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Pediatric PROGRESS

JULY 2019

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

SNACK ATTACKS: Screen time's relationship with unhealthy snacking in adolescents.

GROWING PAINS & GAINS: An **ENDO 2019** study shows a link between obesity and precocious puberty in boys.

NEWBORN CONUNDRUM: Addressing the challenges treating infants with differences in sex development.

A DELICATE BALANCE:

New Society guideline on treating older patients with diabetes

PAYING TRIBUTE:

Remembering Lewis Braverman & Elizabeth Barrett-Connol



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Committee on Diversity and Inclusion: 25 Years Celebrating Diversity in Endocrinology **R** rom my perspective, valuing a diverse and inclusive global community is essential to furthering the field of endocrinology, enriching the biomedical workforce, improving the care and outcomes of endocrine patients, and ensuring the ongoing growth and development of our organization. Over the past 25 years, we have committed to creating unique opportunities to support the recruitment, retention, and engagement of diverse talent in endocrinology and increase the visibility and participation of underrepresented groups within the organization.

Through the dedicated efforts of the Minority Affairs Committee (MAC), now known as the Committee on Diversity and Inclusion (CoDI), we have a robust portfolio of activities specifically designed to meet our goal to develop and support a diverse and inclusive network of clinician, researcher, and educator members and leaders who promote health, advance research, and work to eliminate endocrine health disparities in our local, national, and global communities. For the Society, diversity and inclusion is defined broadly to encompass all aspects of diversity – culture, age, ethnicity, race, gender, nationality, professional level, and sexual orientation.

Currently one of our premier programs, the Future Leaders Advancing Research in Endocrinology Program (FLARE) is a thriving and highly successful leadership training program that has equipped students, fellows, and junior faculty of underrepresented groups with leadership skills that strengthen their confidence as biomedical researchers. Since 2013, FLARE has trained 125 fellows through a



Valuing a diverse and inclusive global community is essential to furthering the field of endocrinology, enriching the biomedical workforce, improving the care and outcomes of endocrine patients, and ensuring the ongoing growth and development of our organization.



multi-faceted program approach to leadership development that includes a skills workshop, structured mentoring network and collaborative opportunities, and an internship program. On a personal note, it has been a privilege to have directed the FLARE program since its inception. I want to acknowledge the devoted faculty and Society members who have taught and mentored our FLARE trainees and all the Endocrine Society staff such as Kirsta Suggs, who has supported the program since its inception, and Tracy Williams, who coordinates many of its activities.

Our annual meeting (ENDO) programming offers myriad opportunities to network with diverse groups of endocrinologists and engage in scientific discussion around minority healthcare and health disparities. In addition to scientific symposia that cover the latest advances in issues related to these topics, the CoDI offers workshops such as "Impacting Perceptions and Bias

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There are many exciting opportunities within the Endocrine Society that promote cultural diversity while building an inclusive community for all endocrinologists to thrive.

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in Healthcare and Research" to address unconscious bias and collaboratively identify strategies to reduce bias in these settings. Our Health Disparities Poster Previews featured six top-scored posters on endocrine-related health disparities to help build awareness around health disparities research. The LGBTQ and Allies Reception was created this year to provide a networking opportunity to anyone interested in connecting with endocrine professionals and to advocate for the lesbian, gay, bisexual, and transgender community. This reception at ENDO 2019 was very popular and drew significant attendance.

Perhaps one of our most successful and sustained ENDO events that builds connections and collaborations amongst diverse groups is the Mentoring and Poster Reception. This reception provides a networking opportunity for researchers of diverse groups at all levels of training and the opportunity for students, fellows, and junior faculty to present their research. We had a lively group of 200 attendees with a record number of 45 poster presenters who received feedback on their presentations. Advisors also met with mentees at topic tables to address career challenges facing underrepresented minority investigators.

There are many exciting opportunities within the Endocrine Society that promote cultural diversity while building an inclusive community for all endocrinologists to thrive. I want

to acknowledge and congratulate all the past and current members and chairs of MAC and CoDI for their tireless efforts and contributions to creating programming that has supported and nurtured all of our members. Activities have ranged from the Shortcourses in Endocrinology program that has reached thousands of students at minority-serving institutions, to the Minority Access Program that trained undergraduate students from underrepresented minority groups. We have and will continue to embrace internal and external outreach activities. student and professional development activities, and efforts that reduce endocrine-related health disparities through integrated activities.

I am excited about the progress we've made and look forward to an even greater impact in the future.

If you have any comments or questions, please let me know at president@endocrine.org.

- E. Dale Abel, MD, PhD, President, Endocrine Society

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FROM THE EDITOR



A Closer Look at Pediatric Endocrinology

This month's issue focuses on pediatric endocrinology with a cover story on a newly discovered link between male precocious puberty and obesity in boys ("Pediatric Obesity and Male Precocious Puberty: A Link Established," p. 24). While well documented in girls, this new Chilean study conducted by Veronica Mericq, MD, from the University of Chile, Santiago, and her team shows a connection of both central and total adiposity with earlier pubertal events in boys. Similar to how the supposed higher risk of breast cancer in girls who experienced puberty early, boys could have concerns later in life, according to Mericq. "It has been postulated that precocious puberty in boys could be related to higher incidence of testicular cancer in adulthood," she says.



From puberty, we go back in time a bit to birth and the phenomenon of difference in sex development (DSD) in infants, a condition not as rare as once believed. These patients present a diverse number of challenges to the clinicians, not to mention the parents and patients themselves. The article, "A Newborn Conundrum: Differences in Sex Development in Infants," by senior editor Derek Bagley on page 28, states that genetic research has been vital to quickly diagnose and manage babies born with DSD. However, Vincent Harley, PhD, from the Hudson Institute of Medical Research in

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Australia, maintains that education for both the parents and clinicians is key for successful care of these patients. "Still, we don't know the long-term impact of atypical genitalia on the psychological state of the child," he says.

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Long periods of screen time are already considered a risk factor for poor metabolic health in adolescents (and adults, for that matter).

"

While preparing this month's issue, I had what would be considered a meta moment. As I was reviewing the article "Heavy Player One" (p. 34) — an in-depth look at how too much screen time can often lead to unhealthy snacking and thus impact the metabolic health of adolescents — I myself had just poured out a sizable portion of Zen Party Trail Mix to munch while I edited. It made me think about my own less-than-stellar habits during my own screen time, which, as a magazine editor is significant. However, trail mix is a bit more of a healthier option than, say, pizza rolls or Hot Pockets.

The article, also by Bagley, states that long periods of screen time are already considered a risk factor for poor metabolic health in adolescents (and adults, for that matter). Moreover, screen time "seems not to be totally independent from other behavioral risk factors, such as unhealthy eating habits," according to Beatriz Schaan, PhD, Universidade Federal do Rio Grande do Sul, Porto Allegre, Brazil, who adds that "if adults limit their screen time and avoid unhealthy snacking, they will collaborate to make a healthier environment at home." And probably at work too. Just saying...

- Mark A. Newman, Editor, Endocrine News



Eunice Kennedy Shriver National Institute of Child Health and Human Development

Dear Colleagues,

We are writing to inform you of a new clinical trial designed to investigate the safety and efficacy of pegvisomant (Somavert), a growth hormone receptor antagonist, in children with gigantism. For this study, we seek patients 2-18 years of age with growth hormone excess and inadequate response to transsphenoidal surgery or radiation therapy, or patients deemed inappropriate candidates for these treatments.

The study involves the administration of pegvisomant for 12 months. Pegvisomant is already approved by FDA for medical therapy of acromegaly in adults and it is listed as one of the initial adjuvant medical therapies on acromegaly at the latest Endocrine Society Guidelines. The studies in adults have shown significant improvement of the IGF-1 levels after pegvisomant administration, with up to 97% of patients achieving normalization of the IGF-1 levels. However, there are currently no studies on the safety or efficacy of the medication in children.

During the study the patient will need to travel to the NIH for three visits (baseline, 6 months and 12 months). Additional blood tests and height/weight measurements are required between these visits.

NIH will cover the expenses for all the laboratory and imaging studies. Pfizer (who is one of the funding agents of the study) will provide the medication at no cost for the participant. Additional coverage of the expenses for travel to and from the NIH will be provided for the patient and one adult legal guardian.

We would be happy to discuss any further questions you may have. Please contact either of us at the email addresses below. We look forward to hearing from you.

Best wishes,

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V. Craig Jordan, OBE, DSC, PhD, Honored by Queen Elizabeth II



n June 7, 2019, Buckingham Palace announced that Her Majesty Queen Elizabeth II appointed V. Craig Jordan, OBE, as Companion of the Most Distinguished Order of St. Michael and St. George (CMG) for services to women's health.

The award recognizes Jordan's discovery of Selective Estrogen Receptor Modulators (SERMs) as the first multifunctional medicines for women that can treat several diseases simultaneously. These medicines switch on or switch off estrogen target tissue sites around a woman's body to treat or prevent osteoporosis and breast cancer. Specific SERMs can decrease coronary heart disease, strokes or relieve dyspareunia.

