

APRIL 2018

THE LEADING MAGAZINE FOR ● ENDOCRINOLOGISTS

Endocrine news

MOVING TARGETS

When immunotherapy takes aim at various forms of cancer, endocrinopathies are often in the line of fire. While most endocrinologists are familiar with how to treat this “collateral damage,” new treatment protocols will likely evolve with experience.

WINNERS CIRCLE:

Q&A: ENDO 2018 Knock Out Rounds Champs

HIRSUTISM TREATMENT:

New guideline stresses patient guidance.

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Hormone Science to Health

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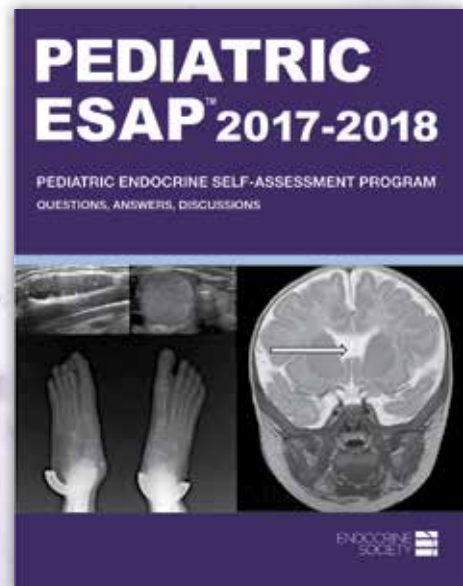
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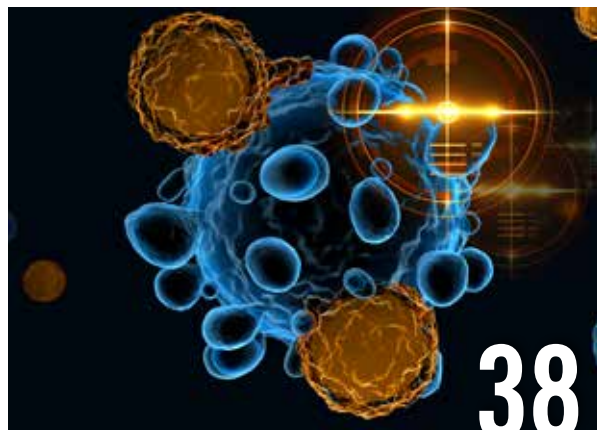
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As **ENDO 2018** settled in for its 100th meeting in Chicago, McCormick Place was packed with attendees from all over the world to get a look at the latest in cutting-edge science and research, as well as to commiserate with colleagues near and far. If you weren't one of the throngs of thousands who descended on the Windy City over St. Patrick's Day weekend, we've provided just a few highlights of what will suimpact the future of endocrinology science and practice for years to come.

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Introducing New Endocrine Society President: Susan Mandel

THE ENDOCRINE SOCIETY IS PLEASED TO welcome its president for 2018 – 2019, Susan Mandel, MD, MPH, who took office at the closing of ENDO 2018. Director of the Clinical Endocrinology and Diabetes Division at the University of Pennsylvania Health System in Philadelphia and professor of Medicine at the University of Pennsylvania, her work focuses on thyroid disease and especially thyroid disease and pregnancy.

“I was certainly honored and humbled when I was elected by members of our organization,” Mandel says. “I will be working with a talented and diverse Council who will provide guidance during the next year.”

Mandel succeeds Lynnette Nieman, MD, as the Society continues its rotation of presidents who represent its core constituencies: basic researchers, clinical researchers, and clinical practitioners. Mandel earned her undergraduate degree at Harvard University and her medical degree at Columbia University. Mandel has been with the University of Pennsylvania since 1997. She has been recognized in *Philadelphia* magazine’s annual Top Docs each year since 2004 as well as by *America’s Top Doctors* and *Best Doctors in America*.

Mandel decided to become an endocrinologist in part after hearing a series of lectures on neuroendocrinology at Columbia. “It was the most interesting medicine because everything seemed to make sense,” she says. “You had to know the physiology, the interactions, the concept that it wasn’t just one organ, but that endocrinology is in fact the entire body.”

Mandel did her fellowship at Brigham and Women’s Hospital in Boston, thinking she wanted to be a neuroendocrinologist because she was fascinated with pituitary hormones. There she came under the mentorship of Reed Larsen, MD, a senior physician at Brigham and Women’s and a professor of medicine at Harvard University. “Reed took me aside one day

and drew the pathways of thyroid hormone metabolism on a napkin,” Mandel says. “He told me he had a research project. So, I went to talk to him and he said to me, ‘I have an idea. I think that women who are hypothyroid need to take more thyroid hormones when they’re pregnant. But nobody has proved that. Why don’t you go figure out a way to do the study and come back to me, and then we can do the study.’” So Mandel came up with a retrospective study to address this, which led to her first paper published in the *New England Journal of Medicine*. She values this experience as prismatic because it highlights the values of mentorship, intellectual curiosity, with outcomes benefiting patient care.

Now that Mandel is a mentor herself, she promotes her fellows the same way, pushing them to look for and seize opportunities that harmonize with their own interests and to take the initiative to further their careers. “My goal is to get everyone around me working at the highest level they can to achieve their own goals,” she says.

And it’s not just her fellows that keep her going, it’s her patients, her work in helping them live as well as they can. “It’s not about their endocrine disorder, which for most of my

“
I'm not going to know what exactly we look like at the end of my 12-month term, but I am the president who is curating the Society and we will begin that journey together in the next 12 months. I am optimistic that we will reach many milestones and get a lot of things done.”
”

patients is thyroid cancer,” Mandel says. “It’s about their life—how does this affect their lives and those around them? How can I get them back to the life that they want? My job is to facilitate that journey.”

Mandel’s main goals for her presidency are linked to the ongoing work of the Society’s fourth strategic plan (SP4), a different kind of journey and an ambitious project that

“

My goal is to get everyone around me working at the highest level they can to achieve their own goals.

”

will continue even after her term is up. She says now that the SP4 process has started it’s important to implement and actualize ideas and ensure that the project represents input from many diverse groups: including international, early-career, established members, as well as those whose careers span the spectrum from scientific investigation to clinical practice.

One of the outcomes of SP4, she says, is to provide even more opportunities for member engagement. “I’m not going to know what exactly we look like at the end of my 12-month term,” she says. “But I am the president who is curating the Society and we will begin that journey together in the next 12 months. I am optimistic that we will reach many milestones and get a lot of things done.” ^{EN}

BY DEREK BAGLEY

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FROM THE **EDITOR**


ENDO: Better Than Ever

ENDO 2018 IN CHICAGO HAS COME AND GONE, AND I TEND TO say the same thing every year post-ENDO: “That was my best ENDO ever!” But this year it’s true (just like it was last year, and the year before that, and the year before that, etc.). The truth is: ENDO simply keeps getting better and better.

Aside from sitting in on some amazing sessions and checking out the exhibits and the posters in the ENDOExpo, one of my favorite activities each year is meeting you. Whether you catch me in the Information Booth or between sessions, I was able to engage in some really great discussions about science and research, the future of endocrinology, as well as what you would like to see us cover in the magazine. Just as ENDO itself gets better each year, likewise we hope you feel our wrap up of the event gets better, so this year we’ve expanded our coverage to a whopping 16 pages with lots of photos to give those of you who missed ENDO 2018 a feel for what it was like this year (p. 24). For those of you who were able to attend, our hope is that it can serve as a reminder of a great event (and inspire you to trek to New Orleans next March for ENDO 2019!).

We’re also featuring a roundtable Q&A with the three early-career basic scientists who emerged victorious at this year’s Knock Out Rounds, which took place at ENDO 2018 on Saturday March 17. It was another stellar group of young researchers, so we thought that “putting them under a microscope” in the magazine would be an even better way to reward them (p. 50)

This month’s cover story takes a deep dive into cancer treatment and how the endocrine system can become an unwitting “innocent bystander” when it gets in the way of treatments meant to eradicate cancer cells. “We think now that the immune system is really capable of mediating anti-tumor activity against almost any type of tumor,” says Howard Kaufman, MD, immediate past-president, Society for Immunotherapy of Cancer and a faculty member of the Massachusetts General Hospital, Boston, in Eric Seaborg’s article “Moving Targets” on page 44. “There are some types that have been holdouts that haven’t responded, and we are trying to understand why that is the case. We think eventually most cancers might be amenable to at least some form of immunotherapy.”

Enjoy the photo-packed ENDO 2018 wrap-up article, and let’s all start preparing for ENDO 2019 down in New Orleans next March! 

— Mark A. Newman, Editor, *Endocrine News*

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Remembering Lawrence A. Frohman, MD 1935 – 2018

BY SHLOMO MELMED, MD



Lawrence Frohman, who passed away March 4, 2018, enjoyed a long and distinguished career as a brilliant neuroendocrinologist who made groundbreaking discoveries in the hypothalamic control of metabolism and growth hormone production, and the genetics of familial growth hormone-secreting tumors.

He performed pioneering work on the control of GH secretion and identified and partially purified a GH releasing factor from pancreatic and lung tumors, which preceded the isolation of GHRH. He developed one of the first RIAs for rat GH and published extensively on regulation of GH secretion and on GHRH expression and action. He was a master teacher of basic and clinical scientists, and excelled at clinical care and professional service.

He directed the Endocrinology Division at Michael Reese in Chicago and at the University of Cincinnati and was Edmund F. Foley professor and chair of medicine at the University of Illinois at Chicago (1992–2001), where he successfully built research, education, and clinical programs for MD and PhD physicians and scientists, many of whom are now in leadership positions throughout the U.S., Europe, Latin America, and Japan.

Larry garnered myriad prestigious professional awards including the 2018 Endocrine Society Laureate Award for Outstanding Leadership, which was bestowed within a few weeks of his passing. He was also recipient of the Society's Rorer Clinical Investigation Award, an Honorary Member of the Japanese Endocrine Society, and the Bane Scholar and Distinguished Faculty Award winner at the University of Illinois. He chaired the NIH Endocrinology Program Advisory Group and is best remembered for

shepherding the NIDDK National Hormone and Pituitary Program, assuring generations of investigators of rigorously produced pituitary reagents available worldwide.

He assumed myriad leadership positions and was president of the Pituitary Society and the Central Society for Clinical Research, served on the Endocrinology Study Section, the VA Endocrinology Merit Review Board, FDA Endocrine-Metabolism Committee, and chaired the USP Expert Advisory Endocrinology Committee. He provided longstanding exemplary skilled service to multiple Endocrine Society Committees, including Nominating, Program, Journals Management, Finance and Audit, chair of Membership and Development, and Council member.

As a colleague and mentor, he will long be remembered as a self-effacing leader who was a true prince of endocrinology. We miss his warmth and exceptional insights as his honorable legacy continues to enrich our Society.

Above all, Larry will be remembered as a dedicated and outstanding scholar who displayed the finest sensitivity, kindness, and gentleness. He was a selfless, engaged, and warm role model for scores of young and old physicians and scientists. As one of the most distinguished leaders of the Endocrine Society, he was so looking forward

to receiving the Outstanding Leadership Award and was determined to celebrate with his wife Barbara in Chicago, their hometown, and yet this was sadly not to be.

“
Larry will be remembered as a dedicated and outstanding scholar who displayed the finest sensitivity, kindness, and gentleness. He was a selfless, engaged, and warm role model for scores of young and old physicians and scientists.
”

Endocrine Society Awards Inaugural Baxter Prize to Women's Health Entrepreneur

French physician and researcher André Ulmann, MD, PhD, received the Endocrine Society's first-ever John D. Baxter Prize for Entrepreneurship for his advances in women's health and rare endocrine conditions.

Ulmann founded HRA Pharma and built the company into a leader in women's health and treatments for orphan diseases. The company revolutionized the treatment of uterine fibroids, the formation of benign tumors on the uterus that can



cause irregular bleeding and reproductive complications, by developing a treatment that reduced the rate of hysterectomy surgeries. In addition, HRA licensed or developed emergency contraceptives and drugs for treating rare conditions including adrenal cancer and hypercortisolism. Ulmann led the company from 1996 to 2009 as CEO and served as chairman until 2016.

Ulmann received the inaugural Baxter Prize at **ENDO 2018**, the Endocrine Society's 100th Annual Meeting & Expo, during a ceremony on March 17. The \$50,000 prize is awarded biennially to recognize scientists or healthcare providers who have demonstrated entrepreneurship by leveraging endocrine research to improve patient care.

"André Ulmann's work has improved the lives of thousands

of women and patients with rare disorders," says immediate past-president Lynnette K. Nieman, MD. "His pioneering work bringing new treatments to market in 90 countries has eliminated the need for surgeries for many women with fibroids and improved the quality of patients' lives. We are thrilled to honor his numerous achievements."

Before founding HRA Pharma, Ulmann served as medical director and head of clinical research for Roussel-Uclaf and Hoechst-Marion-Roussel with global responsibility in the fields of endocrinology, immunology, neurobiology, and bone diseases. Prior to that, he was international project leader for the development of mifepristone as medical director of Laboratoire Roussel, France. He identified several potential uses for this molecule, including as an emergency contraceptive and a treatment for uterine fibroids and Cushing's syndrome.

Ulmann is currently the CEO of Cemag, a service and investment company, and serves as a consultant for several start-up companies. He wrote a book about his career entitled *Le Combat D'un Médecin Pour Les Femmes*. He was awarded the French Légion d'Honneur.

"It is truly an honor to be the first recipient of the Endocrine Society's Baxter Prize, which recognizes innovation in our field," Ulmann says. "I became an entrepreneur because I saw potential to meet women's unfilled medical needs. I am grateful for the prize, which will support my ongoing work in the women's health sphere."

The Baxter Prize was established in memory of Endocrine Society past-president John D. Baxter, MD, who was a world-renowned scientist known for being the first to clone the human growth hormone gene. During his career, he made many fundamental medical discoveries and translated them into clinical therapies that had far-reaching implications in the fields of biotechnology and genetic engineering, benefiting the health and welfare of patients worldwide. He passed away in 2011. The Baxter family endowed the prize in his memory.

Endocrine Society and Other Experts Strongly Disagree with the ACP's Guidance for Higher Blood Glucose Targets for People with Type 2 Diabetes



Together, the Endocrine Society, the American Diabetes Association (ADA), the American Association for Clinical Endocrinologists (AACE), and the American Association of Diabetes Educators (AADE) strongly disagree with the American College of Physicians' (ACP's) proposed new guidance that suggests higher blood glucose targets for people with type 2 diabetes.

While there is agreement on individualization of treatment based on patient-specific factors, with the aim of protecting those at highest risk, the ACP's recommendation of blood glucose targets for A1C "from 7 to 8 percent" could prevent many patients from receiving the full benefits of long-term glucose control. We are also concerned that the broad range suggested by ACP's guidance is too large to apply to "most patients with type 2 diabetes" and has the potential to do more harm than good for many patients for whom lower blood glucose targets may be more appropriate, particularly given the increased risk of serious complications such as cardiovascular disease, retinopathy, amputation, and kidney disease, which are the result of higher blood glucose (A1C) levels.

While ACP's guidance is only one additional percentage point, this may equate to a difference of nearly 30 points when blood glucose is measured in mg/dl. This difference in the lower and higher A1Cs in the range ACP also has been shown to have clear differences in microvascular complications from large, multicenter randomized trials of patients newly diagnosed with type 2 diabetes.

The ACP's new guidance, "Hemoglobin A1C Targets for Glycemic Control with Pharmacologic Therapy for Nonpregnant Adults with Type 2 Diabetes Mellitus: A

Guidance Statement Update From the American College of Physicians," was published in the *Annals of Internal Medicine* on March 5, 2018. It was developed based on analysis of the same international clinical trials for people with type 2 diabetes (ACCORD, ADVANCE, VADT, and UKPDS) reviewed by each of the other organizations, including the Professional Practice Committee for the ADA's 2018 *Standards of Medical Care in Diabetes* and the recommendations of AACE and AADE. However, ACP's interpretations of the findings of the studies did not account for the differences in the patient populations of these studies.

In addition, their recommendations do not consider the positive legacy effects of intensive blood glucose control confirmed in multiple clinical trials, particularly for those newly diagnosed with type 2 diabetes, and, therefore, are not reflective of the long-term benefits of lower A1C targets. ACP's guidance also does not consider the positive impact of several newer medication classes (SGLT2 inhibitors and GLP-1 receptor agonists) demonstrated in more recent clinical trials to improve mortality and morbidity in high-risk patients with type 2 diabetes. These medications have been associated with low risk for hypoglycemia, have favorable effects on weight, and demonstrate improved cardiovascular disease outcomes.

