NEW RULES: MEDICARE NOW COVERS CGMs

SEPTEMBER 2018

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

INTERNA

Women's Health

ENDOCRINE SCIENCE CONTINUES TO TAKE THE LEAD IN ADVANCING WOMEN'S HEALTH RESEARCH AND TREATMENT.

- Breastfeeding & Obesity: New studies show that breastfed offspring might be at higher risk for obesity.
- Understanding PCOS: Analyzing new research and guidelines for treating Polycystic Ovary Syndrome.
- Gone Fishing: Does a diet rich in seafood increase the chances for pregnancy?

QUALITY TIME:
Making the most of your time at the bench.

TRENDS & INSIGHTS:
Sex, gender differences in research; Insulin secretion in metastatic insulinoma; Group exercise and bone loss; and more.

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ENDOCRINE SOCIETY

Make Your Voice Heard and Cast Your Ballot for New Officers

This year becoming the president of the Endocrine Society has been one of the pinnacles of my professional career. As I look back at all the years I have been involved in this organization, which I consider my professional home, I so value all the friendships I have made and how much I have learned from my colleagues and mentors throughout the years.

I joined the Endocrine Society in 1991 and I have personally experienced how the Society helps members at every stage of their careers. I have served in many of the Society committees, and through this participation, have learned skills that have benefited me in my own professional career. As a new member, attending **ENDO** is an eye-opening experience that may create many other opportunities. However, I encourage everyone to look for ways to engage in other activities as much as possible throughout the year beyond attending the annual meeting.

Many of you are familiar with committees and may have served or expressed interest to serve on a committee. The committee appointments process is a challenging task for the president-elect, who every year reviews a very long list of recommendations to select appointees for a limited number of positions, with most committee terms lasting three years. As part of this year's Strategic Plan, SP4, a Governance Task Force has been created to assess the committees/working groups needed to carry out SP4 goals and the vision of the organization. One of the goals of the task force is to create more opportunities for members to volunteer for more focused tasks or projects and for shorter terms. We hope that by creating these new openings, we will be able to engage more of our talented members who are eager to contribute to our organization and who will one day become our future leaders. The Governance Task Force is meeting in early September, so you will hear more about their recommendations in one of my future letters.

It is through member engagement that the future leaders of the Society emerge, and I want to provide you with some brief information about this year's election which is launching this month.

As you may know, the Nominating Committee is responsible for selecting the candidates for the ballot each year from the names collected via a Society-wide Call for Nominations. The ballot for the 2019 Endocrine Society Election will open on September 11 and will remain open until October 10. The Society leadership is well balanced, and each year a president-elect, a vice president, and a Council-designated seat are elected from one of the three constituencies — basic scientists, clinical scientists, and physicians-in-practice — with the candidates for each of the positions coming from a different constituency. The positions on the ballot for the 2019 election are: president-elect (clinical scientist); vice president (physician-in-practice); Council (one basic scientist seat and two "at large" seats).

Our Society has an outstanding group of qualified candidates on the ballot, and I encourage all our voting members to participate in this very important activity. To facilitate the voting process, a link to the electronic ballot is now available in the Society's website. Please remember to cast your vote and remind your colleagues as well. This is *your* Society, and your participation in the election is important!

Thank you for your participation. If you have any questions or comments, please contact me at **president@endocrine.org** EN

— **Susan J. Mandel,** MD, MPH, President, Endocrine Society

VOTE

2019 ELECTION FOR OFFICERS AND COUNCIL

The polls for the 2019 Election open on September 11, 2018 and we ask for your votes. Members with voting privileges have the opportunity to participate in the election and select their future Society Officers and Council.

Submit your votes on **endocrine.org/election**.

Questions should be directed to election@endocrine.org or call 202.971.3636.

Ballots will be accepted through October 10, 2018.

ENDOCRINE SOCIETY

Hormone Science to Health

FROM THE **EDITOR**

Endocrine Research Leads the Way in Improving Women's Health

Since September is Polycystic Ovary Syndrome (PCOS) Awareness Month, it seemed like the ideal time to take a look at the progress that has been made in terms of research and treatment guidelines for this perplexing condition. In "Polycystic Ovarian Syndrome: The Evolving Picture," (p. 30), writer Kelly Horvath speaks to those involved with updated international treatment protocols, including one that the Endocrine Society helped craft. Since the Endocrine Society first published its groundbreaking Scientific Statement on PCOS in 2015, there has been a flurry of activity. Richard S. Legro, MD, of Penn State College of Medicine and the chair of the task force that developed the statement, says that for the first time in many years pharmaceutical companies are investigating both known and novel mechanisms of PCOS, "which is exciting because we haven't seen this kind of theoretical exploration in 20 years."

Senior editor Derek Bagley looks at a new study recently published in *The Journal of Clinical Endocrinology & Metabolism* that examines the relationship between seafood and the ability for couples to procreate. In "Fish Tales" (p. 18), Bagley reports on the study "Seafood Intake, Sexual Activity, and Time to Pregnancy" by Audrey Gaskins, ScD, of the Harvard T.H. Chan School of Public Health in Boston, et al., that states that couples achieved higher rates of pregnancy when they consumed at least two servings of seafood per week. "While seafood is a recommended component of many healthy eating patterns," Bagley writes, "in the context of fertility, it's largely been studied as a potential source of harm, given that it could be a source of exposure to toxicants such as organochlorines, dioxins, and mercury." Despite all this, new research has shown the benefits of a seafood-rich diet when it comes to fertility. And, as the article points out, couples that have meals together often share … dessert.

Six months later and we're still talking about the science presented at **ENDO 2018** in Chicago last March. In "Wean Some, Lose Some: Breastfeeding & Obesity" on page 36, Horvath looks at three different studies that were presented this year that all showed a curious but indelible link to obesity, or at least the risk of obesity, in breastfed offspring. The studies that are examined are "In BRCA mutation carriers, obesity is linked with increased DNA damage in normal breast gland cells" by Kristy A. Brown, PhD, and

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colleagues from Weill Cornell Medicine in New York; "Breastfeeding may protect high-birthweight infants from childhood obesity" by Hae Soon Kim, MD, of Ewha Womans University College of Medicine in Seoul, South Korea, et al.; and "Overeating during breastfeeding may affect the health of offspring" by Jennifer W. Hill, PhD, and Mengjie Wang, MD, at the University of Toledo College of Medicine and Life Sciences in Ohio. While more research is needed to ascertain if these study results are applicable to humans, the research will no doubt find its way to the many meeting rooms at a future **ENDO**. EN

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

CLARIFICATION:

BCG Vaccine May Lead to Long-Term Improvement in Blood Sugar Levels in Patients with Type 1 Diabetes, Study Shows (Trends & Insights, August 2018)

The results of this study were based on a small sample of patients — three patients who received the BCG vaccine and three patients who received a placebo — who continued insulin treatment and were followed in an uncontrolled fashion for an eight-year observation period, and the most likely contributor to HbA1c lowering in a person with type 1 diabetes (insulin treatment) was not adjusted for in the analyses. Further research is needed. A previous version of this article seemed to imply that the BCG vaccine alone restored normal blood sugar levels. That is not the case; we regret the error.

Society Introduces New Meeting Code of Conduct

With the approval of Council, the Endocrine Society has a new Meeting Code of Conduct and a process to report possible harassment.

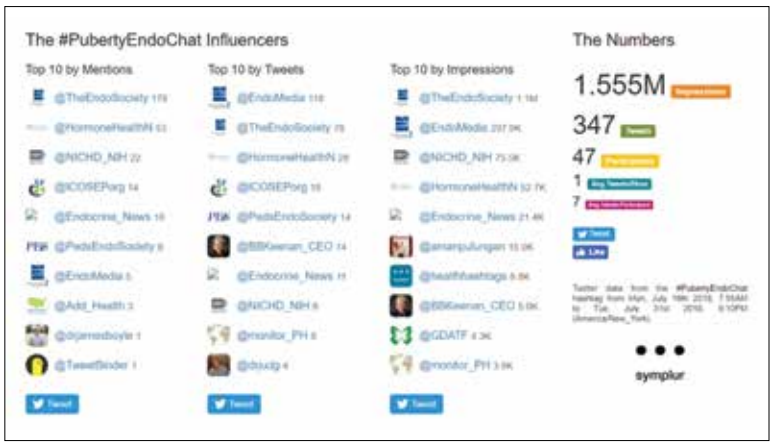
The Code outlines the expectations for professional behavior at Society activities and events, the process for reporting and evaluating complaints, and the consequences for unacceptable behavior. Meeting environments should foster open dialogue and the exchange of scientific ideas, promote equal opportunities and treatment for all participants, and be free of any form of harassment and discrimination.

According to Endocrine Society CEO Barbara Byrd Keenan, the creation of the new Meeting Code of Conduct was all about safety and respect. "Our Council has created this new Meeting Code of Conduct to ensure that anyone who attends a Society event feels like they are a part of the endocrinology community without any fear," she says. "We all have the same goals to advance the science and practice of endocrinology."

All participants are expected to treat others with respect and consideration and demonstrate professional conduct at all Endocrine Society meetings, activities, and events, and to alert staff or venue security of any dangerous or inappropriate situations or if anyone is in distress. With specific examples of expected and improper behavior, the Meeting Code of Conduct provides specific guidance as the Society is committed to providing a safe and welcoming environment for all that is free of any form of harassment and/or discrimination.

The Code and process are available on the Society's website **www.endocrine.org/conduct** and will be publicized at Endocrine Society activities and events. For additional information on the Meeting Code of Conduct, please contact Wanda Johnson, chief program officer at **wjohnson@endocrine.org.**

Puberty Twitter Chat Engages Key Stakeholders



On July 26, the Endocrine Socity conducted a Twitter chat about puberty that provided science-based information on the transition to adulthood to parents and consumers.

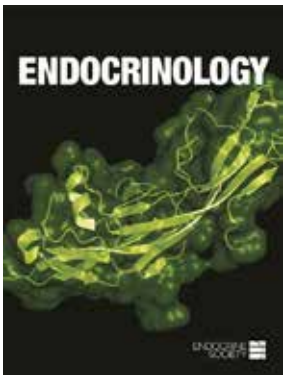
The curated conversation generated more than 1.5 million impressions – a measure of how many times Twitter users saw our hashtag – according to the social media analytics firm Symplur. As a result of the Twitter chat, we tracked more than 1,000 visits to our digital resources, including the Hormone Health Network's video, website, and social media profile pages to learn more about us and our work.

High-profile participants included invited guests from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the Pediatric Endocrine Society. Moderators Alicia Diaz Thomas, MD, MPH, and Christine Burt Solorzano, MD, shared the latest science-based information on puberty with the International Coalition of Organizations Supporting Endocrine Patients, which represents parents of children with endocrine conditions.

Endocrinology Launches Early Career Review Board

After the Early Career Forum at **ENDO 2018** in Chicago, a new opportunity that gives early career members the chance to review papers that appear in *Endocrinology* was born.

As a member of the Early Career Review Board, early career members have the chance to review papers that appear in *Endocrinology*. This opportunity is open to all early career members as long as they have a doctoral degree and have published at least three papers in a peer-reviewed journal with one as either first author or first co-author.



Endocrinology began soliciting nomination for early career reviewers (ECRs) in June. Potential ECRs can self-nominate or be nominated by a past *Endocrinology* reviewer and will be a subset of the main reviewer pool. ECRs will contribute third reviews of a manuscript, which may be appended to the authors' notification at the discretion of the associate editor.

According to *Endocrinology* editor-in-chief Teresa K. Woodruff, PhD, in the July issue, this process will teach the ECR the difference between a good critique and an unjustified criticism of a paper. "It may take 10 reviews or it may take 50 reviews, but the goal is to provide an on-ramp and a roadmap to peer review for new members of our community," she writes, adding that ECRs will be recognized annually in the journal. The goal is to find 30 ECRs for the pilot year and then assess the outcomes.

For more information or to become a member of the Early Career Review Board, write with details to Claudia Barrett at **cbarrett@endocrine.org.**

NDEP's *Guiding Principles for Diabetes Care* Gets an Update

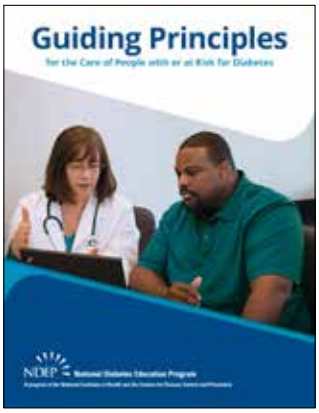
The National Diabetes Education Program's (NDEP) *Guiding Principles for the Care of People with or at Risk for Diabetes* received an update in August, according to the National Institute for Diabetes and Digestive and Kidney Diseases (NIDDK).

This recent update reflects new and changing evidence that has evolved over the last several years, including:

- Emphasis on the importance of diabetes self-management education and support, and of providing patient-centered care using shared decision making and individualized care
- Development of a new Principle 6: Address Overweight and Obesity in the Management of Diabetes

This resource provides a set of 10 clinically useful principles highlighting areas of agreement in diabetes prevention and management that will help healthcare teams improve treatment for adults with or at risk for diabetes.

The Endocrine Society is one of 20 professional societies and organizations that advocate the use of NDEP's *Guiding Principles for the Care of People with or at Risk for Diabetes.*



The U.S. Department of Health and Human Services' National Diabetes Education Program is jointly sponsored by the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) with the support of more than 200 partner organizations. EN

BY DEREK BAGLEY
Senior Editor

Carefully Considering Sex and Gender Differences Leads to More Rigorous, Relevant Research

> "Sex- and gender-informed perspective "increases rigor, promotes discovery, and expands the relevance of biomedical research."