Jordan was also awarded the Endocrine Society's 2018 Gerald D. Aurbach Laureate Award for Outstanding Translational Research for the discovery and development of SERMs applied to address the treatment and prevention of major diseases in women.

"This was a huge surprise to be appointed a CMG by Her Majesty Queen Elizabeth II," Jordan says. "This is reserved for ambassadors and defenders of the U.K. But there is a small category for British subjects who become 'the first' in a foreign country. SERMs is a 'first' in women's health."

Jordan's work on this group of medicines was initiated at the Worcester Foundation for Experimental Biology (1972 – 1974) in Massachusetts and continued at the University of Leeds, UK (1974 – 1979). He advocated reinvention of a failed contraceptive ICI 46,474 discovered by AstraZeneca, to become the world's most successful breast cancer treatment, tamoxifen. Jordan's specific contribution over two decades (1973 – 1993), resulted in his appointment as Officer of the Most Excellent of the British Empire (OBE) for services to International Breast Cancer Research in 2002.

The CMG recognizes extraordinary leadership and exceptional accomplishment in the diplomatic service, security services or overseas service by British citizens in foreign countries.

The nomination was made by both the University of Leeds and Zeneca Pharmaceuticals.

INTOUCH



Braverman with former trainees in Boston last year: From left to right, Alan Farwell, MD; Jennifer Lawrence, MD; Lewis Braverman, MD; Caroline Apovian, MD; and Vin Tangpricha, MD, PhD.

BY VIN TANGPRICHA, MD, PHD

Remembering Lewis E. Braverman, MD, 1929-2019

ewis Braverman, MD, will be dearly missed by countless number of former fellows, colleagues and friends.

Braverman, most recently a professor of medicine at Boston University School of Medicine and chief of the Section of Endocrinology, Diabetes, and Nutrition, was an internationally recognized leader in the field of thyroid research for his contributions that spanned over six decades.

Examples of his contributions include studies leading to the understanding of the Wolff-Chaikoff effect; the demonstration of peripheral conversion of T4 to T3 and to other iodinated products; description of iodine deficiency in the U.S. and worldwide; and the recognition of amiodarone-induced thyroid dysfunction, among several other important contributions. He published over 500 peer-reviewed manuscripts on the topics of iodine metabolism and thyroid dysfunction. He also served as editor for several editions of Werner and Ingbar's *The Thyroid*.

In 1951, Braverman completed his undergraduate degree in biology at Harvard College followed by medical school at Johns Hopkins University in 1955. He returned to his hometown of Boston to complete his internship at the Beth Israel Hospital followed by two years of military service in France. He returned to Boston to complete residency at the Harvard Unit at Boston City Hospital and joined the prestigious Thorndike Laboratory under the direction of Dr. Sid Ingbar. He subsequently served as chief of endocrinology at Tufts St. Elizabeth's Hospital (1962-1975), chief of endocrinology at University of Massachusetts Medical Center (1975-1998), and then chief of endocrinology at Boston University in 1999 where he remained as a faculty member until his retirement in 2017. He valued patient care and kept a busy thyroid practice throughout his academic career. He had a special ability to connect with his patients who followed him throughout his career at different institutions.

Through the years, Braverman provided outstanding service to the Endocrine Society. He was the editor-in-chief of *The Journal of Clinical Endocrinology & Metabolism* from 1989 to 1993. In 2007, he was recognized with the Endocrine Society's Robert H. Williams Distinguished Leadership Award. He was also an integral part the American Association of Clinical Endocrinologists and the American Thyroid Association (ATA), where he received numerous awards and served as president.

He enjoyed mentorship of fellows and junior faculty. He served as mentor on numerous National Institutes of Health career development awards, dissertation committees, research projects, and manuscripts. His former trainees span the globe and include several endocrinology chiefs and senior academic faculty. His door was always open for fellows and faculty to discuss new projects, to manage challenging patients, and to provide career advice. He always took the time to get to know trainees and colleagues on a personal level. He drew large crowds at every endocrine meeting that he attended where former fellows and colleagues queued in line to greet him.

Braverman was a warm and caring individual who gave so much of his time to his patients, trainees, and colleagues. He was a gentle giant of his time and will be missed by all who were fortunate to have known him.

- TANGPRICHA IS PROFESSOR OF MEDICINE, EMORY UNIVERSITY SCHOOL OF MEDICINE, ATLANTA, GEORGIA. HE WROTE ABOUT HIS CAREER IN A PAST INSTALLMENT OF THE "WHY ENDOCRINOLOGY?" COLUMN.

Remembering Elizabeth Barrett-Connor, MD, 1935-2019



The endocrine community is mourning the loss of Elizabeth Barrett-Connor, MD, who died on June 9 at her home in La Jolla, Calif., and who was known for her long-running study on aging, which led to a better understanding of diabetes, cardiovascular disease, menopause, and bone health.

Barrett-Connor, the distinguished professor in the Department of Family Medicine and Public Health at University of California San Diego School of Medicine, received the Endocrine Society's 2018 Fred Conrad Koch Lifetime Achievement Laureate Award for her "paradigm-shifting contributions in endocrine physiology and the role of hormones in disease pathogenesis (focus on gender differences) in cardiovascular disease, diabetes, osteoporosis, and breast cancer," according to the award citation written by Nanette Santoro, MD, from the University of Colorado School of Medicine in Aurora. "It is hard to imagine the existence of any other individual whose work reflects such staggering impact."

Considered a pioneer in public health, Barrett-Connor was the founder of the Rancho Bernardo Heart and Chronic Disease Study, a prospective population-based study that is currently in its 47th year and is one of the longest, continuously funded, NIH observational cohorts in existence. From this study, she explored coronary heart disease (CHD) risks, delineated differences in CHD mortality between the sexes, and exposed hyperlipidemia and diabetes as risk factors. Barrett-Connor then served as principal investigator (PI) or co-PI for numerous clinical trials examining the role of estrogens/selective estrogen modulators on cardiovascular outcomes, lifestyle interventions on diabetes severity, and bone-specific medications on osteoporotic fractures.

In its obituary from June 20, *The New York Times* states that Barrett-Connor was "among the first to show that diabetes removes the usual advantage that women have in avoiding heart disease; that increasing potassium in the diet may protect against stroke; and that drinking lots of caffeinated coffee over a lifetime can lead to low bone mineral density in women who do not also drink milk daily."

"The hallmarks of Barrett-Connor's enduring success — a driving quest for the truth, rigorous scientific discipline, and a joyful passion — have infused every aspect of her career, whether as investigator, lecturer, teacher, or mentor," according to Santoro. "She has helped make women more visible in the endocrinology field, not by example of her own shining star, but by her constant recognition of light coming from others."

Santoro adds that Barrett-Connor's scientific discipline and ability to identify methodological flaws make her an ultimate "seeker of truth."

TRENDS & INSIGHTS

Review Details Long-Term Cancer Treatment's Effects on Endocrine System

E ndocrine disorders are common in people who received cancer treatment in childhood and adulthood, especially as life expectancy in these patients continues to rise with the advancement of these treatments, according to a paper recently published in *Endocrine Reviews*.

The review, by Judith Gebauer, of the University Hospital of Schleswig-Holstein in Luebeck, Germany, et al., points out that therapy-related late effects of cancer treatment have become increasingly recognized during the past 20 years and that endocrine disorders are among the most frequent of these effects. Children are more susceptible than adults, and up to 50% of longterm childhood cancer survivors will develop an

endocrine disorder. "The risk for the development of late effects critically depends on the oncological treatment regimen used," the authors write. "Details of these regimens have been applied to predict the individual risk for certain long-term sequelae and form the basis for the structured lifelong surveillance suggested by various international guidelines."

According to the authors, most data are based on the late effects of treatment in former childhood cancer patients for whom specific guidelines and recommendations already exist, but the data on the effects in adults are not as robust. Surveillance of adults who develop cancer ends after those patients see five years of no recurrence of their cancer. And since the likelihood of developing cancer increases with age, adults who develop cancer later in life won't live as long even if their cancer is successfully treated. However, life expectancy is increasing overall, which means more and more adult cancer survivors are experiencing late complications from their cancer treatments.

The authors then detail the mechanisms by which various therapies affect the endocrine system: Radiotherapy can damage cells and DNA, affecting endocrine organs like the thyroid and pituitary gland, while chemotherapy can contribute to oxidative stress and tissue damage, for example. Cancer treatments can even lead to further malignancies in the thyroid and other endocrine organs.

The increasing success of cancer treatment has become a kind of double-edged sword — the number of cancer survivors is rapidly growing, but they are suffering the long-term consequences of the cancer and subsequent treatments. Because of this, the authors call on the medical community to conduct novel research and clinical approaches to limit these late effects of cancer treatment. "Until then," the authors write, "an optimally integrated followup service urgently needs to be developed where endocrinology should play an essential part."

