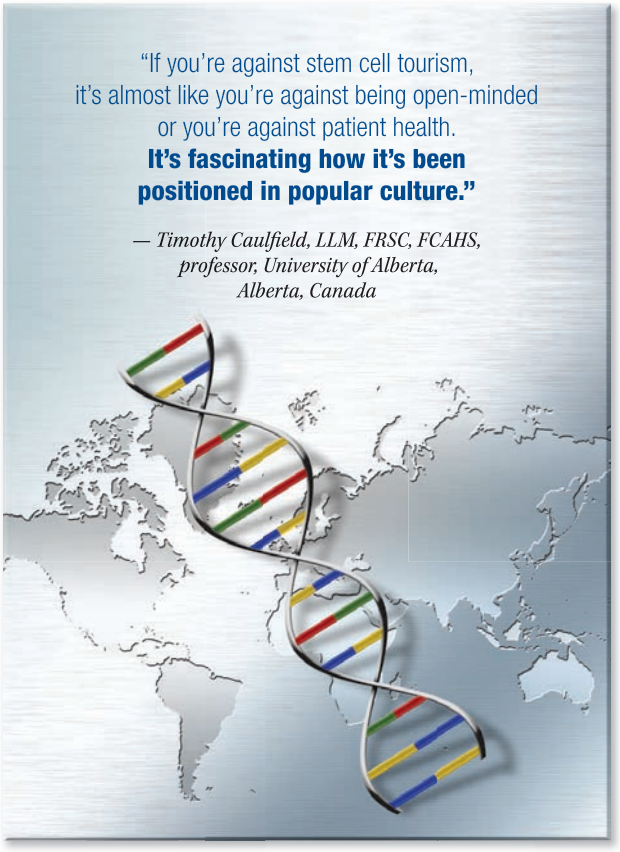
Balancing Act

Stem cell treatments are very expensive, so patients do talk to their doctors about stem cell treatments before packing up and heading out. It can be tempting to be dismissive of their questions. Taking a condescending tone or being overly negative when trying to dissuade a patient from risking so much can seriously harm the doctor/patient relationship. Appeals to reason can be met with bitter defensiveness. On the other hand, according to Caulfield, research has shown that if a physician takes a neutral approach or says "I don't know," patients will take that as an endorsement. So it then becomes a delicate balancing act when responding to their questions.

Indeed, doctors play an important role in this context, so it's crucial for them to think about ways to constructively engage with their patients when these questions arise. "Physician/patient discussions are one of the most effective tools that we can use to curb this phenomenon in a constructive way," Caulfield says.

The best way for physicians to engage with their patients in a positive way is to communicate some basic truths to them, which can be very persuasive. "For [doctors] just to be able to provide patients with the tools to investigate in a more critical manner is valuable," Caulfield says. "Ensuring that physicians have resources that they can point patients to is helpful because then they're just trying to give the patients the tools and support that they need to make an informed decision." For instance, doctors can refer their patients to the International Society for Stem Cell Research's *Patient Handbook on Stem Cell Therapies,* or even Caulfield's own numerous publications. Patients also need to understand what constitutes a clinical trial, and whether any potential therapy they are exploring has been adequately investigated in a well-run, statistically relevant clinical trial that has been published in a peer-reviewed journal.

In fact, Deal was able to point patients to Caulfield's work to dissuade the family of her young patient from traveling to Asia for treatment of her septo-optic dysplasia-associated blindness. However, Deal noted that a child of another family who had received stem cell therapy for a similar condition prior to Deal's discussions with her patient's family developed ataxia; the family is convinced the stem cell treatment is responsible.



Hope for the Future

Still, web-based, direct-to-consumer marketing is rampant, and the promises made on these websites are not accurate, because there is very little oversight. The only regulatory tools that exist are largely complaint-driven, so they do little to keep these clinics and websites in check. Caulfield says he'd like to see regulatory agencies be more aggressive with these clinics and websites that they have jurisdiction over.

But that may be a hard fight yet. Stem cell tourism has reached the status of complementary and alternative medicine in the minds of many patients. "If you're against stem cell tourism, it's almost like you're against being open-minded or you're against patient health," Caulfield says. "It's fascinating how it's been positioned in popular culture."

Ultimately, stem cell tourism, its marketing techniques, and its "scienceploitiation," hurt legitimate stem cell research by creating patient expectations and confusing the regulatory process. "It confuses even the research agenda," Caulfield says. "All this inappropriate marketing is bad for the good stuff." EN

— Bagley is the associate editor of Endocrine News. *He wrote about the highlights of ENDO 2015 in the May issue.*

Belly Flops: BARIATRIC SURGERY COMPLICATIONS

While bariatric surgery has been shown to improve a number of metabolic conditions, some patients experience negative outcomes. Educating both the clinician and the patient is vital, as is lifelong follow-up.

By Glenda Fauntleroy

Nearly 35% of adults — about 78 million people — in the U.S. are obese. Of that number, approximately 11 million have a body mass index of 40 or higher, which makes them a candidate for weight loss surgery.

However, only a very small percentage of the extremely obese turn to bariatric surgery as treatment. For those who do have the surgery, it has shown to improve or resolve many obesity-related conditions including type 2 diabetes, high blood pressure, obstructive sleep apnea, and heart disease.

For some patients, the outcomes are not as successful. Post-surgical complications can arise creating several acute health emergencies. The most common are diarrhea and dumping syndrome, hypoglycemia, bone loss, and vitamin deficiencies.

The Endocrine Society's recently published *Endocrine and Metabolic Medical Emergencies* devotes a chapter to the topic and reports that these emergencies can occur after each of the three types of bariatric procedures: Roux-en-Y gastric bypass, laparoscopic adjustable gastric banding, and laparoscopic sleeve banding.

The chapter's authors call for awareness of these complications by both the treating clinicians and the patients who are considering surgery. "With bariatric surgery, the main challenge to being able to make these safe and effective procedures, is, number one, proper patient selection," says co-author Jeffrey Mechanick, MD, clinical professor Medicine, Endocrinology,

AT-A-GLANCE

- For some bariatric surgery patients, several acute health emergencies can occur, including diarrhea and dumping syndrome, hypoglycemia, bone loss, and vitamin deficiencies.
- With bariatric surgery, the main challenge to being able to make these safe and effective procedures, is proper patient selection.
- The risk of acute health emergencies remains high, necessitating lifelong follow-up.

Diabetes and Bone Disease at New York's Mount Sinai Hospital.

"You can easily see that there may be patients who are not followed by physicians and who wake up one day and see themselves as being very obese and then see a magazine advertisement for some doctor who does a lot of bariatric surgery and they think it's a quick fix," Mechanick adds. "So they call the doctor, travel to another state, and they have the procedure. It may be just one doctor in one clinic, they may or may not be accredited, and then [patients] go back home where nobody really has the expertise to follow them."

Mechanick says these are the patients and the scenario that's at highest risk for post-operative complications.

John Morton, MD, president of the American Society for Metabolic & Bariatric Surgery (ASMBS), differs and says that while the scenario of patients flying to out-of-town clinics occasionally occurred in the past because the surgeries weren't often covered by insurance, things are different now.

"Bariatric surgery is pretty routinely covered by insurers, and as a result the insurers actually insist that patients come to accredited centers," Morton says. "It's a requirement."

Morton, who has performed more than 2,000 bariatric procedures, says the overall message of ASMBS is that bariatric surgery is both safe and effective.

"The national 30-day mortality rates at this point are 0.1%, which makes it as safe as removal of the gallbladder or hip or knee replacement," he explains.

"That being said, there are potential opportunities for complications after surgery. I think the one thing that we all agree upon is that these patients are unique patients and deserve specialized care, and that specialized care is delivered in an accredited center."

"With bariatric surgery, **the main challenge to being able to make these safe and effective procedures, is, number one, proper patient selection.**"

— Jeffrey Mechanick, MD, clinical professor, Medicine, Endocrinology, Diabetes and Bone Disease, Mount Sinai Hospital, New York

Emergencies, Post-Op

Diarrhea and Dumping. About 10%–15% of patients experience fecal incontinence following bariatric surgery, according to the book chapter. The diarrhea and dumping syndrome is often accompanied by symptoms of abdominal pain and cramping, nausea, flushing, and light-headedness.

Hypoglycemia. Postprandial hypoglycemia may also develop but without any related abdominal pain or nausea. These rare hypoglycemia events can be severe, reports the chapter, with patients having blood glucose levels of 15–40 mg/dL.

