THE LEADING MAGAZINE FOR 🦳 ENDOCRINOLOGISTS

INTERNATIONAL

MAY 2017

On the MARCH

FOR

Science

FOR

Abby & Mallory

Type I Diabetes 4 shots Every Day to live

GRANddaughters

On April 22, the Endocrine Society joined the hundreds of thousands of people around the world who took part in the first March for Science to show the world how important scientific research is to everyone regardless of age, race, political affiliation, profession, or nationality.

Endocrine News was there with exclusive coverage and photos.



**GENDER GAP:** A look at the lack of women in the lab



Hormone Science to Health

# Endocrine

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

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## COVER STORY

# $\mathbf{22}$ | Taking it to the Streets

On Saturday April 22, tens of thousands of people gathered in Washington, D.C., and around the country, to show their support for scientific research. The Endocrine Society and *Endocrine News* were on the front lines in the nation's capital.

### **BY DEREK BAGLEY**

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# 18 | Hidden Fissures: Hip Fracture Rate Ends Years-Long Decline

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### BY DEREK BAGLEY

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### BY KELLY HORVATH



# The March for Science: Taking it to the Streets

## N AN UNPRECEDENTED EVENT, THOUSANDS OF PEOPLE TOOK

to the streets of Washington, D.C., and more than 600 other cities around the world, to show their support for scientific research in the first official March for Science. Not only was the Endocrine Society there in full force but so was *Endocrine News*. Senior editor Derek Bagley (pictured, interviewing Society president Lynnette K. Nieman, MD) was another face in the crowd — along with Endocrine Society members and staff — who braved the intermittent downpours in an effort to support science. His story about this historic



day, "Taking it to the Streets," can be found on page 22, along with more photos from the event courtesy of his wife, Beth, who, lucky for us, is a photography pro.

For the fourth year in a row, Derek has tackled the arduous task of preparing a wrapup of some of the highlights from **ENDO 2017**, which took place in Orlando, Fla., last month ("ENDOMANIA," p. 30). While the article touches on only a few of the highlights of the activities, events, programs, and scientific breakthroughs that were presented at **ENDO**, you can find several stories that cover some of the presented studies in more detail at **www.endocrinenews.org**.

Personally, **ENDO 2017** was the most successful **ENDO** I've attended since becoming editor of *Endocrine News*, largely due to being available to meet and greet so many of you in a manner I have not had the chance to do in past years. It was rewarding and even heartwarming to find myself face to face with so many Society members who've written for the magazine in the past ... or who will be writing for the magazine soon.

The endocrine clinicians and scientists are the heart of what makes the Endocrine Society such an important, well respected organization. It's also what makes *Endocrine News* the number one magazine among its competitors. Like the Society, our strength is in our members, and judging from all the amazing endocrinology pros I met in Orlando, *Endocrine News* and the Endocrine Society will continue to raise the bar and be the leader in advancing the science and practice of endocrinology.

- Mark A. Newman, Editor, Endocrine News





THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

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BY GLENDA FAUNTLEROY

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#### www.endocrine.org





PRESIDENT'S VIEWPOINT



# Introducing the New President: Lynnette Nieman, MD

**HE ENDOCRINE SOCIETY IS PLEASED TO** welcome its president for 2017 - 2018, Lynnette Nieman, MD, who took office April 4. A senior investigator and chief of the Endocrinology Consultation Service at the National Institutes of Health (NIH) Clinical Center, her

work focuses mostly on disorders of cortisol, though she has also worked on antiprogestins, leading to two commercialized products.

"I am honored to serve our members," Nieman says, "and excited to work with our members and talented staff and CEO to develop our fourth strategic plan (SP4) to move the Society forward."

Nieman succeeds Henry Kronenberg, MD, as the Society continues its rotation of presidents who represent its core constituencies: basic researchers, clinical researchers, and clinical practitioners. She graduated from Smith College and attended medical school at SUNY Buffalo. Nieman has been with the NIH since 1982, and in that time she has authored or co-authored more than 200 papers and won numerous awards, including the NIH Director's Award, the NIH Clinical Teacher of the Year Award, and the Endocrine Society's Distinguished Physician

award. "I've been lucky to have a lot of different experiences related to investigation and its oversight," she says, "including 11 years as the clinical director of Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and five years as the director of the (NIH Intramural) Office of Human Subjects research. I'm currently working on development of standard templates for protocols within the intramural program."

Nieman's interest in endocrinology stems from her love of complex systems and solving puzzles, as well as the appeal of

66 [I have] two main goals for [my] presidency: First, to have an inclusive process for the development of SP4 goals that will meet many needs of the Society's diverse and global membership. Second, to consider how we can individually, and as a Society, extend our influence — whether by extending our basic research findings to other fields, translating it to clinical investigation, commercializing our results, mentoring others, or educating the public about what we do.



workings of the endocrine system. She says she thinks most physicians choose fields that mesh with their personalities. "I advise our fellows to go into a field that seems exciting, and that sometimes reading The Journal of Clinical Endocrinology & Metabolism (ICEM) or other journals can help figure that out," she says. "Also, recognizing serendipity and opportunities often pulls us one way or the other. For me, I was drawn to the titles on reproduction and cortisol, and fortuitously, RU486 (mifepristone) had recently been developed when I joined the NIH as a fellow. From then on I had a schizophrenic career that 'focused' on cortisol and progesterone."

the complex physiologic and cellular

"It was eye-opening to me that we could improve diagnosis, change treatments, and make a big difference in people's lives through our research," Nieman continues. "Recently I chose to work on human subjects policy to hopefully streamline and

facilitate the ability of other clinical investigators to carry on their important work. I worry that we are losing clinical investigators from the field."

Nieman first joined the Society in the 1980s, after her mentor in Buffalo, N.Y., Pepper Davis, and the "NIH gurus"

logy Consultation Service at lth (NIH) Clinical Center, orders of o worked 5 to two recommended membership. Her first annual meeting was in 1983, and since then, she has been an extremely active member. "I became a member of the 'Membership Committee' (no longer exists) sometime in the 1980s," she says. "From there, I served on a number of other committees, chaired two guidelines, and participated in a number of previous strategic plans. That's my 'involvement' from a statistical perspective; from a personal perspective I have made many friends, benefited from the wisdom of so many colleagues, and had the intellectual pleasure of thinking about how things work."

Nieman says she has two main goals for her presidency: First, to have an inclusive process for the development of SP4 goals that will meet many needs of the Society's diverse and global membership. Second, to consider how we can individually, and as a Society, extend our influence — whether by extending our basic research findings to other fields, translating it to clinical investigation, commercializing our results, mentoring others, or educating the public about what we do.

"I'd like to see the Society become an umbrella organization that interacts in new ways with other groups, organizations, government bodies and patient groups," Nieman says. "Not sure exactly how that will 'look,' but I think we will have overarching goals in this direction with SP4."





# *Functional Hypothalamic Amenorrhea* A NEW STANDARD FOR CARE

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# Some Key Points from the Functional Hypothalamic Amenorrhea Guideline:

- A thorough work-up is essential as Functional Hypothalamic Amenorrhea (FHA) is a diagnosis of exclusion
- Optimal treatment of the condition is controversial with the primary focus on eliminating the energy deficit that stems from undernutrition, over-exercise, or both
- Affected women may have difficulty conceiving, which merits oversight of a reproductive endocrinologist

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

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new Scientific Statement issued by the Endocrine Society advises healthcare providers on ways to spot hormonal causes of hypertension that can be cured with surgery or treated effectively with medication.

Without effective screening, common hormonal causes of hypertension, such as the disorder termed "primary aldosteronism," often go undiagnosed and untreated. This can leave individuals with these conditions at greater risk of developing cardiovascular disease, renal disease leading to dialysis, or even death.

Hypertension affects one in four American adults, according to the Scientific Statement. In about 15% of these cases, hypertension is caused by hormone, kidney, or other disorders. The rate can be as high as 50% among children and 30% among young adults.

"Without appropriate lab tests, some common endocrine disorders are nearly indistinguishable from a routine case of hypertension," says Endocrine Society Past-President William F. Young, Jr., MD, MSc, of the Mayo Clinic in Rochester, Minn., and the chair of the task force that authored the Society's Scientific Statement. "Screening for underlying causes of high blood pressure can save lives. This new resource offers healthcare providers valuable guidance on when to suspect a hormone disorder and how to test for it."

Hypertension can be the first sign of any of 15 endocrine disorders. Potential causes of high blood pressure can include tumors that produce adrenal hormones such as aldosterone and adrenaline, thyroid disorders, obstructive sleep apnea, or acromegaly. The Scientific Statement delves into the number of people affected by the 15 endocrine disorders and the screening process for these disorders.

The most common endocrine cause of high blood pressure is

# Society Issues Scientific Statement to Improve Detection of Curable Forms of Hypertension

primary aldosteronism, which occurs when the adrenal glands produce too much of the hormone aldosterone. This causes a build-up of aldosterone, which normally balances blood levels of sodium and potassium. The resulting excess sodium can raise blood pressure levels.

As many as one in 10 people with high blood pressure may have this condition, according to the Society's Clinical Practice Guideline on management of primary aldosteronism. Individuals with primary aldosteronism face an increased risk of cardiovascular problems, including death and stroke, compared to individuals who have similar blood pressure levels that are not caused by an underlying endocrine condition.

"Healthcare providers should consider primary aldosteronism screening for most people who have hypertension," Young says. "The condition can be easily treated and often cured when it is diagnosed. Early detection also reverses the elevated risk of cardiovascular events and kidney failure in this population."

Other authors of the statement include: David A. Calhoun, University of Alabama at Birmingham, Birmingham, Ala.; Jacques W.M. Lenders, Radboud University Medical Centre, Nijmegen, the Netherlands, and University Hospital Carl Gustav Carus, Technische Universität in Dresden, Germany; Michael Stowasser, University of Queensland School of Medicine, Greenslopes Private Hospital, and Princess Alexandra Hospital, Queensland, Australia; and Stephen C. Textor, the Mayo Clinic, Rochester, Minn.

The statement, "Screening for Endocrine Hypertension: An Endocrine Society Scientific Statement," was published online in the Society's journal *Endocrine Reviews* at **endocrine.org/ hypertension**.

The statement was published in the April issue of *Endocrine Reviews*.





# Endocrine Society Members Share 2017 Harrington Prize for Innovation in Medicine

he fourth annual Harrington Prize for Innovation in Medicine has been jointly awarded to Endocrine Society members Daniel J. Drucker, MD, and Joel F. Habener, MD, for their discovery of incretin hormones and for the translation of these findings into transformative therapies for major metabolic diseases such as diabetes. They share the award with Jens J. Holst, MD, DMSc.

