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Endocrine INNOVATIONS: A Year of Scientific Breakthroughs

Endocrine science has proven once again that it is on the leading edge of new discoveries that will improve the lives of patients around the world for generations to come. Editors from Endocrine Society journals share their top picks for the biggest advances in endocrine research.

SURVIVAL SKILLS: Treating adult survivors of childhood cancers

DECEMBER 2018

ROAD WARRIORS: Check out the Endocrine Society's roadshow debut in Texas!



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Endocrine

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2018: A Year of Accomplishments & Milestones

would like to dedicate this last communication of the year to highlight some, but not all (due to space constraints) of the innovative and essential work that is being done by our committees. It has been a busy year and I want to thank our hardworking members and staff for their commitment and time.

Our Advocacy and Public Outreach Core Committee (APOCC) continues to provide insightful review and feedback on both policy letters and guidance on legislation endorsement. In the spring and the fall, Society members went to Capitol Hill to focus on advocacy for biomedical research funding, insulin pricing, and diabetes self-management training. The committee has also participated in five online advocacy campaigns and I encourage our members to respond to our advocacy emails soliciting your support to contact your congressional leaders — it's just a few clicks!

The Clinical Affairs Core Committee (CACC) has been involved in reviewing the Society's new insulin affordability position statement. The CACC conducted a Clinician Hill Day in early October to advocate for increased access to diabetes self-management training services and to provide education on the impact from rising insulin costs. The committee held a Congressional Briefing on diabetes for Congressional staff which was so well attended that it was standing room only.

The Research Affairs Core Committee (RACC) continues to provide innovative initiatives for our Society to support the research community and to increase opportunities for researcher engagement. This fall, the RACC organized meetings with the directors and/or senior staff of several NIH Institutes. These meetings strengthened our relationships with key institutes that fund endocrine research and we identified opportunities to share information about institute priorities and funding opportunities with endocrine scientists. The **committee** has provided insight and guidance on several important NIH policy changes.

In the educational meetings area, the Annual Meeting Steering Committee (AMSC) is adding its final touches to a stellar program for **ENDO 2019** in New Orleans. The Committee has developed a robust and diverse program of high quality and cutting-edge science, as well as the latest updates in clinical care. This will be a must-attend meeting and I hope to see you all in New Orleans!

The Clinical Endocrinology Update Steering Committee (CEU) added a second program this year — CEU East in Miami and CEU West in Anaheim. Both meetings were very well attended with a total combined attendance of 780,

66 This is just a snapshot of the tremendous amount of work that our members and staff have been doing over the past year. a record attendance. The committee is already discussing plans for next year's East and West meetings. As always, the quality of presentations was stellar and the program attracted international attendees.

The Clinical Endocrine Education Committee (CEEC) continues its oversight of several programs and activities. The Fellows Training Series, which develops online modules on specific endocrine topics to enhance education, is working on a rare endocrine diseases online module. The In Training Exam (ITE) Steering Group is conducting a final review of its exam content, to be available in early January. Over 95% of all U.S. fellowship programs register their fellows to take the ITE. The Endocrine Educators Group is planning sessions for **ENDO 2019** targeted to optimizing the education skills of our members.

The Trainee & Career Development Core Committee (TCDCC) continues working on planning **ENDO** programming around career and professional development. At **ENDO 2019**, they will continue to hold the Early Career Day and the very popular Career Development Workshops. This year they are introducing a half-day professional workshop on bioinformatics pathways, interactions, and resources. They are also creating a podcast series on career guidance. In collaboration with the Committee on Diversity and Inclusion (CODI), the TCDCC will be supporting the development of the Endocrine Society Speakers Bureau, where junior faculty can post short videos to showcase their research and presentation abilities, allowing for dissemination to and review by our members who are planning future programs.

CODI will celebrate the Society's 25th anniversary of designation and promotion of programs to enhance diversity in all aspects of the Society's work; we will celebrate our accomplishments through an online recognition campaign, *Endocrine News* articles, and events at **ENDO 2019**. CODI also continues to work on its yearly **ENDO** programming. New activities planned next year at **ENDO** include an Unconscious Bias in Healthcare and Research symposium and LGBT and Allies Reception. In its seventh year, the Future Leaders Advancing Research in Endocrinology (FLARE) program is expanding to include trainees and junior faculty. They are also developing an Online FLARE community and considering other activities to enhance the engagement of FLARE participants and alumni. The Hormone Health Network (HHN) continues to positively impact the health and well-being of communities by translating the science of endocrinology for patients and the public. At **ENDO 2019**, HHN will feature a new weboptimized version of its website **hormone.org**. As part of this overhaul, the committee members have spent countless hours over the past year reviewing, updating, and re-cataloging content to make it more user-friendly and easier to navigate.

This is just a snapshot of the tremendous amount of work that our members and staff have been doing over the past year. I would like to thank all the other committees, working groups, and task forces that I did not mention but who are working very hard on numerous projects and initiatives to improve endocrinology worldwide. From the bottom of my heart, thank you.

- Susan J. Mandel, MD, MPH, President, Endocrine Society



CLAIM MOC POINTS

As a board-certified physician, you need to earn 100 MOC points every five years. The end of 2018 marks the first five-year deadline since the implementation of ABIM's continuous MOC program. Claim your points by December 31, 2018, from any 2018 Endocrine Society educational activities you participated in.

STILL NEED POINTS? VIEW OUR MOC ACTIVITIES. LEARN MORE AT ENDOCRINE.ORG/CME

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FROM THE EDITOR



2018 Highlights of Endocrine Research & Treatments

or the fourth consecutive year, we are running "Eureka! The Year's Biggest Discoveries in Endocrine Science." This topic has proved to be so popular in the past that we decided to make this an annual feature (p. 20). This year's roundup is put together by Kelly Horvath who spoke with several editors from the Endocrine Society's scientific journals for their input on new breakthroughs that could easily affect the future of endocrine science for years to come.

Among the new research included in this year's wrap-up are:

- Four cardiovascular studies recommended by JCEM associate editor, Robert H. Eckel, MD, that covered everything from low-densitylipoprotein cholesterol and mortality to CVD risk factors in diabetes;
- A paper that links our gut to our brain, recommended by *Endocrine Reviews* editor-in-chief Daniel J. Drucker, MD;
- A study that detailed the effects of diabetes on patients with tuberculosis was praised by *Journal of the Endocrine Society* (JES) associate editor Takashi Kadowaki, MD, PhD;
- Research that gives credence to the notion that tissues communicate via signaling proteins in extracellular vesicles, was lauded by Gregory R. Steinberg, PhD, an associate editor of *Endocrine Reviews*; and
- JES associate editor Ana Claudia Latronico, MD, PhD, recommended an article from that journal that highlighted the cardiovascular health of transgender individuals which exposed an urgent need for additional research on how best to support this growing population as well as the effects of hormone therapy on cardiovascular health.

On page 38, Eric Seaborg delves into the details of the Endocrine Society's clinical practice guideline on treating adult survivors of childhood cancers in "Staying Alive". The new guideline, "Hypothalamic-Pituitary and Growth Disorders in Survivors of Childhood Cancer: An Endocrine Society Clinical Practice Guideline," is a great summary and practical document for endocrine providers, according to Sogol Mostoufi-Moab,

Endocrine news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

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Designer: Catherine C. Neill, CNJ Creative, LLC www.cnjcreative.com

Prepress & Printing: The Sheridan Group www.sheridan.com

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Endocrine News informs and engages the global endocrine community by delivering timely, accurate, and trusted content covering the practice, research, and profession of endocrinology.



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The mission of the Endocrine Society is to advance excellence in endocrinology and promote its essential and integrative role in scientific discovery, medical practice, and human health.

> Endocrine News* is published 12 times a year by the Endocrine Society, 2055 L Street, NW, Suite 600, Washington, DC 20036 Phone 202-971-3636 • Fax 202-736-9708 www.endocrine.org.

Print ISSN 2157-2089 Online ISSN 2157-2097 Copyright © 2018 by the Endocrine Society. All rights reserved.

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Advertising appearing in this publication does not constitute endorsement of its content by *Endocrine News*^{*} or the Endocrine Society. MD, MSCE, assistant professor of pediatrics in the divisions of endocrinology and oncology at the Children's Hospital of Philadelphia, who reviewed the guideline as it was being prepared. "It is also a helpful document for endocrinologists

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The goal of this new program is to present information from members about how the Endocrine Society can better support basic scientists, early career members, and trainees in reaching their career goals in the field of endocrinology.

"

assuming care for adult survivors of childhood cancer to continue the long-term surveillance of various endocrine organ systems impacted by cancer therapy, as most of these patients will continue to experience endocrine-related abnormalities well into adulthood," Mostoufi-Moab tells Seaborg.

On page 32, Jessica Harris writes about the debut of the Endocrine Society's roadshow that traversed the Lone Star State in "Road Warriors." The goal of this new program is to present information from members about how the Endocrine Society can better support basic scientists, early career members, and trainees in reaching their career goals in the field of endocrinology. Judging from the photos at the events in Houston and Dallas, this debut was a freshman success story, and future roadshows are planned...maybe in your state. Stay tuned!

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- Mark A. Newman, Editor, Endocrine News



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WHY ENDOCRINOLOGY?

"ENDO Be All"

BY LINDSEY S. TREVIÑO, PHD, ASSISTANT PROFESSOR, Division of Health Equities, Department of Population Sciences, City of Hope, Duarte, Calif.

y father lives with diabetes. There is a strong history of the disease in my family, with many family members being diagnosed with (and some even dying young from complications of) the disease. Our family is a pretty typical one in South Texas, where diabetes, obesity, and cardiovascular diseases are prevalent. As such, I became familiar with endocrinological health outcomes well before I truly understood how the various endocrine organs and hormones throughout the body make it possible to live a long, healthy life.

My academic interest in endocrinology, on the other hand, began when I was an undergraduate at St. Mary's University in San Antonio, Texas, where I participated in the Maximizing Access to Research Careers (MARC) Undergraduate Student Training in Academic Research (U*STAR) program. Through this program, I conducted summer research in prostate cancer with Dr. Jamboor K. Vishwanatha and in reproductive biology with Dr. O. David Sherwood. Both of these experiences sparked my enthusiasm for endocrinology and convinced me that I should attempt to pursue a career in biomedical research. Early career research experiences seem to be common among the many successful scientists that I know, and I am glad that the Endocrine Society supports such opportunities through their Summer Research Fellowships.

Later, as a graduate student at Cornell University, my love for endocrinology continued to blossom. I joined the laboratory of Dr. Patricia A. Johnson and participated in research focused on investigating the role of steroid hormones in the development and/or progression of ovarian cancer in the hen, an animal model that develops ovarian cancer with a high spontaneous incidence. As I learned more about the role of hormones in human reproductive biology and disease, I came to the realization that endocrinology is the "ENDO be all" (paraphrased from an ENDO t-shirt). In truth, where would any of us be without hormones?

The more I learned about the effects of hormones, the more I wanted to know about their operation. I therefore chose to pursue a postdoc at Baylor College of Medicine (BCM), a mecca for studying the mechanism of hormone action. At BCM, I joined the laboratories of Drs. Nancy L. Weigel and Dean P. Edwards and we investigated the regulation of progesterone receptor (PR) activity by cell signaling pathways in breast cancer cells. Dr. Weigel and Dr. Edwards are both active members of the Endocrine Society, and they encouraged me to join the Society and attend ENDO.

My involvement with the Endocrine Society has been transformational for my career and has cemented my love for all things endocrine. In 2013, I was selected for the inaugural class of the Future Leaders Advancing Research in Endocrinology (FLARE) program. FLARE was a gamechanger for me, providing me with opportunities to serve as a mentor to junior scientists, as a committee/task force member, and as an advocate on Capitol Hill. These experiences have greatly expanded my professional network to include renowned endocrine scientists across disciplines

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

(such as my FLARE mentor Dr. Teresa Woodruff) who continue to educate me about all of the wondrous facets of endocrinology.

One such facet is the rapidly expanding field of endocrine disruptor research. My interest in endocrine disruptors had been piqued early on in my training, but it was not until I joined Dr. Cheryl Walker's laboratory at Texas A&M Health Science Center (now at BCM) that I began work

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Ultimately, I hope that my laboratory's research will contribute to a reduction in health inequities due to environmental exposures and will provide potential therapeutic targets for precision medicine approaches to treat endocrine disease in high-risk populations.

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in this field in earnest. Our work focused on determining the mechanisms underlying epigenetic dysregulation by environmental exposures. These studies provided the foundation for my interest in developing my independent research program at City of Hope focused on investigating endocrine disruptors and epigenetics in the context of diseases with known disparities, including cancer, obesity, and diabetes. Ultimately, I hope that my laboratory's research will contribute to a reduction in health inequities

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

due to environmental exposures and will provide potential therapeutic targets for precision medicine approaches to treat endocrine disease in high-risk populations.

Throughout my training, I have learned that the life of an academic scientist can be tough (failed experiments, rejected manuscripts, unfunded grants, etc.). However, I have also learned that if you love what you do, you can overcome challenges that come your way. I love endocrine science, and this love has helped propel me forward, through success as well as through setbacks. Along the way, I have also been supported by my mentors (those previously mentioned, as well as Dr. Mark Roberson and Dr. Andrea Gore) and inspired by their contributions to our field. As I embark on the next chapter of my career, I hope to share my passion with the next generation of endocrine scientists and support them through their own paths of discovery as we collectively advance the field of endocrinology.



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EndoCares: DC Reached Over 400 People at Mexican & Peruvian Consulates



n Saturday November 17, the Endocrine Society held its second iteration of EndoCares: DC, its global outreach program for healthcare providers, patients, and the general public.

This year, EndoCares followed a health fair format focused on diabetes awareness, and it was held simultaneously at the Mexican and Peruvian consulates, a first for the program and the consulates themselves. EndoCares: DC is part of a larger outreach effort, linking the work the Society does abroad to the ex-pat community in the U.S.