Investigators should carefully consider sex and gender differences when conducting research, according to the authors of a paper recently published in *Endocrine Reviews*.

The review, by Janet W. Rich-Edwards, PhD, of Brigham and Women's Hospital in Boston, et al., makes the case that sex- and gender-informed perspective "increases rigor, promotes discovery, and expands the relevance of biomedical research" and lays out considerations and best practices for researchers to achieve these goals.

Sex differences exist in every facet of medical research, from cell to population to treatment, the authors write. Gender determines health because gender can influence environment and determine access to resources. Sex differences exist in symptoms, and the authors point out that there is even a "sex bias" in gene expression. "In short," the authors write, "the rigor of research depends on researchers' understanding of the ways in which sex and gender influence the biologic systems they study."

But there is an apparent lack of literature regarding sex differences, or at least true sex differences. The authors argue that researchers should keep in mind the historic neglect of women in clinical studies and the sex of animals and cells in basic research. "Furthermore, as argued below, the proliferation of ill-considered and often unplanned sex difference inquiries leads to a literature of contradictions," the authors write. "Thus, the absence of evidence for sex differences is not necessarily evidence of the absence of sex differences."

The authors are aware that the very concept of gender is complex and shifting, and they write that new measures of gender are likely to emerge, but again, there are few studies addressing this complexity. Some researchers have proposed methods for distinguishing gender from sex, but the authors point out that many of these methods are problematic. "Such measures of gender are often measures of gender inequality," the authors write. "Many times they are based on national or state-level statistics, rather than more granular individual or household data."

The review covers a lot – the authors address issues of motivation, subject selection, sample size, data collection, analysis, and interpretation, considering implications for basic, clinical, and population research. The authors argue that any apparent sex differences should be approached with caution, and researchers should honestly address how well their studies rule out bias, confounding, and chance. "Even statistically significant sex differences may be due to chance or bias, instead of true heterogeneity of exposure–disease associations or of treatment effects," the authors write.

Findings: The authors conclude by writing that investigators must address collecting and analyzing data by sex adequately, otherwise the "noise" created by multiple testing across all our datasets may drown out the signal of true sex differences. "Furthermore, in human studies it is important to investigate the impact of both sex and gender to illuminate fundamental, modifiable causes of disease and avoid a reflexive attribution of seeming sex differences solely to biology," they write. "If we address these design and analytic issues skillfully, then we have the chance for new insights for men and women that will be critical for the next generation of scientific and therapeutic discoveries in this age of precision medicine."

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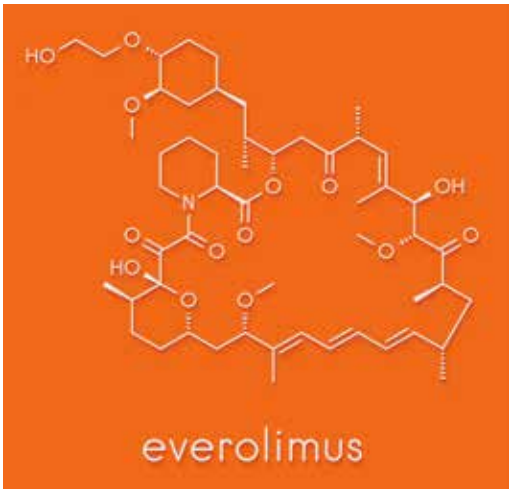
HTTPS://ACADEMIC.OUP.COM/ENDOCRINESOCIETY

Anticancer Agent Also Suppresses Insulin Secretion in Metastatic Insulinoma

The immunosuppressant and anticancer agent everolimus has been shown to directly suppress insulin secretion in metastatic insulinoma, independently of the drug's effect on tumor growth, according to a study recently published in the *Journal of the Endocrine Society.*

Researchers led by Takeshi Miyatsuka, MD, PhD, of the Department of Metabolism and Endocrinology, Juntendo University Graduate School of Medicine in Tokyo, Japan, write that everolimus has been used to treat neuroendocrine tumors and has been found to increase survival rates in progression-free patients with advanced pancreatic neuroendocrine tumors. The drug also can be used to control hypoglycemia in patients with malignant insulinoma. "Thus, whereas everolimus has been proved to be effective in the management of insulinoma, it remains unclear as to whether everolimus directly suppresses insulin secretion in pancreatic beta-cells, independently of tumor regression," the authors write.

The authors report on a case of a 53-year-old woman with insulinoma treated with everolimus, whose lab data was frequently measured, so the authors were able to see the rapid changes in insulin levels when they discontinued and then restarted the everolimus, showing that everolimus directly suppresses insulin secretion, independently of its effect on tumor regression. To confirm this finding, the researchers performed in vitro experiments using mouse insulinoma cells (MIN6) and human induced pluripotent stem cell (hiPSC)–derived insulin-producing cells demonstrated that everolimus inhibited glucose-stimulated insulin secretion (GSIS), even after accounting for cell growth rates.



The authors write that their in vitro experiments showed that everolimus suppresses GSIS, but insulin secretion is not significantly changed under low glucose conditions. However, their clinical case showed immediate and significant suppression of hyperinsulinemia under low glucose conditions during fasting. "Although there is no direct explanation for this difference, it is possible that everolimus suppressed the dysregulated hyperinsulinemia during the postprandial period, which has been reported in patients with insulinoma, and subsequently improved sustained hypoglycemia during fasting," the authors write. "Alternatively, everolimus might improve hyperinsulinemia independently of blood glucose levels *in vivo*, in contrast with the in vitro findings in this study."

Findings: **Based on these findings, the authors conclude that both a patient with metastatic insulinoma and in vitro experiments demonstrated that everolimus directly suppresses insulin secretion, independently of its tumor regression effect.**

> "Alternatively, everolimus might improve hyperinsulinemia independently of blood glucose levels in vivo, in contrast with the in vitro findings in this study."

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Women with Polycystic Ovary Syndrome Dissatisfied with Medical Care

> This study provides context about the current beliefs about medical care in women with PCOS with the goal of identifying factors, which could be targeted to improve patients' overall medical experiences.

A U.S.-based survey of women with polycystic ovary syndrome (PCOS), a common condition characterized by reproductive and metabolic problems, points to distrust and lack of social support from healthcare providers as major contributing factors in their negative medical care experiences, according to a study recently published in the *Journal of the Endocrine Society*.

Researchers led by Marla E. Lujan, PhD, of Cornell University in Ithaca, N.Y., point out that patient beliefs about their medical care are used to evaluate healthcare quality and inform clinical practice guidelines. However, there are few data evaluating patient-provider relationship in PCOS, and previous studies haven't made clear whether medical experiences with PCOS influence patient beliefs during treatment of general medical concerns. "To that end, our primary objective was to examine whether there were differences in trust and beliefs about social support between women with and without PCOS with types of physicians (i.e., PCP, specialists) and/or other healthcare providers (i.e., nurse practitioners, physician assistants)," the authors write. "Our secondary objective was to examine whether trust in physicians varied between the types of health concerns (i.e., general vs PCOS-related). This study provides context about the current beliefs about medical care in women with PCOS with the goal of identifying factors, which could be targeted to improve patients' overall medical experiences."

This cross-sectional study included 332 U.S.-based women — 134 with and 198 without PCOS. The study found that women with PCOS believe primary care physicians are well qualified to treat general health concerns, but trust their opinions less when addressing issues related to PCOS. This may be because of the limited information these women receive from healthcare professionals about the disorder and the significant lag time between PCOS symptom onset and diagnosis. A survey published in *The Journal of Clinical Endocrinology & Metabolism* in December 2016 found many women with PCOS consulted three or more healthcare providers and waited at least two years for a diagnosis.

"This research provides new and important evidence pertaining to deficiencies in trust and social support from healthcare providers that may contribute to negative medical experiences for patients with PCOS," says Lujan. "Our study suggests that physicians can improve the patient-provider relationship by tailoring their advice to acknowledge the broad impact that PCOS has on women's lives and to listen to patient concerns without judgement. These efforts can potentially bring about continuity of care for women with PCOS."

Findings: In the current survey, women who had PCOS also reported arguments with their physicians and an overall lack of emotional support and empathy. It's especially important to provide the right information about emotional counseling to these patients as they often suffer from anxiety and depression, which are associated with PCOS. "PCOS is a complex medical condition that requires lifelong care," says co-investigator, Annie W. Lin, PhD, RD, of Cornell University. "Improving the patient-provider relationship is an important first step to ensuring a successful long-term partnership focused on providing patients with timely and appropriate care."

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Community-Based Exercise Does Not Prevent Bone Loss During Weight Loss in Older Adults

Community-based weight loss does not prevent bone loss in older adults who are actively losing weight, according to a study recently published in the *Journal of Bone and Mineral Research*.

Researchers led by Kristen M. Beavers, PhD, MPH, of Wake Forest University in Winston-Salem, N.C., evaluated 187 older adults with obesity and cardiovascular disease and/or metabolic disease over an 18-month period in a community-based trial and then followed up at 30 months. They looked at weight loss alone (WL), weight loss plus aerobic training (WL + AT), and weight loss plus resistance training (WL + RT). They determined areal bone mineral density (aBMD) through DXA scan and volumetric bone mineral density (vBMD) through CT scan, and they measured biomarkers of bone turnover. "Total hip aBMD was reduced by 2% in all groups at 18 months, with a primary analysis showing no significant treatment effects for any DXA, biomarker, or CT outcome," the authors write. "After adjustment for WL and follow-up at 30 months, secondary analyses revealed that total hip [−0.018 (−0.023 to −0.012) g/cm2 versus −0.025 (−0.031 to −0.019) g/cm2; p = 0.05] and femoral neck [−0.01 (−0.009 to 0.008) g/cm2 versus −0.011 (−0.020 to −0.002) g/cm2; p = 0.06] aBMD estimates were modestly attenuated in the WL + RT group compared with the WL group. Additionally, lumbar spine aBMD was increased in the WL [0.015 (0.007 to 0.024) g/cm2] and the WL + RT [0.009 (0.000 to 0.017) g/cm2] groups compared with the WL + AT [−0.003 (−0.012 to 0.005)g/cm2] group. "

"If minimizing bone loss during active weight loss proves necessary to offset long-term skeletal fragility, then our results suggest that resistance exercise may need to be coupled with other intervention strategies to maximize skeletal benefit," Beaver says

Findings: Based on these results, the authors write, "community-based exercise does not prevent bone loss during active [weight loss] in older adults; however, adding [resistance training] may help minimize long-term hip bone loss." Additional research should seek to elucidate the mechanisms underlying weight-loss–induced bone loss, so that safe and effective strategies can be designed to preserve all aspects of bone health in dieting older individuals, the authors continue. EN

> "If minimizing bone loss during active weight loss proves necessary to offset long-term skeletal fragility, then our results suggest that resistance exercise may need to be coupled with other intervention strategies to maximize skeletal benefit."

2018 Clinical Endocrinology Update/Endocrine Board Review

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

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

www.endocrine.org/ebr/2018
www.endocrine.org/ceu/2018miami
www.endocrine.org/ceu/2018anaheim

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

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

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

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

Seattle, Washington, September 14 — 17, 2018

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

http://grs-igf2018.com

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

Boston, Massachusetts, September 26 — 28, 2018

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

www.criticalmedboston.com

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

Truckee, California, September 26 — 29, 2018

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

https://gimeducation.mayo.edu/

88th Annual Meeting of the Thyroid Association

Washington D.C., October 3 — 7, 2018

This meeting is designed for the community of endocrinologists, basic scientists, internists, surgeons, nuclear medicine scientists, pathologists, trainees, nurses, physician assistants, advanced practice providers, and other health care professionals who wish to broaden and update their knowledge of the thyroid gland and its disorders. A customized educational track will be available to trainees to enhance their meeting experience.

www.thyroid.org/88th-annual-meeting-ata/

Magee-Womens Research Summit

Pittsburgh, Pennsylvania, October 8 — 10, 2018

Magee-Womens Research Institute at the University of Pittsburgh announces the

inaugural Magee-Womens Research Summit. This conference will serve as a premier forum for scientific exchange on topics related to early human development and women's health and wellness across the lifespan.
https://mageesummit.org/

8th Great Lakes Nuclear Receptor Conference (GLNRC)

Minneapolis, Minnesota, October 18 — 19, 2018

The mission of the GLNRC is to spur research and collaboration among scientists from academia and industry in the area of nuclear receptors. The conference is designed to provide an innovative format that establishes a setting for intimate, informal gatherings of established principal investigators, young faculty, and trainees. Organized by leading researchers of nuclear receptors, GLNRC is held every other year at different institutions in the Great Lakes area. The sixth meeting will take place at the University of Wisconsin-Madison.
www.glnrc.umn.edu

2nd Annual Weill Cornell Medicine Pituitary Symposium Pituitary Disorders Across the Age Spectrum

New York, N.Y., October 19, 2018

This CME course is a comprehensive overview and discussion of the evaluation, management, and treatment of the pituitary tumor. This year's conference, comprised of lectures, case-based talks, and Q&A panel sessions, will concentrate on pituitary disorders in specific populations – children, pregnant women, men and women during childbearing years, and the elderly, with special sessions on pituitary surgery, medical management, and radiation therapy for those populations.
www.cvent.com/d/rgqsll

Third United States National Conference on Prevention of Diabetes

Atlanta, Georgia, November 16 — 18, 2018

The Third National Conference on Prevention of Diabetes is a global forum that will feature constructive debates around one of the most important public health issues, the prevention of diabetes and its complications. Although there has been progress made toward the prevention of diabetes and its complications, there is still a long way to go and many lessons to be learned. This conference provides the opportunity for all attendees to participate in high quality scientific discussions on principles of diabetes prevention and listen to the experiences from diabetes prevention programs that have been implemented in various countries.
www.diabetes-prevention.us

World Congress Insulin Resistance Diabetes and Cardiovascular Disease

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

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

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

SPOTLIGHT

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

Nashville, Tennessee, October 11 – 15, 2018

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

This year's multi-track schedule offers a plethora of options for all attendees including pre-conference courses, hands-on skills labs, and an industry sponsored symposium. Interdisciplinary research, education sessions, and policy programming will focus on the latest breakthroughs in the science of obesity. Conference programming will cover the full interdisciplinary spectrum and features leading experts in their respective fields.