Findings: "In conclusion," the authors continue, "late endocrine complications after cancer therapy constitute common health issues in long-term cancer survivors and require lifelong surveillance. For many cancer entities, focus is shifting from surviving cancer to living beyond cancer, and therefore, early diagnosis and treatment of sequelae are essential to ensure a good quality of life and to reduce late morbidity and mortality."







Life expectancy is increasing overall, which means more and more adult cancer survivors are experiencing late complications from their cancer treatments.





To put this in human terms, if your great grandmother was exposed to BPA during her pregnancy and none of your other relatives ever came into contact with BPA, your brain would still show these effects.

??

Mouse Study Finds BPA Exposure Has Transgenerational Effects on Gene Linked to Autism

ransgenerational bisphenol A (BPA) exposure may contribute to autism, according to a mouse study published in *Endocrinology*.

Researchers led by Emilie F. Rissman, PhD, of the University of Virginia School of Medicine in Charlottesville, Va., and North Carolina State University in Raleigh, N.C., point out that animal



studies have linked BPA to anxiety, aggression, and poor learning and social interactions. Studies of human populations report associations between BPA and neurobehavioral issues like attention deficit hyperactivity disorder and autism.

"Exposure of mouse fetuses to BPA disrupts formation of nerve cell connections in the brain, and this is a transgenerational effect," Rissman says. "To put this in human terms, if your great grandmother was exposed to BPA during her pregnancy and none of your other relatives ever came into contact with BPA, your brain would still show these effects." In this mouse study, researchers tested mice descended from those exposed to BPA for social recognition and found that they showed a social behavioral deficient like autistic behavior. Mice whose great grandmothers were exposed to BPA during pregnancy were more active and took longer to habituate to strangers than other mice. More strikingly, they didn't explore the new mice that were introduced to the group.

In order to assess the mechanism for these effects, the researchers examined differential expression of genes related to post-synaptic density formation and function and found *Shank1* — which codes for one of the scaffolding proteins in the post-synaptic densities — particularly noteworthy. *Shank1* mutations have previously been identified in patients with autism. *Shank1* knockout mice exhibited communication deficits but performed better than controls in the radial maze. "Interestingly, *Shank1* microdeletions are

present in some male autistic patients, but in females the same microdeletion is associated with anxiety, not ASD," the authors write. "Perhaps these data speak to the differences in male and female autistic symptomology and these geneby-environment interactions have sexspecific effects."

Findings: "In summary," the authors conclude, "our findings represent the first report of transgenerational BPA actions on one of the genes associated

with autism in humans. This unique gene-byenvironment relationship is correlated with a social behavioral deficient in mice that has relevance to autistic behavior. Because these effects are retained for generations after BPA exposure, even an immediate prohibition on use of BPA in plastics, epoxy resins, thermal paper, and other products will not provide remediation."

"Even if we ban all BPA right now, that will not change these long-term effects on the brain," Rissman says.

Study Shows Dapagliflozin Reduces Progression of Kidney Disease, Renal Death in Patients with Type 2 Diabetes

he sodium-glucose co-transporter 2 (SGLT2) inhibitor dapagliflozin seems to reduce the progression of kidney disease or renal death in patients with type 2 diabetes, according to data from the Phase III Dapagliflozin Effect on Cardiovascular Events (DECLARE)-TIMI 58 trial that was presented at the American Diabetes Association annual meetingin San Francisco and simultaneously published in the *Lancet Diabetes & Endocrinology.*

Researchers led by Ofri Mosenzon, MD, of Hadassah Hebrew University Hospital in Jerusalem, Israel, point out that for years angiotensin-converting enzyme inhibitors or angiotensin receptor blockers have been the basis of treatment of diabetic kidney disease, but patients taking these drugs still had a higher risk of adverse renal and cardiovascular outcomes than people without diabetes. "Novel treatments are therefore needed to both prevent and slow progression of chronic kidney disease in patients with type 2 diabetes," the authors write.

SGLT2 inhibitors have been shown to slow the decline of renal function across several clinical trials, like the EMPA-REG OUTCOME trial and the CANVAS and CREDENCE trials. "Here we report results of detailed analyses of renal outcomes of the DECLARE-TIMI 58 trial, including components of the cardiorenal and renal-specific composite outcomes, subgroup analysis of these composite outcomes, and change in [estimated glomerular filtration rate (eGFR)] at different timepoints, in order to investigate the renal effects of dapagliflozin in this large and diverse study population," the authors write.

This analysis evaluated 17,160 patients with type 2 diabetes and predominantly preserved renal function, irrespective of underlying atherosclerotic cardiovascular disease. The results showed a

47% reduction with dapagliflozin in the relative risk of the composite renal-specific outcome of kidney function decline, or renal death (excluding cardiovascular death) compared to placebo. Dapagliflozin reduced the relative risk of a cardiorenal composite of kidney function decline, ESRD, or renal or cardiovascular death by 24% compared to placebo.

The authors write that there are several important differences between the renal outcome data from DECLARE-TIMI 58 and those from the EMPA-REG OUTCOME and CANVAS trials, including a lower prevalence of established atherosclerotic cardiovascular disease, better renal function at baseline, and longer median follow-up.

The authors also note the distinctions between the DECLARE-TIMI 58 trial and the CREDENCE trial, which was the first large-scale outcome trial of an SGLT2 inhibitor (canagliflozin) with a renal primary outcome to be completed. In CREDENCE and similar dedicated renal outcome trials, all participants have prevalent nephropathy, while in DECLARE-TIMI 58, participants did not have substantially reduced eGFR at baseline and most had normoalbuminuria. "Therefore, the population was at much lower risk of adverse renal outcomes. Thus, our findings for the effects of dapagliflozin on renal outcomes could have important implications for the early prevention of diabetic kidney disease," the authors write.

Findings: "In conclusion," the authors write, "in the DECLARE-TIMI 58 trial, dapagliflozin treatment led to substantial reduction in the risk of clinically significant renal deterioration in a large and diverse population of patients with type 2 diabetes."

AstraZeneca sponsored this trial and is marketing dapagliflozin as FARXIGA. Novel treatments are therefore needed to both prevent and slow progression of chronic kidney disease in patients with type 2 diabetes.

"

ENDOCRINE ITINERARY



2019 Clinical Endocrinology Update/ Endocrine Board Review

CEU East: Miami, Florida, Sept. 5 – 7, 2019

CEU West/ EBR: Seattle, Washington, Sept. 17 – 21, 2019 Once again this year, endocrine clinicians from around the world will have a choice about which Clinical Endocrinology Update (CEU) they choose. CEU East will take place in Miami, while CEU West/Endocrine Board Review (EBR) will land on the West Coast in Seattle.

Miami's Intercontinental Hotel will be the location of the 2019 CEU East, September 5 – 7, and the Hyatt Regency Seattle will be where the joint meeting of the EBR and CEU West take place on September 17 – 21. Each year, CEU brings together hundreds of endocrine clinicians for a unique learning experience and opportunities to network with expert faculty and colleagues. Attend the 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. Unlike other board preparation meetings, the Endocrine

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

www.endocrine.org/ebr/2019

Early Registration: Now – August 1, 2019

The American Society for Bone and Mineral Research (ASBMR) 2019 Annual Meeting

Orlando, Florida September 20 – 23, 2019

The ASBMR Annual Meeting boasts nearly 100 education sessions and 1,100 poster presentations in four informationfilled days. The conference includes hands-on workshops focused on the latest technologies and research tools using model datasets, meet-the-professor sessions, the ASBMR Discovery Hall, an exhibition hall that provides attendees with a truly immersive experience, with access to new science, new knowledge, new tools, and new contacts all in one location. www.asbmr.org

Assisted Reproductive Technology (ART) World Congress 2019

New York, New York October 10 – 11, 2019

The New Hope Fertility Center in New York will host the Assisted Reproductive Technology World Congress, bringing together researchers, physicians, clinicians, and specialists to discuss cutting-edge research and procedures in reproduction assistance. Topics of this year's conference will include oocyte and embryo cryopreservation — a critical view, the assessment of embryo ploidy using timelapse imaging system and conventional morphological grading, automated and semi-automated vitrification and rewarming, and awakening follicles in POI women. art2019.cme-congresses.com

Cardiometabolic Health Congress

Chicago, Illinois October 11 – 13, 2019 CMHC is the largest, U.S.-based,

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multidisciplinary conference that is solely focused on the management of cardiometabolic risk and the prevention of cardiovascular and metabolic disease. This event allows today's busy healthcare professionals a uniquely exclusive opportunity to learn, internalize, and integrate real-world solutions into their toolboxes, and ultimately, their clinical practices and patient care.

www.cardiometabolichealth.org/2019/ chicago-14th-annual-cmhc.html

89th Annual Meeting of the American Thyroid Association

Chicago, Illinois

October 30 - November 3, 2019

The ATA Annual meeting is open to the community of endocrinologists, internists, surgeons, basic scientists, nurse practitioners, and other healthcare professionals who wish to broaden and update their knowledge of the thyroid and thyroid cancer. www.thyroid.org/89th-annual-meeting-ata/