The two consulates hosted more than 400 Mexican and Peruvian citizens from all age groups, from babies to senior citizens, including a 94-year-old Peruvian ex-pat. More than 30 volunteers – medical students, health policy students, physical therapists, and nurses – from the George Washington University School of Medicine & Health Sciences,

as well as three Society members, offered attendees the opportunity to learn how to measure their A1c levels, their blood pressure, and their body mass index. Through partnerships with other organizations, attendees were also offered free flu shots, HIV testing, endometriosis guidance, eye exams, domestic violence counseling, and information on affordable health insurance options.

"EndoCares in the U.S. is a bit different to what we do abroad, because by approaching the general public we focus on awareness and education," says Lucia Tejada, PhD, the Endocrine Society's director of development & strategic partnerships, who spearheaded this initiative. "Therefore, we try to fight diabetes by flagging signs and suggesting behavioral modifications. Through A1c testing we also find a few cases of prediabetes, and those people get immediate guidance from our very own members on-site."

Besides the Mexican and Peruvian consulates, other partners included DC Healthlink, Novo Nordisk, Abbott Nutrition, Walgreens, Emerson Diversity Health Foundation, La Clinica del Pueblo, Ventanilla de Salud, Latina Endometriosis, and the U.S.

From here, Mexico and Peru will help coordinate regional educational efforts in the Latin American region, including outreach and support to the national endocrine organizations. "[November 17] was a landmark in our EndoCares initiative," says Endocrine Society chief executive officer Barbara Byrd Keenan, FASAE, CAE. "Rafael Laveaga, Consul General of Mexico and Lissette Nalvarte, Consul General of Peru, agreed to build upon the EndoCares program held in their respective consulates for future U.S.-based efforts and to support our efforts in their countries and the Latin American region." – *Derek Bagley*

Endocrine Society CEO Barbara Byrd Keenan, FASAE, CAE, with Rafael Laveaga, Consul General of Mexico, and Lissette Nalvarte, Consul General of Peru.



EndoBridge 2018 Celebrates Six Years of Bridging the World of Hormones

The sixth annual meeting of EndoBridge[®] co-hosted by the Society of Endocrinology and Metabolism of Turkey, Endocrine Society, and European Society of Endocrinology, took place in Antalya, Turkey October 25-28, 2018.

The meeting was held in English with simultaneous translation into Russian, Arabic, and Turkish. Accredited by the European Council, the three-day scientific program included 24 stateof-the-art lectures, 16 interactive case discussion sessions, and poster case presentations providing a comprehensive update across hormonal disorders.

"We have reached the highest number of international delegates, countries, and cases this year," says Bulent Yildiz, MD, a faculty member at Hacettepe University School of Medicine in Ankara and the founder and president of EndoBridge. "EndoBridge 2018 brought together 578 physicians and scientists from 41 countries and over 90 cases were presented. As usual, participants had a great opportunity to interact and participate in discussions with global leaders of endocrinology and share their experience and expertise."

The seventh annual EndoBridge[®] will take place in Antalya, Turkey, October 24–27, 2019. Further information can be found at **www.endobridge.org**.



From left to right: Fusun Saygili, MD, executive committee member, The Society of Endocrinology and Metabolism of Turkey; Susan Mandel, MD, president, Endocrine Society; Bulent Yildiz, MD, founder and president, EndoBridge; and AJ van der Lely, MD, president, European Society of Endocrinology.

INTOUCH



Society Members Named to NCCC

hree Endocrine Society members have been appointed to the National Clinical Care Commission. The Commission will evaluate and provide recommendations on federal programs related to complex metabolic or autoimmune diseases that result from insulinrelated issues, such as diabetes.

The Society and its fellow Diabetes Advocacy Alliance members have supported the effort to establish the Commission, which will help the country undertake more proactive and innovative approaches to diabetes and its disease complications.

Society members serving on the Commission are:

- William Herman, MD, MPH, was elected to be the Commission's chairman at its initial meeting Oct. 31. Herman, who was jointly nominated by the Society and the American Diabetes Association, is director of the Michigan Center for Diabetes Translational Research at the University of Michigan in Ann Arbor, Mich.
- Ayotunde Dokun, MD, PhD, FACE, is chief of endocrine service, Division of Endocrinology, Diabetes, and Metabolism at Regional One Health System in Memphis, Tenn. Dokun runs a translational research laboratory that studies the molecular mechanisms of vascular complications in diabetes.
- M. Carol Greenlee, MD, FACP, FACE, is faculty co-chair of the Center for Medicare and Medicaid Innovation Transforming Clinical Practice Initiative in Grand Junction, Colo. A clinician with more than 30 years' experience in private practice, she co-chaired the American College of Physicians (ACP) Medical Neighbor workgroup and was a lead author of the ACP position paper "The Patient-Centered Medical Home Neighbor." She also serves on the *Endocrine News* Editorial Advisory Board.

The Commission consists of 23 voting members, including 11 heads of federal agencies. U.S. Department of Health and Human Services Sec. Alex Azar appointed 12 non-federal experts in prevention, care, and epidemiology of complex metabolic or autoimmune diseases that result from insulin-related issues.

The Office of Disease Prevention and Health Promotion (ODPHP) will provide management and support services for the Commission's activities.

TRENDS & INSIGHTS



BY DEREK BAGLEY Senior Editor



66

A functioning adrenal clock may be required to maintain GC rhythms in humans. reducing alterations in metabolic. hemodynamic, and cognitive function observed under conditions linked to irregular light exposure including shift work, jet lag, and light at night.



Adrenal Clock May Help Maintain Circadian Rhythms During Chronic Aberrant Light Exposure

recent animal model shows that the adrenal clock may help stabilize the circadian Glucocorticoid rhythm in response to chronic exposure to aberrant light cycles, according to a study recently published in *Endocrinology*.

Researchers led by William C. Engeland, PhD, of the Department of Neuroscience at the University of Minnesota in Minneapolis, point out that the misalignment of circadian rhythms that occurs chronically in shift work and jet lag contributes to adverse health effects and that the superchiasmatic nucleus (SCN) had been shown in previous work to be sufficient to maintain these rhythms.

However, the SCN clock may only help to maintain circadian rhythms during a normal 24-hour light cycle. "Whether the adrenal clock is important for maintaining GC rhythmicity during chronic exposure to an aberrant LD cycle is unknown," the authors write. "To address this possibility, we have generated a novel adrenal cortex-specific *Bmal1* knockout (KO) mouse and examined the hypothesis that the adrenal clock is required to maintain the circadian GC rhythm during aberrant light exposure produced by an ultradian 3.5:3.5h (T7) LD cycle." *Endocrine News* caught up with Engeland and his team to talk about this new study and what it could mean for people who work shifts or suffer from chronic insomnia or jetlag.

Endocrine News: First off, what was the impetus of this study? What made you want to look at the adrenal clock's role in maintaining circadian rhythms?

William C. Engeland: The circadian glucocorticoid (GC) rhythm is thought to be dependent on a molecular clock in the suprachiasmatic nucleus (SCN) and a peripheral clock in the adrenal cortex that is synchronized by SCN-dependent signals. However, adrenal cortex-selective clock disruption does not alter circadian GC rhythms, suggesting that the central SCN clock is solely responsible for light entrainment of glucocorticoid rhythms under normal environmental day-night cycles. We were interested in determining if the adrenal clock was important for maintaining the circadian GC rhythm during chronic exposure to aberrant light cycles.

EN: It seems the adrenal clock is not necessary to maintain normal circadian rhythm during a normal light-dark cycle, but according to your results, it may be necessary during chronic exposure to aberrant light. Can you speak more to that?

WCE: Based on the premise that the SCN clock and the adrenal clock require synchronization to maintain timing of GC rhythms, we exposed mice to aberrant light produced by an ultradian T7 light cycle (alternating 3.5-hour periods of light and dark) in an attempt to desynchronize the SCN and adrenal clock. Our results showed that circadian (~24 hour) GC rhythms were still maintained under T7 LD, suggesting that the SCN and adrenal clock remain synchronized under aberrant light exposure. In contrast, circadian GC rhythms were lost in mice in which the core clock gene, *Bmal1*, was selectively deleted in the adrenal cortex. These findings led to our conclusion that the adrenal clock is necessary to prevent desynchronization of the circadian GC rhythm under aberrant light exposure.

EN: Can you tell us about the process of producing these *Bmal1* knock-out mice, and what these new animal models could mean for future studies of the circadian clock?

WCE: We generated a novel adrenal cortex-selective *Bmal1* null mouse using a Cre-LoxP strategy in collaboration with David Breault and colleagues at Harvard Medical School. By intercrossing mice expressing aldosterone synthase-Cre recombinase (ASCre/+) with floxed *Bmal1* mice, we obtained adrenal cortex-selective *Bmal1* deletion in adulthood by taking advantage of the capability of the rodent adrenal to undergo postnatal transdifferentiation. Future work using these mice can examine whether a functioning adrenal clock is required for rhythms in adrenocortical responses to stress and to ACTH.

EN: It appears the adrenal clock acts to maintain

normal circadian rhythms and protect against increases in corticosterone responses. What implications do these findings have in the clinical setting?

WCE: Our work highlights the importance of the adrenal clock in rodents to maintain the circadian GC rhythm during aberrant light exposure. A functioning adrenal clock may be required to maintain GC rhythms in humans, reducing alterations in metabolic, hemodynamic, and cognitive function observed under conditions linked to irregular light exposure including shift work, jet lag, and light at night. Additionally, our study indicates that Bmal1 may act in part by repressing GC responses to ACTH. We have identified dysregulated adrenals genes in Bmal1 null mice exposed to aberrant light that may be responsible for increasing steroidogenesis. Additional work is required to determine whether dysregulation of adrenal Bmal1 contributes to forms of hyperadrenocorticoidism observed clinically.



Additional work is required to determine whether dysregulation of adrenal *Bmal1* contributes to forms of hyperadrenocorticoidism observed clinically.

99

Most Frequent Pathogenic Mutation in *RET* Carries Very Low Lifetime Risk of Medullary Thyroid Cancer

The most frequent pathogenic mutation in the rearranged during transfection (*RET*) mutation — p.Val804Met — carries with it a very low lifetime risk of medullary thyroid cancer (MTC), which could mean the American Thyroid Association's (ATA) recommendation of prophylactic thyroidectomy as standard for all *RET* mutation carriers is inappropriate, according to a study recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Clare Turnbull, MD, PhD, of The Institute of Cancer Research in Sutton, U.K., write that in 1993 the RET protooncogene was definitively identified as the gene underlying multiple endocrine neoplasia type 2 (MEN2) and that germline mutations have subsequently been detected in nearly all families with MEN2A, MEN2B, and familial medullary thyroid cancer (FMTC), with emergence of a distinct pattern of genotype-phenotype correlation. "More recently, the American Thyroid Association (ATA) categorized RET mutations based on age-related penetrance of MTC," the authors write. "The 2009 ATA guidance adopted classes A through D (with D as the most severe); in the 2015 revisions, they were updated to 'moderate,' 'high,' and 'highest' risk of MTC, with accordant guidance on timing of prophylactic thyroidectomy for unaffected RET mutation carriers."

The researchers wanted to estimate penetrance figures, unbiased by ascertainment, for MTC, so they analyzed 61 *RET* mutations that the ATA has deemed disease-causing in population wholeexome sequencing data. They used the analyses of the observed allele frequencies in about 51,000 individuals from the Exome Aggregation Consortium (ExAC) database that were not contributed via The Cancer Genome Atlas (TCGA; non-TCGA ExAC), assuming lifetime penetrance for MTC of 90%, 50%, and unbounded. The group calculated the maximum number of mutant alleles that they would expect to observe in non-TCGA ExAC data for a pathogenic *RET* mutation. "In brief," the authors write, "this method leverages the logic that a fully penetrant allele cannot be more common than the disease it causes."

Fifty of the 61 disease-causing mutations were not detected in this cohort, and of the 11 mutations present, nine were in the moderate risk category and two were in the high-risk category. p.Val804Met shows a frequency greater than fivefold higher than that of any other pathogenic *RET* mutation, the researchers found. "For all other pathogenic *RET* mutations, the observed frequency is consistent with a lifetime penetrance of MTC of >90%, whereas for *RET* p.Val804Met, the observed frequency is not even consistent with a lifetime penetrance of 50%," the authors write. "We go on to demonstrate that the observed frequency of p.Val804Met in non-TCGA ExAC supports a lifetime penetrance of MTC for p.Val804Met of 4%."

The authors go on to point out that even with an unrealistically high estimate of lifetime risk of MTC in combination with implausible estimates of allelic heterogeneity (45%) and genetic heterogeneity (40%) the observed frequency of p.Val804Met still only equates to a penetrance for MTC of 46%.

The ATA currently recommends prophylactic thyroidectomy for all *RET* mutation carriers, but based on the results of this study, that recommendation should be clarified, Turnbull and her group write.

Findings: "Inevitable prophylactic surgery may be a reasonable presumptive model for the carriers of most *RET* mutations who have close relatives affected by disease," they write. "However, for individuals with *RET* p.Val804Met, ascertained through population-based testing [i.e., with no (or an only distant) family history of disease], truly prophylactic thyroidectomy is likely inappropriate."



The authors go on to point out that even with an unrealistically high estimate of lifetime risk of MTC in combination with implausible estimates of allelic heterogeneity (45%) and genetic heterogeneity (40%) the observed frequency of p.Val804Met still only equates to a penetrance for MTC of 46%.





The authors also note that lifestyle interventions have limited success in early pregnancy to prevent GDM, because the processes leading to GDM begin before pregnancy.

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Biomarker Risk Score May Identify Women at Risk for Gestational Diabetes

The predictive ability of a biomarker risk score beyond established risk factors may help identify women at risk of developing gestational diabetes (GDM) before conception and help with tailoring targeted prevention strategies, according to a study recently published in the *Journal of the Endocrine Society*.