Attendees will have the opportunity to meet face-to-face with over 4,000 surgeons, researchers, physicians, and healthcare professionals from across the globe during the exhibit. Additional networking events offer further opportunities for attendees from all fields to collaborate with others who are part of other leading obesity organizations.

In addition, attendees will enjoy all Nashville, the City of Music, has to offer with a wide variety of dining options featuring Southern fare, endless entertainment in the home of country music, and countless attractions for all ages.
Make plans to attend ObesityWeek now at www.obesityweek.com.

INTERNATIONAL **ITINERARY**

European Association for the Study of Diabetes 54th Annual Meeting

Berlin, Germany, October 1 — 5, 2018

The European Association for the Study of Diabetes (EASD) will hold its annual meeting in Berlin, Germany, where more than 1,200 talks and presentations on the latest in diabetes research will be presented. Study Groups will focus on specific aspects of diabetes and its complications while creating a network for specialists in the respective field.

www.easd.org/annual-meeting/easd-2018

Keystone Symposia on Drivers of Type 2 Diabetes from Genes to Environment

Seoul, South Korea, October 7 — 11, 2018

This meeting will address the unresolved gaps in the etiopathogenesis of diabetes and focus on the latest advances that are linked to its molecular drivers. Topics discussed at the symposia include systemic regulation of adipocytes in diabetes, physiological drivers in hunger and energy homeostasis, and metabolic control in diabetes.

www.keystonesymposia.org

EndoBridge 2018

Antalya, Turkey, October 25 — 28, 2018

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

www.endobridge.org

International Conference on Diabetes & Metabolism

Dubai, UAE, October 15 — 17, 2018

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

www.metabolicdiseases.conferenceseries.com/

Immunology of Diabetes Society Congress

London, UK, October 25 — 29, 2018

The Immunology of Diabetes Society (IDS) is a scientific society dedicated to improving understanding and treatment of type 1 diabetes. IDS organizes this Congress every 18 months in major centers in Europe, North America, and Asia at which there are scientific presentations to further this goal. All researchers with an interest in the immunology of diabetes and autoimmunity, as well as those interested in gaining a greater understanding of the disease and the development of new therapeutic strategies, are encouraged to attend the Congress. The event will include presentations from leading speakers in the field, oral and poster presentations, and opportunities for networking and discussion to move toward the common goal of understanding and eradicating type 1 diabetes.

www.ids2018.org

17th International Congress on Hormonal Steroids and Hormones and Cancer

Stellenbosch, South Africa, November 26 — 29, 2018

The objective of this conference is to promote interaction and discussion within the field of steroid hormones and hormone-dependent cancers. The conference will consist of a keynote lecture, plenary lectures, and oral and poster presentations. This conference also includes built-in time for networking as attendees enjoy the Stellenbosch winelands.

www.ichshc2018.co.za

18th International Congress of Endocrinology and 53rd SEMDSA Congress

Cape Town, South Africa, December 1 — 4, 2018

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

www.ice2018.org

2020 LAUREATE AWARDS

CALL FOR NOMINATIONS

DEADLINE: DECEMBER 16, 2018

- Fred Conrad Koch Lifetime Achievement Award
- Gerald D. Aurbach Award for Translational Research
- International Excellence in Endocrinology Award
- Outstanding Clinical Investigator Award
- Outstanding Clinical Practitioner Award
- Outstanding Educator Award
- Outstanding Innovation Award
- Outstanding Leadership in Endocrinology Award
- Outstanding Mentor Award
- Outstanding Public Service Award
- Outstanding Scholarly Physician Award
- Richard E. Weitzman Outstanding Early Career Investigator Award
- Roy O. Greep Award for Outstanding Research
- Sidney H. Ingbar Award for Distinguished Service

NOMINATE TODAY

The Endocrine Society's Laureate Awards are the highest honors bestowed by the Society to recognize the paramount achievements in the endocrinology field including, but not limited to, seminal research, clinical investigation, translational research, mentorship, and non-traditional activities to support developing countries.

Nominate on your own schedule—nominations are now accepted throughout the year. Submissions made after the deadline will be considered for the 2021 award cycle.

- Web resources offer tips for first-time nominators and answers to frequently asked questions
- Need to update a current nomination package? Find out how!

Awards will be honored at ENDO 2020: the 102nd Annual Meeting in San Francisco, California, March 28–31, 2020.

Get started now by visiting endocrine.org/laureate.

Questions? Contact us at laureate@endocrine.org.

ENDOCRINE SOCIETY

Hormone Science to Health

> "A few recent studies have found reproductive benefits with higher marine long-chain omega 3 fatty acid intake, of which seafood is the primary source, which led us to wonder whether seafood intake, when looked at as a whole, was good or bad **when it came to fecundity and what we should be recommending to couples trying to get pregnant."**

— **AUDREY GASKINS**, ScD, Harvard T.H. Chan School of Public Health, Boston, Mass., and lead author of the paper, "Seafood Intake, Sexual Activity, and Time to Pregnancy," which was published in the May issue of *The Journal of Clinical Endocrinology & Metabolism*, discussing her study linking seafood intake to increased pregnancies in couples trying to start a family in "Fish Tales: Does Seafood Consumption Increase Fecundity?" on page 32.

BY THE NUMBERS

19%

New Parks Associates research shows 19% of U.S. broadband households now own two or more connected health devices, a modest increase from 16% in mid-2017.

— **SOURCE:** CONNECTED HEALTH SUMMIT

2

Just two weeks without much activity can have a dramatic impact on health from which it is difficult to recover, according to researchers who studied overweight older adults at risk of developing type 2 diabetes.

— **SOURCE:** *JOURNAL OF GERONTOLOGY*

12%

People who drink two to three cups of coffee per day have a 12% lower risk of early death than people who don't drink coffee at all.

— **SOURCE:** *U.S. NEWS AND WORLD REPORT.*

1 IN 6

At some point, one in six Americans will suffer from depression, with an estimated 16 million afflicted by the debilitating illness every year. And yet 56% of American adults with the disease do not receive treatment, in large part because of the stigma that still surrounds mental illness.

— **SOURCE:** *AARP, THE MAGAZINE*

FROM THE CENTURY OF ENDOCRINOLOGY TIMELINE

1923

Nobel Prize in Physiology or Medicine Awarded to Frederick G. Banting and John J.R. Macleod

In 1923, the Nobel Prize in Physiology or Medicine was awarded jointly to Frederick Grant Banting and John James Rickard Macleod "for the discovery of insulin."

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

QUOTABLE QUOTES

"One sometimes finds, what one is not looking for. When I woke up just after dawn on September 28, 1928, I certainly didn't plan to revolutionize all medicine by discovering the world's first antibiotic, or bacteria killer. But I suppose that was exactly what I did."

— ALEXANDER FLEMING (1881 – 1955), SCOTTISH PHYSICIAN, MICROBIOLOGIST, AND PHARMACOLOGIST. HIS BEST-KNOWN DISCOVERIES ARE THE ENZYME LYSOZYME IN 1923 AND THE WORLD'S FIRST ANTIBIOTIC SUBSTANCE BENZYLPENICILLIN (PENICILLIN G) FROM THE MOLD PENICILLIUM NOTATUM IN 1928, FOR WHICH HE SHARED THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE IN 1945 WITH HOWARD FLOREY AND ERNST BORIS CHAIN.

FISH TALES:

Does Seafood Consumption Increase Fecundity?

BY DEREK BAGLEY

For couples trying to conceive, a diet rich in seafood may prove to be advantageous in their efforts to start a family. According to a new study, just two servings of fish per week not only improved various biological markers, but also increased the number of times the couples were intimate.

This past May, a study appeared in *The Journal of Clinical Endocrinology & Metabolism* that said greater seafood intake among couples trying to get pregnant was associated with higher sexual intercourse frequency and fecundity, bringing hope to couples who may be having trouble conceiving.

The authors of the paper wrote in their conclusion that couples achieved these results when they consumed eight or more servings of seafood per cycle, or about two servings per week. Seafood, of course, is an important source of protein and other nutrients for women who are or may become pregnant, but concerns about mercury levels in fish have led some women to avoid seafood altogether when trying to conceive.

According to the lead author of the paper "Seafood Intake, Sexual Activity, and Time to Pregnancy," Audrey Gaskins, ScD, of Harvard T.H. Chan School of Public Health in Boston, Mass., while seafood is a recommended component of many healthy eating patterns, in the context of fertility it's largely been studied as a potential source of harm, given that it could be a source of exposure to toxicants such as organochlorines, dioxins, and mercury.

The Food and Drug Administration and the Environmental Protection Agency says that 90% of the fish eaten in the U.S. is low in mercury and safe to eat. And although the agencies recommend two to three servings of lower-mercury fish per week, 50% of pregnant women still eat far less than the recommended amount. Gaskins lays out a few reasons for that second statistic: The first is the aforementioned concern about environmental

> **"A few recent studies have found reproductive benefits with higher marine long-chain omega 3 fatty acid intake, of which seafood is the primary source, which led us to wonder whether seafood intake, when looked at as a whole, was good or bad when it came to fecundity and what we should be recommending to couples trying to get pregnant."**
>
> — AUDREY GASKINS, SCD, HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH, BOSTON, MASS

contamination and fear of exposure, especially to methyl mercury. "A great example of this is in January 2001 there was a well-publicized federal advisory recommending that pregnant women limit consumption of certain fish because of concerns about mercury contamination," she says. "Not surprisingly, subsequent research showed that after the dissemination of these federal recommendations, pregnant women reduced their consumption of fish, including tuna, dark meat fish, and white meat fish."

Beyond that, seafood is usually more expensive than other sources of protein, which prices out a lot of people, so they go for cheaper options like chicken and beef. "The third reason which also comes up frequently is that many people just don't like the taste of seafood," Gaskins says.

Despite all this, research is starting to show the benefits of a seafood-rich diet when it comes to fertility. "A few recent studies have found reproductive benefits with higher marine long-chain omega 3 fatty acid intake, of which seafood is the primary source, which led us to wonder whether seafood intake, when looked at as a whole, was good or bad when it came to fecundity and what we should be recommending to couples trying to get pregnant," Gaskins says.

Angling for Couples

In a prospective cohort study, Gaskins and her colleagues followed 500 Michigan and Texas couples from the Longitudinal Investigation of Fertility and the Environment (LIFE) Study for one year to determine the relationship between seafood intake and time to pregnancy. Participants recorded their seafood intake and sexual activity in daily journals.

The researchers chose to recruit couples from these two states because they comprised individuals residing in four Michigan counties with reported exposure to persistent organochlorine chemicals (i.e. Berrien, Calhoun, Ingham, Kalamazoo) and 12 counties in Texas (i.e. Aransas, Brazoria, Calhoun, Chambers, Fort Bend, Galveston, Harris, Jefferson, Matagorda, Montgomery, Nueces, and Orange) with presumed exposure to persistent environmental chemicals.

"Moreover, we were particularly interested in couples with ties to the angler community as they would be more likely to consume

seafood from these local water ways," Gaskins says. "The original aim of the cohort was to assess the effect of environmental chemicals, specifically persistent chemicals such as PCBs, on fertility. Since seafood is one potential route of exposure to persistent chemicals, we collected information on this variable."

The researchers found that 92% of couples who ate seafood more than twice a week were pregnant at the end of one year, compared to 79% among couples consuming less seafood. The association between seafood and faster time to pregnancy was not completely explained by more frequent sexual activity, suggesting other biological factors were at play. These could include effects on semen quality, ovulation, or embryo quality.

Correlation Does Not Equal Causation

Gaskins says that several previous studies have found positive associations between omega fatty acid intake and seafood intake and semen quality parameters, lending support to the idea that higher seafood intake could increase the quantity and quality of sperm. Among women, dietary intake of docosapentaenoic acid (which is found in seafood) was associated with a lower risk of anovulation, and dietary intake of total marine omega-3 polyunsaturated fats was associated with increased luteal-phase progesterone concentrations, suggesting beneficial effects of seafood on ovulation and menstrual cycle function.

AT A GLANCE

- Greater seafood intake among couples trying to get pregnant is associated with higher sexual intercourse frequency and faster time to pregnancy.
- Although 90% of fish in the U.S. is safe to eat, people eat far less fish than the recommended amount for a variety of reasons.
- Research is starting to show the benefits of a seafood-rich diet when it comes to fertility, but there's still more research needed.

> **"If we were to study a population which primarily consumed predatory fish, which tends to be high in environmental chemicals, we might find that overall, the detriments of consuming seafood (because of exposure to these toxicants) far outweigh the potential reproductive benefits. Future research will have to evaluate this further."**
>
> — AUDREY GASKINS, SCD, HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH, BOSTON, MASS

Finally, two separate infertility cohort studies have shown that embryo quality measures were improved among women with higher fish intake, supporting a favorable role of seafood intake on early embryo development.

Another interesting finding in this study was the daily odds of sexual intercourse were 39% higher when both partners consumed seafood on the same day, supporting the popular theory that seafood is an aphrodisiac. But Gaskins is cautious here; correlation doesn't equal causation.