The Endocrine Society, ADA, AACE, and AADE remain firmly committed to protecting the more than 29 million Americans with type 2 diabetes from its serious complications by recommending individualized care that can improve their lives and reduce their risk of complications. The human impact of one percentage point is serious — to their daily lives, their families, friends, and loved ones — and their long-term quality of life and health outcomes.

Safer Named First Executive Director at Mount Sinai Center for Transgender Medicine and Surgery

Joshua Safer, MD, an internationally renowned clinical endocrinologist and authority on transgender medicine, has joined the Mount Sinai Health System as executive director of the Center for Transgender Medicine and Surgery (CTMS), the first and only center in New York — and one of a few pioneers nationwide — to provide transgender patients with a comprehensive and integrated system of care.


Safer, the Center's first executive director, will also serve as a senior faculty member at the Icahn School of Medicine at Mount Sinai. "There is a massive gap in transgender medical care that needs to be filled," Safer says. "The Mount Sinai center will serve as a model of medical care delivery for transgender and gender non-conforming individuals. Mount Sinai's position as a leading academic medical center will be leveraged to develop programs to train the next generation of physicians in transgender healthcare."

In response to the growing need for treatment for transgender individuals, Mount Sinai launched the nation's first transgender surgery and psychiatric medical fellowships in 2017. Little evidence-based data exist to guide transgender healthcare decisions. Safer's arrival will provide the opportunity for Mount Sinai to establish scientific research initiatives to advance the field.

Safer was most recently the founding medical director of the Center for Transgender Medicine and Surgery at Boston Medical Center and Boston University School of Medicine. He earned his medical degree from the University of Wisconsin and completed his internal medicine residency at Mount Sinai Beth Israel and his endocrinology fellowship at Beth Israel Deaconess Medical Center in Boston.

Safer's research focus is on demonstrating the health and quality-of-life benefits of increased access to care for transgender patients. His current and past sources of funding support include the National Institutes of Health and a number of private foundations.

President of the United States Professional Association for Transgender Health (USPATH) and the steering committee co-chair of the international transgender research consortium, TransNet, Safer also serves on the Global Education Initiative committee for the World Professional Association for Transgender Health (WPATH), on the Standards of Care revision committee for WPATH, and as a scientific co-chair for WPATH's international meeting. In addition, he is a past president of the Association of Specialty Professors, the umbrella organization for leaders in internal medicine subspecialty education, and a former secretary-treasurer of the national endocrinology program director organization, the Association of Program Directors in Endocrinology and Metabolism (APDEM).

Safer was a co-author of the Endocrine Society guidelines for the medical care of transgender patients and serves on the *Endocrine News* Editorial Advisory Board. 





Why NOT Endocrinology?

BY SHEHZAD TOPIWALA, MD, FACE, Institute of Endocrinology, Diabetes, Health & Hormones (IEDHH), Doctors Clinic Diagnostic Center, Panama City, Fla.; Dubai Healthcare City, Dubai, UAE

I was born and raised in the cosmopolitan city of Mumbai, India. In the final quarter of the past century,

India's collective cerebral talent emerged powerfully and constituted its major intellectual export to the western hemisphere.

Like thousands of other freshly minted physicians, I was blessed to find a scintillating opportunity to train in the U.S. By the time my endocrinology fellowship commenced in New York, we were well into the new millennium.

By then, endocrine disorders had become the scourge of modern times. One of the most compelling reasons for me to pursue this track was to ameliorate the unrestrained onslaught on human health from these preventable conditions. Today, I am grateful to be part of this unique tribe of endocrine clinicians, promoting hormone health globally.

So what drew me compulsively toward the endocrinology arena? Aside from the typical cognitive allure offered by its perplexing content, I also deployed a process of elimination. Within a year of medical school, I realized I was not cut out for any type of surgery due to my lack of manual dexterity. I also enjoyed extracting

historical clues from my patients, but alas, children would not cooperate during interrogation. So, pediatrics was out. As for radiology and other non-clinical branches, they all lacked direct patient interaction. Then, only a year into my internal medicine residency, I realized that the subject was too broad for me to become an authoritative expert. Hence, I decided to subspecialize.

“

One of the most compelling reasons for me to pursue [endocrinology] was to ameliorate the unrestrained onslaught on human health from these preventable conditions.

”

My migraine would certainly be exacerbated by a cardiology fellowship and practice thereafter. I noted how nephrology could be intense and demanding as well. Neurology and rheumatology, although stimulating, were not gratifying given the intractable conditions that were involved. I somehow was not enthused about pulmonology or gastroenterology, perhaps owing to those specialties' procedural components. Hematology and oncology were too morbid for my liking.

Therefore, endocrinology seemed like an obvious choice. It would give me a decent lifestyle, while dealing with lifestyle disorders. Many endocrinologists I've known worldwide attribute their fitness mantra to endocrinology, and they agree

with me when I say that had I not been an endocrinologist, I don't think I would personally be as healthy. Indeed, many of them have stemmed the tide of aging and look exceptionally youthful, even decades later when I encounter them at international conferences!

If you would like to share your story with our readers around the world, contact Editor Mark A. Newman at mnewman@endocrine.org.

I must acknowledge the role of academic stalwarts in India and the U.S. who inspired me to assimilate principles of endocrine science in a joyful manner. The thrill of clinching mysterious diagnoses and the delight of alleviating reversible endocrinopathies represent unparalleled experiences of my lifetime.

Be that as it may, private practice is quite a contrast! Having practiced for nearly a decade on two vastly different continents, I can vouch for the fact that at least when it comes to community endocrine set-ups, the daily routine encompasses mainstream diabetes and thyroid care. Even though it provides a sense of pride that I am playing my role in chronic cardio-metabolic risk mitigation, I confess burnout is inevitable. Often, healthcare systems and the inherently complex nature of diabetes management preclude optimal treatment strategies. High volumes and patient factors can further exasperate one. This was one key dimension I was not forewarned of earlier in my career.

However, in retrospect I would not trade endocrinology for any other realm of medicine. Ultimately, it facilitates an excellent lifestyle without being consumed entirely by work. Minimal to no after-hour calls and emergencies are indeed a plus in an already stressful life. However, I am not nor have I ever been simply “in it for the money.” I find this resonates with most of my endocrinology colleagues as well. Of course, I also have several friends in various parts of the world who are very enterprising endocrinologists and reap substantive rewards for their entrepreneurial spirit!

In conclusion, I must profess I particularly relish the fancy jargon-like allusions (‘ACTH-dependent endogenous hypercortisolism due to macro-corticotrophinoma.....’ or ‘pseudo-pseudo hypoparathyroidism’). A non-expert is overawed upon hearing these, and it definitely adds to the enigmatic charm of the field! ^{EN}

EDITOR'S NOTE: The opinions and views of the author do not necessarily represent those of *Endocrine News* or the Endocrine Society.

NEW GUIDELINES ADDED

Clinical Decisions Made Easy at Your Fingertips

FEATURING THREE NEW GUIDELINES:

- Diagnosis of Cushing's Syndrome
- Functional Hypothalamic Amenorrhea
- Endocrine Treatment of Gender-Dysphoric/ Gender-Incongruent Persons



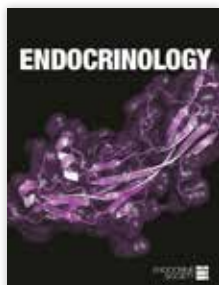
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BY DEREK BAGLEY
Senior Editor



Fracking Chemicals May Alter Mammary Gland Development, Animal Study Finds

Chemicals used in unconventional oil and gas (UOG) operations — fracking and directional drilling — may alter mammary gland development, according to a study recently published in *Endocrinology*.

The study, led by Susan Nagel, PhD, of the University of Missouri, and Laura N. Vandenberg, PhD, of the University of Massachusetts, is yet another indictment of endocrine-disrupting chemicals (EDCs), especially those used in UOG operations. The researchers point out that more than 1,000 chemicals have been identified in fracking fluids and waste water and/or have been reported to be used by the industry. “Many of these chemicals are known developmental and reproductive toxicants,” the authors write. “Furthermore, recent evaluations found that >100 of these chemicals are known or suspected [EDCs], and water samples collected in drilling-dense or UOG wastewater-affected areas of the United States have exhibited disruption of the estrogen, androgen, progesterone, glucocorticoid, and thyroid receptors.”

Two previous studies exposed mice to a 23-chemical mixture of UOG compounds (UOG-MIX) that are commonly used in these operations. In those studies, the mice displayed altered endocrine organ function and serum hormone concentrations. In the first study, male mice exposed to environmentally relevant doses of UOG-MIX showed decreased sperm counts, increased serum testosterone concentrations, and alterations to the weight of organs like the heart and thymus. In the second study, the researchers evaluated the female siblings and found that these mice had alterations to number and developmental stages of ovarian follicles. The mice

also had alterations to the weight of several organs, including the uterus, ovary, and heart.

The researchers hypothesized that UOG chemicals would similarly disrupt the mice’s mammary gland development, since, as the authors write, the mammary gland is a hormone-sensitive organ that is responsive to multiple endocrine inputs during early development. They exposed female mice to varying doses (3; 30; 300; 3,000 µg/kg/d) of UOG-MIX from gestational day 11 to birth. The mice showed no effects on mammary gland development before puberty, but the mice exposed to the 300 or 3,000 µg/kg/d doses of UOG-MIX developed more dense mammary gland epithelial ducts. Females exposed to the lowest dose had an altered ratio of apoptosis to proliferation in the mammary epithelium. “Furthermore,” the authors write, “adult females from all UOG-MIX-treated groups developed intraductal hyperplasia that resembled terminal end buds (i.e., highly proliferative structures typically seen at puberty).”

Findings: The authors conclude that these results suggest that the mammary gland is sensitive to mixtures of chemicals used in UOG production at exposure levels that are environmentally relevant. They go on to write that the evidence for an association between UOG operations and breast cancer is inadequate and that these results suggest that further studies are needed to address this gap. “Future studies are needed to evaluate the many additional chemicals used in, and produced by, UOG processes to better quantify the concentrations of these and other contaminants in environmental samples and to assess the effects of exposure during other sensitive windows of development, including pregnancy and lactation, puberty, and the aging female,” the authors write.

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Many of these chemicals are known developmental and reproductive toxicants,” the authors write. “Furthermore, recent evaluations found that >100 of these chemicals are known or suspected [EDCs], and water samples collected in drilling-dense or UOG wastewater-affected areas of the United States have exhibited disruption of the estrogen, androgen, progesterone, glucocorticoid, and thyroid receptors.”

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Researchers Suggest Possible Biomarker for Diabetic Cardiomyopathy



Alterations in the myocardial ghrelin-GHSR1a system may predict diabetic cardiomyopathy (DCM), according to a study recently published in the *Journal of the Endocrine Society*.

Researchers led by Savita Dhanvantari, PhD, of the Lawson Health Research Institute in London, Ontario, Canada, point out that DCM is characterized by progressive cardiac dysfunction, and that the early stages of DCM represent a latent subclinical phase marked by diastolic dysfunction, oxidative stress, derangements in Ca²⁺ homeostasis, and altered substrate utilization, resulting in myocardial lipotoxicity. The authors go on to write that ghrelin and its receptor, the growth hormone secretagogue receptor 1a (GHSR1a), are new molecules of interest that may track the progression of heart disease and the cardiomyopathy of diabetes, and they hypothesized that GHSR1a could also be a biomarker for DCM.

The researchers used streptozotocin (STZ) to induce DCM in two sets of mice: The first group comprised adult mice treated with 35 mg/kg STZ for three days, and the second group comprised neonatal mice treated with double that amount at days two and five after birth. Group one showed mild fasting hyperglycemia eight weeks after the last injection. Group two showed severe fasting hyperglycemia one to three weeks after the last injection. “In group [one], left ventricular function was slightly impaired as measured by echocardiography, and Western blot analysis showed a significant decrease in myocardial GHSR1a,” the authors write. “In group [two],

GHSR1a levels were also decreased as assessed by Cy5-ghrelin(1–19) fluorescence microscopy, and there was a significant negative correlation between GHSR1a levels and glucose tolerance.”

The researchers saw significant positive correlations between GHSR1a and ghrelin and between GHSR1a and sarcoplasmic reticulum (SR) Ca²⁺-ATPase 2a (SERCA2a), a marker for contractility, but not between GHSR1a and B-type natriuretic peptide, a marker for heart failure. “The strong positive correlation suggests that GHSR1a activation by ghrelin may function to regulate cardiomyocyte contractility through control of Ca²⁺ flux from the SR,” the authors write.

The authors note that ghrelin may be a possible biomarker in heart failure. “Our results seem to indicate that cardiac tissue levels of ghrelin, together with GHSR1a, may be more appropriate markers of early cardiac dysfunction and may indicate changes in intracellular Ca²⁺ homeostasis in cardiomyocytes,” the authors write.

Findings: They go on to cite a study involving tissue biopsies from 12 patients with chronic heart failure that showed that both immunoreactive GHSR1a and GHSR1 mRNA levels were dramatically increased in patients with end-stage heart failure. “Therefore,” the authors conclude, “it appears that myocardial GHSR1a levels are altered differently in early-onset DCM and in end-stage heart failure. We are currently investigating a role for cardiac ghrelin and GHSR1a as an integrated system biomarker for the onset of DCM and heart failure



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The metabolic and cognitive relevance of Thr92AlaD2 has been noted previously in different populations but not always universally replicated. More recently, this same group reported that temporal lobe samples from Thr92AlaD2 carriers showed transcriptional alterations in processes typically associated with neurodegenerative diseases.

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Researchers Observe Genotype that Increases Odds of Alzheimer's, Dementia in African Americans

Researchers may have discovered a factor that contributes to racial discrepancies in developing Alzheimer's disease (AD) or dementia, according to a study recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Antonio C. Bianco, MD, PhD, of University of Chicago, point out that a common single nucleotide polymorphism in DIO2, Thr92AlaD2, is associated with a transcriptome typically found in neurodegenerative diseases in postmortem human brain tissue. The authors write that the metabolic and cognitive relevance of Thr92AlaD2 has been noted previously in different populations but not always universally replicated. More recently, this same group reported that temporal lobe samples from Thr92AlaD2 carriers showed transcriptional alterations in processes typically associated with neurodegenerative diseases.

“In the current study,” the authors write, “we tested the hypothesis that carriers of the Thr92AlaD2 polymorphism have an increased risk for incident Alzheimer's disease.” They also note that the epidemiology and tissue pathology of AD vary by ethnicity. For instance, African Americans (AAs) are more likely to have mixed tissue pathologies compared to clinically matched European Americans (EAs).

The study was performed at Rush University Medical Center in Chicago. The researchers analyzed data from 3,054 AAs and 9,304 EAs; the primary population came from community-based



cohorts from Chicago and northeastern Illinois, as well as religious clergymen from across the U.S. Secondary analyses came from a representative sample of the U.S. population. The team found that AAs with the Thr92AlaD2 polymorphism had 1.3 times higher odds of developing AD, and AAs from the secondary population with Thr92AlaD2 had increased odds of developing dementia and were 1.35 times more likely to develop cognitive impairment not demented (CIND). Meta-analysis showed that AAs with Thr92AlaD2 had 1.3 times increased odds of developing AD/dementia. EAs showed no association between Thr92AlaD2 and AD, dementia, or CIND.

Findings: “Our results show that in these large, well-characterized, populations the Thr92AlaD2 polymorphism is associated with development of AD in AAs, but not EAs,” the authors conclude. “This, in addition to concurrent transcriptional evidence, supports the hypothesis that Thr92AlaD2 is a risk factor for neurodegenerative disease in AA.”


Androgen Receptor Signaling Linked to PCOS Phenotypes, Animal Study Finds

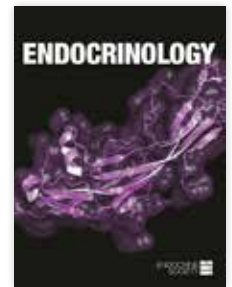
Androgen receptor (AR) signaling is responsible for key reproductive and metabolic polycystic ovary syndrome (PCOS) phenotypes, according to an animal study, the results of which were published recently in *Endocrinology*.