Researchers led by Sylvia E. Badon, PhD, of the Division of Research at Kaiser Permanente Northern California in Oakland, point out that GDM is a common complication during pregnancy, occurring in 5% to 9% of pregnancies, and that GDM carries with it a number of long- and short-term consequences for mother and child, including increased risk of diabetes and cardiovascular disease in the mother and increased risk of diabetes in the child.

The authors write that several biomarkers measure before pregnancy have been individually associated with the risk of GDM, but "previous studies have not examined the ability of multiple preconception biomarkers considered together, beyond established risk factors, to improve prediction of GDM. To the best of our knowledge, a preconception biomarker risk score has not yet been developed and assessed." Therefore, the researchers aimed to develop a preconception biomarker risk score and test it to see how well it predicted GDM.

From 1984 to 1996, female Kaiser Permanente Northern California members were invited to complete a comprehensive health examination [multiphasic health checkup (MHC)] upon enrollment. The researchers conducted a nested case-control study within the larger cohort of women who participated in the MHC. "Of the 27,743 women, 15- to 45-year-olds who participated in the MHC from 1984 to 1996, 4,098 subsequently became pregnant and gave birth before 31 December 2010; had questionnaire and clinical data, including serum samples, available; and were free of recognized diabetes," the authors write. "Women diagnosed with GDM were considered cases. Two controls were selected for each case from among women who did not meet the GDM case definition during the study period." For this study, 256 confirmed cases of GDM with valid biomarker measurements were included.

High-risk levels of sex hormone-binding globulin (SHBG; <44.2 nM), glucose (>90 mg/dL), total adiponectin (<7.2 μ g/mL), and homeostasis model assessment-estimated insulin resistance (HOMA-IR) (>3.9) were independently associated greater odds of GDM. "For each unit increase in the biomarker risk score, odds of GDM were 1.94 times greater (95% CI: 1.59, 2.36)," the authors write. "A biomarker risk score including only SHBG and glucose was sufficient to improve prediction beyond established risk factors (age, race/ethnicity, body mass index, family history of diabetes, previous GDM; area under the curve = 0.73 vs 0.67, P = 0.002)."

Based on these results, the authors conclude that a preconception biomarker risk score, including SHBG, glucose, adiponectin, and HOMA-IR — measured, on average, seven years before pregnancy — was associated with future GDM risk; however, a biomarker score, including only SHBG and glucose, may be sufficient to improve substantially the predictive ability for GDM beyond established GDM risk factors. The authors also note that lifestyle interventions have limited success in early pregnancy to prevent GDM, because the processes leading to GDM begin before pregnancy, as this study shows.

Findings: "Identification of women at high risk for future GDM before pregnancy would allow for preconception interventions to attempt to alter the modifiable pathophysiologic pathways underlying the altered biomarker levels that we identified here," the authors write.

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Analysis Estimates the Positive Impact of Empagliflozin on Life Expectancy in Adults with Type 2 Diabetes and Established CVD



reatment with empagliflozin may impact life expectancy positively in adults with type 2 diabetes and established cardiovascular disease, according to results from the EMPA-REG OUTCOME trial recently published in Circulation. Using actuarial methods and assuming that the demonstrated beneficial effects of empagliflozin remain consistent with long-term use, empagliflozin was estimated to extend life expectancy by one to 4.5 years on average, depending on age, when compared with placebo. This analysis suggests that treatment with empagliflozin could add years of life. Boehringer Ingelheim and Eli Lilly and Company are marketing the drug as Jardiance.

Researchers led by Brian Claggett, PhD, of the Division of Cardiovascular Medicine at Brigham

and Women's Hospital in Boston, conducted an analysis of data from 7,020 people included in the EMPA-REG OUTCOME trial that showed estimated life expectancy increased across all ages when adults were treated with empagliflozin as compared to those treated with placebo. Specifically, estimated mean survival in people aged 45 years was 32.1 years with empagliflozin versus 27.6 years with placebo, resulting in a mean survival difference of 4.5 years. In people aged 50, 60, 70, and 80 years old, the mean survival difference with empagliflozin compared to placebo was an additional 3.1 years, 2.5 years, 2 years, and 1 year, respectively.

"For a 60-year-old living with type 2 diabetes, who has already had a cardiovascular event, previous studies estimate that life expectancy could be reduced by up to 12 years compared with someone of the same age without these conditions," Claggett says. "This latest analysis estimates that empagliflozin could prolong such a person's life span by, on average, 2.5 years."

Findings: The primary EMPA-REG OUTCOME trial results, published in the *New England Journal of Medicine* in September 2015, demonstrated a 38% relative risk reduction in cardiovascular death and a 32% relative risk reduction in all-cause mortality with empagliflozin in people with type 2 diabetes and established cardiovascular disease, compared with placebo, over a period of 3.1 years. Modeling based on the EMPA-REG OUTCOME trial data was used to quantify the potential benefit of empagliflozin on residual life span.



This latest analysis estimates that empagliflozin could prolong such a person's life span by, on average, 2.5 years.

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ENDOCRINE ITINERARY



New Orleans, Louisana March 23 – 26, 2019

KEY DATES

LATE BREAKING ABSTRACTS January 16 – February 13, 2109 HOUSING DEADLINE February 22, 2109 With over 7,000 attendees, nearly 2,000 abstracts, and over 200 other sessions, **ENDO 2019** is the leading global meeting for endocrinology research and clinical care. Join us for the most well attended and valued translational endocrinology meeting in the world. Bringing together leading experts, researchers, and the most respected clinicians in the field, **ENDO 2019** represents a convergence of science

and practice that highlights and facilitates breakthrough discoveries in the field of endocrinology. Spend time connecting with peers and colleagues, exchanging ideas and information, and getting out in front of the latest trends and advancements in hormone health. The meeting also hosts other satellite and pre-conference events.

www.endocrine.org/endo2019

55th Clinical Diabetes and Endocrinology Institute Annual CME Conference

Snowmass, Colorado, January 15 – 19, 2019

The 55th Clinical Diabetes and Endocrinology Institute Annual CME Conference will address gender-affirming hormone therapy, gestational diabetes, precision medicine for thyroid tumors, Cushing's disease, neuroendocrine diseases, obesity therapies, the new ADA/EASD guidelines for type 2 diabetes management, menopause, diabetes technologies, and much more.

www.njhealth.org/diabetes-conference

MEN 2019: 16th International Workshop on Multiple Endocrine Neoplasia

Houston, Texas, March 26 – 29, 2019 In keeping with the spirit of the original MEN workshop, MEN2019 will focus on emerging topics in the genesis and therapy of malignant endocrine tumors associated with multiple endocrine neoplasia. The goal of the workshop will be to provide an outline for basic and clinical research focused on these malignant manifestations. The meeting will bring together local and international experts on multiple endocrine neoplasia to focus on these subjects. A significant portion of the meeting will be spent in workshops centered on emerging topics and the development of an international roadmap for future research and clinical trials, and the remainder of the meeting will be composed of large group didactic sessions. https://www.mdanderson.org/conference

Endocrine Fellows Series: Type 1 Diabetes Care and Management New Orleans, Louisiana March 19–21, 2019,

This comprehensive conference is for adult and pediatric endocrine fellows interested in type 1 diabetes. The unique and highly sought-after program is an opportunity to learn from leaders in the field through interactive sessions. The curriculum is specially designed to support early career endocrinologists by enhancing skills with comprehensive education not typically taught in

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fellowships and providing the opportunity to connect with thought-leaders and peers. https://www.endocrine.org/T1Dfellows

International Pituitary Congress New Orleans, Louisiana March 20 – 22, 2019,

The Sixteenth International Pituitary Congress will present an exciting group of member and guest international experts in pituitary problems. It will include distinguished clinicians and clinical researchers, fellows in training, and experts in basic science. There will be cutting-edge in-depth topics that will permit each attendee to become familiar with the latest trends in pituitary endocrinology. The format of the meeting is intended to facilitate maximum interaction and free exchange of ideas among the participants and speakers. http://pituitarysociety.org



2019 Clinical Endocrinology Update

Seattle, Washington September 17 – 19, 2019

Each year CEU brings together hundreds of endocrine clinicians for a unique learning experience and opportunities to network with expert faculty and colleagues. Attend the 71st CEU to receive the most trusted and clinically relevant information about recent advances in the field of endocrinology. The educational programming at CEU appeals to clinicians at all levels of practice, as well as fellows and other members of the clinical practice team. www.endocrine.org/ceu

Photo: Shutterstock.com

INTERNATIONAL ITINERARY

1st BES-Mayo Course in Advanced Endocrinology 2019 Dhaka, Dhaka, Bangladesh, January 24 – 25, 2019

The Advanced Course in Endocrinology is a collaboration between the Bangladesh Endocrine Society (BES) and the Mayo Clinic, Rochester, Minn. It is a twoday intensive and interactive learning course covering all aspects of clinical endocrinology.

http://www.bes-mayo.com

Keystone Symposia on Functional Neurocircuitry of Feeding and Feeding Disorders

February 10–14, 2019, Alberta, Canada

The goal of this conference is to gather international leaders in the neural control of feeding and energy homeostasis, along with leaders in the pathophysiology of feeding and energy homeostasis. The conference will broaden the field by covering fundamental advances in the neural circuitry underlying feeding, while including entire sessions devoted to anorexia nervosa, disease cachexia, and feeding disorders across the lifespan. Additionally, while past Keystone Symposia conferences on the neuronal control of appetite have been heavily focused on the hypothalamic control of homeostatic feeding, this symposium will feature entire sessions devoted to brainstem and telencephalic control of feeding.

http://www.keystonesymposia.org/19J8

ATTD 2019

Berlin, Germany, February 20 – 23, 2019

The 12th International Conference on Advanced Technologies and Treatments for Diabetes (ATTD 2019) focuses on technology in diabetes and how healthcare professionals and patients can use those technologies for the best outcomes in treatment. International experts will discuss breakthroughs in diabetes treatments, technological innovations, and showcase the latest developments in new insulin analogues, delivery systems, pumps, glucose sensors, closed-loop systems, and much more. Featuring the International Fair of New Technologies, this conference will highlight start-ups and emerging companies displaying cutting-edge technologies.

https://attd.kenes.com/2019#.W9CXKIWnHbg

World Peptide Congress

April 17–18, 2019, Tokyo, Japan

The World Peptide Congress will bring together world-class biochemists, scientists, professors, and scholars to concentrate on "Accelerating Current Innovations in Peptide Research." Peptides play important roles in living body systems by controlling, directing, and coordinating inter- and intra-cellular communications and cellular function and this conference will focus on the latest stimulating patterns and advancements in the field of peptide science.

https://www.meetingsint.com/conferences/peptide

DASHBOARD

Cancer survivors can experience the entire gamut of endocrine disorders, affecting all endocrine organs, so it was not feasible to address the full spectrum of adverse outcomes in a single guideline. Therefore, we decided to focus on disorders of growth and anterior pituitary function in this initial guideline as they are among the most common endocrine disorders seen."

> - CHARLES A. SKLAR, MD, Memorial Sloan Kettering Cancer Center, New York, who chaired the guideline committee that wrote "Hypothalamic-Pituitary and Growth Disorders in Survivors of Childhood Cancer: An Endocrine Society Clinical Practice Guideline" in "Staying Alive" on page 38.



PRESIDENTIAL ARCHIVES

Rosalyn Sussman Yalow

1978-1979 Endocrine Society President

Rosalyn S. Yalow, PhD (1921 – 2011) was a medical physicist who co-developed the radioimmunoassay (RIA) technique for measuring hormones and other biological substances and became the second woman to win the Nobel



Prize in Physiology or Medicine (together with Roger Guillemin and Andrew Schally.) RIA ushered in a new era in the field of endocrinology, making possible major advances in diagnosing and treating hormonal problems related to diabetes, growth, thyroid function, and fertility. Five years after she received the Nobel, Yalow spoke to a group of schoolchildren about the challenges and opportunities of a science career. "Initially, new ideas are rejected," she told them. "Later they become dogma, if you're right. And if you're really lucky you can publish your rejections as part of your Nobel presentation!" The number of people with diabetes that will be left without insulin by 2030. By 2030, 79 million adults with type 2 diabetes are expected to need insulin to manage their condition and if current levels of access remain, only half of them will be able to be able to get an adequate supply.

-SOURCE: LANCET DIABETES AND ENDOCRINOLOGY



YEARS

MILLION

The number of babies born in the U.S. between 1987 and 2015 through the use of IVF or other assisted reproductive technologies.

- SOURCE: U.S. SOCIETY OF ASSISTED REPRODUCTIVE TECHNOLOGY

The gap between the life expectancy of the richest and poorest sectors of society in England, according to new research. The life expectancy of women in the most deprived communities was 78.8 years compared to 86.7 years in the most affluent group. For men, the life expectancy was 74.0 years among the poorest compared to 83.8 years among the richest.

- SOURCE: LANCET PUBLIC HEALTH





CLAIM MOC POINTS

As a board-certified physician, you need to earn 100 MOC points every five years. The end of 2018 marks the first five-year deadline since the implementation of ABIM's continuous MOC program. Claim your points by December 31, 2018, from any 2018 Endocrine Society educational activities you participated in.

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For the fourth year running, *Endocrine News* talks to editors from Endocrine Society publications to get the scoop on the top endocrine discoveries of 2018.

rogress, as they say, is slow, an axiom perhaps nowhere truer than in the field of medicine. Achieving major breakthroughs can take decades of research and scientific effort. But when that "Eureka!" moment does come, it should be duly recognized. This article compiles highlights from what stood out to eight editors from *The Journal of Clinical Endocrinology & Metabolism* (JCEM), *Endocrine Reviews*, and *Journal of the Endocrine Society* (JES) as the most important endocrinology studies of 2018.

