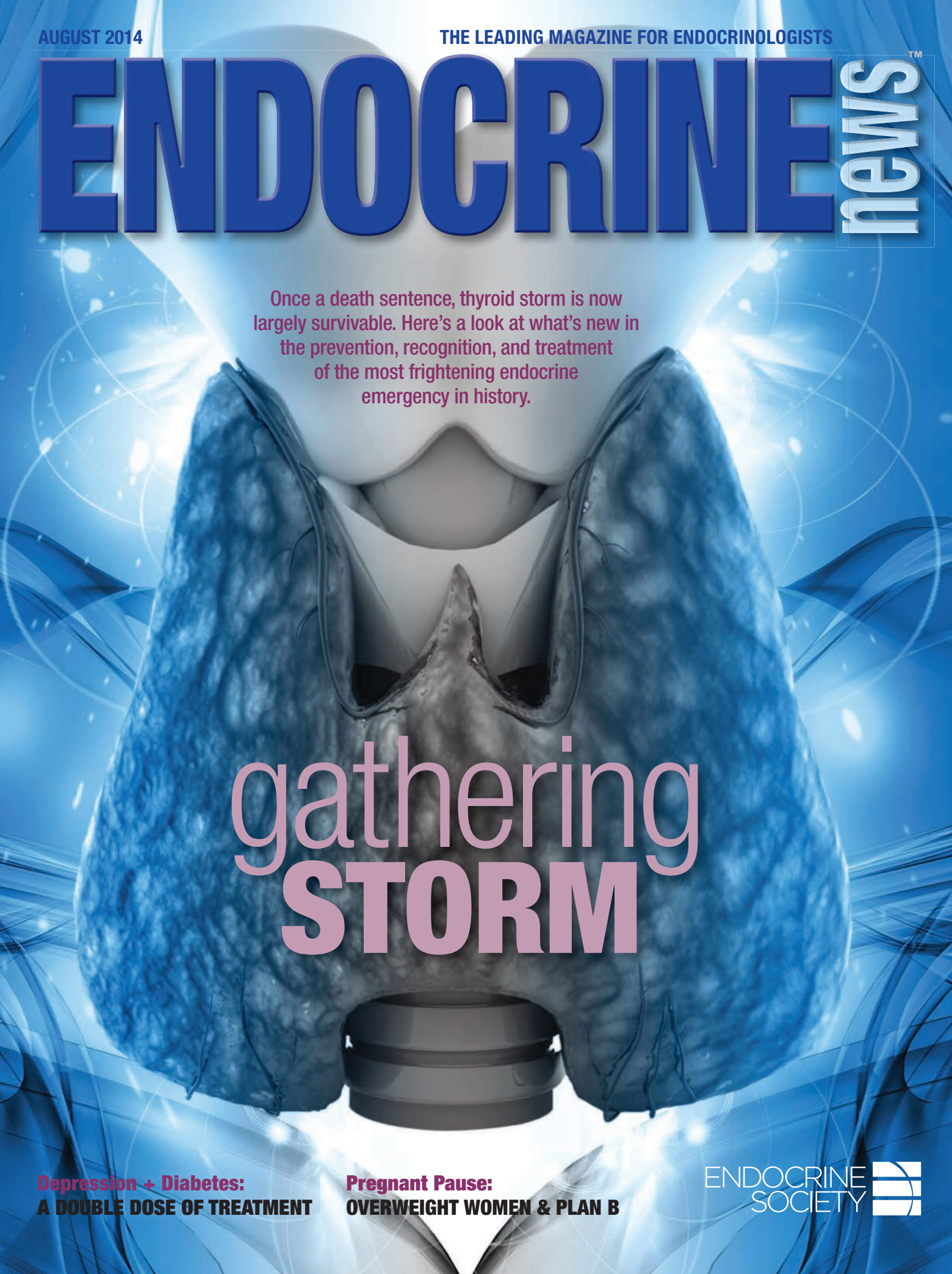
AUGUST 2014

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

ENDOCRINE news™

Once a death sentence, thyroid storm is now largely survivable. Here's a look at what's new in the prevention, recognition, and treatment of the most frightening endocrine emergency in history.



gathering STORM

Depression + Diabetes:
A DOUBLE DOSE OF TREATMENT

Pregnant Pause:
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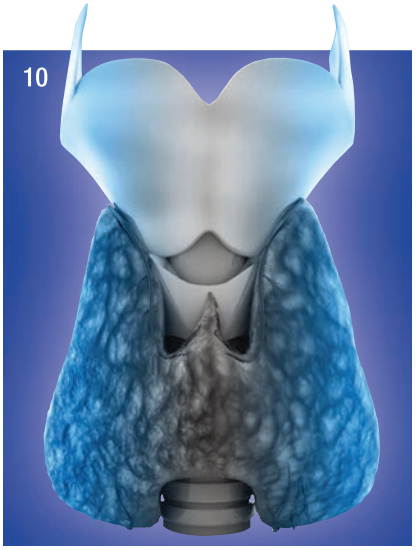

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ENDOCRINE SOCIETY
Hormone Science to Health

ENDO 2015 Will Debut New Endocrine Science Research Even Earlier

Richard J. Santen, MD

This past year, in my president-elect role, I gained a deeper appreciation of the past presidents' extraordinary vision and leadership that have contributed to the outstanding success of the Society over the years. I would specifically like to thank past-president Bill Young and immediate past-president Teresa Woodruff for their commitment and devotion to the Endocrine Society.

I would like to congratulate Teresa Woodruff, the Annual Meeting Steering Committee (AMSC), and staff for making **ICE/ENDO 2014** a record-breaking meeting in all areas. This meeting had the highest number of scientific registrants and overall attendees in **ICE** and **ENDO** history. More than 10,000 registrants representing 96 countries attended the meeting. The Society received more than 3,200 scientific abstracts, which is another record-breaking number. And not only did we break all our previous records, the scientific program was outstanding as many of you can attest.

I am hopeful that **ENDO 2015** will be another exceptional meeting both in attendance and content.

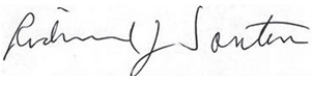
One of my first tasks as president-elect was to appoint the AMSC chairs for the **ENDO 2015** meeting. With **ENDO 2015** moving to March, the planning timeline for the meeting has been compressed this year. The AMSC chairs and committee have been selected and include Mathew Ringel as overall chair and Sue Moenter, Marc-Andre Cormier, and Carol Wysham as basic, clinical science, and clinical practice co-chairs, respectively. The AMSC has already met and developed an outstanding scientific program, which will be featured in more detail in next month's *Endocrine News*. As many of you know, the registration for **ENDO 2015** has already opened. Please mark your calendars for the **ENDO 2015** dates: Thursday, March 5 to Sunday, March 8, 2015. Also note that the abstract submission will launch on September 17, 2014, with a closing date of November 11, 2014.

The new spring timing of **ENDO** ensures that endocrine science will receive extra attention ahead of the summer and fall meetings. The best clinical trials will be showcased in special sessions. Visit ***www.endo2015.org***, and click on the "Abstracts and Awards" button to learn more about the exceptional benefits of submitting your clinical trial abstract to **ENDO** including options for fast-track publication and focused media attention.

As many of you have heard me mention before, my biggest passion and the main focus of my presidential year is to empower the next generation of endocrinologists. I have briefly discussed some of the plans and initiatives that are being considered to create innovative programs that enhance the recruitment, retention, and development of early-career endocrinologists beyond their training completion. This focus influenced an additional task as president-elect, the appointment of committee members. Much effort was devoted to the identification and appointment of next-generation members, a process that worked out well.

The Society's awards program is an important way to recognize and honor our outstanding members. Your input is vital, and I would encourage you and your colleagues to submit your nominations starting next month. Each year, the Endocrine Society presents awards totaling over half a million dollars to foster achievement and recognize excellence in endocrine science and medicine. From undergraduate students to those in established careers, the awards recognize all three constituencies; basic researchers, clinical researchers, and clinical practitioners. In late September, the Society will begin the 2015 awards season with calls for applications for the numerous Society trainee and early-career awards and travel grants. In 2014, trainee abstract awards and travel grants and research fellowships were awarded to nearly 500 trainees and early-career professionals. The details of these awards, including application requirements and submission deadlines for 2015, are on the Society's website, under Awards tab.

I am beginning my presidency full of energy, optimism, and fully committed to the Endocrine Society. If you have any questions or comments, feel free to contact me at **president@endocrine.org**. I look forward to a productive and successful year for the Endocrine Society. EN



Richard J. Santen, MD
President, Endocrine Society

ENDO 2015

Here are some brief **ENDO 2015** highlights:

- Presidential Plenary topics and speakers
  - » Personalized Menopause Management: Role of Genetics in Responses to Therapy: James N. Ingle, MD, Mayo Clinic, Rochester, Minn.
  - » Personalized Menopause Management: Biomarker Data that Informs Decision Making: JoAnn E. Manson, MD, DrPH, Brigham & Women's Hospital, Harvard, Boston
- 16 plenary lectures covering topics such as diabetes, obesity, cancer, reproduction, and signaling
- All new Meet the Professor, symposia, Society guideline, and Master Clinician sessions

ENDOCRINE SOCIETY

AUGUST 2014

ENDOCRINE news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

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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.

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Mark A. Newman

Our cover story this month, "Gathering Storm" (p. 10), details one of the most frightening endocrine emergencies physicians are faced with, the thyroid storm. At one time, this confounding condition was a death sentence. Fortunately, thanks to research and a better understanding of just exactly what thyroid storm is, it now has a survival rate between 80% and 100%. Difficult to diagnose and tricky to treat, this disorder still has no definitive cause, but according to Colonel Henry B. Burch, MD, professor of medicine and chair of the Endocrinology Division of the Uniformed Services University of the Health Sciences, in Bethesda, Md., the key to a patient's survival is simply "making the diagnosis."

Terri D'Arrigo writes on another topic that is all too common: treating diabetes in patients who are also suffering from depression. In "Depression, Distress, and Diabetes" (p. 16), Jeffrey S. Gonzales, PhD, associate professor, Department of Medicine, Department of Epidemiology and Population Health, Albert Einstein College of Medicine in New York, says that "even if you're a very sensitive endocrinologist who knows about depression and wants to get your patient appropriate care, insurance plans may separate mental health benefits from diabetes treatment [in a way that makes teamwork among clinicians difficult]. It's like chopping people up into different diseases."

As the obesity epidemic continues its rampage, it's amazing to see how it affects so many aspects of daily life, even how it impacts pregnancy and birth control. In "Pregnant Pause" on page 24, Melissa Mapes writes about how the over-the-counter female oral contraceptive levonorgestrel — or "Plan B" — has an unusually high failure rate in overweight women. Since this is currently the only affordable emergency contraception available for women over the counter, heavier women might have to seek out a "Plan C."

If you were fortunate enough to be in Chicago for **ICE/ENDO 2014** then you saw firsthand the voluminous amount of research that was presented. On page 20, associate editor Derek Bagley gives an overview of some of the data presented at the conference. From studies on the burgeoning epidemics of diabetes and obesity to new findings on hormones and pregnancy and endocrine-disrupting chemicals, clinicians from all corners of the field of endocrinology gave some compelling presentations. As a bonus, it was a great way for me to find ideas for 2015, which is closer than you think!

Speaking of 2015, if you have any story ideas or topics you'd like to see covered in *Endocrine News*, don't hesitate to drop me a line at ***mnewman@endocrine.org***. EN

Mark A. Newman
Managing Editor, Endocrine News

By Derek Bagley

EXPOSURE TO EDCS MAY LESSEN QUALITY OF LIFE IN FUTURE GENERATIONS

Studies on rats have shown that endocrine-disrupting chemicals (EDCs) impact not only future generations, but also how these descendants respond to stress during adolescence. A new study, published in the journal *Endocrinology,* has revealed that the sexes differ profoundly in these effects. That is, females with a history of exposure respond very differently to stress and exhibit phenotypes that are much more compromised than males.

Researchers led by David Crews, PhD, of the University of Texas at Austin, wrote that the legacy of exposures to EDCs "has permanently altered the present and future health of humans and wildlife." The paper makes the distinction between "context-dependent" epigenetic modifications, which are not heritable because the germ cells are not affected, and "germline-dependent" epigenetic modifications, which "manifest each generation even in the absence of the causative agent." They wrote: "This is the case for several EDCs, notably, vinclozolin, bisphenol A, and tributyltin. Such transgenerational modifications affect all levels of biological organization, from gene regulation to behavioral interactions of conspecifics."

"I have shown previously the transgenerational effects of EDCs on behavior of the descendant generations (F3), (Crews et al. PNAS, 2007)," Crews, says. "More recently, this was extended to a novel two-hit, three-generations apart model to demonstrate how restraint stress experienced during adolescence of the F3 descendants changes their physiology, neural metabolism, and gene expression in adulthood."

Crews and his team focused on vinclozolin, a commonly used fungicide with demonstrated anti-androgenic properties. They used the two-hit, three-generations apart model, testing how F3 descendants of rats given in utero exposures to vinclozolin reacted to stress in their own lives, focusing on sexually dimorphic phenotypic outcomes. The scientists subjected the adult rats, male and female F3 vinclozolin- or vehicle-lineage, stressed or non-stressed, to a battery of tests, behaviorally characterizing them, measuring hormone levels, and analyzing brain function and anatomy.

"Results showed that the effects of ancestral exposure to vinclozolin converged with stress experienced during adolescence in a sexually dimorphic manner," the authors wrote. "Debilitating effects were seen at all levels of the phenotype, including physiology, behavior, brain metabolism, gene expression, and genome-wide transcriptome modifications in specific brain nuclei." There were dramatic differences in the reactions between males and females, with females significantly more vulnerable to the transgenerational effects of vinclozolin on anxiety but not sociality tests.