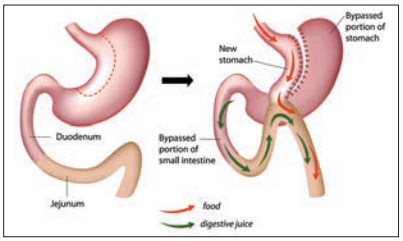
"What we find is that sometimes patients aren't hungry, which is an effect of the surgery where the hunger hormones, ghrelin, is actually decreased substantially after surgery," Morton explains. "As a result, patients don't feel hungry and sometimes skip meals. It's important to know that if they skip meals that can lead to hypoglycemia."

Bone fractures. Bariatric surgery increases the risk of a fracture by twofold, according to a 2014 study in *Osteoporosis International*. The study evaluated 258 patients — 90% of whom had a first gastric bypass at the Mayo Clinic. The average time to first fracture was around two to three years, says the study's co-author Kurt Kennel, MD, of the Division of Endocrinology, Metabolism and Nutrition at the Mayo Clinic.

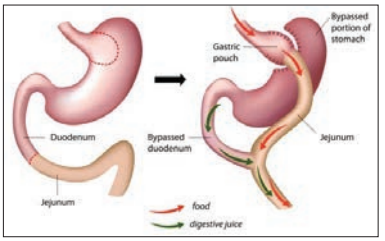
"We were more concerned that because fractures occur quite a few years after the surgery, providers would not recognize the potential connection," he says. "Still, a fracture at any point in time could be disruptive."

Kennel believes providers should consider the

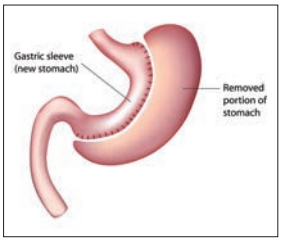
Mini Gastric Bypass



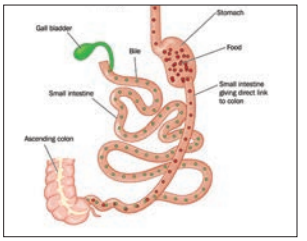
Roux-en-Y Gastric Bypass



Vertical Sleeve Gastronomy



Duodenal Switch



potential for bariatric surgery to have an adverse effect on bone when the patient already has established osteoporosis or, perhaps, in menopausal women with multiple risk factors for osteoporosis. "In such patients, providers want to make sure that patient is already receiving evidence-based osteoporosis screening and management prior to bariatric surgery," he says.

Vitamin deficiencies. Nearly a quarter of patients who had restrictive procedures will develop a vitamin deficiency, says Kimberly Gudzune, MD, assistant professor at Johns Hopkins University School of Medicine. Gudzune authored a 2013 study in *Obesity Surgery* that found although vitamin deficiencies are common after bariatric surgery, they vary by the type of surgery performed.

"Patients who undergo gastric bypass or a malabsorptive surgery like a duodenal switch are more likely to have vitamin deficiencies than patients who have a restrictive procedure such as adjustable gastric banding," she says.

Gudzune says that once a vitamin deficiency is identified, dietary change alone is not usually sufficient to correct the deficiency.

"Most patients need to be on vitamin supplements for the rest of their lives, so we need to make sure that patients continue to receive adequate nutrition and supplementation in order to avoid complications of severe vitamin deficiencies," she explains.

The Need for Lifelong Care

Mechanick's chapter ends with, "the risk of these conditions remains high, necessitating lifelong follow-up." He doesn't specify, however, who should provide the lifelong care or how frequent it should occur.

"We clearly avoid any kind of turf or political issues by stipulating who is providing that lifelong follow-up, but you can easily see that if it's somebody who is complicated and has a lot of nutritional problems, then a physician with expertise in nutrition," Mechanick explains. "If it's somebody with hormonal or endocrine problems, an endocrinologist. And in all those cases, it can still even be a knowledgeable internist or general practitioner."

Morton says the ASMBS is a big believer in follow-up. "Our policy has always been that patients should be followed-up in that bariatric surgery center," he explains. "The usual routine is most surgeons will see their patients at two weeks, three months, six months, and one year and then, every year annually."

"Most surgeons like to see patients annually because there may be surgery-specific questions that come up, but all of us try to work very closely with their referring doctors in making sure they get good coordinated care," Morton says.

"There are potential opportunities for complications after surgery. I think the one thing that we all agree upon is that these **patients are unique patients and deserve specialized care, and that specialized care is delivered in an accredited center."**

— John Morton, MD, president, American Society for Metabolic & Bariatric Surgery

Coordinating Efforts

There's a growing effort to make obesity treatment such as bariatric surgery more available to this country's extremely obese. Last year, the ASMBS sponsored the Obesity Summit where about 26 different medical societies came together to discuss how best to educate patients, provide care, and coordinate that care.

"There's still a lot of reluctance around referring physicians to even discuss bariatric surgery because they don't feel equipped about how to talk to patients about obesity treatment options," Morton says. "So, I think that's still a big thing that they have to overcome, but working together we can do it."

This year's Obesity Summit will be held September 18–19 in Chicago. EN

— Fauntleroy is a freelance writer based in Carmel, Ind., and a regular contributor to Endocrine News. *She wrote about diabetes and dietary supplements in the April issue.*

REGISTER NOW

SEPTEMBER 8-12, 2015

CLINICAL ENDOCRINOLOGY UPDATE 2015

ENDOCRINE BOARD REVIEW

INTERCONTINENTAL MIAMI HOTEL MIAMI, FL

ENDOCRINE BOARD REVIEW

SEPTEMBER 8-9, 2015

CLINICAL ENDOCRINOLOGY UPDATE

SEPTEMBER 10-12, 2015

ENDOCRINE.ORG/MIAMI

ENDOCRINE SOCIETY

FAIRYTALES: Dispelling Pediatric Thyroid Cancer Myths

Misrepresentations surround the occurrence, causes, and treatment of thyroid cancer in the pediatric patient population. It's not as "rare" as once thought, and despite its treatability, there is still a ways to go in separating fact from fiction.

By Kelly Horvath

The mantra in recent years in the world of pediatric thyroid nodules has been that although nodules occur more rarely than in the adult population, they are more likely to be malignant. However, only half of that statement has proven true. Pediatric thyroid nodules do have a fivefold increased risk of malignancy, but, just as with adult nodules, the incidence of thyroid nodules and thyroid cancer is increasing. In "Cancer Incidence Rates and Trends among Children and Adolescents in the United States, 2001–2009," published in *Pediatrics*, study authors analyzed data from the National Program of Cancer Registries and Surveillance, Epidemiology, and End Results to confirm this increase. They suggest several possible causes, including environmental factors such as certain toxins or radiation exposure, but a definitive cause has not been identified.

Not So Rare

"Pediatricians and endocrinologists are seeing more cases of differentiated thyroid cancer, papillary in particular — more frequently than for what 'rare' would be a fair description," says Andrew J. Bauer, MD, FAAP, medical director of the Thyroid Center at the Children's Hospital of Philadelphia (CHOP), and associate professor, Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania. "Although some of this increase can likely be attributed to incidental findings on head and neck imaging, Bauer says much of it really is an increased incidence, and not just of subclinical lesions. "To compare it to a cancer that most people know about, papillary thyroid cancer has roughly the same incidence as non-Hodgkin lymphoma in the U.S. adolescent population, with an estimated incidence of 18 to 20 per million."

AT-A-GLANCE

- Thyroid cancer incidence increased among the overall U. S. pediatric population from 2001–2009, particularly among adolescents ages 15–19 years, at an annual percentage change rate of 4.9 per million.
- Roughly 25% of pediatric thyroid nodules are likely to be malignant, compared to 5%–10% of adult thyroid nodules.
- Children with thyroid cancer suffer significant emotional stress in coping with their disease, despite its "treatability."

Other Myths

Being very rare is not the only long-held belief about pediatric thyroid cancer that does not hold up under the microscope. Bauer co-chaired a task force that included 14 experts from seven countries and was sponsored by the American Thyroid Association (ATA) to author the first "Guidelines on the Evaluation and Management of Thyroid Nodules and Differentiated Thyroid Cancer in Children and Adolescents", which was just published in April. Seeking treatment at a center experienced in pediatric thyroid cancer is a key recommendation. "It's extremely treatable, but it is a cancer, so it still needs to be approached thoughtfully. Patients need to see physicians who understand how to stratify treatment," Bauer says. He urges primary care physicians who find pediatric nodules to refer the patient to an endocrinologist. "The endocrinologist should be the gatekeeper and will look at the ultrasound to determine whether a fine needle aspiration biopsy is necessary. We're trying to educate pediatricians and family physicians not to skip this important step in the evaluation process."