Researchers led by Pamela L. Mellon, PhD, of the University of California, San Diego, point out that animal models have proven to be a valuable resource in studying PCOS mechanisms and pathways, which is important since PCOS is the most common reproductive disorder in women. Mellon's team had previously shown that continuous exposure to aromatase inhibitor letrozole (LET) in mice produces many hallmarks of PCOS, including elevated testosterone (T) and luteinizing hormone (LH), anovulation, and obesity. "In the present study," the authors write, "we sought to determine whether [AR] actions are responsible for any of the phenotypes observed in LET mice." They go on to write that understanding

specific contributions to androgens to LET PCOS phenotypes will allow insight into the mechanisms underlying reproductive and metabolic dysfunction in this model and lay the groundwork for combining transgenic mouse models with LET treatment to study the pathogenesis of PCOS.

The researchers implanted female mice with LET or placebo control (CON), and then treated the mice with an AR antagonist or vehicle control. "Flutamide treatment in LET females reversed elevated T levels and restored ovarian expression of *Cyp17a1* (critical for androgen synthesis) to normal levels," the authors write. "Pituitary expression of *Lhb* was decreased in LET females that received flutamide treatment, with no changes in expression of *Fshb* or *Gnrhr*. Flutamide treatment also restored estrous cycling and reduced the number of ovarian cyst-like follicles in LET females. Furthermore, body weight and adipocyte size were decreased in flutamide-treated LET females."

Findings: Based on these results, Mellon and her team demonstrated that blocking AR with the AR antagonist flutamide ameliorates or reverses PCOS phenotypes in the LET mouse after only a couple of weeks. Furthermore, the authors note that PCOS phenotypes similar to ones they found to be reversed with flutamide treatment in LET females have been improved with antiandrogen treatment in animal and human models. "Altogether," the authors conclude, "we have shown that many reproductive and metabolic aspects of the LET PCOS phenotype can be attributed to AR signaling, establishing the relevance and importance of this model for the study of mechanisms underlying PCOS." 



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We in the endocrinology community need to be familiar with the basic idea behind these medications our oncology colleagues are utilizing. They unleash the immune system to fight malignancies. And while they seem to be very effective in combatting the malignancies for which they are designed, they cause a lot of endocrine-related adverse events.”

— MATTHEW J. LEVINE, MD, Scripps Clinic Division of Diabetes and Endocrinology, San Diego, Calif., from “Moving Targets: Immunotherapy and Endocrinopathies” on page 44.

FROM THE CENTURY OF
ENDOCRINOLOGY TIMELINE

2001: *Endocrine News* First Published

Endocrine News is a monthly news and feature magazine published by the Endocrine

Society as a benefit for members and other interested parties. The magazine provides an in-depth look at trends in the field of endocrinology as well as a closer look at recently published research.

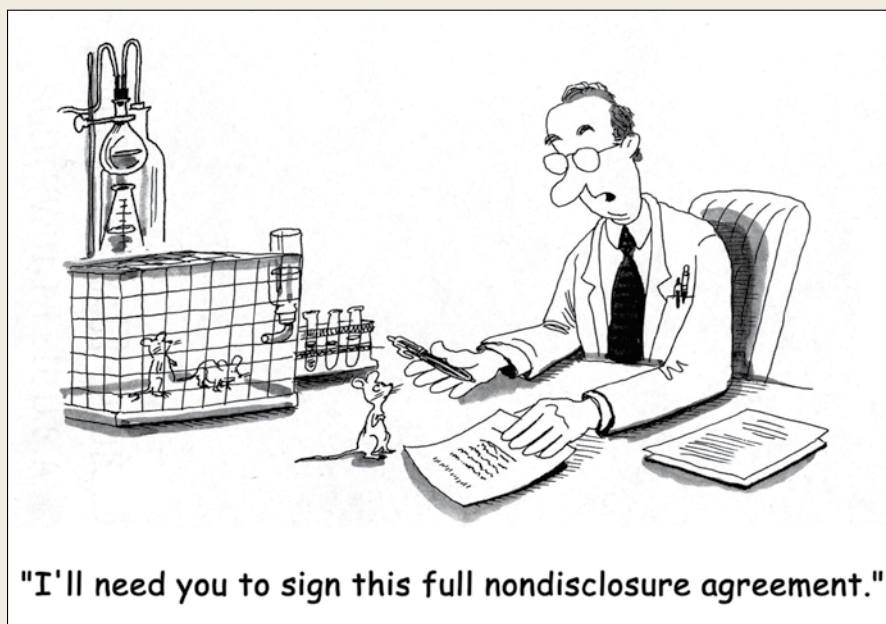
Additionally, the editorial content in *Endocrine News* provides its audience with helpful information, insight, and education about the field and practice of endocrinology and endocrine research. *Endocrine News* informs and engages the global endocrine community by delivering timely, accurate, and trusted content covering the practice, research, and profession of endocrinology

For more about the Century of Endocrinology, go to: www.endocrine.org/timeline.

300

The number of years since there have been any advances in male contraception.

— SOURCE: STEPHANIE PAGE, MD, PHD/ENDO 2018 PRESS CONFERENCE



>40%

Of 16- to 19-year-olds are obese.

— SOURCE: PEDIATRICS

2018 Clinical Endocrinology Update/Endocrine Review Board

**CEU/EBR East: Miami, Fla.
Sept. 4 – 8, 2018**

**CEU West: Anaheim, Calif.,
Oct. 18 – 21, 2018**

www.endocrine.org/ebr/2018

www.endocrine.org/ceu/2018miami

www.endocrine.org/ceu/2018anaheim

Early Registration: Now – August 3, 2018



This year, endocrine clinicians from around the world will have a choice of which CEU they choose. CEU/EBR East will take place in Miami in September, while CEU West will land on the West Coast in October.

Miami's Intercontinental Hotel will be the location for the joint meeting of the 2018 Clinical Endocrinology Update (CEU)/ Endocrine Board Review (EBR) East from September 4 – 8, and the Hyatt Regency Orange County in Garden Grove, Calif., will be where CEU West takes place on October 18 – 21. Each year CEU brings together hundreds of endocrine clinicians for a unique learning experience and opportunities to network with expert faculty and colleagues. Attend the 70th CEU to receive the most trusted and clinically relevant information about recent advances in the field of endocrinology. The educational programming at CEU appeals to clinicians at all levels of practice, as well as fellows and other members of the clinical practice team.

Unlike other board preparation meetings, the Endocrine Society's EBR courses offer a comprehensive mock-exam format with case-based American Board of Internal Medicine–style questions forming the bulk of the presentations. Each section follows the ABIM blueprint for the board exam, covering the breadth and depth of the certification/recertification examination. Each case will be discussed in detail, with the correct and incorrect answer options reviewed. The mock exam appeals to endocrine fellows who have completed or are nearing completion of their fellowship and are preparing to take the board certification exam. Practicing endocrinologists may appreciate the EBR's comprehensive self-assessment of endocrinology either to prepare for recertification or to update their practice.

Endocrine Summit

Mumbai, India, April 28 – 29, 2018

This annual program will bring high-quality education to Indian endocrinologists. The goal of the program is to foster relationships with endocrinologists around India, while providing insights into translational medicine and clinical care across a variety of disciplines. At this year's Endocrine Summit, the six faculty members will present in-depth lectures on adrenal, bone, obesity, pituitary, thyroid, and reproductive topics.

www.endocrine.org/meetings

ADA 78th Scientific Sessions

Orlando, Florida, June 22 – 26, 2018

The Scientific Sessions offers researchers and healthcare professionals an opportunity to share ideas and learn about the significant advances in diabetes research, treatment, and care. Over the course of five days, attendees will receive exclusive access to original research presentations, take part in engaging exchanges with diabetes experts, and expand professional networks with attendees from around the world.

<https://professional.diabetes.org>

9th International Congress of Neuroendocrinology

Toronto, Ontario, Canada, July 15 – 18, 2018

At the ICN 2018, 64 state-of-the-art speakers and eight plenary lecturers will cover the excitement of modern neuroendocrinology from molecules to behavior, across four main themes – metabolism, reproduction, stress, and timing. Highlights include four concurrent symposium sessions, poster sessions with networking opportunities, and top research in neuroendocrinology from around the world.

www.icn2018.org

EndoBridge 2018

Antalya, Turkey, October 2 – 28, 2018

Jointly organized by the Endocrine Society, European Society of Endocrinology, and the Society of Endocrinology and Metabolism of Turkey, EndoBridge will provide a comprehensive update in the field of endocrinology. Held on October 25–28, 2018, in Antalya, Turkey, this meeting is designed for the clinical endocrinologist. The official language of the meeting is English, but simultaneous translation will be available in Russian, Arabic, and Turkish.

www.endobridge.org

18th International Congress of Endocrinology and 53rd SEMDSA Congress

**Cape Town, South Africa,
December 1 – 4, 2018**

The Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) is hosting ICE 2018 with the 53rd annual SEMDSA Congress. The Program Organizing Committee is currently putting together a stimulating program including cutting-edge academic endocrinology for basic scientists and clinicians.

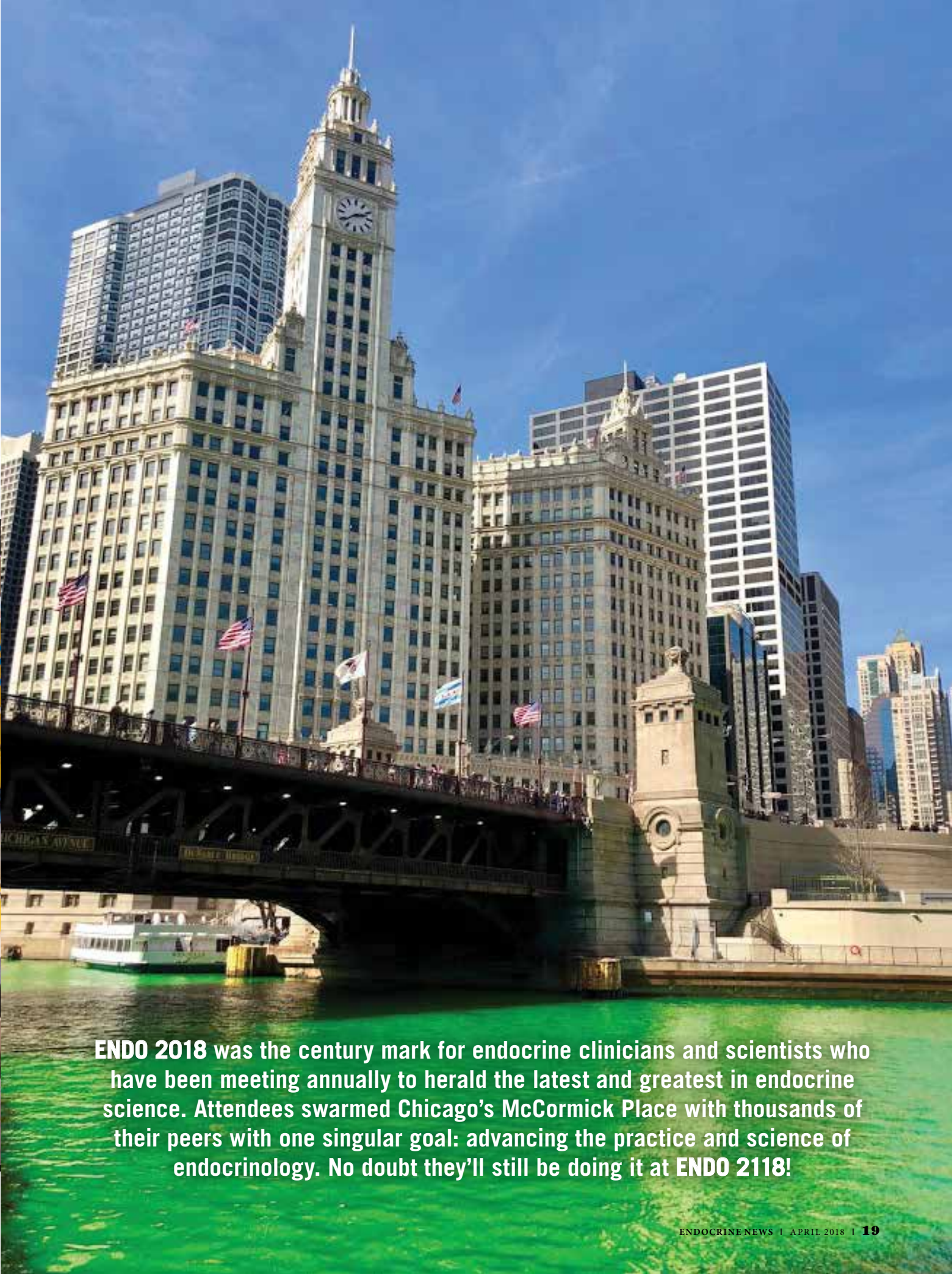
www.ice2018.org

ENDO 2018: BY DEREK BAGLEY AND MARK A. NEWMAN

A Centennial CELEBRATION



CONFERENCE PHOTOGRAPHY BY CHRISTINA SHOOK, CHICAGO PHOTOGRAPHY BY BETH BAGLEY



ENDO 2018 was the century mark for endocrine clinicians and scientists who have been meeting annually to herald the latest and greatest in endocrine science. Attendees swarmed Chicago's McCormick Place with thousands of their peers with one singular goal: advancing the practice and science of endocrinology. No doubt they'll still be doing it at **ENDO 2118!**



“**ENDO 2018**
was one for the
record books.”



s **ENDO 2018** settled in for its 100th meeting in Chicago, McCormick Place was packed with attendees from all over the world to get a look at the latest in cutting-edge science and research, as well as to commiserate with colleagues, many of whom traveled from around the world. If you weren't one of the throngs of almost 8,000 who descended on the Windy City over St. Patrick's Day weekend, we've provided just a few highlights of what will surely impact the future of endocrinology for years to come.

Patients' Stories

Every year, besides the newest in research and technology in the world of endocrinology, **ENDO** tries to bring something fresh to the program. This year in Chicago was no different. **ENDO** featured three patient-centered sessions, in which the clinician brought a patient to speak about his or her condition. There had been a bit of controversy over this decision; questions were raised about the need for such sessions at **ENDO**. Still, at a purely scientific program like **ENDO**, it can be useful to inject a little bit of humanity into the proceedings.

Take Stacy Lloyd, a patient of Peter Kopp's, a clinician at Chicago's Northwestern University. She was diagnosed with pheochromocytoma at age 10, a condition diagnosed funnily enough by her grandfather, since he recognized the same symptoms that his daughter, Stacy's aunt, had. "It was like a lightbulb went on in the room," Stacy says.

Surgeons removed the tumor, but Stacy remained symptomatic. Further tests revealed more tumors, and she was diagnosed with Von Hippel-Lindau (VHL) disease. For Stacy, her treatment is never entirely over, but she's surrounded herself with doctors she trusts and stays active in the non-profit VHL Alliance, dedicated to research and education to raise awareness of VHL.

But Stacy's main worry is passing VHL on. She attends genetic counseling with her family. Kopp says that there is a need to establish a family pedigree, which could provide clues as to who might carry the mutation. These meetings have also revealed some things that clinicians might not always be aware of when treating patients with inherited endocrinopathies. For instance, family members who don't carry the mutation may harbor feelings of guilt, which need to be addressed, Kopp says.

Still, Stacy says, she is part of the first generation that gets to weigh options carefully and thoroughly when considering having children. Although, she says, getting married to someone is "signing someone up for the unknown."

Or there's Craig Stubing, a patient of Anne Peters' (of the University of Southern California), who trains for and competes in marathons while dealing with his type 1 diabetes. He was diagnosed at age 13. He's now 30, and he feels like he finally has a handle on keeping his A1C in range when he runs, but that wasn't always the case.



The Endocrine Society booth, amidst the cutting-edge technology on display in the ENDOExpo, is a popular destination for members from around the world.

He had played hockey in high school but stopped sports entirely during college (“I got busy with other things”), and when he decided he wanted to run in marathons, it was difficult for him to find the correct balance of carbs and bolus insulin.

Peters offered suggestions to Stubing so he could compete and keep his blood sugars within a healthy range, but it was still trial and error there for a while. Stubing sees his story as yet another example of individualizing treatment. “What I do now is vastly different than what you told me to do back then,” he tells Peters.

Finally, during the final session of ENDO, two high school students sat at the front of the room and took questions from Courtney A. Finlayson, MD, as well as the audience. Sawyer, a high school junior, is transitioning from female to male and has been on testosterone for a year and a half. Kylie, a high school freshman, is transitioning from male to female and has been on estrogen for two years and puberty blockers for three years.