The researchers concluded by stating that the consequences of "global contamination and stressful experiences encountered by living descendants is likely to have its own specific risk for males and females for a given spectrum of adverse outcomes. Importantly, the gene expression patterns generally support the functional behavioral and brain transcriptome differences that were observed. The implications of these results for the protection of human health and endocrine-based questions target questions of morbidity and the quality of life."

"The most significant aspect of this paper is the striking difference between females and males at all levels, from physiology, behavior, brain chemistry, and gene expression in neural networks," Crews says. "Females are much more sensitive when these two elements (ancestral exposure and stress during adolescence of the descendants) are combined. This, in turn, provides a new way of viewing the effects of nature (ancestral exposure) and nurture (stress during adolescence) in shaping the adult phenotype and the importance of sex differences. The latter is very much in line with the recent mandate by NIH to consider both sexes in future studies in biomedical research. Finally, it illustrates the value of considering how modern day animals whose ancestors have been exposed to EDCs perceive and respond differently to common challenges in their life history."

COUPLES WITH HIGH CHOLESTEROL TAKE LONGER TO CONCEIVE

Couples may take longer to conceive a child when one, or both partners, has high cholesterol, according to a new study published in the *Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Enrique F. Schisterman, MS, PhD, of the National Institutes of Health's Eunice Kennedy Shriver National Institute of Child Health and Human Development in Bethesda, Md., examined the rate of pregnancies among 501 heterosexual couples trying to conceive in Michigan and Texas from 2005 to 2009. Of the couples who were part of the Longitudinal Investigation of Fertility and the Environment (LIFE) study, 347 became pregnant over the course of 12 months, 54 couples did not conceive a child, and 100 couples withdrew from the study, including some whose plans to have a child changed.

The scientists measured the total and free amounts of cholesterol in the blood of the couples and found that couples in which one or both partners had high levels of cholesterol took longer to become pregnant.

The authors concluded that serum-free cholesterol concentrations in both men and women are associated with time to pregnancy, highlighting the importance of cholesterol and lipid homeostasis for male and female fecundity. "In addition to raising the risk of cardiovascular disease, our findings suggest cholesterol may contribute to infertility," Schisterman says. "Our results suggest prospective parents may want to have their cholesterol checked to ensure their levels are in an acceptable range."

PEOPLE WITH T2D ACHIEVE SUPERIOR OUTCOMES WITH INSULIN PUMPS VS. INSULIN INJECTIONS

Patients with type 2 diabetes achieve better glucose control with insulin pumps than their counterparts who administer multiple daily injections, according to a study recently published in *The Lancet*.

Researchers led by Yves Reznik, MD, of the Endocrinology and Diabetes Department, CHU Côte de Nacre, in Caen Cedex, France, wrote, "Many patients with advanced type 2 diabetes do not meet their glycated haemoglobin targets, and randomised controlled studies comparing the efficacy of pump treatment and multiple daily injections for lowering glucose in insulin-treated patients have yielded inconclusive results. We aimed to resolve this uncertainty with a randomised controlled trial (OpT2mise)."

The global, randomized, controlled study analyzed 331 patients, ranging in age from 30 to 75 years, from Canada, Europe, Israel, South Africa, and the U.S. The results showed that those using insulin pumps achieved a mean A1C (average blood glucose) reduction of 1.1% compared to only a 0.4% reduction by those using multiple daily injections. This improvement in glucose control was achieved without any episodes of severe hypoglycemia. In addition, those in the insulin pump group lowered the total daily dose of insulin by more than 20%. There was no difference in weight gain between the two groups.

The authors concluded, "In patients with poorly controlled type 2 diabetes despite using multiple daily injections of insulin, pump treatment can be considered as a safe and valuable treatment option."

PCOS LINKED TO **LOW-GRADE INFLAMMATION DURING PREGNANCY**

Women who have polycystic ovary syndrome (PCOS) are more likely to experience chronic low-grade inflammation during pregnancy than their healthy counterparts, according to research recently published in the *Journal of Clinical Endocrinology & Metabolism (JCEM)*.

Investigators led by Stefano Palomba, MD, of the Arcispedale of Santa Maria Nuova of Reggio Emilia in Reggio Emilia, Italy, evaluated 150 pregnant women who had PCOS and 150 pregnant women of about the same age and body mass index, tracking biological markers of inflammation. They found that expectant mothers with PCOS had significantly higher markers of inflammation, including white blood cell counts and C-reactive protein.

"Women who have PCOS often exhibit low-level inflammation," Palomba says. "Our research found this state of inflammation worsens during pregnancy. Other studies have identified a connection between inflammation biomarkers and pregnancy complications such as pre-eclampsia and gestational diabetes. The abnormal inflammation seen in women with PCOS may be a factor in the development of these conditions."

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gathering STORM

One of the most confounding endocrine emergencies in history, thyroid storm is no longer a death sentence. Here's a look at what's new on the horizon in the prevention, recognition, and treatment of this once fatal malady.

By Kelly Horvath

Once approaching 100% mortality only a century ago, thyroid storm remains one of the most life-threating endocrine emergencies at a 10% to 20% mortality rate even with advances in prevention, recognition, and treatment. Though rare, the confluence of circumstances that aggravates thyrotoxicosis so drastically leaves devastation in its wake, failing prompt treatment.

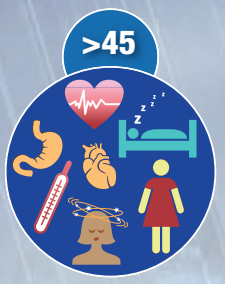
Chasing the Storm

Accounting for the persistently high mortality rate is that multiple body systems are pushed beyond their ability to compensate for the existing high thyroid hormone (TH) level. "Each of the features of uncomplicated hyperthyroidism is exaggerated to an extreme in thyroid storm, leaving not a second to lose," says Colonel Henry B. Burch, MD, professor of medicine and chair of the Endocrinology Division of the Uniformed Services University of the Health Sciences, in Bethesda, Md., endocrinology consultant to the Office of the U.S. Army Surgeon General, and Endocrinology Service at the Walter Reed National Military Medical Center, in Bethesda.

The definitive cause, however, remains elusive. "Our best clue is a list of known precipitants associated with a sudden increase in thyroid hormone in the circulation," Burch says (see box, p. 12). "Therefore, the key to survival is making the diagnosis."

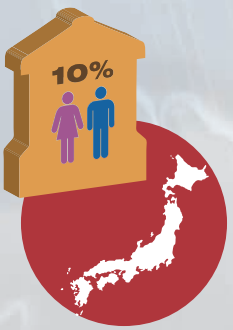
Making the diagnosis is not quite so straightforward, however. Patients can present with symptoms of sepsis, stimulant intoxication, or coma; go undiagnosed and, therefore, untreated; and die from multisystem decompensation. To further complicate diagnosis, there is no such thing as the "typical patient." Although universally accepted criteria do not exist for diagnosing thyroid storm, in 1993, Burch and colleague Leonard Wartofsky, MD, professor of medicine, Georgetown University School of Medicine and editor-in-chief of the *Journal of Clinical Endocrinology & Metabolism*, introduced the empirically derived, Burch-Wartofsky-Point-Scale (BWPS) to assess the likelihood of thyroid storm based on quantitative clinical criteria.

About 200 million people worldwide have some form of thyroid disease.
— Thyroid Foundation of Canada



Thyroid storm is assessed by the Burch-Wartofsky score. A score above 45 suggests thyroid storm.
— Medical Clinics of North America

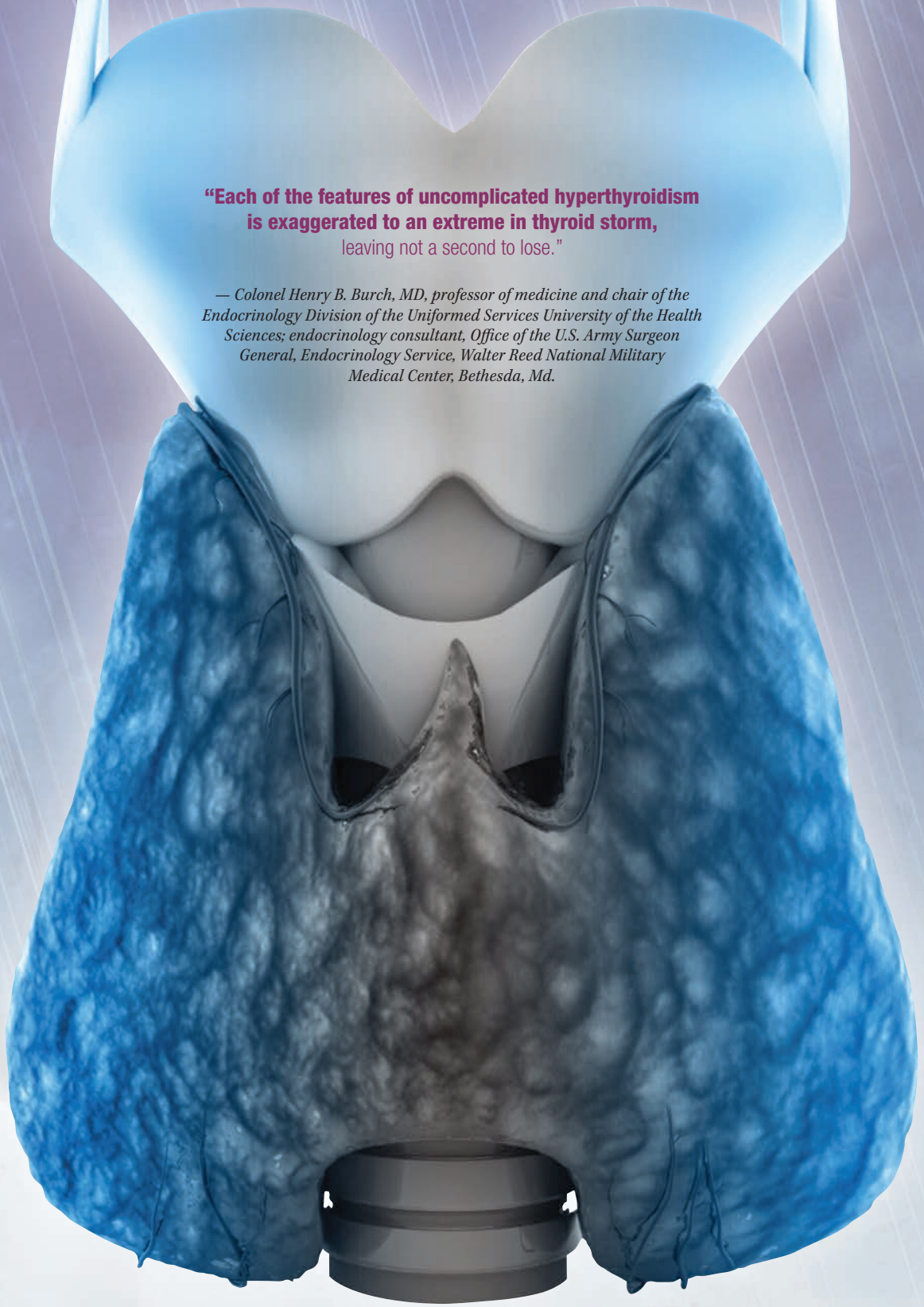
Atrial fibrillation can occur in up to 40% of patients with thyroid storm.
— Endocrinology, Diabetes & Metabolism Case Reports



Thyroid storm has a more than 10% mortality rate in Japan.
— Thyroid

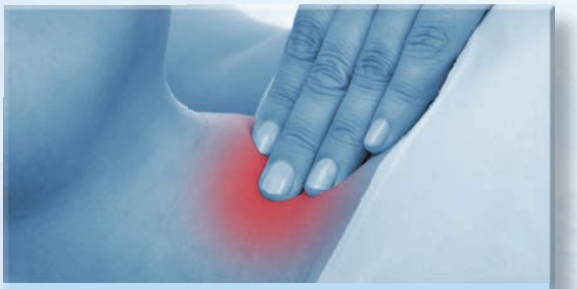
"Each of the features of uncomplicated hyperthyroidism is exaggerated to an extreme in thyroid storm, leaving not a second to lose."

— Colonel Henry B. Burch, MD, professor of medicine and chair of the Endocrinology Division of the Uniformed Services University of the Health Sciences; endocrinology consultant, Office of the U.S. Army Surgeon General, Endocrinology Service, Walter Reed National Military Medical Center, Bethesda, Md.



AT-A-GLANCE

- The cardinal manifestations of thyroid storm are fever, disproportionate tachycardia, neurologic disturbances, and gastrohepatic dysfunction.
- Recognizing and avoiding precipitants in a hyperthyroid patient is key for clinicians to prevent tipping over into a thyrotoxic crisis.
- Be alert for systemic decompensation in a patient with established thyrotoxicosis as well as for unusual presentations, such as coma or those that resemble stimulant drug intoxication or sepsis.