"Pediatricians and endocrinologists are seeing more cases of differentiated thyroid cancer, papillary in particular — more frequently than for what 'rare' would be a fair description."

— Andrew J. Bauer, MD, FAAP, medical director, Thyroid Center at the Children's Hospital of Philadelphia, and associate professor, Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania

Given the increased risk of malignancy in pediatric thyroid nodules, performing a biopsy might seem like a waste of time and money. "But that's not the best approach," Bauer says. "Not all nodules need biopsy, and not all nodules need surgery." Fine needle aspiration (FNA) is a low-risk procedure, whereas thyroid surgery carries a significant risk of long-term complications. Forgoing FNA might save money in the short term, but doing what might have been an unnecessary surgery and causing hypoparathyroidism or damage to the recurrent laryngeal nerve is hardly cost-effective. Moreover, the patient's quality of life may be significantly impaired. "A biopsy will provide the information you need to make the right decision as far as continuing to watch with ultrasound or moving to surgery, as well as optimizing and individualizing the extent of surgery," Bauer says.

James D. Sidman, MD, director of ENT and Facial Plastic Surgery at the Children's Hospitals and Clinics of Minnesota, and professor of Otolaryngology and Pediatrics at the University of Minnesota Medical School, agrees that a careful physical evaluation and management process is critical. "Don't jump to a CAT scan," he urges, "because the contrast can delay treatment. By far and away, the most frequent type of cancer we see is papillary carcinoma, which responds well to treatment and has a 95% – 100% remission rate when treated first by surgery and then by radioactive iodine therapy. The response should be, do an ultrasound." He also agrees that much of the time FNA is in order. "But it can be controversial," he says. "Some argue that putting a child

"In the pediatric population, where almost all thyroid cancers are papillary, a pediatric ENT surgeon may be required because it's not a simple thyroidectomy. **Papillary cancer patients may need to have a modified radical neck dissection to strip out all of the lymph nodes."**

— James D. Sidman, MD, director, ENT and Facial Plastic Surgery, Children's Hospitals and Clinics of Minnesota; professor of Otolaryngology and Pediatrics, University of Minnesota Medical School, Minneapolis

through the sedation necessary for FNA is futile if the nodule is, say, a 2-cm solid nodule by ultrasound and would probably be removed anyway."

Sidman also cautions physicians to have a high index of suspicion for the multiple endocrine neoplasia syndromes, which he sees about once a year. "If a child tests positive for the RET proto-oncogene, that patient might need to have a total thyroidectomy — you might not be able to do watchful waiting with that patient." According to Bauer, the decision should be based on what the specific mutation is as well as the family history, referring to the recently updated ATA guidelines is the best place to start.

Sidman and Bauer agree saying that referral to the appropriate surgeon with plenty of material experience is key because a pediatric thyroidectomy is quite different from an adult thyroidectomy. "In the pediatric population, where almost all thyroid cancers are papillary, a pediatric ENT surgeon MAY BE required because it's not a simple thyroidectomy," Sidman says. "Papillary cancer patients MAY need to have a modified radical neck dissection to strip out all of the lymph nodes." Bauer says the surgery should carry less than a 3% to 5% risk for serious complications, which requires a surgeon who performs 30 or more surgeries a year.

Opportunities to Improve Approach to Care

A hot topic gaining traction in pediatric thyroid cancer is molecular evaluation. "A biopsy is not always either benign or malignant, cancer or not cancer," Bauer explains. "The reality is, about 25% of people fall into this gray zone in which you don't have normal-looking cells but you don't have cells that are clearly cancerous. In that case, we don't know what the right surgery is, because if it's benign, you didn't need surgery, and if it's malignant, you needed a total thyroidectomy and not a lobectomy." Researchers have been finding adjunct ways of looking at the biopsy in adults, such as specific gene expression classifier panels or oncogene panels that test for RET/PRC rearrangements and RAS or BRAF mutations, molecular alterations that predict whether that gray-zone biopsy is more likely to be benign or to be cancer and how the patient might respond to treatment. "We're just starting to explore these tests in pediatrics, and we need more research to figure out how to use them with kids," Bauer says, who presented an abstract on this topic at the ATA annual meeting in October 2014.

Another important new topic concern is quality of life for children and adolescents diagnosed with thyroid cancer. "People tend to say things like, 'If you're going to have cancer, thyroid cancer is the one to have because it's so treatable,' and patients hate that," Bauer says. According to an abstract that he will co-present at the American Academy of Pediatrics in October 2015, kids shoulder the same posttraumatic stress burden with thyroid cancer as with, for example, Hodgkin lymphoma. "It's good to say it's very treatable, but don't dismiss it. It's not really true that anyone is lucky to have thyroid cancer," he says. "That it's treatable is a nice place to start, but that's not the end of the story. The question is, what can we do to take better care of these patients, to individualize their treatment, and to maintain this excellent outcome? To dismiss thyroid cancer because it is very treatable isn't fair to the patient." EN

— Horvath is a freelance writer based in Baltimore, Md. She wrote about the link between obesity and breast cancer in the March issue.

NOW AVAILABLE

Toujeo®

insulin glargine 300U/mL

SANOFI

US.GLT.15.01.133

Q&A

When Bad Fat Goes GOOD

Endocrine News talks to Philip Kern, MD, at the University of Kentucky about the phenomenon of "beige" fat and what it means for the future of obesity research.

By Melissa Mapes

Heat usually melts fat — like butter in a sunbeam — but in mammals, cold may actually burn off adipose tissue. For "brown fat," this is no surprise. Brown fat exists mostly in infants and mammals that live in low-temperature environments, working as an efficient heat source for the body. Unfortunately, adult humans are generally covered in "white fat," which until now was thought to be of little use aside from a cushion.

Philip Kern, MD, professor at the University of Kentucky and director of the Barnstable Brown Diabetes and Obesity Center, discovered that white fat can turn "beige" when exposed to cold. Interestingly, obese subjects demonstrated far less "beiging" in their adipose samples than subjects at a healthy weight.

Kern spoke to *Endocrine News* about his findings and described the techniques used in fat-testing experiments.

***Endocrine News*: What are the main differences between white, beige, and brown fats?**

Phillip Kern: All mammals have the ability to fight off cold exposure to varying degrees. When a bear is storing up fat for the winter, a lot of that is brown fat because it has to generate heat to stay warm in its cave. Brown fat has a lot of mitochondria, which normally generate ATP, but "uncoupling protein" allows the mitochondria to dissipate the energy in the fat and provide warmth.

Humans evolved to survive as hunter-gatherers. A newborn baby has to be able to stay warm, so babies have substantial amounts of brown fat located around the neck and between the scapula and central back. This has been known for a long time.

In addition to brown fat, we discovered that our white fat has the ability to not become brown exactly, but become something in-between. That's why it's called beige.

The subcutaneous white fat that surrounds our bodies actually can turn on some of the same genes that are found in brown fat. When it does, it causes our white fat to also dissipate energy as heat. It doesn't become as active as the brown fat. Brown fat is like a thermogenic machine.

Adults have some brown fat, but not much — maybe 10 or 15 grams — whereas we probably have 20 – 50 kilos or more of white fat. So if we can turn on our thermogenic machinery in our white fat, even to a small extent, it could potentially be very significant in terms of burning up calories.

EN: What other methods are used to test this cold exposure process?

PK: If I were to take an average adult right now and do a PET-CT scan, which is a clinical scan that will identify brown fat, chances are that I would not find any. However, if I then chilled this person, which has been done in a variety of ways, and repeated the PET-CT scan, some of the brown fat would probably come out. To chill the core body, researchers have performed experiments where they wrap participants in a vest and circulate ice water through it.

What I did, firstly, was take fat biopsies from regular people in the summer versus the winter — just abdominal subcutaneous fat. And I found that the genes involved in beiging, that cause thermogenesis, were about fourfold higher in the winter.

The increase in these thermogenic genes was not present or was minimally present in obese subjects,

CRYOTHERAPY: Weird fad or weight-loss miracle?

