

Endocrine news

JULY 2018

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

INTERN

Pediatric PROGRESS:

The Vital Role of Endocrine Science in Advancing Children's Health

- New research from **ENDO 2018** sheds light on the harm EDCs can inflict on the unborn.
- Are essential oils an endocrine disruptor? We look at a study from **ENDO 2018** that caused quite a stir.
- Despite surgical success, younger patients often are not offered this option. Could provider bias play a role?
- Girl Power! How one Virginia tween improved her glycemic control while winning her middle school science fair!

Q&A:

Charles Sklar, MD, details the new Society guideline on childhood cancer.

TRENDS & INSIGHTS:

Bone metabolism, maternal diabetes, acromegaly and cancer, and more.

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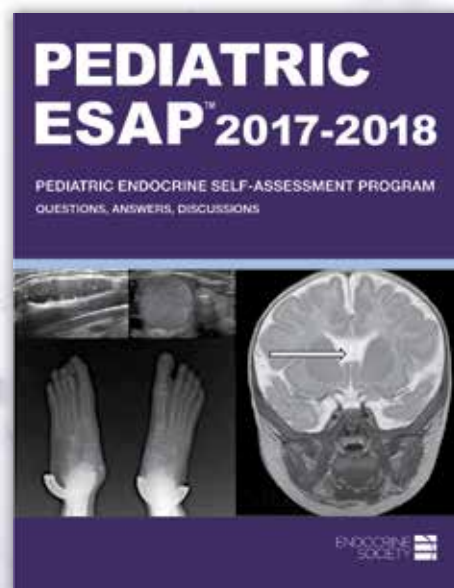
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A Busy Agenda for Society Leadership

The first three months of my presidency have been productive. I would like to share with you some highlights of the major activities that have taken place recently.

In early May, the Annual Meeting Steering Committee (AMSC) met to begin planning for **ENDO 2019** in New Orleans. The three-day meeting took place in Washington, D.C., and 42 AMSC members were in attendance. The main objectives of the meeting were to stimulate exploration, enrich the sense of community, and enhance fundamentals. We focused on emerging science as well as innovative content and its delivery. There will be many opportunities for ENDO attendees to engage through networking and mentoring activities. I would like to thank our terrific AMSC chairs (Greg Brent, overall chair; W. Lee Kraus, basic science chair; Ghada El-Hajj Fuleihan, clinical science chair; and Susan Sherman, physician-in-practice chair) for their outstanding leadership and contributions to this very difficult but exciting work. I will provide more details on the **ENDO 2019** scientific program and other planned activities in a future letter.

On May 10, we held this year's first Researcher Hill Day attended by a diverse group of members who conduct research to advocated for NIH funding and educate congressional offices about the value of endocrine-related research. Participants included members from the Advocacy and Public Outreach Core Committee (APOCC), the Research Affairs Core Committee (RACC), Council, the Early Career Forum at **ENDO 2018**, and the Society's Future Leaders Advancing Research in Endocrinology (FLARE) program.

I welcome you to participate in a future Endocrine Society Hill Day. We will have future Hill days focused on research, planned for September 13, and on clinical issues, planned for October 1. **If you are interested, please contact govt-prof@endocrine.org.**

We have begun the implementation process for our new Strategic Plan, SP4! In June, the Governance Task Force (GTF) met and focused on learning about strategies for good governance, developing guiding principles that will guide the task force's work, envisioning our desired future and discussing potential paths forward. The following day, the GTF, Council and several invited guests met for a Governance Workshop and contributed additional insight and perspectives.

Council held its first meeting under my presidency in June. In addition to the regular business meeting, members discussed some new initiatives to add to member value — more to come in future letters.



Governance Workshop participants at the June 8, 2018 meeting in Washington, D.C.

The Nominating Committee also met in June to select the slate of candidates for election that will be launched in early September. I thank all of our members who submitted


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What a talented and diverse membership we have. Our member leaders are critical to the future of our society.

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suggestions online; what a talented and diverse membership we have. Our member leaders are critical to the future of our society. PLEASE VOTE when you receive your personalized email notification.

Lastly, I would like to call your attention to a special July issue of *Endocrine News* dedicated to the Clinical Endocrinology Update (CEU) meeting. In response to last year's successful CEU, we will be having two meetings this year, CEU East and West. The CEU East meeting will be held in Miami, Fla., on Sept. 6-8 (Endocrine Board Review will be on Sept. 4-5.) CEU West will be held in Anaheim, Calif., on Oct. 19-21. CEU provides you with an opportunity to receive the latest updates in diagnosis and treatment options.

I look forward to seeing many of you at CEU! If you have any questions or comments, please contact me at president@endocrine.org 

— Susan Mandel, MD, MPH, President, Endocrine Society

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FROM THE **EDITOR**

Endocrinology and the Littlest Patients



This month's issue of *Endocrine News* focuses on how the practice and science of endocrinology impacts the youngest patients of all. From embryos in the womb to young adults battling obesity, we have done our best to cover all stages of childhood this month.

Provider bias is apparently a factor when young patients with obesity are seeking solutions. While various weight loss surgeries have proven the most effective, many doctors don't recommend this option, and new research alleges that much of this is due to bias of the healthcare provider. In "Preconceived Notions" by senior editor Derek Bagley (p. 22), Fatima Cody Stanford, MD, MPH, MPA, laments losing some of her patients too soon. "I have lost very young patients," she says. "I lost two patients, one at the age of 11, one at the age of 26 from obstructive sleep apnea, but they both had severe obesity. And I don't like to go to funerals."

From the oldest kids to the youngest, new studies presented at **ENDO 2018** shed new light on the effects of endocrine-disrupting chemicals (EDCs) on the unborn. In "Parental Guidance: Exploring the Dangers of EDC Exposure In Utero," by Kelly Horvath (p. 28), one study focuses on BPA and brain development and another looks at how DEHP exposure can lead to infertility in males. Despite both studies being animal studies, Deborah Kurrasch, PhD, from the University of Calgary in Canada says that she generally advises pregnant women to be careful with their use of plastics and to follow "good plastic guidelines," adding that if "plastics are old and showing signs of distress, throw them out. Use glass when you can."

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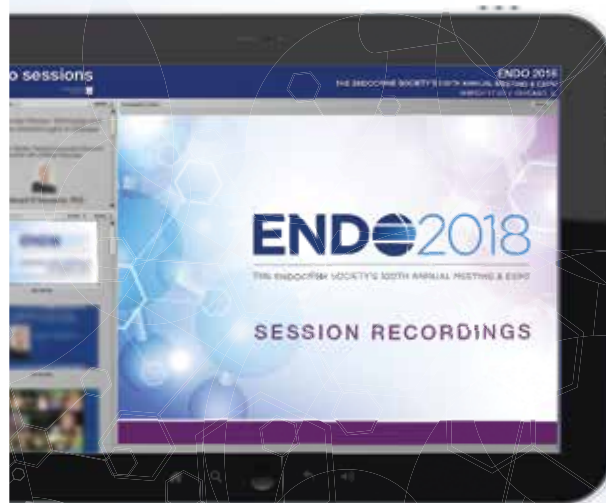
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Another study from **ENDO 2018** in this same topic area caused quite a stir when it was released last March. The issue at hand deals with the possibility of essential oils and whether they have endocrine-disrupting tendencies. Specifically, a new study shows that certain compounds in lavender and tea tree oils could be a causal factor of gynecomastia in prepubertal boys. According to one of the study authors, J. Tyler Ramsey, a postbaccalaureate research fellow at the National Institute of Environmental Health Sciences, our society deems essential oils safe in “Are Essential Oils an Endocrine Disruptor?” by Derek Bagley on page 18. “However,” Ramsey says, “they possess a diverse amount of chemicals and should be used with caution because some of these chemicals are endocrine disruptors.”

We also have a patient’s story by Eric Seaborg appropriately titled “Girl Power,” on page 34, detailing how 12-year-old Claire Engler created her own continuous glucose monitor system with the help of her father, David. This is strictly a patient’s story and details what Claire and her family — along with the help of doctors and online communities along the way — went through to get Claire’s A1C to acceptable levels. And in so doing, Claire has become somewhat of an expert on her own care: “My A1C decreased from an average of 7.5% — ranging from 6.9% to 8.0% — over almost ten years of diabetes, to 6.0% in my first six months of OpenAPS use. This is almost to the non-diabetic range. This happened at an age when A1C is usually at the highest due to body changes and insulin resistance.”

Claire’s tale is the type of story I hope to feature more in the future because it tells the stories that many in the profession do not have access to otherwise. So if you know of patients’ stories that should be shared with the readers of *Endocrine News*, please feel free to contact me at mnewman@endocrine.org. 

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



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Endocrinology: Here, There, and Everywhere

BY MARIA FERNANDEZ, PHD, Assistant Investigator, CONICET, Buenos Aires, Argentina

My first contact with the field of endocrinology occurred when I was in my third year of college. I was taking a biological chemistry class as part of my master's in biology at the School of Sciences in the University of Buenos Aires. I remember one of my professors, Juan Carlos Calvo, talking about hormones and their effects in the body. I knew I wanted to do something in that direction, so, after that class finished, I asked him if he knew anyone who would want a student in their lab. He said he would ask around, and soon after I was interviewing with Victoria Lux and her group, in the neuroendocrinology lab at the Institute of Biology and Experimental Medicine (IByME), CONICET.

I did my master's thesis on the effects of GnRH in an experimental ovarian tumor under the direction of Dr. Lux. After graduating, I started to work on my PhD on the effects of bisphenol A on the rat neuroendocrine system, under the direction of Carlos Libertun and Dr. Lux. Soon after starting my project, I realized that my deepest interest was to study how environmental contaminants are able to interact with the natural hormones of the body to alter their effects and functions. I realized that I would need more experience on *in vitro* and molecular techniques to elucidate the mechanisms of action of endocrine disruptors. When I was in my last year of graduate school, I decided to pursue a postdoc abroad to get training and experience in those techniques. In 2008, I had the opportunity of traveling to **ENDO** as an awardee of the International Endocrine Scholars Program. During the conference, I met Nicholas Webster, professor of medicine at the University of

California, San Diego (UCSD), and then I decided to go to the U.S. for a postdoctoral position in neuroendocrinology.

After getting married and defending my PhD thesis, all between February and March 2009 — and yes, I did everything in that order! — my husband and I traveled to the U.S. The first few months were a little difficult; everything was new to us, and we didn't know anyone in San Diego except for my boss. Things got better when we started to make new friends with people from all over the world. My husband started to study English (our native language is Spanish), and we both felt that we had arrived at our home away from home.

But what about the postdoc? It took me some time to get adjusted to the new place, but I was really excited about working at UCSD. At the beginning, I felt that I was bothering everyone all the time — Where is the ice machine? Where do you keep this or that reagent? Of course, things got better as I got used to the new place and people. For me, it was not only a very interesting working experience, it was a very enriching cultural one as well. People from China, India, Japan, Korea, different parts of Europe, to name a few places, were all working together in the same department. I spent almost five years in that lab and worked incredibly hard. I collaborated on different projects, met principal investigators from different departments, mentored undergraduate students, and obtained very interesting results on the effects of PPAR γ in metabolism and reproduction. After spending four years in the U.S., my husband and I decided that it was time to go back home.



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

We wanted to start our family, and my husband had not been able to get a full-time job, as we were on a J visa at that time. I applied for an assistant investigator position at the National Research Council (CONICET) in Argentina in the Laboratory of Neuroendocrinology at the IByME. I was selected, so in February 2014, we flew back home.

Adjusting again to our home country was not easy. We had been gone for almost five years, and a lot of things happened during that time. The first difficult thing was to re-adjust to a “big city.” In San Diego, our life was more relaxed (except for the fact that I worked a lot, and had crazy schedules, but we scientists do that all the time, right?); we found time to go to the beach, to hang out with friends, to enjoy the sun. Buenos Aires, on the other hand, is like any other big city; lots of traffic, everyone is in a hurry all the time. Also, during our first year back home, I got pregnant, so I had to not only get used to the country but to also being a mom!

I have been back home for four years now. Things are a little hard for us these days as it is difficult to get grant money in Argentina, not only for new investigators like myself, but also for more established ones. Often, lab directors buy supplies with their own money to keep research going because even when grants are awarded, it takes lots of time for money to come through.

The economy in Argentina is changing constantly and priorities shift all the time. However, I try to stay positive, and I like challenges. I am lucky to be working in an excellent research institute, the IByME, and to have great mentors and colleagues. I continue to stay in touch with my postdoc adviser, Dr. Webster, who is also one of my mentors, and with other PIs from UCSD, like Pam Mellon (who donated the cells lines that I am using in my research). I try to publish the best I can and to apply for national and international grants to study *in vivo* effects of endocrine disruptors on the neuroendocrine system. I am also mentoring MSc students and developing collaborations as I try to grow as a basic and translational endocrinologist. This may sound naïve to many, but I have hope that things will get better soon. We just need to keep motivating ourselves in the times of adversity. ^{EN}

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Endocrine Society Shares ASAE Power of A Awards for Diabetes Relief Efforts

The Diabetes Emergency Relief Coalition, composed of the Endocrine Society and seven other leading diabetes care and research organizations, has been recognized by the American Society of Association Executives (ASAE) with two 2018 Power of A Awards for providing critical diabetes supplies to regions impacted by Hurricanes Harvey and Irma.

The Coalition received the Gold Power of A Award as well as the Summit Power of A Award, the highest recognition for associations that make exemplary commitments to solving problems and creating a stronger world.

“ We are proud to join with other leading diabetes organizations to tackle this important public health issue and thrilled to see ASAE recognizing our work as well as ADA’s leadership in convening this coalition.”