Drucker is a senior scientist with the Lumenfeld Tanenbaum Research Institute in Toronto, and a professor at the University of Toronto. He received his MD from the University of Toronto in 1980. Habener is professor of medicine at the Massachusetts General Hospital, Harvard Medical School. He received his MD in 1970 from the University of California – Los Angeles.

The Harrington Prize for Innovation in Medicine, established in 2014 by the Harrington Discovery Institute at University Hospitals in Cleveland, Ohio, and the American Society for Clinical Investigation (ASCI), honors physician-scientists who have moved science forward with achievements notable for innovation, creativity, and potential for clinical application. Habener and Holst are recognized for their discovery of the hormone glucagon-like peptide 1 (GLP-1), and Drucker for translating the discovery into breakthrough treatments for diabetes. The work of these three investigators, and Drucker in particular, has also resulted in the discovery and clinical development of glucagon-like peptide 2 (GLP-2) for intestinal disorders (short bowel syndrome).

A committee composed of members of the ASCI Council and the Harrington Discovery Institute Scientific Advisory Board reviewed 58 nominations from 49 institutions and five countries before selecting the 2017 recipients.

In addition to sharing a \$20,000 honorarium, Holst, Habener, and Drucker jointly delivered the Harrington Prize Lecture at the 2017 Association of American Physicians/ ASCI/American Physician Scientists Association Joint Meeting on April 21, and published an essay in the *Journal of Clinical Investigation*.



# Freelance Reporter Receives Endocrine Society Award for Excellence in Science and Medical Journalism

indsey Konkel, a New Jersey–based freelance reporter, received the Endocrine Society's annual Award for Excellence in Science and Medical Journalism.

Konkel was honored at the Society's 99th Annual Meeting & Expo in Orlando, Fla., for her coverage of how exposure to endocrinedisrupting chemicals (EDCs) can affect the development of the placenta. The winning article, "Lasting Impact of an Ephemeral Organ: The Role of the Placenta in Fetal Programming," was published in *Environmental Health Perspectives* in July 2016.

In her article, Konkel explains how environmental stresses such as chemical exposure in the womb can raise an individual's risk of developing diseases later in life.

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

More information on the Endocrine Society Award for Excellence in Science and Medical Journalism is available at: https://www. endocrine.org/news-room/journalism-award. Endocrine Society Applauds CMS Announcement on Therapeutic CGM Coverage Expansion



he Endocrine Society praised the decision to extend access to therapeutic continuous glucose monitors (CGMs) to older Americans on intensive insulin therapy for diabetes.

The Centers for Medicare & Medicaid Services (CMS) announced new coverage criteria for CGM devices Thursday. The guidance states that all Medicare individuals who have type 1 or type 2 diabetes and who use intensive insulin therapy can access therapeutic CGM devices (i.e., Dexcom G5) to monitor their blood glucose levels.

For many years, the Society has advocated to expand coverage for CGMs to the Medicare population. The Society is pleased with the new coverage criteria and looks forward to continuing work with CMS to ensure patients have access to these lifesaving tools.

In its Clinical Practice Guideline on diabetes technology issued in September 2016, the Society recommended CGMs as the gold standard of care for adults with type 1 diabetes. CGMs are primarily used to help in the management of type 1 diabetes, although the devices also can be useful for people with type 2 diabetes, particularly those at risk for severe hypoglycemia.

CGMs measure glucose levels in the fluid between the body's cells every few minutes throughout the day and night. The technology can tell the user whether glucose levels are rising or falling, and monitor trends from the past several hours. The devices also feature alarms to warn users when glucose levels are too high or too low.

Studies of CGMs have shown that individuals with type 1 diabetes are able to maintain better control of their blood sugar without increasing episodes of hypoglycemia when blood glucose levels drop to dangerously low levels, compared to those who self-monitor blood glucose with periodic fingersticks. **INTOUCH** 

# Hotamisligil Named to Seven Bridges' Scientific Advisory Board

okhan Hotamisligil, MD, PhD, from the Harvard School of Public Health, has been named one of six members of the newly formed Scientific Advisory Board for biomedical data analysis company, Seven Bridges.

This new advisory board will formalize relationships with leading global experts in genomic medicine, bioinformatics, and cancer research. The board members will also advise on the company's product designs and strategies for cloud-based biomedical data analysis, as well as share their knowledge about key challenges and opportunities in the field of genomic research.

Hotamisligil is a 2015 Endocrine Society Laureate Award winner, having received the Roy O. Greep Award for Outstanding Research. In his current capacity, Hotamisligil is the James S. Simmons Professor of Genetics & Metabolism, chair, Department of Genetics & Complex Diseases; director, Sabri Ülker Center for Metabolic Research; and an associate member, Harvard-MIT Broad Institute, Harvard Stem Cell Institute, Joslin Diabetes Center. He earned his MD at Ankara University in Turkey, and his PhD from Harvard University. He has focused his research efforts on the molecular and genetic basis of common and complex diseases, particularly obesity, diabetes, and heart disease.



His research examines the mechanisms of nutrient sensing and response pathways as they relate to immune and metabolic homeostasis. He is an internationally recognized leader with seminal contributions including the discoveries that defined immunological components of obesity and diabetes, discovery of novel hormones regulating lipid and glucose metabolism, and endoplasmic reticulum as a key organelle regulating cellular and organismic metabolism, and its role in obesity, insulin resistance, and diabetes.

Hotamisligil pursues interdisciplinary paths, collaborations, and industry alliances toward development of novel preventive and therapeutic strategies against chronic metabolic diseases. His work has resulted in more than 180 highly cited papers and resulted in multiple patents. He has been recognized with fellowships and awards including Markey, Pew, and AAAS Fellowships, the Outstanding Scientific Accomplishment Award of ADA, Wertheimer Award from IASO, Koç Science Award, TUBITAK Science Award, Roy Greep Award of the Endocrine Society, and the International Danone Prize.

## ENDOCRINE ITINERARY



### **Endocrine Board Review 2017**

### Chicago, III., September 26 - 27, 2017

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

### **19th European Congress** of Endocrinology

#### Lisbon, Portugal, May 20 - 23, 2017

The largest European gathering of endocrinologists and endocrine scientists from around the world converge at this annual meeting with the aim of shaping the future of endocrinology to improve science, knowledge, and health across Europe and beyond.

www.ece2017.org

# American Diabetes Association's 77th Scientific Sessions

San Diego, Calif., June 9 – 13, 2017 The Scientific Sessions offers researchers and healthcare professionals the unique opportunity to share ideas and learn about the significant advances in diabetes research, treatment, and care. Over the course of five days, participants will receive exclusive access to more than 3,000 original research presentations, take part in provocative and engaging exchanges with leading diabetes experts, and expand professional networks with over 13,000 professional attendees from around the world.

www.professional.diabetes.org

### Rapid Signaling & Genomic Hormone Action in Health & Disease

Snowmass, Colo., June 11 – 16, 2017 Hormone researchers from around the world will be attending the FASEB Science Research Conference focused on steroid hormone receptors. This five-day event will focus on nuclear and steroid hormone receptor and signaling pathway crosstalk in cancer, metabolism, neuroscience, immunology, and reproduction. www.faseb.org/src/micro/Site/ SteroidHormones/home.aspx

### Dimensions in Diabetes

Mumbai, India, June 17 – 18, 2017 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 SunPharma, the two-day program brings in eight faculty members to present in-depth lectures on diabetes and its comorbidities. www.endocrine.org

### EndoBridge 2017

Antalya, Turkey, October 19 – 22, 2017 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. info@endobridge.org

### **19th ASEAN Federation of Endocrine Societies 2017** Yangon, Myanmar,

#### November 9 - 12, 2017

ASEAN Federation of Endocrine Societies (AFES) is an association of seven endocrine societies in Southeast Asia with a conference held every two years. With an extensive program covering a broad array of topics, various networking opportunities, poster sessions, continuing medical education, updates on new products and technologies at the AFES Expo, keynote speakers, and more, AFES 2017 is a "must-attend" event in Asia and one of the most recognized congresses among the clinicians and researchers in endocrinology. www.afes2017myanmar.com

### Translational Reproductive Biology and Clinical Reproductive Endocrinology 2017

New York, N.Y., November 16 – 19 The objective of this conference is to offer an authoritative 2017 update for reproductive clinicians and researchers, focusing on new translational developments in the field of reproductive biology and physiology, as well as clinically relevant patient-care issues. The conference aims to offer basic scientists and clinicians a unique and intimate framework for interactions and exchanges of ideas around paradigm changes and imminent new developments of significance. www.afes2017myanmar.com



## WHY ENDOCRINOLOGY?

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The advent of molecular

biology and gene-targeting

experiments clarified that

estrogen and progesterone

receptors ER and PR are

requisites for uterine

preparation for implantation

in mice. However, whether

the preimplantation embryo

is a direct target for steroid

hormones remains unclear.

# The Birth of an Endocrine Researcher

**BY S.K. DEY, PHD,** Lova Riekert Chair and Professor; Director, Division of Reproductive Sciences; Professor, Division of Developmental Biology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

y journey into reproductive endocrinology began with my education as a graduate student in Calcutta University in the late 1960s. My first mentor, Dr. Mukerjee, encouraged me to contemplate the molecular significance of reproductive events. During one of our many discussions, he explained his fascinating idea that glycogen moves from the base to the apex of the luminal epithelium prior to implantation under the influence of estrogen in the

rat uterus. Glycogen is broken down into glucose to provide energy products that support embryo growth for implantation. I started a project to disrupt this conversion using sodium malonate to block the tricarboxylic acid cycle (TCA cycle) in pregnant rats with the hope of inhibiting implantation. To my surprise, I found that reproduction actually improved with the birth of healthy pups.

I was so intrigued by this response that I spent hours in the library stacks, researching through huge volumes of biological abstracts. I found a paper that showed blocking the TCA cycle shunted carbohydrate metabolism through the pentose phosphate pathway, generating NADPH, a cofactor for steroidogenesis. I did not have access to sophisticated tools that could measure steroid levels, so I used several relatively simple

approaches to test this hypothesis. The findings helped me finish my PhD degree. Today, increasing numbers of studies follow in this trend to describe metabolic pathways and their roles during pregnancy. We now have a better understanding of steroidogenesis and metabolic impact on the female reproductive system. After immigrating to Kansas University Medical Center to obtain my postdoctoral training in 1973 in Dr. Dickmann's laboratory, I came up with the idea that embryonic estrogen plays a role in implantation. This idea sprung from my literature review on the ovarian estrogen requirement for implantation in mice and rats, but ovarian estrogen is not essential for implantation in many species, including pigs, rabbits, hamsters, and guinea pigs; progesterone alone can support implantation

> in these animals. I immediately began studying steroidogenic enzymes in preimplantation rat embryos by utilizing simple histocytochemistry. We published our initial work on rats in the *Journal of Reproduction and Fertility* in 1974.