PRECIPITANTS OR TRIGGERS of Thyroid Storm

Conditions associated with a rapid rise in thyroid hormone levels

- Withdrawal of antithyroid drugs
- Radioiodine therapy
- External beam radiation therapy
- Thyroid "poisoning" (overdose of thyroid hormone)
- Vigorous thyroid palpation
- Iodinated contrast dyes
- Thyroid bed trauma
- Thyroid surgery

Conditions associated with an acute or subacute nonthyroidal illness

- Nonthyroidal surgery
- Infection
- Cerebrovascular accident
- Pulmonary thromboembolism
- Parturition
- Diabetic ketoacidosis
- Emotional stress

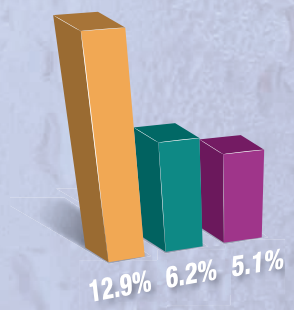
From Warnock and Burch, Endocrine Press, 2014

Yet even a single day for the clinician to arrive at the diagnosis can be too late. "You need a good clinical indication," Burch says. These include signs of systemic decompensation, such as cardiovascular dysfunction (e.g., congestive heart failure, cardiomyopathy, cerebrovascular accident, pulmonary thromboembolism) gastrointestinal (GI) dysfunction, and central nervous system (CNS) disturbance (e.g., anxiety, psychosis, global hyperkinesis), in addition to signs and symptoms of hyperthyroidism, such as high temperature, tachycardia, hyperdefecation, and a high TH level. "Then you throw everything you've got in your arsenal at it."

However, making the diagnosis is by no means simply a matter of a TH level increased beyond what constitutes hyperthyroidism or thyrotoxicosis. In fact, the BWPS awards a score independently from TH level. "It's not a level—it's a patient's ability to compensate," says Stephanie L. Lee, MD, PhD, director of the Thyroid Health Center of the Boston Medical Center, and associate professor of Medicine at Boston University School of Medicine. The degree of excess TH is not necessarily more profound than that seen in uncomplicated thyrotoxicosis, but a catalyst, such as infection or childbirth, causes the patient to decompensate and tip over into thyroid storm. "The diagnosis is clinical, based on the presence of a known precipitant plus thermodynamic dysregulation and cardiovascular, CNS, and GI dysfunction," Lee says, "and a key point is that the fever is out of context with any existing infection."

In 2012, Takashi Akamizu, MD, PhD, of Wakayama Medical University, Japan, and the Japanese Thyroid Association (JTA), introduced a qualitative diagnostic system. "Diagnostic Criteria, Clinical Features, and Incidence of Thyroid Storm Based on Nationwide Surveys" published recently in *Thyroid*, was the largest case series of thyroid storm conducted to date, comprising retrospective analysis of 282 definite and 74 suspected cases from 2004 to 2008. Their system grades thyroid storm based on the existence of one or more of the five BWPS diagnostic criteria plus thyrotoxicosis. TS1 (definite) includes CNS plus one other manifestation or three manifestations other than CNS. TS2 (suspected) includes two manifestations other than CNS or history of thyroid disease, presents with exophthalmos and goiter, and meets either of the criteria for definite cases.

"The JTA system was also largely empirically derived and includes features that mirror those in the BWPS," Burch says. The difference lies in its sensitivity. "The JTA system may result in the selection of a slightly smaller group of patients for aggressive therapy," Burch adds. However, the finer point remains that thyroid storm is not simply a matter of TH level — it's a much more complicated clinical picture and a more complex etiology. Therefore, the two diagnostic systems may work most effectively in tandem. "There was a significant correlation between our diagnostic criteria and the BWPS, suggesting that both the BWPS and our criteria are helpful in diagnosing thyroid storm," Akamizu says. "As the next obvious step, therapeutic procedures that aim for a better prognosis should be created."



White non-Hispanic women were most likely to have had treatment for thyroid disease in 2008 (12.9%). This was higher than the treatment rates for Hispanic (6.2 percent) or black non-Hispanic (5.1%) women.

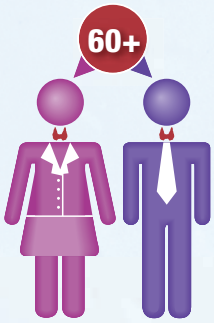
— Agency for Healthcare Research and Quality

Graves' disease is the most common cause of hyperthyroidism.

— American Thyroid Association

Weathering the Storm

Catching thyroid storm in the impending stage promotes the best chance of patient survival. The treatment approach is three-pronged: 1) make the diagnosis sufficiently early; 2) determine etiology and treat to reverse (e.g., antibiotics for infection); and 3) resuscitate and initiate supportive care (e.g., antipyretics, fluids, nutrition, telemetry, invasive monitoring), all of which happens concurrently. "Then there are caveats that make medical treatment very complicated," Lee says. Reducing the TH concentration and preventing its peripheral actions must happen (optimally within 48 hours), as clinicians have known since the 1920s, but treating with iodine, which blocks both synthesis and release, can

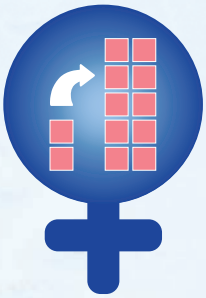


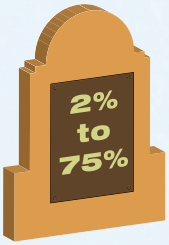
Hyperthyroidism is more likely in people older than 60.

— National Endocrine and Metabolic Diseases Information Service (NEMDIS)

Women are two to 10 times more likely than men to develop hyperthyroidism.

— NEMDIS





Even if diagnosed early, reported mortality rates for thyroid storm have ranged from 2% to 75% in hospitalized patients. *— Thyroid*

only be done at least one hour after antithyroid drug (ATD) therapy has been instituted. Propylthiouracil (PTU) blocks the synthesis of thyroid hormones and inhibits the peripheral conversion of T4 to T3, but because of the risks associated with PTU, "you have to balance how severely T3 toxic the patient is with how severely they are decompensating, and then switch to a safer drug, such as methimazole," Lee explains. Because the thyroid gland is unique in that it stores pre-formed TH, blocking synthesis is not enough to eliminate the excess TH; therefore, iodine must also be given. β-Blockers (e.g., propranolol) treat target organ effects. If this combination of drugs is unsuccessful in lowering thyroid hormone levels, dialysis and plasmapheresis can be undertaken as a last resort—"when your back is against the wall," Lee adds.

Another possible complication to watch for can result from cooling the extremely hyperthermic patient with blankets or alcohol baths, which paradoxically can raise the temperature if the patient starts to shiver, Lee says.

Storm Abatement

With proper treatment, improvement is generally seen within two days, and full recovery is seen in one week. "Then plan for definitive therapy," Burch says. "Once the patient is euthyroid, institute radioiodine or thyroidectomy, noting that with radioiodine, iodine given during treatment of thyroid storm must be cleared over several weeks."

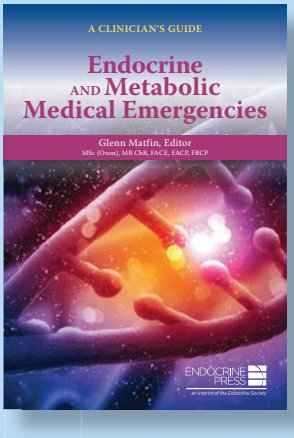
Two vital points for clinicians are to educate patients and to avoid precipitants. "Patients should be alert for fever or confusion, and clinicians should avoid abrupt ATD discontinuation (unless there is a major adverse drug effect), pretreat high-risk patients with ATDs before radioiodine therapy, and avoid surgery in thyrotoxic patients — completely correct thyrotoxicosis before elective surgery," Burch says.

With the mortality rate still so relatively high, this confounding syndrome warrants continued research into effective treatment. As experts agree, early detection is critical, but with the physiologic complexity that thyroid storm entails, early detection may not always suffice. EN

— Horvath is a freelance writer based in Baltimore, Md. She wrote about childhood obesity in the July issue.

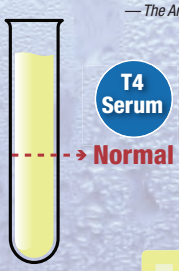
OnPOINT from the Endocrine Society

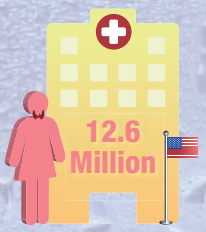
Henry B. Burch, MD, along with Alicia L. Warnock, MD, and David S. Cooper, MD, authored a chapter on treating thyroid storm in ***Endocrine and Metabolic Medical Emergencies*** from Endocrine Press, the first publication from the Society's new book imprint. Copies can be purchased at **www.press.endocrine.org.**



Patients with complicated thyrotoxicosis have T4 serum concentrations greater than twice the upper limit of normal.

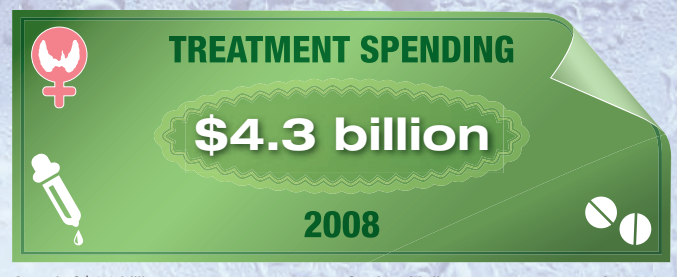
— The American Journal of Medicine





In 2008, 12.6 million women in the U.S. reported being treated for thyroid disease.

— AHRQ



A total of $4.3 billion was spent on treatment for thyroid disease among women in 2008.

— Agency for Healthcare Research and Quality (AHRQ)

Patients with complicated thyrotoxicosis are more likely to be uninsured or covered by Medicaid.

— The American Journal of Medicine

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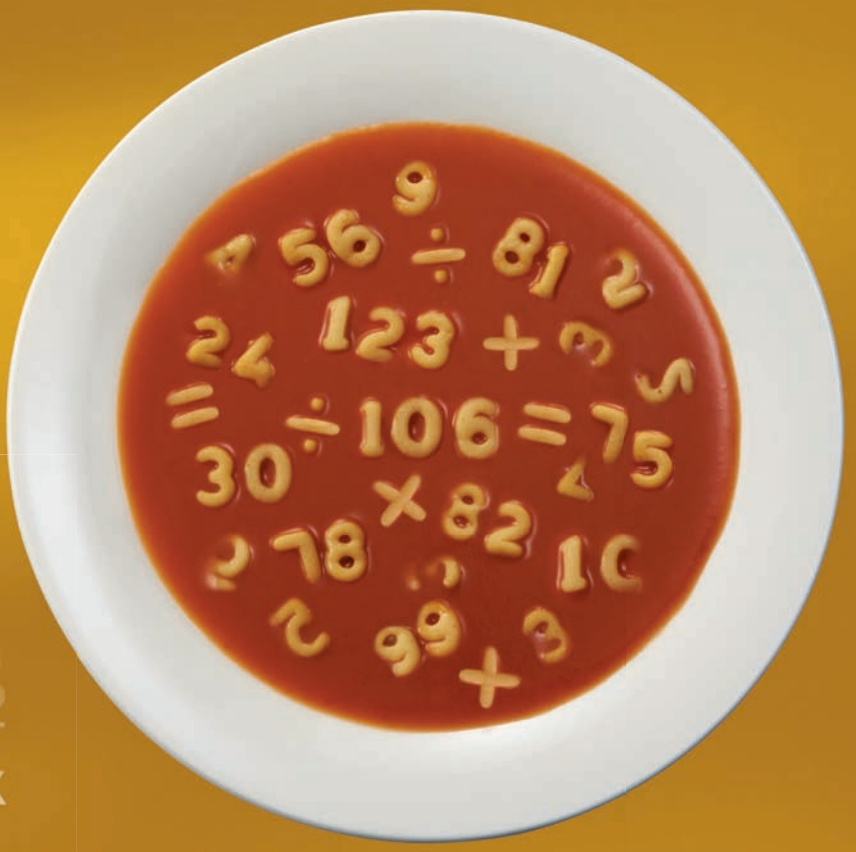

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Depression, Distress, and

When a diabetic patient is also dealing with depression, there are myriad issues to consider for both the physician and the patient. Everything from diabetes distress and medications to alcohol consumption can affect both conditions.

By Terri D'Arrigo

For people with diabetes, depression acts as a magnifier. It can worsen the pain of diabetes-related neuropathy and wreak havoc on blood glucose by disturbing appetite and sapping the energy required for regular physical activity. Diverse studies such as the Diabetes and Aging Study and the Pittsburgh Epidemiology of Diabetes Complications Study suggest that people with both diabetes and depression have more than twice the risk of early mortality than people who have only diabetes.

According to a May 2013 paper published in *SelfCare*, roughly 11% of adults with diabetes have major depression, and 31% have clinically relevant depression, harking back to a 2001 study in *Diabetes Care*. With statistics like that, it's a given endocrinologists will encounter patients with diabetes who are struggling with depression.

Yet more recent evidence, such as research presented by Lawrence Fisher, PhD, professor of family and community medicine at the University of California–San Francisco at the American Diabetes Association's 74th Scientific Sessions in June 2014, suggests that depressive symptoms in people with diabetes often point not to clinical depression, but to diabetes distress, a separate, if similar, condition. Whereas depression is overarching, diabetes distress is about the emotional burdens of managing diabetes in particular.