— BARBARA BYRD KEENAN, FASAE, CAE, ENDOCRINE SOCIETY CEO

The Coalition is a hurricane relief effort launched by the American Diabetes Association (ADA), JDRE, and Insulin for Life in August 2017. The Endocrine Society joined the effort 24 hours later and together, the coalition provided almost 4,000 pounds of diabetes supplies to those individuals without access to water and electricity. In addition, the group coordinated with nearby hospitals to help get patients the care they needed.

The Society staff worked tirelessly to support the coalition. The staff raised \$2,500 for Insulin for Life, a Florida-based charity that served as a key supplier and staffed a hotline to identify needs throughout affected areas. The Society is currently working with the coalition to build permanent infrastructure to respond to future disasters.

“We are proud to join with other leading diabetes organizations to tackle this important public health issue and thrilled to see ASAE recognizing our work as well as ADA’s leadership in convening this coalition,” says Endocrine Society CEO Barbara Byrd Keenan, FASAE, CAE. “Thanks to the coalition’s unified efforts, people with diabetes have been able to maintain access to crucial supplies in emergency situations.”

To prepare for this year’s hurricane season, the Coalition is building a permanent infrastructure to respond and support people with diabetes who are impacted by future disasters. The Coalition is focusing on preparing people with diabetes by raising awareness of the need for a diabetes emergency plan while engaging and mobilizing healthcare professionals to prepare for the next emergency response. In times of need, healthcare providers will be able to reach Coalition volunteers at 1-314-INSULIN to find out how to connect to diabetes supplies.

The Power of A Awards showcase how associations leverage their unique resources to solve problems, advance industry and professional performance, kickstart innovation, and improve world conditions. ASAE is a membership organization of more than 21,000 association executives and industry partners representing 9,300 organizations. Its members manage leading trade associations, individual membership societies, and voluntary organizations across the U.S. and in nearly 50 countries around the world.



Endocrine Society Revamps Online Career Center

Endocrinologists are gaining new resources to help them move up the career ladder with the launch of the Endocrine Society's revamped online career center, EndoCareers.

The Society partnered with Health eCareers™, the leading career resource for healthcare, to provide job listings targeted to endocrine scientists and clinicians. Endocrinology-specific jobs will be posted on the Society's EndoCareers site, connecting more than 18,000 Society members worldwide to healthcare employers looking to hire.

Currently, there are fewer than 6,500 endocrinologists in the U.S. to care for the millions of patients who suffer from common hormonal disorders like diabetes, thyroid disease, infertility, and osteoporosis. The Society's online career center will help medical centers and healthcare practices find talented professionals to join their team.

"One of our main priorities as an organization is to support our members through all stages of their careers," says Endocrine Society CEO Barbara Byrd Keenan, FASAE, CAE. "Our new

online career center creates a one-stop shop for job listings and professional development resources to make it easier for endocrinologists to climb the career ladder."

The career center allows endocrinology professionals to upload a searchable resume and sign up for job alerts. The single access point includes valuable articles, enriched employer profiles, access to CV consultations, and other tools created specifically to support professionals throughout their careers. The resources complement the Society's educational resources and online courses, which include information geared toward helping young professionals establish careers in the endocrinology field.

To highlight these resources, the Society will hold an in-person job fair at **ENDO 2019**. The meeting includes a day-long career development workshop where students, fellows, and postdoc members can gain valuable insights and connect with today's leading endocrinology experts. **ENDO 2019** will take place March 23 — 26 in New Orleans, La.

To check out EndoCareers online, go to: www.endocrining.org/careers.

Endocrine Society Launches New Podcast

International experts delve into the latest advances in hormone research and clinical care on the Endocrine Society's new podcast.

The *Endocrine News* podcast's first two episodes explore efforts to develop a male birth control pill and the risk of novel cancer therapies triggering diabetes and other endocrine complications. Episodes are available to download or stream on the Society's website and at the iTunes store.

"Hormones impact so many aspects of our daily lives, including our diet, sleep, breathing, movement, and growth," says the Endocrine Society's chief communications officer Aaron Lohr, one of the podcast's hosts. "Hormones also are at the root of chronic conditions that affect millions, including obesity and diabetes. We created the *Endocrine News* podcast to give scientists and healthcare providers a convenient way to stay up to speed on advances in the field."

Stephanie Page, MD, PhD, professor of medicine at the University

of Washington in Seattle, Wash., describes a prototype male pill in the inaugural episode. The second episode features Anupam Kotwal, MBBS, of the Mayo Clinic in Rochester, Minn., discussing cases of autoimmune diabetes diagnosed in cancer patients who were treated with novel anti-cancer agents called immune checkpoint inhibitors. These drugs block certain proteins that otherwise would keep the immune system in check and prevent it from killing cancer cells. Both Page and Kotwal presented their work at the Society's 100th annual meeting, **ENDO 2018**.

Future episodes will highlight basic and clinical research breakthroughs as well as trends in clinical care.

The podcast is easily downloaded to a phone or tablet and can be listened to on the go. Listeners also can access it for free at <https://www.endocrine.org/podcast> from a computer at home or the office. **EN**





BY DEREK BAGLEY
Senior Editor

TRENDS & INSIGHTS

South Asian Immigrants Exposed to Pesticides Have Increased Risk of Diabetes

South Asian immigrants exposed to higher levels of organochlorine (OC) pesticides also are at a higher risk of developing diabetes, meaning there could be a positive association between these pesticides and incidence of diabetes, according to a study recently published in the *Journal of the Endocrine Society*.

Researchers led by Martyn T. Smith, PhD, of the Division of Environmental Health Sciences, School of Public Health at the University of California in Berkeley, write that South Asians living in the United Kingdom are two or three times more likely to have type 2 diabetes than their white counterparts, and that South Asians develop type 2 diabetes at a lower body weight, blood lipid level, and age compared to other ethnic groups. "One possibility is that South Asians have a higher exposure to organochlorine (OC) pesticides, which have been associated with diabetes mellitus in European, American, and Korean populations," the authors write.

They go on to note that South Asians have been exposed to higher levels of OC pesticides for longer periods of time, so the team hypothesized: "1) baseline levels of OC pesticides are higher in South Asian immigrants than European whites in the London area; and 2) diabetes mellitus is associated with OC pesticide exposure in South Asians." One hundred-twenty South Asians of Tamil or Telugu descent and 72 European whites were recruited into the London Life Sciences Population (LOLIPOP) Study cohort. Plasma levels of *p,p'*-dichlorodiphenyldichloroethylene (*p,p'*-DDE), *p,p'*-dichlorodiphenyltrichloroethane (DDT), β -hexachlorohexane (β -HCH), and polychlorinated biphenyl-118 (PCB-118) were analyzed by gas-chromatography mass spectrometry. South Asian cases and controls were categorized by binary exposure (above versus below the 50th percentile) to perform logistic regression, the authors write.

Tamils had three to nine times higher levels of OC



pesticides, and Telugus had nine to 30 times higher levels of OC pesticides than European whites. "Odds of exposure to *p,p'*-DDE above the 50th percentile was significantly greater in South Asian diabetes cases than controls, OR= 7.00 (2.22, 22.06 95% CI). Odds of exposure to β -HCH above the 50th percentile were significantly greater in the Tamil cases than controls, OR= 9.35 (2.43, 35.97 95% CI)," the authors write.

The researchers acknowledge that there are limitations to their study, including the small sample size, the fact that OC pesticides might not contribute independently to diabetes risk but may act through similar mechanisms, and that diabetes risk may depend on timing and dose of cumulative OC pesticide levels as opposed to current measurements of single analytes or chemical classes. However, these findings add to the growing number of studies linking OC pesticides to diabetes and may implicate another endocrine-disrupting chemical, which may be an underappreciated contributor to disparities in metabolic disease risk.

Findings: Based on their findings the authors conclude: "South Asian immigrants have a higher body burden of OC pesticides than European whites. Diabetes mellitus is associated with higher *p,p'*-DDE and -HCH concentrations in this population. Additional longitudinal studies of South Asian populations should be performed."



“
...these findings
add to the
growing number
of studies linking
OC pesticides
to diabetes and
may implicate
another endocrine-
disrupting chemical,
which may be an
underappreciated
contributor to
disparities in
metabolic disease
risk.

”

Review Proposes Best Practices for Diagnosing, Treating Klinefelter Syndrome

A paper recently published in *Endocrine Reviews* presents a comprehensive look at Klinefelter syndrome (KS), a rare disease that poses diagnostic challenges and remains largely misunderstood in the medical community.

The review, by Claus H. Gravholt, MD, PhD, of the Department of Endocrinology and Internal Medicine (MEA) at Aarhus University Hospital in Norrebrogade, Denmark, et al., points out that many patients with KS are misdiagnosed or remain undiagnosed, as there is insufficient insight into the prevalence and causes of different syndrome-associated traits that may impact adversely on prognosis. They write that current attempts at providing guidelines may underestimate morbidity and mortality, and that previous guidelines relied on expert consensus that did not include a broad base of professionals working with KS patients.

The authors write that KS prevalence is estimated to be about 152 cases per 100,000 newborn males, but only 25% of KS patients are accurately diagnosed, and many of these diagnoses are not made until adulthood. KS patients usually have small testes, infertility, hypergonadotropic hypogonadism, and cognitive impairment. “Available data show that diagnosis of KS is often seriously delayed, and frequently a diagnosis is never made, illustrating that new diagnostic avenues should be implemented,” the authors write. “Late diagnosis or non-diagnosis extend to all sex chromosome syndromes.” They go on to call for population-based, neonatal screening, since screening would enable early establishment of appropriate treatment. However, given how rare KS is, it will likely take a long time to “demonstrate associations between early diagnosis, continuous specialized care, and improved long-term outcomes,” the authors write.

KS is associated with a lower socioeconomic status, which could explain the increased risk of morbidity

and mortality. The authors write that KS affects all aspects of socioeconomic status, including educational achievement, cohabitation, fatherhood, employment, and income. KS is also associated with hypogonadism, which in turn is associated with greater risk of metabolic syndrome, type 2 diabetes, cardiovascular disease, breast cancer, and extragonadal germ cell tumors.

The treatment for both the physical symptoms and the subsequent quality-of-life measures is testosterone replacement therapy (TRT). However, the authors write that the effects of this therapy have not been rigorously studied. “There is only scant evidence that TRT in infants and boys has positive effects on cognitive and social functions, and no good evidence for this in adolescence or adulthood,” they write.

This review covers a lot of ground, because, as the authors write, men with KS “face a bewildering array of medical, neurocognitive, and social problems, which are only beginning to become apparent in recent years.” The authors conclude the review with a number of questions for moving forward: Is the testicular demise inevitable, or is there a possibility for rescuing testicular function, thus possibly avoiding infertility and the need for testosterone substitution? Why is it so difficult to diagnose KS? How detrimental is late diagnosis to the life of KS males? Would early diagnosis improve the lives of males with KS materially?

Findings: The authors then write: “It is clear that the current diagnostic approach is not sufficient, and we advocate for the incorporation of diagnostics of sex chromosome abnormalities, including KS, into neonatal screening programs. It is currently not clear which methodology would be most appropriate to use in a neonatal screening program, and therefore the costs of such an intervention is not yet clear.”

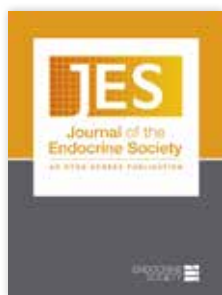


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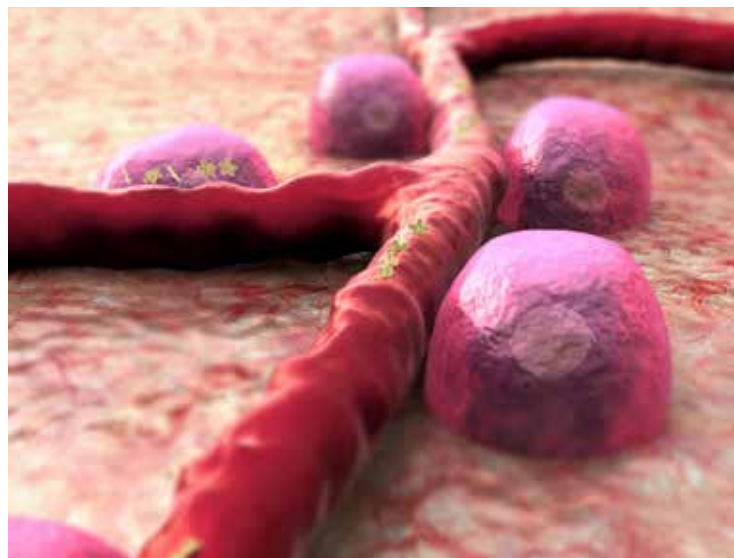
Fetal Exposure to Maternal Diabetes Can Cause Sexually Dimorphic Beta-Cell Dysfunction



“

The researchers speculate that the alterations in insulin secretion are from a beta-cell defect, and not beta-cell loss, since insulin secretion in response to the combination of arginine and glucose, which in theory reflects beta-cell mass, was unaffected.

”



Beta cells on the pancreas surface, insulin and leukocytes inside the blood vessel

Fetal exposure to maternal diabetes predisposes beta-cell dysfunction in adult offspring, but this dysfunction is different between males and females after intravenous (IV) glucose stimulation, according to a study recently published in the *Journal of the Endocrine Society*.