Although remaking the field in a single swoop is not likely to happen, it is hard to overstate the enormous leaps forward that endocrinologists made this year, publishing vital research that will ultimately improve peoples' lives. From developing new clinical tools, to unmasking health threats, to elucidating new intracellular communication pathways, to clarifying disease mechanisms, taken together, these important breakthroughs provide a snapshot of this year's unalloyed endocrinology gold.

Testosterone Therapy Explained

As reported in *Endocrine News*' 2017 "Eureka!" article, Alvin M. Matsumoto, MD, professor at the University of Washington, associate director of the VA Puget Sound Geriatric Research, Education and Clinical Center and an associate editor for JCEM, cited several male reproductive endocrinology papers from The Testosterone Trials as well as one reporting on a harmonized reference range for testosterone levels as landmark achievements. This year, he highlights new guidelines that provided important clinical implications of those collective findings. "The revised Endocrine Society guideline on testosterone treatment of men with hypogonadism is an important ongoing clinical contribution to the field," Matsumoto says. "Testosterone Therapy in Men with Hypogonadism: An Endocrine Society Clinical Practice Guideline," by Bhasin, S., et al. (an Endocrine Society-appointed task force of 10 medical content experts including Matsumoto and a clinical practice guideline methodologist) and published in JCEM in March, updates 2010 guidelines with graded, evidence-based differences regarding how hypogonadism is diagnosed and managed. In short, the diagnosis is made in men who demonstrate signs and symptoms of testosterone deficiency as well as "unequivocally and consistently low serum testosterone concentrations." Relatedly, using accurate assays for measuring testosterone and repeating those measurements is essential, which is now possible in part owing to "Harmonized Reference Ranges for Circulating Testosterone Levels in Men of Four Cohort Studies in the United States and Europe," by Travison, T.G., et al., one of the studies Matsumoto cited for last year's wrap-up.

In men meeting the criteria, testosterone therapy is recommended, particularly in men with diseases of the hypothalamic-pituitary-testicular system; however, in men planning fertility or with certain cancers or other enumerated conditions, testosterone therapy is not recommended. Additionally, for men ages 65 years and older, testosterone therapy should not be routinely prescribed; rather, its appropriateness should be gauged on a case-by-case basis after explanation of the uncertainties of the long-term risks and benefits of treatment.





In "Effects of Aspirin for **Primary Prevention in Persons** with Diabetes Mellitus," by the ASCEND Study Collaborative Group, 15,480 adults with diabetes but without CVD were randomized to receive 100 mg of aspirin daily or matching placebo. Over the course of about seven years, those in the aspirin group experienced significantly fewer vascular events, including MI, stroke or transient ischemic attack. or death from any vascular cause than those in the placebo group; however, they experienced significantly more major bleeding events, such as intracranial hemorrhage, sight-threatening bleeding event in the eye, gastrointestinal bleeding, or other serious bleeding. One of the most significant aspects of the new guideline is its emphasis on patient education and shared decision making between patient and provider. In "Ungraded Good Practice Statements," the task force underscores the importance of explaining potential risks and benefits of therapy and any associated concerns to the patient in order to keep these fundamental good practices front-of-mind for clinicians. "Like most areas of medicine, hypogonadism and testosterone treatment is an area where evidence is incomplete," Matsumoto says. "The Endocrine Society clinical practice guideline provides an ongoing, up-to-date summary of evidence and the quality of evidence that clinicians can use to inform their practice. Guidelines are not cookbooks; they can only supplement, not be a substitute for, good clinical judgment."

Three More Reasons to Stay Heart Healthy (and a Cautionary Tale on Aspirin)

Also an associate editor for JCEM as well as professor at the University of Colorado Anschutz Medical Campus in Aurora, Robert H. Eckel, MD, selected four cardiovascular papers, two published in *JAMA*, and two from the *New England Journal of Medicine* as the studies he found most impactful in endocrinology this year.

From the April issue of *JAMA*, "Association Between Baseline LDL-C Level and Total and Cardiovascular Mortality After LDL-C-lowering: A Systematic Review and Meta-analysis," by Navarese, E.P., et al., showed that lowering low-density-lipoprotein cholesterol (LDL-C) in patients with higher baseline LDL-C levels reduced mortality from cardiovascular events as well as of total mortality. Nearly 300,000 patients from 34 trials were treated with either intensive or less-intensive LDL-C-lowering therapy consisting of statin only (less intensive) or some combination of higher-dose statins, ezetimibe, and proprotein convertase subtilisin-kexin type 9 (PCSK9)-inhibiting monoclonal antibodies (intensive). Meta-regression showed that the intensive LDL-C-lowering therapy reduced mortality as well as the secondary end points of myocardial infarction (MI), cerebrovascular events, revascularization procedures, and major cardiovascular events.

"All-cause mortality reduction is what we all want," Eckel says. "LDL-C being higher before lowering is the best predictor."

66 Like most areas of medicine, hypogonadism and testosterone treatment is an area where evidence

is incomplete. The Endocrine Society clinical practice guideline provides an ongoing, up-to-date summary of evidence and the quality of evidence that clinicians can use to inform their practice. **Guidelines**

are not cookbooks; they can only supplement, not be a substitute for, good clinical judgment."

> — ALVIN M. MATSUMOTO, MD, PROFESSOR, UNIVERSITY OF WASHINGTON; ASSOCIATE DIRECTOR, VA PUGET SOUND GERIATRIC RESEARCH, EDUCATION AND CLINICAL CENTER, SEATTLE; ASSOCIATE EDITOR, JCEM

"Association of Cardiovascular Health Level in Older Age with Cognitive Decline and Incident Dementia," from the August issue of *JAMA*, by Samieri, C., et al., definitively answered the question many have long wanted to know: Does the suspected association really exist?

In a French cohort study, 6,626 individuals ages 65 years or older without history of cardiovascular disease (CVD) or dementia at baseline in 1999 had systematic in-person neuropsychological testing through 2016. Using the American Heart Association's "My Life's Simple 7" tool, researchers scored participants with a total derived from values assigned to each of the tool's seven metrics. Optimally, these are being a nonsmoker; having a body mass index <25; regularly engaging in physical activity; eating fish twice a week or more and fruits and vegetables at least three times a day; and maintaining cholesterol <200 mg/dL, fasting glucose <100 mg/dL, and blood pressure <120/80 mm Hg. Participants were also given a global cardiovascular health score. The more optimal cardiovascular health metrics a person exhibited correlated with lower risk of cognitive decline.

"CVD risk factor control is among the best things we can do to stave off what we all do not want — loss of memory as we age," Eckel says. "Also stay active and use your brain."

The two studies from *NEJM*, published in August and October, respectively, concern type 2 diabetes and cardiovascular health. In "Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus," by the ASCEND Study Collaborative Group, 15,480 adults with diabetes but without CVD were randomized to receive 100 mg of aspirin daily or matching placebo. Over the course of about seven years, those in the aspirin group

experienced significantly fewer vascular events, including MI, stroke or transient ischemic attack, or death from any vascular cause than those in the placebo group; however, they experienced significantly more major bleeding events, such as intracranial hemorrhage, sight-threatening bleeding event in the eye, gastrointestinal bleeding, or other serious bleeding.

The upshot, according to Eckel is: "Aspirin may work in reducing CVD events in high-risk patients with diabetes without known CVD disease, but not without more risk of serious bleeding; so, in general, don't go there."

"Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes," by Rawshani, A., et al., investigated whether reducing type 2 diabetes patients' high risk of death and cardiovascular events is possible. The researchers matched up 271,174 Swedish patients with type 2 diabetes with 1,355,870 controls according to age, sex, and county. They then assessed the type 2 diabetes group for the presence of five risk factors - elevated glycated hemoglobin and LDL-C levels, albuminuria, smoking, and high blood pressure - and followed-up for about five years to quantify the risk for adverse outcomes including death, MI, stroke, and hospitalization for heart failure) as well as to explore how each of the five risk factors is linked with those outcomes. They found that a high glycated hemoglobin level was the strongest predictor of stroke and MI, and smoking was the strongest predictor of death in patients with type 2 diabetes. On the upside, patients with type 2 diabetes whose five riskfactor variables were within target ranges demonstrated the same degree of risk of death, MI, and stroke as that of the control group.



"No surprise," Eckel says, "but fewer CVD risk factors with diabetes leads to better outcomes than more risk factors."

What Does Your Gut Say?

Endocrine Reviews editor-in-chief Daniel J. Drucker, MD, and senior scientist at the Lunenfeld Tanenbaum Research Institute of the Mt. Sinai Hospital in Toronto, Ontario, points to a paper that establishes a direct connection between our guts and our brains. "A Neural Circuit for Gut-Induced Reward," by Han, W., et al., and published in *Cell* in September showed that optogenetic stimulation of vagal sensory neurons that innervate the gut induced dopamine release in mice and motivated them to sustain the resulting reward sensations.

"Gut enteroendocrine cells (EECs) have been classically viewed as sensors of the local nutritional and microbial environment that communicate information via the synthesis and release of circulating peptide hormones," Drucker says. "The current study expands the versatility of EECs to encompass direct and rapid communication with the enteric, peripheral, and central nervous systems via synthesis and release of neurotransmitters and highlights how EECs serve as central cellular relays for transmission of information from the external environment to convey information about nutrient availability, mucosal integrity, and luminal inflammation to distal organs and the peripheral and central nervous systems."

Exercise Tissue Talk

Also from *Endocrine Reviews*, associate editor Gregory R. Steinberg, PhD, and professor of medicine at McMaster University in Hamilton, Ontario gives "Extracellular Vesicles Provide a Means for Tissue Crosstalk during Exercise" top billing. By Whitham, M., et al., and published in *Cell Metabolism* in January, this study lends further credence to the notion that tissues communicate via signaling proteins circulating in extracellular vesicles (EVs).

"It is now well established that exercise elicits beneficial effects across the entire body, but how a contracting muscle communicated directly with other organs to exert these effects was not understood," Steinberg says. In the current study, Whitham and colleagues used high-performance liquid chromatography tandem mass spectrometry to identify muscle-derived cytokines (myokines) that are packaged within EVs and released from contracting muscles during cycling.

They found that more than 300 proteins were increased with cycling and that the EVs tend to cluster in the liver. More research to identify their function is planned. In the meantime, the existence of an exercise-induced EV proteome suggests that inter-tissue communication during exercise stimulates essential biologic processes at the cellular level. "These may be important for mediating the beneficial effects of exercise across the body," Steinberg says.

High Plasma Leptin and Frailty in Older Adults

Four associate editors for the *Journal of the Endocrine Society* weighed in with their selections, each taken from JES.

Takashi Kadowaki, MD, PhD, and principal investigator at the Kadowaki Lab at the University of Tokyo Hospital in Japan chose two articles. In "Plasma Leptin Concentration and Sympathetic Nervous Activity in Older Adults with Physical Dysfunction," by Shibasaki, et al., published in September, researchers examined the relationship between plasma leptin concentration, physical function, and sympathetic nervous system activity in 69 frail Japanese adults 75 years old and older. They found that a higher plasma leptin level is significantly negatively associated with physical function, independent of age, sex, and body mass index. No correlation was found, however, between plasma leptin levels and the sympathetic nervous system, possibly due to the participants' older ages.

Furthermore, leptin concentration was higher in obese subjects with muscle wasting, suggesting a failure of the sympathetic nervous system's feedback system. "This study represents an interesting contribution to the knowledge about the relationships between leptin and autonomic cardiovascular regulations and metabolic status in obese sarcopenia," Kadowaki says.

Diabetes Exacerbates Tuberculosis

Kadowaki also mentioned "The Negative Clinical Impact of Diabetes on Tuberculosis: A Cross-Sectional Study in New Jersey," by Lardizabal, A., et al. "In this article, researchers have revealed an important correlation of tuberculosis (TB) and diabetes in the U.S. compared to previous reports in different places globally," Kadowaki says. "The authors have provided a cross-sectional comparison of tuberculosis cases with and without diabetes in a TB clinic," he says. After excluding TB patients with HIV infection, they reviewed 73 cases of TB and found that extent of disease on chest x-ray was higher for diabetes-positive cases compared to diabetes-negative cases and that diabetes-positive cases had higher evidence of cavitation on chest x-ray and were slightly more likely to have positive sputum cultures than diabetes-negative cases.

"The paper offers a clinical look at tuberculosis in the United States that might otherwise be overlooked," Kadowaki says.

Transgender Population Health

Another JES associate editor, Ana Claudia Latronico, MD, PhD, and professor at Sao Paulo University in Brazil, selected "Health and Cardiometabolic Disease in Transgender Adults in the United States: Behavioral Risk Factor Surveillance System 2015," by Nokoff, N.J., et al., and published in April. In an effort to fill an information gap on a burgeoning population, this study used national survey data to look at differences in cardiometabolic disease among subgroups of transgender adults including femaleto-male (FTM), male-to-female (MTF), and gender nonconforming (GNC) as well as compared these differences with the health status of cisgender adults in the U.S.

Researchers found that, compared to cisgender adults, the FTM subgroup was less likely to be insured. They also found that GNC-F adults were more likely to have poor mental and physical health than cisgender women. Although they expected to find that the MTF subgroup would have higher rates of MI than both cisgender women

66 ...Researchers have revealed an important correlation of tuberculosis (TB) and diabetes in the U.S. compared to previous reports in different places globally. The authors have provided a crosssectional comparison of TB cases with and without diabetes in a TB clinic."

— TAKASHI KADOWAKI, MD, PHD, PRINCIPAL INVESTIGATOR, KADOWAKI LAB, UNIVERSITY OF TOKYO HOSPITAL, JAPAN



and men, they found instead that MTF had more MI than only cisgender women.

These findings expose an urgent need for additional study on how best to support the health of the growing transgender population as well as to learn more about the effects of hormone therapy, which a large segment of transgender people use, on cardiovascular health.