Before they spoke, Stephen M. Rosenthal, MD, of the University of California, San Francisco, laid out the barriers that remain to treating transgender children



Aaliyah Riccardi from the University of Connecticut School of Medicine participates in the mentoring poster session.



This packed session on treating patients with hypoglycemia in one of the largest halls in McCormick Place clearly indicates how important this complication is to endocrinologists.

optimally, including the fact that all the medications available to prescribe are off-label and therefore might not be covered by insurance. And these are medications that are necessary for blending in once these patients transition, since blocking puberty earlier in a male transitioning to female will halt the development of a deeper voice, for instance.

The costs for these medications alone would be enough to take its toll on any family, but there's also the issue of preserving fertility. "Just because someone is transgender," he says, "doesn't mean they aren't interested in preserving fertility." But again, these costs can be astronomical, which means that many of these patients may never have kids.

Then the audience heard from Amy Tishelman, PhD, a senior attending psychologist for the Disorders of Sex Development-Gender Management Service (DSD-GeMS) at Boston Children's Hospital. She touched on the vocabulary associated with treating transgender children, including the fact that the word "transgender" itself is a blanket term for an entire spectrum of gender identities. "It takes a lot of empathy to

understand when someone tells you their gender, what they firmly believe their gender identity to be," she says.

And Tishelman says that while yes, many transgender children are bullied and may become depressed, it doesn't have to be that way. The main way to combat these feelings in transgender children is through support. Of course, that means support from family, teachers, friends, and so on. But that also means little things, even in the ways doctors interact with these patients.

Sawyer says that before he started on testosterone, he didn't feel like he was in the correct body. His family and his friends' families were curious more than anything. They had lots of questions, but they were supportive. But at times during his treatment, there were some shortcomings on the part of the team caring for him. He would notice little things like the fact that documents still referred to him by his birth name, rather than his chosen name. "Being on top of the language would be helpful," he says.

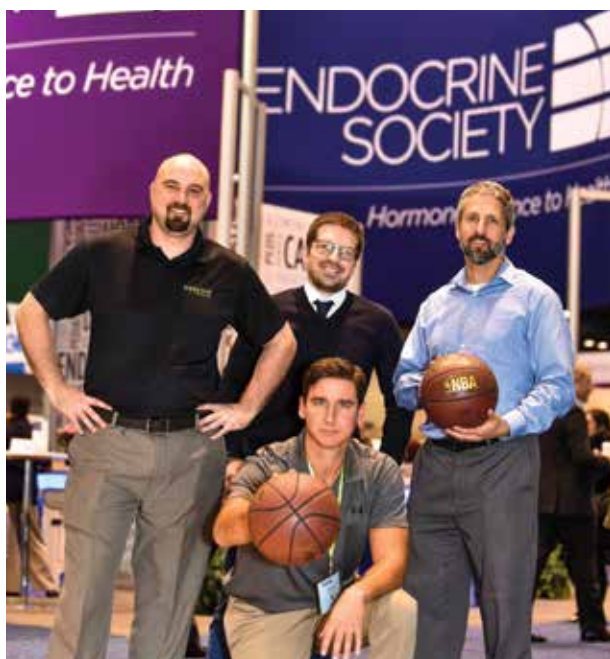
(Continued on page 33)

JOB BOARD

PLACE YOUR JOB POSTING HERE



The Job Board on the EXPO floor had myriad opportunities for attendees at all professional levels.



The March Madness Lounge allowed attendees to show off their basketball skills between sessions.



No buyer's remorse for this proud shopper who made a stop at the ENDO Store.

The Future of Endocrinology attended ENDO2018's Early Career Forum



All of the 2018 attendees of the ENDOCareers Early Career Forum, an all-day pre-conference event on Friday March 16. Presentations included how to get the most out of **ENDO 2018**; clinical and research career options; tips on CVs and job searches; how to handle negotiations; creating a mentoring relationship; achieving an optimal work/life balance; effective networking; and much more. Endocrinologists starting out in their careers are well prepared thanks to the Early Career Forum held each year at ENDO.





MAIGEN M. BETHEA
PhD student, University of
Alabama at Birmingham

My ENDO 2018 WRAPPED

From beta-cell and miRNAs in metabolism oral sessions to the St. Patrick's Day tradition of dyeing the river green, Chicago proved to be quite the host for the 100th Annual meeting and **Expo** of the Endocrine Society.

As a first-time attendee, I wanted to be a sponge and absorb as much information as I possibly could. My journey started the day before the conference at the Early Career Forum sponsored by the Trainee and Career Development Core Committee (TCDCC) at the Endocrine Society. At this forum, I was immersed in a day-long workshop where the focus was enriching the professional development of endocrine trainees and early-career professionals. Topics included personal career journeys, career paths within endocrinology, job searching, negotiation strategies and techniques, achieving life balance, along with effective networking.

Day one was spent obsessing over the scientific talk I'd been selected to give in the "Regulation of Beta-cell Stress, Function, and Survival" session. Once I delivered the talk, I received a mixture of thought-provoking questions along with suggestions to improve my study design from big names in the field. This was one of the first times I've received such feedback in all my years of presenting at large conferences similar to **ENDO** (e.g., American Diabetes Association and Experimental Biology).

I spent the remainder of my time caught up in the infectious energy that comes from being alongside thousands of the most talented endocrine clinicians and researchers from all over the world. It was an incredible experience to network and learn with the other attendees. So what does this first-timer think about **ENDO 2018**? In short, **ENDO** has become my favorite professional conference, and I'll definitely be attending next year's conference in New Orleans!



Diane M. Donegan (left) speaks at a session on interview skills for clinical practice jobs at the Early Career Forum. An Early Career participant asks a question during one of the sessions at this day-long event.



At the Science Hub on the ENDOExpo floor, Matthew Bouchonville, MD, from the University of New Mexico, discusses the success he's had in using Endo ECHO in his practice.

Combating Fake Endocrine News

Here's a question: What makes endocrinology a prime target for Internet myths? Jonathan Leffert, MD, of the North Texas Endocrine Center, gave an interesting talk aimed at laying out these myths and trying to debunk them. Endocrine diseases can present with “vague” symptoms, which can frustrate patients, so they turn to the Internet to try to grasp their conditions. It's difficult for patients to differentiate between fact and fiction when it comes to endocrinopathies, as well as the fact that endocrinology can be a long process: One step leads to the next, and things can take time to figure out. “Remember that patients are frustrated,” he says. “Take that into account. I thought when I went into practice that I was going to fix everyone who had some terrible disease. That's not always the case.”

According to Leffert, the best approach to debunking myths about thyroid disease is to differentiate yourself from alternative medicine doctors, to explain that you are an expert on these diseases and explain in laymen's terms the normal physiology of the thyroid and the meaning of thyroid function tests. Or

when it comes to dealing with myths about low testosterone (or “low T,” a term that only came along once TV ads started airing), differentiate yourself from primary care physicians and urologists, and discuss the assays and the subsequent evaluations from the endocrinologists' perspective — specifically looking for the causes of low testosterone in young men.

And, as we in *Endocrine News* covered last year, the best way to debunk myths about adrenal fatigue, Leffert says, is to explain that adrenal fatigue is not recognized by the endocrine community, that there's no evidence to support such a diagnosis. The symptoms don't match adrenal insufficiency, and although adrenal supplements are a common treatment, it's not clear what exactly is in these medications.

Overall, Leffert stresses, endocrinologists need to be compassionate and understanding when it comes to these patients. “Don't send them away empty-handed,” he says. “Don't prescribe medications outside of your comfort zone but try to do something that makes them feel better, even if it's just listening to them.”



Researchers discussing and defending their scientific findings posted in the EXPO hall is one of the many mainstays of ENDO each year.



There's always time for an impromptu meeting on the EXPO floor.

Opioids & Endocrinology

Opioids have been grabbing headlines for the past couple of years. They've become an epidemic, and the U.S. is right in the center of it. In 2014, the U.S. used almost 70% of the world's opioids. And it's not just pain management physicians prescribing these drugs. Family medicine doctors, cardiologists, neurologists, nephrologists, and so on, are all prescribing opioids to their patients for acute and chronic pain. Of course, these drugs can lead to addiction and even death, but their effects on the endocrine system haven't been covered as extensively as the more pressing side effects.

Niki Karavitaki, MSC, PhD, of the University of Birmingham, United Kingdom, gave a talk on how chronic use of opioids can lead to multiple endocrinopathies. Currently, there is a lack of robust data on the prevalence of opioid-induced endocrinopathies and on predictive factors for who will develop them, she says. But opioid use has been associated with hypogonadism and adrenal insufficiency.



The Thyroid Ultrasound Workshop has advanced and introductory sessions for attendees to learn about the use of ultrasound in diagnosing thyroid nodules and performing ultrasound-guided fine-needle aspirations.

According to Karavitaki, opioids suppress the hypothalamus/pituitary/gonad system and reduce bone mineral density. These drugs also suppress adrenocorticotrophic hormone and glucocorticoid secretion. And opioid-induced hypogonadism remains under-diagnosed, partly because men may be embarrassed to tell their doctors they're suffering from lower libido or ability to perform, and partly because there is an under-appreciation for this connection among physicians. Karavitaki argues that doctors treating men on opioids need to think about testing testosterone levels, as well as the need for more studies and the development of guidelines since these drugs are so prevalent.

And while the government and physicians' groups are still struggling with the best ways to tackle this epidemic, an audience member stood up and commented on a possible easy solution, especially as it relates to how opioids affect the endocrine system. "If you tell men up front that opioids decrease sex drive and make them feel weaker, they will often opt for alternative treatment," she says.

A Focus on Endocrine Disruptors

One of the studies highlighted on Monday revolved around new mice studies that explain how exposure to bisphenol A (BPA) during pregnancy can lead to altered brain development later in life for the fetus. "Decades of research in over 1,000 animal and 100 human epidemiological studies have demonstrated a link between BPA exposure and adverse health outcomes," says lead researcher Deborah Kurrasch, PhD, associate professor at the University of Calgary in Calgary, Canada. She adds that this is especially true for the developing brain, which is particularly sensitive to the estrogen-promoting effects of BPA during gestation. "Indeed, several human studies have now correlated early life BPA exposure with behavioral problems later in childhood, suggesting BPA permanently alters brain development that leads to lasting effects on neural functioning."

The U.S. Food and Drug Administration (FDA) along with other governmental agencies around the world, declare BPA to

(Continued on page 37)



RICARDO CORREA, MD,
Es. D, FACP, FACR, CMQ, Warren Alert
School of Medicine, Warren, R.I.

GETTING “WOWED” at ENDO 2018

This year, **ENDO 2018**, the most important meeting in the field of endocrine science at the national and international level, brought many interesting and outstanding lectures and activities that captured the attention of the participants.

Personally, I was most impressed with the Early Career Symposium and the International Seminar Series. The addition of new topics such as the importance of academic medicine, negotiations, mentoring, and advice for international medical graduates (IMGs) made this symposium a tremendous success. Reviewing the feedback and opinions of the participants, it's obvious that the Endocrine Society really cares about the future of endocrinology and provides tools to create a strong group of young clinical and research endocrinologists.

The Presidential lecture by Lynnette Nieman, MD, on translating basic discovery into reproductive health was one of my favorite sessions of **ENDO 2018**. She explained the perfect interconnection between the bench and bedside research in hormone science.

There were several oral presentations that deserve special mention because they are top-notch topics in endocrinology. “The Predictors of survival in Adrenal Cortical Carcinoma (ACC): An analysis from the National Cancer Database” by Sri Harsha Tella, MD, was an outstanding investigation on this topic, and the research uncovered many unanswered questions. This was ground-breaking work in the field. “FGF-21 Mediates Energy Expenditure” by Karyne Vinales, MD,

illustrated that this growth factor determines weight change independent of age, gender, and race. Also, the featured poster on “Novel Treatment (SGLT2i) for Type B Insulin Resistance” by a team from Brown University opens a new research world for management of this rare condition and cases of severe insulin resistance.

Finally, the minority and diversity symposium was superior; the level of scientific quality of the poster presentations and the networking organization were very impressive and reflects the keen interest of the Endocrine Society in working with all its members.

ENDO 2018 has been the best meeting I have attended in the past 10 years. An excellent way to celebrate 101 years of the Endocrine Society.

Outgoing Endocrine Society President Lynnette Nieman, MD, at the Presidential Plenary session on Saturday morning.





Attendees from around the world stopped by the Endocrine Society booth to show their professional pride as part of the #IAMENDOCRINOLOGY campaign to highlight the rich diversity in this exciting field.

be safe. One reason for this disparity is the absence of a smoking gun, according to Kurrash: “If BPA is so toxic to developing brains, then where is the evidence of defective brains? Our study is the first to use environmentally relevant doses of BPA and show exposure to the chemical during brain development can affect the timing of the birth of nerve cells, or neurons.”

However, Kurrash is encouraged that the general public has been educating itself about the dangers of BPA and other potential endocrine disruptors. “Although there is still work to be done to translate these rodent effects to human pregnancy, this research could provide expectant mothers with important information on what to avoid to best protect their babies.”

A similar mouse study on EDCs focused on typical consumer products and their potential link to decreased sperm counts and sperm quality among men. Potentially frightening, this study showed that the effect of EDCs could actually extend beyond more than one generation. According to lead author Radwa Barakat, BVSC, MSc, of the College of Veterinary Medicine, University of Illinois at Urbana-Champaign, “Sperm counts among men have dropped substantially over the last few decades, but the reason for such an alarming phenomenon is not known. These results suggest that when a mother is exposed to an endocrine disruptor during pregnancy, her son and the son’s future generations may suffer from decreased fertility or hormone insufficiency.”

Barakat and her team gave pregnant mice one of four doses of di-(2-ethylhexyl) phthalate (DEHP), which is among the most widely used EDCs. It is found in a wide array of industrial and consumer products, including PVC piping and tubing, cosmetics, medical devices and plastic toys. The doses were administered from 11 days after they conceived until birth.

Adult males born to these mice were bred with unexposed female mice, to produce a second generation of mice. Young adult males from this second generation were bred with unexposed females to produce a third generation. When each generation of mice was 15 months old, the researchers measured sex hormone levels, sperm concentrations, and sperm motility or movement (a potential sign of infertility).

In second-generation males, only those descended from mice in the highest DEHP exposure group had abnormal reproductive results — lower testosterone concentration, sperm levels, and sperm motility. Third-generation males descended from DEHP-exposed mice also exhibited reproductive abnormalities at age 15 months, even those descended from mice that received a lower dose of the chemical. The researchers were surprised to find that the lowest DEHP dose group exhibited the greatest abnormalities.

“This study underscores the importance of educating the public to try their best effort to reduce their exposure to this chemical and also the need to substitute this chemical with a safer one,” Barakat says.

Is the Male Pill Closer to Reality?

It's been almost two years since *Endocrine News* wrote about the possibility of a male birth control pill in the June 2016 issue. New research presented at **ENDO** reveals that a potential male pill appears to be safe when used daily for a month, with hormone responses consistent with effective contraception.

Like the female pill, the experimental male pill — called dimethandrolone undecanoate (DMAU) — mixes the activity of an androgen-like testosterone and a progestin and is taken once a day. This is a major step forward in the development of the one-a-day male pill, says the study's author Stephanie Page, MD, PhD, professor of medicine at the University of Washington, Seattle. "Many men say they would prefer a daily pill as a reversible contraceptive rather than long-acting injection or topical gels, which are also in development," she says.

According to Page, progress toward a male birth control pill has been stymied because available oral forms of testosterone may cause liver inflammation and they clear the body too quickly for once-daily dosing, which leads to a second daily dose. However, DMAU contains undecanoate, a long-chain fatty acid, which Page says slows this clearance. DMAU is being developed by the NIH, Eunice Kennedy Shriver National Institute of Child Health and Human Development, which funded this study.

The study included 100 healthy men, ages 18 to 50 years, and took place at the University of Washington Medical Center and at Harbor-UCLA Medical Center in Torrance, Calif., (led by co-author Christina Wang, MD). The investigators tested three different doses of DMAU (100, 200, and 400 mg) and two different formulations inside the capsules (castor oil and powder). Each dose group included five subjects who were randomly assigned to receive an inactive placebo and another 12 to 15 men who received DMAU. Subjects took the drug or placebo for 28 days once daily with food. DMAU must be taken with food to be effective, Page notes.