Cryotherapy spas are springing up in cities across the nation, claiming weight loss, reduced symptoms of arthritis, and other health benefits. Patrons stand in a big box cooled to -130 degrees Fahrenheit for three minutes — keeping only their heads out of the container.

Several cryotherapy companies called Kern to ask, "Do you think stepping into these machines a couple times a week would stimulate beige adipose tissue?" He responded, "It probably would!"

However, he went on to say that, "So would shoveling snow in Green Bay. And so would chasing polar bears in Alaska on the ice flows."

Kern does believe that beige fat has therapeutic potential but does not think there is enough evidence to fully support cryotherapy claims.

suggesting that as people become obese, they may lose this ability to beige.

We also gathered some volunteers and took a fat biopsy on the anterior thigh on one leg. Then we put an ice pack on the other leg and took a biopsy four hours after. We saw the same thing. An acute exposure [to cold] caused an increase in the beiging genes.

EN: Can beige fat turn back into white fat after the cold exposure passes?

PK: Yes. First of all, we need to know a lot more about this, but we believe that our white fat cells have certain plasticity to them. If there is a stimulus, like cold exposure, then many of these white fat cells can become beige. But if cold exposure passes, they can then go back to white again. So it is really a bidirectional pathway depending on the stimulus.

EN: What are the next stages of research?

PK: I want to better understand the role of the immune system in this process. I mentioned that obese subjects do not seem to beige up their white fat as well. I think one of the reasons is because obese subjects tend to have more inflammation — including inflammation in their fat tissue. I think that there's an inhibitory effect of this chronic inflammation on the beiging process.

There is evidence in the literature that the immune system is important in beiging. Now, most of this has been done in mice, but there is a suggestion that a cold stimulus seems to trigger a variety of inflammatory cytokines, which actually stimulate the beiging process.

So you have this conundrum. On the one hand, you have this evidence that inflammation inhibits beiging, but then on the other hand you have evidence from a different angle that suggests it is an important part of it.

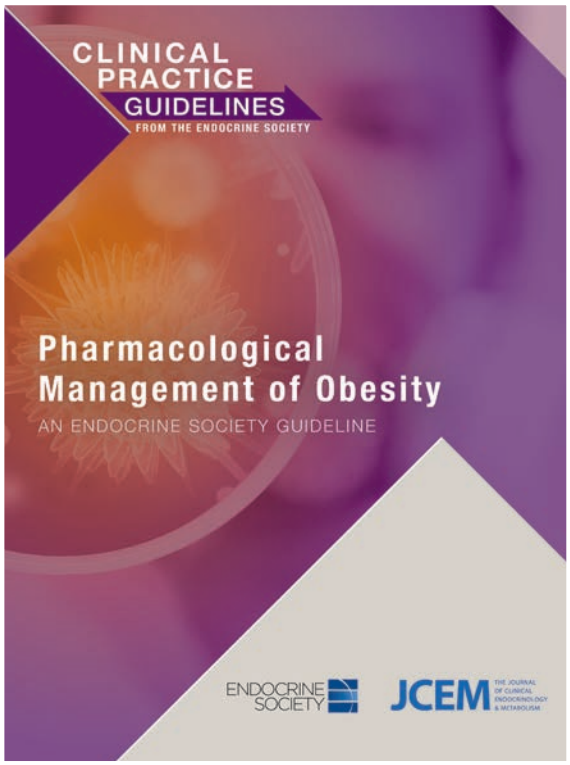
It probably depends on what kind of inflammation. Inflammation can be bad, or it can actually be part of a natural process. I think that is the key thing to try to figure out right now. EN

— Mapes is a Washington, D.C–based freelance writer and a regular contributor to Endocrine News. *She wrote about the artificial pancreas in pediatric patients in the May issue.*

OnPOINT from the Endocrine Society

Pheochromocytoma and Paraganglioma: Kern's study can be found in the December 2014 issue of *The Journal of Clinical Endocrinology & Metabolism,* titled "The Effects of Temperature and Seasons on Subcutaneous White Adipose Tissue in Humans: Evidence for Thermogenic Gene Induction."

CLINICAL PRACTICE GUIDELINES
FROM THE ENDOCRINE SOCIETY



A NEW STANDARD FOR CARE

The Pharmacological Management of Obesity

THE LATEST BEST PRACTICE ADVICE

Available Now!

The Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline is the most up-to-date best advice on the pharmacological treatment of obesity. Chaired by Caroline Apovian MD, these newly published recommendations will help clinicians manage obesity in patients who have been unsuccessful with diet and exercise alone. The guideline includes:

- Rationale for the pharmacological treatment of Obesity
- Weight profiles of medications
- Weight management in patients with diabetes, HIV/AIDS, hypertension, depression, and others

Peer-reviewed and developed by a team of experts, the Society's Clinical Practice Guidelines provide the highest quality, actionable recommendations for physicians in a clinical setting.

GET YOUR FREE DOWNLOAD AT
ENDOCRINE.ORG/CPG

ENDOCRINE SOCIETY

DOCTOR'S ORDERS

As electronic health records are adopted by more and more practices, it's becoming evident that they have created an increased workload. Using a scribe may be key to improving your office's productivity.

By Kurt Ullman

The introduction of electronic health records (EHR) has brought about two often-voiced concerns from the physician. One is that they are cumbersome and impact negatively on physician productivity. The other is the structure means a doctor's time and attention is split between the patient and the computer, to the detriment of the former.

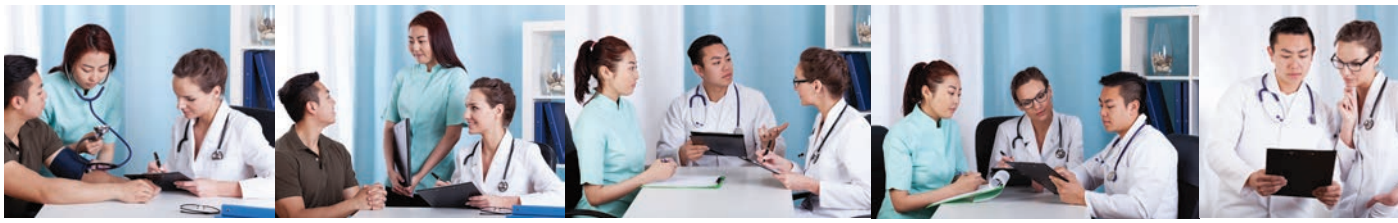
One way to address both of these is to add a position to the practice known as a scribe. These are unlicensed individuals, usually with a medical background, who do the necessary data entry and management under the supervision of a physician or independent practitioner.

"What the scribe does is give back to doctors time lost to pointing, clicking, and typing," says Kevin Brady, president of Physician Angels, Inc., a provider of virtual scribe services. "It makes no sense to have your $300 an hour doctor doing $15 an hour data entry work. The scribe frees up the doctor to focus on the patient, see more patients, and still get home at a decent hour."

More Patient/Doctor Interaction

The scribe also impacts on the patient-doctor interaction and may help increase patient satisfaction scores. Before, the doctor had to spend a certain amount of time with their back to the patient while working with the computer. Scribes give providers an opportunity to maintain eye contact and lessens patient concerns about the doctor treating the computer instead of the patient.

Generally, the scribe is a person who has at least some knowledge of medical terminology. Most practices use a medical assistant (MA) or registered nurse (RN) for the position. A practice considering a scribe will need to make sure they understand the latest requirements for scribes in order for that encounter to be acceptable under the Centers for Medicare and Medicaid Services' Meaningful Use rules. Although some organizations train and certify medical scribes, there are no widely accepted criteria for scribe training and employment requirements.



One way to utilize scribes is as an employee with that as their only function within the practice. They can interact remotely using video and/or audio conferencing from another room in the practice's offices or at some central location.

Another way is to use staff already on board and working with the physicians. In this model, the scribe is often an MA or RN who sets up the room, gathers initial information such as vital signs, reason for the visit, and medication lists before the patient sees the physician. They then stay in the room during the visit and enter data as needed.

"In many cases, the practice won't need to employ additional people," says Jeffrey Daigrepont, senior vice-president of the Coker Group in Alpharetta, Ga. "It is often repurposing a person already in the office. Most were probably already involved in note taking to a certain extent even before the EHR was implemented."