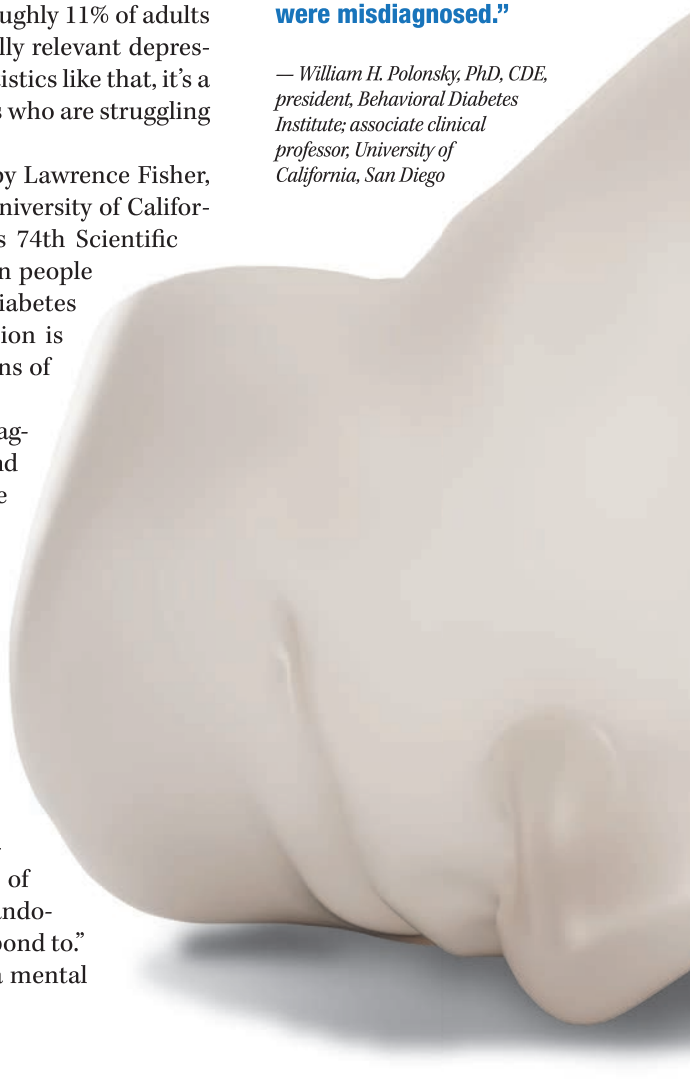
"Over the past few years, we have found that many cases diagnosed as depression really were more specific to how fed up and discouraged people were with their diabetes. Sometimes people were misdiagnosed," says William H. Polonsky, PhD, CDE, president of the Behavioral Diabetes Institute and associate clinical professor at the University of California, San Diego. "The catch is that if a patient has diabetes distress, giving that person an antidepressant is not going to make it go away."

Considering the time constraints of an office visit, endocrinologists tend to shy away from discussing their patients' emotional state, says Jeffrey S. Gonzales, PhD, associate professor in the Department of Medicine and the Department of Epidemiology and Population Health at the Albert Einstein College of Medicine in New York. "Endocrinologists often feel unprepared to deal with the question of depression with diabetes. They can feel like it's opening a Pandora's Box, or probing for things they may not have time to respond to."

Although a diagnosis of depression should come from a mental

"Over the past few years, we have found that many cases diagnosed as depression really were more specific to how fed up and discouraged people were with their diabetes. **Sometimes people were misdiagnosed."**

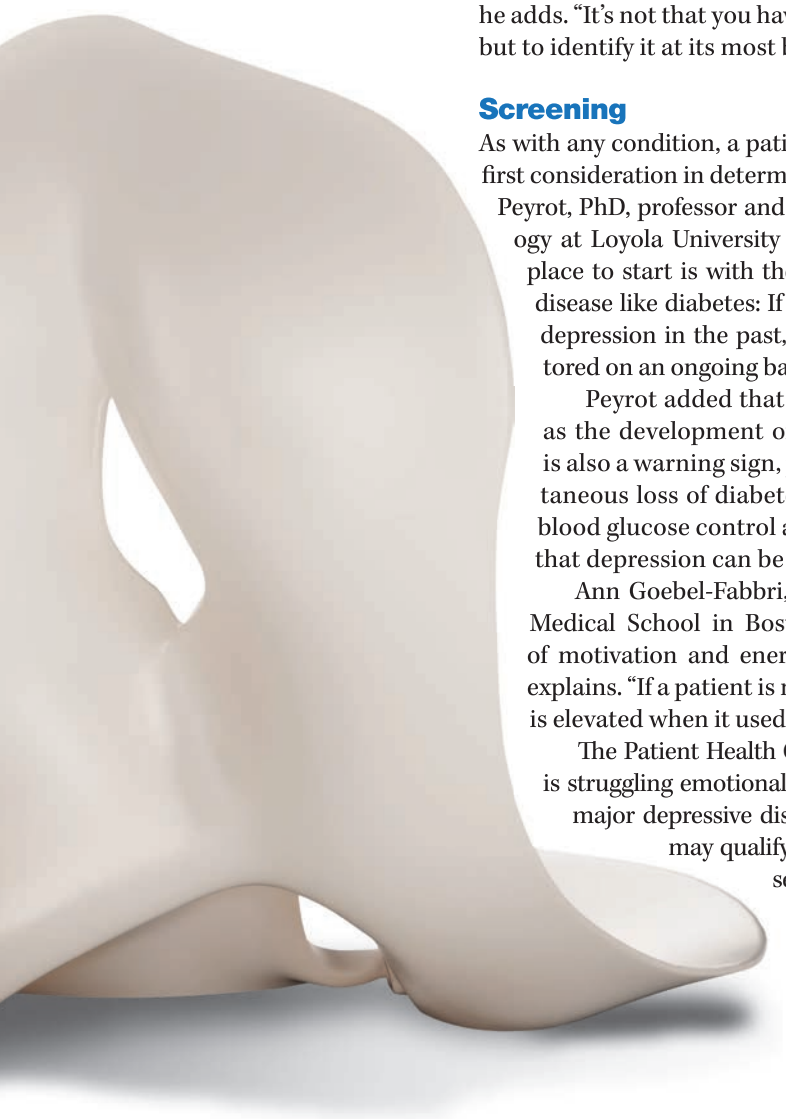
— William H. Polonsky, PhD, CDE, president, Behavioral Diabetes Institute; associate clinical professor, University of California, San Diego



DIABETES

AT-A-GLANCE

- Symptoms of depression overlap with those of a similar condition, diabetes distress, which is about the emotional burdens of managing diabetes in particular. Screening and treatment for diabetes distress are distinct from screening and treatment for depression.
- Endocrinologists should discuss alcohol use with their patients with diabetes, as alcohol abuse may indicate that the patient is struggling with depression or diabetes distress.
- Antidepressants and other drugs prescribed by mental health professionals may contribute to hypoglycemia, hyperglycemia, or both. Whenever medications are added, patients should be counseled to monitor their blood glucose more closely.



health professional, endocrinologists are in an excellent position to notice a decline in their patients' emotional well-being and make a preliminary determination about diabetes distress, he adds. "It's not that you have to fix the problem in 15 minutes, but to identify it at its most basic level."

"Endocrinologists often feel unprepared to deal with the question of depression with diabetes. They can feel like it's opening a Pandora's Box, or probing for things they may not have time to respond to."

— Jeffrey S. Gonzales, PhD, associate professor, Department of Medicine, Department of Epidemiology and Population Health, Albert Einstein College of Medicine, New York

Screening

As with any condition, a patient's medical history should be the first consideration in determining risk for depression, says Mark Peyrot, PhD, professor and chair of the Department of Sociology at Loyola University Maryland, in Baltimore. "The best place to start is with the idea that depression is a chronic disease like diabetes: If someone has been diagnosed with depression in the past, he or she should be closely monitored on an ongoing basis. It's a high level of alert."

Peyrot added that a major downturn in health, such as the development of a diabetes-related complication, is also a warning sign, particularly if there is also a simultaneous loss of diabetes control. "I wouldn't say that patients with poor blood glucose control are at an exceptionally high risk for depression, but that depression can be one of the reasons why they have poor control."

Ann Goebel-Fabbri, PhD, assistant professor of psychiatry at Harvard Medical School in Boston, agrees. "The hallmark of depression is lack of motivation and energy, and diabetes management requires both," she explains. "If a patient is not meeting the optimal glycemic target and the A1c is elevated when it used to be in the healthy range, that could be a red flag."

The Patient Health Questionnaire 9 offers a quick way to see if a patient is struggling emotionally, says Peyrot. "It's based on diagnostic criteria for a major depressive disorder. If there is a high symptom count, the patient may qualify for a diagnosis of depression and it would be worth sending the patient to [a mental health professional] who can make that determination."

But if the results are not clear, endocrinologists should take the time to drill down and assess the patient for diabetes distress, says Polonsky. "Ask

them how they feel about their diabetes, and if they can tell you one thing about their diabetes that is driving them crazy. That can give you an immediate sense of how big a problem you're looking at, and to what degree they are really grappling with diabetes distress," he says. "People with type 1 may say they feel like they never get a break. People with type 2 may say they are frustrated with trying to lose weight. Both may say they are tired of not reaching their goals despite their best efforts."

Tools such as the Diabetes Distress Scale 17, developed by Polonsky, Fisher, and their colleagues, contains questions designed to zero in on diabetes distress.

Endocrinologists should also discuss alcohol use, says Joshua J. Neumiller, PharmD, CDE, FASCP, associate professor in the Department of Pharmacotherapy at Washington State University's College of Pharmacy in Spokane. "People who are depressed may self-medicate with alcohol but often will not share this unless specifically asked," he says, adding that endocrinologists may find clues in a patient's glycemic control and could approach the subject that way. "Depending on what a patient drinks and how much, alcoholic beverages can have a considerable impact on glycemia. Alcohol use is also associated with delayed hypoglycemic reactions. This is very much an under-recognized phenomenon and worth looking into."

Treatment

Basic screening and a few targeted questions can provide a starting point for treatment. If the assessments strongly indicate diabetes distress, the patient may need to go no further than the endocrinologist's office to address it.

"With diabetes distress, the endocrinologist, diabetes nurse educator, or other clinicians in the endocrinology practice may be best qualified to talk to the patient because treatment will focus on better diabetes management," says Gonzalez.

However, if screening points to clinical depression, then a referral to a mental health professional is in order. The challenge there is fragmentation in healthcare.

"Even if you're a very sensitive endocrinologist who knows about depression and wants to get your patient appropriate care, insurance plans may separate mental health benefits from diabetes treatment [in a way that makes teamwork among clinicians difficult]," says Gonzalez. "It's like chopping people up into different diseases."

Endocrinologists or their staffs may have to do some legwork to find mental health professionals for appropriate referrals, says Goebel-Fabbri. "Be aware that many mental health providers will not have experience with diabetes, its treatments, and its goals. You may have to search for providers you can imagine your patients working with and keep a list."

She adds that the dearth of mental health professionals knowledgeable about the finer points of diabetes care may require endocrinologists to be proactive in communicating with counselors. "Information about diabetes should come from the diabetes team," she says. "It's unfair to burden the patient with teaching a counselor about it. Physicians and counselors will need to talk to each other." EN

— D'Arrigo is a health and science writer based in Holbrook, N.Y., and a regular contributor to Endocrine News. *She wrote about treating diabetes concurrently with cancer in the July issue.*

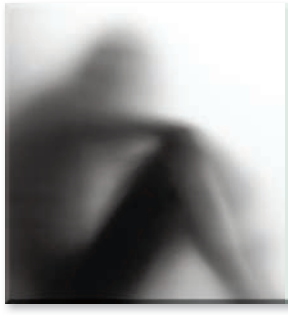
Going OFF SCRIPT

Joshua J. Neumiller, PharmD, CDE, FASCP, associate professor in the Department of Pharmacotherapy at Washington State University's College of Pharmacy in Spokane, encourages endocrinologists to stay abreast of any medications their patients with diabetes may be prescribed by mental health professionals and counsel their patients accordingly. "Many drugs are associated with case reports of hypoglycemia, hyperglycemia, or both, so whenever medications are added, patients should be made aware of the need to watch their blood glucose."

These drugs include amitriptyline, aripiprazole, bupropion (which is also prescribed for diabetic peripheral neuropathy), desipramine, duloxetine, nortriptyline, and venlafaxine, among others. He adds that some antidepressants, such as fluoxetine, can enhance the effects of diabetes drugs and raise the risk of hypoglycemia.

"It always comes down to risk versus benefit," Neumiller says. "If there are glycemic changes, providers will need to work together to determine if the patient is realizing sufficient benefits from the psychiatric medications to warrant their continued use, or whether it would be better to look at nonpharmacologic or alternative approaches to management."

— TD



TOOLS for Screening

Diabetes Distress Scale 17
http://familymedicine.medschool.ucsf.edu/pdf/bdrg/scales/DDS_all.pdf

Patient Health Questionnaire 9
http://www.integration.samhsa.gov/images/res/PHQ%20-%20Questions.pdf

*Data are from a 2006–2007 multinational survey, of which 2,334 patients were considered very high risk (defined as CHD plus two or more major risk factors). National Cholesterol Education Program (NCEP) Adult Treatment Panel III U.S. optional goal is <70 mg/dL (1.8 mmol/L). Countries in this analysis included the United States, Canada, Spain, the Netherlands, France, Taiwan, Korea, Brazil, and Mexico.

Reference: 1. Waters DD, Brotons C, Chiang CW, et al. Lipid treatment assessment project 2: a multinational survey to evaluate the proportion of patients achieving low-density lipoprotein cholesterol goals. *Circulation.* 2009;120:28-34.

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ONE FOR THE RECORD BOOKS

Another year, another annual meeting gone by, and another set of records broken. If you weren't in Chicago in June, here's just a small sample of the leading-edge research presented at ICE/ENDO 2014.

By Derek Bagley

The Endocrine Society and the International Society of Endocrinology held their joint meeting in Chicago for the first time since 1996, and **ICE/ENDO 2014** attracted more registrants in the history of the Endocrine Society at over 10,000, researchers submitted a record-breaking 3,273 abstracts, and attendees sat in on more than 350 presentations.

The event, as always, featured an all-star cast of speakers, both seasoned veterans and up-and-comers, delivering a wealth of exciting new developments, groundbreaking research, and information for advancing the state of endocrinology from bench to bedside. And while it was impossible to cover everything in the massive McCormick Place, here are some of the myriad highlights from **ICE/ENDO 2014**.