When asked about the biological reason for this association, she says that the short answer is they're not sure. Shellfish like oysters are high in zinc, and studies have shown that in humans, dietary zinc intake has a positive correlation with testosterone levels and in rats that zinc therapy improves sexual competence. "However," she says, "given that we did not measure zinc intake in our study and zinc is found in many other foods other than seafood, we felt uncomfortable making this link. It is also possible that couples who consume higher amounts of seafood together share more meals and thus more time together (including nights) which may be a behavioral explanation for the association we observed with sexual activity."

Going Back for Seconds

But there's still work to be done. For example, the researchers point out that they weren't able to obtain daily dietary assessments from participants since it would have been too burdensome. Therefore, they couldn't evaluate whether the men and women who ate more seafood also had a healthier diet. In their study, however, seafood intake was not associated with income or education which led them to believe that seafood may not be as tightly correlated with a healthy diet in this population (as it is in others).

Gaskins also says that they do not have a good biomarker of seafood intake and therefore they have to rely on self-reported intake when doing research. "There are proxies for seafood intake that we can measure in the blood — for example, levels of long chain omega 3 fatty acids, which are derived from seafood, but this is not a perfect biomarker as people can consume these long chain omega fatty acids from supplements as well," she says.

And in their conclusion, Gaskins and her team write that further research is needed to study the effects of eating predatory fish, which tend to have higher levels of environmental chemicals and mercury and could actually produce adverse health effects. Predatory fish such as swordfish and sharks have higher concentrations of these chemicals because of bioaccumulation which starts when algae absorbs small quantities of these chemicals at the beginning of the food chain.

"In the U.S., the majority of fish that we eat is from non-predatory fish which limits our potential exposure to high levels of environmental chemicals," Gaskins says. "Therefore, we're likely getting most of the benefits of fish and very few of the potential downsides due to environmental contamination. However, if we were to study a population which primarily consumed predatory fish, which tends to be high in environmental chemicals, we might find that overall, the detriments of consuming seafood (because of exposure to these toxicants) far outweigh the potential reproductive benefits. Future research will have to evaluate this further."

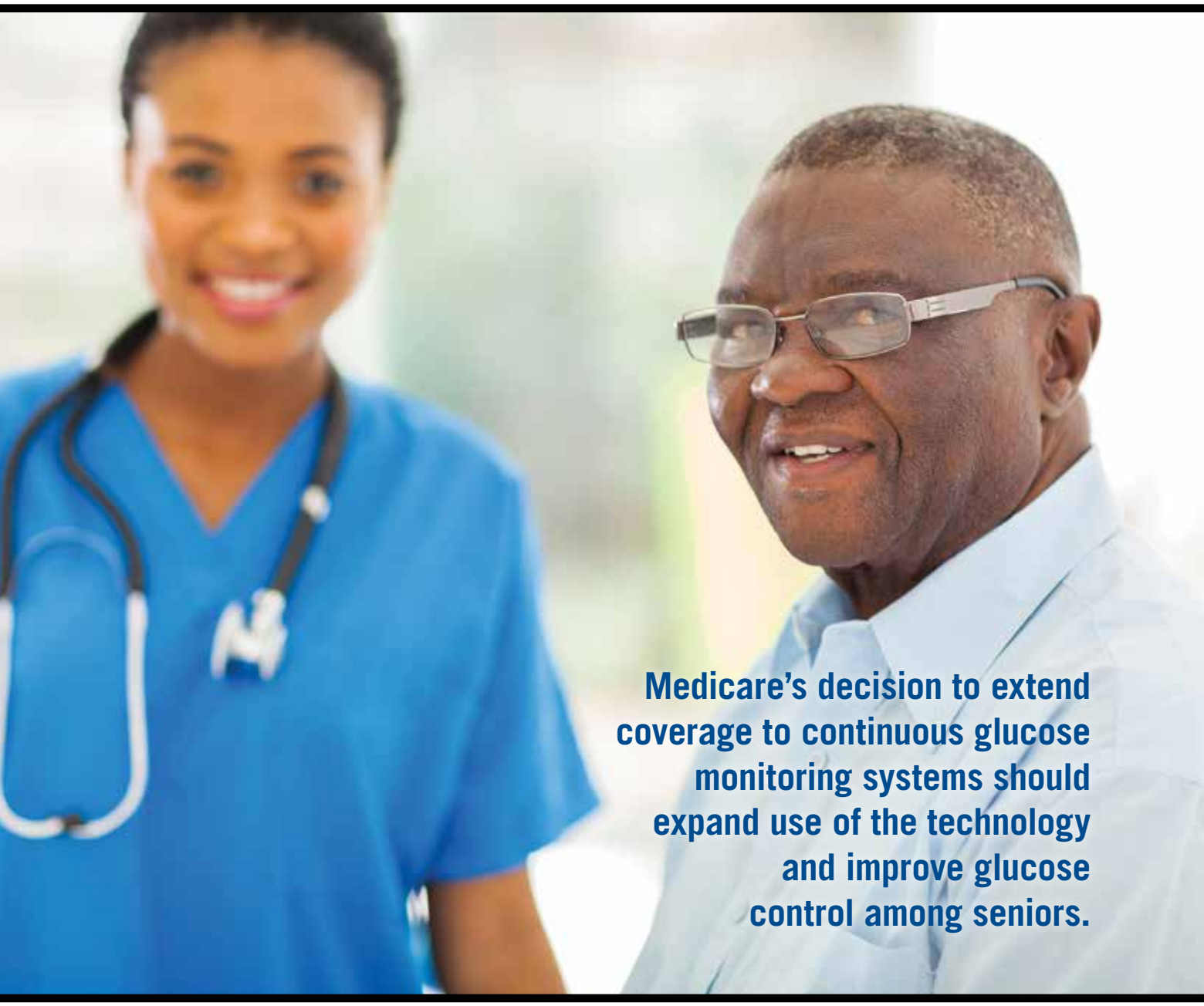
For now, Gaskins and her team conclude that their research suggests that both men and women should aim to consume at least two servings of low-mercury seafood per week for the maximum fertility benefit. "Furthermore," she says, "we saw no detrimental effect of higher seafood intakes on fecundity in men or women suggesting that couples may see benefits of seafood intake above and beyond the two servings per week suggestion." EN

BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. IN THE AUGUST ISSUE, HE WROTE ABOUT MANAGING ACROMEGALY PATIENTS AFTER THEY'VE BEEN SUCCESSFULLY TREATED OR EVEN CURED.

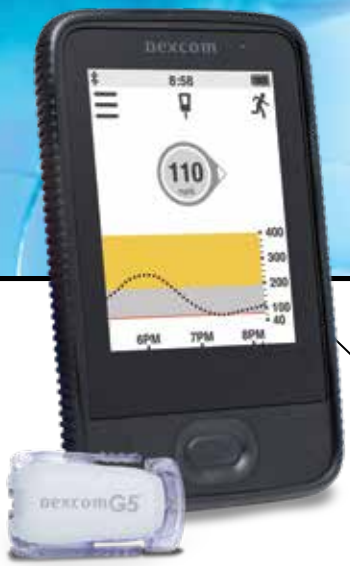
BY ERIC SEABORG

NEW RULES:

Medicare Now Extends Coverage of CGMs



Medicare's decision to extend coverage to continuous glucose monitoring systems should expand use of the technology and improve glucose control among seniors.



The Dexcom G5 continuous glucose monitoring (CGM) system is one of two CGM choices that Medicare now covers. The system consists of the sensor, transmitter, and display device. *Image courtesy of Dexcom, Inc.*

New Medicare rules that extend reimbursement to include continuous glucose monitoring (CGM) systems are already leading to greater use among the senior population of a technology shown to improve glycemic control, and the trend is expected to grow.

"Some patients had been waiting for over two years for these sensors to be covered by Medicare. They are really happy about having access now," says Grazia Aleppo, MD, associate professor of medicine and director of the Diabetes Education Program at Northwestern University, who has moved quickly to introduce patients to the technology. "We also have many patients who are happy Medicare started covering therapeutic CGM because they had been paying for it out of pocket."

Older patients may find CGM even more beneficial than younger patients, according to Andrew J. Ahmann, MD, professor of medicine and director of the Harold Schnitzer Diabetes Health Center at Oregon Health and Science University: "Older patients are more at risk for hypoglycemia. They are more likely to have hypoglycemia at the same level of glucose control. They are also more susceptible to damage from hypoglycemia, both in terms of cardiovascular events as well as falls, fractures, and other consequences."

Aleppo says CGM is a useful tool for managing patients: "When the systems are downloaded, one can see much more clearly the challenges of glucose fluctuations these patients are facing. Mealtime insulin-to-carbohydrate ratios can be adjusted, as well as basal insulin doses and correction factors. We can work with the patient on bedtime glucose levels and show them what can be modified to decrease fluctuations both in the low glycemic range and in the high glycemic range." The patients who often benefit the most are long-term type 1 diabetes patients with hypoglycemia unawareness, having lost the feeling of the symptoms of low glucose.

Medicare requires the clinician to provide documentation for patients to qualify for coverage. A patient must inject insulin three or more times a day or have an insulin pump, perform at least four measurements a day with a home blood glucose monitor, and require frequent insulin adjustments based on these measurements. The clinician must also confirm that the patient is capable of using the technology.

And although CGM tends to be associated with type 1 patients, the Medicare rules do not differentiate between diabetes types, as the qualifying factor is insulin dependence.

A senior woman is having a smart sensor attached by a medical specialist and is introduced to the CGM device. For either system, patient training is a key to success.

The FreeStyle Libre system, one of two Medicare choices, is a continuous glucose monitoring system consisting of a handheld reader and a sensor worn on the back of the upper arm. *Image courtesy of Abbott Diabetes Care Inc.*

The Choices

A key next step is to help the patient choose which of the systems available is the best fit — the Dexcom G5 CGM or the Abbott FreeStyle Libre Flash Glucose Monitoring System.

The Dexcom G5 consists of a small sensor that the patient places under the abdominal skin. It measures interstitial glucose every five minutes and transmits the results in real-time to a receiver. In addition to the readings, the receiver displays trend arrows indicating whether and how quickly a patient's glucose level is trending up or down. It can be set to sound an alarm at selected levels when glucose goes too high or too low. (The Dexcom G5 can be used with a smart phone, but Medicare currently does not support this use.)

The FreeStyle Libre's sensor, which is about the size of two stacked quarters, attaches to the upper arm. It makes regular glucose readings that the user accesses with a scanner. The scanner displays the readings and trend arrows, but does not have an alarm to notify the user of an impending glycemic event.

The Dexcom provides real-time CGM, whereas the FreeStyle Libre is generally considered intermittent scanning CGM or "flash glucose monitoring because you have to put a reader device up to the sensor to get a reading," Ahmann says. In addition, clinicians have more experience with the Dexcom because it has been on the market longer.

> **Older patients are more at risk for hypoglycemia.** They are more likely to have hypoglycemia at the same level of glucose control. They are also more susceptible to damage from hypoglycemia, both in terms of cardiovascular events as well as falls, fractures, and other consequences."
>
> — ANDREW J. AHMANN, MD, PROFESSOR OF MEDICINE; DIRECTOR, HAROLD SCHNITZER DIABETES HEALTH CENTER, OREGON HEALTH AND SCIENCE UNIVERSITY, PORTLAND

The Dexcom G5 requires calibration twice a day by the patient, using fingerstick measurements, whereas the FreeStyle Libre requires no calibration by the user, which may make it a better fit for patients who have difficulty getting blood from their fingers as well as those who simply desire a simpler system.

At the end of March, the Food and Drug Administration approved a new Dexcom model — the G6 — that removes this difference by requiring no calibration. It is scheduled to begin shipping in early June, but it has not been approved for coverage by Medicare, and a Dexcom spokesperson could not give an estimate for how long it might take to gain that approval.

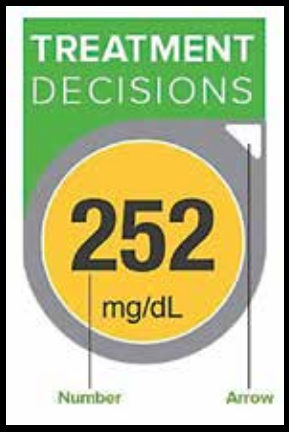
Differences in the Two Systems

Aleppo says that the real-time data from the Dexcom and its alerts of impending problems make it particularly suited to patients whose hypoglycemia unawareness might lead them "to manage their fear of hypoglycemia by overeating, taking less insulin, being afraid of exercise, being afraid of driving, and eating unnecessary bedtime snacks to avoid overnight events. Patients sleep better because they know that the alarms can notify them or their companion. For people who have preserved feeling of hypoglycemia, the Freestyle Libre is a great tool — convenient and informative. Scanning the flash reader is painless and can be done several times a day. Some patients prefer to be notified about impending hypo- or hyperglycemia, whereas others do not want to hear the alarms."

Ahmann agrees that the Dexcom might be preferred by patients who have hypoglycemic episodes: "If you want the most data, you would certainly want the Dexcom platform because it provides more information and has the alarms. The Freestyle Libre is a little simpler for the older patient or others who aren't as comfortable with the technology."

AT A GLANCE

- **Medicare has begun covering continuous glucose monitoring systems, which is leading to more seniors using systems shown to improve glycemic control.**
- **There are two FDA-approved systems available that offer different strengths that appeal to different patient situations.**
- **CGM can improve glucose control in patients regardless of age or education level, but it requires training to optimize the benefits.**



Guidance on CGM Trend Arrows

The Endocrine Society has provided guidance on how to use the trend arrows by publishing "Using Continuous Glucose Monitoring Trend Arrows in the Management of Adults with Diabetes: A Practical Approach to the Dexcom G5 CGM System" in the December issue of the *Journal of the Endocrine Society* and online at https://academic.oup.com/jes/article/1/12/1445/4642923. Aleppo and Ahmann both served on the panel that drew up these recommendations.