A third model seen in the U.S. uses a scribe that is employed by a third party. The scribes can work from anywhere in the world.

"The virtual or remote scribe is in a HIPAA-secure facility with an audio connection allowing them to monitor the interaction and ask questions as needed," Brady explains. "They are logged in to the EHR under their own unique identifier and chart the encounter in real time."

Information Specialist

The scribe is not a transcriptionist taking down everything the doctor says. Instead, he or she listens carefully to the conversation the provider is having with the patient and populates the chart based on what is being said. This means the doctor vocalizes information that may have just been written down on paper notes before. This can help impart to the patient additional information on his or her condition and what the provider feels are important aspects of care.

The way that works best for a given practice will differ. The more repetitious the interventions are, the more a scribe can do to populate the charts from templates. The personality of the individual physician may also have an impact, as it requires a certain amount of trust in the abilities of the scribe and some relinquishment of control.

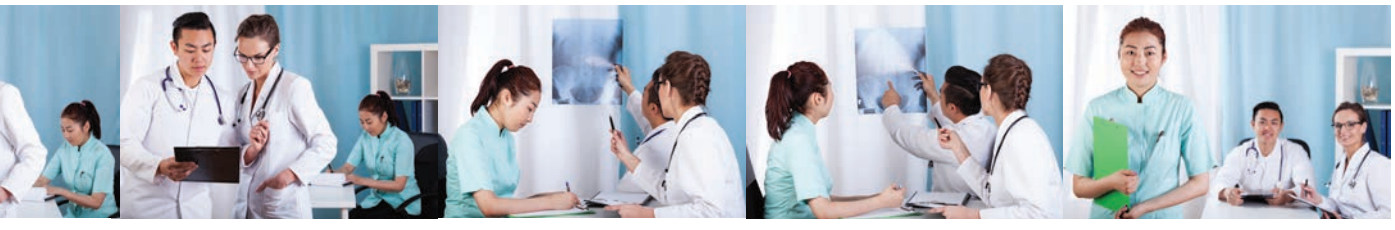
At the end of the visit, the doctor will need to look over the information entered into the electronic records and add anything that is needed. After confirming that all is in order, the physician can then sign the record and go on to the next patient.

"The doctor remains responsible for the note whether or not they entered it directly," Daigrepont says. "I would not suggest that the scribe be given the authority to do the capturing for reimbursement. The provider really needs to be the one determining the level an encounter should be billed to avoid unwanted liabilities if there is an audit."

In the end, the motivations of the physicians are largely based on two things. One is seeing more patients. Some studies suggest the average specialist can schedule as many as seven additional patients a day.

"Some just don't want to work until 7 or 8 every night," Brady says. "This is a quality of life issue so the provider can see their family and not spend their entire life at the office." **EN**

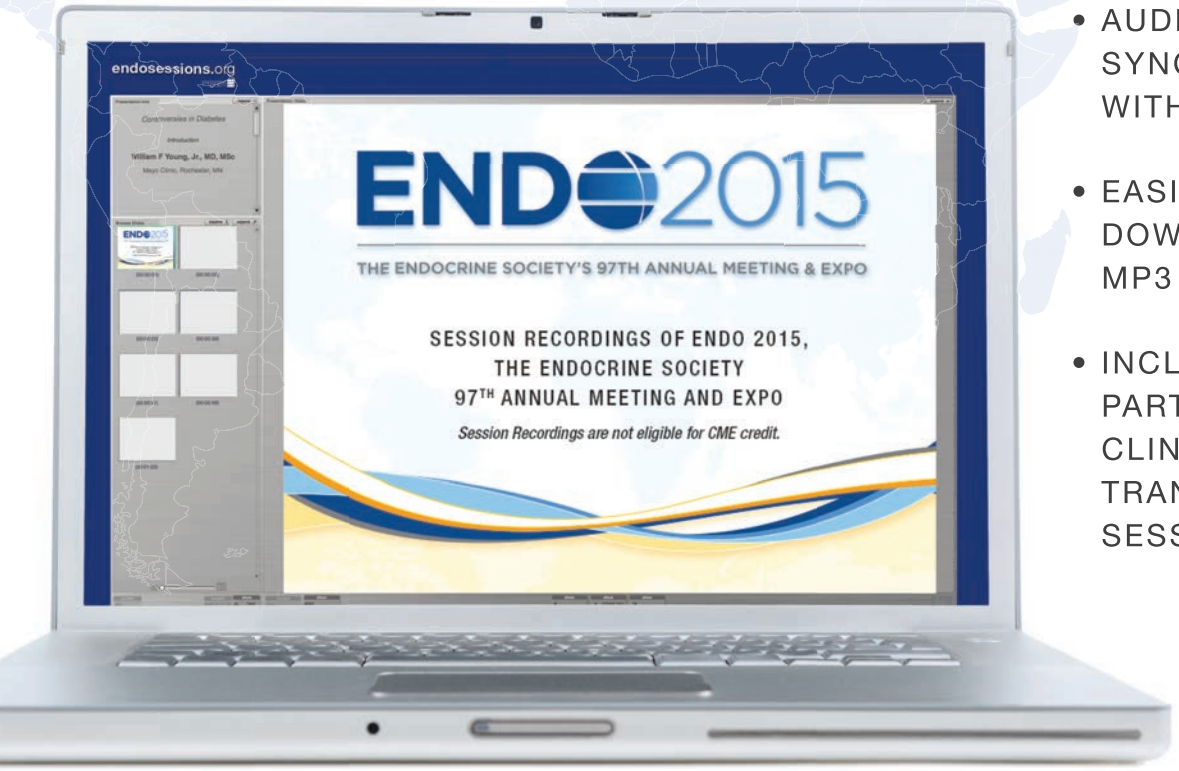
— Ullman, RN, MHA, is an Indiana-based freelance writer with nearly 30 years of experience. He wrote about making the move from a private practice into a group setting in the February issue.



ENDO 2015

SESSION RECORDINGS

ACCESS THE MEETING ONLINE ANY TIME WITH MORE THAN 100 LECTURES FROM ENDO 2015:



- AUDIO SYNCHRONIZED WITH SLIDES
- EASILY DOWNLOADABLE MP3 FILES
- INCLUDES PARTICIPATING CLINICAL AND TRANSLATIONAL SESSIONS

GET YOUR SESSION RECORDINGS TODAY

Nonmember: $375 | Member: $250 | Early Career/In-Training Member: $200

endosessions.org

ENDOCRINE SOCIETY

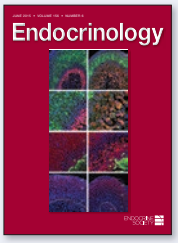
The following studies, among others, will be published in Endocrine Society journals. Before print, they are edited and posted online in each journal's Early Release section. You can access the journals at ***www.endocrine.org***.

Daily or Cyclical Teriparatide Treatment in Women with Osteoporosis on No Prior Therapy and Women on Alendronate • Felicia Cosman, Jeri W. Nieves, Marsha Zion, Patricia Garrett, Simon Neubort, David Dempster, and Robert Lindsay • *Cyclic TPTD over two years improves BMD similarly to daily treatment in women who remain on ALN, despite only 50% of the TPTD dose. However, there does not appear to be a BMD advantage to cyclic administration in treatment-naïve women for up to 24 months.*

Effects of Denosumab and Calcitriol on Severe Secondary Hyperparathyroidism in Dialysis Patients with Low Bone Mass • Chien-Liang Chen, Nai-Ching Chen, Huei-Lung Liang, Chih-Yang Hsu, Kang-Ju Chou, Hua-Chang Fang, and Po-Tsang Lee • *Denosumab allows for supra-physiologic doses of calcitriol resulting in decreased parathyroid secretion and parathyroid hyperplasia. Supervised administration and weekly laboratory and clinical monitoring of serum calcium are recommended during the first month to prevent hypocalcemia.*

Therapeutic Effectiveness of Screening for Multiple Endocrine Neoplasia Type 2A • Andreas Machens and Henning Dralle • *Screening efforts need to focus on sporadic-appearing MTC to deplete the pool of unrecognized carriers of ATA level B and A mutations and enable earlier pre-emptive thyroidectomy in their offspring.*