A total of 83 men completed the study, including giving blood samples, for hormone and cholesterol testing, on the first and last days of the study. At the highest dose of DMAU tested, 400 mg, subjects showed "marked suppression" of levels of their testosterone and two hormones required for sperm production. The low levels, Page says, are consistent with effective male contraception shown in longer-term studies. "Despite having low levels of circulating testosterone, very few subjects reported

symptoms consistent with testosterone deficiency or excess," Page adds.

While all groups taking DMAU did have weight gain and decreases in HDL (good) cholesterol, Page says both were mild; all subjects passed safety tests, including markers of liver and kidney function. "These promising results are unprecedented in the development of a prototype male pill," Page says. "Longer-term studies are currently under way to confirm that DMAU taken every day blocks sperm production."

As Page notes at the press conference at **ENDO** on March 18, "This is the first significant breakthrough in male contraception in 300 years when the condom was invented."

Essential Oils Under the Microscope

They have been heralded as alternative therapies for everything from weight loss, skin care, anxiety, in recipes, and even as insect repellants and household cleansers. Now essential oils may have another label: endocrine disruptor.

A new study from the National Institute of Environmental Health Sciences (NIEHS), gives further evidence to a possible link between abnormal breast growth in young boys — prepubertal gynecomastia — and regular exposure to lavender or tea tree oil.

Needless to say, the results of this study have caused something of an uproar in the alternative medicine world. One manufacturer of essential oils even went so far as to issue a response to the study! "Our society deems essential oils as safe," according to J. Tyler Ramsey, a postbaccalaureate research fellow at NIEHS, and lead investigator. "However, they possess a diverse amount of chemicals and should be used with caution because some of these chemicals are potential endocrine disruptors."

Male gynecomastia occurring before puberty is relatively rare, but a growing amount of cases have been reported to coincide with topical exposure to lavender and tea tree oil. But when exposure to the oils ceased, the condition went away. NIEHS researchers, including Kenneth Korach, PhD, a co-investigator for the new study, previously found laboratory evidence that lavender and tea tree oil have estrogenic (estrogen-like) properties and anti-androgenic (testosterone inhibiting-like) activities, meaning they compete or hinder the hormones that control male characteristics, which could affect puberty and growth.

See You Next Year
ENDO 2019
New Orleans, LA • March 23-26, 2019




Under Korach's direction, Ramsey and his NIEHS colleagues analyzed eight components that are common and mandated for inclusion in the oils. Four appear in both oils: eucalyptol, 4-terpineol, dipentene/limonene, and alpha-terpineol. The others were in either oil: linalyl acetate, linalool, alpha-terpinene, and gamma-terpinene. Using *in vitro* experiments, the researchers applied these chemicals to human cancer cells to measure changes of estrogen receptor- and androgen receptor-target genes and transcriptional activity.

All eight chemicals demonstrated varying estrogenic and/or anti-androgenic properties, with some showing high or little to no activity, the investigators reported. Ramsey said these changes were consistent with endogenous, or bodily, hormonal conditions that stimulate gynecomastia in prepubescent boys. "Lavender oil and tea tree oil pose potential environmental health concerns and should be investigated further," he says.

According to Ramsey, there is further concern: Many of the tested chemicals appear in dozens of other essential oils, which are available without a prescription and are not regulated by the FDA. Going forward, the public needs to be aware of these findings before using these trendy medical

alternatives for whatever purpose they see heralded in their social media feeds or in online advertising.

From patients telling their own stories to the impact of headline-grabbing issues affecting endocrine science and practice alike, **ENDO 2018** was one for the record books. However, this article barely scratches the surface. Much of the research presented at **ENDO** has already been posted online (www.endocrinenews.org), but we will also be covering it more in-depth in the months to come in *Endocrine News*, both in print and online.

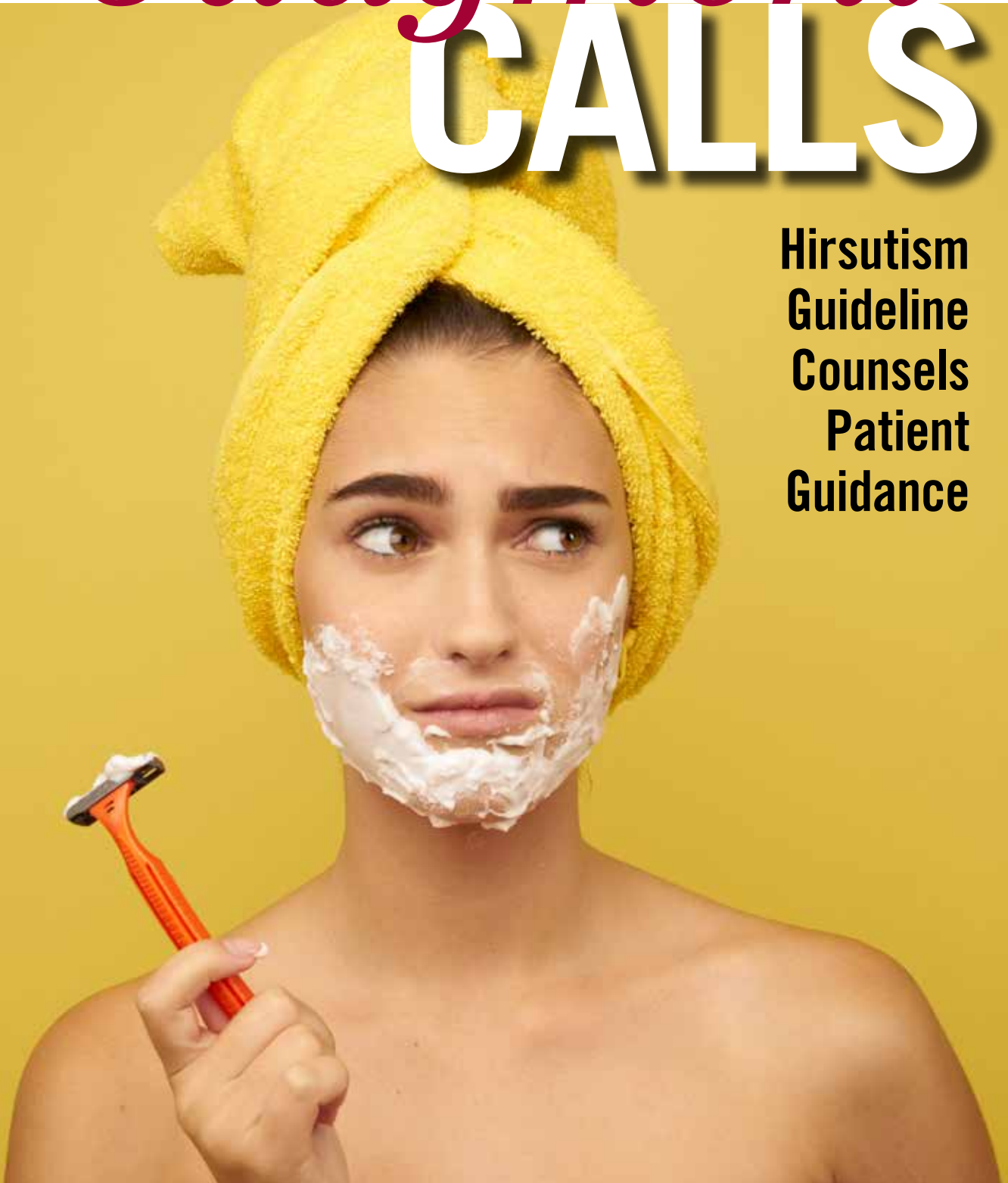
Hopefully this wrap-up made you green with envy, rivaling the Chicago River on St. Patrick's Day! Never fear, there's plenty of time to plan for **ENDO 2019**, March 23 – 26 in one of the most culturally significant cities in the country: New Orleans! As you hear on the streets of the French Quarter: "Laissez les bon temps rouler!" 

BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS* AND NEWMAN IS THE EDITOR. **ENDO 2018** WAS THE SIXTH ANNUAL CONFERENCE FOR BOTH AND THEY ARE EAGERLY ANTICIPATING **ENDO 2019** IN NEW ORLEANS!

BY ERIC SEABORG

Judgment CALLS

**Hirsutism
Guideline
Counsels
Patient
Guidance**



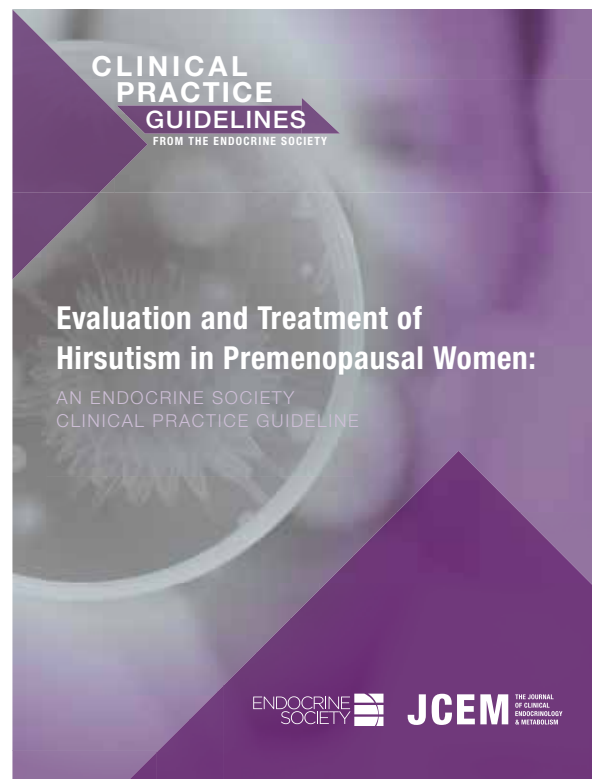
According to a new treatment guideline from the Endocrine Society, endocrinologists should base treatment of hirsutism on the distress and perceptions of the patient, not their opinion of its severity.

A newly released Endocrine Society guideline on treatment of hirsutism does not make major changes from the 2008 version, but it does make a host of tweaks and updates regarding both treatment and diagnosis based on the latest knowledge.

“To maintain the quality of the guideline, we did an updated literature review and meta-analysis to see if there was a compelling reason to change any of our treatment recommendations,” says Kathryn A. Martin, MD, a faculty member in the Reproductive Endocrine Unit at Massachusetts General Hospital in Boston, who chaired the task force that drew up the guideline.

“Hirsutism is common, occurring in 5% to 10% of all women. It is usually a sign of an underlying endocrine disorder, most commonly polycystic ovary syndrome (PCOS),” Martin says. “The Endocrine Society has a separate guideline on the diagnosis and treatment of PCOS. Our task was to focus on the evaluation and management of hirsutism and not other aspects of PCOS. We hope that women who present with any degree of hirsutism will be offered an endocrine evaluation followed by appropriate therapy as outlined in the guideline. Treatment options include pharmacologic treatment, direct hair removal methods, or both.”

Many clinicians have treated hirsutism based on their judgment of the severity of the hair growth. But the new guideline reinforces the notion put forth in the previous



version that the need for treatment should be the patient's call, not the physician's. “Treatment should be based on the level of distress the woman is experiencing,” Martin says. “Some women are distressed by a little bit of hair growth, while others with very severe hair growth may not be as distressed.”

Martin adds that one important message to clinicians is that they should not ignore the patient's cosmetic concerns “just because you think their hirsutism is minimal or mild,” she says. “We now know how distressing any degree of hirsutism can be. It is associated with anxiety and depression, so we do want clinicians to take it seriously.”

More Evidence Confirming Practices

Two other areas where additional evidence reinforced their previous recommendations were the choice of oral contraceptive and hair removal through photoepilation.

The previous guideline found that all formulations of oral contraceptives are equally effective for treatment of hirsutism. Even so, one school of thought has maintained that because hirsutism is associated with high levels of

CHANGES IN TREATMENT

While the new version of the guideline does not differ greatly from the 2008 edition, there have been several modifications:

- ▶ For women with mild hirsutism and no evidence of an endocrine disorder, the new guideline suggests that initial therapy can be either pharmacologic therapy that targets androgen production and action or direct hair removal methods, consistent with the approach of offering treatment options based on the patient's preferences. "For other women with patient-important hirsutism, we suggest starting with pharmacological therapy and adding direct hair removal methods if needed," the statement says.
- ▶ Although the statement recommends against combination therapy as a standard first-line approach, the committee added a recommendation that in treating women with severe hirsutism who are experiencing a high level of distress, it is reasonable to start with combined pharmacological therapy of both oral contraceptives and anti-androgens.
- ▶ The previous guideline advised against the use of the anti-androgen flutamide, and the revised version strengthens this recommendation. "Clinicians prescribing flutamide started using it at lower and lower doses, saying it was safe. We found plenty of evidence that even at lower doses it is not safe, so we made a definitive recommendation that you should avoid it under any circumstances," Martin says. "It causes liver toxicity, and we couldn't justify giving it to an otherwise healthy young woman when there are other drugs that are very effective."
- ▶ Hirsutism is most often caused by polycystic ovary syndrome, so the guideline writers added a recommendation that first-line treatment should include the lifestyle changes of diet and exercise, especially for patients with obesity.

“ We hope that women who present with any degree of hirsutism will be offered an endocrine evaluation followed by appropriate therapy as outlined in the guideline.

Treatment options include pharmacologic treatment, direct hair removal methods, or both.”



— KATHRYN A. MARTIN, MD, TASK FORCE CHAIR; FACULTY MEMBER, REPRODUCTIVE ENDOCRINE UNIT, MASSACHUSETTS GENERAL HOSPITAL, BOSTON

androgens, birth control pills containing progestins, which are considered “anti-androgens,” must be more effective. But a meta-analysis of an increasing number of studies in the literature suggested that “all available birth control pills seem to be equally effective for hirsutism, so it really doesn't matter which one you use,” Martin says.

“This version has more detail on the uses, efficacy, and safety of photoepilation — hair removal using laser and intense pulsed light,” Martin says. “In 2008, we were less enthusiastic about recommending it for patients, but this time there were more clinical trials that had been published. We were very comfortable saying it is effective therapy for women with light skin and dark hair. But it is less effective and sometimes associated with complications in women with darker skin, especially those with Middle Eastern and Mediterranean ancestry. Some women with dark skin get unusual complications. One is called paradoxical hypertrichosis, which is a type of hair growth that is not hirsutism. Instead of having a reduction in their facial hair, patients end up with a lot more facial hair. And it is not just in the areas where they laser, it is all over their face, and no one knows why.”

Broadened Diagnostic Testing


The guideline broadens the suggestions for biochemical testing. “We now suggest testing the serum total testosterone level of all women with hirsutism,” Martin says, in contrast to the previous guideline's suggestion that only those with moderate-to-severe hirsutism be tested.

The guideline also recommends broadening testing when:



“This version [of the CPG] has more detail on the uses, efficacy, and safety of photoepilation — hair removal using laser and intense pulsed light,” Martin says. “In 2008, we were less enthusiastic about recommending it for patients, but this time there were more clinical trials that had been published.”

- Patients who have a normal serum total testosterone concentration in the presence of moderate-to-severe hirsutism or other clinical evidence of hyperandrogenemia should have their serum free testosterone concentrations measured.
- Hyperandrogenemic women should be screened for non-classic congenital adrenal hyperplasia (NCCAH) due to 21-hydroxylase deficiency by measuring early morning 17-hydroxyprogesterone levels in the follicular phase. Patients with amenorrhea or infrequent menses should be tested on a random day.
- Women with hirsutism whose family history or ethnicity puts them at high risk for NCCAH should have their 17-hydroxyprogesterone levels measured even if their serum total and free testosterone concentrations are normal.