Novel Indian Hedgehog (IHH) Gene Mutations Implicated in Growth Disorders

Latronico also mentioned a JCEM paper in pediatric endocrinology from February. "IHH Gene Mutations Causing Short Stature with Nonspecific Skeletal Abnormalities and Response to Growth Hormone Therapy," by Vasque, G.A., et al. "It is an excellent paper with novel findings in the genetic of short stature," Latronico says. Among 290 patients with autosomaldominant short stature, researchers performed whole exome sequencing to screen for defects in the IHH gene that regulates endochondral ossification. They uncovered 10 variants that were present in higher numbers than in cohorts without a growth disorder. Some phenotypes had a good response to recombinant human growth hormone therapy.

Detection Bias in Adrenal Adenoma

JES associate editor Paul M. Stewart, MD, FRCP, FMedSci, executive dean and professor at the University of Leeds School of Medicine in the United Kingdom, chose "The Lateralizing Asymmetry of Adrenal Adenomas," by Hao, M., et al., from March.

In cross-sectional and longitudinal studies of 1,376 patients, Hao et al., found that left-sided adenomas were discovered in 65% of patients, right-sided adenomas in 21%, and bilateral adenomas in 14%. Among unilateral adenomas, 75% were left-sided. Notably, left-sided adenomas were significantly more prevalent than right-sided adenomas in each size except the largest, at \geq 30 mm, which suggests that right-sided adenomas may be harder to find, rather than being rarer.

"This study has a surprising outcome and highlighted the predominance of left-sided adrenal adenoma diagnosis, something that many endocrinologists (including myself) had not even thought about," Stewart says. "One would expect a 50:50 split in adrenal adenomas across the right and left glands as in, for example, in other bilateral organs such as breast and testicular cancer, but this has not been the case and has important clinical consequences."

Apart from raising the obvious question of "why," the implications are that adenomas may be getting missed by clinicians. In the case of right-sided disease, this could mean that the tumor has progressed to a large size by the time of diagnosis. Additionally, when bilateral disease is unrecognized, associated conditions will be more difficult to identify and treat. Hao and team urge clinicians to be aware of the lateralizing detection asymmetry while evaluating imaging of patients with adrenal adenomas. This study has a surprising outcome and highlighted the predominance of left-sided adrenal adenoma diagnosis, something that many endocrinologists (including myself) had not even thought about. One would expect a 50:50 split in adrenal adenomas across the right and left glands as in, for example, in other bilateral organs such as breast and testicular cancer, but this is not been the case and has important clinical consequences."

> - PAUL M. STEWART, MD, FRCP, FMEDSCI, EXECUTIVE DEAN AND PROFESSOR AT THE UNIVERSITY OF LEEDS SCHOOL OF MEDICINE IN THE UNITED KINGDOM; ASSOCIATE EDITOR, JES

BPA: Stay Away!

Finally, "Experimental BPA Exposure and Glucose-Stimulated Insulin Response in Adult Men and Women," by Stahlhut, R.W., et al., published in October, was chosen by JES associate editor Bülent O. Yildiz, MD, professor at Hacettepe University School of Medicine in Ankara, Turkey, as his top JES pick of 2018. On the basis of findings from animal studies as well as cross-sectional and epidemiological studies in humans that demonstrated disrupted glucose homeostasis on exposure to bisphenol A (BPA), researchers investigated whether BPA alters insulin/C-peptide secretion in humans, using a dose of 50 μ g/ kg body weight, the amount considered the maximum safe daily dose by both the U.S. Food and Drug Administration and the Environmental Protection Agency.

In two exploratory cross-over studies, non-diabetic participants were tested with and without oral BPA exposure (and thus served as their own controls). In the first experiment, eight healthy young men took the oral glucose tolerance test so that researchers could measure early and late-phase insulin response. Serum HbA1c demonstrated marked within-subject differences in insulin and C-peptide levels between BPA and control sessions. In the second, five men and three postmenopausal women (including a study author) were tested with the hyperglycemic clamp, which allowed glucose to be stabilized prior to dosing of BPA or control, and only late response measured. These results did not replicate the strong positive relationship between HbA1c and the change in insulin response between BPA and control sessions from the first experiment, but they did show the opposite — a significant percentage decrease between control and BPA sessions in late-phase insulin and the maximum concentration of C-peptide as well as an inverse relationship between the percentage change in later-phase C-peptide with HbA1c.

Although this study created some controversy, its implications for U.S. regulatory entities are quite clear. What has been considered a safe dose of exposure, in fact, alters the insulin/ C-peptide response to a glucose challenge (by at least a couple of different mechanisms), which may suggest that BPA plays a role in triggering insulin resistance. Clinically, this suggests that anyone predisposed to insulin resistance might consider finding ways to reduce BPA exposure.

HORVATH IS A FREELANCE WRITER IN BALTIMORE, MD., AND A FREQUENT *ENDOCRINE NEWS* CONTRIBUTOR. SHE WROTE ABOUT THE LINK BETWEEN OBESITY AND BREASTFEEDING IN THE SEPTEMBER ISSUE.

NAKING

Breakthroughs in Adrenocortical Carcinoma

With a brutal five-year survival rate below 40%, adrenocortical carcinoma is not only rare, it is also somewhat misunderstood. New research may shed light on this condition and even provide a path to future treatment options.

BY KELLY HORVATH

drenocortical carcinoma (ACC) is an aggressive orphan malignancy that confers a less than 35% survival rate at five years. In addition to its aggressiveness, up to 60% of ACC is associated with hormonal access, with patients presenting with Cushing syndrome (hypercortisolism), Conn syndrome (hyperaldosteronism), or virilization in women (androgen excess). Many patients present late and with metastatic disease, which contributes to poor survival. Surgical resection is first-line therapy, but many tumors are unresectable or recur. Other treatments for ACC have been shown to have minimal benefit, ACC being a devastating diagnosis.

Although it is rare (with an incidence of 0.7-2.0 cases/million habitants/ year), in 2013, four patients with ACC were seen at the University of Colorado Hospital's CU Cancer Center in Denver, providing clinicians and researchers with an unusual opportunity to gain insight into the disease. They were seeking treatment by a multidisciplinary team led by Margaret E. Wierman, MD, and Stephen Leong, MD, co-directors of an Adrenal Neoplasm Program forging new territory in the field. Katja Kiseljak-Vassiliades, DO, had joined Wierman's lab as a fellow, to explore mechanisms of endocrine tumorigenesis, which has been her interest since early in medical training. "The mechanisms of endocrine tumorigenesis seem to be different than those of classic human malignancies," she explains. "In pituitary tumors, for example, some of the molecular mechanisms that we see even in advanced malignancy are present, such as epithelial mesenchymal transition, although these tumors never metastasize. So, I think we can learn from these indolent tumors and inform common human malignancies by understanding what the differences are and, with the most aggressive tumors, such as adrenocortical carcinoma and anaplastic thyroid carcinoma, how the molecular signature affects cancer growth and prognosis."

Preclinical Models Move the Field Forward

When the four patients with ACC presented to the clinic, Kiseljak-Vassiliades says, "we quickly realized that there were no good treatments for these patients. Our team examined what kind of preclinical models and research were available in adrenal cancer. However, progress was slow because preclinical models were scarce, with no animal models available." The team at CU started treating the patients with mitotane, an insecticide-based adrenolytic and currently the only FDA-approved drug for adrenal cancer, and communicated with other adrenal cancer experts around the country, including Gary Hammer, MD, at the University of Michigan Rogel Cancer Center in Ann Arbor and Mouhammed Habra, MD, FACP, FACE, from the MD Anderson Cancer Center, in Houston, Texas, to establish an effective clinical protocol.

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I think we can learn from these indolent tumors and inform common human malignancies by understanding what the differences are and, with the most aggressive tumors, such as adrenocortical carcinoma and anaplastic thyroid carcinoma, how the molecular signature affects cancer growth and prognosis."

- KATJA KISELJAK-VASSILIADES, DO, UNIVERSITY OF COLORADO HOSPITAL, CU CANCER CENTER, DENVER

The real breakthrough came when the team collaborated with the gastrointestinal (GI) tumor group including Stephen Leong, MD, and Todd Pitts, MD at University of Colorado, who had developed patient-derived xenografts (PDXs) in colorectal cancer and advised the endocrine team to develop similar models for adrenal cancer. The CU adrenal tumor team's two 2018 studies, "Development of new preclinical models to advance adrenocortical carcinoma research," published in Endocrine-Related Cancer, and "Elucidating the Role of the Maternal Embryonic Leucine Zipper Kinase in Adrenocortical Carcinoma," published in Endocrinology, show how the first two ACC cell lines (CU-ACC1 and CU-ACC2) and two corresponding mouse models of the disease can be used to identify and target potential tumorigenic pathways underlying ACC.

Although attempts at preclinical models had been made before, they were unsuccessful, largely because the animals could not survive the accompanying steroid hormone production when tumors were implanted. Kiseljak-Vassiliades and Adwitiya Kar, PhD, a postdoctoral fellow in the lab, in collaboration with their endocrine surgeons, Christopher Raeburn, MD, and Maria Albuja-Cruz, MD, have been able to implant a variety of ACC tumors "This is a big step for the field," Kiseljak-Vassiliades says. "One of the things that we have really championed here is the technique to create PDXs, which the GI colorectal group has refined."

Got MELK?

Now that the models are available, novel therapies can be sought. "One of the biggest deficiencies in the field right now is lack of targeted therapy. All the therapies used in other cancers that have been tried in ACC have not been very successful in patients, and so our focus has been to find new druggable targets," Kiseljak-Vassiliades says. The team started with identifying the kinases in ACC that have previously shown to have moderate success on other human malignancies. Because most ACC are not associated with targetable genetic mutations, they reasoned that pinpointing problems in the DNA damage response pathway could lead to effective ACC treatment. Analyzing publicly available expression data sets, they found that maternal embryonic leucine zipper kinase (MELK) was one of the most upregulated kinases in adrenal cancer compared to normal tissue. Then, using their newly developed ACC tumor cell lines, they demonstrated that the MELK inhibitor OTSSP167 suppressed tumor growth. Though exciting, still to be tested is what additional therapy should be used along with a MELK inhibitor, as most kinase inhibitors develop resistance eventually, according to Kiseljak-Vassiliades. The team has studies underway to evaluate OTSSP167 more closely and determine what off-target effects it might have along with what other kinases it inhibits. "A single arm kinase inhibitor is probably not going to be the answer," Kiseljak-Vassiliades says, "but it might be something that is going to prolong the patient's life as we are currently trying to find new and better targets."

OTSSP167 is now in phase I studies in solid tumors (mostly breast), and, on the basis of preclinical in vivo data not yet published, the team hopes to move the drug into phase II studies in patients with adrenal cancer once the phase I studies are completed. "Whether giving patients MELK inhibitor would potentially change their outcome or decrease the tumor burden to get them to surgery, is a question we hope to address," Kiseljak-Vassiliades says. "When we studied OTSSP167 in mice, it showed a very modest decrease in tumor size and seemed rather to prevent tumors from progressing."

Humanized Mouse Model

There's more. A third study the team presented at **ENDO 2018** and soon to be submitted for publication details the development of another novel preclinical model in a mouse that has a human immune system derived from cord blood-derived hematopoietic stem cells. The team treated the mouse with either control or immunotherapy with the PD-1 blocking antibody pembrolizumab. The mice receiving the treatment showed significantly lower tumor volume than the control group. The researchers simultaneously treated the ACC patient that the PDX was derived from with immunotherapy, and the patient has had a lasting response with 79% tumor reduction — many metastases disappeared, most of them shrank significantly, and the patient has had no progression or new metastases in the last 18 months.

Call to Arms

"The field is getting excited about these new preclinical models because, for the first time, we can test new drugs and new compounds in preclinical models before going to phase I studies in humans," Kiseljak-Vassiliades says. "It is important to test a drug — even mitotane, that has been approved for patients, should be retested in preclinical models to study its mechanism further and identify which tumor types it would be most efficacious against. Although these studies are moving the field along, the field itself is very behind those of some of the common human malignancies. To make progress, it takes effort and multisite collaboration as well as additional research funding for this orphan endocrine cancer."

HORVATH IS A FREELANCE WRITER IN BALTIMORE, MD., AND A FREQUENT ENDOCRINE NEWS CONTRIBUTOR. SHE WROTE ABOUT NEW RESEARCH TO TREAT PCOS IN THE SEPTEMBER ISSUE.

AT A GLANCE

- For the first time, a team from University of Colorado established two new adrenocortical carcinoma (ACC) cell lines and corresponding patient-derived xenograft (PDX) preclinical models: CU-ACC1 and PDX from a perinephric metastasis in a patient with an aldosterone-secreting tumor and CU-ACC2 and PDX from a liver metastasis in a patient with Lynch syndrome.
- In vivo studies demonstrated that the maternal embryonic leucine zipper kinase inhibitor, OTSSP167, ablated tumor growth in the PDX mouse models of ACC.
- A patient treated with mitotane plus pembrolizumab showed 79% tumor reduction as well as fewer and no new metastases almost two years after starting treatment, demonstrating that immunotherapy may have a role in some patients with metastatic ACC.

ROAD BARRIORS: Endocrine Society Debuts Its Roadshow in Texas

BY JESSICA HARRIS

PEOPLE LIKE YOU CAN'T DO THAT

Genevieve Neal-Perry, MD PhD Professor, Department of Obstetrics and Gynecology and Women's Health Division Director, Reproductive Endocrinology and Infertility

During Neal-Perry's career development talk at Baylor College of Medicine, she highlighted the importance of persevering through adversity.

The Endocrine Society embarked on its first ever roadshow across the Lone Star State to learn directly from members how it can better support basic scientists, early career members, and trainees in reaching their career goals, as well as how to improve the member experience for the broad range of professionals who call the Society their scientific home. hat do a neuroscientist, a diabetes nurse, and a transgender endocrinologist have in common? They all call the Endocrine Society their professional and scientific home.