Aberrant TGFβ Signaling Contributes to Dysregulation of Sphingolipid Metabolism in Intrauterine Growth Restriction • Sarah Chauvin, Yoav Yinon, Jing Xu, Leonardo Ermini, Julien Sallais, Andrea Tagliaferro, Tullia Todros, Martin Post, and Isabella Caniggia • *Altered TGFβ signaling in IUGR placentae causes dysregulation of sphingolipid metabolism, which may contribute to the increased trophoblast cell death typical of this pathology.*



Control of Polyamine Biosynthesis by Antizyme Inhibitor 1 is Important for Transcriptional Regulation of Arginine Vasopressin in the Male Rat Hypothalamus • Michael P. Greenwood, Mingkwan Greenwood, Julian F. R. Paton, and David Murphy • *The authors have identified Azin1, and hence by inference polyamines, as novel regulators of the expression of the AVP gene.*

OPG Treatment Prevents Bone Loss During Lactation But Does Not Affect Milk Production or Maternal Calcium Metabolism • Laleh Ardeshirpour, Cristina Dumitru, Pamela Dann, John Sterpka, Joshua VanHouten, Wonnam Kim, Paul Kostenuik, and John Wysolmerski • *These studies demonstrate that RANKL signaling is a requirement for bone loss during lactation, and suggest that osteoclast activity may be required to increase osteoblast numbers during lactation in preparation for the recovery of bone mass after weaning. These data also demonstrate that maternal bone loss is not absolutely required to supply calcium for milk production unless dietary calcium intake is inadequate.*

Adrenal Development in Mice Requires GATA4 and GATA6 Transcription Factors • Sergei G. Tevosian, Elizabeth Jiménez, Heather M. Hatch, Tianyu Jiang, Deborah A. Morse, Shawna C. Fox, and Maria B. Padua • *These results reveal a requirement for GATA factors in adrenal development and provide a novel tool to characterize the transcriptional network controlling adrenocortical cell fates.*

Central Fibroblast Growth Factor 21 Browns White Fat via Sympathetic Action in Male Mice • Nicholas Douris, Darko Stevanovic, Ffolliott M. Fisher, Theodore I. Cisu, Melissa J. Chee, Ngoc Ly Nguyen, Eleen Zarebidaki, Andrew C. Adams, Alexei Kharitonenkov, Jeffrey S. Flier, Timothy J. Bartness, and Eleftheria Maratos-Flier • *These data indicate that FGF21 can signal in the brain to activate the sympathetic nervous system and induce adipose tissue thermogenesis.*

Minireview: Role of Intracellular Scaffolding Proteins in the Regulation of Endocrine G Protein-coupled Receptor Signaling • Cornelia Walther and Stephen S.G. Ferguson • *This review focuses on GPCR interacting PSD95-Disc Large-Zona Occludens (PDZ) domain containing scaffolds in the regulation of endocrine receptor signaling as well as their potential role as therapeutic targets for the treatment of endocrinopathies.*

Homeodomain Proteins SIX3 and SIX6 Regulate Gonadotrope-specific Genes During Pituitary Development • Huimin Xie, Hanne M. Hoffmann, Jason D. Meadows, Susan L. Mayo, Crystal Trang, Sunamita S. Leming, Chiara Maruggi, Shannon W. Davis, Rachel Larder, and Pamela L. Mellon • *In summary, SIX3 and SIX6 play distinct but compensatory roles in regulating transcription of gonadotrope-specific genes as gonadotrope cells differentiate.*

Participants at the hypoglycemia roundtable, hosted by the Endocrine Society and Merck, came from the realms of patient advocacy, the federal government, quality improvement organizations, professional societies, and more, all to discuss increasing the level of awareness about this disorder.

Society Holds Roundtable on Hypoglycemia to Increase Awareness

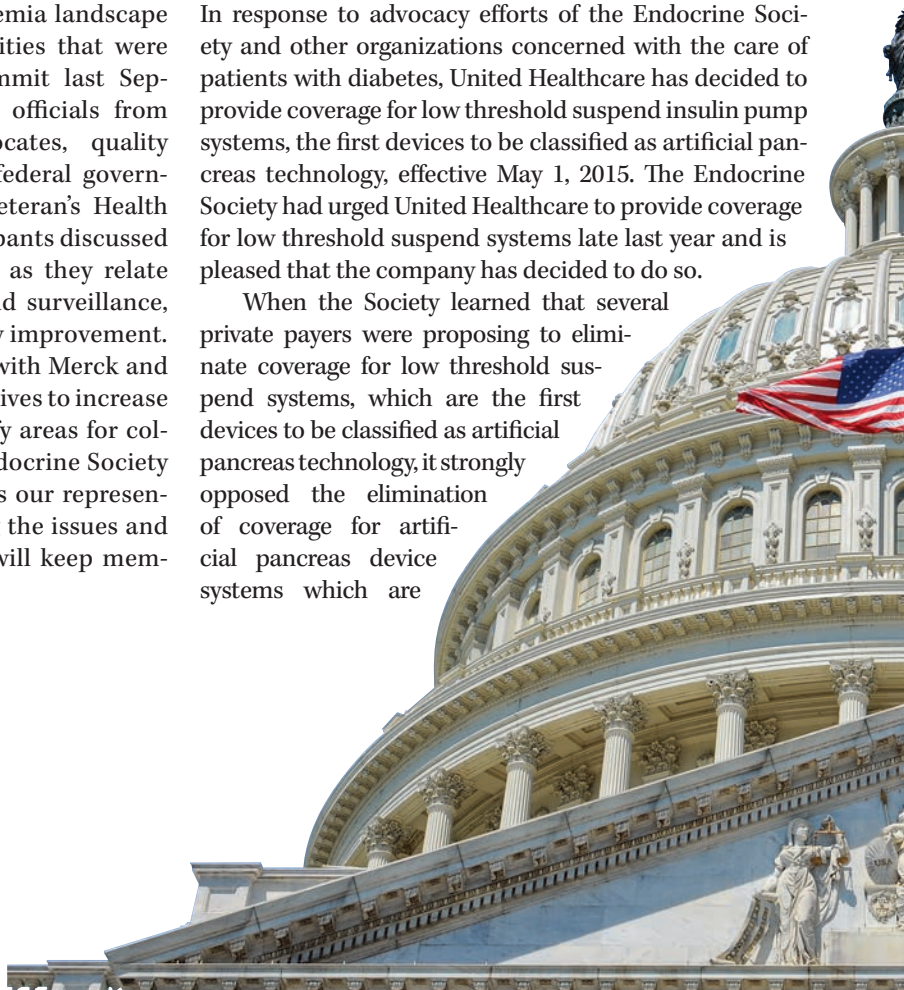
On April 29, the Society co-hosted a roundtable with Merck to discuss the current hypoglycemia landscape and to delve deeper into policy priorities that were identified at our diabetes policy summit last September. The roundtable featured key officials from professional societies, patient advocates, quality improvement organizations, and the federal government, including NIDDK, CDC, and Veteran's Health Administration. At the meeting, participants discussed various perspectives on hypoglycemia as they relate to the patient experience, research and surveillance, issues in the clinical setting, and quality improvement.

The Society will continue working with Merck and participants at the roundtable on initiatives to increase awareness of hypoglycemia and identify areas for collaboration. Tony McCall, MD, PhD, Endocrine Society Vice President for Clinical Science, was our representative and did a masterful job distilling the issues and providing context for next steps. We will keep members apprised of the follow-up.

Society Advocacy Prompts United Healthcare Coverage of Low Threshold Suspend Devices

In response to advocacy efforts of the Endocrine Society and other organizations concerned with the care of patients with diabetes, United Healthcare has decided to provide coverage for low threshold suspend insulin pump systems, the first devices to be classified as artificial pancreas technology, effective May 1, 2015. The Endocrine Society had urged United Healthcare to provide coverage for low threshold suspend systems late last year and is pleased that the company has decided to do so.