The 37th Annual Meeting of The Obesity Society

Las Vegas, Nevada, November 3 – 7, 2019 The Obesity Society (TOS) will hold its 37th Annual Meeting at ObesityWeekSM—a unique, international event focused on the basic science, clinical application, surgical intervention, and prevention of obesity. ObesityWeek brings together world-renowned experts in obesity to share innovation and breakthroughs in science unmatched around the globe. This year, the international conference will focus on diabetes. Attendees will enjoy the diverse educational opportunities, networking events, and scientific synergies offered in sessions, and joint symposia with numerous peer-related organizations. www.obesityweek.com

INTERNATIONAL ITINERARY

28th European Diabetes Congress

Edinburgh, Scotland, July 17 – 18, 2019

The Euro Diabetes 2019 Conference invites academic scientists, endocrinologists, surgeons, primary care physicians, pharmaceutical industrial delegates, and students from across the globe to network and learn about the latest advancements, growth, and research in diabetes and endocrinology. The theme of the conference is "Recent Advancements and Developments for Changing Life of Diabetes World." wvw.diabetesexpo.com

SLENDO 2019

Colombo, Sri Lanka, August 1 – 3, 2019

SLENDO 2019 is jointly organized by the South Asian Federation of Endocrine Societies (SAFES), the Sri Lanka College of Endocrinologists (SCLE,) and the International Society for Endocrinology. Over the course of three days, delegates will have an opportunity to take part in more than 170 sessions that include plenaries, symposia, workshops, and meet-the-professor sessions from international experts. The free paper sessions offer researchers and trainees the chance to showcase cutting-edge research while sharing ideas with others in the field. There will be awards for young investigators, offering the winners of the free paper sessions a travel grant to travel to ICE Buenos Aires in 2021 to showcase their work. https://slendo.lk

IBPS Summer School on Endocrine Disruptors

Paris, France, August 25 – 31, 2019

Organized by the Institut de Biologie Paris-Seine, this international summer school is targeted primarily, but not exclusively, to PhD students and post-docs focusing on the topic of endocrine disruptors. Over the course of five days, attendees will attend lectures and collaborate on work focused on the research of endocrine disruptors. In addition to the coursework and networking opportunities, guests will have the opportunity to explore Paris with others in their field.

https://sites.google.com/view/ibps-summer-school-disruptors/home

EndoBridge 2019

Ayatall, Turkey, October 24 – 27, 2019

Jointly organized by the Endocrine Society, European Society of Endocrinology, and the Society of Endocrinology and Metabolism of Turkey, EndoBridge focuses on "bridging the world of endocrinology" and will provide a comprehensive update in the field of endocrinology. This meeting is designed for the clinical endocrinologist. The official language of the meeting is English, but simultaneous translation will be available in Russian, Arabic, and Turkish.

http://endobridge.org

International Prader-Willi Syndrome Conference

Havana, Cuba, November 13 – 17, 2019

The 10th international meeting of the International Prader-Willi Syndrome Organisation (IPWSO), this conference is a unique event focused solely on Prader-Willi Syndrome. The event is a multi-disciplinary event for networking, sharing knowledge, and collaboration opportunities for a vast audience including scientists, caregivers, physicians, policymakers, and more.

www.ipwsoconference.org





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DASHBOARD

66 A lot of physicians look at somebody 70 and above [and] say, '[their problems are] part of the aging process, we don't have to do too much.

We now know that even older [patients with diabetes] live for many more years, so the guideline stresses that they should be fully treated to reduce the acute effects [as well as] the chronic complications of diabetes."

> - DEREK LEROITH, MD, PHD, Mount Sinai School of Medicine, New York; chair, guideline-writing committee for the Endocrine Society's "Treatment of Diabetes in Older Adults: An Endocrine Society Clinical Practice Guideline" in "A Delicate Balance: Treating Older Diabetes Patients" on page 40.



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the percentage of

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The percentage by which new cases of diabetes have decreased in the U.S. since a peak in 2009. This indicates that ongoing efforts to stop the country's diabetes epidemic appear to be working.

- SOURCE: CENTERS FOR DISEASE CONTROL AND PREVENTION







Nearly 1 in 4 Americans struggle to afford their prescription drugs

More than 4 in 10 Americans in poor health struggle to afford their prescription drugs -SOURCE: UNITED STATES PUBLIC INTEREST GROUP



Pediatric Obesity and

Male Precocious Puberty: A LINK ESTABLISHED

While the connection has been well-established between obesity and precocious puberty in girls, a Chilean study presented at **ENDO 2019** establishes a link in boys.

BY KELLY HORVATH

ccording to statistics from *Pediatric Obesity* — Assessment, *Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline* as well as *Endocrine Facts and Figures: Obesity*, the pediatric obesity epidemic continues to be a global health threat. In the U.S., pediatric obesity affects 16.9% of children and adolescents, while another 31.8% meet the criteria for overweight, with the multitude of associated risks for long-term health complications and comorbidities looming in adulthood.

In addition to the health problems it may cause, pediatric obesity also seems to disrupt the endocrine system in multiple ways. One such disruption is seen with precocious puberty in girls. Until now, evidence suggesting that pediatric obesity also initiates early puberty in boys has been conflicting, with some studies showing a correlation only with overweight status and some finding that pediatric obesity actually delays puberty. A new study, however, may just settle the controversy.

Blooming Too Early

In research presented at **ENDO 2019**, Verónica Mericq, MD, from the Universidad De Chile in Santiago, and team demonstrate an association of both central and total adiposity with earlier pubertal events in boys. Their longitudinal follow-up study included 527 Chilean boys who were participants in the Growth and Obesity Chilean Study (GOCS) starting at age four. After weight, height, and waist circumference were measured and body mass index (BMI) calculated, testicular volume was evaluated starting at around age seven with a Prader orchidometer.

They define obesity as two standard deviation scores (SDS) greater than BMI, which equates to the U.S. definition — equal to or greater than the 95th percentile (of the 2000 Centers for Disease Control and



The most promising link between obesity and puberty is the adipokine–leptin–insulin axis and its interaction with the kisspeptin system, which is an important regulator of puberty."

- VERÓNICA MERICQ, MD, UNIVERSIDAD DE CHILE, SANTIAGO, CHILE

Prevention sex-specific BMI-for-age growth charts). They define precocious gonadarche in boys as a testicular volume greater than 3 ml before nine years of age in either testicle and precocious pubarche as the appearance of pubic hair before age nine, based on the Tanner scale. The defined age at gonadarche and pubarche onset as happening midway between two consecutive visits. The association between obesity and precocious puberty was analyzed through a logistic regression model, with the odds ratio and confidence interval corresponding to 95%.

The team found a positive and statistically significant association between total body obesity and precocious puberty from four to seven years of age, with 45 boys (9.1%) starting puberty early. Compared to boys with healthy weights, boys with obesity had a 2.7 times higher risk of early-onset puberty. They also analyzed BMI as a continuous variable, and the association held up, as it did for central obesity and precocious puberty. For central obesity, which is a more reliable indicator of increased fat mass, the risk was 6.4 times higher. The rates of both central and total adiposity increased among the boys during the study period, from 22.0% to 28.6% and 11.8% to 17.4%, respectively.

"The underlying mechanisms are not yet fully understood, and whether earlier onset of puberty is based on the activation of the hypothalamic–pituitary–gonadal axis is unclear," Mericq says. "The most promising link between obesity and puberty is the adipokine–leptin–insulin and its interaction with the kisspeptin system, which is an important regulator of puberty. However, peripheral action of adipose tissue (e.g., via other adipokines, aromatase activity) could also be involved in changes to the onset of puberty."

As prior studies have shown, other potential mediators linking the onset of puberty to obesity include nutritional



Boys who are "early bloomers" could have an increased risk of behavioral problems because their bodies have matured before their brains have processed the changes.

factors, epigenetics, and endocrine-disrupting chemicals, she explained. Toxic environmental stress has also been implicated.

Double Jeopardy

So, in addition to the physical burden and health risks that pediatric obesity confers as already described, these children are also at risk for a host of the physical, psychological, social, and emotional problems associated with precocious puberty itself.

On the physical side, precocious puberty has been correlated with type 2 diabetes and adult-onset asthma. The bones of these children stop growing earlier because such growth ceases toward the end of puberty, meaning they may have shorter stature than expected. Their physical childhood is cut short because their bodies show evidence of physical maturity, which can likewise make them vulnerable to bullying and lead to depression, substance abuse, and having sex earlier, consequences possibly related to the stress of being a so-called "early-bloomer" and not being on the same development wavelength as peers. "Early puberty might increase the risk of risk-behavior problems," Mericq says. For these children, their bodies have physically matured before their brains are ready to process this metamorphosis.