Researchers led by Jean-François Gautier, MD, of the Department of Diabetes and Endocrinology, Lariboisière Hospital in Paris, France, point out that fetal exposure to maternal diabetes is associated with altered glucose-stimulated insulin secretion at an adult age, but that males and females regulate glucose homeostasis differently, and whether fetal exposure to maternal diabetes predisposes to alteration in insulin secretion in a sexually dimorphic manner is unknown. “To address this issue, we studied oral and [IV] glucose-stimulated insulin secretion in adult male and female offspring following fetal exposure to maternal diabetes,” the authors write.

The researchers compared data from 29 adult nondiabetic offspring of mothers with type 1

diabetes (ODMs) and 29 nondiabetic offspring of fathers with type 1 diabetes (ODFs). They measured insulin secretion in response to oral glucose and insulin secretion rate in response to intravenous glucose ramping. “In response to oral glucose, male and female ODMs displayed a reduced insulin secretion. In contrast, in response to graded intravenous glucose infusion, only female ODMs (not males) exhibited

decreased insulin secretion,” the authors write.

The researchers speculate that the alterations in insulin secretion are from a beta-cell defect, and not beta-cell loss, since insulin secretion in response to the combination of arginine and glucose, which in theory reflects beta-cell mass, was unaffected. Male beta-cell dysfunction may be different after fetal exposure to type 1 diabetes because testosterone via the androgen receptor in beta cells may compensate for the insulin secretory defect during IV glucose stimulation, the authors write.

Findings: Based on these results, the authors conclude: “[F]etal exposure to maternal diabetes predisposes to beta-cell dysfunction in male and female adult offspring. However, this beta-cell defect is characterized by a sexual dimorphism following IV glucose stimulation, suggesting that males are protected against or can compensate for the deleterious effect of maternal hyperglycemia on fetal beta cells.”

READ THIS AND OTHER ENDOCRINE SOCIETY JOURNAL ARTICLES AT
[HTTPS://ACADEMIC.OUP.COM/ENDOCRINESOCIETY](https://academic.oup.com/EndocrineSociety)

Researchers Find Slightly Elevated Cancer Incidence in Patients with Acromegaly

Cancer incidence rates are slightly elevated in patients with acromegaly, according to a meta-analysis recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Jens Otto Lunde Jørgensen, MD, DMSc, of the Department of Endocrinology and Internal Medicine at Aarhus University Hospital in Norrebrogade, Denmark, point out that acromegaly has been associated with an increased risk of cancer, since growth hormone (GH) and insulin-like growth factor 1 (IGF-1) are implicated in cancer promotion. Acromegaly is associated with thyroid and colorectal cancer in particular, but the researchers note that all studies have found this association, and it's not known whether mortality from cancer is increased by acromegaly. "A major reason for the inconsistent epidemiological data on cancer risk is differences in study design, and the need for population-based studies persists," the authors write.


The team conducted a nationwide population-based cohort study to examine the long-term risk of cancer incidence and mortality in patients with acromegaly, as well as a meta-analysis of the literature on cancer standardized incidence ratios (SIRs) in acromegaly. The study looked at 529 acromegaly cases from 1978 to 2010. They compared incident cancer diagnoses and mortality with national cancer rates estimating SIRs.

The study identified 81 cases of cancer after excluded cases of cancer diagnosed within the first year. "SIRs were 1.4 (95% CI, 0.7 to 2.6) for colorectal cancer, 1.1 (95% CI, 0.5 to 2.1) for breast cancer, and 1.4 (95% CI, 0.6 to 2.6) for prostate cancer. Whereas overall mortality was elevated in acromegaly (SIR 1.3; 95% CI, 1.1 to 1.6), cancer-specific mortality was not," the authors write.

The meta-analysis showed a SIR of overall cancer of 1.5 (95% CI, 1.2 to 1.8). SIRs were elevated for colorectal cancer, 2.6 (95% CI, 1.7 to 4.0); thyroid cancer, 9.2 (95% CI, 4.2 to 19.9); breast cancer, 1.6 (1.1 to 2.3); gastric cancer, 2.0 (95% CI, 1.4 to 2.9); and urinary tract cancer, 1.5 (95% CI, 1.0 to 2.3). "In general, cancer SIR was higher in single-center studies and in studies with <10 cancer cases," the authors write.

The authors note that while the meta-analysis supported their finding that cancer risk is increased in patients with acromegaly, the meta-analysis revealed potential sources of bias. Cancer incidence risk was increased in single-center studies and was lower when the researchers excluded studies with fewer than 10 cases, suggesting selection or sample bias. "It is possible that the patient population in single centers represents difficult cases with previous treatment failure and increased comorbidity," the authors write. "It is also possible that the comparator group in single-center studies derived from screening programs, which poses the risk of healthy user bias."

The authors go on to write that surveillance bias might have existed in cases of thyroid cancer, since acromegaly enlarges the thyroid, which may lead to overdiagnosis of occult thyroid cancer, "and endocrinologists are generally more likely to focus on endocrine diseases."

Findings: Taking the results of the cohort study and the meta-analysis together, the authors conclude there is "only a slightly elevated overall risk of cancer in patients with acromegaly." And while these results should not deter patients or healthcare professionals from following cancer surveillance guidelines, the authors write, "our findings agree with the previously drawn conclusion that excessive GH in humans is not a serious cancer risk." 



“

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2018 Clinical Endocrinology Update/Endocrine Board Review

**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 17, 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 (ABIM)-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.

Heart in Diabetes

Philadelphia, Pennsylvania, July 13 – 15, 2018

Heart in Diabetes is a unique medical conference bringing together world-renowned clinical leaders in diabetes and cardiovascular disease. The program is designed to evaluate the state-of-the-art clinical data focusing on the management of the heart and kidneys in patients with diabetes. The goal is to align cardiologists, endocrinologists/diabetologists, iridologists, and nephrologists in their understanding and development of appropriate comprehensive clinical management plans for very high-risk patients.

www.heartindiabetes.org

2018 Santa Fe Bone Symposium

Santa Fe, New Mexico, August 3 – 4, 2018

The Santa Fe Bone Symposium is an annual forum devoted to advances in the science and economics of osteoporosis, metabolic bone disease, and assessment of skeletal health. Presented by the Osteoporosis Foundation of New Mexico, this meeting is for healthcare providers, scientists, and researchers with a special interest in bone disease, and for bone densitometry technologists who seek a high level of knowledge in their field. (*The Endocrine Society's Endocrine Fellows Series: Osteoporosis and Metabolic Bone Conference is held August 1 and 2 in Santa Fe.*)

awards@endocrine.org

9th International Congress of the Growth Hormone Research and IGF Societies

Seattle, Washington, September 14 – 17, 2018

The International Congress of the Growth Hormone Research and IGF Societies will gather researchers and practitioners to provide an opportunity to learn from them and to share data. Initially organized by the GRS, the last several meetings have been jointly hosted by both the GH Research and IGF Societies.

<http://grs-igf2018.com>

Principles of Critical Care Medicine for the Non-Intensive Care Specialist

Boston, Massachusetts, September 26 – 28, 2018

Keeping pace with the rapid changes in evidence-based critical care medicine is a challenge for specialty-trained intensivists; for non-intensivists, the challenge of staying up to date may be overwhelming. This CME course is intended to provide core clinical critical-care skills to healthcare providers who are not trained as intensivists, but whose clinical duties involve taking care of critically ill patients. The focus of this course will be to highlight recent important evidence-based advances in the practice of modern critical-care medicine.

www.criticalmedboston.com

Grit for Women in Medicine: Growth, Resilience, Inspiration, and Tenacity

Truckee, California, September 26 – 29, 2018

This course is designed to empower women and men in medicine with the skills and resources to remove barriers and bias of women in leadership positions, specifically in healthcare. Leaders in business and healthcare will present evidence-based strategies to promote professional development and enhance personal well-being. Nationally, there is a large number of female clinicians reporting burnout, which has a potential effect on patient experience, compliance, and outcomes. This course will address the growing need for improved clinician wellness and development for a gender balanced leadership healthcare team.

<https://gimeducation.mayo.edu/>

88th Annual Meeting of the Thyroid Association

Washington, D.C., October 3 – 7, 2018

This meeting is designed for the community of endocrinologists, basic scientists, internists, surgeons, nuclear medicine scientists, pathologists, trainees, nurses, physician assistants, advanced practice providers, and other healthcare professionals who wish to broaden and update their knowledge of the thyroid gland and its disorders.

A customized educational track will be available to

trainees to enhance their meeting experience.
www.thyroid.org/88th-annual-meeting-ata/

Magee-Womens Research Summit **Pittsburgh, Pennsylvania, October 8 – 10, 2018**

Magee-Womens Research Institute at the University of Pittsburgh announces the inaugural Magee-Womens Research Summit. This conference will serve as a premier forum for scientific exchange on topics related to early human development and women's health and wellness across the lifespan.

<https://mageesummit.org/>

Obesity Week – The Obesity Society and American Society for Metabolic and Bariatric Surgery Joint Meeting

Nashville, Tennessee, October 11 – 15, 2018

ObesityWeek is an international event focused on the basic science, clinical application, surgical intervention, and prevention of obesity. By combining both American Society for Metabolic & Bariatric Surgery (ASMBS) and The Obesity Society (TOS) annual meetings, ObesityWeek brings together world-renowned experts in obesity to share innovation and breakthroughs around the globe. This year, the international conference will focus on the heart, the cardiac component of obesity.

www.obesityweek.com

World Congress Insulin Resistance Diabetes and Cardiovascular Disease

Los Angeles, California, November 29 – December 1, 2018

Offering three days of CME, the World Congress Insulin Resistance Diabetes and Cardiovascular Disease is a state-of-the-art program featuring distinguished global experts presenting unique topics and lectures on the most innovative clinical research and basic science in cardiometabolic disorders. The Congress is a premier global meeting dedicated to diabetes, obesity, lipids, cardiovascular disease, and energy balance.

<https://www.wcir.org/>

INTERNATIONAL ITINERARY

Dimensions in Diabetes

Mumbai, India, July 14 – 15, 2018

This annual program will bring high-quality clinical education to Indian endocrinologists. The goal of the program is to foster relationships with endocrinologists around India while providing a clinical update in the field of diabetes. Supported by Sun Pharmaceuticals, the two-day program brings in eight faculty members to present in-depth lectures on diabetes and its comorbidities.

www.endocrine.org/meetings

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

Brazilian Congress of Endocrinology and Metabolism

Belo Horizonte, Brazil, August 7 – 11, 2018

Brazil's largest event in endocrinology, the Brazilian Congress of Endocrinology and Metabolism enters its 33rd year. The scientific program focuses on international updates in all areas of endocrinology, metabolism, and diabetes, including topics from the basic overview of each area to the most consolidated clinical practices. The event will also feature the latest national scientific findings available at the poster session and oral presentations.

www.endocrino.org.br/cbem-2018/

Endocrine Society of Australia and The Society for Reproductive Biology Annual Meeting

Adelaide, Australia, August 19 – 22, 2018

Featuring combined international Endocrine Societies, attendance is anticipated to exceed 700 delegates representing a variety of specialties including endocrinology, cell and molecular biology, reproductive biology, gynecology, pharmacology, and rheumatology. Key themes for the meeting include dynamic endocrine testing, transgender endocrinology, endocrine control of reproduction,

neuroendocrinology, and a focus on women's health.
www.esa-srb.org.au/

International Conference on Diabetes & Metabolism

Dubai, UAE, October 15 – 17, 2018

This international conference highlights recent advancements related to diabetes and cholesterol metabolism. The scientific sessions emphasize diabetes mellitus, diabetes complications, endocrinology, obesity, metabolic syndrome, epidemiology of diabetes, cholesterol metabolism, lipid metabolism, cardiovascular diseases, hypercholesterolemia, and recent advances in treatments and therapies.

www.metabolicdiseases.conferenceseries.com/

EndoBridge 2018

Antalya, Turkey, October 25 – 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. 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

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“When we look at patients who have lost weight through diet and exercise versus those who have lost weight with weight loss surgery, we see the person who’s lost weight with diet and exercise more favorably. Like, ooh, they deserve to lose the weight. We’ve placed a moral judgment against that person that needed to utilize that tool, and I just see it as a tool, which is weight loss surgery.”

— **FATIMA CODY STANFORD, MD, MPH, MPA**, Harvard Medical School and Massachusetts General Hospital, Boston, discussing provider bias in considering weight loss surgery for younger patients in “Preconceived Notions: Provider Bias, Young Patients, and Weight Loss Surgery,” on page 30.

7



The number of teaspoons of added sugar consumed by a U.S. toddler (age 19 – 23 months) on any given day.

— SOURCE: CDC.

FROM THE CENTURY OF ENDOCRINOLOGY TIMELINE

1972 – 1978

Newborn Screening for Congenital Hypothyroidism

From 1972 – 1978, screening began for neonatal congenital hypothyroidism in the U.S., Canada, England, Japan, and some other countries. In most cases of congenital hypothyroidism, problems with the thyroid start in the womb. Because the gland is missing, incomplete, or in the wrong place, the body does not produce enough thyroid hormone. Missing or low levels of the hormone lead to abnormal growth and development, as well as slower intellectual functioning. Simply providing thyroid hormone at normal levels can prevent the effects and health problems of congenital hypothyroidism.

— SOURCE: NICHD MISSION AND SCIENTIFIC ACCOMPLISHMENTS: CONGENITAL HYPOTHYROIDISM

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

BY THE NUMBERS

71%

The percentage of all deaths globally caused by noncommunicable diseases such as heart disease, diabetes, and breast and colon cancer, including the deaths of 15 million people per year ages 30 to 70.

— SOURCE: WORLD HEALTH ORGANIZATION GLOBAL ACTION PLAN ON PHYSICAL ACTIVITY AND HEALTH 2018 – 2030

More than 1/3

The percentage of Americans using prescription drugs with potential side effects that may contribute to depression and suicidal thoughts.