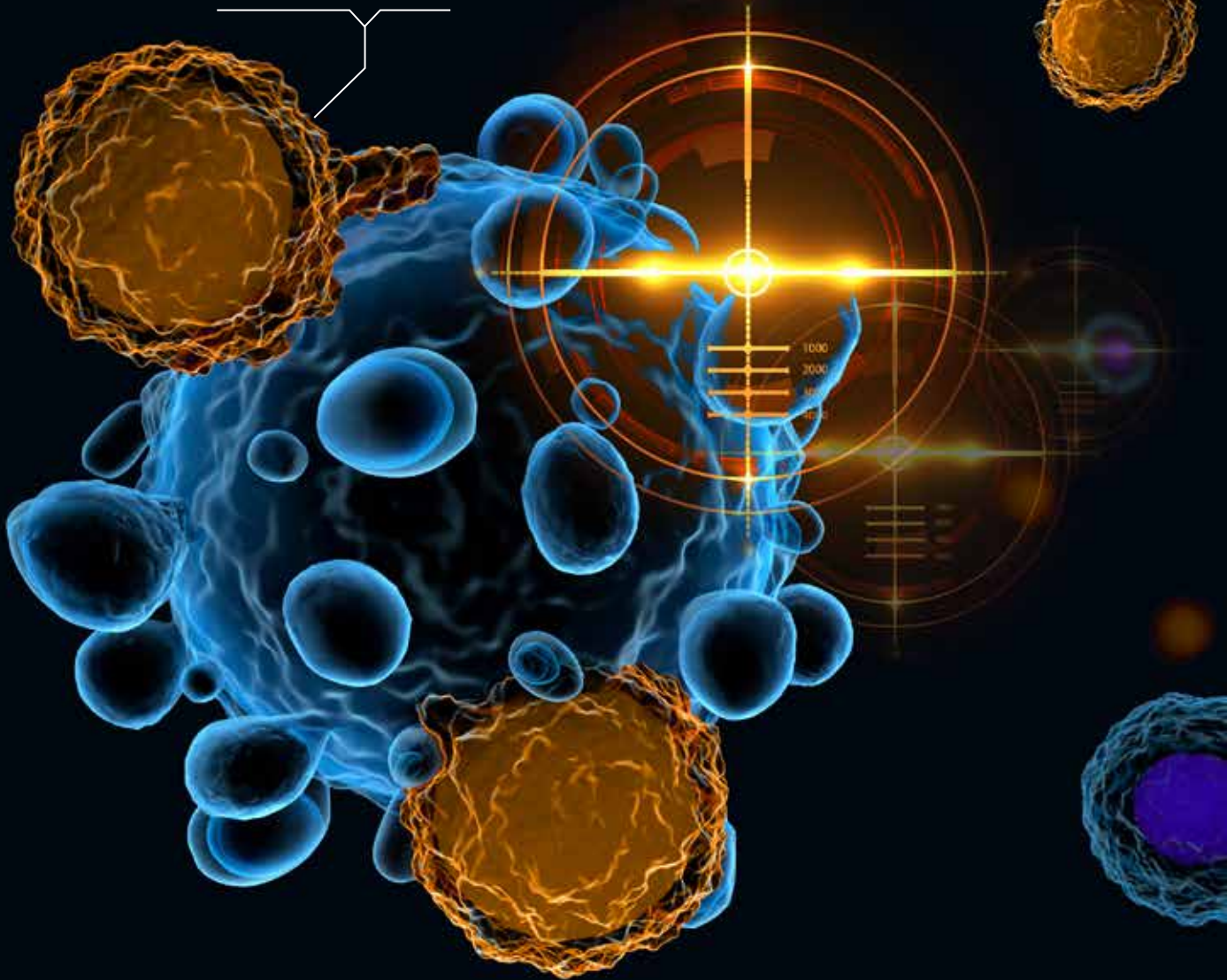
In addition to the Endocrine Society, “Evaluation and Treatment of Hirsutism in Premenopausal Women: An Endocrine Society Guideline” was cosponsored by the Androgen Excess and Polycystic Ovary Syndrome Society and the European Society of Endocrinology. It will be published in the April issue of *The Journal of Clinical Endocrinology & Metabolism*, and is available online at: www.endocrine.org/hirsutismCPG. 

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT A NEW SCIENTIFIC STATEMENT ON TREATING PATIENTS WITH DIABETIC MICROVASCULAR DISEASE IN THE FEBRUARY ISSUE.

AT A GLANCE

- ▶ Hirsutism is distressing to many patients. Because it is associated with anxiety and depression, treatment should be guided by the patient’s perceptions, not the clinician’s opinion of its severity.
- ▶ Hirsutism is most often caused by an endocrine disorder such as polycystic ovary syndrome (PCOS), so clinicians should focus on the underlying problem, if present, in addition to the hirsutism. If the patient has PCOS, this could include treating irregular menstrual cycles as well as metabolic problems such as obesity and an increased risk of type 2 diabetes. Women with hirsutism and PCOS are typically started on estrogen-progestin contraceptives; an anti-androgen is added after six months if the patient feels there has not been enough improvement.
- ▶ Photoepilation has proven to be an effective treatment for hirsutism, particularly for patients with light skin and dark hair but should be avoided among patients with dark skin.

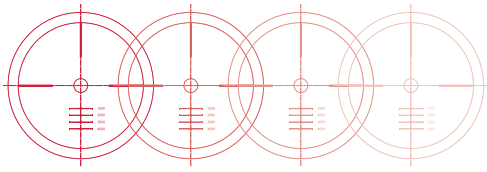
3d illustration of immune system T cells
targeting and attacking cancer cells



Immune checkpoint inhibitors unleash the immune system on cancer to great effect and increase survival rates. However, switched-on immune cells set their sights on other targets, many times the endocrine system.

MOVING Targets:

BY ERIC SEABORG



Immunotherapy and Endocrinopathies

Immunotherapy has boosted survival rates for some of the most recalcitrant forms of cancer with an approach that is revolutionizing the field. But as the treatment beats back cancer, serious side effects strike many patients. Endocrinopathies — particularly involving the thyroid, pituitary, and pancreas — are among the most common and important of these.

“We in the endocrinology community need to be familiar with the basic idea behind these medications our oncology colleagues are utilizing,” says Matthew J. Levine, MD, of the Scripps Clinic division of diabetes and endocrinology in San Diego. “They unleash the immune system to fight malignancies. And while they seem to be very effective in combatting the malignancies for which they are designed, they cause a lot of endocrine-related adverse events.”

AWAKENING T CELLS

Immunotherapy attacks cancer’s secret weapon — its ability to hide from the immune system by keeping immune cells from recognizing tumor cells as invaders. The immune system contains checks and balances that keep the body from harming itself, and several years ago researchers discovered some “checkpoints” on T cells that act as brakes on their aggressiveness, including the proteins PD-1 (for programmed

death 1) and CTLA-4 (for cytotoxic T-lymphocyte-associated protein 4). Many tumor cells express the ligands for these checkpoint receptors, and when triggered, the checkpoint proteins provide a brake or “off switch” that inhibits the T cell from attacking the tumor cell.

Researchers exploited these discoveries to develop drugs they dubbed immune checkpoint (ICP) inhibitors — monoclonal antibodies aimed at PD-1, PD-L1, and CTLA-4 to block the proteins from binding to the tumor cells, thereby taking off the brakes and allowing the T cell to recognize and attack the tumor cells.

The Food and Drug Administration (FDA) approved the first ICP inhibitor in 2011, and the therapy is now in use for advanced or metastatic melanoma, non-small-cell lung cancer, metastatic squamous cell carcinoma of the head and neck, kidney cancer, urothelial cancer, and Hodgkin lymphoma. And they are in clinical trials for many other cancer types.

TARGETS IN THE ENDOCRINE SYSTEM

“Over the last two years there has been an explosion of using these drugs, and as a side effect of that treatment, we are starting to get a significant referral of patients to endocrine clinics with the onset of new autoimmune problems that are targeting the

FDA-Approved ICP Inhibitors

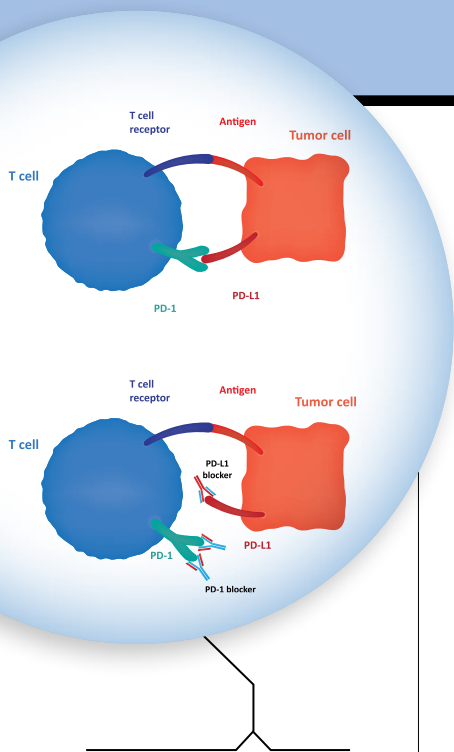
Anti-CTLA-4 drugs:
Ipilimumab

Anti PD-1 drugs:
Nivolumab, Pembrolizumab

Anti PD-L1 drugs:
Atezolizumab, Durvalumab, Avelumab



Programmed death-ligand 1 (PD-L1) protein, 3D rendering. Produced by tumor to suppress the immune system. Blockers of the PD-L1 and PD-1 interaction are an important new anticancer drug class.



Cancer Immunotherapy (Nivolumab). The PD-1/PD-L1 Blockade: (top figure) The PD-1/PD-L1 interaction protects the cancer cell from immune destruction; (bottom figure) Blocking the PD-1/PD-L1 interaction allows T cells to destroy tumor cells.

patient's endocrine system," says Mark S. Anderson, MD, PhD, a professor and researcher at the University of California San Francisco Diabetes Center.

The problem is that when these drugs take off the brakes, the T cells can attack the patient's own tissues — and the thyroid, pituitary, and adrenal glands as well as pancreatic islets are of particular concern for these immune-mediated problems.

When Levine and his colleagues at Scripps reviewed the charts of 103 patients who received ICP inhibitors, they found that some 32% developed an endocrine immune-related adverse event. A 2016 study by Joshi et al. in *Clinical Endocrinology* found that thyroid dysfunction occurs in up to 15% of patients, hypophysitis in up to 9%, and adrenalitis in about 1%. Other reports put the incidence of type 1 diabetes at 1% or more.

The agents appear to affect tissues differently. CTLA-4 inhibitors are associated more with hypophysitis, whereas PD-1 blockade is implicated more in thyroid dysfunction.

The Joshi study found that the mean onset of endocrine side effects is nine weeks after the initiation of therapy, with a wide range of onset from five to 36 weeks. Levine's team found that most endocrine adverse events occurred between the second and fifth infusion. Several occurred after the first infusion, and one occurred after 14 infusions. There are literature reports of problems occurring even later in the infusion process, so patients must be monitored through a wide time frame.

TREATMENT: STANDARD YET EXPERIMENTAL

For the most part, recommended treatment for these conditions is generally the same whether they result from ICP treatment or develop on their own or under other circumstances. The treatment approach may depend on a condition's severity and how soon it was detected, especially as it relates to whether the cancer treatment can continue.

“ We think now that the immune system is really capable of mediating anti-tumor activity against almost any type of tumor. There are some types that have been holdouts that haven't responded, and we are trying to understand why that is the case. **We think eventually most cancers might be amenable to at least some form of immunotherapy.**”

— HOWARD KAUFMAN, MD, IMMEDIATE PAST PRESIDENT, SOCIETY FOR IMMUNOTHERAPY OF CANCER; FACULTY MEMBER, MASSACHUSETTS GENERAL HOSPITAL, BOSTON

“Sometimes the thyroid issues that come up as a result of these medications are consistent with thyroiditis — a transient phenomenon where a person can develop an overactive thyroid, then an underactive thyroid. By its nature, it normalizes over time,” Levine says.

Hypothyroidism can be treated with conventional hormone replacement, and hyperthyroidism can also be treated conventionally.

Although some sources have recommended treating hypophysitis with high-dose glucocorticoid therapy, various studies have found that high-dose therapy did not improve outcomes. They suggest that physiologic glucocorticoid replacement dosing may avoid additional adverse consequences.

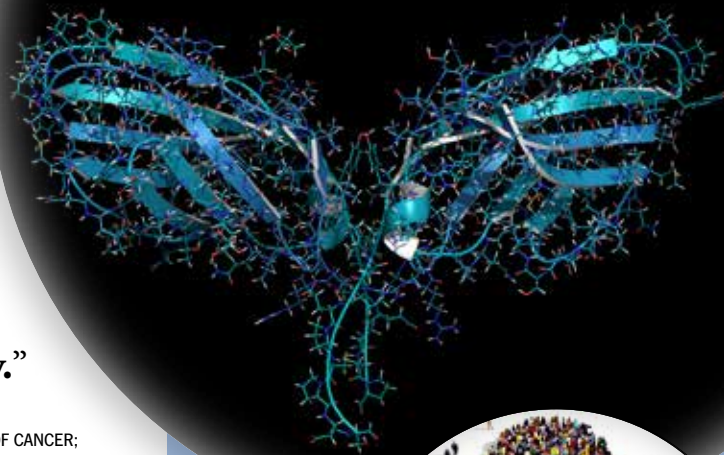
Primary hypoadrenalism due to ICP inhibitor treatment should be treated with conventional hormone replacement following current guidelines.

UNIQUE DIABETES

The tripping of an autoimmune disease such as type 1 diabetes should come as no surprise, but Anderson says: “It's remarkable how quickly it can happen. The glucose will be normal at one infusion and then sky high at the next. We are getting patients who have glucoses well over 500 mg/dL, diabetic ketoacidosis, and low insulin c-peptide levels. Taken together, this picture points to an acute onset of a unique form of type 1 diabetes.”

Although there seems to be interim consensus on treatment recommendations, Levine notes that the field is so new that it is lacking in protocols on treatment and about whether ICP treatment can be continued while side effects are treated. Patients generally receive panels of laboratory tests from their oncologists, but the field also

CTLA-4 (Cytotoxic T-lymphocyte-associated protein 4, CD152) protein. CTLA4 blocking antibodies are used in cancer therapy (immune checkpoint blockade therapy).



AT A GLANCE

- ▶ Immune checkpoint inhibitors to treat cancer are exploding in use. Their success could revolutionize the field.
- ▶ As immunotherapy unleashes the patient's immune system to attack cancer, T cells can also attack the patient's other tissues, with the endocrine system at particular risk.
- ▶ Most endocrinologists will be familiar with how to treat these endocrinopathies, but the protocols for treatment will evolve with experience.



IMMUNOTHERAPY

“ We in the endocrinology community need to be familiar with the basic idea behind these medications our oncology colleagues are utilizing. They unleash the immune system to fight malignancies. And while they seem to be very effective in combatting the malignancies for which they are designed, they cause a lot of endocrine-related adverse events.”

— MATTHEW J. LEVINE, MD, SCRIPPS CLINIC
DIVISION OF DIABETES AND ENDOCRINOLOGY,
SAN DIEGO, CALIF.


lacks protocols on the extent and timing of testing. The question of how often the endocrinopathies are reversible and how many will require indefinite treatment is another that only experience will answer.

EARLY TREATMENT PAYS

Patients need to be told to be frank about their symptoms and resist any temptation to hide them out of fear that they could be taken off the ICP inhibitors, according to Howard Kaufman, MD, immediate past president of the Society for Immunotherapy of Cancer and a faculty member at Massachusetts General Hospital in Boston: “If we can intervene when the side effects are minimal, the likelihood that they will stay on the treatment is higher. With all of these side effects, the earlier they are identified and treated, the more rapidly they seem to come under control.”

Another challenge comes from patients who don't realize their symptoms are side effects of the ICP inhibitors or misunderstand their implications. “They go to the emergency room and say, ‘I'm on chemotherapy.’ The poor emergency room doctor may be misled or may not understand that immunotherapy is really different from chemotherapy,” Kaufman says. Kaufman gives his patients cards explaining about their ICP inhibitor treatment, but not everyone carries them.

Most endocrinologists are seeing these patients as a result of referrals from oncologists. But the potential for patients to show up at endocrine clinics seeking treatment for side effects will grow. ICP inhibitors are currently used mostly in large centers, but many more agents are in development and trials. As more come on the market and the indications for their use expand, they will inevitably spread throughout the healthcare system and endocrinologists will need to be prepared to manage these patients.

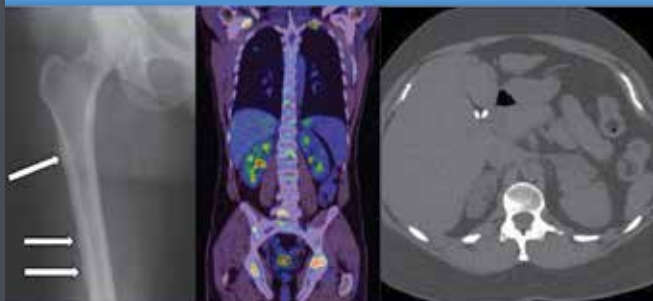
“We think now that the immune system is really capable of mediating anti-tumor activity against almost any type of tumor,” Kaufman says. “There are some types that have been holdouts that haven't responded, and we are trying to understand why that is the case. We think eventually most cancers might be amenable to at least some form of immunotherapy.” 