> The timing was a stroke of luck, as Brian Heap at Cambridge University, UK, published a report in *Nature* that pig blastocysts have the capacity to produce estrogen. In collaboration with Dr. Johnson, I expanded on these studies to rabbit blastocysts and found they also have the capacity to synthesize estrogens. Several years later, in collaboration with Michael Waterman at Vanderbilt, we found that mouse blastocysts lack aromatase, the enzyme for estrogen synthesis. Several findings conclusively determined that rabbit, pig,

and horse blastocysts have the capacity to synthesize estrogens, while the mouse and rat embryos have limited, if any, estrogensynthesizing machinery, although they can metabolize steroid hormones. Researchers are still interested to know whether preimplantation estrogen secretion by the ovary or embryo plays a crucial role in human implantation.

As the Endocrine Society embarks on its second century, Endocrine News will continue to tell the stories of how endocrinologists chose this remarkable field. If you would like to share your story with our readers around the world, contact Editor Mark A. Newman at **mnewman@endocrine.org**.

I continued my work in reproductive biology with a focused lens on molecular pathways and how the endocrine systems impacted the pathways. From these early successes, I was able to develop a reproductive biology laboratory at Kansas University Medical Center that steered the course of reproductive endocrinology through molecular biology approaches, a research lens that continues in reproductive sciences today. The advent of molecular biology and gene-targeting experiments clarified that estrogen and progesterone receptors ER and PR are requisites for uterine preparation for implantation in mice. However, whether the preimplantation embryo is a direct target for steroid hormones remains unclear. We provided evidence in our early follow-up studies that preimplantation ovarian estrogen secretion on day four of pregnancy in mice has a dual role as primary estrogen and catecholestrogens with distinct targets. While primary estrogen acts via uterine ER to prepare the uterus for implantation, catecholestrogens formed locally in the uterus from the primary estrogen participate in blastocyst activation.

It remains a mystery how catecholestrogens mediate activation of blastocystsa. Although nuclear ERa is present in both active and dormant blastocysts, dormant blastocysts do not respond to estradiol and fail to attain implantation competency in vitro. In contrast, dormant blastocysts do respond to catecholestrogen 4-OH-E2 and become implantationcompetent in vitro. The ERa antagonist ICI-182,780 fails to reverse this response, suggesting that nuclear ERa signaling is not critical to blastocyst activation.

These observations surprised me in light of other recent findings that ERa, ERB, and efp mRNAs are expressed in preimplantation embryos. Examining the direct roles of estrogens and/or progesterone in preimplantation embryo function and how steroid hormone signaling in the embryo and uterus are coordinated for implantation is an ongoing and actively debated question in the field of reproductive endocrinology.



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## DASHBOARD

**I think that science is separate from politics and religion and that investing in science is like investing in life. It's a fundamental thing that we can never let up on.** I think what a lot of people don't realize is that an investment often doesn't come true right away. It takes years or decades, but the things that science finds, other minds apply to new endeavors and new aspects of health. There's no dollar in science that I think is really wasted."

— RICHARD LEGRO, MD, the Endocrine Society's secretary-treasurer and a clinical scientist with Penn State College of Medicine in State College, Pa., discussing why he participated in the March for Science in "Taking It to the Streets" on page 22.

#### FROM THE CENTURY OF ENDOCRINOLOGY TIMELINE

**1942:** Klinefelter's Syndrome Described



Klinefelter's syndrome was first described by Harry Klinefelter, Jr., Edward C. Reifenstein, Jr., and Fuller Albright, Jr. (Society president, 1946-1947), in their article, "Syndrome Characterized by Gynecomastia, Aspermatogenesis without A-Leydigism, and Increased Excretion of Follicle-Stimulating Hormone," published in the Journal of Clinical Endocrinology in November 1942 (Volume 2, Number 11, pages 615-627). By the late 1950s, researchers discovered that men with Klinefelter syndrome had an extra sex chromosome, resulting in a chromosomal arrangement of XXY; the usual male arrangement is XY.

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





Total number of times the **ENDO 2017** smart phone app was downloaded.

# **24** million

The number of people who would lose insurance coverage under the Trump Administration's American Health Care Act.

> - SOURCE: CONGRESSIONAL BUDGET OFFICE



How much the risk of fractures could be reduced in individuals who regularly consume extra virgin olive oil.

- SOURCE: PREVENCION CON DIETA MEDITERRANEA (PREDIMED)

# — Cushing's Disease: — U.S. Annual Cost Burden



- SOURCE: ENDOCRINE FACTS & FIGURES (WWW.ENDOCRINEFACTS.ORG)



# **Can Intensive Medical Treatment Reverse Type 2 Diabetes?**

ype 2 diabetes can be reversed with intensive medical treatment using oral medications, insulin, and lifestyle therapies, according to a study published in The Journal of Clinical Endocrinology & Metabolism.

Researchers led by Hertzel C. Gerstein, MD, MSc, FRCPC, of McMaster University and Hamilton Health Sciences in Hamilton, Ontario, Canada, randomly divided 83 individuals with type 2 diabetes into three study groups. One group received standard diabetes care, while the other two groups received an intensive metabolic intervention where they were provided with a personalized exercise plan and a suggested meal plan that reduced their daily calorie intake by 500 to 750 calories a day. These study participants met regularly with a nurse and dietitian to track their progress and received oral medications and insulin at bedtime to tightly manage their blood glucose levels. One group underwent the intervention for eight weeks, while the other was treated intensively for 16 weeks. After the intervention, individuals in both groups stopped taking diabetes medications and were encouraged to continue with lifestyle changes. Participants in all three groups received usual diabetes care if they experienced a diabetes relapse.

Study participants had their average blood glucose levels from the past two to three months measured at eight, 20, 28, and 52 weeks to gauge how well their blood sugar was controlled. They also undertook oral glucose tolerance tests.

Three months after the intervention was completed, 11 out of 27 individuals in the 16-week intervention group met HbA1C criteria for complete or partial diabetes remission, compared to four out of 28 individuals in the control group. Three months after finishing the eight-week intervention, six out of 28 individuals in that group met the same criteria for complete or partial diabetes remission.

Findings: The authors conclude: "A short course of intensive lifestyle and drug therapy achieves on-treatment normoglycemia and promotes sustained weight loss. It may also achieve prolonged, drug-free diabetes remission and strongly supports ongoing studies of novel medical regimens targeting remission." They go on to write that despite the study's limitations (short follow-up, standard diabetes care for patients after the trial), "this trial clearly shows that a multifaceted intensive metabolic strategy that targets normoglycemia and weight loss using pharmacological and lifestyle approaches may achieve remission, is acceptable to patients, and may be easily translated into clinical practice."

"By using a combination of oral medications, insulin and lifestyle therapies to treat patients intensively for two to four months, we found that up to 40% of participants were able to stay in remission three months after stopping diabetes medications," says the study's first author, Natalia McInnes, MD, MSc, FRCPC, of McMaster University and Hamilton Health Sciences. "The findings support the notion that type 2 diabetes can be reversed, at least in the short term not only with bariatric surgery, but with medical approaches."



Whole-Body Vibration May Be as Effective as Exercise

hole-body vibration — sitting or lying on a vibrating machine to contract and relax muscles — may be as effective at benefitting metabolic health as exercise, according to an animal study recently published in *Endocrinology*.

Researchers led by Alexis M. Stranahan, PhD, of the Medical College of Georgia in Augusta, point out that whole-body vibration (WBV) has gained attention as a potential exercise mimetic, but data on direct comparisons to exercise are lacking. The team examined two sets of five-week-old male mice — a wild-type group and a leptin receptor-deficient group — for 12 weeks. Mice from each group were assigned to sedentary, WBV, or treadmill exercise conditions. The mice in the WBV group underwent 20 minutes of WBV at a frequency of 32 Hz with 0.5g acceleration each day. Mice in the treadmill group walked for 45 minutes daily at a slight incline. The mice were weighed each week.

The researchers found that exercise and WBV caused the mice in those groups to lose weight and gain enhanced glycemic control. Mice who ran on the treadmill or had WBV also showed modest positive skeletal responses. Obese mice gained less weight after exercise or WBV than obese mice in the sedentary group, although they remained heavier than normal mice. Exercise and WBV also enhanced muscle mass and insulin sensitivity in the genetically obese mice. Although there were no significant effects in the young healthy mice, the low-intensity exercise and WBV protocols were designed for successful completion by obese mice.

**Findings:** The authors conclude that, "taken together, these observations indicate that whole-body vibration recapitulates the effects of exercise on metabolism in type 2 diabetes." They also go on to note that "WBV warrants further investigation as a strategy to attenuate risk factors for cardiovascular and metabolic diseases."

These results are encouraging," says the study's first author, Meghan E. McGee-Lawrence, PhD, of Augusta University in Augusta, Ga. "However, because our study was conducted in mice, this idea needs to be rigorously tested in humans to see if the results would be applicable to people."



Recent Survey Finds Many Adults with Diabetes Unaware of Their Increased Risk for Certain Serious Illnesses

any adults with diabetes are unaware of their increased risk for certain serious illnesses, according to a recent national, online consumer awareness survey sponsored by Merck and the American Diabetes Association, and conducted by Harris Poll.

In the survey of 1,003 U.S. adults ages 18 years and older diagnosed with diabetes, respondents were twice as likely to recognize the potential for adults with diabetes to develop kidney disease (72%) and heart disease (67%), than serious infectious diseases such as pneumococcal disease, including pneumonia, meningitis, or an infection of the blood (36%), compared to adults without diabetes. While published data show that adults with diabetes are approximately three times more likely to develop pneumococcal disease compared to healthy adults of the same age, only 35% of respondents believed they were at least somewhat personally likely to get pneumococcal pneumonia/ pneumococcal disease. In addition, less than half of those surveyed (43%) responded that they had discussed the risk factors for pneumococcal pneumonia/pneumococcal disease with their doctor.

Findings: "These data illustrate that patients with diabetes are not fully aware of their risk of other serious illnesses," says American **Diabetes Association Immediate Past Chief Scientific & Medical** Officer Robert E. Ratner, MD, "and that there is a critical communication gap between patients and their healthcare providers about the risks for serious illness, including pneumococcal pneumonia or pneumococcal disease, flu, and hepatitis B for adults with diabetes. Because people with diabetes have increased risks for these diseases and more complicated medical courses when they contract them. healthcare providers should seek to initiate discussions with patients to bridge the information gap, as recommended in our Standards of Care."