Diabetes Diagnosis and Management

The day before **ICE/ENDO 2014** officially kicked off, attendees gathered for the Endocrine Society's Diabetes Diagnosis and Management (DDM), a daylong, interactive workshop that focused on current issues in clinical diabetes management, namely cardiometabolic comorbidities and new treatment options, because the "prevalence of congestive heart failure in type 2 diabetes patients is quite high," according to Darren K. McGuire, MD, MHSc, of the University of Texas Southwestern Medical Center in Dallas. And Samuel Dagogo-Jack, MD, MSc, of the University of Tennessee Health Science Center in Memphis, says that patients with type 1 diabetes have "10 times the risk for cardiovascular disease." The challenge, then, is that diabetic patients who develop heart conditions, or are at risk of developing

these comorbidities, need to be handled differently and with greater care, and they may not always fit into neat, strict algorithms.

"We need to make good decisions based on what we know," says Robert Eckel, MD, of the University of Colorado Anschutz Medical Campus in Aurora, in his presentation updating attendees on the ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults.

Left: A full house listens intently to the newest developments in Diabetes Diagnosis and Management. *Below:* Robert Eckel, MD, of the University of Colorado, updates attendees on the ACC/AHA guideline on the treatment of blood cholesterol to reduce ASCVD risk in adults.

Of course, diagnosing and managing diabetes, and one of its major causes, obesity, is such a major issue in endocrinology that many of the plenary lectures, symposia, meet-the-professor sessions, and case management forums comprising **ICE/ENDO 2014** were dedicated to that very issue. Diabetes and obesity once again took center stage, because the obesity epidemic is still increasing. Steven R. Smith, MD, of the Translational Research Institute for Metabolism and Diabetes in Orlando, Fla., warns that by 2030, 10% of the U.S. population will be "severely obese." It seems like such a simple solution: Patients just need to lose weight. But as the various presentations at **ICE/ENDO 2014** covering obesity proved, that solution is anything but simple.

A "Losing" Battle

The battle to help obese patients lose weight starts with getting them to eat less. Weight loss comes with eating fewer calories. The course of action usually starts conservatively, with lifestyle changes, such as a strict diet and exercise routine, and then progresses to drug therapy. New research presented at **ICE/ENDO 2014** showed that the drug liraglutide, in combination with diet and exercise, led to significant weight reduction, as well as improvement in cardiovascular risk factors, based on a study of more than 3,700 overweight and obese nondiabetic adults.

Researchers led by Carel Le Roux, MD, PhD, of the Diabetes Complications Research Center at University College Dublin in Ireland, showed that on average, patients treated with 3 mg of liraglutide lost 5.4% more of their body weight than their counterparts on the placebo, achieving a total of 8%. The patients who received liraglutide also saw better improvements in their blood pressure and cholesterol. Presenting investigator David Lau, MD, PhD, of the University of Calgary, in Alberta, Canada, says that liraglutide, "as an adjunct, results in significant weight loss and cardiovascular risk improvements."

"Current obesity options are limited," Le Roux says. "There is a need for new treatment options for people who struggle with obesity and obesity-related diseases that can help in reducing their weight."

But when patients don't respond to drug therapies, surgery is the next step. Bariatric surgery, once considered extreme, is becoming more and more widely accepted as a safe and effective tool for managing obesity and even diabetes. Researchers at Brigham and Women's Hospital in Boston showed that gastric bypass improved diabetic patients' quality of life better than diet and exercise. Donald Simonson, MD, MPH, ScD, and his team found that weight loss surgery not only led to improvements in diabetic patients' physical and mental health, it also led to patients reporting improvements in the adverse effects of weight on their quality of life, such as self-esteem, sex life, public distress, and work.

Roux-en-Y gastric bypass (RYGB) surgery is also an acceptable therapeutic option for reducing the risk of heart disease in obese patients with T2D, according to researchers at the Joslin Diabetes Center in Boston. Su Ann Ding, MBBS, a research fellow at the Center, and her team found that patients who had RYGB surgery lost more weight than their counterparts in a lifestyle and medical modification group. The surgical group also saw better improvements in their blood sugar control, blood pressure, and cholesterol levels.

"There is emerging evidence highlighting the potential health benefits of bariatric surgery in managing obese patients with type 2

diabetes," says Ding. "In the past, lifestyle advice and medications provided the mainstay of treatment for this group of patients, but despite the substantial improvements in pharmacotherapy for adults with type 2 diabetes, many patients still do not achieve targeted health goals."

Hormones and Pregnancy

But what about obese patients for whom surgery is not an option, but have health goals they'd like to reach? Investigators in China showed that pregnant women who engage in an intensive lifestyle modification program early, in their first trimester, gain less weight and experience fewer pregnancy complications like gestational diabetes and preeclampsia, for which obesity is a risk factor.

The study's lead researcher, Guanghui Li, MD, PhD, of Capital Medical University in Beijing touched on the fact that obesity is now a global problem. "In the past," she says, "Chinese people were mostly thin, but now more and more are becoming obese." Li also pointed out that they found how hard it is for obese women to modify their lifestyles. "Healthcare providers should pay more attention to make practical and effective intervention strategies for obese pregnant women to enhance their compliance with the recommendations," she says.

Indeed, pregnant women may experience a variety of complications during their terms, but perhaps the most devastating is miscarriage. Researchers in the U.K. may have found a way to effectively predict a woman's risk of miscarriage by measuring blood kisspeptin levels.

Ali Abbara, MBBS, BSc, MRCP, a clinical research fellow in the Department of Investigative Medicine at Imperial College in London, presented findings of the first study showing that a single plasma kisspeptin level test during pregnancy can identify the risk for miscarriage in asymptomatic women. The investigators found that women who miscarried during the study had 60% lower kisspeptin levels than their healthy counterparts.

According to the authors of the study, miscarriage (pregnancy loss prior to 24 weeks of gestation) is the most common complication of pregnancy, affecting one in five pregnancies. Abbara says, "Being able to identify women at high risk of miscarriage may allow for improved monitoring and management of these pregnancies." However, Abarra warned against administering kisspeptin to at-risk women to prevent miscarriage, saying that may be something available "very far in the future."

Endocrine-Disrupting Chemicals

An issue that is certainly at hand right now is the call for the elimination of endocrine-disrupting chemicals (EDCs), which, as their moniker suggests, can cause damaging health effects by disrupting hormone function in the body.

Hydraulic fracking, a process of injecting numerous chemicals and millions of gallons of water deep underground to extract natural gas, has been repeatedly shown to cause adverse health effects in people, but as research presented at **ICE/ENDO 2014** showed, the endocrine-disrupting activity of those chemicals may be worse than previously thought.

Chris Kassotis, a PhD student at the University of Missouri in Columbia, and his team studied 24 fracking chemicals found in water samples collected from documented fracking spills in Garfield County, Colo. Many of the chemicals were found to block the estrogen receptor, androgen receptor, progesterone receptor, glucocorticoid receptor, and thyroid hormone receptor, all of which are necessary to stay healthy.

But many of these EDCs aren't just found around spill sites; they're found in consumer plastics, especially ones with hard plastics, and more and more research is pointing to their detrimental effects. The industrial chemical in question is bisphenol A (BPA), which has been shown to cause all kinds of health problems, and now research is incriminating these chemicals in even more diseases and disorders.

BPA exposure can hinder the effectiveness of a drug designed to target inflammatory breast cancer, an aggressive form of breast cancer with one of the worst survival outcomes. Gayathri Devi, PhD, an associate professor at Duke University in Durham, NC, explains that the reason for these poor outcomes is the high rate of treatment failure, and he says environment factors may explain this. Devi says, "This, to the best of our knowledge, is the first study to show BPA's effects in altering effectiveness of a targeted drug treatment approved for use in breast cancer patients, including those with inflammatory breast cancer."

Now that everyone's been back home and back to work for a month or so, it's time to start marking your calendars for the next meeting: **ENDO 2015** taking place in March, in sunny San Diego, so bring sunglasses. The future of endocrinology looks bright. EN

— Bagley is the associate editor of Endocrine News. *He wrote about competition in the April issue.*

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Pregnant Pause

The "Plan B" contraceptive pill has a remarkable failure rate in larger women.

By Melissa Mapes

Physicians may want to think twice before suggesting the "Plan B" pill to patients in need of emergency contraception (EC).

The results of a large European study show that the popular form of EC, levonorgestrel 1.5 mg, (Plan B pill) loses its potency in women weighing about 165 pounds and does not work at all in women weighing 175 pounds or more. Since the average weight of a woman in the U.S. is 166.2 pounds according to the U.S. Centers for Disease Control and Prevention (CDC), women have few options but to take a gamble on the only approved form of over-the-counter emergency contraception.

The study originally set out to compare the effectiveness of different types of EC. It studied the outcomes of the levonorgestrel "morning after" pill and the ulipristal acetate pill known as "Ella" in about 2,000 women. The lead author, Anna Glasier, MD, honorary professor of Obstetrics and Gynecology at the University of Edinburgh, in Scotland, and a world-renowned expert on EC, decided the data would be more practical if it could be used to identify at-risk patients.

"Somewhere between 90% to 95% of women who take emergency contraception do not appear to be at great risk of pregnancy, so if you could work out who was genuinely at risk, it might help you as a clinician," she explains.

She and her team conducted a meta-analysis and found a worrisome pattern: Levonorgestrel consistently failed in heavier women. Generally, levonorgestrel prevents about 50% of pregnancies that would have occurred without intervention, but when Glasier factored in weight, the effectiveness changed drastically. Women with a body mass index (BMI) of 25 or higher experienced decreased efficacy, and the pill stopped working entirely in obese women with a BMI of 30 or higher. In fact, obese women that took levonorgestrel were slightly more likely to become pregnant, 5.8%, than women who did not take EC at all, 5.6%. The number of obese women included in the study was small, but still statistically significant.

These findings elicited a change in the patient information packets of the European levonorgestrel EC that reflects the drug's impotence in overweight and obese women. The FDA is currently reviewing the evidence and considering a change to U.S. labels, but most women are still unaware of the drug's limited efficacy. Reports by National Public Radio state that physicians treating overweight and obese patients regularly see women who became pregnant after taking the Plan B pill.

This glaring issue was overlooked because the original research used to bring the Plan B pill to market did not focus on a representative sample of women in the

AT-A-GLANCE

- Obese women that took levonorgestrel were slightly more likely to become pregnant than women who did not take emergency contraception at all.
- The original research used to bring Plan B to market did not focus on a representative sample of women in the U.S. and Europe.
- Ella bested Plan B by half, with about 50% fewer pregnancies than those taking levonorgestrel.
- The only affordable, convenient form of emergency contraception for women in the U.S. is over-the-counter levonorgestrel, and it is for sale without any warning of its ineffectuality in larger women.

U.S. and Europe. It obtained approval from the FDA based on data from the World Health Organization in which the average BMI of participants was too small to see the effects of weight. "If you look at the first study, they reported the BMI and the mean was 22 with a standard deviation of plus or minus three. So these were not, by and large, very heavy women," Glasier explains.

More Weight, Less Efficacy

Several theories exist as to why the levonorgestrel pill fails in women over a certain weight: the dilution of the steroids in a larger blood volume; hormones becoming sequestered in fat cells; or the drug might be metabolized differently in a larger person. Yet nothing is definitive. "There is a lot of evidence that certain contraceptives are less effective in heavier women, although the studies haven't really been of really good quality. None, including ours, have been designed to look specifically at the relationship between effectiveness and weight," Glasier says.

Quite possibly, a larger patient simply needs a larger dose of the drug. "It is not really surprising because if you do studies on animals you dose them on a weight basis; however many milligrams per kilogram. The only reason that we don't do that with human medication is because it would just be so horribly complicated," Glasier continues.

The only consolation to the dismal success rate of levonorgestrel is that resulting infants are not adversely affected if a patient still becomes pregnant. Glasier insists there is no evidence for concern over a baby's future health due to a mother ingesting Plan B or the Ella pill. That said, women should definitely be advised to consider other options.

Ella proved to be more effective than levonorgestrel regardless of weight and definitely performed better on overweight and obese women. Ella bested Plan B by half, with about 50% fewer pregnancies than those taking levonorgestrel. For both drugs, pregnancy risk is elevated by additional factors unrelated to a patient's weight. Women who had intercourse around the time of ovulation had a fourfold increase in the likelihood of pregnancy compared to women having sex outside the window of fertility. Those who had unprotected sex after using either pill type were also more likely to get pregnant.

The IUD Option

Due to these mitigating factors, Glasier recommends the copper intrauterine device (IUD) as a first line of defense. It offers a 95% success rate as emergency contraception, making it the most effective option by far. "The big advantage, of course, is that once it's in place you can keep it in place and it is a highly effective ongoing contraceptive until you want to get pregnant and fertility comes back to normal within a week."

Ideally, of course, women should avoid the need for EC entirely by getting a copper or Mirena IUD or a hormonal implant before an emergency arises. Glasier describes these options as "independent of compliance," meaning that patients do not need to remember to take a daily pill or follow other such instructions. But when it is too late for preventative steps, the copper IUD is the way to go.

Unfortunately, an IUD is not available from pharmacies and a lot of women do not like the idea of having a foreign object inserted into their cervix. In the U.S., it is much more expensive than taking an emergency contraception tablet. A lack of health insurance coverage could make the costs prohibitive, and the extra steps involved may deter some patients from taking action.

The Ella pill also requires a visit to a doctor and a prescription, which prohibits some women from access. Glasier still recommends this option over Plan B if a woman is not willing or able to obtain a copper IUD.