— SOURCE: AMERICAN DIABETES ASSOCIATION



80%

The number of older Americans (ages 50 – 80) that approve of marijuana use for medicinal purposes.

— SOURCE: UNIVERSITY OF MICHIGAN/AARP

\$60 BILLION

The amount lost due to fraud and improper Medicare payments annually.

— SOURCE: CMS

ENDOCRINE FACTS AND FIGURES

Endocrine Facts and Figures is a compendium of epidemiological data and trends related to a spectrum of endocrine diseases.

All information is sourced from peer-reviewed publications and reviewed by a group of experts in the field.



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Visit endocrinefacts.org to view the reports, watch interviews with experts, and sign up to receive future content alerts when new information is published.



Are
Essential
Oils an

ENDOCRINE DISRUPTOR?

BY DEREK BAGLEY

An ENDO 2018 presentation that linked essential oils to gynecomastia in prepubertal boys caused a bit of an uproar in the spring. The study authors detail what their research means, why certain populations should be mindful of essential oil use, and the importance of future studies.



A study presented this past March at ENDO 2018 in Chicago raised yet another concern in the growing problem of endocrine-disrupting chemicals (EDCs), providing further evidence of a suspected link between prepubertal gynecomastia and regular exposure to lavender or tea tree oil. According to researchers, key chemicals in these common plant-derived oils act as EDCs, which may cause prepubescent boys to develop enlarged breast tissue.

Lavender (LO) and tea tree oil (TTO) are among the so-called “essential oils” that have become popular as alternatives for medical treatment, personal hygiene and cleaning products, and aromatherapy. Various consumer products contain lavender and tea tree oil, including some soaps, lotions, shampoos, hair-styling products, cologne, and laundry detergents.

“Our society deems essential oils as safe,” says study researcher J. Tyler Ramsey, a postbaccalaureate research fellow at the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health. “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. Kenneth Korach, PhD, the senior scientist for the new NIEHS EDC study, previously found laboratory evidence that lavender and tea tree oil showed endocrine-disrupting activities.

In that study, published in the *New England Journal of Medicine* (NEJM) in 2007, Korach and his team concluded that once the boys stopped using the products, the gynecomastia resolved. “Furthermore,” they wrote, “studies in human cell lines indicated that the two oils had estrogenic and antiandrogenic activities. We conclude that repeated topical exposure to lavender and tea tree oils probably caused prepubertal gynecomastia in these boys.”

“The current study is based on our original observations published in the *NEJM* linking lavender and tea tree oils to the incidence of male prepubertal gynecomastia,” Ramsey and Korach write in an email to *Endocrine News*. “At the time, we tested whether lavender or tea tree oil had any hormonal activities and found that they were estrogenic and also antiandrogenic.”



“ Our society deems essential oils as safe. However, they possess a diverse amount of chemicals and should be used with caution because some of these chemicals are potential endocrine disruptors.”

—J. TYLER RAMSEY, A POSTBACCALAUREATE RESEARCH FELLOW, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, RESEARCH TRIANGLE PARK, N.C.

Surprising Outcomes

Under Korach's direction, Ramsey and his NIEHS colleagues went a step further. From the hundreds of chemicals that comprise lavender and tea tree oil, they selected for analysis eight components that are common and mandated by the International Standard Organization for inclusion in the oils. “We wanted to study the essential oils to determine what specific components in lavender and tea tree oil could potentially possess hormonal activity,” according to Ramsey and Korach. “We also wanted to know which of the components would have either or both of the estrogenic or antiandrogenic activities, as well as the mechanisms by which these components activate estrogen receptor alpha and the androgen receptor. In our previous studies, only lavender and tea tree oil were examined, and the precise mechanisms by which they act were not determined.”

Four of the tested chemicals appear in both lavender and tea tree 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 says these changes were consistent with endogenous, or bodily, hormonal conditions that stimulate gynecomastia in prepubescent boys.

“There were a few surprising outcomes that we did not expect when we first started these experiments,” according to Ramsey and Korach. “Many of the components differentially

elicited hormonal activity, and some had no activity at all. These are interesting results because it shows that some components, not all, are potential endocrine disruptors.”

Providing Clarity

Of course, whenever a study like this is made public, it will make some waves. When *Endocrine News* first broke the news on social media during **ENDO 2018** in March, the Twitter account received a few strong responses, demanding to know what this means for people who use essential oils or expressing concerns about the study itself. A press release from the Australian Tea Tree Industry Association pointed out what it perceived as flaws in the study and expressed its disappointment by saying, “this sensationalization of data from Ramsey *et al.* at **ENDO 2018** has caused undue concern for consumers of [tea tree oil] around the world.”

The group goes on to write in its opinion, “Since the 2007 *NEJM* paper...multiple investigators have demonstrated the flaws in linking TTO (as well as LO and other essential oils) to endocrine disruptor activity.”

Indeed, the Research Institute of Fragrance Materials in 2013 published a paper in the *International Journal of Toxicology* that disputed Korach and his team's 2007 findings. However, other studies have confirmed that the oils had hormonal activity.

Still, Ramsey and Korach are confident in their data. And they're not looking to ruin the essential oils industry; they're looking to raise awareness about what chemicals are found in “essential” products people use every day. When asked about any pushback to their current work, they only offer that they have addressed many of these concerns in the full



"There were a few surprising outcomes that we did not expect when we first started these experiments. Many of the components differentially elicited hormonal activity, and some had no activity at all. These are interesting results because it shows that some components, not all, are potential endocrine disruptors."


— J. TYLER RAMSEY, POSTBACCALAUREATE RESEARCH FELLOW, AND KENNETH KORACH, PHD, PRINCIPAL INVESTIGATOR, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, RESEARCH TRIANGLE PARK, N.C.

manuscript. "When the manuscript is published, we hope it will provide clarity to those with questions."

Lingering Questions

Ramsey and Korach acknowledge that what was presented at **ENDO** and the subsequent publication isn't the final word on the health effects of essential oils. Their work warrants further investigation, and there are more questions to answer.

Many of the chemicals Ramsey, Korach, and their team tested appear in at least 62 other essential oils. Another cause for concern is that essential oils are available without a prescription and are not regulated by the U.S. Food and Drug Administration. The public should be aware of these findings and consider all evidence before deciding to use essential oils.

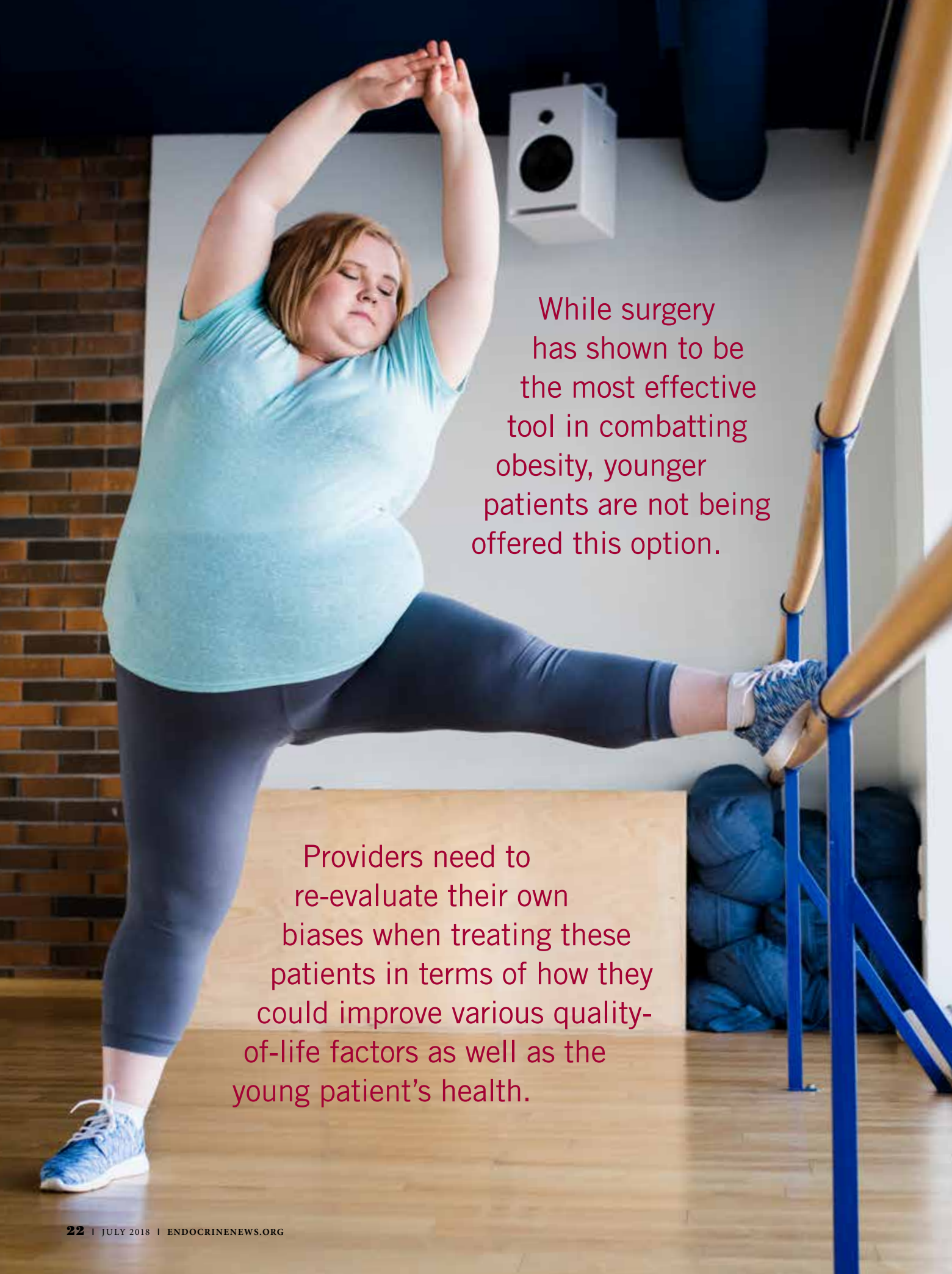
And no matter the pushback from interested parties, the current evidence shows that oils possess components that are potential endocrine disruptors. The current study provides more evidence between the established link of essential oil use and the potential for development of prepubertal gynecomastia. "Based on clinical case studies," Ramsey and Korach write, "susceptible individuals that use lavender and tea tree oil products develop prepubertal gynecomastia, but when they stop using the products, the condition subsides." 

BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT HOW TELEHEALTH IMPROVED DIABETES OUTCOMES IN VA PATIENTS IN THE MAY ISSUE.



AT A GLANCE

- ▶ New research shows that some components of essential oils, deemed safe and found in a variety of products people use every day, may be endocrine disruptors that cause prepubertal gynecomastia in young boys.
- ▶ Industry and other interested parties have pushed back on the findings, but the researchers are confident in their data.
- ▶ The current study shows a link between essential oils and enlarged breast tissue in prepubescent boys, and the condition resolves once the boys stop using the products.



While surgery has shown to be the most effective tool in combatting obesity, younger patients are not being offered this option.

Providers need to re-evaluate their own biases when treating these patients in terms of how they could improve various quality-of-life factors as well as the young patient's health.

Preconceived **Notions:**

BY DEREK BAGLEY

Provider Bias, Young Patients, and Weight Loss Surgery

Fatima Cody Stanford, MD, MPH, MPA, an instructor of medicine and pediatrics at Harvard Medical School and an obesity medicine physician at Massachusetts General Hospital, treats children and young adults with severe obesity — defined as having a body mass index (BMI) above 40.

One of Stanford's young adult patients presented to her clinic with a BMI of 58. When this young woman first came to the clinic, she told Stanford about her struggles to find a job. She had gone to a local retailer to apply for a job and was quickly told she would not qualify for the position.

Severe obesity continues to trend upward, and along with the physical comorbidities like type 2 diabetes, obstructive sleep apnea, and heart disease, severe obesity carries with it other intangibles. There remains a significant bias against people with obesity and severe obesity. "Persons who have severe obesity are often overlooked or undervalued with regards to their working environment," Stanford says. "And we do know that they have a lower likelihood of acceptance into advance degree programs."

If a pediatric patient has severe obesity early in life, it means an earlier onset of comorbid conditions, which means they're going to have a higher degree of morbidity and earlier mortality, not to mention an impacted socioeconomic status, increased risk of depression, decreased quality of life, and so on.

Stanford and her collaborators Karen Campoverde-Reyes, MD, a research fellow at Harvard Medical School and Massachusetts General Hospital; and Madhusmita Misra, MD, MPH, a professor of pediatrics at Harvard Medical School and chief of pediatric endocrinology at Massachusetts General Hospital,



There is this bias against individuals with severe obesity, but within the medical community there also seems to be a bias against performing this major surgery on teenagers and young adults.

“ I have lost very young patients. I lost two patients, one at the age of 11, one at the age of 26 from obstructive sleep apnea, but they both had severe obesity. And I don’t like to go to funerals.”