# Childhood Exposure to Chernobyl Radiation Linked to Increased Risk of Thyroid Nodules

hildren who were exposed to radiation following the Chernobyl nuclear accident in April 1986 may have an increased risk of developing thyroid nodules, according to a study recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Elizabeth K. Cahoon, SM, MHS, PhD, of the Radiation Epidemiology Branch, DCEG, at the National Cancer Institute in Bethesda, Md., point out that internal radiation exposure during childhood is an important risk factor for thyroid cancer, but whether internal radiation exposure during childhood is related to thyroid nodules isn't known, so they set out to study whether there was an association between internal I-131 radiation dose and thyroid nodules in young people who were exposed to Chernobyl radiation as children.

Cahoon and her team screened 11,970 residents of Belarus who were children (18 or younger) at the time of the Chernobyl accident for thyroid disease. Thyroid palpation, ultrasonography, blood and urine analysis were performed, and medical follow-up was given when appropriate. The investigators measured excess odds ratios per Gray scale at five years old at the time of the accident for any thyroid nodule and for grouped nodules.

The researchers found that risk of any thyroid nodule increased with internal I-131 dose and with younger age at exposure for a given dose. "The EOR/Gy (95%CI) for neoplastic nodules (3.82;0.87, 15.52) was significantly higher than for non-neoplastic nodules (0.32;<0.03, 0.70) and did not vary by size; while the EOR/Gy for non-neoplastic nodules did vary by size (P=0.02) and was 1.55 (0.36, 5.46) for nodules  $\geq$ 10 mm and 0.02 (<-0.02, 0.70) for nodules <10 mm in diameter. EORs/Gy for single and multiple nodules were comparable," they write.

**Findings:** The authors conclude that "childhood exposure to internal I-131 is associated with increased risk of neoplastic thyroid nodules of any size and non-neoplastic nodules ≥10 mm." They go on to write that these results support the theory that children exposed to radiation may be more susceptible to developing cancer.

Hip fracture rates had been declining for years — but a new analysis shows the decline has stopped. Could a decrease in testing rates and a fear of drug side effects be to blame?

# HIDDEN Fissures

# **Hip Fracture Rate Ends Years-Long Decline**

### **BY ERIC SEABORG**

he U.S. and other developed countries have made steady progress in recent years in bringing down the rate of hip fractures in the elderly. But that favorable curve has leveled off in the U.S., according to an abstract presented at the fall meeting of the American Society for Bone and Mineral Research (ASBMR).

The researchers who performed the analysis suggest that the factors contributing to the new trend include cuts in Medicare reimbursement for dual-energy x-ray absorptiometry (DXA) testing leading to fewer people being tested, fewer at-risk patients being diagnosed, and media reports scaring patients off anti-osteoporotic bisphosphonates.

The study examined Medicare data for women over age 65 from 2002 through 2014. It found that DXA testing and osteoporosis diagnoses peaked in 2008 to 2009, then began to decline. The hip fracture rate declined linearly from 884 fractures per 100,000 women age 65 and over in 2002 to 740 in 2012. At that point, the fracture rate leveled off through 2014.

"This analysis suggests the trend of decreasing hip fracture rates in the U.S. may be over. Other studies have shown a decrease in osteoporosis prescriptions over this period of time," the study says.

# Drop in Testing, Drop in Diagnoses

The decline in the number of tests tracks with a steep drop in Medicare reimbursement for DXA testing, says the lead author of the study, E. Michael Lewiecki, MD, clinical assistant professor of medicine at the University of New Mexico School of Medicine in Albuquerque and past-president of the International Society for Clinical Densitometry, which generated the data in the study. The national average for Medicare payment for DXA testing was \$139 in 2006, which was cut to \$82 in 2007, and then to \$42 today.

That reimbursement level is well below the cost of performing the test, Lewiecki says. Faced with below-cost reimbursement, many practices stopped offering the test — substantially decreasing the convenience and availability of the tests for patients. "DXA testing and diagnosis of osteoporosis started declining in 2009, two years after Medicare decreased office-based DXA reimbursement to levels below the cost of providing the service," according to the abstract.

# CALL TO ACTION

The ASBMR is so concerned about the state of affairs that it issued a "Call to Action to Address the Crisis in the Treatment of Osteoporosis" that has been endorsed by 38 organizations, including the Endocrine Society. It says that "the field as a whole must take action to aggressively reduce fracture risk in our aging population" in response to "a crisis caused by the declining rate of testing, diagnosis, and treatment of high-risk patients."

As part of the response, the organization recommends better education programs for healthcare professionals: "Despite compelling data that bisphosphonates reduce both risk of a second fracture and reduce death in those patients who have had a hip fracture, many clinicians do not have the necessary information or resources available to help their patients make informed decisions to prevent hip fractures."

The call to action also advocates that:

- governmental organizations provide more support for programs to reach the highest-risk patients;
- public and private insurers cover effective services to improve diagnosis and treatment of highestrisk patients; and
- health systems adopt quality measures that incentivize screening and treatment of high-risk individuals.

From a public health standpoint, **if hip fracture rates are higher than expected**, **it is certainly a concern** because of the personal burden of hip fractures, the increase in disability and death, and the high medical costs associated with hip fractures."

> – E. MICHAEL LEWIECKI, MD, CLINICAL ASSISTANT PROFESSOR OF MEDICINE, UNIVERSITY OF NEW MEXICO SCHOOL OF MEDICINE, ALBUQUERQUE

# **Fear of Bisphosphonates**

Another potential contributing factor is that prescriptions for osteoporosis drugs began to drop even before the decline in diagnoses. The advent of bisphosphonates in the 1990s was one likely factor in the decline of fracture rates, but prescriptions for them began plummeting around 2008 to 2009 with media reports of their side effects. "The media began talking about osteonecrosis of the jaw and atypical femur fractures, and blowing their frequency way out of proportion," says Ethel Siris, MD, professor of medicine at Columbia University Medical Center in New York City, who also contributed to the study. "These two side effects are not nearly as common as people seem to think. For example, the rate of osteonecrosis of the jaw from osteoporosis dosing of these drugs — in contrast to doses used for metastatic bone cancer — is very low. It is a rare problem, but the news media make it sound like it happens every week."

The ASBMR notes on its website: "The number of fractures that are prevented with treatment far outweighs the risk of atypical femur fractures and osteonecrosis of the jaw. Treatment of women with osteoporosis for up to five years would result in fewer than one atypical femur fracture caused per 100 osteoporotic fractures prevented."

# **The Many Fracture Factors**

Lewiecki notes that the exact reasons for both the decline in fractures and the plateau in this decline are not clear. The use of bisphosphonates and other drugs does not entirely explain the decline in fractures, and factors like improvements in lifestyle — and even the rise in obesity — could be associated with better bone density. And factors tugging on the negative side include "the publicity about calcium supplements possibly causing cardiovascular disease and confusion about how much vitamin D is needed," Lewiecki says. "And primary-care doctors, who manage most patients with osteoporosis, are overwhelmed



with many competing healthcare priorities. They have limited time in patient encounters, and often osteoporosis doesn't rise to the point that it is discussed in office visits."

The timing of the news of the decline in diagnoses is somewhat ironic because it coincides with an effort by the National Bone Health Alliance and a coalition of groups that includes the Endocrine Society to expand the definition of osteoporosis beyond T-scores to include patients who have an elevated fracture risk based on additional criteria such as their World Health Organization Fracture Risk Algorithm (FRAX) scores. (See "Breaking Bad," in the December 2015, *Endocrine News*.)

"Although causality cannot be clearly established," the abstract notes, "there is a plausible chain of events from reduced DXA reimbursement to fewer DXA providers to fewer DXAs performed to fewer women diagnosed to fewer being treated, all leading to an increase in fractures above expected levels." And if that is the case, the reimbursement rates could be penny wise and pound foolish because "the increase in fracture-related expenses is likely to outweigh the modest savings to Medicare from decreased DXA reimbursement and fewer DXAs performed."

"From a public health standpoint, if hip fracture rates are higher than expected, it is certainly a concern because of the personal burden of hip fractures, the increase in disability and death, and the high medical costs associated with hip fractures," Lewiecki concludes.

# AT A GLANCE

- A new study shows that a years-long decline in hip fractures among older women has leveled off.
- Factors contributing to the new trend seem to be a decline in the rate of testing, leading to a decline in the number of diagnoses combined with a reluctance of at-risk patients to take drugs of proven efficacy.
- The American Society for Bone and Mineral Research has responded to this development by issuing a "call to action" to address the "crisis in the treatment of osteoporosis."

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT A VARIETY OF NEW OPTIONS TO TREAT OBESITY IN THE MARCH ISSUE.

# NO SIDES

# IN SCIENCE

### **BY DEREK BAGLEY**

# Taking it to HESTRES

On Saturday April 22, hundreds of thousands of people around the world took to the streets to show their support for scientific research in the March for Science. The Endocrine Society was not only a sponsor but an avid participant as members and staffers alike raised their voices — and often humorous signs — to show their support for science.

t was a soggy, chilly April afternoon, but the nasty weather didn't stop 15,000 people from rallying around the National Mall in downtown Washington, D.C., and then marching to the Capitol building, all in the name of celebrating science.

The March for Science, the first event of its kind, coincided with Earth Day and took place not only in Washington, but in more than 600 cities around the world. It was a day when scientists left their labs, created imaginative and hilarious signs, and took to the streets to reaffirm the very real impact that science has in every person's life, whether they realize it or not. It was a day when more than 100 different organizations representing every field of science — from physics to paleontology to medicine stood up to let the world know that science is crucial and non-partisan, no matter how many people would like to see science politicized.





6 6 An attack on science is an attack on health and an attack on medicine, so I think we're all in this together."

> — RICHARD LEGRO, MD, SECRETARY-TREASURER, ENDOCRINE SOCIETY; CLINICAL SCIENTIST, PENN STATE COLLEGE OF MEDICINE, STATE COLLEGE, PA.

# **No Science Dollar Is Wasted**

The Endocrine Society was a proud sponsor of the March for Science, since endocrine scientists continue to make remarkable contributions in areas of critical national interest, including diabetes, obesity, the microbiome, cancer, bone health, fertility, and so much more. But continuing to make advancements such as these depends on funding, which could be in jeopardy as the Trump administration has proposed very deep cuts to the National Institutes of Health (NIH) funding in 2018. President Donald Trump, for his part, released a statement the day of the March, saying "rigorous science is critical to [his] administration," but he's still proposing slashing the NIH budget by 20%, which could have drastic effects on health outcomes in the future, especially as diabetes and obesity numbers continue to rise.

"I think that science is separate from politics and religion and that investing in science is like investing in life," says Richard Legro, MD, the Endocrine Society's secretary-treasurer and a clinical scientist with Penn State College of Medicine in State College, Pa. "It's a fundamental thing that we can never let up on. I think what a lot of people don't realize is that an investment often doesn't come true right away. It takes years or decades, but the things that science finds, other minds apply to new endeavors and new aspects of health. There's no dollar in science that I think is really wasted."