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT THE ENDOCRINE SOCIETY'S LATEST SCIENTIFIC STATEMENT ON OBESITY IN THE MARCH ISSUE.

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Winners Circle

BY MARK A. NEWMAN

A Roundtable with the 2018 Knock Out Round Champs



One of the highlights of ENDO each year is witnessing the up and coming talent in the world of endocrine science present their research at the Knock Out Rounds. *Endocrine News* spoke to this year's winners, Angela Odle, Juilee Rege, and Daniel Ferguson about their experience, their research, and their futures.



Angela Odle

postdoctoral research fellow in the Department of Neurobiology and Developmental Sciences at the University of Arkansas for Medical Sciences, in Little Rock

“

With the current rates of obesity in our country, both in children and adults, we need to address increasing complexity of reproductive difficulties. It is crucial that we define the mechanisms behind impaired fertility in obese and overweight populations.

”

One of the highlights of **ENDO 2018** was the game show-like atmosphere of the Knock Out Rounds, where more than a dozen young researchers did their best to persuade a panel of judges that their three-minute presentation was the best.

Since its debut at **ENDO 2016** in Boston, the Knock Out Rounds have proven to be one of the most popular events at the conference. This year, 13 early-career basic science researchers were pitted against each other as they presented short, focused presentations highlighting the rationale for their science rather than strictly focusing on the outcomes. Each contestant was allowed only three minutes per presentation along with a single slide to illustrate their work.

Serving on the panel of judges were Jonna Frasor, PhD, Department of Physiology and Biophysics, University of Illinois at Chicago; Gregory A. Brent, MD, UCLA; and yours truly, representing *Endocrine News*. Once again, the event was kept on track and on time by the Endocrine Society's own chief communications and marketing officer, Aaron Lohr.

“These were all very talented young researchers who did a great job presenting their research in engaging and easy-to-understand terms,” Frasor says. “This is such an important skill for researchers to make a lay audience really understand the work that they do in the lab day in and day out. Each of these researchers did a remarkable job. I was thoroughly engaged.”

This year, Angela Odle a postdoctoral research fellow in the Department of Neurobiology and Developmental Sciences at the University of Arkansas for Medical Sciences, in Little Rock, was the first-place winner, as well as the People's Choice winner, which was decided by online voting of those in the audience who voted via the **ENDO 2018** app on their phone. Second-place honors went to Juilee Rege, a postdoctoral fellow in the laboratory of Dr. Bill Rainey in the Department of Molecular and Integrative Physiology at the University of Michigan, Ann Arbor. Daniel Ferguson, a postdoctoral research scholar in the Internal Medicine Division of Endocrinology, Metabolism, and Lipid Research at Washington University School of Medicine in St. Louis, placed third. They took time from their busy research projects and navigating the sessions in McCormick Place to share their thoughts about their presentations, their research, and what they see for the future of their research as well as their careers in endocrinology.

What was it like explaining your research to a room full of scientists and clinicians?

Angela Odle: I was surprised by how much fun I had both participating in and listening to the KO Rounds. We are all so used to talking about our research on a day-to-day basis with people in our own little world that we can sometimes forget how much jargon we actually use. I enjoyed the challenge of trying to make everyone in the room understand the basis of my work. I felt like the organizers did a great job of creating a positive atmosphere and making the session enjoyable for everyone.

Juilee Rege: The Knock Out Rounds was a fun experience. Explaining my research to scientists and clinicians not in my area of research was challenging but exciting. I think that the format of the Knock Out Rounds was a great tool to get people with other endocrinology backgrounds interested in the research that I do. I am glad I could communicate the clinical and translational significance of my research to a broad scientific audience.



Juilee Rege

postdoctoral fellow in the laboratory of Dr. Bill Rainey in the Department of Molecular and Integrative Physiology at the University of Michigan, Ann Arbor

“

I am glad I could communicate the clinical and translational significance of my research to a broad scientific audience.

”

Daniel Ferguson: It was a bit intimidating, but I really do appreciate the perspective of both researchers and clinicians.

How did you prepare differently once you learned more about the Knock Out Rounds?

AO: We were instructed not to summarize our posters/abstracts, so I was careful not to include too much data from the start. However, what little data I did include initially had to be edited even further once I realized I couldn't possibly give enough background for each different component. I only included one type of data that I felt was interesting and representative of the kind of work that we do in our lab. Keeping a talk down to three minutes is challenging! I wrote down everything I wanted to say, and then kept cutting, editing, and practicing until I could consistently stay within the time limit.

JR: The Knock Out Rounds is a difficult but exciting concept where you get only three minutes and one slide to convey your research to a lay audience. It is challenging for researchers to communicate their work and its implications in a way that is accessible and meaningful to a broad audience. The Knock Out Round audios from the previous **ENDO** meetings posted on the **ENDO** website definitely helped me to exactly understand what needed to be highlighted in my talk. As far as the preparation was concerned, I tried to put forth my science in such a way that it was simple and less jargon-y. Input from my lab folks and an hour-long session with RELATE, a communications training and community engagement program on campus designed to improve the dialogue between researchers and different public audiences, helped significantly.

DF: The three-minute time limit was the biggest factor in deciding what did or didn't get added into the talk and how to say it.

Tell us a little bit about your presentation and why you feel your study was so important.

AO: I spent the first part of my presentation discussing reproduction and nutrition, and how the two systems are thought to communicate. I made sure to point out what components are known, and what is still being investigated. I also felt that it was important to remind the audience WHY it is important that our reproductive system is capable of receiving signals about the body's nutritional stores. I then focused in on the pituitary, where our research takes place. I introduced a hypothesis, showed one set of data, and then formed a conclusion based on that data.

With the current rates of obesity in our country, both in children and adults, we need to address increasing complexity of reproductive difficulties. It is crucial that we define the mechanisms behind impaired fertility in obese and overweight populations.

JR: My work focuses on the production of bioactive androgens in pre-pubertal children. Testosterone has been the conventional measure of androgen activity in pre-pubertal children all this while, but our study has pointed out that 11-ketotestosterone — an adrenal-derived 11-oxygenated derivative of



Daniel Ferguson

postdoctoral research scholar
in the Internal Medicine
Division of Endocrinology,
Metabolism, and Lipid
Research at Washington
University School of Medicine
in St. Louis

testosterone — could in fact represent a major androgen source in this population. I feel this study is important because we need to expand our repertoire of biomarkers to include this new androgen for diagnosis of childhood androgen excess disorders for more accurate diagnosis and in turn better health outcome.

DF: The work is important because our treatment induces such a dramatic decrease in metabolic abnormalities (obesity, diabetes, and fatty liver) associated with hormone deficiency, specifically leptin deficiency, and it can also be applied to lipodystrophy, which is a much larger patient population.

What are your future plans with the study that you presented at the Knock Out Rounds?

AO: I presented limited data on luteinizing hormone secretion from female mice with (normal) and without (mutant) gonadotropin leptin receptors, showing that our mutants did not produce a normal LH surge. I plan to use in vitro studies to show the mechanisms behind leptin's actions in the gonadotropin, specifically with regard to this important hormonal event.


JR: I want to dive deep into the study of this novel derivative of testosterone at both molecular as well as translational level. In addition, I hope to apply this knowledge in non-adrenal-related hyperandrogenic disorders in children and women.

DF: To publish the work.

Where do you see yourself in the next five years in the field of endocrinology?

AO: That is a tough question! I really enjoy the field I am in now. Researchers in the area of reproductive endocrinology are some of the most intelligent and generous scientists you will come across. I'd like to become an independent academic researcher with a strong spirit of collaboration. It is collaboration that has allowed our group to be successful and move out of our comfort zone into more cutting-edge territories. In five years, I imagine myself still attending the **ENDO** meetings, maybe as a young principal investigator, sitting in the audience, voting for my student in the 2023 KO rounds.

JR: My long-term career goal is to establish a strong independent research program in the area of adrenal-related hyperandrogenism. My current goals all revolve around obtaining scientific independence, including obtaining funding. I have been exceptionally fortunate to have Dr. William Rainey and Dr. Richard Auchus at the University of Michigan as mentors who have 1) broadened my research horizons; 2) acquainted me with the strengths and weaknesses of various study designs and interpretations; 3) helped me develop a sense of self-critique toward my own work; 4) provided guidance on developing a service portfolio; and 5) encouraged me to maintain a work/personal life balance. I hope to continue this tradition as mentoring and establishing a legacy of successful mentees is very important to me.

DF: Not sure of the exact position, but my main passion is to perform translational research to solve problems in the clinic (bench to bedside). 

“

My main passion is to perform translational research to solve problems in the clinic (bench to bedside).

”

Shock TO THE System

BY GLENDA FAUNTLEROY



From electrocutions to deadly fires, a variety of accidents and deaths in the lab have been linked to a lack of proper electrical safety. While maintaining a safe research environment is vital to pass inspection, it's also vital in saving lives.

In August 2005, tragedy struck the campus of Cleveland State University when distinguished researcher, Tarun Mal, was killed in a laboratory accident. The 42-year-old biology professor was electrocuted as he plugged equipment into an electrical outlet.

And at the University of Hawaii in March 2016, postdoc Thea Ekins-Coward lost her arm in a laboratory explosion caused from a static electricity charge that ignited a tank containing a highly flammable pressurized mixture of hydrogen, oxygen, and carbon dioxide, according to *Science* magazine. The final report found that the tank was not grounded, and the ignition probably happened “when the statically charged researcher touched the metal housing of the gauge.” The university was ultimately found to have systemic safety failures in the lab.

Horrible electrical accidents like these are an unfortunate occurrence in laboratories across the country. The major hazards associated with electricity in the laboratory are electrical shock or electrical fire. Oftentimes, however, such electrocutions and electrical fires could have been avoided if the laboratory had been aware of safety hazards and taken appropriate measures to correct.

Careful Compliance

Laboratories are stocked with electrically powered equipment used on a daily basis. Whether it's vacuum pumps, stir plates, UV lamps, or refrigerators, all electrical equipment can pose a serious hazard if not properly maintained or improperly used.

While universities have their own individual safety compliance standards, many refer to

ELECTRICAL SAFETY MUST-DOS

Make sure your team follows these precautions to lower the risk of personal injury or damage to important laboratory electrical equipment:

- ▶ Inspect wiring of equipment before each use.
- ▶ Replace all frayed or damaged electrical cords immediately.
- ▶ Use only equipment with three prongs (ground) in the laboratory.
- ▶ Use extension cords only temporarily. Otherwise, request installation of a new outlet.
- ▶ Equip all electrical power outlets in wet locations with ground-fault circuit interrupters (GFCIs) to prevent electrocutions. GFCIs are designed to “trip” and break the circuit when a small amount of current begins flowing to ground.
- ▶ Know the location and how to operate shut-off switches and/or circuit breaker panels and use these devices to shut off equipment in the event of a fire or electrocution.

codes and standards set by the National Fire Protection Association (www.nfpa.org) — the global organization devoted to eliminating death, injury, property and economic loss from fire, electrical, and related hazards. Laboratories on university campuses and institutions are regularly inspected to ensure that they adhere to established safety codes.

The laboratory of Daniel Gorelick, PhD, assistant professor in the Department of Cellular & Molecular Biology, at Baylor College of Medicine, Houston, Texas, is inspected once a year, and he says his team is reminded not to overload circuits.

“This means limiting our use of power strips, and never plugging one power strip into another,” says Gorelick. “We are also prohibited from using electrical space heaters.”

On some campuses, safety inspections are done even more frequently.

“We are inspected twice a year, and principal investigators are asked to do a quarterly self-inspection,” says Andrea C. Gore, PhD, professor and Vacek Chair of Pharmacology, at the University of Texas at Austin.


Gore says the school’s Environmental Health & Safety’s general lab inspection list includes checking for frayed or torn electrical cords on instruments, an extension cord that is used permanently, a blocked electrical panel, and improper use of cords/receptacles. All of these are code violations.

For inspector Mark Yanchisin at the University of Florida, finding these types of violations as well as more egregious ones is far too common.

As the university’s Clinical and Laboratory Safety Program Manager, Yanchisin and his team are charged with inspecting the research and teaching labs of about 1,000 principal investigators each year. With the main campus and another 40 or so research sites around the state, it equates to about 3,000 labs. Their goal is to act as a facilitator in resolving non-compliance laboratory safety issues and to train lab staff for safe use of equipment and hazardous materials.

“We never cease to be surprised by what people do when they think they’re saving time,” says Yanchisin. “The PIs have university credit cards and will buy supplies at a hardware store and attempt an electrical job themselves,” he says. “Self repairs are our worse culprits.”

“When we inspect a lab, we often find code violations that weren’t there the previous year,” he adds. “It just means it has to be ripped out, so in the end it was a waste of the PI’s time and money.”

His advice: Ask if you have a question or don’t know the answer or codes. Don’t cut corners. And have new equipment or lab changes checked by an electrician or your safety inspector officers. 

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COMPILED AND WRITTEN BY COURTNEY CARSON

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Congress Passes FY 2018 Funding Bill with \$3 Billion Increase for NIH



Six months late and after five temporary stopgap continuing resolutions and two brief partial government shutdowns, the FY 2018 appropriations process is finally completed. After multiple delays, congressional negotiators released a \$1.3 trillion spending bill March 22 as the clock ticked closer to a March 24 shutdown deadline. Leaders originally planned to release the details of the bill earlier in March, but the spending talks remain mired in fights over immigration, gun control, and healthcare. The House of Representatives and Senate passed the bill with less than 24 hours until the deadline.

Despite the extended fight, the final bill represents a **huge victory** for the Endocrine Society.

The spending bill (HR 1625) provides a **\$3 billion** increase for the National Institutes of Health (NIH) for a total budget of \$37.084 billion. This funding level exceeds the recommendation approved by the Senate Appropriations Committee last summer! That amount includes \$496 million for projects funded by the 21st Century Cures Act and \$500 million for opioid research. Funding increases were made possible by legislation passed last month that raised statutory spending caps in the federal budget.

The bill also includes:

- ▶ Increases to every NIH institute and center above their FY 2017 levels
- ▶ No restrictions on federal funding for fetal tissue or stem cell research
- ▶ A provision prohibiting any caps on facilities and administrative costs (e.g., indirect costs)
- ▶ Language stating that the NIH is expected to use the increased funding to support an increase in the number of new and competing research project grants
- ▶ Language mandating that the NIH continue its focus on emerging investigators and first-time renewals of young investigators with actions to significantly reduce the average age of an NIH-supported new investigator
- ▶ New language clarifying that the Dickey Amendment does not prohibit the Centers for Disease Control and Prevention (CDC) from awarding grants to study gun violence
- ▶ A provision directing the NIH to delay enforcement of the new clinical trials definition
- ▶ Significant funding increases for the other federal agencies, including a \$1 billion increase for the CDC
- ▶ \$8.1 million increase for the National Diabetes Prevention Program
- ▶ Endocrine Society-recommended report language recognizing certain hormone assays need harmonization
- ▶ A compromise on controversies surrounding the Title X family planning grant program, which will receive flat funding in FY 2018. While Republicans have sought

Take Action

Join the Endocrine Society advocacy campaign to increase research funding in FY 2019 by visiting endocrine.org/takeaction.

Learn more about how you can get involved in the Society's advocacy and the March for Science at endocrine.org/advocacy.

for years to eliminate the program because some of its funding goes to Planned Parenthood, negotiations over the bill were prolonged because Democrats wanted to prevent the administration from making changes that could affect Planned Parenthood and other abortion providers. The bill no longer has that restriction and instead contains language that would require grant recipients to “encourage family participation” when minors seek family-planning services.

The Endocrine Society was certainly not the only group advocating for funding increases, but we were one of the most vocal. We thank our members who joined in our efforts by sending emails to Congress, participating in our Hill Days and briefings, and rallying for medical research. Your work made a difference! We now begin working on FY 2019 appropriations and increases for our program priorities.

Endocrine Society Announces 2018 Diabetes Champion Award Winners



Sen. Susan Collins (R-ME)



Sen. Jeanne Shaheen (D-NH)



Rep. Tom Reed (R-NY)



Rep. Diana DeGette (D-CO)

During its 100th annual meeting, the Endocrine Society announced it will present the co-chairs of the Congressional Diabetes Caucus, Senators Susan Collins (R-ME) and Jeanne Shaheen (D-NH) and Representatives Tom Reed (R-NY) and Diana DeGette (D-CO) with a special Diabetes Champion award. This award is a result of the Diabetes Caucus co-chairs' continuous dedication to improving the lives of people with diabetes, their families, and their physicians.