Step-by-Step Training

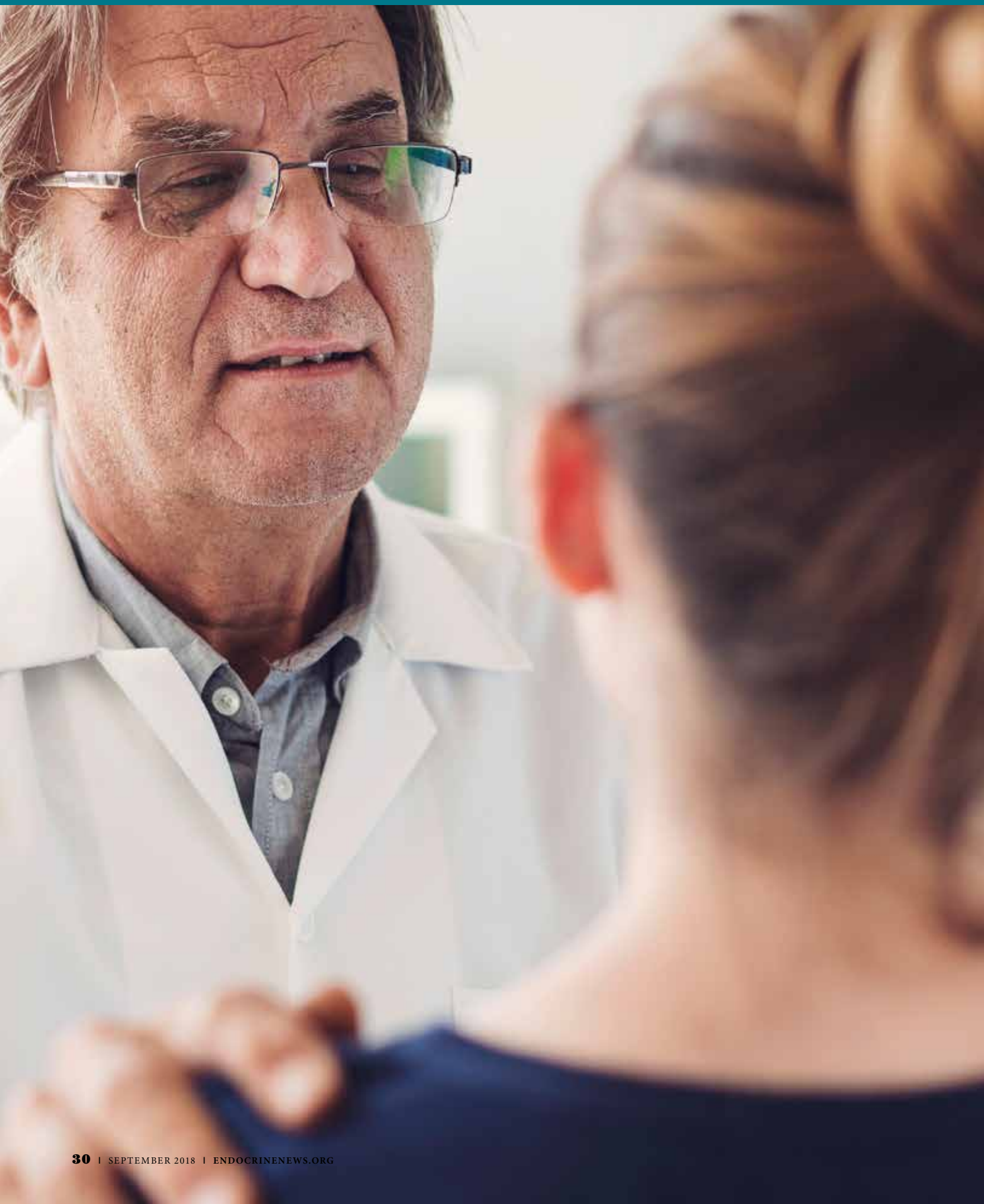
For either system, patient training is a key to success. "The majority of the training is done by our certified diabetes educators, who already know the patients well," Ahmann says. "Our educators go through a formatted approach to teach patients how to use it technically, and then teach them how to use the information to their best benefit."

Aleppo said that education is a multi-step process, starting with becoming comfortable with the sensor before going on to learning about the arrows and dosing. "We teach patients very slowly. We have to make sure they are comfortable with the information they get. You need to first make sure they understand what the alert means, what the up and down arrows mean. Then you can talk about adjusting the insulin dose based on the trend arrows before a meal."

Ahmann said that the DIaMonD study demonstrated that CGM improves glycemic control in patients with type 1 diabetes regardless of age: "There was no difference in benefit whether they were younger or older. The DIaMonD trial showed not only that age didn't make a difference, but neither did level of education or ability in mathematics. That study convinced us that this can be effective therapy for older patients, and some of the limitations that we might assume probably don't exist. But you still need somebody who is going to embrace it. There are certainly some older patients who are averse to technology."

Both Aleppo and Ahmann say that one of the weaknesses of the Medicare approval is that it does not allow the use of the Dexcom mobile phone app, which can be particularly useful in the older population who have some cognitive decline and may need the help of family members to foresee and manage glycemic events. Both are hopeful that this rule may be revised in the near future. EN

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA., AND A FREQUENT *ENDOCRINE NEWS* CONTRIBUTOR. HE WROTE ABOUT ADVANCES IN TREATING HYPOPARATHYROID PATIENTS IN THE AUGUST ISSUE.



POLYCYSTIC OVARY SYNDROME: The *Evolving* Picture

BY KELLY HORVATH

September is Polycystic Ovary Syndrome (PCOS) Awareness Month and is the ideal time to chart the progress made by researchers and clinicians around the world on behalf of the millions of adolescent and adult women with this disorder. Hopefully, updated treatment protocols will ease some of the concerns of patients and physicians regarding this often-perplexing condition.

As reported last year in *Endocrine News*, polycystic ovary syndrome (PCOS) remains a confounding condition for patients, clinicians, and researchers alike, despite being both the target of multiple ongoing investigations and the most common endocrinopathy in women of reproductive age, affecting more than 10 million women worldwide, many of whom have yet to be diagnosed. In fact, women with PCOS wait a frustratingly long time to get the diagnosis and make visits to multiple healthcare professionals before beginning treatment or receiving counseling or other support.

The results of a U.S.-based survey of 332 women released last month in the *Journal of the Endocrine Society* show just how distressing this condition characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology can be for women. In "Trust in physicians and medical experience beliefs differ between women with and without polycystic ovary syndrome," researchers led by Marla E. Lujan, PhD. found that women with PCOS report negative interactions with their healthcare providers, as compared to women who have regular periods. They may feel that they are not being taken seriously by their healthcare providers, that their healthcare providers lack empathy, and that they are not receiving enough support

> "Regarding pathogenesis, PCOS is most likely the result of multiple factors that are connected and act in a concerted way. The individual contribution of each of those factors — **primary ovarian abnormalities, neuroendocrine alterations, genetic polymorphisms, epigenetic modulators, and an increase in the amount of fat stored ectopically** — may be different in each patient."

— LOURDES IBÁÑEZ, MD, PHD, INSTITUT DE RECERCA PEDIÀTRICA HOSPITAL SANT JOAN DE DÉU, BARCELONA, SPAIN

Oral contraceptive hormones are used to prevent pregnancy and treat other medical conditions, such as PCOS.

about their health concerns, even while this condition demands lifelong management. *[Editor's Note: See more about the JES study in Trends & Insights on page 10.]*

Symptoms include wide-ranging metabolic and reproductive health effects with accompanying psychological features like anxiety and depression, all of which combine to have a profound impact on the patient's quality of life. Some evidence points to PCOS possibly resulting from the body's incapacity to effectively store fat, leading to increased hepatic and visceral adiposity and, in turn, insulin resistance and androgen excess. It is thus associated with other metabolic disorders, such as type 2 diabetes and obesity, as well as an increase in cardiovascular disease risk factors.

Time for Changes

However, since the release of the Endocrine Society's groundbreaking November 2015 *Scientific Statement on the Diagnostic Criteria, Epidemiology, Pathophysiology, and Molecular Genetics of Polycystic Ovary Syndrome*, "there has been a flurry of activity," says Richard S. Legro, MD, of Penn State College of Medicine and chair of the task force that developed the statement, which focused on etiology and diagnostic criteria, insofar as earlier diagnosis was deemed essential to ameliorating the long-term effects of PCOS. At that time, many researchers also considered the condition to be inappropriately, even misleadingly, named, which was perhaps thwarting the likelihood of earlier diagnosis. "I think that's not a priority right now," Legro says. "With what's currently in the research pipeline, there are larger issues than the name."

"We're seeing pharmaceutical companies explore both known and novel mechanisms," Legro continues, "which is exciting because we haven't seen this kind of theoretical exploration in 20 years." He

points to two key areas that look promising: genetics and anti-Müllerian hormone (AMH). Several meta-analyses of genome-wide association studies (GWAS) have identified at least 14 new genetic variants that could confer susceptibility to PCOS, and researchers have been investigating the role of AMH in the hypothalamic–pituitary–ovarian axis and how it might be involved in pathogenesis.

International Guideline Helps Clinicians Provide Better Care

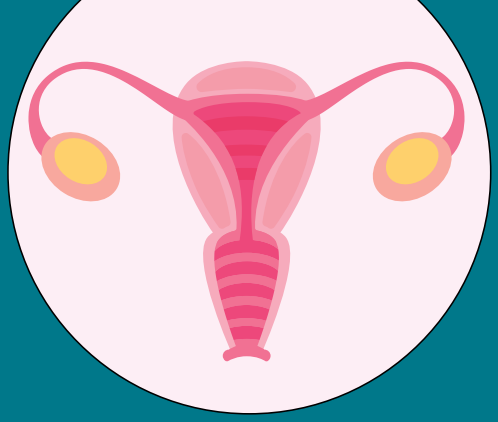
There's even more to be hopeful about, according to Legro, with the release of *International evidence-based guideline for the assessment and management of polycystic ovary syndrome 2018*. Designed to "assist clinical decision making and support optimal patient care," the guideline was undertaken by a consortium of 37 international societies, including the Endocrine Society, from 71 countries. Lead author Helena Teede, MBBS, FRACP, PhD, of Monash University in Melbourne, Australia, explains what has evolved in diagnosis, treatment, and management of PCOS.

"In diagnosis, the key differences in the new guideline are around the Rotterdam diagnostic criteria," Teede says. Until now, the Rotterdam criteria have been controversial and inconsistently adopted. "Here they have been grounded in evidence, internationally endorsed, but also modified," she explains. Further, ultrasound has been downgraded to a third-line diagnostic criteria in adult women and not recommended for diagnosis in women within eight years of menarche. "AMH is also not recommended in diagnosis at this time," she adds.

In treatment, medical and infertility therapy were extensively reviewed. Says Teede: "A key change is in recommending low-dose, safer combined oral contraceptive pill (COCP) preparations and recommending against first-line use of higher-dose ethinyl estradiol, cyproterone acetate COCPs, which have long been the mainstay of COCP therapy in PCOS." When and when not to use metformin is also clarified. Regarding infertility, evidence shows that most women with PCOS-related infertility achieve reproduction with therapies safer and cheaper than in vitro fertilization, which has been downgraded to third-line infertility therapy in those with PCOS-related infertility alone.

In management, the importance of individualized and multidisciplinary approaches is underscored. "Metabolic screening is more refined and personalized based on both PCOS status and the presence of other risk factors," Teede says. "The role of ethnicity and culture in PCOS has likewise been highlighted." Preventing weight gain with specific guidelines regarding diet and exercise from adolescence is recommended. Maintaining a healthy weight mitigates downstream metabolic and reproductive effects as well optimizing overall health.

"The high prevalence of depressive and anxiety symptoms, PCOS's impact on quality of life, and other psychological manifestations have been strongly highlighted, with screening for anxiety and depression recommended," Teede says.