The rain kept coming ... but so did the marchers!



The Endocrine Society's chief innovation officer Rob Bartel (left) showing his support for the National Institutes of Health.





Everyone's favorites from Muppet Labs, Beaker and Dr. Bunsen Honeydew are avid supporters of science, especially experimental science.

**Chief a global perspective.** The problems that we have in the United States are problems in other places, and we'd like to be able to help."

- LYNNETTE K. NIEMAN, PRESIDENT, ENDOCRINE SOCIETY



Endocrine Society secretary-treasurer Richard Legros, MD, and president Lynnette Nieman, MD, show their support for hormone science.

# Muppets, Dinosaurs, and Scientists...Oh My!

Still, the organizers of the March for Science insisted that this was not a protest but a ceremony — a testament to evidence-based research and peer review in the search for answers that could improve lives and influence public policy. And in truth, it could be viewed as a party. Celebrities and science luminaries showed up. (Questlove, of the band The Roots, hosted an event; Bill Nye spoke, as did Mona Hanna-Attisha, who first raised awareness of the water crisis in Flint, Mich., and Lydia Villa-Komaroff who discovered mammalian insulin in bacterial cells.)



Even in the pouring rain, colorful and thoughtful signs outnumbered umbrellas, and their creators were proud to show them off. Some favorites included: "What do we want? Evidence-based research! When do we want it? After peer review!" and "There is no plan-et B" and "Got science? It does everybody good." Rob Bartel, Endocrine Society chief innovation officer, carried a sign that read "Fund NIH Bigly," and Jessica Harris, a specialist in the Society's government and public affairs department, carried a sign that quoted astrophysicist Neil Degrasse Tyson: "The good thing about science is that it's true whether or not you believe in it." Some marchers even took the opportunity to dress as their favorite Muppet scientists or wear full T-Rex costumes.

And that was just in Washington. Six hundred more cities had their streets filled with similar scenes, which led to massive amounts of media exposure. Google "March for Science," and dozens of articles will appear. The hashtag #marchforscience was at the top of Twitter's trends all weekend long. A retweet from the Society's EndoMedia account garnered 37,000 impressions (times viewed), a record for that account.

For Endocrine Society president Lynnette K. Nieman, MD, a clinical scientist with the NIH in Bethesda, Md., that exposure is a lynchpin of the March. "I think one of the things the March means is to call attention to regular people, the public, to science," she says. "To also let people know what the breadth of science is, from computing and physics to healthcare. And then also to interest young people in going into science, particularly young girls, because they tend not to do that."

# THE TRUTH IS OUT THERE

IS OUT THERE (Seriously. It's Called PEER-REVIEWED RESEARCH.)

DON'T COVER

**666** Local policy makers need to hear that their constituents value continued scientific progress and the incorporation of scientific evidence into policy. We hope that after participating in this event, scientists will continue to participate in advocacy and that members of the public will continue to demand attention to science in all policy making."

– JOANNA SPENCER-SEGAL, MD, PHD, UNIVERSITY OF MICHIGAN, ANN ARBOR, MEMBER OF THE STEERING COMMITTEE FOR THE MARCH FOR SCIENCE

# "We're All in This Together"

The March for Science was just the beginning. The Endocrine Society is committed to remaining a visible leader and continuing to offer activities to keep members engaged for as long as necessary. Federal funding of biomedical research has led to major accomplishments in endocrinology such as understanding: how the hormone insulin works, resulting in treatments for diabetes; the effects of hormones such as aldosterone on the heart, leading to new treatments for heart failure; and thyroid hormones, resulting in the development of new, better, and safer therapies for patients with thyroid disorders. Removing one-fifth of the budget of the organization that made all this possible seems, well, ill-advised. "An attack on science is an attack on health and an attack on medicine," Legro says. "So I think we're all in this together."

March for Science organizers are crafting plans for all scientists and supporters of science to remain active on a local level, according Joanna Spencer-Segal, MD, PhD, University of Michigan, Ann Arbor, a member of the Steering Committee for the March for Science. "Local policy makers need to hear that their constituents value continued scientific progress and the incorporation of scientific evidence into policy," she says. "We hope that after participating in this event, scientists will continue to participate in advocacy and that members of the public will continue to demand attention to science in all policy making. A continued partnership between scientists and the public is one of the long-term goals of this event."

Nieman adds that people can be active and activists in various ways. "Some people have a march they can go to," she says. "Some people can email their senators and congressmen or their heads of state in Europe and other parts of the world. This is not just an American movement, but it's important from a global perspective. The problems that we have in the United States are problems in other places, and we'd like to be able to help."

During the march to the Capitol building, a chant went up: "Science is real, not what you feel!" That's true; as Harris's poster quoting Tyson said, good science is based on evidence and reason, and is therefore real, no matter what you believe. Or to put it more succinctly, as in the case of one sign: "I can't believe I have to march for facts."

BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT THE HIGHLIGHTS OF **ENDO 2017** ON PAGE 30 OF THIS ISSUE.



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# END



Attendees of **ENDO 2017** in Orlando, Fla. shared the Orange County Convention Center with throngs of WrestleMania devotees as part of a massive WWE event. Thankfully, there were no "smackdowns" as both groups intermingled nicely, but once again **ENDO** proved why it is still the reigning champion in heralding cuttingedge endocrine research to endocrinology professionals from around the world.

# ENDOCRINE SOCIETY

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and staff leaned into. After all, what's **ENDO** itself if not a spectacle — a chance to show off the fruitions and breakthroughs and products that are the results of sometimes years of hard

work. Obstacles overcome. Challenges tackled. The Wrestlemania of endocrinology.

At first blush, it could seem like an odd mixture of people. Neither group was cordoned off from the other, so at any time you could see clinicians and researchers posing for pictures with men and women wearing colorful shirts depicting their favorite wrestlers or wearing ornate championship belts around their waists or over their shoulders. An interesting dynamic, and one that Endocrine Society members

he Orange County Convention Center in Orlando, Fla. — at seven million square feet — is one of the largest hospitality centers in the U.S., a fortunate vastness in that over the first weekend of April the center hosted not only thousands of endocrinologists from around the world, but thousands more World Wrestling Entertainment enthusiasts in town to attend Wrestlemania — a high-flying and

hard-hitting spectacle.

# **Promising Results of Long-Lasting Growth Hormone**

For instance, recombinant human growth hormone (rhGH) is the gold standard for treating children and adults with growth hormone deficiency (GHD), but those daily injections can be a burden on children and their families, which can compromise treatment or even lead to noncompliance. However, **ENDO 2017** saw two oral presentations and three poster presentations on the promising effects of somavaratan, a novel long-acting rhGH fusion protein currently in clinical development for treatment of GHD in children and adults. The drug, developed by Versartis, is intended to reduce the burden of injection therapy by requiring only two injections a month. The hope is that fewer injections would lead to improving compliance and treatment outcomes. Phase 3 trials are set for later this year.

According to Bradley S. Miller, MD, PhD, a pediatric endocrinologist with the University of Minnesota, with current daily injection therapy, patients miss anywhere from 15% to 77% of their injections. Miller, a co-author of the research on somavaratan presented at **ENDO 2017**, treats a number of children and young adults with GHD. He says the goal is to look at the maximum height these patients should be able to achieve with rhGH therapy — an expected height based on their parents' heights — but with daily injections they've never been able to achieve that goal. "I think if we can take out the compliance issue, we can get closer to that goal," he says. "This kid should end up right where they belong because they're getting the right dose and that's going to lead to better outcomes."

*Endocrine News* last July published an article that looked at growth hormone (GH) research — the drug's risks and rewards — and the experts agreed that long-lasting GH treatments would benefit patients. **ENDO 2017** provided an opportunity for

**66** After all, what's **ENDO** itself if not a spectacle?"





endocrinologists and industry to show they're on top of it. The Phase 2 data that Miller presented were the results of three years on therapy — children received 2.5mg per kg of somavaratan twice a month and then were increased to 3.5mg twice a month, which is the Phase 3 dose. Miller says that with the Phase 3 dose, they're seeing IGF-1 peaks moving into the upper half of the normal range. "I think there's going to be good efficacy with the treatment," he says.

# Tag Team Cage Match: Diabetes & Obesity

Still the twin baddies — diabetes and obesity — loom, but again ENDO 2017 provided the opportunity to show off interesting strategies defeating them, no matter how daunting the challenges.

Anne Peters, MD, of the University of Southern California and a practicing endocrinologist in Los Angeles, talked about her experience treating poorer patients with diabetes, especially how regulatory agencies create unnecessary burdens when treating these patients. *Endocrine News* last month touched on how formularies make it hard for poorer patients to get life-saving insulin, and Peters agrees that a change is needed. She says that she spends too much of her time just writing prior authorizations just to get patients the insulin they need. "I believe we need to fight hard to change the formularies," she says.

Or consider this: Insulin pump manuals are written at an 11th-grade level. Many of the patients in this socioeconomic class might not have finished high school. Or English is their second language. Which leaves it to the physician to spend time showing their patients how these pumps work. Of course, these regulations and arbitrary rules and reading levels burden the physicians as well, but Peters has some advice to avoid getting discouraged. "Prior auths and regulatory agencies can make practicing medicine hard," she says, "but create an environment in your practice that doesn't burn you out."



Gary "The Hammer" Hammer, MD, PhD, Millie Schembechler Professor of Adrenal Cancer; director – Endocrine Oncology Program, University of Michigan, Ann Arbor, got into the spirit of sharing the Orange County Convention Center with Wrestlemania. As the chair of the Society's Annual Meeting Steering Committee, Hammer and his fellow committee members definitely earned a championship belt for making ENDO 2017 a success!

ALL ENDO 2017 PHOTOGRAPHY BY CHRISTINA SHOOK



# Achieving a Lifelong Goal

One of my major goals has always been to attend an international scientific congress and present my research. What could be better than having the opportunity to do just that at **ENDO 2017**?

However, my experience at **ENDO** exceeded all expectations! From ease of the registration process to the caliber of the professionals who spoke to my own learning experience was so much more rewarding than I could have imagined.

It was invigorating to be among other endocrine scientists from around the world, exchanging ideas and discussing the rewards and difficulties of performing scientific research. The topics presented ran the gamut regardless of your professional focus; basic research, clinical, translational, and basic/clinical were all well represented. There was certainly no shortage of knowledge!

Of course, the greatest honor was being able to present my research. I presented my work in an oral poster session, and it was an unforgettable experience I can barely put into words. I am so grateful that there is an event like **ENDO** where I can be part of the larger scientific community. My desire to do research has only intensified, so bring on **ENDO 2018**, **ENDO 2019**, **ENDO 2020**, and beyond!