When the Society learned that several private payers were proposing to eliminate coverage for low threshold suspend systems, which are the first devices to be classified as artificial pancreas technology, it strongly opposed the elimination of coverage for artificial pancreas device systems which are



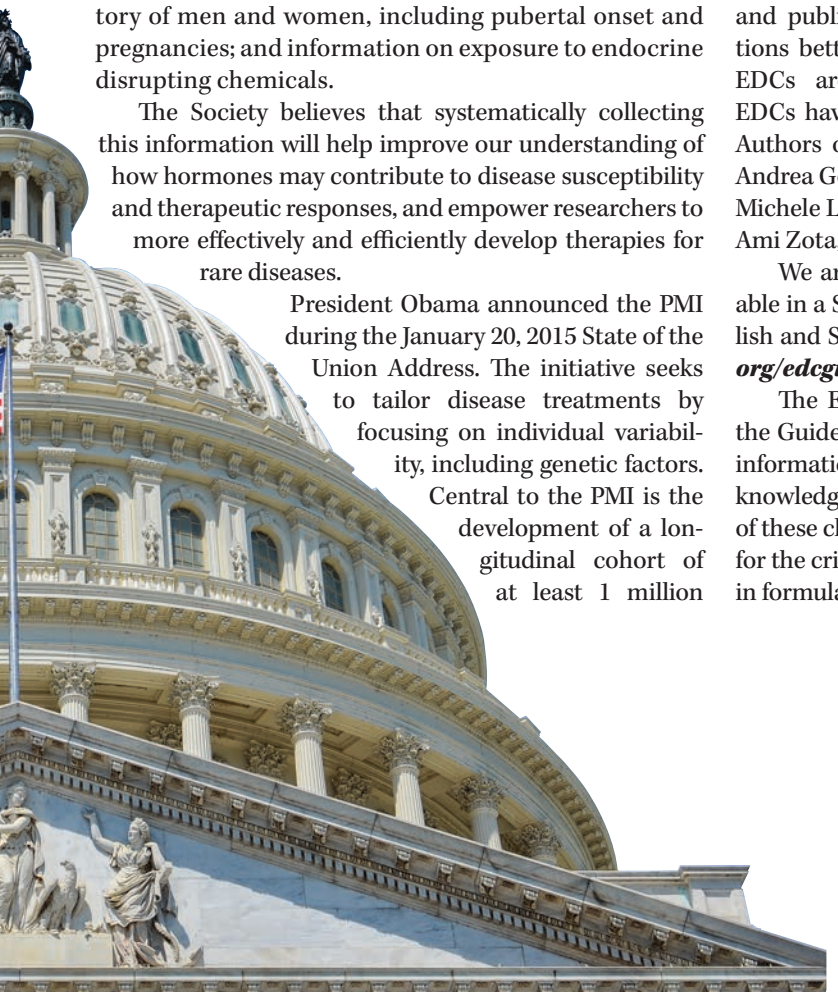
FDA-approved and have been used in numerous countries for several years.

The Society has received responses from several other payers stating that they were reviewing their policies and would have a determination in the coming weeks. The Society will continue to advocate on behalf of coverage for the next generation of technologies that could pave the way for the artificial pancreas and will update its members when additional information becomes available.

Endocrine Society Recommends Including How Hormones Contribute to Disease Susceptibility in Precision Medicine Initiative

The Obama Administration is moving ahead with its Precision Medicine Initiative (PMI), a research effort to revolutionize how we improve health and treat disease by creating a new model of patient-powered research that promises to accelerate biomedical discoveries and provide clinicians with new tools, knowledge, and therapies to select which treatments will work best for which patients. Recently, the National Institutes of Health (NIH) sought feedback on the "characteristics, purpose, or other overall aspects in the development and implementation of a large U.S. precision medicine cohort." The Society recommended that the PMI include: information on the hormonal status of the cohort; a careful assessment of women at various reproductive stages and during pregnancy; fertility history of men and women, including pubertal onset and pregnancies; and information on exposure to endocrine disrupting chemicals.

The Society believes that systematically collecting this information will help improve our understanding of how hormones may contribute to disease susceptibility and therapeutic responses, and empower researchers to more effectively and efficiently develop therapies for rare diseases.



President Obama announced the PMI during the January 20, 2015 State of the Union Address. The initiative seeks to tailor disease treatments by focusing on individual variability, including genetic factors. Central to the PMI is the development of a longitudinal cohort of at least 1 million Americans. Data from the cohort will include biological specimens, such as DNA samples, linked to electronic health records. President Obama would like to spend $215 million on the initiative with $130 million allotted to NIH for research, plus $10 million to the FDA to aid in developing regulatory approaches, and $5 million offered to assist in health IT interoperability. PMI is also a target for funding in legislation developing in both the House of Representatives and the U.S. Senate.

Endocrine Society – IPEN Guide on Endocrine Disrupting Chemicals Now Available in Spanish

Last December the Endocrine Society and IPEN, a leading global network of 700 non-governmental organizations (NGOs) working to establish and implement safe chemicals policies and practices, collaborated on the publication of *Introduction to Endocrine Disrupting Chemicals (EDCs): A Guide for Public Interest Organizations and Policy Makers.* The purpose of the Guide is to raise global awareness about EDCs and help global policymakers, government leaders, and public interest organizations better understand what EDCs are and the impact EDCs have on human health. Authors of the Guide are Endocrine Society members: Andrea Gore, PhD, David Crews, PhD, Loretta Doan, PhD, Michele La Merrill, PhD, MPH, Health Patisaul, PHD, and Ami Zota, ScD, MS.

We are pleased to announce the Guide is now available in a Spanish translation. Copies of the guide in English and Spanish are available at ***http://www.endocrine.org/edcguide***.

The Endocrine Society and IPEN are disseminating the Guide and hope that greater awareness gained by its information will lead to additional programs to enhance knowledge of EDCs, to foster new research into the effects of these chemicals, and to promote a greater appreciation for the critical need for endocrine principles to be applied in formulating EDC policy and regulations. EN

Society Staff Changes
Signal Forward Momentum

On April 16, Endocrine Society CEO Barbara Byrd Keenan announced a number of staff changes that will further propel the organization forward as it concentrates on three new priorities: leadership development, global strategy, and knowledge integration.

Rob Bartel, director, Education, has been promoted to senior director, Knowledge Integration and New Product Development. According to Keenan, the term "knowledge integration" originated in the artificial intelligence field as the process for identifying existing and new information and knowledge and combining them in different ways to generate even newer knowledge. "For us, it means working across all of our content assets to combine, connect, and extend them to create new, better, useful, and profitable programs and services," she says. "He will serve as our internal 'entrepreneur' working across the Society to bring new ideas to purposeful and profitable life."

A new position, senior director, Strategy & Planning, has been created and is filled by new hire Amanda Perl, who began on April 28. Perl will be charged with managing the process for articulating, focusing, and monitoring the Society's 3 Horizon Planning effort and serve as staff lead on the leadership development and global strategy priorities. Perl will also be managing the Society's EndoCares program, a campaign to improve the lives of patients around the world with endocrine diseases.

Perl comes to the Society from the Institute of Food Technologists where she was the vice president of Development and managing director of Certification. In these capacities, she served as the special projects leader for new launch initiatives, leadership development, global partnerships and alliances, strategic planning, and grant management.

Steve Poston, the Society's director of Information Technology, will be adding office services to his responsibilities as director of Information Technology and Office Services. "Steve has prior experience in administration and facilities management so this is a natural move for the Society," Keenan says.

These changes have been on the horizon since November when the Council agreed upon the three new priority areas. In addition, the Society will be launching EndoCares, a global social responsibility initiative. "We clearly need additional capacity to comprehensively develop these programs as we do not have the bandwidth to handle the expanded workload," Keenan explains. "To accomplish this at this point in time, we will be reallocating several vacant staff positions to support these efforts."

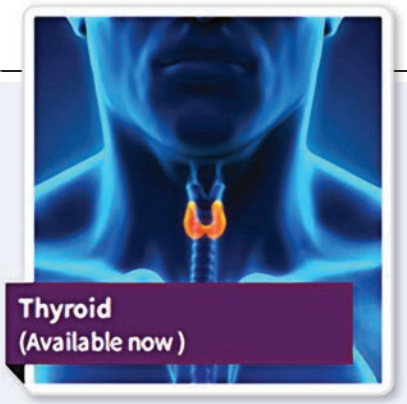
According to Keenan, these staffing changes are exciting developments for the Society, and the timing is finally right. "This was not possible when we needed to conduct two ENDOs in nine months and handle special projects that only are done every few years like the ACCME reaccreditation and the Membership Needs Assessment, as well as new projects like Facts & Figures and the Workforce Study," she explains. "These past efforts are a testament to the resilience, dedication, and competence of our staff." EN

Announcing the **Endocrine Cases Program**

The Endocrine Society is proud to announce a new, exclusive member benefit — Endocrine Cases. Envisioned and developed by immediate past president Richard J. Santen, MD, this online tool allows members to submit their most challenging clinical cases and have Society experts weigh in.