A global organization of over 18,000 members, the Endocrine Society is unique in its inclusiveness. Our members come from 122 countries, bringing their expertise to every facet of the endocrine field. They are clinical, basic science, and translational medicine investigators, healthcare providers, and educators who cover the spectrum of career stages from students to emeritus professors. They not only lead breakthrough discoveries, they also apply this knowledge in the treatment of their patients with hundreds of hormonerelated conditions such as diabetes, obesity, osteoporosis, thyroid disorders, and infertility.

But while this professional diversity is one of our strongest assets, it has also presented the organization with a challenge. At a time when endocrine scientists and endocrinologists look for ways to focus on their particular areas of expertise, the value of being part of a global community may appear less important. So, how can we maintain that personal touch for each of our 18,000+ members around the world? How can we help each of our members be successful in their various career tracks, and in so doing, make endocrinology a more attractive field for graduate students and medical residents? And, how can we ensure that we remain the professional home for so many different groups of experts? As it turns out, the most effective way to answer these questions is also the most straightforward: go to our members and ask.

Welcome to the Endocrine Society Roadshow.

What is the Roadshow?

A cross between an educational outreach program and a real-time member survey, the Endocrine Society Roadshow is a series of in-person visits to laboratories, clinics, hospitals, and academic institutions. During these visits, our leadership and staff meet with faculty, students, and trainees in a variety of formats that range from seminars to roundtables to one-on-one meetings.

In addition to meeting with members, the Roadshow team



Genevieve Neal-Perry, MD, PhD, Rona Yoffe Sonabend, MD, Assistant Professor at Baylor College of Medicine, Stephanie Sisley, MD, Assistant Professor at Baylor College of Medicine, and Robert Lash, MD, at Texas Children's Hospital discussing Baylor's innovative approaches to trainee education.



Lash with Society member Philipp E. Scherer, PhD, in his diabetes lab discussing ways to improve **ENDO** 2019 for basic scientists. also meets with institutional staff who specialize in professional development, diversity and inclusion, and educational curricula. The goals of the Endocrine Society Roadshow are simple: to meet members where they are – their labs, their clinics, their offices – to learn about their work, to discuss how we can improve the member experience, and to understand how we can best support our members at all stages of their careers. By meeting with all of these groups where they work and learn, we gain unique insight into the opportunities and challenges that our members encounter in their day-to-day lives.

The inaugural Endocrine Society Roadshow stops took place October 24-26, 2018 at Baylor College of Medicine (Houston, TX) and University of Texas Southwestern Medical Center (Dallas, TX). Over these three days, our vice president of basic science, Genevieve Neal-Perry, MD, PhD, professor of obstetrics & gynecology, University of Washington, Seattle, and our chief professional and clinical affairs officer Robert Lash, MD, gave talks to basic science and clinical audiences, met members in their offices, toured their labs, and held roundtable sessions with graduate and postdoctoral students and fellows.

First Stop: Houston

The Endocrine Society Roadshow got off to a great start at Baylor College of Medicine (BCM) in Houston. Hosted and organized by members Carolyn Smith, PhD, professor, molecular & cellular biology and senior associate dean of graduate education, and Marco Marcelli, MD, professor, medicine and interim section chief, endocrinology, the itinerary included a career development talk for graduate students as well as meetings with career development staff, endocrine fellows, and pediatric endocrinologists at Texas Children's Hospital.

In Neal-Perry's career development talk, "People Like You Can't Do That," she described her own journey through graduate and medical schools, why she became an Endocrine Society

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Mentors are critical to your success, but they cannot fix all of your problems.

You are equally responsible and you have to be an active, not passive, participant in your career development. But at the end of the day, it's not whether you get knocked down; it's whether you get back up again and press forward."

— GENEVIEVE NEAL-PERRY, MD, PHD, PROFESSOR OF OBSTETRICS & GYNECOLOGY, UNIVERSITY OF WASHINGTON, SEATTLE; VICE PRESIDENT OF BASIC SCIENCE, ENDOCRINE SOCIETY

member, and the value the Society brings to trainees and early career faculty. She gave advice to the students in the room about the importance of perseverance, having multiple mentors, and the power of networking. "Mentors are critical to your success," she emphasized, "but they cannot fix all of your problems. You are equally responsible and you have to be an active, not passive, participant in your career development. But at the end of the day, it's not



Standing room only at Neal-Perry's talk at UTSW.



The line for Neal-Perry's talk at UTSW.

whether you get knocked down; it's whether you get back up again and press forward."

Next Stop: Dallas

After visiting Baylor College of Medicine, the Roadshow team traveled to Dallas to meet with members at University of Texas Southwestern Medical Center (UTSW). Society members Carole Mendelson, PhD, professor, biochemistry and obstetrics & gynecology and former Society vice president, basic science, and Perry Bickel, MD, chief, Division of Endocrinology, organized a busy two-day itinerary that included a basic science talk, endocrine grand rounds, a women's faculty reception, career development roundtables with postdocs and endocrine fellows, and several one-on-one meetings with basic science and clinical members.

One major highlight of the visit was Neal-Perry's basic science talk, "Vitamin D and Female Reproduction: A Role Beyond Bone Health," which was delivered to a packed room of UTSW faculty, graduate students, and postdoctoral trainees. Following the talk, Neal-Perry held a roundtable discussion with a group of those students where she learned about their research, spoke about her own background in endocrine science, and highlighted career development opportunities that the Endocrine Society offers young scientists. Neal-Perry



666 Many [graduate students and postdoctoral trainees] don't even realize that they are performing endocrine research. I am concerned that our students are too narrowly focused in their training and lack the breadth that I believe necessary to survive in today's basic research environment."

 CAROLE MENDELSON, PHD, PROFESSOR, BIOCHEMISTRY AND OBSTETRICS & GYNECOLOGY, UNIVERSITY OF TEXAS SOUTHWESTERN, DALLAS advised trainees that many of the career development opportunities offered to our members also serve as the foundation on which they can build their national and international presence, a metric often used for promotion.

A recurring theme throughout the Roadshow team's discussions with basic scientists and program directors was that many students and faculty define their research too narrowly, which can limit their careers and ultimately weaken the endocrine field. "Many [graduate students and postdoctoral trainees] don't even realize that they are performing endocrine research," Mendelson says. "I am concerned that our students are too narrowly focused in their training and lack the breadth that I believe necessary to survive in today's basic research environment."

For Mendelson, the comprehensive topic of Neal-Perry's talk (i.e., vitamin D and reproductive endocrinology) and the story of her personal journey to become an endocrine scientist were the kinds of topics that students need to hear throughout their training.

The Roadshow team also learned that medical students and residents currently do not have the opportunity to see patients with the breadth of endocrine disorders. "Medical students and residents are not getting enough exposure to the wide range of interesting endocrine disorders," explains Society member and Division chief Perry Bickel, MD, "and this is in part because much of their clinical experience takes place in the hospital, where there is a narrower spectrum of endocrine disease."

Following his Endocrine Grand Rounds talk on gestational diabetes, Lash held an Endocrine Self-Assessment Program (ESAP) review session with a group of endocrine fellows, which highlighted the variety of diseases and conditions that endocrinologists treat. "It was fascinating to hear about [the fellows'] research and clinical interests, and I was particularly impressed with their



The campus of the University of Texas Southwestern Medical Center, located in Dallas, was the second stop on the Endocrine Society's debut Roadshow.

discussions on a difficult set of questions from the Society's ESAP program," Lash says.

Lessons Learned & Looking Ahead

In Texas, the Endocrine Society Roadshow served two main functions: to meet our members (and future members) where they are, and to find out how we can better support our members, particularly basic scientist early career members and trainees. Members were candid in their feedback about how they view the Society and the future of the endocrine field and workforce. Throughout our three days "on tour" a few key messages resonated:

• Members want a personal connection with their Society and its leadership.

• Basic scientists need to know how we can provide value beyond meetings and publications.

• Trainees and early career members want more information on possible career tracks and development opportunities available to them, especially if they want a career outside of a lab.

• Medical students and internal medicine residents need more (and earlier) exposure to different aspects of endocrinology in order to foster an interest in the field and strengthen the endocrine workforce.

Thanks to the success of the inaugural Endocrine Society Roadshow stops, the future of the program is looking bright. Planning has already begun for where we will travel in 2019, and our leadership is eager to engage more of our membership. By learning directly from our members how we can improve their experience with the Society and how we can better support the new generation of endocrine professionals, we demonstrate the value and importance of being part of a united and global endocrine community.

If you're interested in hosting the Endocrine Society at your institution, please contact Jessica Harris at *jharris@endocrine.org* for more information.

HARRIS IS THE SPECIALIST, EXTERNAL POSITIONING AT THE ENDOCRINE SOCIETY. SHE LAST APPEARED IN ENDOCRINE NEWS IN JANUARY WHEN SHE WROTE ABOUT HOW MEMBERS CAN GET INVOLVED WITH THE SOCIETY'S ADVOCACY EFFORTS.

STAYING ALIVE:

Treating

Cancer Survivors

While childhood cancer survival rates continue to climb, there could still be endocrine complications for these survivors in adulthood. A new Endocrine Society guideline lays out screening and treatment recommendations for clinicians who treat these resilient patients.



s cancer therapy continues to improve, the number of survivors of childhood cancers is increasing accordingly. And because up to half of these patients will develop hormone disorders as side effects of their cancer therapy, endocrinologists can expect to see more and more of them.

To help physicians provide state-of-the-art screening and treatment, an expert committee from the Endocrine Society recently published a new clinical practice guideline.

"Our new guideline addresses the growing risk of endocrine disorders among childhood cancer survivors and suggests best practices for managing pituitary and growth disorders commonly found in this population. The guideline stresses the importance of life-long screening of these survivors for earlier detection and optimal patient care," says Charles A. Sklar, MD, of the Memorial Sloan Kettering Cancer Center in New York City, who chaired the guideline committee.

This patient population is projected to continue to grow, as the overall five-year survival rate has climbed to nearly 80%. "For some of the more common cancers, such as acute lymphoblastic leukemia and Hodgkin lymphoma, five-year survival rates are in the 90% range," Sklar says. "It is estimated there will be 500,000 survivors of childhood cancer in the U.S. by 2020."

Focused on Common Disorders

"Cancer survivors can experience the entire gamut of endocrine disorders, affecting all endocrine organs, so it was not feasible to address the full spectrum of adverse outcomes in a single guideline," Sklar says. "Therefore, we decided to focus on disorders of growth and anterior pituitary function in this initial guideline as they are among the most common endocrine disorders seen."

There are some existing guidelines that address this population, but they have been produced mainly by pediatric oncologists and are aimed at general practitioners. This guideline is the first aimed at endocrinologists.

"Our guideline is focused on the treating endocrinologist, so we discuss the kind of testing that is needed, we provide assistance in interpreting the test results, and we give general recommendations for management, which is really above and beyond the existing guidelines," Sklar says. Endocrinologists at a few academic centers with oncology programs see a large number of these patients, but there are many small programs that see fewer patients. "This guideline is really geared to people who encounter these patients infrequently, and feel somewhat insecure in management," Sklar says.

Irradiated Organs

"This guideline applies to a very large group of cancer diagnoses," Sklar says, with the main common denominator being that "radiation is the single biggest culprit in causing endocrine problems." Hypothalamic, pituitary, and growth disorders can follow on the heels of cancers involving brain tumors, tumors of the head and neck, leukemia and other disorders requiring bone marrow transplant, and solid tumors in which patients are exposed to total body irradiation.

"Radiation-induced hypothalamic-pituitary dysfunction is both dose- and time-dependent," Sklar says. "At doses less than 30 Gy, one sees primarily growth hormone deficiency and precocious puberty, whereas at doses greater than 30 Gy, additional deficits of luteinizing hormone/folliclestimulating hormone, thyroid-stimulating hormone, and adrenocorticotropic hormone are seen, often years after the completion of cancer therapy. Although the testing for and treatment of many of these disorders in cancer survivors are like those in the non-cancer population, the guideline emphasizes key differences and unique features and findings that are specific to the cancer survivor."

For example, the guideline recommends that survivors of some cancers should be periodically assessed for central precocious puberty, but that clinicians cannot rely on testicular size as an index of pubertal status in patients who have been exposed to gonadal toxic therapy because they may manifest small testes for their stage of puberty.

Examples of some conditions for which the guideline recommends using the same diagnostic strategy and treatment approach for cancer survivors as the general population include luteinizing hormone/follicle stimulating hormone deficiency, thyroid-stimulating hormone deficiency, and adrenocorticotropic hormone deficiency.

Growth and Growth Hormone

Some of the most detailed and significant sections of the guideline deal with short stature and growth hormone deficiency because "impaired linear growth and short adult height are the most common side effects in survivors exposed at a young age to central nervous system, spinal, or total body irradiation," Sklar says.

The guideline suggests "against using growth hormone in cancer survivors who do not have growth hormone deficiency to treat for short stature and/or poor linear growth following spinal irradiation." It advises using "the same provocative testing to diagnose growth hormone deficiency in childhood cancer survivors as are used for diagnosing growth hormone deficiency in the noncancer population." And it recommends "offering growth hormone treatment in childhood cancer survivors with confirmed growth hormone deficiency" but suggests "waiting until the patient has been one year

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The guideline is a great summary and practical document for endocrine providers. It is also a helpful document for endocrinologists assuming care for adult survivors of childhood cancer to continue the long-term surveillance of various endocrine organ systems impacted by cancer therapy, as most of these patients will continue to experience endocrine-related abnormalities well into adulthood."

> - SOGOL MOSTOUFI-MOAB, MD, MSCE, ASSISTANT PROFESSOR OF PEDIATRICS, DIVISIONS OF ENDOCRINOLOGY AND ONCOLOGY, CHILDREN'S HOSPITAL OF PHILADELPHIA, PHILADELPHIA, PA.

Childhood cancer survivors need to be monitored as they continue into adulthood, to keep an eye out for potential endocrine disorders, as an ongoing screening process over the months and years.

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disease-free, following completion of therapy for malignant disease, before initiating growth hormone treatment."