AT A GLANCE

- **PCOS has a phenotypic spectrum and varying symptoms; therefore, it should be approached from an individualized, yet multidisciplinary standpoint.**
- ***International evidence-based guideline for the assessment and management of polycystic ovary syndrome 2018* clarifies diagnosis, management, and treatment options for primarily adult women with PCOS. Notably, modified Rotterdam criteria are now clearly evidence based and endorsed for diagnosis, capturing those women in need of care early, while avoiding overdiagnosis. Extensive patient and health professional resources are now freely available at https://www.monash.edu/medicine/sphpm/mchri/pcos/resources.**
- ***An International Consortium Update: Pathophysiology, Diagnosis, and Treatment of Polycystic Ovarian Syndrome in Adolescence* clarifies diagnosis, management, and treatment options for adolescents with PCOS. Notably, diagnostic criteria are stricter than for adults, given that many of the clinical biochemical findings are part of the pubertal process and the maturation of the hypothalamic–pituitary–ovarian axis. (These stricter diagnostic guidelines for adolescents are also reflected in the 2018 evidence-based guideline.)**

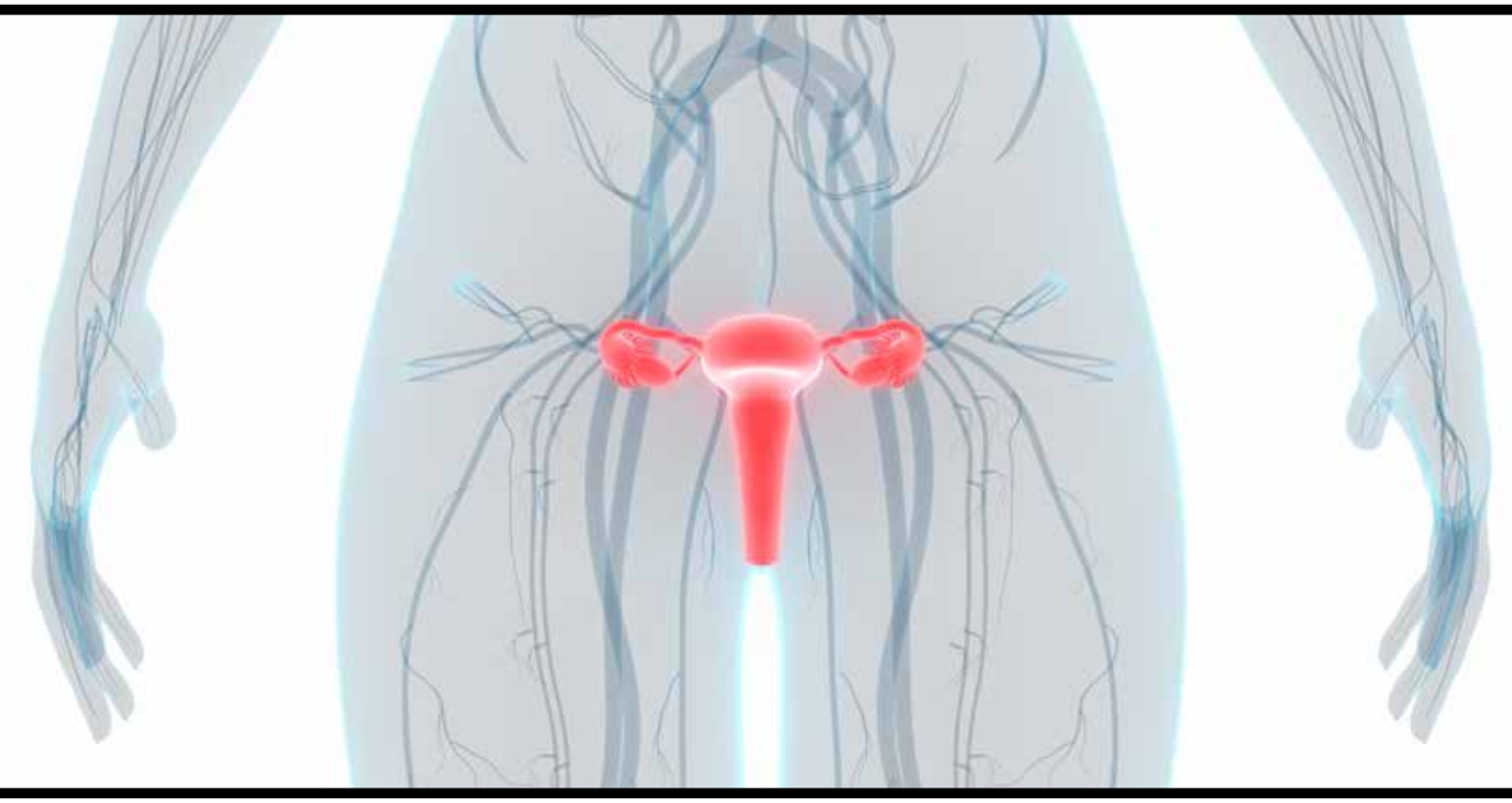
> A key change is in recommending low-dose safer combined oral contraceptive pill (COCP) preparations and **recommending against first-line use of higher-dose ethinyl estradiol, cyproterone acetate COCPs,** which have long been the mainstay of COCP therapy in PCOS."
>
> — HELENA TEEDE, MBBS, FRACP, PHD, MONASH UNIVERSITY, MELBOURNE, AUSTRALIA

Perhaps most importantly — and, as if in answer to the patients who have recently reported dissatisfaction with their treatment — the guideline emphasizes the need for partnership in care. "The education and empowerment of women with PCOS has been enabled by the guideline translation tools freely available at **www.monash.edu/medicine/sphpm/mchri/pcos** and on the iTunes "AskPCOS" app," Teede says.

International Consortium Update Guides PCOS Care for Adolescents

Another very important piece of the PCOS puzzle is differentiating adolescents, who present a particular challenge for diagnosis. "The issue remains that adolescents are in a metabolic state of evolution, and more lenient diagnostic criteria for adults such as Rotterdam are not appropriate until more than one year or closer to two years post-menarche has occurred," says Sharon E. Oberfield, MD, director, Division of Pediatric Endocrinology Diabetes and Metabolism at Columbia University in New York and co-author of the 2015 Endocrine Society Scientific Statement. "Prematurely branding an adolescent with the diagnosis of PCOS, when she is maybe only minimally at risk is very disheartening and could be fraught with problems of self-image later on."

But there's good news here as well. In *An International Consortium Update: Pathophysiology, Diagnosis, and Treatment*



of Polycystic Ovarian Syndrome in Adolescence, published in November 2017 in *Hormone Research in Paediatrics*, co-lead author Lourdes Ibáñez, MD, PhD, from the Institut de Recerca Pediàtrica Hospital Sant Joan de Déu, in Barcelona, Spain, and team (including co-lead authors Oberfield and Selma F. Witchel, MD, of the Children's Hospital of Pittsburgh in Pennsylvania) explains: "There are new insights regarding the potential factors playing a role in the pathophysiology of androgen excess, and also novel approaches in the management of the entity based on these new insights." Whereas formerly, the tendency was for clinicians to derive directions for assessment, management, and treatment of adolescent PCOS from proposed adult guidelines, the update makes clear that adolescents must be approached quite differently.

"The two recommended criteria for adolescent PCOS are reminiscent of the National Institutes of Health criteria," Ibáñez says. "They are stricter than the Rotterdam criteria, which are considered inappropriate for adolescents." The first is menstrual irregularity, which is now specifically defined: In girls who are at least two years beyond menarche, menstrual irregularity can present as persistent oligomenorrhea (cycles >45 days), secondary amenorrhea (absence of cycles >3 months), dysfunctional uterine bleeding, or even primary amenorrhea (never had a period).

(Note, this definition of menstrual irregularity in adolescents was refined in the 2018 evidence-based guideline: In girls less than one year post-menarche, irregular cycles are considered normal pubertal development. In those one to three years post-menarche, cycles lasting <21 to >45 days are considered irregular, and in girls more than three years post-menarche onwards, cycles lasting <21 to >35 days are considered irregular. In girls more than one year post-menarche, secondary amenorrhea — absence of cycles >3 months — is considered irregular).

The second is biochemical or clinical evidence of androgen excess, manifesting as high total testosterone and/or high free androgen index or progressive hirsutism and/or severe cystic acne, respectively. Furthermore, other causes of androgen excess, such as congenital adrenal hyperplasia, hyperprolactinemia, hypothyroidism, and androgen-producing tumors must be ruled out.

It's important to note that the 2018 international guideline largely aligns with this 2017 update on adolescence, with specific points of difference being the aforementioned details of menstrual irregularity definitions as well as a strengthened recommendation that ultrasound not be used to diagnose PCOS within eight years of menarche, as Teede explains.

Closeup of infected sebaceous glands and red acne on the chin of a young woman who has PCOS. Inflamed skin and acne are caused by a hormone imbalance (male hormones in females).

Although PCOS in adolescence should be approached differently, it shares at least one important commonality with PCOS in adults: individualization. "Regarding pathogenesis, PCOS is most likely the result of multiple factors that are connected and act in a concerted way," Ibañez says. "The individual contribution of each of those factors — primary ovarian abnormalities, neuroendocrine alterations, genetic polymorphisms, epigenetic modulators, and an increase in the amount of fat stored ectopically — may be different in each patient." Ectopic fat, in particular, deposited in viscerae rather than subcutaneous adipose tissue, may drive pathogenesis. This can happen when there is an upward mismatch between weight at birth and weight at adolescence, because the girl has gained weight disproportionately.

"PCOS is not a disorder starting after menarche that must be silenced with an oral contraceptive; rather, it may be the result of a body mass index mismatch that may start early in life," Ibañez says. For adolescents with PCOS, the update focuses on lifestyle intervention to lose excess weight as the first-line treatment. The effects of lifestyle can be enhanced with medications, for example, by a low-dose combination of insulin sensitizers and an anti-androgen.

The Big Picture

A lot has changed in the past few years regarding diagnosis, management, and treatment of PCOS: Controversies have been settled, approaches have been clarified, and mechanisms have begun to be elucidated. But the key change, according to Oberfield, is "a desire to educate all stakeholders regarding overall evaluation and management of PCOS, now across the lifespan." EN

HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT THE DANGERS OF EDC EXPOSURE IN UTERO IN THE JULY ISSUE.

From new research linking BRCA mutations and DNA damage to the effects of breastfeeding on offspring, three studies presented at ENDO 2018 in Chicago all share a common if not always obvious connection: Obesity is often in the genes, but it is far from inevitable.

Wean Some, Lose Some: BREASTFEEDING & OBESITY

BY KELLY HORVATH

Three studies presented at **ENDO 2018** in March kept attendees abreast of what is happening in research concerning the mammary gland. One zooms in on the BRCA mutation, and the other two elucidate aspects of breastfeeding. Interestingly, all three are tied together with another common thread — avoiding obesity. Taken together, these studies underscore the importance of maintaining a healthy weight.

> "…other problems come along with early puberty, like glucose disruption, which is an indicator for prediabetes. **We think our findings to some extent can alert endocrinologists and their patients with early puberty to watch for other health problems after they become adults."**
>
> — MENGJIE WANG, MD, MS, UNIVERSITY OF TOLEDO COLLEGE OF MEDICINE AND LIFE SCIENCES, TOLEDO, OHIO

Good News for BRCA Mutation Carriers

In "In BRCA mutation carriers, obesity is linked with increased DNA damage in normal breast gland cells," lead researcher Kristy A. Brown, PhD, and colleagues from Weill Cornell Medicine in New York, N.Y., took a molecular-level look at the tie between obesity and breast cancer development in BRCA mutation carriers, as evidenced in clinical observations.

BRCA mutation, as is well known, means that the carrier's DNA repair enzymes are faulty, and tumors are not kept in check as they otherwise might be; therefore, these women have an increased risk of breast and ovarian cancer. Brown and team hypothesized that obesity or increased body mass index (BMI) may be associated with higher levels of DNA damage in the normal breast epithelium of carriers. They recruited 82 women who had identified BRCA mutations and generated tissue microarrays, a technique that allows more than 100 different patient samples to be viewed on a single slide. With the microarrays, they used immunofluorescence to stain for gamma-H2AX foci, a histone mark occurring when DNA is damaged. "One of the first observations we made was that BMI was associated with more of these gamma-H2AX foci in breast tissue, which is an indication of higher levels of DNA damage. This is important as it is hypothesized that DNA damage can lead to tumor formation if not properly repaired," Brown says.

An additional arm of the study involved determining whether a relationship existed between this DNA damage and previously characterized players in the obesity–breast cancer link, the estrogen biosynthetic enzyme, aromatase, as well as crown-like structures, which are inflammatory foci also found in the breast. "We found a positive correlation between these two factors and the formation of DNA damage foci. We are currently undertaking additional studies to be able to establish causation," Brown says.

They also used an animal model of obesity to see whether obesity alone would be sufficient to cause this effect. After feeding formerly cancer-free mice a high-fat diet, the researchers assessed the amount of DNA damage in the mouse mammary glands.

"What we found was similar to the studies in the BRCA mutation carriers — there was an increase in DNA damage in the normal mammary gland of the mice," Brown explains. "What becomes more interesting is that after we submitted these mice to caloric restrictions, we saw reduction in the number of these focal points, suggesting that DNA damage may be preventable or even reversible."

Many more studies will be needed to confirm this idea, but these results are encouraging, perhaps even empowering, for carriers nonetheless. In women with the mutation for whom cancer development is highly probable, maintaining a healthy lifestyle and a healthy BMI becomes critical in order to limit exposure to factors that have negative effects in the breast. "Through diet and exercise, women in that population may be able to reduce their risk of breast cancer, which is supported by a seminal **study*** by Mary-Claire King, published in *Science* in 2003, which showed that avoiding obesity decreases the penetrance of breast cancer in BRCA mutation carriers."

The team is very much interested in causation and will be investigating whether obesity-associated factors may be responsible for the increase in DNA damage as well as whether that leads to tumor formation. "The current study is really a first look at what's happening to the DNA," Brown says. "Which factors are involved and whether there is a way to intervene is part of ongoing studies."

Large-for-Gestational Age Children May Gain Advantage from Breastfeeding

In "Breastfeeding may protect high-birthweight infants from childhood obesity," lead researcher Hae Soon Kim, MD, of Ewha Womans University College of Medicine in Seoul, South Korea, and team studied 38,039 children in three groups — low birthweight (≤2,500 grams), normal birthweight (2,500–4,000 grams), and high birthweight (≥4,000 grams) — starting from birth and evaluating their growth development in relation to their birthweight at regular checkpoints.

*Breast and Ovarian Cancer Risks Due to Inherited Mutations in *BRCA1* and *BRCA2*. *Science 24 Oct 2003: Vol. 302, Issue 5645, pp. 643-646, DOI: 10.1126/science.1088759*

Artist's rendering of damaged DNA

AT A GLANCE

- **BRCA mutation carriers with obesity show increased evidence of DNA damage, suggesting that avoiding obesity, and even exercising and/or reducing caloric intake to reverse obesity, may decrease the likelihood of developing cancer in carriers.**
- **Breastfeeding mouse dams who consumed a high-fat diet passed on increased risks of obesity, diabetes, early puberty, and reduced fertility to their male and female offspring.**
- **Infants born with high birthweights are more likely to develop obesity in childhood, but this likelihood is significantly reduced if they are exclusively breastfed for their first six months.**

> What we found was similar to the studies in the BRCA mutation carriers — there was an increase in DNA damage in the normal mammary gland of the mice. **What becomes more interesting is that after we submitted these mice to caloric restrictions, we saw reduction in the number of these focal points, suggesting that DNA damage may be preventable or even reversible."**
>
> — KRISTY A. BROWN, PHD, WEILL CORNELL MEDICINE, NEW YORK, N.Y.