"In addition, it has been postulated that precocious puberty in boys could be related to higher incidence of testicular cancer in adulthood," she says. This parallels the purported higher risk of breast cancer that girls experiencing early puberty face.

Boys Will Be Boys

Obesity continues to confound researchers and clinicians alike. Although no one fully understands this many-headed hydra and how its pervasive injury to body systems unfolds, experts believe that prevention is the key to battling it. Once it has already occurred, reversing it in a long-lasting way is exceedingly difficult.

"Our results suggest that controlling the obesity epidemic could be useful in decreasing the risk for early puberty," said Mericq. Preventing pediatric obesity can be largely achieved by promoting a healthy diet and encouraging regular activity, according to *Pediatric Obesity* — *Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline.*

Maintaining a healthy weight might just let boys be boys.



AT A GLANCE

- In the past few decades, the rate of childhood obesity has skyrocketed worldwide, with a demonstrated link to precocious puberty in girls; that link was also established for boys in a recent Chilean study.
- Both total and central body obesity in Chilean boys evaluated starting at age four are associated with precocious gonadarche, defined as greater than 3 ml testicular volume before age nine.
- Of 527 total boys, 45, or 9.1%, entered puberty before age nine, with total obesity conferring a 2.7 times higher risk of starting puberty early, and central obesity 6.4 times higher risk.

HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT NEW PROGRESS IN ACHIEVING MALE HORMONAL CONTRACEPTION IN THE JUNE ISSUE.

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Conuce An A Newborn Difference in Sex Development in Infants

BY DEREK BAGLEY

ach year, Nayla Leon, MD, and Alejandra Reyes, MD, clinical geneticists based in Mexico City, Mexico, encounter more than 50 families with babies born with ambiguous genitalia — cases that can be challenging for clinicians, as diagnosis and management involves myriad decisions, and precise diagnosis is essential for management of a slew of issues the child may face.

Not as rare as previously thought, babies born with differences in sex development can present a vast array of challenges to clinicians, as well as to parents and the patients themselves. These cases require an experienced team of specialists from a variety of disciplines to ensure healthy and normal development.



Difference in sex development (DSD) cases are complex genetically and clinically, potentially with a hundred different causes. They can be present at birth with ambiguous genitalia. Some forms are life-threatening and should be treated immediately. Others are mild and can be treated when the child is older. Variations in more than 40 genes have been associated with DSD, but most cases do not receive a definitive diagnosis.

Increasing genetic information is improving DSD diagnosis and patient management, and while previous studies have shown that about one in 4,500 babies are born with ambiguous genitalia, recent research has shown that ambiguous genitalia in newborns may be more common than previously thought.

Leon and Reyes traveled to the Hudson Institute of Medical Research in Clayton, Victoria, Australia, to work with Vincent Harley, PhD, to develop a clinical algorithm to diagnose DSD based on a systematic review of the literature, which they published earlier this year in *The Lancet*. "We felt there was a need to describe the many forms of the condition (some 48 forms are described) and to provide a pathway for clinicians to navigate to achieve a diagnosis," Harley says. "In the past four years, five diagnostic algorithms have been published, being mainly clinical in scope or focused on molecular aspects. We designed a diagnostic tree that integrates traditional clinical practice with molecular diagnosis and emerging technologies."

Around this time, Banu Kucukemre Aydin, MD, of Istanbul University in Turkey, was studying the frequency of DSD with ambiguous genitalia in babies born in her country and found that not only was the frequency of ambiguous genitalia higher than in previous studies, but there may be a connection between the health of the mother and DSD. She and her colleagues published their work in the *Journal of the Endocrine Society*. "There was limited data available on the exact incidence of DSD with genital ambiguity at birth and most of the published studies were coming from Western countries, in which consanguinity rates are lower than our country," Aydin says. "That's why we wanted to determine the frequency of ambiguous genitalia in our population."

Here, we'll take a look at both papers and what they mean for babies born with ambiguous genitalia and DSD patients, their families, and the (ideally) multidisciplinary teams who care for them.

Quick, Definitive Diagnosis

Rapid diagnosis is of the utmost importance in children born with ambiguous genitalia. A quick, definitive diagnosis minimizes unnecessary testing, such as a battery of endocrine tests, multiple physical examinations, and imaging studies. At the heart of it is that parents want to know whether their baby is a girl or a boy. A faster diagnosis of a baby with a DSD can shorten this period of anxiety.

The good news is that technological advances have opened up several avenues to reaching a faster diagnosis. "We are in a genome revolution and in the DSD field, genetic testing is fast becoming the first-line approach," Harley says. "The standard battery of endocrine tests and imaging analysis as first-line studies is being superseded by genetic analyses."

However, Harley and his colleagues are fully aware that there are vulnerable communities, such as those in developing countries with no access to large-scale genetic testing. "We have suggested the classical approaches of endocrine analysis and imaging evaluation, but also detailed their limitations when used in isolation," Harley says. "We recommended that clinicians in vulnerable communities align with international consortia (e.g., DSD-TRN in the U.S., I-DSD in Europe) and research institutes or centers of excellence in DSD research to access genetic testing."

The algorithm developed by Leon, Reyes, and Harley captures 48 different possible DSD diagnoses into a single tree, and while it won't increase the number of patients identified with ambiguous genitalia (which can be easily diagnosed through clinical examination), Harley says that his hope for these babies is that the algorithm will help increase molecular diagnosis to well above 30%, the currently reported proportion of patients who receive a molecular diagnosis.

66 Education is key to ease parents' anxiety and to delay surgery. Still, we don't know the long-term impact of atypical genitalia on the psychological state of the child."

- VINCENT HARLEY, PHD, HUDSON INSTITUTE OF MEDICAL RESEARCH, CLAYTON, VICTORIA, AUSTRALIA

AT A GLANCE

- Difference in sex development (DSD) cases are heterogenous and can present challenges to clinicians.
- Researchers are employing genetic research to quickly diagnose and manage babies born with differences in sex development, as well as to explore potential connections between the mother's health and DSD.
- Optimal medical management of patients with DSD requires a multidisciplinary team of specialists.

66 There was limited data available on the exact incidence of DSD with genital ambiguity at birth and most of the published studies were coming from Western countries, in which consanguinity rates are lower than our country. That's why we wanted to determine the frequency of ambiguous genitalia in our population."

- BANU KUCUKEMRE AYDIN, MD, ISTANBUL UNIVERSITY, ISTANBUL, TURKEY

Not So Rare Anomaly

But the number of babies identified with ambiguous genitalia may actually be higher than previously reported. In a prospective study, Aydin and her team examined 14,177 newborns, all examined at birth; data on weeks of gestation, birth weight, and length were collected. "A structured questionnaire was used for data collection. Quigley and Prader scales were used for phenotypic grading. Clinical and genetic investigations were performed," the authors write. Eighteen babies with ambiguous genitalia were found among 14,177 newborns – or 1.3 in 1,000, far more than the previously reported one in 4,500. Aydin says that the reason for this is that past studies were mostly done retrospectively or using registries with a possibly lower capture rate.

But Aydin is careful here, pointing to the study's limitations, such as the fact that it was held in tertiary hospitals, to which complicated pregnancies are referred, causing a selection bias. "Additionally, in Turkey, the consanguineous marriage rate is high, causing a higher incidence of autosomal recessive diseases," Aydin says.





And again, the genetic approach is important, uncovering a possible connection between the mother's health and a diagnosis of DSD in her baby. Fifteen newborns were diagnosed with 46, XY DSD, which occurs in male infants when the body can't use testosterone properly or the testicles do not develop properly. Birth weight was lower in babies with 46, XY DSD than healthy babies, and preeclampsia was a common condition in those pregnancies. "It is believed that early placental dysfunction creates immune alteration and vascular disorder and causes preeclampsia," Aydin says. "In addition to our results, a Danish Nationwide Cohort Study reported that boys of mothers with preeclampsia had the highest occurrence of cryptorchidism and hypospadias, increasing with preeclampsia severity."

Aydin says that the Danish researchers posited that preeclampsia and genital anomalies share common etiologic factors and that placental dysfunction and androgen deficiency in early pregnancy are important in the etiology of male genital anomalies. "There are also other studies suggesting similar conclusions; readers can find some of which in our discussion section," she says.

Multidisciplinary Treatment Team

DSDs are highly heterogeneous, clinically and genetically unique. In every case, it is crucial to consider the needs, wishes, and concerns of the patients and their families. In babies born with ambiguous genitalia, the parents and, in the future, the patients, need psychological support and comprehensible information. "The heterogeneity of these conditions makes it difficult for parents to get specific advice from reliable sources online," Harley says. "The DSD multidisciplinary team [specialists in surgery, urology, endocrinology, psychology, psychiatry, radiology, nursing, and clinical genetics] needs to review each case individually for the optimal medical management. Psychosocial assessment is also required to strengthen the parent's and patient's ability to cope with the condition."