— FATIMA CODY STANFORD, MD, MPH, MPA,
INSTRUCTOR OF MEDICINE AND PEDIATRICS,
HARVARD MEDICAL SCHOOL; OBESITY
MEDICINE PHYSICIAN, MASSACHUSETTS
GENERAL HOSPITAL, BOSTON

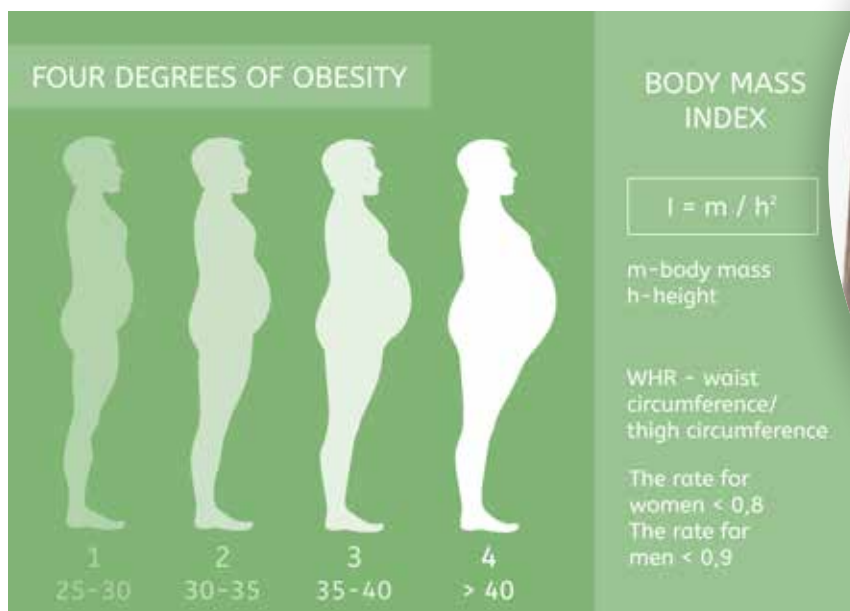
at **ENDO 2018** presented results from their study that found only a small percentage of teenagers and young adults with severe obesity undergo weight loss surgery even though it’s considered the most effective long-term weight loss therapy. The investigators concluded that a possible reason for the underutilization of weight loss surgery in this patient population is a lack of education and awareness among healthcare providers and the public regarding surgical treatment of obesity.

The results also speak to the bias against people with severe obesity, even among medical professionals.

No Surprises

Stanford, Campoverde-Reyes, and Misra looked at the frequency of weight loss surgery in 14- to 25-year-olds treated at eight academic health systems that participate in a web-based clinical data research network called ARCH (Accessible Research Commons for Health). Four of the institutions are in Boston: Beth Israel Deaconess Medical Center, Boston Children’s Hospital, Boston Medical Center, and Partners Healthcare, which comprises Massachusetts General and Brigham and Women’s Hospital. The others are Washington University School of Medicine in St. Louis, Mo., Morehouse School of Medicine in Atlanta, Ga., University of Texas Health Science Center at Houston, and Wake Forest Baptist Medical Center in Winston-Salem, N.C.

They identified people with severe obesity using the diagnostic billing code for a BMI of 40 or more. They found that about 0.7%, or 18,008, of the more than 2.5 million patients ages 14 to 25 had a diagnosis of severe obesity, the investigators



reported. The percentage of patients with severe obesity who underwent weight loss surgery ranged from 0.4% at Boston Children's Hospital to 21.5% at Partners Healthcare. The other percentages were 1.4% at Boston Medical Center, 2.3% at Beth Israel, and 2.5% at Washington University. The other institutions performed too few weight loss surgeries (fewer than 10) to report percentages.

"I wanted [the results] to surprise me, but [they] did not," Stanford says.

She again points to a low level of education in the treatment of severe obesity among medical students, residents, and attending physicians as a reason for her team's findings. But it's not just that. Stanford also sees a continuing bias toward people with severe obesity, in which people tend to presume it's just a "lifestyle choice," that if they could just eat less and exercise more, the pounds would melt away. "That's actually not founded on science that we know about obesity," she says. "I think there's a bias that plays a large role. When we look at patients who have lost weight through diet and exercise versus those who have lost weight with weight loss surgery, we see the person who's lost weight with diet and exercise more favorably. Like, ooh, they deserve to lose the weight."

"We've placed a moral judgment against that person who needed to utilize that tool, and I just see it as a tool, which is weight loss surgery," she continues.

Weight loss surgery criteria for teenagers and young adults is the same as the criteria for the adult population. Patients with moderate obesity (BMI of 35 to 39.9) and a comorbid condition like type 2 diabetes or heart disease would be candidates, and patients with a BMI of 40 or above would meet the criteria without a comorbid condition. Still, these patients would have to have tried lifestyle changes, but if everything has been exhausted, then physicians should consider weight loss surgery.



AT A GLANCE

- ▶ Severe obesity in younger patients means not only an earlier onset of comorbidities but an impacted socioeconomic status and decreased quality of life.
- ▶ There remains a bias against patients with severe obesity, even in the medical community.
- ▶ Researchers have found that institutions perform too few weight loss surgeries on young people with severe obesity, even though weight loss surgery is the best tool for long-term weight loss.



“ We think about the high impact diseases such as obesity, **but we don’t think about the fact that it affects hiring. It affects socioeconomic status. It affects quality of life. It affects depression.** These things are all inter-related, and so treating that child or adolescent with severe obesity sooner really can play a large role in setting them on an upward trajectory pretty early in life.”

— FATIMA CODY STANFORD, MD, MPH, MPA,
INSTRUCTOR OF MEDICINE AND PEDIATRICS,
HARVARD MEDICAL SCHOOL; OBESITY
MEDICINE PHYSICIAN, MASSACHUSETTS
GENERAL HOSPITAL, BOSTON

“I Don’t Like to Go to Funerals”

So there is this bias against individuals with severe obesity, but there also seems to be a bias against performing this major surgery on teenagers and young adults. But for Stanford, the benefits of the surgery far outweigh the risks of worsening comorbid conditions. And for her, it’s personal. The week before Stanford spoke with *Endocrine News*, she was at a funeral for a 38-year-old man who passed away from a heart attack. He had obesity that led to cardiac disease. “This is the reality of what happens on the ground,” Stanford says. “I have lost very young patients. I lost two patients, one at the age of 11, one at the age of 26 from obstructive sleep apnea, but they both had severe obesity. And I don’t like to go to funerals.”

Of course, a lot of times children and teenagers with severe obesity are dealt that hand from the beginning. Their parents and grandparents suffered from obesity, but the medical community can’t change family histories. And these are deaths that could have been prevented. “There is a high likelihood that they’re going to have severe obesity, and they develop issues much like their parents and grandparents and suffering a sudden cardiac death at 38 is not out of the realm of normal,” Stanford says. “And so I would say it’s more hassle for us not to intervene.”

Working to Do Better

In the March issue of the journal *Obesity*, Turner, et al., published a paper titled “Current Knowledge of Obesity Treatment Guidelines by Health Care Professionals,” that concludes “provider understanding of appropriate clinical care for obesity is inconsistent with evidence-based recommendations. As coverage for behavioral counseling services and pharmacotherapy expands, it is imperative that healthcare professionals understand how to effectively leverage these treatment modalities to optimize health outcomes for patients with obesity.”



Stanford also sees a continuing bias toward people with severe obesity, in which people tend to presume it's just a "lifestyle choice," that if they could just eat less and exercise more, the pounds would melt away. "That's actually not founded on science that we know about obesity," she says.

The authors also write that the "impact of pervasive weight stigma on [healthcare provider] understanding of ideal approaches to obesity management should not be discounted when considering systematic drivers of suboptimal or absent obesity care."

"I think that we can work to do better despite the level of training we have," Stanford says. "Or we're going to continue to fail our patients and our obesity rates are going to continue to proliferate, and we're going to start to see it earlier and younger. We see patients die much earlier than they need to of chronic diseases like heart disease associated with obesity."

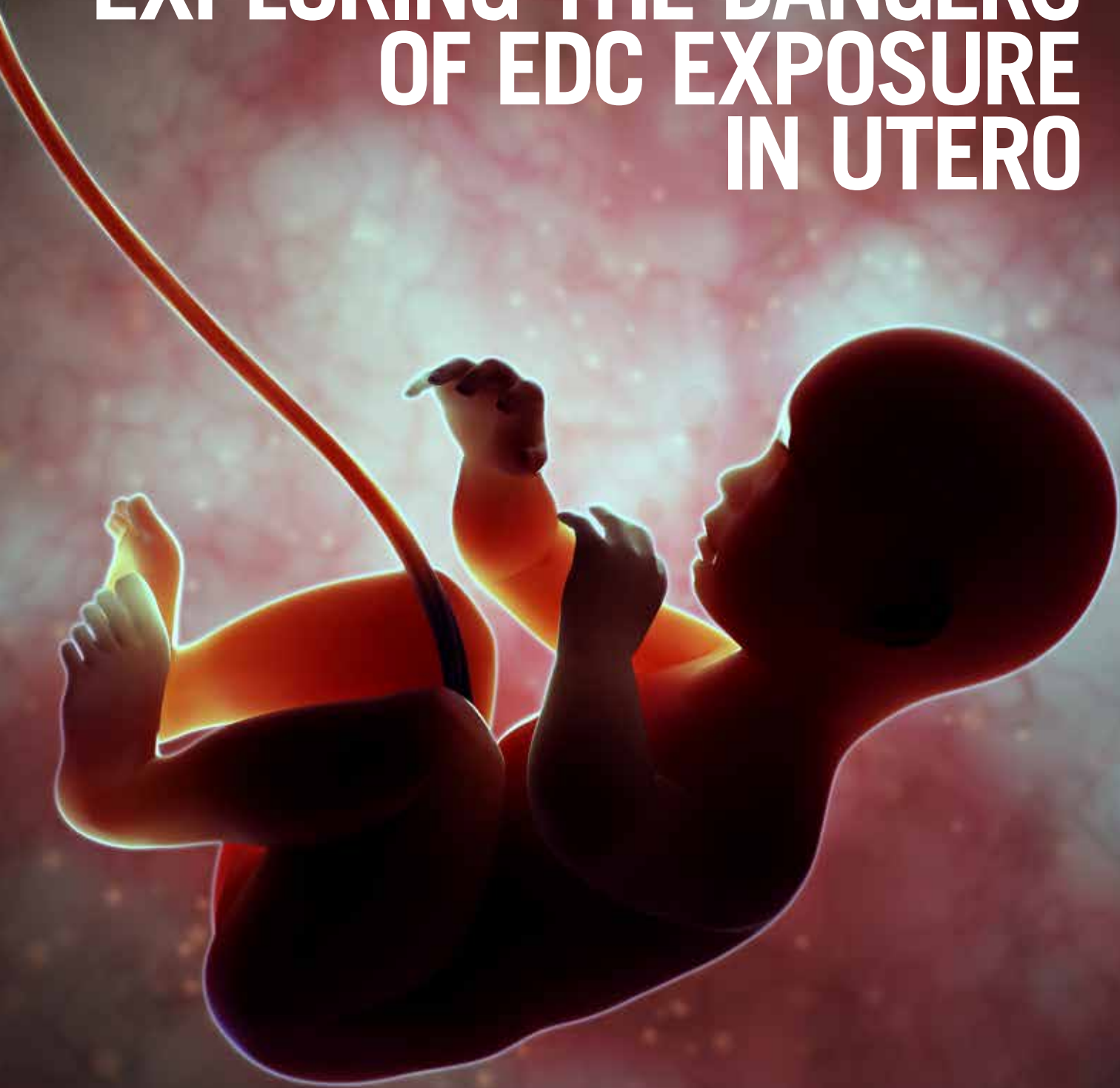
Stanford sent her patient with the BMI of 58 to surgery. Her BMI dropped to 28. She went back to the same retailer, the same hiring manager, with the same resume and was hired on the spot. It was kind of a bittersweet victory, but this patient

was bold enough to address the issue with the hiring manager, saying, "Look, I'm the same person. I came in before two and a half years ago, and you told me I wasn't qualified. And you hired me, but there's no difference, and I really think you should really look at your policies regarding hiring."

"When we think about obesity in our large population, we only think about the disease process," Stanford says. "We think about the high impact diseases such as obesity, but we don't think about the fact that it affects hiring. It affects socioeconomic status. It affects quality of life. It affects depression. These things are all inter-related, and so treating that child or adolescent with severe obesity sooner really can play a large role in setting them on an upward trajectory pretty early in life." ^{EN}

Parental Guidance:

EXPLORING THE DANGERS OF EDC EXPOSURE IN UTERO



The research presented at **ENDO 2018** ran the gamut in terms of endocrine science breakthroughs. Of particular interest were studies that took a closer look at how offspring could be harmed by endocrine disruptors — specifically BPA and DEHP — while still in the womb.

BY KELLY HORVATH

Two studies presented at **ENDO 2018** in March, the Endocrine Society's 100th annual convention, provide further evidence that in utero exposures to chemicals and other substances can have profound effects for the individual's life span and even beyond the directly exposed individual to future generations.

Neurogenesis and BPA: Wires Tangled

In "Exposure to low levels of BPA during pregnancy can lead to altered brain development," lead researcher Deborah Kurrasch, PhD, at the University of Calgary in Canada, and team exposed pregnant mice to environmentally relevant levels of bisphenol A (BPA) to investigate



“ It is tempting to think that DEHP may be a contributing factor to the decreased sperm counts and qualities in modern men compared to their previous generations.

This study therefore finds the importance of educating the public to try their best effort to reduce their exposure to this chemical and also of the need to substitute this chemical with a safer one.”

— RADWA BARAKAT, BVSC, MSC, PHD STUDENT, UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN, URBANA

whether exposure to BPA during gestation would affect brain development and, if so, what lasting effects the exposure might have on behavior from birth onward.

Environmental exposure to the xenoestrogen BPA and other endocrine-disrupting chemicals (EDCs) is known to increase the risk for many health problems, including such endocrine disorders as impaired fertility, diabetes, and obesity; cardiovascular disorders; several cancers; and behavioral changes in children. BPA is also known to cross the placenta, thereby exposing fetuses.