- LUIZ FONTE BOA, MASTER STUDENT, FEDERAL UNIVERSITY OF RIO DE JANEIRO, BRASIL And it's not just the poorer patients in cities like Los Angeles who are underserved. Patients who live in rural areas with access only to their primary care physician (PCP) — who may not be adequately trained to treat complex cases of diabetes — suffer less than optimal health outcomes as well. But a study presented at ENDO 2017 showed that PCPs and community health workers in New Mexico gained confidence in their ability to manage patients with complex diabetes by participating in a videoconferencing educational program led by diabetes specialists.

The program is called Endo ECHO, based on a model developed in 2003 at the University of New Mexico Health Sciences Center, and was detailed by endocrinologist Matthew Bouchonville, MD, CDE, in the September 2015 issue of *Endocrine News*. The program connects PCPs and community health workers at 10 rural health centers in the state with experts from Project ECHO, including endocrinologists, nurses, certified diabetes educators, behavioral health specialists, and social workers. Program participants include one selected PCP at each health center, who will become a local expert in managing complex diabetes. The experts' weekly two-hour videoconferencing sessions present diabetes education and mentoring on actual cases of deidentified patients with diabetes.

To evaluate the success of Endo ECHO in equipping the care providers, the researchers surveyed participants before the program and a year into the four-year program about their self-efficacy to manage patients with complex diabetes. Survey respondents included 13 PCPs and 10 community health workers. Respondents reported improvement in all measures of self-efficacy for complex diabetes management. Overall selfefficacy scores, on a seven-point scale, improved from an average of 2.6 to 6.0 in community health workers and from 3.7 to 5.8 in PCPs. Examples of self-efficacy measures for the PCPs included confidence in their ability to manage complex insulin regimens and to screen for diabetic complications. Self-efficacy measures for community health workers included confidence in their ability to advise on self-care and motivate behavioral change.

"Primary care providers and community health workers who participated in Endo ECHO say they feel better equipped to manage patients with complex diabetes — and are more willing to do so instead of referring them to a faraway specialist," says Bouchonville, the study's lead investigator and an assistant professor at the University of New Mexico School of Medicine in Albuquerque.



# **Gut Reaction**

Of course, these are just a couple of the ways endocrinologists are approaching the diabetes fight. And now obesity has tagged in, but endocrinologists are showing they're up for the challenge with some interesting and novel ideas.

Research has shown that an underlying cause of obesity may be an impaired gut microbiota composition, and a study presented at **ENDO 2017** showed that noninvasive electromagnetic brain stimulation technique helps obese people lose weight, partly by changing the composition of their intestinal bacteria.

Researchers led by Livio Luzi, MD, professor and head of endocrinology at the IRCCS Policlinico San Donato and the University of Milan in Italy recruited three men and 11 women, ages 22 to 65, with obesity as shown by a body mass index (BMI) of 30 to 45 kg/m2. They randomly assigned the study subjects to two groups for five weeks to receive 15 sessions three times per week — of either deep transcranial magnetic stimulation (dTMS) (to the insula and prefrontal cortex deep in the brain) or a sham stimulation as a control. Before and at the end of treatment, subjects provided stool samples for microbiota analysis.

The research team also measured blood levels of glucose, insulin, pituitary gland hormones, and neurotransmitters such as norepinephrine. Pituitary hormones play a key role in regulating appetite, and recent research shows that norepinephrine and other neurotransmitters affect microbiota composition, Luzi says.

After five weeks of treatment, subjects receiving dTMS lost more than 3% of their body weight and more than 4% of their fat — significantly more than controls did, Luzi reports.

Results of the fecal analysis demonstrated that, after five weeks, dTMS-treated subjects had greatly increased quantities of several beneficial bacterial species with anti-inflammatory properties, such as are found in healthy people. The control group, however, had no clinically relevant alterations in their microbiota composition, Luzi says. He also reported that changes in the abundance of other bacterial species correlated with improvement of metabolic and hormonal parameters, including glucose, insulin, several pituitary hormones, and norepinephrine.

"These changes suggest a beneficial effect of dTMS on both weight loss and change in microbiota composition," Luzi says. "Our research shows the innovative ability of dTMS in exerting anti-obesity effects through alteration of the gut-brain axis."

# **Knockout Rounds**

Knockout Rounds, a new offering that debuted at **ENDO 2016** in Boston to raves and a standing-room-only crowd, proved so popular that a second round was included this year. The Knockout Rounds give presenters three minutes and one slide each to share their findings. This innovative program, named in allusion to the famous genetic technique, provides basic science trainees the opportunity to present and highlight the significance of their research in front of a diverse audience.

Participants were graded on a scale of one to five (one being the best score) in three categories: oral presentation, use of graphics, and how well the data translated to a lay audience. All of the presentations were extremely interesting and even entertaining, with clever use of slides and graphics, and well rehearsed oral presentations.



# Learning from the Experts

The Endocrine Society has once again outdone itself this year by organizing a terrific annual meeting with thousands of participants from all over the world. It was impressive to see the broad amount of research topics covered in so many different ways. Poster sessions, oral presentations, meet-the-professor sessions, and even Knockout Rounds, just to mention some of the offerings, kept you busy and excited throughout the day.

Having many of the key persons in the different research areas at the same place not only provided the opportunity to learn from the experts, but it also motivated me to broaden my view to find common ground with [people in] fields I have not initially considered. It was also insightful to follow workshops focused on career development, especially for the young professionals, where learning opportunities were provided on various topics ranging from starting up a lab to communicating your research with the media.

I was fortunate to present our work with both an oral presentation and during a news conference, which additionally enhanced my personal overall experience with **ENDO 2017**. I am already looking forward to the next **ENDO** meeting in Chicago, which undoubtedly will also be a great success.

--- MESUT SAVAS, MD, MSC, ERASMUS MC, UNIVERSITY MEDICAL CENTER ROTTERDAM, THE NETHERLANDS Lauren Stone, a clinical research coordinator at Massachusetts General Hospital in Boston, won the second day's Knockout Rounds with a presentation that looked at psychological stress-induced ghrelin resistance in rodents and its implications for human mental illness, namely post-traumatic stress syndrome (PTSD). Stone says she didn't expect to even place, given that all the presentations were "stellar." "I was just honored to have the opportunity to give an oral presentation and to be in this fun, health-oriented session," she says.

Speaking about her preparation process, Stone says the first thing she thought of was how to frame the literature. "PTSD is a really significant public health problem," she says, "and there's no preventative treatment for it." She purposefully avoided too much detail and methodology from previous research and presented her own findings using simplified graphs from her graduate thesis in order to clearly show the takeaway message and clinical implications. "This took many iterations," Stone says.

A classically trained ballet dancer, Stone says she doesn't mind "performing," but she does get nervous about what she's going to say, so she practiced her talk with friends and family. "I'm lucky enough to have really good mentors where I work," she says, "so they listened to it as well and gave me some feedback, saying things like 'This isn't clear' and 'You lost me after this part."

Stone studied this topic as an undergraduate, so she is no longer affiliated with that lab, but she says she's looking into medical schools with strong research programs and she'd like to continue working on this specific topic.

# **Global Leadership Academy**

While the Knockout Rounds avoided a sophomore slump, another exciting initiative premiered at ENDO 2017 — the Global Leadership Academy, an international program created to provide formal professional leadership training for endocrinology scientists and practitioners who have reached this uneasy juncture in their careers. Made possible by the sponsorship of Sanofi Peru, this program is geared to those professionals who have completed between five and 10 years of professional training so that young endocrinologists may have the opportunity to improve their "soft skills" that will contribute to their academic and scientific development, according to Cecilia Medina, MD, medical director, Sanofi Peru, who says that "the limited access to such integral initiatives in Peru" inspired the company to play a role in launching the Global Leadership Academy. **Couldn't Make It to ENDO 2017?** Experience Endocrine Society educational programming from the convenience of your home or office. The Endocrine Society session recordings are a compilation of digital audio recordings and synchronized slides accessible on your computer, tablet, or phone, or on the go with downloadable mp3 files. For more information, go to www.endocrine.org/meetings/session-recordings.

On April 3, members of the Academy gathered to listen to Cesar and Margaret Boguszewski (husband and wife endocrinologists who both hold MDs and PhDs) tell the story of their incredible journey from growing up in Brazil to pursuing PhDs in Sweden to joining the Endocrine Society to moving back to Brazil to practice endocrinology. Cesar is a clinical scientist who focuses on obesity, endocrine cancer, and the thyroid. Margaret is a pediatric endocrinologist who focuses on development and growth hormone. Their story frames the Global Leadership Academy well, since it shows the impact of international networking, sharing ideas, and strategizing globally. "That's the beauty of working together," Cesar says.

The members of the Academy were also given the chance to suggest improvements or give accolades or tell what they'd like to see as the Academy grows. "I loved that Peru has taken the initiative to identify the top endocrinologist in their country and support their success," says Shannon Whirledge, PhD, of Yale University in New Haven, Conn., and a member of the Global Leadership Academy. "It seemed that because many of the attendees were among their peers, people felt comfortable participating and actively engaging in the Global Leadership Academy. It was a great way to get people connected to the Endocrine Society."

And while Whirledge is happy to see a large Peruvian contingent, she would like to see the Academy and the Society target other countries as this initiative moves forward, specifically countries under-represented within the Endocrine Society. "Alternatively, future leadership academies could target early- and mid-career scientists/physicians with an interest in a similar topic (i.e., the Global Leadership Academy for Diabetes)," she says.

"It would be great for the Endocrine Society to provide opportunities for the Global Leadership Academy attendees to practice what they have learned, potentially through invitations to serve on committees/focus groups, participate in outreach programs, or invited presentations at future meetings," Whirledge continues. "I think this year's Global Leadership Academy was a success and should definitely become a permanent part of the Endocrine Society."

As with every ENDO — and ENDO re-cap — there's always far too much to cover, but hopefully this article gave you a taste of what ENDO 2017 attendees experienced firsthand. Still, ENDO 2017 provided a plethora of research that we've already posted online (www.endocrinenews.org) and will be covering in greater detail in future issues throughout the rest of the year in *Endocrine News*.

Plans are already in place for **ENDO 2018** in Chicago, March 17 – 20, where no doubt more exciting research will be revealed; problems will be solved with elegant solutions; and perhaps even a bombshell revelation or two. To be sure there will be high-flying and hard-hitting endocrine science in the Windy City with or without the wrestling component. It will be another spectacle.

BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT HOW THE COST OF DIABETES CARE IS IMPACTING TREATMENT IN THE APRIL ISSUE.

As the baby-boomer generation — and everyone else gets older, the prevalence of bone-related conditions will continue to increase, disproportionately affecting women. New research shows that menopausal hormone therapy has a beneficial effect on bone strength.