When the cohort reached age six years, the researchers found that 10% of the low-birthweight group, 15% of the normal-birthweight group, and more than 25% of the high-birthweight group had become obese or overweight (pediatric criteria for obesity in South Korea is a BMI of ≥95th percentile for age and sex). However, the risk of obesity was considerably lower when the high-birthweight children were exclusively breastfed during their first six months.

With pediatric obesity now so prevalent, this newly demonstrated benefit of breastfeeding may provide more mothers food for thought.

Breastfeeding Mothers: Avoid Fatty Foods

In "Overeating during breastfeeding may affect the health of offspring," principal investigator Jennifer W. Hill, PhD, and graduate research assistant Mengjie Wang, MD, MS, at the University of Toledo College of Medicine and Life Sciences in Ohio, sought answers on what factors may account for the global penetrance of early puberty. Looking at previous studies, the researchers found childhood obesity commonly cited as a comorbidity; not surprisingly, both of these conditions have increased in incidence around the world. "Epidemiological evidence shows that from 1970 to now, puberty is beginning one year earlier than before. Normally, in girls, it should be 10 to 12 years old, but now early puberty is defined in girls before

[they are] eight years old. And, some believe we need additional diagnostic criteria for people for different regions, so, it may be even earlier than that," Wang says.

The team also knew from a 2014 animal **study**** from the lab of Jens Brüning that a maternal high-fat diet and overeating can affect timing of puberty, in which they figured out that the breastfeeding phase from the date of birth to the weaning date is the most critical window for metabolic functions in the offspring. "Our ideas came from that paper," Wang says. "We want to understand how maternal high-fat diet feeding only during the breastfeeding phase can regulate metabolic and reproductive function in the offspring."

To determine how excess body weight may alter the timing of puberty, they used two groups of C57/BL6 mice, a control group of new mothers and a group who were fed high-fat food (60% of calories from fat) from the date they delivered to weaning. They checked body weight of the offspring every week from week 3 to week 20. To evaluate pubertal development in female mice, they used vagina opening and the first estrous age as markers. "We found that the excess calories during the breastfeeding phase can cause early obesity due to increased fat mass and we also found earlier puberty in those mice," Wang says. Furthermore, glucose tolerance tests showed glucose intolerance and insulin insensitivity. Finally, performing fertility tests of the offspring in adulthood demonstrated such infertility problems as smaller litters, longer times to become pregnant, and lower pregnancy rates.

In the future, Wang and her team plan to pursue such mechanisms as how a maternal high-fat diet might change the microbiota of the offspring and how, in turn, those changes might influence their pubertal development.

The jury is out as to whether these results apply to humans. However, we can provisionally extrapolate some implications, according to Wang. "The first thing I would want to tell a clinician is that a maternal high-calorie diet does advance puberty, so advise your patients to avoid excess calories," she explains. "Second, other problems come along with early puberty, like glucose disruption, which is an indicator for prediabetes. We think our findings to some extent can alert endocrinologists and their patients with early puberty to watch for other health problems after they become adults." EN

**Neonatal Insulin Actions Impairs Hypothalamic Neurocircuit Formation in Response to Maternal High-Fat Feeding, *Cell*, Volume 156, Issue 3, P495-509, January 30, 2014 DOI:https://doi.org/10.1016/j.cell.2014.01.008

HORVATH IS A BALTIMORE-BASED FREELANCE WRITER AND A FREQUENT CONTRIBUTOR TO *ENDOCRINE NEWS*. SHE WROTE ABOUT THE DANGERS OF EDC EXPOSURE IN UTERO IN THE JULY ISSUE.

With so many researchers up to their necks in multi-tasking, it's easy to get distracted by the minutiae of everyday life. *Endocrine News* spoke to a few researchers who shared some of their methods to make the most of their time at the bench.

QUALITY TIME:

Lab Hacks to Maximize Productivity

BY GLENDA FAUNTLEROY SHAW

There is one thing that every laboratory professional can attest — managing the time spent on routine tasks and experiments while maintaining the lab's productivity can be a monumental effort. Meeting deadlines, completing paperwork, and staying connected to staff often require laser focus when chronic time zappers enter the fray.

One startling statistic about a common time abuser: On average, office workers receive at least 200 messages a day and spend about 2.5 hours reading and replying to emails, according to a 2017 *Forbes* article.

We turned to several researchers and principal investigators and asked what tasks they found the most time-consuming and have tried to find methods to streamline.

"Sifting through emails and data organization/management are the two most time-consuming activities for me," says Andrew Demidowich, MD, adult endocrinology staff clinician and principal investigator at the National Institutes of Health in Bethesda, Md..

"If you know of a way to streamline writing grants, I'd love to hear it!" says Daniel Gorelick, PhD, assistant professor in the department of Cellular & Molecular Biology, at Baylor College of Medicine in Houston, Texas.

"My first thought was 'experiments that always work until one day they don't,'" adds Lisa Tannock, MD, chief of the Division of Endocrinology and Molecular Medicine at the University of Kentucky, Lexington.

"I am revising a manuscript and the reviewer suggested an experiment," Tannock explains. "Basically, a Western. We do Westerns all the time, but now for the past month everything is going wrong and we have spent a month troubleshooting. Today's worked, and the only thing different from last week was a new batch of precast gels, but this is not the first time we've tried different gels, so it's possible that we've had several bad batches of gels."

"This is what wastes time, when something that always works suddenly stops. And it happens over and over and over," Tannock adds.

Getting Organized

For Demidowich, staying organized is a matter of checklists and "to do" lists.

Lisa Tannock, MD

> **"This is what wastes time, when something that always works suddenly stops. And it happens over and over and over."**
>
> — LISA TANNOCK, MD, CHIEF OF THE DIVISION OF ENDOCRINOLOGY AND MOLECULAR MEDICINE AT THE UNIVERSITY OF KENTUCKY, LEXINGTON

Daniel Gorelick, PhD

> **"We've also started a laboratory manual, a collection of my lab's commonly used protocols, but also general lab advice and philosophy. Now when we have a rotation or summer student, or even an existing lab member is going to try a new technique, their first stop is the lab manual."**
>
> — DANIEL GORELICK, PHD, ASSISTANT PROFESSOR IN THE DEPARTMENT OF CELLULAR & MOLECULAR BIOLOGY, AT BAYLOR COLLEGE OF MEDICINE

"I have a separate list for clinical (patient care) responsibilities, and a separate list for each project or protocol that I'm working on to help ensure that nothing gets lost or forgotten about," he explains.

"Additionally, for the students on my research team, we have an electronic Standard Operating Procedures (SOP) explaining in detail the 'how to' for the different tasks in our project, from patient recruitment to data entry, to ordering supplies to making sure the patient gets paid their reimbursement."

Demidowich has also created standardized checklists for the students tailored specifically for each visit. "Standardization and organization cannot be emphasized enough in performing good research," he stresses.

Gorelick agrees lab manuals are good solutions. "We've also started a laboratory manual, a collection of my lab's commonly used protocols but also general lab advice (e.g., 'plan X amount of time for this type of experiment') and philosophy (such as 'here are the types of papers we publish and here are the journals we target')," he says. "Now when we have a rotation or summer student, or even an existing lab member is going to try a new technique, their first stop is the lab manual."

> **"I have a separate list for clinical (patient care) responsibilities, and a separate list for each project or protocol that I'm working on to help ensure that nothing gets lost or forgotten about."**
>
> — ANDREW DEMIDOWICH, MD, ADULT ENDOCRINOLOGY STAFF CLINICIAN AND PRINCIPAL INVESTIGATOR AT THE NATIONAL INSTITUTES OF HEALTH, BETHESDA,

Gorelick also shared one tool that offered a good fix. "I read the book *Deep Work* by Cal Newport," he says (*Deep Work: Rules for Focused Success in a Distracted World*). "The tips for focusing on work by eliminating distractions, such as email and web browsing, for defined, concentrated periods of time resonated with me. I try to practice deep work."

He bought each lab member the book and now hopes that when he doesn't respond to their emails immediately, they'll assume he is in the midst of a deep work period.

Andrew Demidowich, MD

Final Hacks

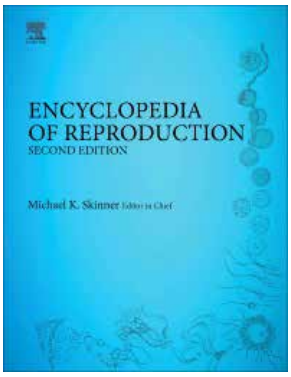
Find small things that can shave off time from your lab day to make it more productive. One main tip is basic planning ahead to keep the lab running smoothly. Making stock master mixes (such as PCR reagents and growth media), labeling reagents clearly, and restocking supplies and reagents during down periods, are a few tips from a recent *Lab Manager* article.

To conquer the email zap, disable push notifications to your phone, mute the volume on your computer, or close your email tab so that messages don't distract you from your current task. Or, try setting "check in" times where you limit checking your email to just three times a day: first thing in the morning, after lunch, and near the end of the day. If that doesn't seem plausible, add in a mid-morning and mid-afternoon email fix. EN

— FAUNTLEROY SHAW IS A FREELANCE EDITOR/WRITER BASED IN CARMEL, IN. SHE IS A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS*.

Updating Your Endocrine Library

COMPILED AND WRITTEN BY COURTNEY CARSON



Encyclopedia of Reproduction, Second Edition

As reproductive health is a fundamental component of an individual's overall health status and a central determinant of quality of life, this book is a timely addition to the literature on the subject. This updated edition comprehensively reviews biology and abnormalities, while also covering some of today's most common diseases, including prostate and breast cancer. Each article provides a comprehensive overview of the selected topic to inform a broad spectrum of readers, from advanced undergraduate students to research professionals. Each chapter also explores the latest advances in reproductive medicine ranging from cloning to stem cells to genomics.
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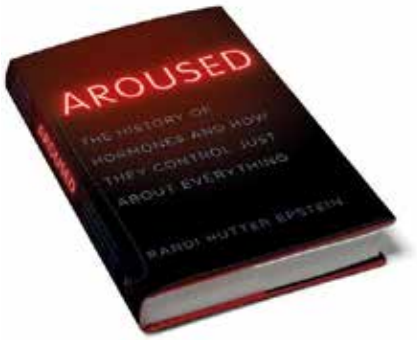
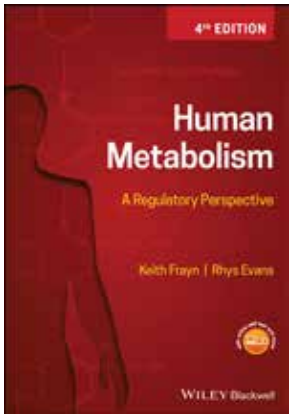
Aroused: The History of Hormones and How They Control Just About Everything



Metabolism, behavior, sleep, mood swings, the immune system, fighting, fleeing, puberty, and sex – these are only some of the areas controlled by hormones. Armed with a healthy dose of wit and curiosity, medical journalist Randi Hutter Epstein takes readers on a journey through the unusual history of these potent chemicals from a basement filled with jarred nineteenth-century brains to a twenty-first-century hormone clinic in Los Angeles.
www.randihutterepstein.com



Human Metabolism: A Regulatory Perspective

The revised and comprehensively updated edition of *Human Metabolism* (formerly *Metabolic Regulation – A Human Perspective*) offers a current review of metabolism and metabolic regulation. The authors explain difficult concepts in clear and concise terms to provide an accessible and essential guide on metabolism. Covering a wide variety of topics including energy balance, body weight regulation, exercise, and how the body copes with extreme situations, this book illustrates how metabolic regulation allows the human body to adapt to many different conditions.
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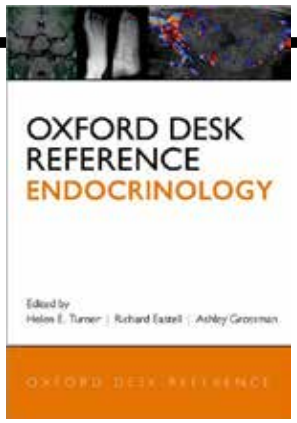
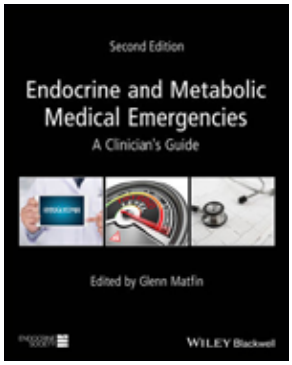


▼ *Oxford Desk Reference: Endocrinology*

This new book provides easy access to evidence-based materials for quick consultation which has been brought together by experts from around the world. The vast spectrum of endocrine disorders is clearly laid out in self-contained topics for easy reference and includes practical treatment for everyday endocrine disorders as well as the management of lifelong chronic endocrine conditions. Chapters are organized according to endocrine glands, disorders, and syndromes with specific sections on the evolution from childhood to adult endocrinology and the needs of geriatric patients.
www.oup.com

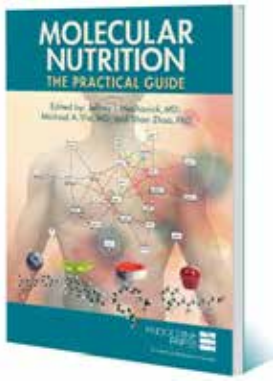
▶ *Endocrine and Metabolic Medical Emergencies: A Clinician's Guide, Second Edition*