A meta-analysis done as part of the evidence base for the guideline on whether growth hormone treatment increases the risk of the development of second tumors concluded that there was not sufficient evidence to indicate any risk, although the studies that have been done are limited and the results are somewhat inconsistent. The treatment is not associated with increased risk of recurrence.

Lifelong Screening

Because endocrine problems can surface years after the end of cancer treatment, physicians need to be vigilant in looking for them in some patients. For example, the guideline recommends lifelong annual screening for thyroid-stimulating hormone deficiency and adrenocorticotropic hormone deficiency in childhood cancer survivors treated for tumors in the region of the hypothalamic-pituitary axis and survivors exposed to 30 Gy hypothalamic-pituitary radiation. In the case of growth hormone deficiency, the trigger level for lifelong periodic clinical assessment is 18 Gy.

"The guideline is a great summary and practical document for endocrine providers," says Sogol Mostoufi-Moab, MD, MSCE, assistant professor of pediatrics in the divisions of endocrinology and oncology at the Children's Hospital of Philadelphia, who was not on the committee but reviewed the guideline as it was being prepared. "You can read it, and save it, and go back to it with questions like, 'When do I start screening for various endocrine disorders after radiation or chemotherapy?' and, 'What parameters should I use to establish the diagnosis of growth hormone deficiency in the survivor population and offer treatment?' It is also a helpful document for endocrinologists assuming care for adult survivors of childhood cancer to continue the long-term surveillance of various endocrine organ systems impacted by cancer therapy, as most of these patients will continue to experience endocrine-related abnormalities well into adulthood."

The guideline, titled "Hypothalamic-Pituitary and Growth Disorders in Survivors of Childhood Cancer: An Endocrine Society Clinical Practice Guideline," appeared in the July issue of *The Journal of Clinical Endocrinology* & *Metabolism* and is available online at https://academic.oup.com/jcem/ advance-article/doi/10.1210/jc.2018-01175/5046572

AT A GLANCE

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- Thanks to improvements in treatment, many more patients are surviving childhood cancers

 but as a side effect of their treatment, a large percentage develop endocrine disorders that require intervention.
- In many cases, screening tests and treatment for endocrine disorders are the same for childhood cancer survivors and the general population — but a new Endocrine Society clinical practice guideline specifies the key differences for treating cancer survivors.
- Endocrine problems can surface years after cancer treatment has ended, so clinicians must be aware that the need to monitor these patients continues into adulthood.

Photo Credit: Angela Lucia Photography

The Art of Scientific Storytelling

When you spend the majority of your life at the bench, you might sometimes forget how to tell your story so that you can spend even more time at the bench through grants and papers. Here is a look at what steps you can take to present your research in a dynamic and impactful manner.

Science is neither art nor story. According the traditional academic viewpoint, it is a rigid set of facts and figures. What if I told you that the art of scientific storytelling is a crucial element for the advancement our field? This may lead you to label me as crazy or think that I am not a real scientist. Perhaps I have been cast in a science-themed reality show called Science or Fake News.

BY KAREN D. CORBIN, PHD, RD

I am actually a card-carrying scientist, an expert in human nutrition and metabolism. After 20 years of traversing the worlds of healthcare and science, I realized that a fundamental barrier exists for translating ideas into solutions: the frequent inability of scientists and other "geeks" to deliver information in a way that is impactful, relevant, and inspires action. This led me to an important conviction. By sharing my gift of translating complex scientific information in a way that is accessible to a broad range of audiences, I can exponentially increase my contributions to science by helping others catalyze their ideas. To accomplish that, I launched a brand called Geeks that Speak* to inspire and empower scientists to become powerful storytellers. I believe there are three reasons we need to embrace the art of storytelling within our daily science life.

The standard academic box pushes us to think mainly about one person: me, me, me! What do I need to focus on to advance my own ideas? What do I need to do to advance my own career (i.e., get papers and grants)? This leads us to frequently approach storytelling with an inward focus. We create presentations based on the data we feel is most important and we shove as much data as possible in the time allocated for our talks. If we instead tell stories with an outward focus, we will convey our ideas in meaningful ways that make an impact. This increases our chances of reaching the next member of our study team, an investor, or our next boss.

When we build our own personal science story, we tend to be laser focused on a specific narrow topic. That is how the most successful scientists have made



66...a fundamental barrier exists for translating ideas into solutions: the frequent inability of scientists and other "geeks" to deliver information in a way that is impactful, relevant, and inspires action.

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their mark. In this era of global reach and transdisciplinary science, stories should be built with the intent of solving an important problem. This allows diverse groups of scientists and innovators to bring their best to the table to accomplish a shared goal. By doing this, we change the narrative away from the narrow and predictable and towards solution-based approaches that require out-of-the-box innovation. This will lead to ideas that go far beyond those tucked away in the corners of our laboratories.

By far the most important reason why scientific storytelling is not just a trend or an unnecessary waste of time is simple yet profoundly relevant in today's society: Scientific knowledge is powerful. It has the power to heal, the power to give hope, the power to solve the most important problems facing our society. And with great power, comes great responsibility. We have a duty to share what we know. When we do this, we advance our career trajectory, accelerate innovation, and empower society to make better decisions about their lives.

We live in an era of abundant information. Any question can be answered with a search engine that resides in a device that fits into the palm of our hand. This apparent era of knowledge that we live in comes with a huge caveat. Volume of information does not equate to accuracy of information. People today are hungry for truth. Who better to share that truth than those of us who spend our careers in search of it?

To improve the reach of our brilliance, there are three key steps to take:

- First, focus on developing a talk that meets the needs of your audience: What do they know and what additional knowledge can you impart that will be beneficial to them?
- The second has to do less with what you say and more with how you say it. Body language elements such as gestures and eye contact are some of the non-verbal aspects of presentations that elevate the storytelling game.
- Finally, crafting the message with basic elements of traditional storytelling allows the audience to follow the main points with ease. When conveying scientific information, key points should be unambiguously conveyed and build on one another with smooth transitions in between.



You probably have your own hypothesis on the value of spending time refining your storytelling skills. If so, do an experiment to test your hypothesis. Implement some of my recommendations and gather data on how the presentation was received, how you felt after you delivered the information, and the benefits of moving away from "I just want to get this over with" and towards "How can I convey information in a meaningful way to inspire action?" Do it three times to reach statistical significance and let me know what you conclude.

I am confident the experiment will lead you to a different attitude towards storytelling that will enrich your career and broaden your impact on the process of discovery.

Corbin is a faculty investigator at the Translational Research Institute for Metabolism and Diabetes, Orlando, Fla., focusing on nutrition, enterohepatic metabolism, and the mechanisms that drive individual susceptibility to metabolic diseases. She is also the owner and chief geek of Geeks That Speak[®], a company dedicated to maximizing the impact of science through the art of storytelling. She can be reached at geeksthatspeak@gmail.com.

What the Results of the Midterm Elections Mean for Endocrinology

The results of the midterm elections are in. Democrats regained majority in the House of Representatives; Republicans picked up additional seats to grow their majority in the Senate. But what do these results mean for endocrinology and the Endocrine Society's advocacy agenda? To answer these questions, we examined the election results along with the Congress's plans for its agenda.



Midterm Election Results

It wasn't quite the tsunami the Democrats were hoping for, but congressional analysts agree it was at least a slow-rolling ripple, if not a blue wave. The Democrats regained their majority in the House of Representatives. They needed to pick up 23 seats and ended up gaining 39 leaving them with 234 seats to the Republicans' 201. Republicans, however, gained more seats to widen their majority in the Senate ending up with 53 seats to the Democrats' 47. Big losses for the Democrats, especially in what many called "The Year of the Woman," were the defeats of Senators Heidi Heitkamp (D-ND) and Claire McCaskill (D-MO).

There are several important conclusions to draw from the election results. First, we will have a divided Congress with Democrats in the majority in one chamber and Republicans in the majority in the other. Not only will this make it more difficult for President Trump to achieve his legislative goals, but the divided Congress could be even more partisan than we have seen over the last two years and it could lead to gridlock. Because the margins remain relatively close in both chambers, to get legislation passed will require some bipartisan negotiation. This, alternatively, may lead to some bipartisan victories where there is a common mission.

Another clear message we heard at the polls was that healthcare was the most significant issue that voters were thinking about. In exit polling, 50% said healthcare was the most important issue compared with 27% who said it was the economy. Eighty percent of all voters see reducing healthcare costs as the number one priority for the new Congress. Obviously, this will impact our priorities and agenda by elevating our issues, but before we look at how this will impact the new Congress, let's look at what is ahead during Congress's Lame Duck session in November and December.

Lame Duck Session

Before the 116th Congress sworn in in January, the current Congress had to come back to Washington and finish up work it did not complete before the elections. Both chambers returned after Thanksgiving and are scheduled to work until mid-December to contend with several must-pass pieces of legislation, policy fights, and leadership battles.

The top item of business during the Lame Duck is Congress has to prevent a partial government shut-down. Seven appropriations bills were left unfinished before the elections and while Congress passed a temporary stopgap bill to keep the government funded, this will expire December 7. Although funding for the National Institutes of Health (NIH) and much of the Department of Health and Human Services was settled in September, funding has not been finalized for the Food and Drug Administration, Indian Health Service, and several other parts of the government. Complicating the appropriations process is that President Trump has threatened to shut down the government if he does not get the funding he seeks to support a border wall. In addition, some senators have also threatened a standoff unless legislation is passed to protect the Mueller investigation.

In addition to appropriations, the Senate also has to deal with dozens of executive and judicial nominations and several pieces of "must pass" legislation, including reauthorization of the Violence Against Women Act, the Farm Bill, and disaster relief

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legislation. Congressional attention on these issues means the Congress will be somewhat distracted from our policy priorities during the Lame Duck.

Issues for New Congress

As noted above, healthcare dominated voter decisions, so healthrelated issues are likely to take center stage in the new 116th Congress. Here is how we think these issues will fare:

- Appropriations For last few years, we have achieved funding increases for the NIH. Unfortunately, other public health programs like prevention, workforce training, and education, have not gotten as much love from Congress. In the new Congress, Democrat Nita Lowey (D-NY) will become chair of the House Appropriations Committee and Rosa DeLauro (D-CT) will be chair of the L-HHS Appropriations Subcommittee. Both will be in a better position to allocate more money for public health, but that still will not be so easy because the two-year budget deal that raised spending caps imposed by the Budget Control Act of 2011 is to due expire next year. Absent another budget deal, non-defense discretionary programs face statutory cuts of \$55 billion in FY 2020 (about 10% below current spending). Consequently, even with Democrats in the majority in the House, we will have to continue to advocate for funding increases and for raising spending caps.
- Obamacare/Affordable Care Act (ACA) The ACA remains a divisive and politically charged issue. Despite agreement on both sides that there are problems to be addressed and that the law should be updated, doing so will be difficult in a divided Congress. Democrats may try to block or amend administration rules expanding short-term, bare-bones health plans. They also will want to work to bolster the exchanges and possibly examine the idea of "Medicare for All," broadening the federal health insurance program from covering primarily people 65 and older to a single-payer plan covering Americans of all ages. (Plans for a congressional hearing is already in the works). With additional debates over the ACA in the foreseeable future, we will continue to protect access to care, particularly for vulnerable patient groups, including transgender and women's health services.
 - **Drug Pricing** The Democrats takeover of the House has injected new life into efforts to combat high drug prices – perhaps with bipartisan support. House Democratic leaders and President Trump believe they share some common ground over drug pricing and Senate Majority Leader Mitch

McConnell has expressed some openness to addressing the issue next year. Allowing Medicare to negotiate drug prices is key to the solution and has long been a goal of Democrats. Since last summer, the Trump Administration has floated a variety of ideas to bring down prices, so we will have to see if this will play out through regulation or legislation (something attached to a must-pass bill or a bipartisan bill to crack down on delay tactics against approval of generic drugs).

• Other health issues – Congress has also indicated that it plans to give attention to Medicaid expansion, data privacy, reauthorization of the Patient Centered Outcomes Research Institute (PCORI), and the Older Americans Act.

Bottom Line: Many of our issues will take center stage in the new Congress. This includes NIH funding, access to healthcare, and insulin pricing. Success will depend on whether Congress can break through partisan gridlock. The Endocrine Society will continue to focus on our policy priorities (visit **endocrine.org/ advocacy** for complete list) and will continue to follow a nonpartisan strategy to bring all lawmakers to support our issues.

New Congress Strategy

In preparation for the 116th Congress, the Endocrine Society is preparing "Welcome to Congress" packets for all new representatives and senators. The packets will contain fact sheets on several of our priority issues and will help introduce the Endocrine Society as a resource to these offices. We also will be sharing resources with congressional committees with jurisdiction over our issues. In addition, in the spring, we will have a Hill Day focused on research and appropriations issues and will have our members meet with the appropriations committees.

We also hope to involve more of our membership in advocacy activities. In January after the Congress is sworn in, we will launch a special advocacy campaign targeting our members who have a new representative and/or senator. The online campaign will send a letter to these offices introducing our priority issues and ways our members can serve as a resource. We plan to be active on several issues and urge our members to watch out for advocacy alerts. If you have any questions or would like to become more involved in the Endocrine Society's advocacy activities, please contact **govtprof@endocrine.org.**

Endocrine Society Urges Faster Action on EU EDC Strategy



n recent years, the European Union (EU) has made strides in reducing exposures to endocrine-disrupting chemicals (EDCs) through implementing policies, such as the recently adopted criteria to define EDCs in the context of biocides and pesticides laws. However, the legislative landscape for EDCs in other sectors of the economy, such as cosmetics and other consumer products, remains fragmented. Towards the development of a harmonized approach to regulating EDCs, the Endocrine Society has called on the European Commission to update the original 1999 EU Strategy on EDCs to reflect new scientific advances and legislative gaps.