Present real or hypothetical situations and test your hypothesis against what the experts recommend. And if you're an educator, encourage your fellows to use this tool as part of their ongoing training. Unlike textbooks, review articles, or Up To Date, Endocrine Cases lets you provide a set of components specific to a case and receive unique advice from members who've just about seen it all.

Visit ***endocrine.org/Cases*** to learn more about this valuable and informative member benefit.



Society Releases **Endocrine Facts and Figures: THYROID**

The second chapter of Endocrine Facts and Figures was released on April 22 and deals exclusively with the thyroid.

The new chapter follows on the heels of the inaugural chapter on obesity and is only the second chapter in what is planned to be a nine-chapter online tome covering a vast array of endocrine disorders. "Endocrine Facts and Figures" is an effort by the Society to compile the latest peer-reviewed statistics in a single comprehensive resource.

This chapter contains the most current epidemiological and trends data on thyroid nodules and goiters, hypothyroidism, hyperthyroidism, thyroiditis, and iodine deficiency. For more information and to access the latest document, go to ***www.endocrinefacts.org***. EN

Event **CALENDAR**

JUNE 5 – 9, BOSTON *American Diabetes Association Annual Conference* ***www.diabetes.org***

SEPTEMBER 8 – 12, MIAMI
Clinical Endocrinology Update ***www.endocrine.org/ceu***

OCTOBER 9 – 12, SEATTLE *American Society for Bone and Mineral Research Annual Meeting* ***www.asbmr.org***

OCTOBER 17 – 21, CHICAGO
Neuroscience 2015 ***www.sfn.org***

OCTOBER 18 – 23, ORLANDO
Thyroid ITC 2015 ***www.thyroid.org***

NOVEMBER 1 – 7, LOS ANGELES
Obesity Week 2015 ***www.obesity.org***

EXERCISES: ANYTIME, ANYWHERE

Hormone Health NETWORK®
Keep your body in balance

Exercise is key to a healthy endocrine system. When you move, your muscles release hormones. Physical activity has the ability to keep hormones in balance that are necessary for regular functioning (energy level, bone and muscle strength) and help your body cope with symptoms of endocrine conditions such as diabetes and thyroid disorders.

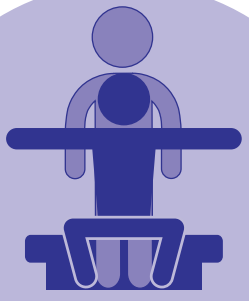
Visit hormone.org for more information.

Exercise doesn't have to be intimidating. You don't have to exercise at a gym for hours at a time. Exercise breaks can be taken by anyone, anywhere—from the office to the classroom.

TRY THESE SIMPLE EXERCISES

"Raise the Roof"
Overhead press with arms

"Tree Pose"
Stand with arms raised above head, palms together, and balance on one leg



"Hot Seat"
Chair squats with legs

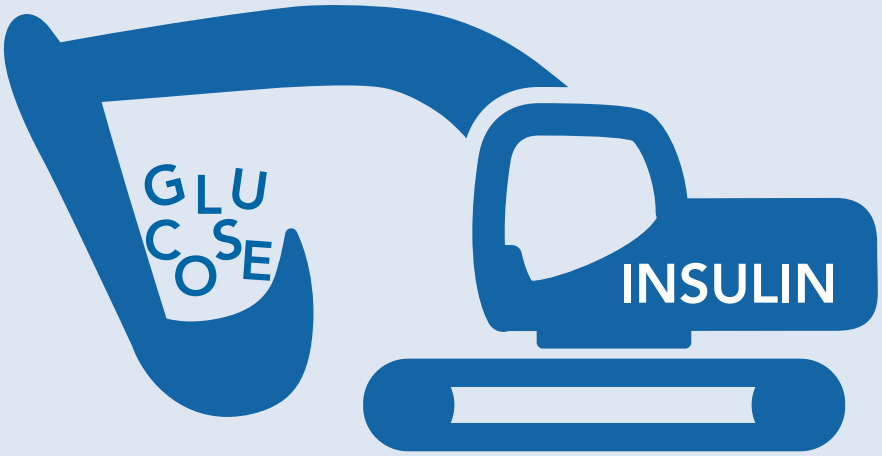
Wall Push-ups
Face a wall, lean in, and push back whole body with arms

"Swim"
Freestyle swim motion with arms

Boxing
Punch the air with arms from chest

WALKING: THE EASIEST EXERCISE OF THEM ALL

SECRET WEAPON AGAINST DIABETES = EXERCISE



Exercise gets the bloodstream moving, which paves a smooth road for insulin to do its job and carry excess glucose (sugar) into cells for energy.

EXERCISE CAN BE MORE DIFFICULT WHEN DEALING WITH EXTREME HORMONE CONDITIONS

- Thyroid function
- Testosterone levels
- Cortisol levels

Consult an endocrinologist to get hormone levels tested.

You have questions. We have answers.
The Hormone Health Network is your trusted source for endocrine patient education. Our free, online resources are available at hormone.org.

Additional editing by Judith Korner, MD, PhD, Columbia University and Guillermo Umpierrez, MD, Emory University

Hormone Health NETWORK® FROM THE ENDOCRINE SOCIETY

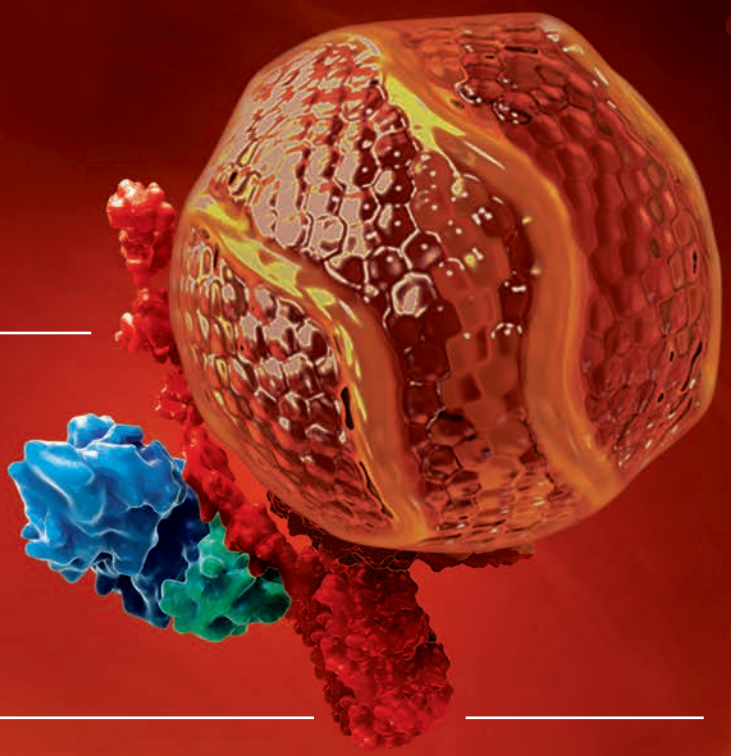
SAVE THE DATE

ENDO 2016

APRIL 1–4, 2016 BOSTON, MASSACHUSETTS

BOSTON CONVENTION AND EXHIBITION CENTER **ENDO2016.ORG**

ENDOCRINE SOCIETY



PCSK9: It has LDL receptors in a serious bind[1]

Recent discoveries show there's an important new factor to consider. PCSK9 is a protein that promotes degradation of the LDL receptor within hepatocytes, thereby increasing plasma LDL-C levels.[2,3] Amgen Cardiovascular is proud to be a leader in PCSK9 research and remains dedicated to deepening our understanding of the critical role it plays in cholesterol metabolism. **PCSK9 means it's time to discuss cholesterol differently.**

Unite the cholesterol conversation at **DiscoverPCSK9.com**.

AMGEN®

Cardiovascular

LDL = low-density lipoprotein; **LDL-C** = low-density lipoprotein cholesterol;
PCSK9 = proprotein convertase subtilisin/kexin type 9.

References: 1. Lambert G, Sjouke B, Choque B, Kastelein JJP, Hovingh GK. *J Lipid Res*. 2012;53:2515-2524. **2.** Zhang D-W, Lagace TA, Garuti R, et al. *J Biol Chem*. 2007;282:18602-18612. **3.** Qian YW, Schmidt RJ, Zhang Y, et al. *J Lipid Res*. 2007;48(7):1488-1498.