Harley goes on to say that non-reversible surgeries continue in children without their consent when conditions are non-life threatening as a result of pressure from parents, cultural norms, and/or societal pressures to normalize the genital appearance. "Education is key to ease parents' anxiety and to delay surgery," Harley says. "Still, we don't know the long-term impact of atypical genitalia on the psychological state of the child."

Aydin and her team plan to do more comprehensive genetic analyses in patients still coming in for follow-up, and she says she sees a near future in which whole genome sequencing will be used as one of the first-line tests for diagnosis of DSD, although some challenges to that remain, including long turnaround times, high costs, a lack of national healthcare system coverage, and difficulties in the interpretation of the results. For now, she says, "It would be good to see the frequency of ambiguous genitalia in other populations with new prospective studies."



How Screen Time and Snacking Impacts Adolescent Metabolic Health

A study presented at ENDO 2019 seems to indicate a link between teens who spend a lot of time in front of a screen and poor metabolic health. Due to the propensity of so many adolescents to snack while they gaze at everything from a television to a cell phone, strategies are needed to address these unhealthy habits.

ere in 2019, we live surrounded by screens: televisions, computers, tablets, phones, and on and on. This is not always necessarily a problem; people use computers for work or they read novels on their tablets or video chat with loved ones around the world.

But as we've entered this brave new world, studies have linked excessive screen time to the growing epidemic of childhood obesity and increased risk for adolescents developing metabolic

BY DEREK BAGLEY



While screen time has been considered a potential risk factor for cardiometabolic health for some time, it is not totally independent from other risk factors such as unhealthy eating habits.

syndrome, which in turn could lead to a higher risk for developing subclinical atherosclerosis and type 2 diabetes as an adult. Metabolic syndrome affects nearly 25.0% of the adult population and approximately 5.4% of children and adolescents in the U.S.

But according to research presented at **ENDO 2019** in New Orleans, these studies have had inconsistent results due to methodological differences among them. "The main question has emerged from literature and the interest of some students in my lab about lifestyle and cardiometabolic health among adolescents," says lead researcher Beatriz Schaan, PhD, of the Universidade Federal do Rio Grande do Sul in Porto Alegre, Brazil. "Screen time has been studied as a potential new risk factor for cardiometabolic health. However, it seems not to be totally independent from other behavioral risk factors, such as unhealthy eating habits."

Unhealthy Patterns

Schaan and her team set out to investigate the association between screen-based sedentary times and metabolic syndrome, and whether this association is modified by children and adolescents consuming unhealthy snacks. The research was part of the Study on Cardiovascular Risks in Adolescents (ERICA), a nationwide school-based survey of Brazilian teens. The study included data on 33,900 teens ages 12 to 17 years.

Schaan says that they first investigated whether the link between screen time and metabolic syndrome was independent of physical activity and total energy intake. "At this point, we observed that including these variables in the analysis reduced the strength of the association between screen time and metabolic syndrome, but did not eliminate it," she says.

High screen time and unhealthy snacking are harmful to adult health too; however, it's difficult to say if our results would be similar if we replicate these analyses in adults. Adult behavior can be easily adopted by youth, so if adults limit their screen time and avoid unhealthy snacking, they will collaborate to make a healthier environment at home."

- BEATRIZ SCHAAN, PHD, UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE, BRAZIL

Next, the researchers turned their focus to eating behaviors — specifically unhealthy snacking patterns — and found an interaction between screen time and unhealthy snack consumption while in front of screens. "This analysis partially changed our interpretation about the results, showing to us that unhealthy snack intake in fact plays a very important role in the association between screen time and metabolic syndrome among adolescents," Schaan says.

The researchers measured the teens' waists and blood pressure, and took blood samples to measure blood glucose, HDL-cholesterol, and triglycerides. Screen time was self-reported and categorized as two or fewer hours a day, three to five hours a day, and more than six hours a day. Snack intake was also self-reported, with answers separated as no (no habit of snacking while in front of a screen) or yes (snacking sometimes or every day). Almost 60% of the teens were female, and the average age was 14.6. Almost half of the teens were physically active; 85% said they usually eat snacks in front of the TV, while 64% usually ate snacks while using the computer or playing video games.

The researchers found 2.5% of the teens had metabolic syndrome. Those who spent six or more hours a day in front of screens were 71% more likely to have metabolic syndrome compared with those who spent less time in front of screens. However, heightened risk was only seen in those who reported usually eating snacks in front of screens. There was no association between screen time and metabolic syndrome among teens who reported no snacking in front of screens. Among teens who reported habitually eating snacks in front of the TV or computer, the risk for metabolic syndrome rose the longer teens spent in front of screens.

"When we observed that total energy intake materially unchanged the association between screen time and metabolic syndrome and decided to explore unhealthy eating behaviors, we thought that the low nutritional quality of the snacks combined with the entertainment in front of screens, which may induce an unhealthy food intake, could be the key for this conundrum," Schaan says. "Thereafter, the results confirmed that hypothesis, at least in part."

Screens, Screens Everywhere

Of course, many health organizations recommend limiting screen time each day, and while that certainly seems like a simple suggestion, it's not always an easy one to follow given the sheer ubiquity of screens — especially in young people's lives. "Indeed, today young people live surrounded by screens and

AT A GLANCE

- Excessive screen time has been associated with the development of metabolic syndrome in adolescents, but these associations aren't always consistent.
- New research presented at ENDO has shown that the association between excessive screen time and metabolic syndrome is modified by unhealthy snacking while in front of screens.
- Strategies to address metabolic syndrome in adolescents should aim at limiting unhealthy snacking during sedentary screen times.



Screen time has been studied as a potential new risk factor for cardiometabolic health. However, it seems not to be totally independent from other behavioral risk factors, such as unhealthy eating habits."

- BEATRIZ SCHAAN, PHD, UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL, PORTO ALEGRE, BRAZIL

it's not always a bad thing," Schaan says. "Thus, limiting the consumption of junky food in front of screens can be easier than avoiding screen-based activities."

Schaan says that she and her team believe that the relationship among screen time and unhealthy snacking and cardiometabolic health in adolescents can be considered synergic or at least complementary. "It is possible that unhealthy snacking occurring in front of a screen is the direct result of more exposure to the screens," she says. "A circular pattern could also be occurring; for example, those who tend to eat unhealthy snacks while in front of a screen also tend to spend more time in front of screens, and this in turn leads to even more eating unhealthy snacks. However, this picture is not completely clear yet and more studies are needed."

Strategies to address metabolic syndrome among adolescents should aim at limiting unhealthy snacking while in front

of screens, Schaan says, which may reduce the strength of the association between total screen time and metabolic syndrome. Moreover, programs to reduce screen time and to adopt policies to incentivize a healthy diet through the media — such as restricting junk-food advertisements during children's shows — can be helpful to improve metabolic health in this population.

For now, Schaan says that the adolescents involved in the study and their parents were very interested in the results, since they could make some relatively simple lifestyle changes that could possibly lower their future cardiovascular risk. "High screen time and unhealthy snacking are harmful to adult health too; however, it's difficult to say if our results would be similar if we replicate these analyses in adults," Schaan says. "Adult behavior can be easily adopted by youth, so if adults limit their screen time and avoid unhealthy snacking, they will collaborate to make a healthier environment at home."



- BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT TESTOSTERONE TREATMENTS IN HYPOGONADAL MEN WITH OBESITY IN THE JUNE ISSUE.



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A Delicate Balance:

Older patients with diabetes can benefit from even more carefully personalized treatment than their younger counterparts. A new Endocrine Society clinical practice guideline provides a new look at how to care for this growing population.

Treating Older Patients with Diabetes

new Endocrine Society clinical practice guideline aimed at treating diabetes patients 65 years and older stresses that longer life expectancies mean that these patients will benefit from treatment similar to that offered younger patients. But it also highlights the need for special care because the population is more susceptible to acute problems such as hypoglycemia that can be triggered by avid efforts to prevent long-term complications.

And because cognitive impairment is more common in older diabetes patients than in their healthier counterparts, providers may need to simplify drug regimens to make them easier for patients to follow.

Providers must resist the outdated belief that because the patients are older, they may not live long enough for potential complications to progress to problems, according to Derek LeRoith, MD, PhD, of Mount Sinai School of Medicine in New York City. LeRoith chaired the committee that developed the guideline.

BY ERIK SEABORG





"A lot of physicians look at somebody 70 and above [and] say, '[their problems are] part of the aging process, we don't have to do too much," LeRoith says. "We now know that even older [patients with diabetes] live for many more years, so the guideline stresses that they should be fully treated to reduce the acute effects [as well as] the chronic complications of diabetes." The guideline provides strategies for providers to find a balance between long-term and short-term goals.

A Tie to Aging

In the U.S., a third of those over 65 have diabetes, and almost half have prediabetes, so the guideline applies to a broad swath of the population. And the aging process is an important part of the equation.

"The underlying pathophysiology of the disease in these patients is exacerbated by the direct effects of aging on metabolic regulation," the guideline says. "Similarly, aging effects interact with diabetes to accelerate the progression of many common diabetes complications."