Their work helped advance the Endocrine Society diabetes agenda and resulted in a number of important wins for the diabetes community over the past year, including: Medicare coverage for therapeutic continuous glucose monitors and the Omnipod, the renewal of the Special Diabetes Program for two years, and the establishment of the National Diabetes Clinical Care Commission.

The Endocrine Society looks forward to continuing its work with the Congressional Diabetes Caucus over the coming year to expand screening, access, and treatment options for patients with diabetes.

Endocrine Society Highlights Challenges in Reducing Outpatient Hypoglycemia at ENDO Session and in JCEM



Attendees at the “Reducing Outpatient Hypoglycemia: An Emerging Opportunity” session at ENDO 2018 learned about clinical tools to help identify patients at risk for hypoglycemia.

The Society continued its work to raise awareness of and reduce the incidence of hypoglycemia at ENDO 2018 with the session, “Reducing Outpatient Hypoglycemia: An Emerging Opportunity.” The attendees heard from Christine Lee, PharmD, PhD, from the Food and Drug Administration, Judith Fradkin, MD, director of the Division of Diabetes, Endocrinology, and Metabolic Diseases at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and Jeffrey Boord, MD, MPH, of Parkview Medical and chair of the Society’s Hypoglycemia Prevention Initiative Steering Committee.

Lee discussed the work of the Safe Use Initiative to further the understanding of hypoglycemia through research on effective risk assessment and engagement with organizations like the Endocrine Society to advance the national dialogue. Fradkin spoke about the work of the NIDDK to support research to improve the management of diabetes and reduce the incidence of hypoglycemia through new technologies such as the closed loop or artificial pancreas systems. The session concluded with a discussion by Boord about the Society’s ongoing work on hypoglycemia. The Initiative will test risk assessment and patient and physician education tools through a pilot project in the primary care setting focused on people with type 2 diabetes who are on insulin and sulfonylureas. The pilot project will undergo initial feasibility testing in the end of 2018 and be launched in early 2019.

Earlier in March, the Endocrine Society published new research in *The Journal of Clinical Endocrinology & Metabolism* finding that clinicians lack the resources to identify, assess, and manage patients who are at a high risk of developing hypoglycemia or episodes of dangerously low blood sugar.

The study examined available resources for managing hypoglycemia and opportunities to incorporate better management strategies in clinical practice. The analysis suggests that efforts to prevent hypoglycemia should focus on helping primary care providers identify high-risk patients who would most benefit from individualized glycemic targets and educating at-risk patients about how to recognize and appropriately manage hypoglycemic events.

While some tools exist to help healthcare providers identify individuals at high risk of hypoglycemia, they are not in widespread use.

The research confirms the need for the Society’s Hypoglycemia Prevention Initiative to improve outcomes in individuals with type 2 diabetes.

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Endocrine Society Participates in Roundtable on Rising Insulin Costs with Representative Diana DeGette



Representative Diana DeGette (second from right) meets with experts from the Endocrine Society and American Diabetes Association to discuss ways to address rising insulin prices.

On March 12, the Endocrine Society participated in a roundtable with Representative Diana DeGette (D-CO) to discuss ways to address rising insulin costs as well as other diabetes medications and supplies. Michael McDermott, MD, an endocrinologist at the University of Colorado — Denver, represented the Society at the event where he shared his perspective on the impact of insulin costs on his patients and practice. The Roundtable gave Rep. DeGette the opportunity to hear from the Endocrine Society and the American Diabetes Association about this problem and potential ways to address it.

The Society has worked with Rep. DeGette over the past few years to identify potential solutions to insulin pricing. Last September, we held a series of focus groups with our members to respond to a request for information from the co-chairs of the Congressional Diabetes Caucus, Representatives Tom Reed (R-NY) and DeGette. As a result of these conversations, the Endocrine Society submitted recommendations for addressing this issue, including:

- ▶ Integrating of formulary and coverage information into electronic health records, including out-of-pocket costs and deductible information

- ▶ Exempting insulin from coinsurance/copayments in high-deductible plans due to its lifesaving nature and high cost
- ▶ Maintaining formularies for a minimum of one year to reduce non-medical switching
- ▶ Examining federal policies to reduce patient cost sharing and to ensure patients benefit from rebates at point of sale
- ▶ Making patient assistance programs less restrictive and more accessible, including a common application that could be utilized for subsequent applications to the same or different program(s).

The Congressional Diabetes Caucus considered these recommendations in drafting a letter to insurers, manufacturers, and pharmacy benefit manufacturers about formularies, non-medical switching, and the accessibility of patient assistance programs. We look forward to continuing to work with Rep. DeGette on this critically important issue. More information about the Society's position can be found at endocrine.org/insulin; recommendations to address insulin pricing are expected from the Congressional Diabetes Caucus later in 2018.

ENDO2018

SESSION RECORDINGS

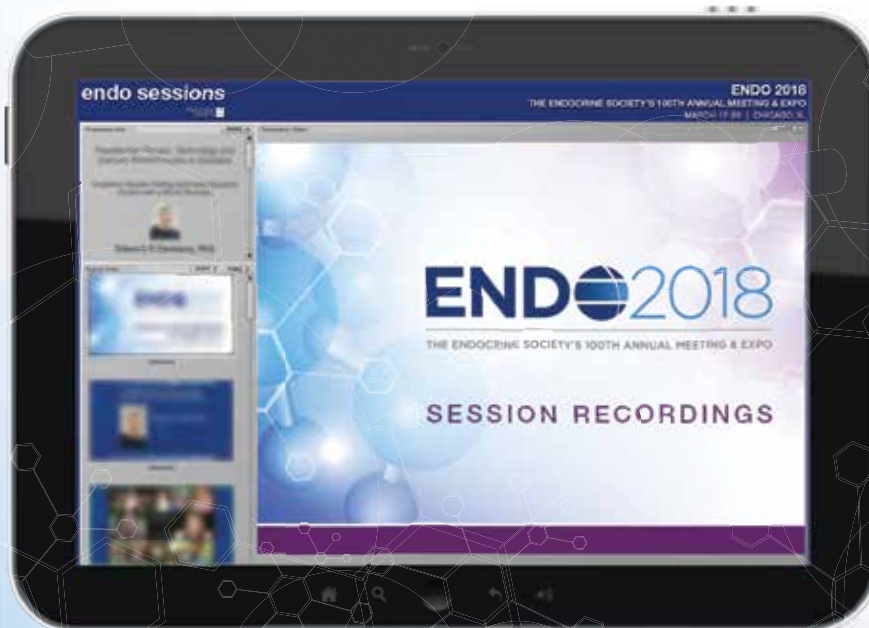
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Endocrine Society Urges Consumer Protections in New Cosmetics Reform Legislation



On February 23, the Senate Health, Education, Labor, and Pensions (HELP) Committee released a discussion draft of the Modernization of Cosmetics Regulation Act. This legislative proposal is intended to advance cosmetics reform by stimulating discussion and feedback from stakeholders and members of Congress. The Endocrine Society has been involved in bipartisan efforts to advance cosmetics reform to ensure that the public is protected from harm from exposure to endocrine-disrupting chemicals (EDCs). We are a strong supporter of the Personal Care Products Safety Act (S. 1113), introduced by Senators Dianne Feinstein (D-CA) and Susan Collins (R-ME).


HELP Committee staff reached out to the Endocrine Society for comments on the Modernization of Cosmetics Regulation Act because of our scientific expertise on EDCs. After a careful review, we expressed concern with the discussion draft, as it did not contain many critical provisions that were included in the Personal Care Products Safety Act and are absolutely necessary to protect consumers from harmful chemicals in cosmetics and other personal care products. In our letter to Committee staff, we identified several requirements for effective regulation, including:

1. A strong safety standard for personal care products, requiring that ingredients pose a “reasonable certainty of no harm under usual, customary, or intended uses.”
2. Authority for the Food and Drug Administration (FDA) to review chemicals and set restrictions, including the ability to issue mandatory product recalls should companies fail to remove dangerous products from the market.
3. Special protections for populations such as pregnant women and adolescents, who may be susceptible to hormonal interference from EDCs.
4. Fee-based structures for the FDA to conduct independent reviews of information provided by manufacturers, including accurate estimates of ingredient concentrations.
5. Public-facing databases providing consumer access to information about chemicals that they are exposed to.

The Endocrine Society will continue to work with the HELP Committee and other stakeholders to advance effective legislative reforms to cosmetics regulation that will improve public health. Stay tuned to the Society’s advocacy webpage at www.endocrine.org/advocacy for opportunities to weigh in on this important issue.

Society Hosts Researcher Networking Sessions at ENDO 2018

One of the many benefits of attending **ENDO** is the opportunity provided to meet with colleagues and network with the endocrine research community. At **ENDO 2018**, Endocrine Society members hosted several new Researcher Networking Sessions with the goal of supporting communities of researchers and facilitating networking among researchers interested in specific topic areas, including endocrine research and bioinformatics; endocrinology-based entrepreneurship; and hormones and aging.

During the networking sessions, participants generated ideas for potential research collaborations and new educational opportunities for researchers. International participants discussed their unique needs and how the Endocrine Society might facilitate information exchange among members in different countries. Each group expressed an interest in further correspondence and helping the Endocrine Society build innovative products and targeted services for member researchers based on their interests and goals. For more information on these groups, or if you are interested in hosting a researcher networking session at **ENDO 2019**, contact Joseph Laakso, director of Science Policy at jlaakso@endocrine.org. 

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Controls aspects of some human behavior (sexual arousal, recognition, trust, anxiety, and mother-infant bonding) and key aspects of reproductive system (childbirth and lactation in women, ejaculation and conversion of testosterone into dihydrotestosterone in men)

SOMATOSTATIN

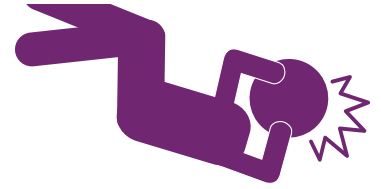
In the central nervous system, works to inhibit other hormones, most notably growth and thyroid-stimulating hormones








THYROTROPIN-RELEASING HORMONE

Stimulates production of thyroid hormone, which plays important role in the body's metabolism, heart and digestive functions, muscle control, brain development, and preservation of bones

that originate in the brain and can lead to serious physical diseases and disorders.

Genetics can also play a role in causing these conditions, and others beyond the central nervous system. **See an endocrinologist to get tested!**



HORMONE	TOO HIGH	TOO LOW
ANTI-DIURETIC HORMONE 	Water retention, diluted blood, seizure	Dehydration, blood pressure drop
CORTICOTROPIN-RELEASING HORMONE 	Diabetes, high blood pressure, osteoporosis, abdominal obesity, acne, dysfunctional menstrual cycle, infertility, muscle loss and weakness (i.e. Cushing's syndrome)	Weight loss, low blood pressure, gastrointestinal distress, anorexia nervosa, increased skin pigmentation in areas not exposed to sun (e.g. hand creases, genitals)
GONADOTROPIN-RELEASING HORMONE 	Disrupted connection between the hypothalamus, pituitary gland, and gonads (i.e. menopause, removal of the testes or ovaries)	Poor bone health, no puberty, infertility (i.e. Kallmann syndrome)
GROWTH HORMONE-RELEASING HORMONE 	Abnormal enlargement of hands, feet, and skull which alter facial features (i.e. acromegaly), diabetes, menstrual disorders	In children—delayed physical growth, delayed puberty In adults—decreased muscle mass and increased body fat
OXYTOCIN 	Beyond the brain, linked to enlarged prostate resulting in urination difficulty	Linked to breastfeeding difficulty in women, and autism/poor social functioning in developing children
SOMATOSTATIN (aka GROWTH HORMONE-INHIBITING HORMONE) 	Beyond the brain, diabetes, gallstones, intolerance to fat in the diet, and diarrhea	Variety of physiological problems, including uncontrolled growth hormone secretion
THYROTROPIN-RELEASING HORMONE 	Weight loss, weak muscles, excessive sweating, excessive menstrual flow (i.e. hyperthyroidism)	Fatigue, depression, weight gain, feeling cold, constipation, dry skin and hair, hair loss, heart problems, dyslipidemia, irregular menstrual cycles (i.e. hypothyroidism)

You have questions. We have answers.

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

Additional editing by Genevieve Neal-Perry, MD, PhD, University of Washington



Evaluation and Treatment of Hirsutism in Premenopausal Women

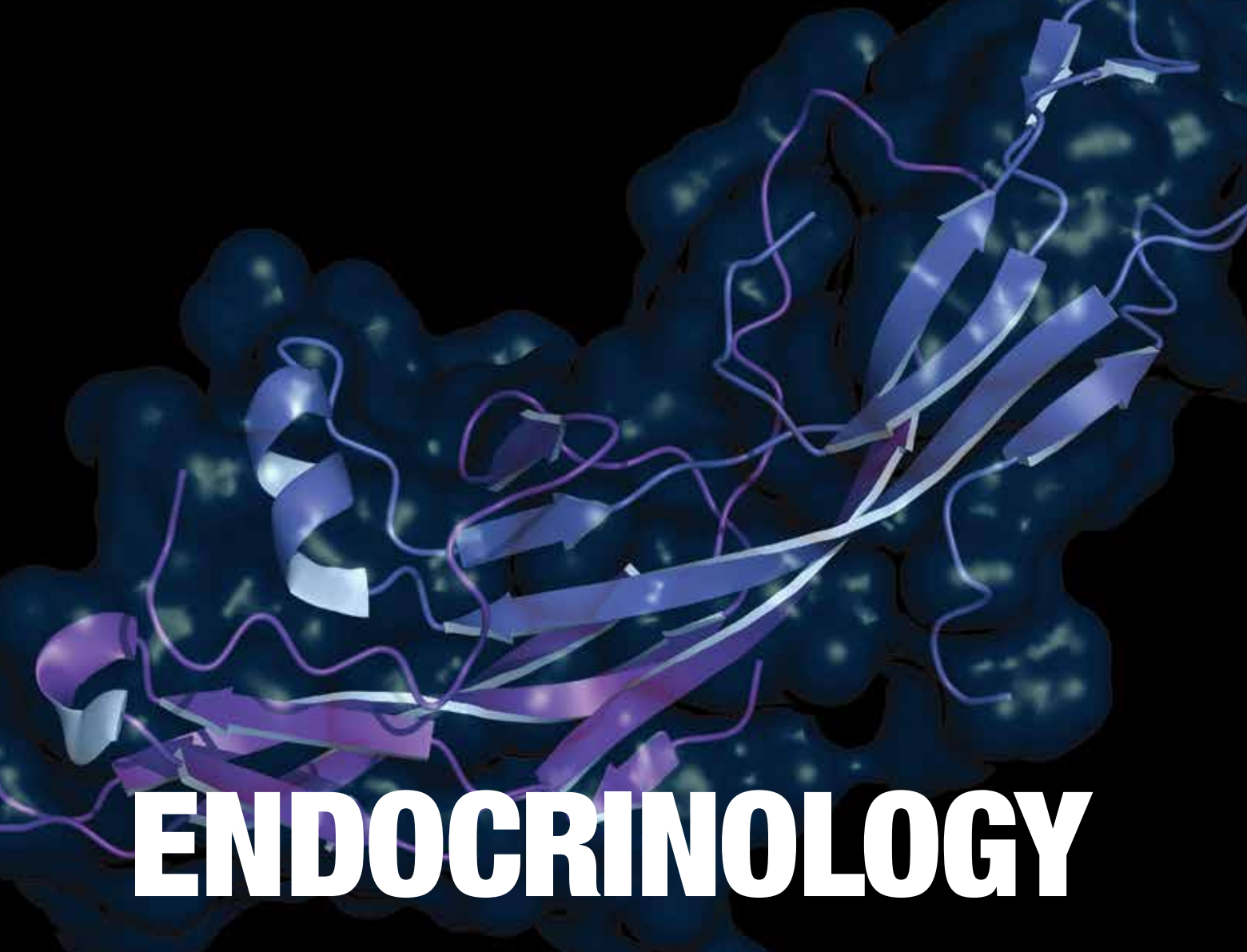
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- ▶ Treating mild cases with medication or direct hair removal.
- ▶ Lifestyle changes, including a healthy diet and exercise.

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