On November 7, the European Commission issued a communication that calls for minimizing exposures to EDCs, increasing research funding, and improving test methods related to EDCs. The communication also announced a "fitness check" that will review existing legislation across sectors to determine if additional action is needed to address EDC exposure through better regulation. We were encouraged by some of these elements of the communication, but we also remain concerned about the lack of concrete details and unclear timeframes for the fitness check and other actions proposed by the Commission. Following the release of the communication, Endocrine Society members travelled to Brussels for a series of meetings with European Union policy makers to discuss our priorities and how we can work with the European Commission, Parliament, and Member States to reduce exposures to harmful EDCs.

We invited the European Society of Endocrinology (ESE) to join us in developing a briefing for Members of the European Parliament (MEPs) and their staffs hosted by MEPs Eric Andrieu and Lieve Wierinck. The event featured presentations from Angel Nadal, PhD, Vera Popovic, MD, PhD, FRCP, and Jorma Toppari, MD, PhD. Nadal and Popovic presented the perspectives of the Endocrine Society and the European Society of Endocrinology and called for additional research funding and a strategy for EDCs that is consistent across sectors with measurable results and action steps. Toppari then described his research program investigating the effects of chemical exposures on male reproductive health. Attendees appreciated the perspectives of expert scientists; following their presentations, speakers fielded questions about how to deal with mixture effects and ways that the EU could take a leadership role in developing safer chemical alternatives for consumer products.

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The following day, Endocrine Society members met with Members of the European Parliament and representatives from several European Commission Directorates-General (DGs) including the office of the Secretariat-General. We explained our concerns about the Communication to update the EDC Strategy and requested more details about the fitness check and other proposed actions by the Commission. Commission representatives appreciated the Endocrine Society's perspective and emphasized that their goal is to develop policies to minimize EDC exposures that are based in science. Towards that end, they offered to continue to meet and work with the Society and our members to ensure that endocrine research strengthens their approach to regulating EDCs.

We are pleased that our advocacy is influencing EU policy makers towards a more effective and harmonized approach to EDCs throughout the EU. However, we recognize that there is much more work to be done and it will be important to maintain pressure throughout the upcoming European Parliament elections so that recent progress is not lost.

For more information on how you can get involved, see the Society's advocacy webpage at **endocrine.org/advocacy**. For more information about EDCs, please visit **endocrine.org/edc.**

CMS Releases Final 2019 Physician Fee Schedule; Delays Revisions to Evaluation and Management Codes Until 2021



he Centers for Medicare and Medicaid Services (CMS) finalized the Medicare Physician Fee Schedule for 2019, which sets physician payment policies and rates under the Part B program.

The final rule included significant changes to how evaluation and management (E/M) services will be paid and documented. Beginning on January 1, 2021, CMS will pay a single rate for E/M outpatient visit levels 2, 3, and 4 (one for established and another for new patients) and level 5 visits will remain unchanged to account for greater complexity. CMS also finalized a complexity add-on code and an extended service code that can be billed with all level 2-4 new and established outpatient visits. To bill the single payment level 2-4 outpatient E/M visit, CMS will require providers to document a level 2 service when using medical decision making or the 1995/1997 guidelines. If providers choose to document using time, they will have to document medical necessity and that they met the current typical time for the reported CPT code. For level 5 visits, providers will be allowed to document using the current 1995/1997 guidelines or the current level 5 definition of medical decision making. Providers can also document a level 5 visit by time: 40 minutes for an established patient and 60 minutes for a new patient.

The delay of these payment policies until 2021 provides the Endocrine Society with additional opportunities to influence the structure of these changes, which are expected to result in a 2% cut in reimbursement for endocrinologists. We will continue to work with our members, federal agencies, and other specialty societies to ensure that these changes have minimal impact on practices. For 2019 and 2020, CMS will continue to use the current coding and payment structure for outpatient E/M visits, and practitioners should continue to use the 1995/1997 guidelines to document them.

In addition to changes to E/M codes, CMS finalized payment policies on several additional issues of importance to endocrinology, including the establishment of codes for virtual check-ins and interprofessional consultations. The agency also finalized changes to the work relative value units for fine-needle aspiration and diabetes self-management training codes. A detailed summary of the policies impacting endocrinologists can be accessed at **endocrine.org/feeschedule**.

Endocrine Society Discusses Collaboration Opportunities with NCI and CSR

n November 8, Endocrine Society members Ruth Keri, PhD, and Matthew Ringel, MD, met with representatives from the National Institutes of Health (NIH) Center for Scientific Review (CSR) and National Cancer Institute (NCI) to discuss research priorities and grant review processes at the NIH.

During the meeting with CSR, the group discussed how the NIH can more effectively share information with endocrine researchers about various opportunities to volunteer on NIH review panels, including as an ad hoc reviewer or early career reviewer. Keri and Ringel noted the breadth of topics and disease areas that endocrine researchers study, and the need to include endocrine expertise where appropriate to ensure that grants investigating hormonal systems are reviewed by individuals with suitable expertise. CSR staff indicated that the Society's volunteer lists are helpful, and that it would be particularly useful to include individuals with clinical or business expertise, even if they aren't necessarily NIH grantees.

During the meeting with NCI, the NCI acting deputy director Dinah Singer, PhD, expressed interest in learning more about new research opportunities in endocrinology, particularly research topics that are underfunded due to open questions or that involve areas at the interface between the missions of NCI and the other institutes at the NIH. She also noted the need to reinforce the basic science community in areas like thyroid biology and ensure that highly motivated young investigators join the field and have mentors to support their development. The group was encouraged by opportunities to engage at workshops and other events where funding priorities are discussed, so that endocrine science is incorporated into future research plans.

Throughout both meetings, participants focused on how to support researchers throughout the entire career trajectory and ensure that there is an adequate pipeline of early and mid-career researchers. Staff at CSR and NCI were very interested to learn more about opportunities to interact with endocrine scientists and learn about the great work our research communities are doing in cancer and other fields at the Society's annual meeting, ENDO.

Endocrine Society Delegation Attends AMA House of Delegates Meeting; Policy on Gender Assignment Surgery Debated



In early November, the Endocrine Society attended the American Medical Association (AMA) House of Delegates meeting to establish policy positions on topics of importance to patients and healthcare providers. Our delegation is comprised of Society members Amanda Bell, MD, Palak Choksi, MD, Shivani Agarwal, MD, Barbara Onumah, MD, Robert Vigersky, MD, and Daniel Spratt, MD. The Society attends the AMA meetings to further our policy agenda by garnering the support of the House of Medicine on issues of importance to our members. This enables us to take that message to Capitol Hill and federal agencies as an additional means of support. In addition to passing policy that supports the Society's priorities, we also fight against passage of policy that will be detrimental to endocrinologists or the patients that they treat.

Policy proposals passed or referred for further study at the House of Delegates meeting that address Society priorities included collection of public health data on sexual

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From left, Dr. Kevin McKinney, Dr. Jonathan Leffert, Dr. Ved Gossain, Dr. Ricardo Correa, Dr. Robert Vigersky, Dr. Shivani Agarwal, Dr. Barbara Onumah, and Dr. Kathleen Figaro, at the Endocrine Section Council meeting during the Interim Meeting of the AMA House of Delegates on Saturday. November 10, 2018.

orientation and gender identity, affirmation that gender identity falls across a spectrum, and ensuring healthy foods are available to all. The most relevant endocrine-related issue debated concerned gender assignment surgery in infants with differences of sex development (DSD). Resolutions have been considered at past AMA meetings that called for a ban on all surgeries until the child is old enough to participate in the decision, unless there is a life-threatening medical need. Opponents of early surgery argue that there are instances where the individual does not identify with the gender chosen for them at the time of birth and ultimately suffers harm. While others do not necessarily believe that surgery should be done at the time of birth in all cases, they do believe that the parents should be able to make the decision for their child based on an understanding of all available options.

These resolutions were ultimately referred to the AMA's Council on Ethical and Judicial Affairs, which offered an ethical opinion at the November meeting. The report does not adjudicate clinical disagreement or prescribe what manner of decision is "correct" or "best," but rather clarifies the values at issue and identified what factors must be considered to arrive at an ethically sound decision in any given patient's unique situation. The report updates existing policy on pediatric decision making and lays out recommendations for physicians who care for these patients, which includes, but is not limited to:

- Develop an individualized plan of care that will best serve the patient, basing treatment recommendations on the best available evidence and in general preferring alternatives that will not foreclose important future choices by the adolescent and adult the patient will become.
- Work with parents/guardians to simplify complex treatment regimens whenever possible and educate parents/guardians in ways to avoid behaviors that will put the child or others at risk.
- Provide a supportive environment and encourage parents/ guardians to discuss the child's health status with the patient. Physicians should offer education and support to minimize the psychosocial impact of socially or culturally sensitive care.
- When it is not clear whether a specific intervention promotes the patient's interests, respect the decision of the patient (if the patient has capacity and is able to express a preference) and parents/guardians.
- When there is ongoing disagreement, seek consultation with an ethics committee or other institutional resource.

The next meeting of the AMA will be in June 2019. We encourage any member with questions or suggestions for resolutions that the Society could sponsor at an upcoming meeting to contact Stephanie Kutler, Director, Advocacy & Policy at **skutler@endocrine.org.**

SURVIVING CHILDHOOD CANCER

A cancer diagnosis is upsetting at any age, but especially when the patient is a child. The care of children, adolescents, and young adults who survived cancer is complex. A 5-year survival rate is greater than 80%, but various therapies used to treat cancer can throw off the endocrine and hormonal system. It is important to know the early and late endocrine symptoms that may develop and possible effects following cancer treatment in survivors.

CHILDHOOD CANCER SURVIVORS

One of the most frequently affected endocrine organs in cancer survivors are the hypothalamus and pituitary gland.

- The hypothalamus produces and releases hormones and links the nervous and endocrine systems through the pituitary glands.
- The pituitary gland is often referred to as the "master gland" and influences other organs in the body. It also produces the growth hormone.
- The growth hormone controls the body's growth. If survivors have too little of the growth hormone, it can lead to health problems, including weight gain and growth failure in young survivors.
- Other hormones that may be affected include fertility hormones released by the pituitary gland such as LH, FSH, and ACTH.

The endocrine conditions facing cancer survivors include:

- Growth failure
- Growth hormones deficiency
- Delayed puberty
- · Amenorrhea or loss of libido
- TSH deficiency
- ACTH deficiency, which is the hormone responsible for cortisol production

Endocrine complications in cancer survivors may be caused by:







Effects from the cancer or tumor

These conditions are diagnosed based on specific clinical evidence, blood tests, and radiological evaluation. Most signs and symptoms are dependent on the affected endocrine gland.

Visit hormone.org for more information.

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GROWTH HORMONE DEFICIENCY FROM THE PITUITARY GLAND



Growth deceleration or lack of growth acceleration with puberty in older children

A decrease in growth rate or a lack of pubertal growth spurt in pre-pubertal children

Adults may experience fatigue, abnormal fat deposition, body composition of fat and lean mass, and elevated cholesterol

FSH AND LH DEFICIENCY FROM THE PITUITARY GLAND

- Delayed or absent puberty
- Secondary amenorrhea (no periods) or loss of libido in sexually mature adults

PRECOCIOUS PUBERTY

Breast development in girls before age 8 or testicular or penis enlargement in boys before age 9.

TSH DEFICIENCY

Fatigue, constipation, slow growth in growing children.

ACTH DEFICIENCY

Fatigue, abdominal pain, weight loss, low blood sugar or low blood pressure, particularly in times of acute illness.

TREATMENT RECOMMENDATIONS

Cancer survivors are encouraged to ask their health care providers about the early or late endocrine developments of their cancer and/or therapy. Based on the diagnosis that is made and the psychological and physical health of the patient, treatments can include thyroid hormone replacement, cortisol replacement, growth hormone therapy, and suppression or induction of puberty.

- Highlight the likelihood of endocrine disorders in CCS and how long of a latency period there can be between completion of treatment and the endocrine disorder and it is recommended that a skilled doctor monitors growth and puberty since each can impact final height outcomes of a child.
- Stimulating testing is a medical test that determines the way a child's endocrine system responds to different types of hormones.
- Childhood cancer survivors should also make sure their doctor has a summary of their treatment history and list of conditions they may be at risk for based on their medical history.

QUESTIONS TO ASK YOUR DOCTOR

- Should any endocrine testing being done should be preformed in any different way than for the general non-cancer survivor?
- Is there any medicine that can impact my child's condition post cancer?
- What are the risk and the benefits of each treatment option?



Patients have questions. We have answers.

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



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PennState Health Milton S. Hershey Medical Center

ENDOCRINOLOGY CLINICAL INVESTIGATOR/SCIENTIST

The Division of Endocrinology, Diabetes, and Metabolism at **Penn State Health Milton S. Hershey Medical Center**, Penn State College of Medicine (Hershey, PA) is seeking an NIHfunded **Clinical Investigator/Scientist** with a focus on basic/ clinical diabetes related research to join an expanding Diabetes program. A highly competitive departmental and institutional start-up package will supplement the candidate's extramural support to strengthen and expand the candidate's ongoing research with the goal of developing novel scholarly initiatives within the division and the institution in the field of diabetes. Joint appointments in Basic Science Departments are anticipated.

The Harrisburg-Hershey area includes the state capitol, a population of 500,000 and offers an excellent combination of low cost of living, excellent schools, cultural activities and attractions that bring millions of visitors each year. We're conveniently located within a short distance to major cities such as Philadelphia, Pittsburgh, NYC, Baltimore, and Washington DC.

Appropriate candidates must possess a MD, MD/PhD or foreign equivalent, NIH funding, the ability to obtain a medical license in the Commonwealth of Pennsylvania.

Qualified applicants should contact:

Andrea Manni, M.D. Professor and Division Chief of Endocrinology Diabetes, and Metabolism c/o Heather Peffley, PHR, FASPR Physician Recruiter Penn State Health hpeffley@pennstatehealth.psu.edu

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