Assessment of vertebral fracture by dual x-ray absorptiometry (DXA)

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# BY KELLY HORVATH **New Study Cuts to the Bone**

According to the Endocrine Society's 2016 Endocrine Facts and Figures Report on Bone and Mineral, more than 34 million people in the U.S. have low bone mineral density (BMD), and another 10 million or more have osteoporosis.

reating an imbalance between bone resorption and formation and leading to a net loss, which sets the stage for osteoporosis to develop. Importantly, although BMD is a major determinant of bone strength and fracture risk, half of fragility fractures occur in those with BMD values in the osteopenic or normal range, suggesting that bone microarchitecture also affects bone strength.

As the global population ages and life expectancy continues to inch upward, the prevalence of age-related conditions like osteopenia and osteoporosis will only increase. Yet, these conditions will lead to occurrence of fractures, which in their turn can markedly impact quality of life by reducing mobility as well as be prohibitively expensive to manage, especially when assisted living or long-term nursing home care is required.

BMD is known to be improved by menopausal hormone therapy (MHT), which is generally given to ameliorate vasomotor symptoms and vaginal



Rendering showng the four stages of osteoporosis. For women, the picture is particularly bleak, as 80% of osteoporosis diagnoses are for women, and women are three times more likely than men to have an osteoporosis-related fracture. This is at least partly because menopause hastens the rate at which women lose bone mass, creating an imbalance between bone resorption and formation and leading to a net loss, which sets the stage for osteoporosis to develop.

**6 6 1** think the real question is if there is a place for MHT as an osteoporosis treatment. Maybe we start to think of MHT as a first-choice treatment for young postmenopausal women."

 GEORGIOS PAPADAKIS, MD, LAUSANNE UNIVERSITY HOSPITAL, SWITZERLAND dryness; however, in 2005, when results from the Women's Health Initiative trial showed increased risk of blood clots, heart disease, stroke, and breast cancer in some women taking MHT, MHT use became somewhat controversial. Since that time, medical organizations including the Endocrine Society have issued statements indicating their consensus that, for most healthy, recently menopausal women, MHT is safe to use for a period of within 10 years of menopause. Such organizations have also stipulated that MHT should be individualized, taking into consideration such factors as quality-of-life priorities as well as the degree of each woman's personal risk.

## **Hot News Flash**

A new study might even have the as-yet-unconverted looking at MHT with fresh eyes. Georgios Papadakis, MD, of the Lausanne University Hospital in Switzerland, and his team of researchers are the first to have investigated whether MHT's positive effects on BMD extend to bone microarchitecture. The team used data gathered from the ongoing OsteoLaus Cohort Study, certain results of which were published in 2012. OsteoLaus was designed to identify women at high risk for fracture based on clinical risk factors for osteoporosis, bone ultrasound of the heel, lumbar spine, and hip BMD, assessment of vertebral fracture by dual x-ray absorptiometry (DXA), and microarchitecture evaluation by trabecular bone score (TBS). Results showed that TBS can be used to predict fracture risk in postmenopausal women, independently of BMD and the Fracture Risk Assessment tool.

OsteoLaus included 1,500 Swiss women ages 50 to 80 years, but any who had undergone bone-modulating treatments were excluded from Papadakis and team's current crosssectional analysis, for a total of 1,279 participants. The main variables considered in this study were age and body mass index (BMI), with researchers also assessing history of fractures as well as current and past use of calcium and vitamin D supplements. Serum vitamin D levels from 1,204 of the participants were also taken into account.

To test their novel hypothesis, researchers divided their 1,279 participants into three categories based on MHT use: 282 current users (22%), 380 past users (30%), and 617 never users (48%), and compared TBS among the groups. In addition to substantiating previous findings that MHT is associated with significantly higher BMD values at all sites, they also found that bone microarchitecture was better preserved among the current and past MHT users, as demonstrated by TBS, which also likely contributed to decreased risk of fracture.

Thus, MHT exerts a protective effect on both bone mass and structure. Interestingly, duration of MHT did not have an effect one way or the other on the results. However, the benefits on bone health did not dwindle with withdrawal from MHT; the increases in BMD values and TBS are seen for at least two more years, explains Papadakis. "What I think is most interesting about our large cohort study is the results of past users. The results of previous studies in this field have been quite contradictory regarding whether there is a very rapid rebound effect after the withdrawal of MHT. We were surprised to find that in past users, effects persist for at least two years after withdrawal," he says.

Potential limitations of the study, titled "The Benefit of Menopausal Hormone Therapy on Bone Density and Microarchitecture Persists After its Withdrawal" and published in *The Journal of Clinical Endocrinology & Metabolism*, include reliance on participant self-reporting of MHT start date and discontinuation and what type of MHT they used, Papadakis adds. Moreover, researchers were not able to determine the amount of estrogen each participant took in. Additionally, this study was cross-sectional rather than randomized.

# **Clinical Implications: Double Duty**

Regarding what the study offers to clinicians, Papadakis says, "I think the real question is if there is a place for MHT as an osteoporosis treatment. Maybe we start to think of MHT as a first-choice treatment for young postmenopausal women." To be effective, researchers now believe that an antiosteoporotic agent should target both bone mass and bone microarchitecture, the latter being a shortcoming of current drug treatments. However, MHT does both, which may make it the more efficacious choice. In most postmenopausal women ages 60 and younger, the benefits of using MHT outweigh the risks. In these women, MHT could be used to both prevent and treat osteoporosis for a period of around five to 10 years, and its effects will likely last for at least two years after treatment withdrawal.

# AT A GLANCE

- Age- and BMI-adjusted analysis showed higher TBS as well as BMD values at the lumbar spine, femoral neck, and total hip (primary endpoints) in current MHT users as compared to past and never users.
- Past MHT users demonstrated higher lumbar spine and total hip BMD and higher TBS than never users. Among past users, early discontinuers (<2 years) had significantly greater residual impact of MHT on TBS and BMD.
- Current and past MHT users had significantly lower 10-year loss of TBS and BMD at the lumbar spine and total hip than did never users.

Papadakis emphasizes that this new facet of MHT does not mean that it should be prescribed to all women or that it should be given indefinitely, despite that the bone health benefits it confers will dissipate. Rather, its role can be thought of as warding off bone fragility and potentially preserving quality of life for a subset of middle-age women with no contraindications to MHT. Though temporary, these advantages could make a considerable difference in women's lives. Furthermore, they would essentially treat two conditions with one form of therapy. "Other osteoporotic treatments can then be reserved for later in life," Papadakis says. "Even when we stop the hormones, we do not need to introduce any immediate replacement treatment because, unlike other osteoporotic treatments, there is no rebound effect."

Future research Papadakis and team would like to undertake includes exploring the association between estrogen and fat mass as well as the role of fat mass on bone health. "What we would like to do next in our cohort is to try to see if the effect on bone passes partly via an effect on fat tissue. Although we are in the very beginning stages of developing this hypothesis, people with excess abdominal fat are in a state of chronic inflammation and also present with an increased risk for fracture by a possibly related mechanism."

HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE LAST MONTH'S COVER STORY ON THE EFFECTS OF CERTAIN FORMS OF CONTRACEPTION AND ENDOCRINE-DISRUPTING CHEMICALS ON VITAMIN D LEVELS IN THE BODY.

# GET EVIDENCE-BASED CLINICAL GUIDELINES CONTENT AT THE POINT OF CARE

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EVIDENCE-BASED CLINICAL CONTENT





*Endocrine News* talks with Catherine M. Gordon, MD, chair of the task force that created the latest Clinical Practice Guideline on functional hypothalamic amenorrhea. She discusses why it was important for the Endocrine Society to release a practice guideline on this topic now and why she thinks it will impact the care patients receive in the future. n March, the Endocrine Society issued a Clinical Practice Guideline advising healthcare providers on ways to diagnose and treat functional hypothalamic amenorrhea (FHA), a condition that develops in female athletes and women who have eating disorders, which causes them to cease menstruation.

Titled "Functional Hypothalamic Amenorrhea: An Endocrine Society Clinical Practice Guideline," the guideline was published online and will appear in the May 2017 print issue of *The Journal of Clinical Endocrinology & Metabolism (JCEM)*.

Hypothalamic amenorrhea occurs when the hypothalamus in the brain slows or stops releasing GnRH, the hormone that controls the menstrual cycle. It often affects adolescent girls or women with low body weight, a low percentage of body fat, a very low calorie or fat intake, and emotional stress. Ballet dancers, figure skaters, runners, and others who burn more calories through exercise than they consume in their diet can be at risk for developing hypothalamic amenorrhea.

*Endocrine News* spoke with Catherine M. Gordon, MD, of Cincinnati Children's Hospital Medical Center in Cincinnati, Ohio, and the chair of the task force that authored the guideline, to find out how the guideline will help dispel some of the myths that exist about the diagnosis and treatment of this condition, as well as the importance of a multi-disciplinary approach to treatment, which should include psychological support.

**Endocrine News:** What was the main reason for the publication of the FHA guideline — what drove the decision and why now?

**Catherine M. Gordon:** FHA is a common problem and can affect patients across the lifespan — adolescent girls, adult women, including women struggling with infertility. Unfortunately, there have been myths circulating about the diagnosis and management of this clinical problem. The most appropriate diagnostic work-up has also been questioned. Through our recommendations, we have tried to dispel these myths regarding the management of FHA. For example, combined oral contraceptive pills do not confer bone protection in these patients, but they continue to be prescribed by clinicians solely for this purpose. The accumulating evidence on this subject led us to recommend short-term transdermal estrogen therapy to select patients when amenorrhea is longstanding despite efforts to correct their "energy deficit." We emphasize that the mainstay of therapy for these patients remains close attention to nutrition, exercise, and alleviating stressors through psychological support, best achieved through a multidisciplinary team.

**EN:** What are your hopes for the impact of the guideline on endocrine standards of care of the patient with FHA?

**CMG:** We hope that our recommendations will raise awareness about FHA and lead to thorough yet standardized work-up for these patients. We also hope that endocrinologists will embrace the concept of multidisciplinary care, with input from medical, nutrition, and mental health specialists as they care for these adolescents and young women.

# **GUIDELINE** RECOMMENDATIONS

### Hypothalamic amenorrhea is a "diagnosis of exclusion," which requires healthcare providers to rule out other conditions that could be interrupting the menstrual cycle.