The research team fed the dams either a diet lacking BPA, a low-dose BPA diet, or a high-dose BPA diet and measured fetal serum concentrations. For context, the low dose fed to the mouse dams resulted in a fetal serum concentration 350-fold lower than what has been reported in human placenta. They then looked at how the fetal brains were developing and found precocious shift in the timing of when neurons were born in the BPA-exposed mice. “The first step in forming a brain is neurogenesis, the process of a progenitor cell becoming a neuron,” says Kurrasch. “These neurons then move to a particular place and form a proper connection. With more neurons developing too early, they probably will not migrate to the correct place to form the needed connections.”

Disrupted neurogenesis is concerning enough, but the researchers

Bisphenol A is primarily used to make plastics, such as these polycarbonate water bottles, while PVC is used extensively due to its low cost, chemical resistance, and ease of jointing. Phthalate plasticizers are essential to the utility of PVC, which is otherwise too brittle.



went on to show that the BPA exposure had lasting effects on behavior. As has been demonstrated in prior studies, BPA can cause hyperexcitability/hyperactivity. Kurrasch and team further validated that fetal exposure caused the mice to wander more than unexposed mice, which preferred to remain close to the walls of the testing chamber, suggesting that the BPA-exposed mice display a decreased awareness of self-preservation. Using the elevated plus maze, a measure of anxiety, they again showed that the mice did not restrict themselves to covered areas but moved about freely, consistent with the notion that mice exposed to BPA during gestation are less cautious.

The team plans to follow up this research by delving more fully into the neurogenesis — specifically what neurons are being affected and what is happening to the potentially premature neuronal connections.

There is a message to heed in the meantime; however, err on the side of caution where plastics are concerned, especially those likely to contain BPA. “Even though this was an animal study,” Kurrasch says, “I generally advise that pregnant women should be careful with their use of plastics, and they should follow ‘good plastic guidelines,’ such as avoiding putting plastics in the dishwasher or the microwave. If the plastics are old and showing signs of distress, throw them out. Use glass when you can.” There is still education to be done concerning plastics and what they expose us to, including BPA. At least in mice, its harmful effects on the brain may be lasting.

Transgenerational Infertility and DEHP

In “Prenatal Exposure to DEHP Leads to Premature Reproductive Senescence in Future Generations,” lead author Radwa Barakat, B.V.S.C., MSc, a PhD student at the University of Illinois at Urbana-Champaign, from the faculty of Veterinary Medicine, Benha University, in Egypt, and team investigated another widely used EDC, the plasticizer di-(2-ethylhexyl) phthalate (DEHP). Knowing that DEHP has been demonstrated to induce infertility in male mice, possibly by interference in fetal testosterone biosynthesis, these researchers wondered whether this effect is transmitted to following generations.

“Sperm counts among men have dropped substantially over the last few decades,” Barakat says. “The reason for such an alarming phenomenon is not known, but chemicals introduced to consumer products have been suspected to be contributing factors. In particular, chemicals that disrupt hormonal action in our body are prime suspects.”

The team fed mouse dams (generation 0) a diet containing 20 µg, 200 µg, 500 mg, or 750 mg/kg/day of DEHP or a diet of tocopherol-stripped corn oil from around the time of fetal gonadal development (gestational day 11) until birth. The adult male offspring (generation 1) were bred with unexposed females, producing generation 2. These adult male offspring were, in turn, bred with unexposed females, producing generation 3. At 15 months, a time when male mice are normally reproductively mature, the researchers measured serum androgen levels, assessed sperm concentration and motility in the cauda epididymis, and examined testicular histology.



AT A GLANCE

- ▶ Because EDCs interfere with endogenous endocrine signaling, perinatal exposure increases the likelihood of lifelong endocrine disruption.
- ▶ Exposure to BPA caused earlier differentiation of progenitor cells into neurons during neurogenesis in mouse fetuses, disrupting formation of appropriate neuronal connections and adversely affecting behavior throughout the lifespan.
- ▶ Male mice prenatally exposed to DEHP as well as their non-exposed offspring for two subsequent generations exhibited abnormal findings on reproductive indices and consequently lost fertility prematurely.

“Even though this was an animal study,” Kurrasch says, “I generally advise that pregnant women should be careful with their use of plastics, and they should follow ‘good plastic guidelines,’ such as avoiding putting plastics in the dishwasher or the microwave. If the plastics are old and showing signs of distress, throw them out. Use glass when you can.”

— DEBORAH KURRASCH, PHD, UNIVERSITY OF CALGARY, CALGARY, CANADA



Results from generation 1 were previously published and showed age- and dose-dependent gonadal dysfunction. As early as seven months, the 750 mg/kg/day group had significantly reduced fertility. At 19 months of age, 86% of the 750 mg/kg/day mice were infertile, compared with 25% of control mice. At this age, all of the DEHP-exposed mice had lower serum testosterone levels, higher serum estradiol levels, and higher luteinizing hormone levels than control mice.

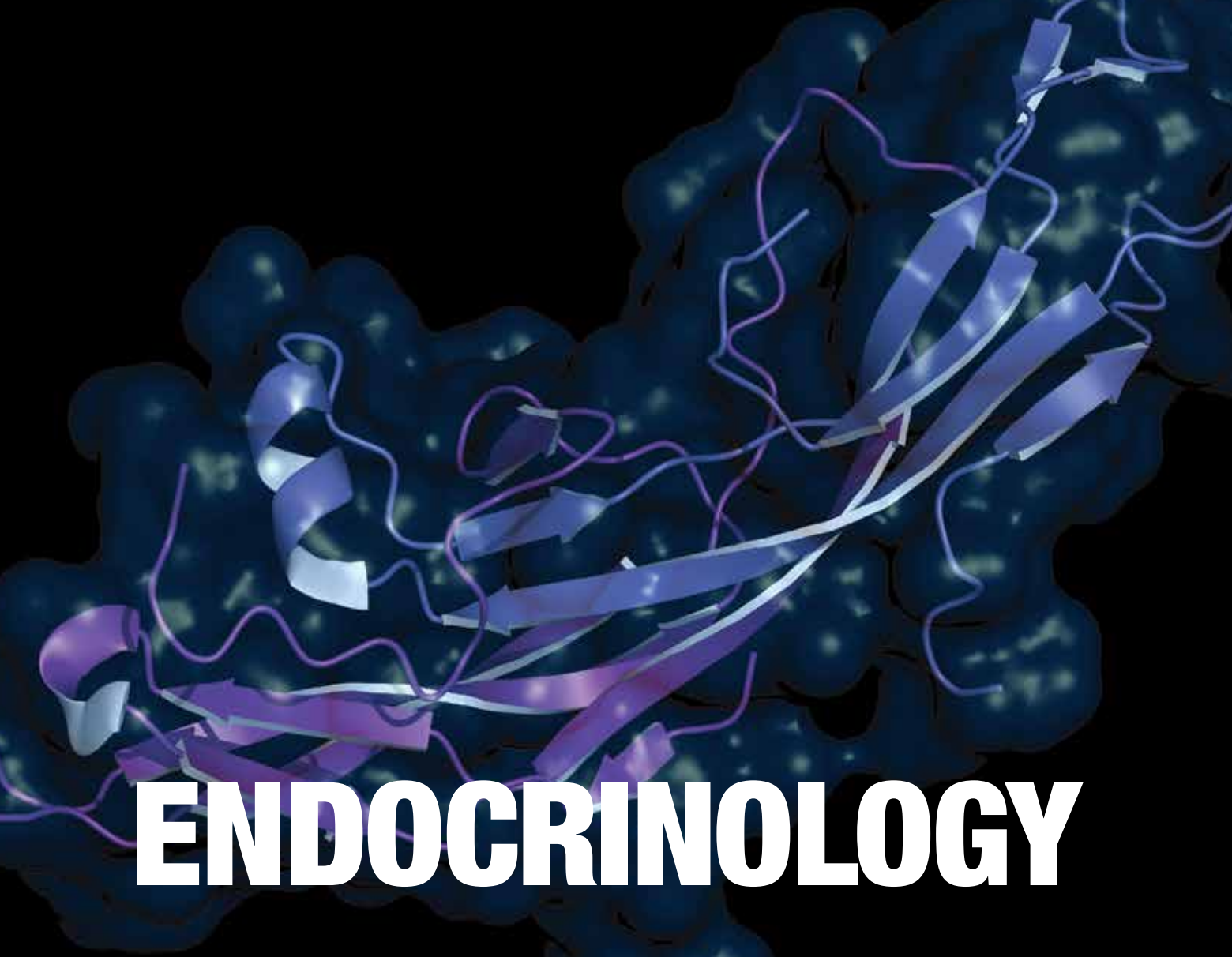
In generation 2, only the offspring of the highest-dose (750 mg/kg/day) group originally exposed to DEHP had abnormal results, including lower serum testosterone concentration; fewer and less motile sperm in the cauda epididymis; and histological evidence of testicular degeneration in the form of germ cell sloughing, which is normally seen in aged mice.

In generation 3, DEHP males continued to exhibit these reproductive abnormalities. However, the researchers were surprised to find that, despite the exposure having happened two generations prior, offspring of all dose exposures were affected, not just the group exposed to the highest dose. Perhaps even more surprisingly, in generation 3, reproductive indices were the least promising of all among the lowest-dose (20 µg/kg/day) group exposed to DEHP.

“Thus, the shape of the non-monotonic dose-response curve (NMDRC) reverses as the level of contamination goes up,” Barakat says. “Some NMDRCs are shaped like U’s, with high responses at low and at high levels of contamination as we found in DEHP-exposed mice.” The difference in effect between low- and high-dose exposures could be caused by anything from saturation of biotransformation pathways or protein-binding sites, to depletion of intracellular cofactors, to differences in ligand affinity and in efficacy of signal transduction.

Says Barakat of these findings: “It is tempting to think that DEHP may be a contributing factor to the decreased sperm counts and qualities in modern men compared to their previous generations. This study therefore finds the importance of educating the public to try their best effort to reduce their exposure to this chemical and also of the need to substitute this chemical with a safer one.” **EN**

HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT THE T TRIALS IN THE JUNE ISSUE.



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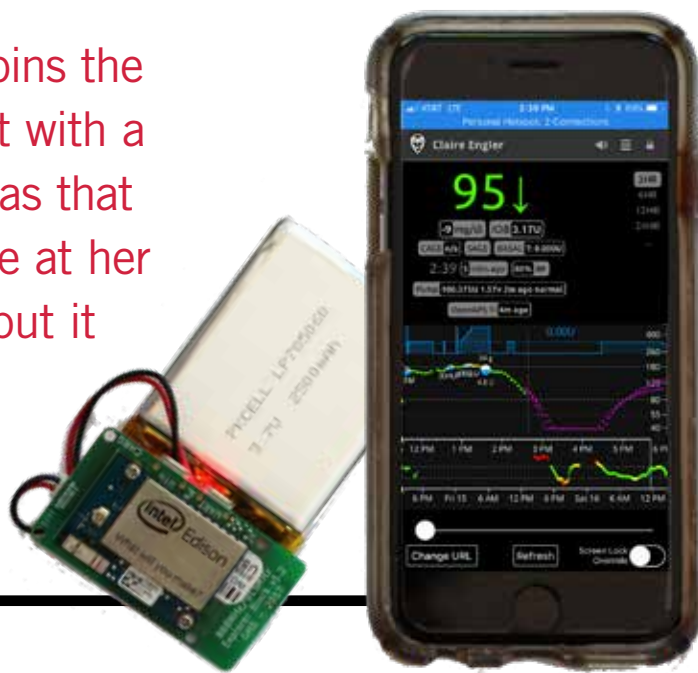


Twelve-year-old Claire Engler does not let type 1 diabetes slow her down, shown here, as she competes with her swim team, The Killer Whales, “armed” with her CGM.
PHOTO: David Engler

GIRL *Power*

BY ERIC SEABORG

Virginia tween Claire Engler joins the #WeAreNotWaiting movement with a do-it-yourself artificial pancreas that not only scored her a big prize at her middle school's science fair, but it has also greatly improved her glycemic control.



Claire's DIY system consists of a Medtronic MiniMed 722 insulin pump, a Dexcom G5 continuous glucose monitor, an Intel Edison pocket-sized computer, and an iPhone.

Claire Engler has had type 1 diabetes for a decade — but for the past six months, her glucose has been almost in the nondiabetic range. The 12-year-old credits this impressive control to the “artificial pancreas” she was showing off recently when *Endocrine News* encountered her at the Burley Middle School Science Fair in Charlottesville, Va., where she took a top prize.

Claire did not invent the system. She teamed up with her father to implement a do-it-yourself rig based on the Open Artificial Pancreas System (OpenAPS) project. (See Disclaimer, page 47.)

“When I heard about the DIY artificial pancreas, I knew right away that was what I wanted to do, both to be healthier and because I thought it would be an awesome project. At first, my dad did not think it was realistic, but after we looked into it more, he was on board,” Claire says.

An Overwhelming Diagnosis

Claire was two years old when one night her parents heard her running the bathroom faucet because she was unable to slake her thirst. For her physical therapist mother, Rebecca, this was the smoking-gun symptom of diabetes, and she and Claire were at her pediatrician's office the next morning. And from there, they were sent to the emergency room.

They were overwhelmed by a diagnosis they found “more stressful than bringing home a newborn,” Rebecca says, adding that they read everything they could find to educate themselves. After about six months of giving Claire insulin shots, their research showed that Claire could benefit from using an insulin pump.



Claire's father, David, amassed a stack of studies to show their pediatric endocrinologist, only to be told, "I wouldn't put a child that young on a pump." They found a physician in Richmond, Va., who agreed with them about the value of a pump and for the next few years made the 70-mile trip down the interstate for Claire's care. David says a pump can be particularly effective for toddlers because they fuel themselves with lots of snacks rather than meals.