For now the most affordable and convenient form of emergency contraception for women in the U.S. is over-the-counter levonorgestrel, and it is for sale without any warning of its ineffectuality in larger women. Those who still become pregnant will have to think of a "Plan C." EN

— Mapes is a Washington D.C.–based freelance writer. She wrote about diabetes social networks in the December issue.

Emergency Contraception LINES OF DEFENSE

- **1st: Copper IUD**
  Works 98-99% of the time and continues to prevent pregnancy for up to 10 years, but fertility will return to normal within a week of removal.
- **2nd: Ulipristal acetate, or "Ella"**
  More effective than the levonorgestrel in women of all sizes but still requires a prescription.
- **3rd: Levonorgestrel, or "Plan B"**
  Only works half the time on average and is unlikely to work at all in women over 175 pounds.

LIGHTEN THE LOAD

If you're burning the midnight oil, you're also using a lot of electricity. Here are some simple tips to make your lab more environmentally friendly.

By Melissa Mapes

At Penn State University, lab buildings cost around $5 to $10 per square foot in utilities, while office space uses under $2 per square foot. This discrepancy is typical across universities and hospitals. An average laboratory will use three to five times more energy than an office or classroom. When you take into consideration water consumption and hazardous waste, the gap grows much larger.

Penn State saved an estimated $672,722 in operating costs after putting in place a comprehensive energy-saving project. But, unfortunately, the financial costs of running "green" programs more often outweigh the monetary savings from smaller energy bills and less trash. This has inhibited most labs from implementing similar environmental plans in the past. However, an increased consciousness about sustainability has caused green initiatives to pop up across the country and world.

The greatest progress has been made at universities like Penn. Many have established internal accountability programs to satisfy the demand among staff, faculty, and students for greener practices. Campus- or hospital-wide cooperation naturally leads to the greatest impact, but there are steps that individuals can take to reduce unnecessary waste as well.

Flip the Switch

We all know to turn off the lights when we leave a room, but there are a lot more switches to hit when exiting a lab. The impact of these many machines buzzing needlessly adds up to a significant electrical drain. Kathryn Ramirez-Aguilar, green labs program manager at the University of Colorado, Boulder, told *The Scientist* that a refrigerated floor centrifuge uses the same energy as a pair of flat-screen televisions when left idle at 4°C.

A lack of awareness about such facts seems to drive a large portion of excess consumption. Ramirez-Aguilar discovered that 11 diffusion pumps used to generate ultra-low pressure conditions were perpetually running in a certain lab. She put five of the pumps on timers to automatically shut off during evenings and weekends,

which saved about 58,000 kWh of electricity and one million gallons of water in a year.

Some of the largest energy consumers are freezers, specifically the ultra-low temperature (ULT) variety. An average ULT takes up 16 to 35 kWh/day, and large universities might have hundreds running across its laboratories all day long. As a secondary effect, the heat from the freezers' motors will, in some cases, throw off the cooling system for an entire building and drive even more waste.

Experts suggest scheduled defrostings and cleaning out of superfluous samples. Labs can also share freezers to decrease the number needed and keep a careful inventory to maximize available space. Samples are often placed in ULTs when a less extreme temperature would suffice. Allen Doyle, sustainability manager at the University of California, Davis, pointed out to *The Scientist* that some researchers keep DNA samples at –80°C when –20° would do the trick.

Smart Inventory

Similarly, lab workers will often order things they do not need. This is especially true when it comes to chemicals. Large organizations and universities with multiple labs can share resources, but all labs should carefully record all inventory to avoid over-ordering or buying additional supplies when there are plenty of stores hidden in the stockroom.

An inefficient lab may allow buckets of chemicals to expire on the shelf while spending extra funds on unneeded replenishments if a smart tracking system is not in place. Ultimately, this leads to additional hazardous waste, as chemicals can be particularly difficult to recycle or dispose of.

The conversion to "green chemicals" can assuage the overall effects of such waste. To assist researchers in finding more environmentally friendly alternatives for their experiments, the Massachusetts Institute of Technology (MIT) tasked its Chemistry program and Environmental Health and Safety Office with developing a "purchasing wizard database." The project is one of several funded with help from the Environmental Protection Agency's (EPA) People, Prosperity, and the Planet grants.

Among the substitutions offered by the database, one of the most common has been ethidium bromide, a gel dye for DNA samples. Because it acts as a mutagen, this chemical can be dangerous to lab workers and causes waste removal issues. The wizard recommended Life Technologies' SYBR Safe in its place. This safer substance can be poured down the drain in many labs, though it does cost more than ethidium bromide.

Sash-ay Away

When you walk away from a fume hood, always close the sash. It provides the largest savings with the least amount of effort — up to $2,000 to $3,000 per year per hood in energy bills. Amorette Getty, co-supervisor of the LabRATS program at the University of California, Santa Barbara, claims that, "A fume hood uses the equivalent of three residential houses' worth of electricity per year."

The staggering consumption comes from the vacuum of air-conditioned lab air into the hood, necessitating the production of more air conditioning. *The Scientist* estimates that most labs require six or more air changes per hour under normal conditions, but an open sash can exponentially raise that amount. By keeping hoods closed for at least half the day, labs may be able to reduce energy needs by nearly 40%.

One easy way to remind scientists and students to close the fume hoods involves stickers. According to Getty, some laboratories have begun placing them on the side of each unit to show the amount of energy use for different heights of the sash, and report significant improvements in compliance.

Human Resources

All programs suggest a designated point person for coordinating green lab activities, from recycling to stickers. They can hold scientists and students accountable for poor practices and reward those that uphold high-efficiency standards. For laboratories that cannot afford a green project staff member, there are numerous self-checklists to assist with eco-friendly aspirations.

Although "going green" may not yet come with financial incentives for smaller operations and individuals, many researchers have come to expect and desire a greater emphasis on waste reduction, recycling, and environmental safety. The reward comes in the form of reputation and a satisfied conscience. EN

— Mapes is a Washington, D.C.–based freelance writer and a frequent contributor to Endocrine News. *She wrote about the state of endocrinology in the June issue.*

Green Lab CHECKLISTS

- Penn State's "What You Can Do In The Laboratory" ***http://sustainability.psu.edu/live/what-faculty-staff-can-do/what-you-can-do-laboratory***
- Duke University's "Guide to the Green Lab Certification Checklist" ***http://sustainability.duke.edu/action/labs/Green%20Lab%20Certification%20Checklist%20Guide.pdf***
- Campus Safety Health and Environmental Managment Association's (CSHEMA) "Green Lab Best Business Practices Checklist" ***http://www.cshema.org/uploadedFiles/CSHEMA_Content/Connect/Communities_of_Practice/Green%20Lab%20Best%20Business%20Practices%20Checklist_Final.pdf***
- Harvard's Green Labs program's "Top Ten Sustainable Lab Actions" ***http://www.green.harvard.edu/programs/green-labs***

STAR QUALITY

The EPA's Energy Star program has various guidelines and the steps needed to turn your lab into an energy-efficient workplace; methods to finance these strategies; products; and even case studies. A plethora of information can be found at ***www.energystar.gov.*** There are even government rebates available for using certain products.

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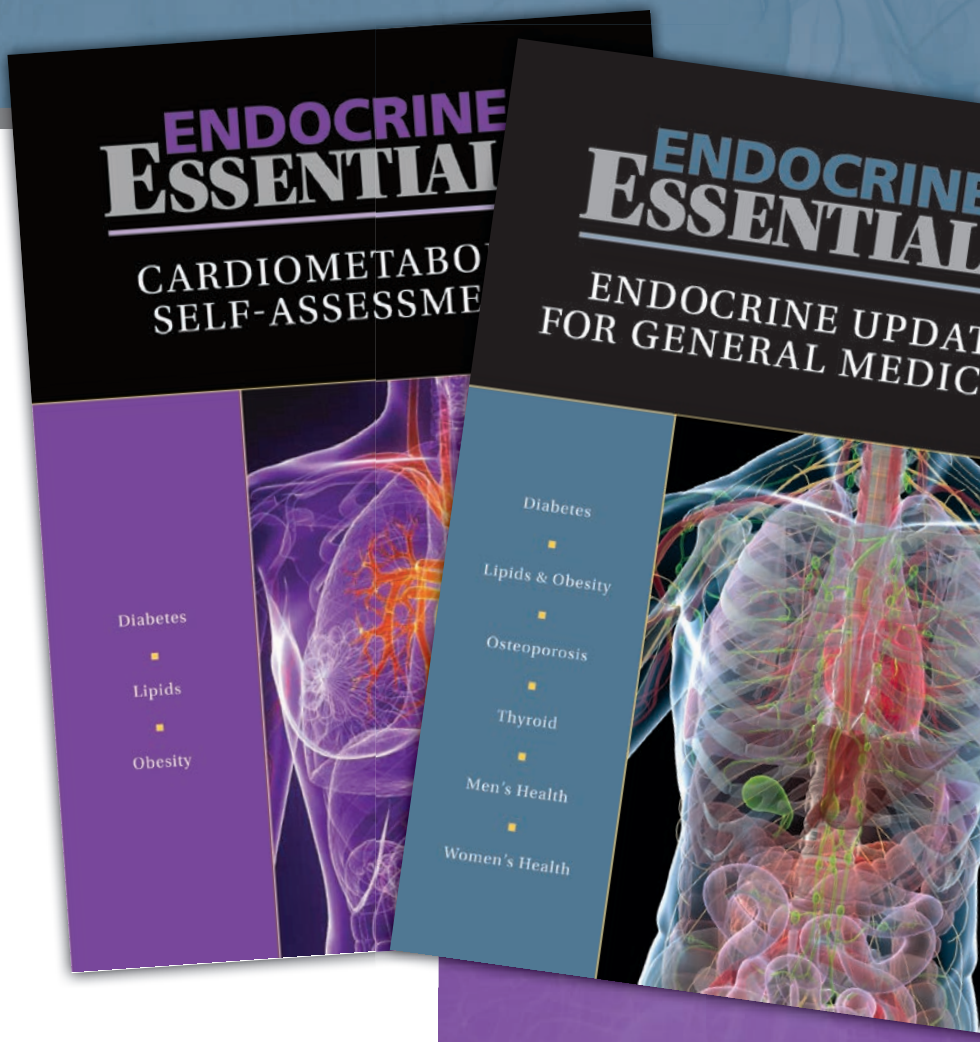
Endocrine Essentials



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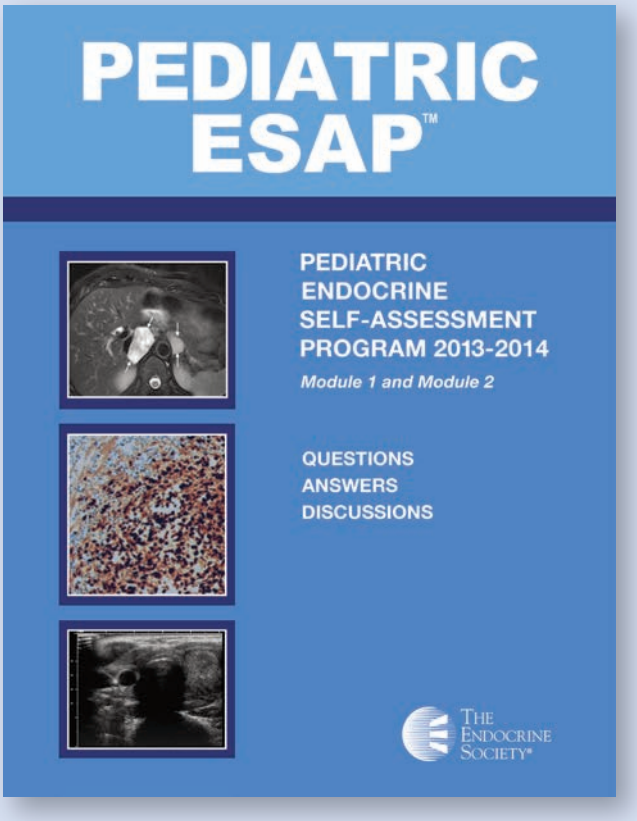

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ENDOCRINE SOCIETY

Endocrine Society Calls on **Congress to Stop Cuts and Keep America Safe and Healthy, Invest in Public Health**

New report documents devastating impacts of deep cuts to biomedical research.

By Mila Becker

On July 15, the Endocrine Society joined with the Coalition of Health Funding (CHF), which represents more than 90 public health advocacy organizations, to call on Congress to prevent further budget cuts to federal health programs.

At a standing-room-only briefing for congressional staff, the CHF released a new report, "Faces of Austerity: How Budget Cuts Hurt America's Health," documenting the dire consequences of Congress' deep cuts to public health programs in recent years. The Endocrine Society contributed to the report by writing a chapter illustrating how cuts in funding for the National Institutes of Health (NIH) have significantly impeded efforts to advance diabetes research.

"On average, a researcher has to write eight to 10 grants to get one.
The likelihood of a scientist with a highly regarded grant application successfully being awarded a grant has dropped from 31.5% in 2000 to a historic low of 16.8% in 2013."

— from the Endocrine Society's chapter of the "Faces of Austerity Report"

Broader Strategy

The report and briefing are part of a broader Society strategy to educate Congress about the impact of budget cuts on public health programs and advocate for prevention of further cuts. Just a tiny fraction of the federal budget goes toward supporting all of our nation's public health needs — everything from preventing disease, to keeping our food and drugs safe, to ensuring that Americans have access to primary care doctors.

Flat federal funding over the last decade has reduced that small pot of money to unacceptable levels. At a time when we should be taking advantage of scientific opportunities and building on previous discoveries, the NIH is operating at a level that is 20% below its FY 2003 budget. The Society wanted to make sure congressional offices understand the impacts of its budget cuts.