- As part of their initial evaluation, women diagnosed with hypothalamic amenorrhea should have a series of laboratory tests to check levels of hormones including estrogen, thyroid hormones, and prolactin. The workup can help identify factors preventing menstruation.
- Hypothalamic amenorrhea patients should be evaluated for inpatient treatment if they have an abnormally slow heart rate, low blood pressure, or an electrolyte imbalance. Careful monitoring is needed in these cases because there is a high mortality rate associated with hypothalamic amenorrhea in the setting of eating disorders, particularly anorexia nervosa.
- Select patients presumed to have hypothalamic amenorrhea should undergo a brain MRI to check for damage to or abnormalities of the pituitary gland or pituitary hormone deficiencies, if they exhibit select signs or symptoms, including a history of severe or persistent headaches; persistent vomiting that is not self-induced; changes in vision, thirst, or urination not attributable to other causes; neurological signs suggesting a central nervous system abnormality; or other clinical signs or test results that suggest pituitary hormone deficiency or excess.



**EN:** How do you expect other medical specialties to be affected by your recommendations?

**CMG:** FHA is a diagnosis that can affect an adolescent girl or adult women. Patients present to pediatric, adult, and reproductive endocrinologists for management of this problem, involving clinicians trained in pediatrics, internal medicine, and obstetrics/ gynecology, respectively. Our task force included experts from many disciplines. For all specialties, our recommendations attempt to provide guidance around the appropriate evaluation for patients who present with FHA as there has been a lack of consistency in current clinical practice. FHA is a "diagnosis of exclusion" meaning that underlying anatomic or organic pathologies must first be ruled out. Our guideline attempts to provide clarity around the appropriate general, endocrine, and imaging evaluations to consider for these patients.

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

**CMG:** In our guidelines, we call attention to the concept of an "energy deficit" that can manifest in an adolescent girl or adult woman from restricted caloric intake, expenditure of calories through exercise, or a combination thereof. There is a misconception that FHA is seen only in the underweight patient, which is not true. Our guidelines review how the seemingly "healthy" teen can present with FHA or the normal-weight but stressed adult with infertility. We also underscore the importance of bone density screening after six months of amenorrhea as bone is one of the tissues most detrimentally affected in these patients. On the treatment front, we underscore the importance of psychological support for both adolescents and adults and select cases where short-term transdermal estrogen therapy may be helpful if a reasonable trial of nutritional, psychological, and/or exercise modifications have not resulted in the return of menses.

Other members of the Endocrine Society task force that developed this guideline include: Kathryn E. Ackerman, MD, MPH, Boston Children's Hospital, Massachusetts General Hospital, Boston, Mass.; Sarah L. Berga, MD, and Jay R. Kaplan, PhD, Wake Forest School of Medicine, Winston-Salem, N.C.; George Mastorakos, MD, Areteio Hospital, Athens, Greece; Madhusmita Misra, MD, MPH, Massachusetts General Hospital, Boston, Mass.; M. Hassan Murad, MD, the Mayo Clinic, Rochester, Minn.; Nanette F. Santoro, MD, University of Colorado School of Medicine, Aurora, Colo.; and Michelle P. Warren, MD, Columbia University Medical Center, New York, N.Y.

The Clinical Practice Guideline was co-sponsored by the American Society for Reproductive Medicine, European Society of Endocrinology, and the Pediatric Endocrine Society. The guideline will be published online at https://academic.oup.com/jcem/article-lookup/doi/10.1210/jc.2017-0131.

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# Forward Progress

The number of women who are in science, technology, engineering, and mathematic (STEM) research fields is only a fraction compared to men. Fortunately, work is being done to help find solutions to reducing this disparity.

### **BY GLENDA FAUNTLEROY**



assidy Sugimoto, PhD, had many positive female role models throughout her science career but realizes there is still a need to increase women's roles in science for future generations. She has, thus, dedicated her work to identifying how gender disparity exists in science.

"I was surrounded by several strong female colleagues, and these women reinforced the fact that women of all types were welcome in academe," Sugimoto tells *Endocrine News*.

## **Representation Matters**

Sugimoto is an associate professor of Informatics at Indiana University in Bloomington, and her research examines the influence of gender on key metrics for success in science. In a published paper in *Nature*, Sugimoto analyzed nearly 5.5 million research papers and more than 27.3 million authorships and found that female authors were underrepresented at a 30% to 70% authorship rate compared with males, and that for every female first author on a scientific paper there were nearly two male first authors.

The researchers concluded that barriers to women in science remain widespread worldwide, whether from the trickledown effects of having fewer female elders in science or the increased opportunities for male researchers to participate in international collaborations.

Sugimoto says that for young female students interested in science academia careers, seeing women in professorial roles is necessary. Images matter.

"My department, which has many tenured female faculty members, currently has very few pre-tenured faculty," Sugimoto adds. "We must remain diligent to avoid moving backwards in our progress towards gender parity in science."

For women in STEM (science, technology, engineering, and

mathematic) fields, the disparity statistics, such as those in research authorships, are fairly common. A May 2016 study from Ohio University reported that one year after they graduate, women with PhDs in science and engineering earn 31% less than do men. The results showed, however, there was a difference in what fields men and women studied. Women completed their PhDs in typically lower-paying fields, such as biology, chemistry, and health rather than engineering, computer science, or physics — fields in which men were more than twice as likely to complete.

Bruce Weinberg, a co-author of the study, said that his results didn't gleam why women are in the fields that tend to pay less. "Perhaps that's just what interested them," he says. "Or were they guided there at a young age by teachers or parents? Or did they try a more male-dominated field but had bad experiences that drove them out? We just don't know."

However, while many studies have shown there is a definite pay gap between men and women in STEM fields, these careers offer opportunities for women to participate in exciting fields of discovery and innovation, and the chance at greater economic success. Women in STEM jobs earn 33% more than those in non-STEM occupations.

"There's a necessity for women involvement in STEM," says Joy Gaston Gayles, an associate professor at North Carolina State University in a school release. "The number of jobs requiring STEM skills outpaces the number of available candidates, so there is a need to engage more females or risk losing our competitiveness in cutting-edge innovations."

## The Search for Solutions

Recognizing the need to empower the next generation of women in STEM careers, two universities have recently received considerable government funding to develop strategies to help improve the statistics.

At Clemson University, an initiative called "ADVANCE: Increasing Participation and Advancement of Women in Academic Science and Engineering Careers" has been funded by a \$3.4 million National Science Foundation (NSF) grant. **6** With the support of NSF ADVANCE, we will be able to accelerate the recruitment and retention of underrepresented scholars across the university and to improve the work environment for all faculty no matter their background or discipline."

- ELLEN GRANBERG, A CO-PRINCIPAL INVESTIGATOR OF THE GRANT

"With the support of NSF ADVANCE, we will be able to accelerate the recruitment and retention of underrepresented scholars across the university and to improve the work environment for all faculty no matter their background or discipline," says Ellen Granberg, a co-principal investigator of the National Science Foundation grant.

The university currently struggles with the number of both women and minorities in STEM faculty positions. Last year across the campus, 35% of full-time faculty were women. In STEM departments, the percentage drops to 19%. And out of 509 STEM faculty members, only one was an African-American woman and two were Hispanic women.

Another research team at Indiana University in Bloomington has also been granted a \$2.2 million NSF grant to identify obstacles that keep women from entering and remaining in STEM careers. The work explores what may be subtle, environmental signals that prove discouraging — anything from the number of men versus women in a room to segregated seating patterns.

Bottom line: Reducing the disparity gender gaps is on the horizon and the work continues.  $\textcircled{\begin{subarray}{c} \end{subarray}}$ 

FAUNTLEROY IS A FREELANCE HEALTH WRITER BASED IN CARMEL, IND., AND A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS*. SHE WROTE PROVIDED TIPS ON REDUCING THE COSTS OF PIPETTES IN THE APRIL ISSUE.

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# HORMONES AND YOUR BONES WHAT YOU NEED TO KNOW

The endocrine system is a network of glands and organs that produce, store, and secrete hormones. Hormones are really important to bone health and strength. Too much or too little of certain hormones in the body can contribute to osteopenia and osteoporosis. These are conditions in which bones become weak and are more likely to fracture or break.

# WHAT IS OSTEOPOROSIS?

Osteoporosis, which means porous bones, is a progressive condition in which bones become weak and more likely to fracture or break. Osteopenia is the more moderate decline in bone mass than occurs in osteoporosis.

Throughout the early part of your life, the amount of bone lost and the amount of bone gained — called bone turnover — remains balanced. Bone mass (size and thickness) increases during childhood and early adult life. After mid-life, more bone is broken down than is formed, and bone mass slowly declines.

# **DID YOU KNOW?**

Bone loss is a natural part of aging, but there are things that you can do to help keep your bones healthy.

- In the United States, 44 million Americans are at risk for osteoporosis.
- 10 million Americans already have osteoporosis.
- Women make up 80% of osteoporosis cases.
- Each year 1.5 million people suffer a fracture from bone loss.

Source: Report from the Surgeon General

# Visit **hormone.org** for more information.

Additional Editing by Ramon E. Martinez, MD, *Miami Beach Community Health Center* 



# OSTEOPOROSIS AND HORMONES

- Menopause during this period, the ovaries make less estrogen; therefore, estrogen-related bone protection is diminished
- Aging in Men they produce less testosterone as they age, which can contribute to bone loss
- Pituitary or Adrenal Gland Tumor

   the body is producing excess cortisol and Cushing's syndrome develops, which can damage bones
- Corticosteroid Medications (Steroids) — long-term use of prednisone and cortisone can affect bone health
- Other Hormone Imbalances including: an over-active thyroid gland, and hyperprolactinemia, in which the pituitary gland produces too much of the hormone prolactin
- Thyroid Cancer and Hypothyroidism — in which treatment might include high doses of thyroid hormone
- Eating Disorders these often lower sex hormone production, which can also result in bone loss and increased risk of osteoporosis

Your doctor can order a bone density test (DXA scan) to determine your risk of bone fractures. If you are over 65 and you do not have any risk factors for osteoporosis, you should still have a bone density test.

# UNCONTROLLABLE RISK FACTORS

- Being over age 50
- Being female
- Menopause
- Family history
- Low body weight (small and thin)
- Being Caucasian or Asian

# CONTROLLABLE RISK FACTORS

- · Diet low in calcium
- Decreased sun exposure, which results in low vitamin D
- · Not eating enough fruits and vegetables
- Little or no exercise
- Cigarette smoking
- Drinking too much alcohol
- Losing too much weight

Therapy with a steroid (such as prednisone) for any significant length of time can also increase your risk.

## TREATMENT

Along with prevention and lifestyle changes, you may need medication to stop bone loss and decrease the risk of fractures. Certain drugs slow down bone loss. If you are taking hormone medications, talk with your doctor to get the most appropriate does to treat your condition.

# **4 STEPS TO PREVENTION**

- Get enough calcium and vitamin D, either through diet or supplements (at least 1,000-1,200 mg of calcium; 400-800 IU of vitamin D daily under age 50 or at least 800-1,000 IU after age 50)
- Do weight-bearing exercises and stay physically fit
- Avoid smoking
- Don't drink too much alcohol



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