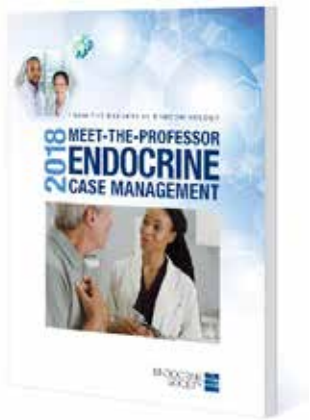
Co-published by the Endocrine Society, *Endocrine and Metabolic Medical Emergencies* is a highly practical and timely clinician's guide which updates existing knowledge and sets standards for the testing, diagnosis, and treatment of endocrine and metabolic emergencies. Special populations included in the second edition range from hospitalized patients with HIV/AIDS to the elderly and pregnant women. Additional topics of focus include various endocrine and metabolic systems including metabolic bone diseases, neuroendocrine tumors, and clinical lipidology.
www.wiley.com



▼ *Molecular Nutrition: The Practical Guide*

Molecular Nutrition investigates the therapeutic and preventative benefits of whole foods-based eating patterns based on the science of food-body interactions. This practical guide integrates new perspectives on nutritional medicine into a 10-step protocol that translates clinical problems into food-based solutions. *Molecular Nutrition explores a new frontier of therapeutic strategies for the treatment,* management, and prevention of hormone and hormone-related illness.
www.elsevier.com





◀ *Meet-The-Professor 2018*

If you missed the conference or are looking for a refresher, Meet-the-Professor examines summaries of cases discussed during the live Meet-the-Professor sessions from **ENDO 2018** in Chicago. This year's edition includes case studies while assessing a clinician's knowledge of all aspects of endocrinology.
www.endocrine.org/store/books-and-publications

September is a Month of Action for NIH Advocacy

While Congress has not yet finalized fiscal year (FY) 2018 federal funding decisions, President Trump has kicked off the FY 2019 federal budget process by submitting his budget request to Congress on February 12. The President's budget proposal calls for approximately $4.4 trillion in total spending. Much of the budget seeks to scale back nondefense programs and streamline review processes for projects.

With the current fiscal year (FY) about to expire on September 30, time is running out for the Congress to complete work on spending bills to fund the government, including the National Institutes of Health (NIH) for the next fiscal year.

Take Action

In recent weeks, Endocrine Society members have been calling, writing, and visiting their representatives in Congress to ensure that proposed funding increases for the NIH become a reality. To ensure your voice is heard and has the greatest effect we urge all U.S. members of the Society to contact their elected representatives with the easy-to-use resources on the Society's website at www.endocrine.org/advocacy by September 30.

When this issue of *Endocrine News* went to press, the Senate passed a combined Labor, Health, and Human Services and Department of Defense (LHHS/DoD) funding package that would tie public health funding, including the NIH, together with funding for defense priorities. The Senate bill would increase funding for the NIH by $2 billion, consistent with the Endocrine Society's request and improving upon the $1.25 billion increase proposed by the U.S. House of Representatives.

Although significant progress has been made by both chambers towards a final LHHS bill, bicameral negotiations will still be necessary to arrive at a final appropriations package before September 30. Unless the bill is completed by that date and signed into law, a continuing resolution (CR) will be required to keep the government open, but only at current-year funding levels.

While a CR would allow the government to function, it causes delays in awarding grants and uncertainty for biomedical researchers who rely on NIH grants to conduct life-saving research. A short-term CR also runs the risk of becoming a series of CRs or even a full-year CR as momentum slows and attention turns to the mid-term elections or other legislative priorities. It is therefore critical that legislators continue to hear from researchers in the remaining days of September about the need to complete work on the LHHS appropriations bill and increase funding for the NIH to the Endocrine Society's recommended level of $39.3 billion in FY 2019.

Endocrine Society Discusses Research Priorities with NIDDK

On September 12, Endocrine Society president-elect Dale Abel, MD, PhD, and secretary-treasurer Richard Legro, MD, met with Griffin Rodgers, MD, MACP, the director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), to discuss emerging research priorities in endocrine science and opportunities to improve outcomes for trainees in endocrine research programs.

During the meeting, Abel thanked the NIDDK for their continued support of the Future Leaders Advancing Research in Endocrinology (FLARE) program, a highly successful initiative which helps trainees from underrepresented minority communities build skills needed to advance their research careers. The group shared stories about FLARE fellows who are now making contributions to the field and are achieving independent research success.

Legro shared new insights on the relationship between polycystic ovary syndrome (PCOS) and insulin resistance and new research priorities for PCOS identified in the Endocrine Society's recent Scientific Statement on PCOS. Participants also discussed the NIH response to the text, recommended by the Endocrine Society and included in the House and Senate appropriations bill report, that called on the NIH to "report on the research that has been conducted on PCOS and its comorbidities to date, identify the gaps in the research, and develop a trans-NIH research action plan."

The Endocrine Society appreciates the opportunity to share our priorities with Rodgers and his leadership team and learn about NIDDKs plans and goals for the coming year. The meeting resulted in concrete opportunities for the Society and NIDDK to work together on in the coming year to advance our shared public health objectives.

Endocrine Society Advocates for Better Physician Reimbursement; Opposes Proposed Revisions to Medicare Evaluation & Management Services

In the 2019 Medicare Physician Fee Schedule proposed rule, the Centers for Medicare and Medicaid Services (CMS) included significant revisions to the way that evaluation and management (E/M) services would be reimbursed and documented.

According to CMS, the proposal is intended to reduce administrative burdens resulting from documentation requirements for complex services by only requiring physicians to document medical necessity and either the medical decision making, time, or existing documentation guidelines for a level 2 visit regardless of the level of service provided. CMS reforms to payment that are linked to this proposed documentation change. The agency is proposing to create a single payment rate for level 2 through 5 new and established patient office visits. To account the decreased reimbursement, the agency is proposing new add-on codes that can be billed for longer, more complex visits.

The Endocrine Society has advocated for revisions to the existing E/M code set for many years, including the revaluation and redefinition of these codes. The current E/M structure is outdated and does not reflect current care that is provided during office visits, particularly those provided by endocrinologists and other cognitive specialists. While we support revisions to the E/M codes, we believe that it must be done in a methodical, evidence-based manner to account for patient complexity, services rendered, and the impact that new technology may have on practice.

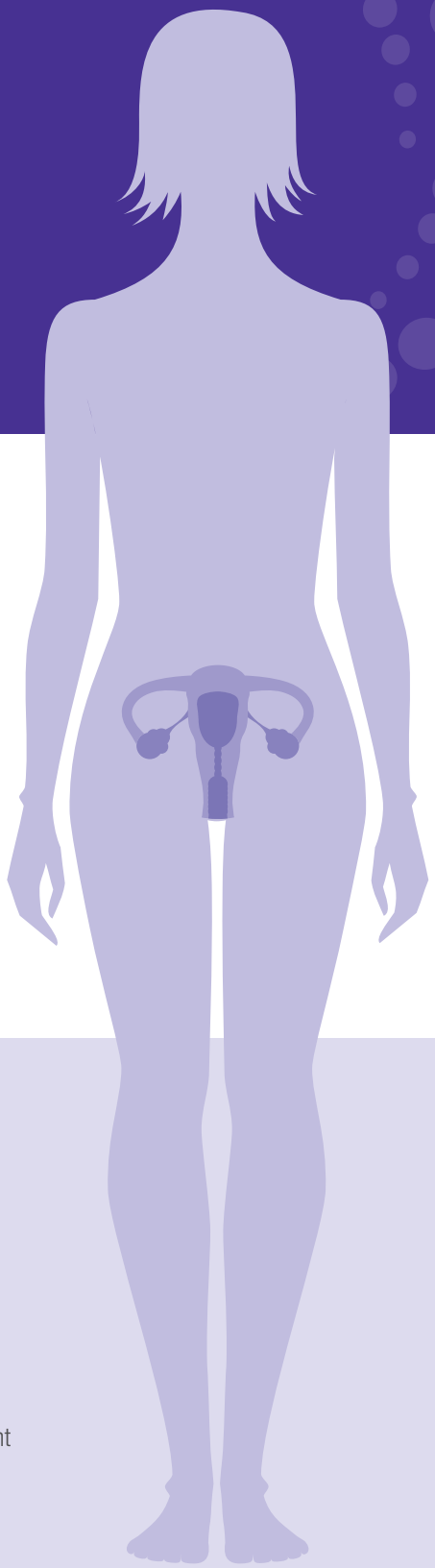
Because CMS' approach reduces the reimbursement for the E/M codes that account for the most complex services, we are concerned that it will reduce access to care and exacerbate existing workforce shortages by forcing physicians to see additional patients to make up the difference in reimbursement. While CMS did propose new add-on codes to address prolonged visits, we do not believe these codes will be used by a significant number of endocrinologists because of the time requirements. We also believe that the effort to consolidate level 2 through 5 E/M codes would penalize specialists, like endocrinologists, who treat more complex patients and require a higher degree of documentation regardless of Medicare's requirements for billing.

In our comments on this proposal, we recommend that CMS delay the implementation of this proposal and use that time to model and consider other alternatives that recognize the complex cognitive work cognitive physicians provide and account for their expertise. While we support efforts to reduce administrative burdens and unnecessary paperwork, CMS should consider the level of documentation that is required for patients of greater complexity in terms of best practices. It is not our expectation that reducing documentation requirements for billing will actually reduce the level of documentation that is required for patients with complex or multiple diseases. We will continue to advocate for revisions to the existing E/M structure that account for the complex specialty care endocrinologists deliver to patients.

To see the full text of our comments to CMS on the proposed 2019 Medicare Physician Fee Schedule Rule, visit ***www.endocrine.org/advocacy/policy-communications****. A summary of the proposed rule with Endocrine Society analysis can be seen at* ***www.endocrine.org/advocacy/priorities-and-positions*** *in the Additional Society Policy Documents section.*

POLYCYSTIC OVARY SYNDROME WHAT YOU NEED TO KNOW

The endocrine system is a network of glands and organs that produce, store, and secrete hormones. Normally, women make small amounts of "male" hormones (called androgens), but women with Polycystic Ovary Syndrome (PCOS) produce slightly higher amounts of androgens. This hormone imbalance causes an assortment of health problems, many of which are related to the reproductive system.



WHAT IS PCOS?

A hormonal disorder that may be characterized by a constellation of symptoms that may include:

- Irregular or absent menstrual periods
- Infertility
- Weight gain (especially at the waist)
- Acne
- Excess hair on the face and body
- Thinning scalp hair
- Skin tags
- Darkening skin
- Depression or anxiety
- Poor sleep

When the body cannot use insulin properly, it secretes more insulin to make glucose available for cells. Often linked to **obesity**, many women with PCOS tend to make too much insulin. The resulting excess in insulin is thought to also boost male hormone or **androgen production** by the ovaries.

POTENTIAL PCOS CAUSES

Although we don't know for sure what causes PCOS and none of these is a direct cause, each one is highly related to the condition.

Insulin Resistance — some women are less sensitive to insulin than normal, which makes their ovaries produce too many male hormones.

Genetics — PCOS appears to run in families, so having a mother or sister with the condition makes you more likely to have it.

Obesity — because women and girls with PCOS are more likely to gain excess weight and women and girls who are obese are more likely to have the condition, there is a tight, but not absolute, link between the two.

Visit hormone.org for more information.

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

Hormone Health NETWORK®
Keep your body in balance

PCOS CAN AFFECT A WOMAN'S:

- Menstrual cycle
- Ability to have children
- Hormones
- Heart
- Blood vessels
- Appearance
- Mental health
- Risk for cancer
- Metabolic syndrome

On ultrasound, the ovaries appear to have a multiple number of small follicles (also called cysts) that are often arranged in a ring around the ovary. Science indicates these are related to arrested egg development and failed ovulation.

DID YOU KNOW?

Women with PCOS often have type 2 diabetes, low levels of good cholesterol (HDL), and high levels of bad cholesterol (LDL) and other blood fats, including triglycerides. These may increase the risk of heart attack or stroke.

PCOS affects **7-10%** of women of childbearing age and is one of the most common causes of infertility.

In the United States, an estimated **5-6 million** women have PCOS.

Sleep apnea may occur in up to **50%** of women with PCOS.

Pregnant women with PCOS appear to have higher rates of:

- Miscarriage
- Diabetes during pregnancy
- Pregnancy-induced high blood pressure (preeclampsia)
- Premature delivery
- Endometrial cancer

Source: U.S. Department of Health and Human Services and National Institutes of Health

TREATMENT

In addition to medications to help manage your symptoms, a healthy diet and brisk physical activity are nearly always part of a treatment plan for PCOS. Attention to blood sugar levels is also very important. Be sure to follow your treatment plan exactly as your doctor prescribes so you can control your PCOS symptoms and reduce risk factors that can change the quality of your life.

5 STEPS TO LIVING BETTER WITH PCOS

- Limit processed foods
- Add more whole grains
- Eat more fruits, vegetables, and lean meats
- Maintain a healthy weight
- Get moving

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**.

Hormone Health NETWORK® FROM THE ENDOCRINE SOCIETY

ENDO 2019

SAVE THE DATE

MARCH 23–26, 2019 **NEW ORLEANS, LA**

ERNEST N. MORIAL CONVENTION CENTER

KEY DATES

ABSTRACT SUBMISSION OPENS: SEPTEMBER 5, 2018

EARLY REGISTRATION OPENS: OCTOBER 25, 2018

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