Public Health Crisis

Nationally, budget cuts have forced the layoffs of more than 50,000 public health professionals who monitor and respond to virus outbreaks, immunize children and the elderly, inspect restaurants, and care for the indigent. Public health departments in 33 states and the District of Columbia have reduced their budgets. Funds for public health overall, let alone the workforce, have been eroding for nearly a decade, and while there will be some limited sequester relief in 2014, sequestration threatens public health programs in 2015 and for years to come unless Congress does something to support a balanced approach to deficit reduction.

"More than 29 million people in this country have diabetes, and we desperately need to do something about it," says Richard J. Santen, MD, Endocrine Society president. "Cuts to health programs are slowing and sometimes halting potentially life-saving research. Investing in biomedical research funding is investing in ourselves, our families, and our communities and should not be further eroded."

The "Faces of Austerity" report is available online at ***www.cutshurt.org***. EN

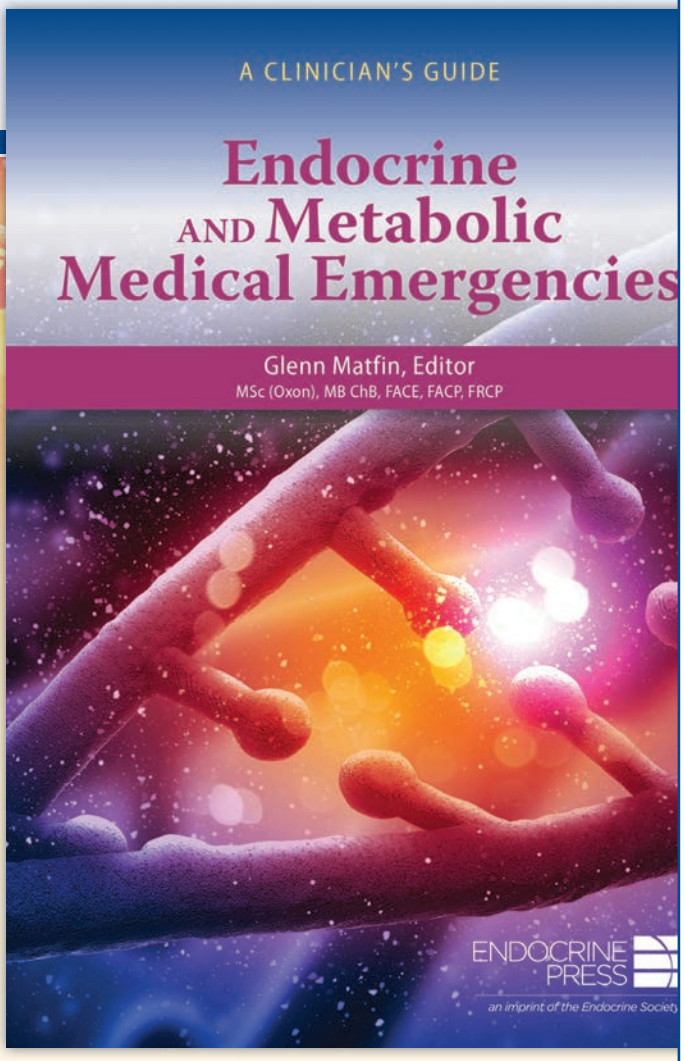
— Becker is the senior director of Advocacy & Policy Programs, at the Endocrine Society.

Take**ACTION**

Please help the Endocrine Society educate Congress about the value of biomedical research and the need to protect NIH from further cuts by participating in the Society's online advocacy campaign. Simply visit the Society's website at ***www.endocrine.org*** and click the Advocacy tab and "Contact Congress" to send a pre-written email to your congressional delegation. In addition, the Society encourages all Twitter users to tweet using the hashtag ***#cutshurt***.

GAIN NEW INSIGHT INTO TREATING COMPLEX ENDOCRINE EMERGENCIES

Editor, Glenn Matfin, MSc (Oxon)



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ENDOCRINE SOCIETY

AFFORDABLE CARE ACT
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Keep your body in balance

These are some of the benefits available under the Affordable Care Act. For further information about how you and your plan are affected, contact your plan administrator.

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Choose your primary care provider and your child's pediatrician within your network.

No lifetime dollar limit on most benefits. Annual dollar limits will be phased out in 2014.

No higher charges or denial of coverage because of a pre-existing condition.

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THE HEALTH INSURANCE MARKETPLACE
healthcare.gov

The Health Insurance Marketplace was established to make buying health coverage easier and more affordable. You can:

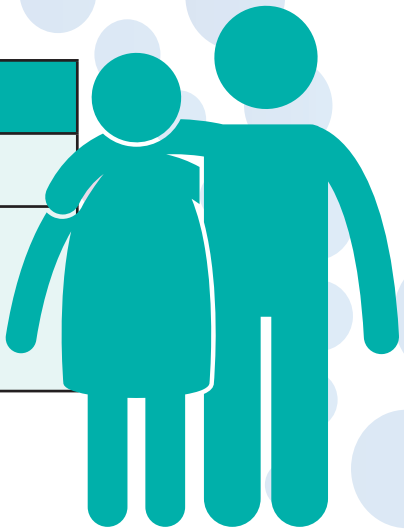
- compare health plans
- find answers to questions
- enroll in a plan that meets your needs

THE NEXT OPEN ENROLLMENT PERIOD:
NOVEMBER 15, 2014–FEBRUARY 15, 2015

WOMEN

- 18.6 million uninsured women have new opportunities for coverage
- Women cannot be charged higher insurance premiums than men
- No referrals from primary care provider before seeking OB-GYN services from participating OB-GYN specialists
- Covered preventive services and screenings include:
  - type 2 diabetes
  - breast cancer mammography

CHILDREN/YOUNG ADULTS



- Young adults can remain on their parents' plan up to age 26
- Many screenings, risk assessments and immunizations for children are covered:
  - congenital hypothyroidism (for newborns)
  - obesity

SENIORS

- Seniors with Medicare receive an annual wellness preventive visit at no cost
- Other preventive services covered include:
  - diabetes screening
  - mammograms
  - bone mass measurement
- Medicare drug discounts increase yearly until the coverage gap is closed in 2020

Patients 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.

Hormone Health NETWORK® FROM THE ENDOCRINE SOCIETY

Endocrine Society Honors
Sen. Dick Durbin with Biomedical Research Champion Award

The Endocrine Society presented U.S. Senate Assistant Majority Leader Dick Durbin (D-IL) with the Biomedical Research Champion Award during a ceremony at **ICE/ENDO 2014** in Chicago.

"I am honored to receive the Endocrine Society's National Biomedical Leadership Award and to share the Society's commitment to federal funding for biomedical research in order to help us live longer and healthier lives," Durbin tells *Endocrine News*.

The award recognizes and commends members of Congress who strive to advance endocrine research and enhance public understanding of health issues pertaining to the field of endocrinology. As a member of the Senate Appropriations Committee, Durbin has worked to accelerate and secure financial support for research.

"Sen. Durbin has led the way in acknowledging the importance of biomedical research to all Americans," says Teresa K. Woodruff, PhD, immediate past-president of the Endocrine Society. "He has fought to increase funding and create new revenue streams for the National Institutes of Health (NIH). I'm proud to honor my senator for his tireless efforts to advance research needed to identify the medical treatments of tomorrow."

In March, Durbin introduced legislation called the American Cures Act. The proposed bill, endorsed by the Endocrine Society, would create a trust fund to support a mandatory funding stream for biomedical research. The bill would increase funding annually for the NIH, Centers for Disease Control and Prevention, Department of Defense Health Program, and Veterans Medical and Prosthetics Research Program at a rate of 5%.

Durbin noted that with diabetes and many other endocrine diseases, the biggest obstacle to better treatments and cures is not lack of science, it's lack of money. "That is why I've introduced the American Cures Act," Durbin says, "which would make federal funding for cutting-edge biomedical research less political and more predictable. I look forward to working with the Endocrine Society on this effort." EN

(L to R): Outgoing Society president Teresa K. Woodruff, PhD, Sen. Dick Durbin (D-IL), and Leslie DeGroot, MD.

Endocrine Society Award for
Excellence in Science and Medical Journalism Awarded

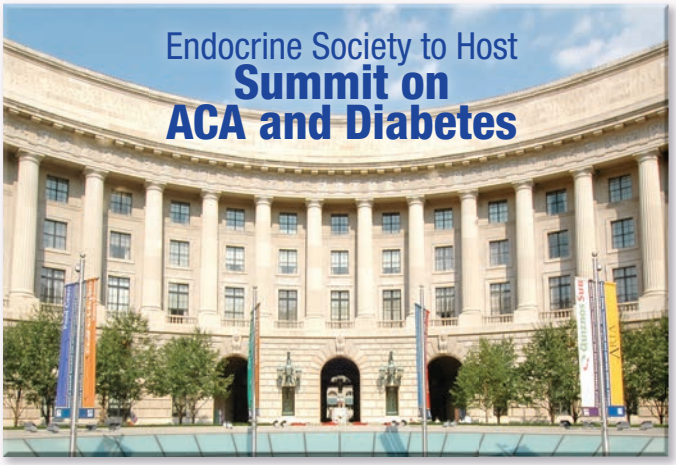
Freelance journalist Cathryn Jakobson Ramin (left) received the Endocrine Society's annual Award for Excellence in Science and Medical Journalism.

Ramin, of Mill Valley, Calif., was honored at **ICE/ENDO 2014** in Chicago, for her winning article, "The Hormone Hoax Thousands Fall For." The article was published in the October 2013 issue of *More* magazine.

Established in 2008, the Endocrine Society created the award to recognize outstanding reporting that enhances the public understanding of health issues pertaining to the field of endocrinology.

In her investigative article, Ramin examined the process of compounding medications and the health risks this can pose to women who are prescribed hormone therapy for hot flashes and other menopausal symptoms. Her coverage found inconsistencies in the level of hormones when identical prescriptions were filled by 12 different compounding pharmacies. She was recognized for her in-depth research and ability to clearly explain how hormones function in terms easily understood by the average reader.

The Award for Excellence in Science and Medical Journalism consists of a presentation at the Society's awards banquet, as well as travel and accommodations to attend the Society's Annual Meeting. EN



Endocrine Society to Host Summit on ACA and Diabetes

On Sept. 12, 2014, the Endocrine Society will host "ACA Implementation: Impact on the Patient with Diabetes" in the Atrium Ballroom of the Ronald Reagan Building in Washington, D.C.

The all-day conference will explore the impact of the Patient Protection and Affordable Care Act (ACA) on patients with diabetes. Specifically, the summit will explore:

- The current state of diabetes care in the U.S., including its epidemiology, prevalence, and challenges relevant to care management.
- The cost of diabetes care and the impact on various stakeholder groups, including individual patients, third-party payers, and healthcare systems.
- Intended benefits of the ACA and how this shift in healthcare policy may impact diabetes care and outcomes.

After the summit, attendees should have a much better understanding of the humanistic and economic burden of diabetes, as well as the challenges of diagnosis, treatment, management, and prevention of long-term complications. They will also get an in-depth appraisal of the ACA—both positive and negative—from various perspectives including those of physicians, private payers, as well as patients. There will also be a vigorous discussion of future healthcare policy recommendations that favor treatment options for patients with diabetes and therapies that could prevent the disease or its progression.

Among the speakers invited to the summit are Robert Vigersky, MD, Endocrine Society past president, director, Diabetes Institute, Walter Reed National Military Medical Center; Ann Albright, PhD, RD, director, Division of Diabetes Translation, Centers for Disease Control and Prevention; Sherita Golden, MD, MHS, associate professor of Medicine/Endocrinology and Metabolism, Johns Hopkins University; Patrick Conway, MD, MSc, deputy administrator for Innovation and Quality and Centers for Medicare and Medicaid Services; Carter Blakey, deputy director, Office of Disease Prevention and Health Promotion; Kelly Close, Close Concerns, as well as White House officials, congressional staff, key policy makers, and more.

The Ronald Reagan Building is located at 1300 Pennsylvania Avenue, NW. For more information, go to ***www.endocrine.org/meetings/policy-summit***. EN

Event CALENDAR

AUGUST 6 – 9, 2014, ORLANDO, FLA.
AADE14 – American Association of Diabetes Educators • *http://www.diabeteseducator.org/ProfessionalResources/AnnualMeeting/CorporateOpps/*

SEPTEMBER 2 – 6, 2014, SAN FRANCISCO, CALIF. Endocrine Board Review and Clinical Endocrinology Update • *Endocrine.org/SF*

SEPTEMBER 12, 2014, WASHINGTON, D.C.
ACA Implementation: Impact on the Patient with Diabetes • *http://www.endocrine.org/meetings/policy-summit*

SEPTEMBER 14 – 17, WASHINGTON, D.C.
10th International Meeting of Pediatric Endocrinology *www.pedsendo.org*

SEPTEMBER 15 – 19, 2014, VIENNA, AUSTRIA
50th European Association for the Study of Diabetes Annual Meeting • *www.easd.org*

Applications Being Accepted for the **Delbert A. Fisher Research Scholar Award**

If you're interested in the history of endocrinology, then you might be the ideal person to present the Clark T. Sawin Memorial History of Endocrinology Lecture at ENDO 2015 in San Diego in March as a recipient of the Delbert A. Fisher Research Scholar Award.

The Endocrine Society is currently accepting applications for the Delbert A. Fisher Research Scholar Award, which provides a $2,000 honorarium award to one recipient annually for scholarly work on the history of endocrinology. Initiated in 2011, the Delbert A. Fisher Research Scholar delivers the Clark T. Sawin Memorial History of Endocrinology Lecture and may submit a summary article to be considered for publication in *Endocrine News*. The application deadline is Aug. 29, 2014.