In a nod to this interplay, the guideline recommends that providers be careful to avoid overtreatment in older patients and design treatment regimens specifically to minimize hypoglycemia.

The guideline encourages clinicians to consider available evidence and a patient's overall health, likelihood to benefit from interventions, and personal values when considering treatment goals such as glucose, blood pressure, and cholesterol. Our framework prioritizes blood glucose targets over the hemoglobin A1c test when managing diabetes in older adults."

- DEREK LEROITH, MD, PHD, MOUNT SINAI SCHOOL OF MEDICINE, NEW YORK; CHAIR, GUIDELINE-WRITING COMMITTEE

Personalizing Treatment

And just as individuals age uniquely, LeRoith emphasizes the need for "personalized medicine. Each individual needs to be evaluated differently." For example, healthier patients without cognitive impairment might pursue good glycemic control using hemoglobin A1c testing and good blood pressure control to prevent complications.

But many older adults with diabetes have co-morbidities such as cognitive impairment, frailty, renal disease, cardiovascular disease, impaired vision, and rheumatoid arthritis that affect diabetes self-management. For these patients, LeRoith says that it may be better to "back off in our goals to make sure that, in our enthusiasm to prevent the long-term complications, we don't cause short-term complications. Overtreating or not following the patients closely enough can lead to problems like hypotension and hypoglycemia."

"The guideline encourages clinicians to consider available evidence and a patient's overall health, likelihood to benefit from interventions, and personal values when considering treatment goals such as glucose, blood pressure, and cholesterol. Our framework prioritizes blood glucose targets over the hemoglobin A1c test when managing diabetes in older adults," LeRoith says.

Diabetes exacerbates the decline in cognitive function that can come with the aging process, and providers should take this into account. In patients with a diagnosis of cognitive impairment, the guideline suggests that "medication regimens be simplified and glycemic targets tailored to improve compliance and prevent treatment-related complications." But when it comes to treating cognitive impairment itself, the guideline recommends the same treatment for diabetes patients as for non-diabetes patients.

Diagnostic Testing Surprise

LeRoith said that one surprise from the literature review that the committee performed in preparation for the guideline related to tests used for diagnosing diabetes. Many conditions that are relatively common in this age group can affect the lifespan of red blood cells in the circulation and therefore affect the accuracy of hemoglobin A1c test results.

Patients who meet the criteria for only prediabetes by fasting plasma glucose or hemoglobin A1c tests may be tipped over to a diagnosis of diabetes if they are given a two-hour glucose post-oral glucose tolerance test. The oral glucose tolerance test may be revelatory in high-risk patients who have conditions or risk factors such as overweight or obesity; a first-degree relative with diabetes; higher risk because of race or ethnicity; or cardiovascular disease, hypertension, or sleep apnea.



AT A GLANCE

- Treatment of older patients with diabetes requires a balancing act to control blood sugar closely enough to prevent long-term complications while avoiding short-term problems, particularly hypoglycemia.
- Because seniors with diabetes experience cognitive impairment at higher rates than their counterparts, simplifying drug regimens can make it easier for patients to adhere to them.
- With patients living longer, tailoring treatment to match a patient's overall health and particular co-morbidities is more important than ever.

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- DEREK LEROITH, MD, PHD, MOUNT SINAI SCHOOL OF MEDICINE, NEW YORK; CHAIR, GUIDELINE-WRITING COMMITTEE



The patient may benefit because a diagnosis of prediabetes can limit treatment options to recommending lifestyle changes, whereas crossing the border into diabetes opens the possibility of prescribing medications.

And on the subject of medications, the guideline recommends metformin as the initial oral medication for glycemic management (in addition to lifestyle management). For those who do not achieve glycemic targets with metformin and lifestyle, the guideline recommends the addition of "other oral or injectable agents and/or insulin." But to reduce the risk of hypoglycemia, it recommends avoiding sulfonylureas and glinides and using insulin sparingly.

Recommendations for Specific Situations

The guideline contains many specific targets and recommendations for managing the common co-morbidities a provider may be called on to treat, including:

- Targeting blood pressure levels of 140/90 mm Hg to decrease the risk of cardiovascular disease outcomes, stroke, and progressive chronic kidney disease;
- Ordering an annual lipid profile and using statin therapy to achieve the recommended lipid levels for reducing absolute cardiovascular disease events and all-cause mortality; and
- Administering annual comprehensive eye exams to detect retinal disease.

"This [guideline] is a good clinical tool," says Anne Peters, MD, director of the University of Southern California Clinical Diabetes Program, who was not on the guideline committee but provided input during the writing and review process. "Many of these older patients require a great deal of individualization of care, and it can be hard to create a 'one size fits all' set of targets. The authors give us a good paradigm for thinking about patients and targets."

The guideline was co-sponsored by the European Society of Endocrinology, Gerontological Society of America, and Obesity Society. Entitled "Treatment of Diabetes in Older Adults: An Endocrine Society Clinical Practice Guideline," it was published in the May 2019 print edition of *The Journal of Clinical Endocrinology* & *Metabolism* and is available online at www.endocrine.org /2019diabetes.

- SEABORG IS A FREELANCE MEDICAL WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT TREATING OSTEOPOROSIS IN POST-MENOPAUSAL PATIENTS IN THE MAY ISSUE.

Action on NIH Appropriations in Congress

s this issue of *Endocrine News* goes to press, the U.S. House of Representatives is considering a package of appropriations bills that would partially fund the federal government in fiscal year (FY) 2020. Among the four bills under consideration is the Labor-Health and Human Services and Related Agencies bill, which includes funding for several of the Society's priorities — the National Institutes of Health (NIH), Diabetes Prevention Program (DPP), and Title X. The Endocrine Society is supporting passage of the package, as it includes a much-needed increase for these programs, including a \$2 billion increase for the NIH, which would bring total funding for the agency to \$41.1 billion next year. The package also includes \$400 million for Title X, which would be the program's first increase in six years, and \$30 million for the DPP, a \$5 million increase over FY 2019.

Although progress in the House is encouraging, there is still a long way to go before a final appropriations bill is enacted and we can count on additional funds for these programs in 2020. As of June 13, votes are currently taking place on multiple amendments to the bill, including politically contentious changes such as the removal of restrictions on fetal tissue research. To encourage swift passage of the bill, Endocrine Society members took action through a new advocacy campaign, wrote to their elected representatives, and participated in Capitol Hill Days to visit congressional offices and directly make the case for more funding for our priorities. However, more work is needed to ensure that the proposed increases become a reality.

The Senate also needs to advance similar appropriations bills before President Trump would have an opportunity to sign the final bills. Furthermore, while negotiations are ongoing toward an eventual deal to raise the Budget Control Act caps and the debt ceiling, both of these issues need to be addressed before any increases to funding levels can be distributed. The Senate has expressed willingness to begin work on FY 2020 appropriations, but it is not clear what their overall spending levels would be in the absence of concrete top-line spending numbers enabled by a deal to raise the budget caps. In addition, the White House has threatened a veto of the House bill because it exceeds President Trump's proposed spending levels.

Endocrine Society members can look forward to more opportunities to influence Congress and help ensure that biomedical research, Title X, and DPP funding are prioritized in the coming weeks and months. To stay informed on this developing issue, we encourage you to check https:// endocrinenews.endocrine.org for more information.



Endocrine Society Opposes Gene Patent Legislation



his May, the Endocrine Society was extremely concerned to learn of a new legislative proposal introduced by Senators Thom Tillis (R-NC) and Chris Coons (D-DE) to amend Section 101 of the Patent Act.

As currently written, the bill would authorize patent protections for products and laws of nature, abstract ideas, and other general fields of knowledge, thereby enabling patents for genes and naturally occurring associations between genes and diseases. The draft bill also states explicitly that any "judicially created exception to patent-eligibility will be abrogated," effectively overturning several recent U.S. Supreme Court rulings establishing that medical diagnostic tests based on blood metabolite levels (*Mayo Collaborative Services v. Prometheus Labs*) and human genes isolated from the body (*Association for Molecular Pathology v. Myriad Genetics*) are not eligible for patent protections.

The Endocrine Society and other members of the biomedical research community immediately recognized the potential challenges that this legislation could impose on researchers who study the relationship between genes and disease and the potential for harm to patients who rely on accurate diagnostic tests for genetic diseases. In June, we joined with a diverse coalition of stakeholders and reached out to Sens. Coons and Tillis to register our opposition to the bill as currently written and argue that genes and other naturally occurring matter and relationships should never be granted to anyone as intellectual property.

We expect that there will be changes to the draft before it is formally introduced in the House or Senate, and we will keep pressure on legislators to ensure that any final bill will not render genes or other natural phenomena and relationships patent-eligible. We will continue to monitor and report on any developments related to this bill, or opportunities for members to weigh in, in *Endocrine News*.

66 Current estimates predict that as many as one in four people already have non-alcoholic fatty liver disease or NASH; increasing public awareness is an important goal of the Society.