By the time Claire was three, she was also on a continuous glucose monitor (CGM) — after her parents documented its advantages well enough to convince their health insurance company to cover it.

A Louder Alarm

So, it's not surprising that someone growing up with the latest technology would be excited to hear about the OpenAPS project. The project was started by a data analyst

named Dana Lewis, a type 1 diabetes patient who simply wanted to make the alarm on her CGM loud enough that she wouldn't sleep through it. As one thing led to another, she and her husband Scott Leibrand, a computer network and systems engineer, developed algorithms using the CGM readings to make insulin dose recommendations. When another member of their online community found a way for communicating with her insulin pump, they "closed the loop" on the feedback system. They shared their success online and continued development of the open source, crowd-sourced system.

The basic components of the OpenAPS artificial pancreas are a CGM, insulin pump, smartphone, and small computer to process the information and communicate with the web.

Claire's system consists of a Medtronic MiniMed 722 insulin pump, a Dexcom G5 CGM, an Intel Edison pocket-sized computer, and an iPhone.

“ When I heard about the DIY artificial pancreas, I knew right away that was what I wanted to do, both to be healthier and because I thought it would be an awesome project.”

— CLAIRE ENGLER, 12, TYPE 1 DIABETES PATIENT, CHARLOTTESVILLE, VA.

The choice of pump is crucial because the user needs to be able to configure it to accept outside commands for insulin delivery, a process the OpenAPS guides the user through. This function exists in some older Medtronic models but not newer ones. “Newer insulin pump models have more advanced security features,” says Pamela Reese, a spokesperson for the Medtronic Diabetes Group.

Manufacturers of medical devices have a strong incentive to prevent users from making modifications that deviate from their Food and Drug Administration (FDA)-approved functioning. The Englers found the old-model Medtronic on Craigslist and drove several hours to a rendezvous at a Cracker Barrel restaurant in southwest Virginia to buy it.

Claire’s computer provides Wi-Fi capacity to upload her CGM readings to the OpenAPS website, where algorithms calculate her upcoming insulin needs for communication to her pump. Claire had to get approval to use her school’s Wi-Fi. School administrators were happy to cooperate when she informed them of the reason she needed it.

Claire’s iPhone displays her CGM readings, insulin recommendations, and trend lines — and so do her parents’ phones, providing them peace of mind and the opportunity to intervene if needed.

Better Control

The system’s results have been striking. “My A1C decreased from an average of 7.5% — ranging from 6.9% to 8.0% — over almost ten years of diabetes, to 6.0% in my first six months of OpenAPS use,” Claire says. “This is almost to the non-diabetic range. This happened at an age when A1C is usually at the highest due to body changes and insulin resistance.”



AT A GLANCE

- ▶ Although not approved or regulated by the Food and Drug Administration, the Open Artificial Pancreas System provides tech-savvy type 1 diabetes patients an approach that many are using to improve their glycemic control.
- ▶ The basic “artificial pancreas” generally consists of a continuous glucose monitor communicating with an insulin pump, with dosing decisions made by a computer using sophisticated algorithms.
- ▶ Do-it-yourself rigs and commercial devices are showing that these closed-loop systems can mimic the pancreas to a remarkable degree.



“ My A1C decreased from an average of 7.5% — ranging from 6.9% to 8.0% — over almost ten years of diabetes, to 6.0% in my first six months of OpenAPS use. This is almost to the non-diabetic range. This happened at an age when A1C is usually at the highest due to body changes and insulin resistance.”

— CLAIRE ENGLER, 12, TYPE 1 DIABETES
PATIENT, CHARLOTTESVILLE, VA.

Before the OpenAPS, Claire had so many hypoglycemic episodes that she'd developed unawareness and did not recognize the sensation. After a month or two on the system, she had fewer hypoglycemic episodes and could feel them when she did. Her body was also more attuned to detecting high blood sugar.

The system is not entirely automated. She gives herself a manual bolus when she eats, which is considered a safety feature of OpenAPS software. “I do fewer fingersticks. Most of my fingersticks now are to check Dexcom accuracy before I give myself a large dose of insulin for meals. I still do checks to confirm a high or low reading before treating. Exercise, stress, and miscalculated meals can lead to rapid changes that Open APS cannot keep up with,” Claire says. She needs fewer overnight checks and generally wakes up with a good blood glucose level. Before this system, “my blood glucose was very unpredictable when I woke up.”

The OpenAPS website notes that it “is not an FDA-approved system or device. It's not manufactured or sold anywhere in the world. It's an open-source designed system that you can choose to build yourself. The DIY part of OpenAPS is important, because there's no customer service if it breaks or stops working — you'll have to fix it yourself. Individuals who build an OpenAPS are essentially doing an experiment, which they have a right to do to/by themselves. That is not a regulated activity by the FDA.”

While Claire's determination and overall attitude is a clear indicator that she will undoubtedly overcome any obstacle that may present itself in the future, creating a homemade CGM from a disparate collection of components is not what most endocrinologists would recommend.

“Claire is certainly an inspiration with a wonderful can-do spirit, but we continue to recommend that patients stick to FDA-approved systems,” says Endocrine Society chief professional and clinical affairs officer Robert Lash, MD. “With diabetes-related technology developing so quickly, patients and physicians will be able to choose from a growing number of innovative, safe, and effective devices.”

Spreading Technology

The 600-plus people currently using the OpenAPS system are those who have access to the technology and know-how to implement its slogan of “#WeAreNotWaiting to reduce the burden of type 1 diabetes.” The Englers certainly benefited from David's professional work as a software engineer, but he says that after getting the software downloaded, he made sure that Claire did most of the work of getting the system running.



Claire's active lifestyle includes soccer, running, playing flute in the school band — and launching into the air at Michigan's Sleeping Bear Dunes National Lakeshore.

Below she shows off the components of her system: sensor, pump, pocket computer, and smartphone.



In June 2017, Medtronic launched the MiniMed 670G, a “hybrid closed loop” insulin pump system that “mimics some of the functions of a healthy pancreas” and “adjusts insulin based on CGM readings,” according to the company’s website.

As one other example — also based in Charlottesville — a system developed at the University of Virginia (UVA) featuring a reconfigured smartphone running advanced algorithms that is linked wirelessly to a blood-sugar monitor and an insulin pump is in the final rounds of “a large-scale trial run by UVA at seven sites across the country. If successful, this study should help take the new system through FDA approval and out there in a year,” according to Boris Kovatchev, PhD, a developer of the system and director of the UVA Center for Diabetes Technology. ^{EN}

DISCLAIMER

Endocrine News and the Endocrine Society do not advocate patients tampering with commercially available glucose-monitoring equipment. However, we felt that this story should be shared with endocrinologists who might have patients currently using or considering creating such a device. — Editor

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT RESEARCH BREAKTHROUGHS REGARDING THE MALE BIRTH CONTROL PILL IN THE JUNE ISSUE.



Q&A:

Charles Sklar



***Endocrine News* talks with Charles A. Sklar, chair of the guideline writing committee that created the latest Endocrine Society Clinical Practice Guideline on hypothalamic-pituitary and growth disorders in survivors of childhood cancers. He discusses why it was important for the Society to publish this guideline now and why he thinks it will help improve the health of pediatric patients for generations to come.**

In July, the Endocrine Society published a Clinical Practice Guideline on treating hypothalamic-pituitary and growth disorders in survivors of childhood cancers. Titled “Hypothalamic-Pituitary and Growth Disorders in Survivors of Childhood Cancer,” this is the first guideline of its kind that the Society has published.

Cure rates for childhood cancers have improved dramatically over the past several decades with an overall five-year survival rate near 80%, according to Charles A. Sklar, MD, from

the Department of Pediatrics at Memorial Sloan-Kettering in New York. “Moreover, for some of the more common cancers such as acute lymphoblastic leukemia and Hodgkin lymphoma, five-year survival rates are in the 90% range. Thus, survivors are an ever-expanding population; it is estimated that there will be 500,000 survivors of childhood cancer residing in the U.S. by 2020.”

Sklar, who is the chair of the guideline writing committee that authored the guideline, adds that while these survival rates are impressive and cause for celebration, “it is important to know that survivors face many challenges including an excess risk of serious medical conditions over time.”

Endocrine News spoke with Sklar to see how this new guideline could serve as an introduction for clinicians who may have not cared for these patients in the past, as well as a benchmark for specific treatments regarding growth disorders and anterior pituitary function.

Endocrine News: What was the main reason for the publication of the hypothalamic-pituitary and growth disorders in survivors of childhood cancer guideline? What drove the decision and why now?

CHARLES A. SKLAR: To address the special issues facing survivors, several general guidelines have been developed, primarily by the pediatric oncology community. These guidelines have been aimed at the generalist caring for survivors and have focused on identifying survivors at highest risk for a variety of common medical disorders

and have emphasized approaches to screening for these complications. As adverse endocrine, metabolic, and reproductive outcomes are highly prevalent among cancer



survivors, endocrinologists, both pediatric and adult, are increasingly likely to encounter such patients in their practice. Thus, it is most appropriate that we develop specific guidelines by and for endocrinologists with the aim of addressing the diagnosis and management of endocrine disorders in this high-risk population.

As survivors can experience the entire gamut of endocrine disorders, affecting all endocrine organs, it was not feasible to address the full spectrum of adverse outcomes in a single guideline. Therefore, we have decided to focus on disorders

“The ultimate aim is to improve the quality of life and reduce morbidity of survivors by facilitating timely diagnosis and appropriate management of endocrine disorders.”

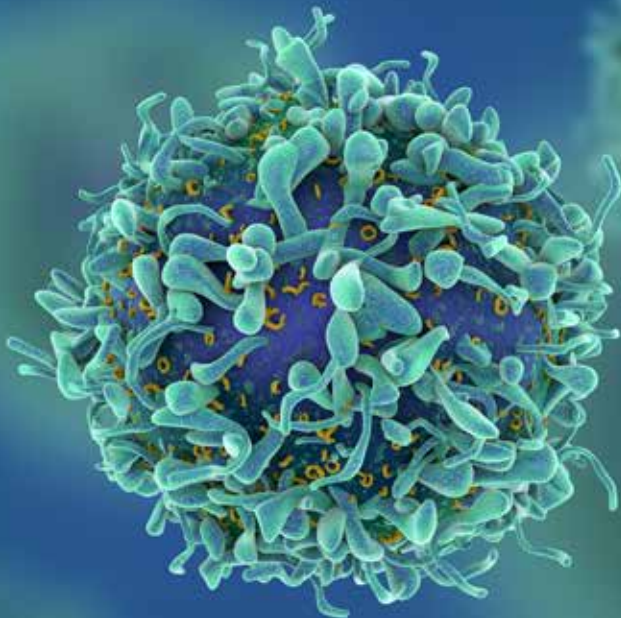


Illustration of cancer cell

of growth and anterior pituitary function in this initial guideline as they are among the most common endocrine disorders seen.

EN: What are your hopes for the impact of the guideline on endocrine standards of care for survivors of childhood cancer with hypothalamic-pituitary and growth disorders?

CAS: It is our hope that providers who are less familiar with this population will appreciate better how the diagnosis and management of these disorders compares to the diagnosis and management in a non-cancer population. While many aspects of care are similar, we have emphasized key differences and unique features and findings that are specific to a survivor population. Of course, the ultimate aim is to improve the

quality of life and reduce morbidity of cancer survivors by facilitating timely diagnosis and appropriate management of endocrine disorders.

EN: What are the key take home messages for patients in this guideline?

CAS: The focus of this guideline is the physician, but the key take-home messages would include: Risk for late effects are dependent upon your prior diagnosis and treatment so knowing this information is essential; for survivors previously exposed to radiation to the brain, new endocrine problems can develop many years after the completion of cancer therapy and, thus, routine follow-up with an appropriate specialist may be required for the patient's lifetime. **EN**

“As adverse endocrine, metabolic, and reproductive outcomes are highly prevalent among cancer survivors, endocrinologists, both pediatric and adult, are increasingly likely to encounter such patients in their practice.”

Schmooze Alarm:

Networking for Scientists



From in-person conferences such as ENDO to online sites like LinkedIn, networking is a vital part of creating professional relationships in and out of the lab.

BY GLENDA FAUNTLEROY SHAW

Networking — “the cultivation of productive relationships for employment or business” — is a must for researchers. Networking affords the opportunities to meet potential collaborators who can enhance your work, provide mentorship, or be avenues to financing funding resources. Meeting new people in your field of work should be a requirement on every scientists’ to-do list. For young scientists, especially, networking can open the door to a vastly brighter future.

Conferences Have Rewards

Attending conferences can offer easy access to colleagues and has long been the tried-and-true method of networking. Whether it’s during the scheduled mixer and networking sessions or during a casual coffee break, meeting colleagues at conferences who share your same interests can have huge benefits. The Endocrine Society, for instance, holds ENDO each spring, and for its more than 7,000 attendees, there are a host of opportunities to make connections.

“I found it to be very beneficial to network with others while at ENDO 2018. I had the opportunity to collaborate with scientific professionals from a variety of subspecialty fields within endocrinology.”

Jeffrey Tyler Ramsey, a postbaccalaureate research fellow at the National Institute of Environmental Health Sciences in Durham, N.C., attended **ENDO 2018** in Chicago for the first time and deems it a “great experience.”

“I found it to be very beneficial to network with others while at **ENDO 2018**,” he says. “I had the opportunity to collaborate with scientific professionals from a variety of subspecialty fields within endocrinology. Furthermore, I met many individuals who provided me different perspectives on my research. Since there were also many professionals familiar with my specific field, I was given new insights on my research that I had not thought of previously.”