The Endocrine Society thanks Dr. and Mrs. Delbert A. Fisher for their generous support, which makes this award possible.

To learn more about the application process, visit: ***http://www.endocrine.org/awards/additional-society-awards/delbert-a-fisher-research-scholar-award***.

Past Clark T. Sawin Memorial History of Endocrinology Lecturers:

YEAR	LECTURER
2014	Eberhard Nieschlag, MD, FRCP, PhD
2013	Jesse Roth, MD
2012	Leonard Wartofsky, MD
2011	Michel F. Holick, MD, PhD
2010	D. Lynn Loriaux, MD, PhD
2009	John W. Funder, MD, PhD
2008	Neena B. Schwartz, PhD
2007	Michael J. Bliss, PhD

Society Journals Make the **Top of the GOOGLE SCHOLAR LIST**

Three of the Endocrine Society's journals were classified as the most influential in their field, according to data released in June by Google Scholar Metrics.

The top publication in Google Scholar's endocrinology category is *The Journal of Clinical Endocrinology & Metabolism (JCEM)*, with *Endocrinology* in the number two slot, and *Endocrine Reviews* rated number four. The Society's *Molecular Endocrinology* also made the top 20 list at number 11.

"The Editors and staff at *JCEM* are very proud of the Google Scholar rankings which confirm what we all believe to be the pre-eminence of *JCEM* amongst 120 journals in endocrinology," says Leonard Wartofsky, MD, MACP, editor-in-chief of *JCEM* and professor of medicine, Georgetown University School of Medicine; Department of Medicine, Washington Hospital Center. "We owe that success to our readers and members who submit their best work for publication and to our reviewers who provide expert critical analysis of the manuscripts submitted leading to publication of only the very best."

This system provides authors a quick and easy way to gauge the influence and visibility of the articles in various scientific journals. It also summarizes recent citations to a number of publications so authors can decide which journals are worthy of their research. Further, the articles are ranked in Google Scholar the same way researchers rank them: weighing the full text of each document, where it was published, who it was written by, as well as how often and how recently it has been cited in other scholarly literature.

Google Scholar ranks journals based on the h-index, which is a measurement that gauges the productivity as well as the impact of a published work by a specific scientist or author. The index is based on the author's most cited papers as well as the number of citations the author has received in other publications.

First suggested in 2005 by Jorge E. Hirsch — the H in h-index — a physicist at the University of California in San Diego, the h-index was developed to address the perceived faults of other measurements such as simply citing the total number of papers. Hirsh felt that by just citing the volume of published works did not necessarily mean said works were of the highest quality. The h-index addresses this conundrum by including the number of citations on a given paper in other scholarly publications.

The other major measurement of journal metrics is the impact factor, which was scheduled to be released at the end of July. EN

— Mark A. Newman

Revamped **Menopause Map Now Online**

The Hormone Health Network (HHN) recently released a "new and improved" Menopause Map™, an updated interactive online tool that is essentially a one-stop source for all things relating to menopause.

"The Menopause Map can be used by women of all ages to learn more about the hormonal changes that occur during all stages of menopause, which include: preparing for menopause, premature menopause, perimenopause, menopause, and postmenopause," says Cheretta Clerkley, director, Hormone Health Network, adding that "women who are currently on this journey should find it useful, and even fun, to use. An additional bonus is that the Network has developed tools for healthcare professionals because they are critical to helping women find the right treatment options. The healthcare professional microsite offers free tools to help medical professionals learn how to use this new interactive tool with their patients."

Clerkley states that HHN is committed to empowering all women when it comes to menopause. "With this in mind, we recognized it was time to provide a refresh of the current map to better educate women of all the stages of menopause, to provide additional information on managing symptoms, and to inform women on where to go for peer-to-peer support resources," she says. "This new version of the tool accomplishes these goals and enhances the women's experience with the map, while keeping the integrity of the original Menopause Map."

The Menopause Map can be accessed at ***www.menopausemap.org***. EN

This new site includes many new features implemented based on feedback from women:

- New and improved design
- Interactive e-magazine
- Print companion magazine
- Conversation starters
- Social media functionality
- Monthly E-newsletter with additional resources and tips
- Microsite with toolkit for health care providers

Hormones and Cancer

Committed to spanning basic, translational, and clinical research on the impact of hormones on all aspects of cancer biology

Benefits of publishing with *Hormones and Cancer*

- Easy-to-use online manuscript submission and tracking system
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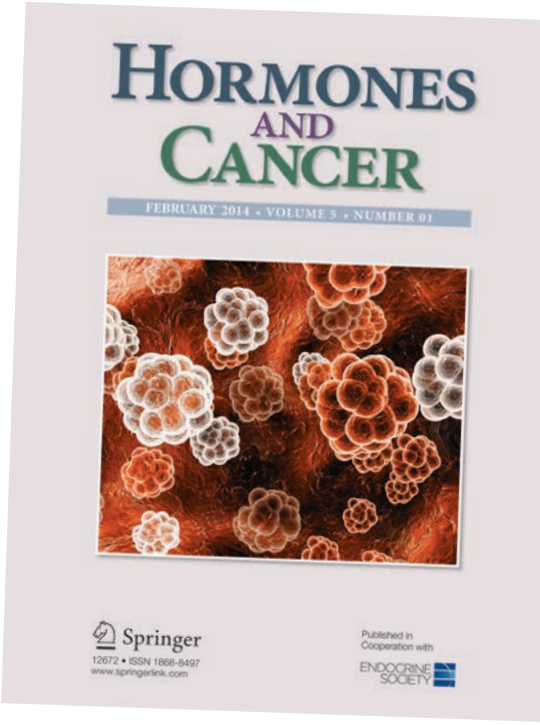

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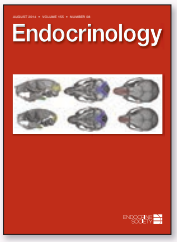
ENDOCRINE SOCIETY

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***.

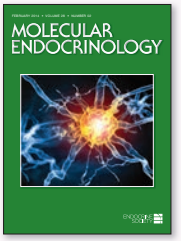
Persistent Apparent Pancreatic β-Cell Defects in Premenarchal PCOS Relatives • Laura C. Torchen, Naomi R. Fogel, Wendy J. Brickman, Rodis Paparodis, and Andrea Dunaif • *DI is decreased in peripubertal FDR girls, and this decrease persists as puberty progresses. These findings suggest that β-cell dysfunction is an early defect in glucose homeostasis preceding decompensation in glucose tolerance in FDR girls. T levels were increased in FDR girls earlier than previously reported, but these changes did not persist suggesting an earlier onset of pubertal increases in glandular androgen secretion in FDR girls.*

Long-Acting Progestin-Only Contraceptives Enhance Human Endometrial Stromal Cell Expressed Neuronal Pentraxin-1 and Reactive Oxygen Species to Promote Endothelial Cell Apoptosis • O. Guzeloglu-Kayisli, M. Basar, J. P. Shapiro, N. Semerci, J. S. Huang, F. Schatz, C. J. Lockwood, and U. A. Kayisli • *LAPC-enhanced NPTX1 secretion and ROS generation in HESCs impair HEEC survival resulting in a loss in vascular integrity, demonstrating a novel paracrine mechanism to explain LACP-induced AUB.*



Intrinsic Expression of a Multiexon Type 3 Deiodinase Gene Controls Zebrafish Embryo Size • Cuicui Guo, Xia Chen, Huaidong Song, Michelle A. Maynard, Yi Zhou, Alexei V. Lobanov, Vadim N. Gladyshev, Jared J. Ganis, David Wiley, Rebecca H. Jugo, Nicholas Y. Lee, Luciana A Castroneves, Leonard I. Zon, Thomas S. Scanlan, Henry A. Feldman, and Stephen A. Huang • *This study indicates that the embryonic deficiency of dio3, once considered only a placental enzyme, causes microsomia independently of placental physiology and raises the intriguing possibility that fetal abnormalities in human deiodination may present as intrauterine growth retardation. By mapping the gene structures and enzymatic properties of all four zebrafish deiodinases, we also identify dio3b as the first multiexon dio3 gene, containing a large intron separating its open reading frame from its selenocysteine insertion sequence (SECIS) element.*

Evidence of Contribution of iPLA2β-Mediated Events During Islet β-Cell Apoptosis Due to Proinflammatory Cytokines Suggests a Role for iPLAβ in T1D Development • Xiaoyong Lei, Robert N. Bone, Tomader Ali, Sheng Zhang, Alan Bohrer, Hubert M. Tse, Keshore R. Bidasee, and Sasanka Ramanadham • *These observations suggest that iPLA2β-mediated events participate in amplifying β-cell apoptosis due to proinflammatory cytokines and also that iPLA2β activation may have a reciprocal impact on ER stress development. They raise the possibility that iPLA2β inhibition, leading to ameliorations in ER stress, apoptosis, and immune responses resulting from LPC-stimulated immune cell chemotaxis, may be beneficial in preserving β-cell mass and delaying/preventing T1D evolution.*



ERβ- and Prostaglandin E2-Regulated Pathways Integrate Cell Proliferation via Ras-Like and Estrogen Regulated Growth Inhibitor in Endometriosis • D. Monsivais, M.T. Dyson, P. Yin, J.S. Coon, A. Navarro, G. Feng, S.S. Malpani, M. Ono, C.M. Ercan, J.J. Wei, M.E. Pavone, E. Su, and S.E. Bulun • *Overall, we demonstrated that E2/ERβ and PGE2, integrate at RERG leading to increased endometriotic cell proliferation and represents a novel candidate for therapeutic intervention.*

Endogenous ω-3 PUFAs Production Confers Resistance to Obesity, Dyslipidemia, and Diabetes in Mice • Jie Li, Fanghong R. Li, Dong Wei, Wei Jia, Jing X. Kang, Maja Stefanovic-Racic, Yifan Dai, and Allan Z. Zhao • *This study shows that endogenous conversion of ω -6 to ω-3 PUFAs via fat-1 strongly protects against obesity, diabetes, inflammation, and dyslipidemia, and may represent a novel therapeutic modality to treat these prevalent disorders.*

Comprehensive Overview of the Structure and Regulation of the Glucocorticoid Receptor • Sofie Vandevyver, Lien Dejager, and Claude Libert • *In this review, we summarize recent knowledge on the distinct GR isoforms and the processes that generate them. We also review the importance of all known transcriptional, post-transcriptional, and post-translational modifications, including the regulation of GR by microRNAs. Moreover, we discuss the crucial role of the putative GR-bound DNA sequence as an allosteric ligand influencing GR structure and activity. Finally, we describe how the differential composition and distinct regulation at multiple levels of different GR species could account for the wide and diverse effects of glucocorticoids.*

Endocrine Scintigraphy with Hybrid SPECT/CT • Ka Kit Wong, Lorraine M. Fig, Ehab Youssef, Alice Ferretti, Domenico Rubello, and Milton D. Gross • *The integration of function depicted by scintigraphy and anatomy with CT has synergistically improved the efficacy of nuclear medicine imaging across a broad spectrum of clinical applications, that include some of the oldest imaging studies of endocrine dysfunction.*

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Endocrinologist Opportunities

Geisinger Health System (GHS) is seeking Endocrinologists for two locations:

- **Endocrinology at Geisinger Wyoming Valley Medical Center (GWV), Wilkes-Barre, Pa.**
- **The Endocrinology team at Geisinger-Patton Forrest, State College, Pa.**

About the Position at GWV

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- Engage in clinical mentoring and educational programs for medical students and family medicine residents on the GWV campus, as well as internal medicine residents on rotation at GWV

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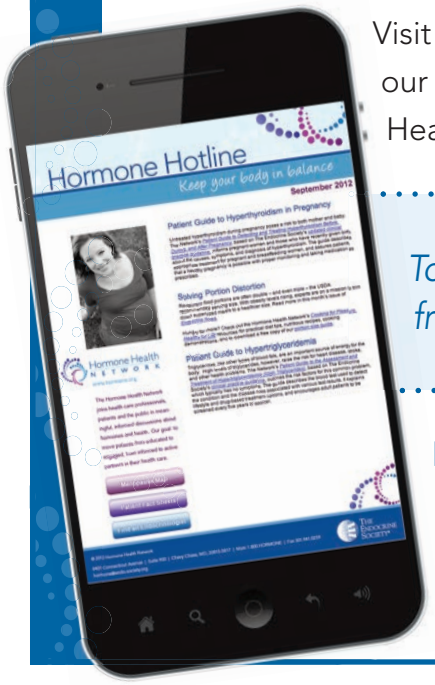

Visit **www.hormone.org** and sign up for *Hormone Hotline*, our monthly e-update, to get the latest news on Hormone Health Network publications and events.

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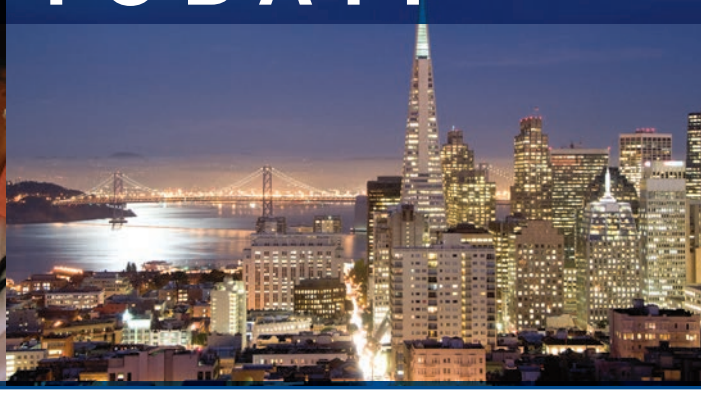

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