Congressional Briefing Raises Public Awareness for International NASH Day

n June 12, we participated in International NASH Day to help raise awareness about non-alcoholic steatohepatitis (NASH) and fatty liver disease.

As part of this effort, which was spearheaded by the Global Liver Institute (GLI), Society member and expert Rita Basu, MD, spoke at a congressional briefing about the role of endocrinology in the screening and diagnosis of NASH and the importance of early detection. As current estimates predict that as many as one in four people already have non-alcoholic fatty liver disease or NASH, increasing public awareness is an important goal of the Society.

We participate in the GLI NASH Council to bring together key stakeholders to quantify and address the disease and have launched a series of educational webinars on treatment. More information can be found at: www. clinicaloptions.com/hepatitis/programs/nash-hot-topics.



Advocating for patients at International NASH Day. Pictured, left to right, are: Kimberly Martinez, NASH patient advocate, GLI Advanced Advocacy Academy, Broken Arrow, Okla.; Nadege T. Gunn, MD, physician investigator, gastroenterology/hepatology, Pinnacle Clinical Research, Austin, Texas; Donna Cryer, JD, president and CEO, patient advocate, Global Liver Institute; Rita Basu, MD, professor, **Division of Endocrinology, Department of** Medicine, University of Virginia, Endocrine Society, Charlottesville; and Zobair M. Younossi, MD, MPH, FACG, AGAF, FAASLD, chairman, **Department of Medicine, Inova Fairfax Medical Campus, Professor of Medicine, Inova Fairfax** Hospital, American Gastroenterological Association, Fairfax, Va.

AMA House of Delegates Considered Many Endocrine-Related Policy Resolutions



he Endocrine Society attended the American Medical Association (AMA) House of Delegates (HOD) in June to establish policy positions on topics of importance to patients and healthcare providers.

Our delegation includes Amanda Bell, MD, Palak Choksi, MD, Shivani Agarwal, MD, Barbara Onumah, MD, Robert Vigersky, MD, and Daniel Spratt, MD. We attend the AMA meetings to further our policy agenda by garnering the support of the House of Medicine, which bolsters our advocacy efforts on Capitol Hill and with federal agencies as an additional means of support. In addition to passing policy that supports the Society's priorities, we also fight against resolutions that will be detrimental to endocrinologists or the patients they treat.

The HOD considered a wide range of resolutions, from Medicare for All to gender equity in medicine. We focused our attention on resolutions that dealt with transgender/gender identity, infertility, contraception, drug pricing, and obesity. We spoke in support of resolutions advocating for physician awareness and patient education on fertility preservation for members of the transgender and non-binary community prior to undergoing gender-affirming therapies and for cancer patients when gonadotoxic treatment is used. We also advocated for a reduction Endocrine Society member Daniel Spratt, MD, Division of Reproductive Endocrinology & Infertility from the Maine Medical Center, Portland, speaks at the American Medical Association House of Delegates meeting in June. Spratt was one of several Endocrine Society members who served as part of a delegation on behalf of the Society.

in the consumption of processed meats and a study on the effects of exposure to glyphosate on health.

Finally, the HOD considered a resolution opposing the requirement for gender-based medical treatments for athletes with disorders of sexual development to compete and agreed that a study is needed to understand the existing research and the impact on athletic competition. We are analyzing the impact of these new policies on our members and will work with the AMA to advance our mutual policy priorities.

We also worked closely with the delegates from the American Association of Clinical Endocrinologists, American Society for Reproductive Medicine, and American Association of Endocrine Surgeons during the meeting on issues of importance to endocrinologists. The Obesity Caucus meeting brought together delegates who have an interest in impacting the obesity epidemic to discuss opportunities to raise awareness of the disease at the HODs meetings and in our communities.

Making Your Voice Heard: Taking Action is Faster and Easier Than Ever Before!

o help our efforts, Endocrine Society launched a new, easy-to-use online advocacy platform that makes having your voice heard easier than ever before!

Our new online platform features a cleaner, more modern look and will help us expand our grassroots efforts in the U.S. and the European Union. Using this new tool, we can better target policymakers with our messaging, build social media campaigns, and collect stories from our members to share with congressional and Parliamentary members.

To learn about our latest campaigns and how to make your voice heard today, visit us at **endocrine.org**/ **takeaction** today!

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message that the House of Representatives needs to pass this.	-State - E	



Get the latest recommendations and treatment strategies, which take into consideration the overall health and quality of life of older individuals with diabetes, defined as age 65 or older.

Recommendation Highlights:

- Simplify medication regimens and tailor glycemic targets in older adults with diabetes and cognitive impairment (i.e. dementia) to improve compliance and prevent treatment-related complications.
- Target blood pressure levels of 140/90 mmHg to decrease the risk of cardiovascular disease outcomes, stroke, and progressive chronic kidney disease.
- > Establish clear blood sugar targets for older adults with diabetes in hospitals or nursing homes while avoiding hypoglycemia.

READ THE GUIDELINE AT ENDOCRINE.ORG/2019DIABETES



Aside from having to deal with your research, grants, safety, and other concerns in your lab, another important task is managing your staff. *Endocrine News* talked to some management pros for basic hacks on how to be a better manager.

BY GLENDA FAUNTLEROY SHAW

MANAGER HACKS: How to Be a Better Boss

t is no secret that having a good boss makes coming to work much easier. With the number of hours spent at the laboratory or office, having a pleasant relationship with a boss can ease the stress of long work weeks. Statistics, however, indicate that many employees may not be doing their best work, and they point to poor managers as a reason.

The Gallup's 2017 State of the American Workplace found that most employees in the U.S. show up to work daily without the "guidance, incentives, and support needed to perform at their best." What's more, only 21% of workers think their performance is "managed in a way that motivates them to do outstanding work." On the flip side, 59% of employees are more likely to be engaged when they are supervised by highly engaged managers rather than actively disengaged managers.

So how can managers be better? While acknowledging that opinions of a manager's performance can differ among the varied personalities in the workplace, experts do agree that following these tips are a good way to please the masses.

Hack #1: Be A Coach

In recent years, managers who succeed have seen their roles shift from "boss" to "coach." In this new role, to be a great manager, one must focus on both the quality and quantity of the interactions with team members. The difference between a boss and a coach appears to fall in the time spent. Coaching relationships require more personal and frequent interactions than usual.

To make your communication more personal, get on a first-name basis with your employees and share their excitement and concerns. Employees value communication from their managers, not just about their roles and responsibilities, but also about what happens in their lives outside of work, according to Gallup. The study revealed that employees who feel their manager is invested in them as people are more likely to be engaged.

LABORATORY NOTES

And all modes of communication can have an impact on engagement, whether in person, email, or even by instant message.

Hack #2: Ask the "Magic" Question

"What do you think?" This is the magic question, writes Jerry Wilson in *151 Quick Ideas to Inspire Your Staff.*

"These are the four most important words in the world; when you ask, you learn. When you learn, you grow. When you ask, you get information and other opinions to help make better decisions," he says.

All too often managers are afraid that asking other people for their opinion will make us "small and trivial, and that we're not capable of making our own decisions," Wilson writes. However, using these four words can be a boost. And when you ask people what they think, be very careful to give credit where credit is due. Be sure to acknowledge employees' feedback with verbal or written recognition. "What gets rewarded gets repeated."

Hack #3: Hire a Coach

We all know being a great boss is challenging. But the good news is that there is help available to turn a so-so or mediocre boss into a good one. Richard Kinsley, CEO and managing partner of the Kinsley Group, uses the term "followership" to describe the skills that talented leaders need. The Kinsley Group, headquartered in Indianapolis, Ind., offers executive coaching services from a team of coaches based in more than 100 countries.





Looking to read more about becoming a better leader? These books are a good start:

- Progress Principle, by Teresa Amabile and Steven Kramer
- Influence, by Robert Cialdini
- Made to Stick, by Chip and Dan Health
- **•** Thinking, Fast and Slow, by Daniel Kahneman
- Quiet, by Susan Cain

SOURCE: "12 BOOKS THAT EVERY LEADER SHOULD READ," BY BOB SUTTON, WWW.LINKEDIN.COM.

"The most frequent request [we get] concerns talented leaders who lack one or more followership skills," Kinsley says.

These necessary manager skills include:

- The ability to recognize when their approach or style might actually be impeding progress;
- The ability to focus on shared objectives those they share with their team, their peers, and the overall organization, not just their own objectives;
- The ability to build and nurture strong professional relationships up, down, and across the organization; and
- The ability to coach, teach, and otherwise enable the success of others.

Executive coaching can help develop these skills through detailed personalized programs.

"All leaders are capable of improvement if they are open to and accept the need to improve," Kinsley says. The key is to be sure to engage coaches who have the requisite credentials to be helpful to their clients, he says. The most effective coaches are those who have experience in their client's world/industry.

- FAUNTLEROY SHAW IS A FREELANCE WRITER BASED IN CARMEL, IND. SHE IS A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS*.

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