Ramsey was selected for an oral presentation, and his research will be included in the annual Research Summaries Book. He was also invited to hold a live press conference on his research, and it was covered by more than 100 national and international media outlets.

“While I usually attend local conferences a few times a year, I can say with certainty that my first time attending a national conference will be something I never forget as I continue on with my career into medicine,” Ramsey adds.

The Introvert Dilemma

It is a fact that conferences are not enjoyable for everyone. Talking to total strangers at a networking event can be an overwhelming anxiety-producing exercise for those

Jeffrey Tyler Ramsey, a research fellow at the National Institute of Environmental Health Sciences in Durham, N.C., during his press conference at **ENDO 2018** in March. He also managed to spend a great deal of time networking with others in his subspecialty within endocrinology. (Editor's Note: Ramsey's research is also featured in "Are Essential Oils Endocrine Disruptors?" on page 18.)





LABORATORY NOTES

These early-career attendees at **ENDO 2018** spent an entire day together before the conference at a variety of sessions, which allowed for ample networking opportunities.

“Meeting new people in your field of work should be a requirement on every scientists’ to-do list. For young scientists, especially, networking can open the door to a vastly brighter future.”

who consider themselves introverts. Since missing out on valuable collaborations is not an option, pushing through a networking event is a must. An article in *The Guardian* offered some helpful tips to survive as an introvert:

- ▶ **Get there early.** Be one of the first people at the event. It can be intimidating to walk in late when conversations and groups have already formed. Even try to connect with other attendees online beforehand. If the conference has a Twitter hashtag, for example, use it to engage with others who will be there.
- ▶ **Ditch the elevator speech.** Don’t worry about saying something clever. Just smile, stick out your hand, and introduce yourself. Skip the small talk that may make you uncomfortable. Jump straight into discussing your research.
- ▶ **Listen.** Let others talk about their work. Ask a few open-ended questions that you can ask anyone you meet: “How did you get started in your career?” or “What are you passionate about?” And be ready to answer these same questions for yourself if asked.

- ▶ **Aim for quality rather than quantity.** If talking to complete strangers doesn’t come naturally, set a goal of meeting just a handful of people. If you come away with just two or three new contacts who you can connect with at a later date, consider the event a success.

Check in Online

Technology has made networking much easier than just 10 years ago. Every professional should extend their reach by creating a profile on popular networking sites such as LinkedIn and Facebook. A search of “endocrinology” on LinkedIn can reveal hundreds of people in the specialty, and it’s not unusual for employers to search these sites for prospective candidates. Also, go through your friends’ online profiles to identify interesting contacts they have and ask for an introduction.

Whatever method you choose, keep in mind that there are plenty of new and interesting people to meet, many who may already have some connection to you through shared schools, research, and friends. You never know what you’ll find until you ask. ^{EN}

Medicare Expands Access to CGM Smartphone Applications

In an important advocacy victory for our members and their patients, Medicare beneficiaries will now be able to use smartphone applications in conjunction with their continuous glucose monitors (CGM).

Over the past year, the Society has advocated for expanded access to this important safety net, which can help protect patients who experience hypoglycemic events. These efforts included numerous meetings on Capitol Hill to engage and educate policy makers about this important access issue. We have also been working on this issue with our colleagues in



the Diabetes Advocacy Alliance, where Meredith Dyer, our director of health policy, serves as a co-chair.

This group met with Principal Deputy Administrator and Director of the Center for Medicare, Demetrios Kouzoukas, just days before the announcement, to underscore the impact that precluding beneficiaries from using CGM technology has on older patients. The Society will continue to work with the Centers for Medicare and Medicaid Services as it revises the coverage determination to mitigate any additional disruptions in patient access to this important technology.

House Appropriations Bills Propose Increase for NIH



On June 14, the House Appropriations Committee released text for its fiscal year (FY) 2019 Labor, Health and Human Services (LHHS), Education and Related Agencies Appropriations spending measure, which includes funding for the National Institutes of Health (NIH).

The House LHHS bill provides an additional \$1.25 billion for biomedical research, which would raise the NIH budget to \$38.3 billion (a 3.4% increase) compared to FY 2018. Within the \$1.25 billion increase, the following funding increases are included to support specific NIH initiatives:

- ▶ \$401 million for Alzheimer's disease research;
- ▶ \$100 million for the Cancer Moonshot research initiative;
- ▶ \$29 million for the Brain Research through Application of Innovative Technologies (BRAIN) initiative;
- ▶ \$147 million for the All of Us research initiative;
- ▶ \$30 million towards the development of a universal flu vaccine; and
- ▶ \$15 million for research on combating antibiotic-resistant bacteria.

After accounting for these targeted initiatives, approximately \$528 million would be applied to the base budgets of the various institutes and centers.

In the weeks and months leading up to the release of the House text, Endocrine Society members called, wrote, and visited their representatives to ensure that Congress appreciated the critical work done by endocrine scientists funded by the NIH and the need to maintain the trajectory of steady, sustainable increases in funding that have been achieved in recent years. Although the proposed increase falls short of the \$39.3 billion that the Endocrine Society requested for FY 2019, we are encouraged that the House prioritized an increase in funding for the NIH during a year where the overall federal budget is extremely restrained.

We also advocated for a component of the NIH budget that does not fall under the LHHS bill. Earlier in the year, the House Appropriations Committee also released the FY 2019 Interior and Environment (I&E) bill, which included a \$3 million increase to a total of \$80 million for the Superfund Research Program (a 3.9% increase). The Superfund Research Program is administered by the NIH under the direction of the National Institute of Environmental Health Sciences (NIEHS).

For both bills, attention now turns toward the Senate where, at the time this article was written, work on both the LHHS and I&E bill continues. Society Members are encouraged to continue to take action in support of increased NIH funding by visiting www.endocrine.org/advocacy.

The Endocrine Society & AMA Address Rising Insulin Prices

The American Medical Association (AMA) House of Delegates met in June to establish policy positions on topics of importance to patients and healthcare providers. The Society attends the AMA meetings to further our policy agenda by garnering the support of the House of Delegates on issues of importance to our members. This enables us to take that message to Capitol Hill and federal agencies as an additional means of support. In addition to passing policy that

supports the Society's priorities, we also fight against passage of policy that will be detrimental to endocrinologists or the patients that they treat.

The House of Delegates offers a means to generate support in the medical community for potential policy solutions to the problem of high insulin prices. At the November 2017 House of Delegates meeting, the Society teamed up

with the American Association of Clinical Endocrinologists (AACE) to introduce a resolution urging the AMA to pursue several initiatives aimed at improving insulin affordability for patients with diabetes. Overwhelming support for addressing insulin costs expressed on the floor of the House of Delegates led to a unanimous vote for the AMA to study these issues and provide a report with findings and recommendations to the House of Delegates.

The resulting report was introduced at June's meeting and is now policy of the AMA. Recommendations for



addressing the high costs and reducing the impact on patients include:

1. Encouraging the Federal Trade Commission and the Department of Justice to monitor insulin pricing and market competition and take enforcement actions as appropriate;
2. Disseminating model state legislation to promote increased drug price and cost transparency and to prohibit standard gag clauses that bar pharmacists from telling consumers about less-expensive options for purchasing their medication;
3. Supporting physician education regarding drug price and cost transparency and challenges that patients may encounter at the pharmacy;
4. Supporting legislation or regulation to ensure that private health insurance carriers declare which medications are available on their formularies by October 1 of the preceding year, and that drugs may not be removed from the formulary or moved to a higher cost tier within the policy year; and
5. Supporting cost-sharing requirements for prescription drugs that consider factors known to affect patient compliance and the development and use of tools and technology to enable physicians and patients to determine the actual price and out-of-pocket costs of prescription drugs prior to making prescribing decisions.

The AMA released a statement on June 13 announcing these recommendations, many of which are consistent with the Society's priorities for addressing and lessening the impact of high insulin prices.

Policy proposals passed or referred for further study at the House of Delegates meeting that address other Society priorities include transgender placement in prison, banning sex assignment surgery in infants with disorders of sex development, barriers to obesity treatment, and integration of scientific evidence in EPA policies. We are analyzing the impact of these new policies on our members and will work with the AMA to advance our mutual policy priorities.



David Tridgell, MD, (left) and Rob Lash, MD, the Endocrine Society's chief professional and clinical affairs officer, visited Capitol Hill recently to educate members of Congress about the impact of rising insulin prices and how it affects patients.

Society Advocates for Insulin Affordability, Supply Chain Transparency

The Endocrine Society took to Capitol Hill to educate policy makers about the impact of rising insulin costs on patients with diabetes and how to begin addressing this critical issue.

Society member David Tridgell, MD, who himself has type 1 diabetes, met with key committees of jurisdiction in both the House and Senate to advocate that Congress take action to expand drug pricing transparency, evaluate the feasibility of passing rebates on at the point of sale without increasing premiums, and bolstering the patient assistance programs offered by manufacturers. Tridgell is an endocrinologist who has authored several pieces on the impact of insulin affordability on himself and his patients, including an OpEd in the *Washington Post* titled, "Insulin is Too Expensive for Many of My Patients. It Doesn't Have to Be."

Addressing the rising cost of insulin is a top priority for the Endocrine Society, which has been working with the

Congressional Diabetes Caucus for more than a year on potential solutions. The Society also submitted testimony to the Senate Special Committee on Aging following its hearing on insulin pricing offering the following recommendations to effect change:

- ▶ Integrating formulary and cost information into electronic health records;
- ▶ Including insulin on preventive drug lists;

- ▶ Ensuring patients receive rebate benefits at point of sale; and
- ▶ Making patient assistance programs more accessible and less restrictive.

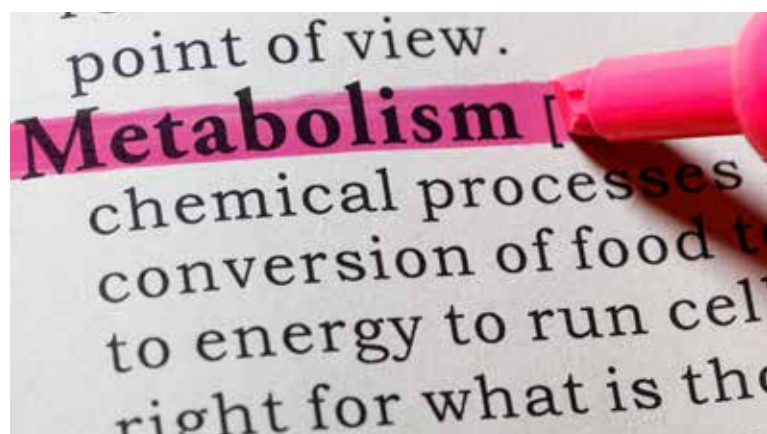
We will continue to monitor and engage with policy makers about this important issue. For more information on how to get involved, including opportunities to advocate on Capitol Hill, contact Meredith Dyer, Director of Health Policy, at mdyer@endocrine.org.

National Conference on Women's Health Issues to Focus on Metabolism Across the Lifespan

On September 26 – 28, the Center for Women's Health Research (CWHR) at the University of Colorado Anschutz Medical Campus will host the 2nd National Conference on Women's Health Research "Sex Differences Across the Lifespan: A Focus on Metabolism." Session topics will include fetal origins of adult disease, heart disease, skeletal health, sleep and circadian physiology, diabetes, and exercise and cardiometabolism. The NIH Office of Research on Women's Health will also be leading a workshop focused on how to study sex as a biological variable.


This conference will gather top scientists from around the country to speak about women's health and the latest research on sex differences. Conference attendees will have the chance to discuss the latest science with colleagues in a productive, collaborative environment featuring interactive sessions, poster presentations, keynote speakers, and a special breakfast to provide the latest research information to the lay community. Attendees will have extensive opportunities for networking, exchanging new ideas, and creating plans for collaborative, interdisciplinary research to tackle unaddressed questions in sex-difference research.

In addition to updates from senior scientists, the conference will showcase the talents of early-career scientists to further the CWHR's mission of mentorship and collaboration across career generations. Attendees may submit abstracts for poster presentations, which will be judged by leading conference



speakers; a subset of the posters will be selected to receive an award.

The CWHR is focused on research to prevent, treat, and cure cardiovascular disease, diabetes, and mental health illness in women (as well as studying sex differences in these areas). In addition, the CWHR is focused on mentoring the next generation of scientists in women's health and educating the public. Research that addresses sex differences will enable future breakthroughs to improve the health of both women and men.

To learn more, register, or submit a poster abstract, visit www.cwhr.org. **Note that the deadline for registration and abstract submission is August 24, 2018.** 

Weight Watchers: Devices to Combat Obesity

COMPILED AND WRITTEN BY COURTNEY CARSON



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◀ Ethicon Echelon Flex

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▶ DietSensor

The DietSensor app was designed to assist patients looking to achieve a weight loss goal, keep weight off after a bariatric procedure, and manage insulin-dependent diabetes. DietSensor helps users conveniently manage conditions such as diabetes and obesity by scanning, analyzing, and logging food and drink in a few seconds from anywhere. Created by two parents following their daughter's type 1 diabetes, DietSensor received numerous plaudits for its use of the DietSensor SCiO scanner, a small, handheld Bluetooth molecular sensor that uses near infrared spectroscopy to determine the chemical makeup of food and drinks.

www.dietsensor.net



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POINT OF CARE TOOLS



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Which help to enhance patient understanding and increase confidence support their overall well-being.



Download Patient Guides

These evidence-based patient resources are a derivative of the Endocrine Society Clinical Practice Guideline used as point of care tools to support patient learning and comprehension.



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