DECEMBER 2016 THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

Endocrinology ENCORE

ENDOCRINE SCIENCE IS ON THE LEADING EDGE OF FINDING NEW WAYS TO ADDRESS THE ISSUES OF AN AGING POPULATION. *ENDOCRINE NEWS* ADDRESSES HOW TREATING THIS DEMOGRAPHIC HAS EVOLVED AND TAKES A CLOSER LOOK AT NEW TREATMENT AND RESEARCH DISCOVERIES THROUGHOUT THE YEAR OF ENDOCRINOLOGY.

- The varied complications of treating older diabetes patients.
- Genitourinary syndrome of menopause: A hidden malady revealed.
- Endocrine scientists discuss the top breakthroughs of the year.
- What are the new treatments, therapies, and products that made headlines in 2016?

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WHY ENDOCRINOLOGY?
How Deena Adimoolam was influenced by her patients.

ENDOCRINE SOCIETY

1916-2016
100 YEARS
OF HORMONE SCIENCE TO HEALTH

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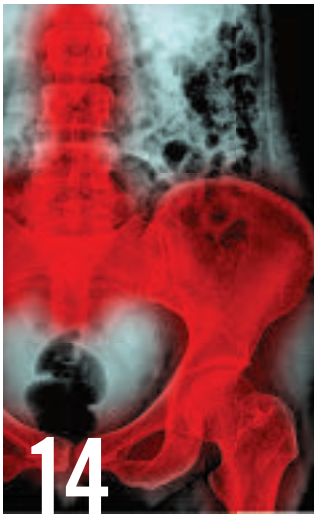
BY DEREK BAGLEY



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JANUARY 2017 MARKS THE DEBUT ISSUE OF THE MERGER OF *ENDOCRINOLOGY* AND *MOLECULAR ENDOCRINOLOGY.*

Editors-in-Chief: Andrea C. Gore, PhD and Stephen Hammes, MD, PhD

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— Peter Fuller, AM, PhD, FRACP, Chair, Publications Core Committee, Endocrine Society, Head, Centre for Endocrinology and Metabolism, *Hudson Institute of Medical Research* and Head, Endocrinology Unit, *Monash Health, Australia*

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Society Journals Posed to Make Ambitious Strides for 2017 and Beyond

LAST JUNE, I HAD THE PLEASURE OF WRITING to the membership about the Endocrine Society's exciting plans to further improve the global reach and impact of our impressive suite of peer-reviewed journals.

As with all scholarly journals these days, the Society's journals face multiple challenges in response to changing technology, increasing competition, and shifting business models. To answer these challenges, early in 2015 the Council approved a Strategic Planning Initiative for our journals program. The Publications Core Committee, chaired by Peter Fuller, worked with Society staff and publishing experts from Kaufman Wills Fusting & Company to formulate a plan to ensure the ongoing excellence of the Society's journals.

With the Council's approval of additional Strategic Planning Initiative funds for 2016, the journals project moved into its implementation phase, which is planned to run through 2018.

In this month's letter, I provide you with updates on the two most ambitious aspects of our journals work, both of which are launching in 2017. These include the launch of our Open Access journal, the *Journal of the Endocrine Society (JES)*, and the merger of our two journals, *Endocrinology* with *Molecular Endocrinology*.

In January 2017, the *Journal of the Endocrine Society* will debut. It will be our first new journal in 30 years, and our first Open Access journal. *JES* opened for submissions in October 2016 and publishes across the Society's mission in all areas of basic science, clinical science, and clinical practice. As an Open Access journal, its content is freely available online worldwide. *JES* publishes research articles, mini-reviews, editorials, and perspectives. Images, case reports, articles about databases and methods, and interactive media are also featured. Key to the success of the journal is the agreement of J. Larry Jameson to be its founding editor-in-chief. An international group of associate editors is working with Larry to attract a broad range of submissions, maintaining the Society's high standards for peer review while ensuring timely publication decisions. Articles will be published continually and within a week of acceptance, with article-level metrics provided.

Also in January 2017, *Endocrinology* — having published for 100 years — and *Molecular Endocrinology* — having published for 30 years — will combine their content and scopes under the joint leadership of Andrea Gore and Steve Hammes as co-editors-in-chief to become the Society's single, comprehensive, basic science journal. Publishing under the retained title of *Endocrinology*, with the added tagline of "Molecular and Physiological Basis of Endocrine Health and Disease" to indicate its expanded breadth, the combined journal will encompass and expand on the scopes of the two journals to provide important insights into endocrine systems and diseases at molecular, biochemical, cellular, genomic, comparative, and organismal levels. Article types will include full-length research articles, mini-reviews, commentaries, rapid communications, technical papers, and resource articles. Article-level metrics will provide feedback to authors on the impact that their articles are having. The editors-in-chief have exciting plans for celebrating the journal's Centennial throughout the year.

These major initiatives in our journals will be facilitated by the formation of a powerful new partnership that the Society has struck with Oxford University Press (OUP). OUP will serve as the exclusive distributor of our journals to the institutional market and will be the online host of digital versions of all of our journals. This new arrangement will result in Society journals and their authors' articles becoming available in more than 2,500 additional libraries around the world.

The exciting and ambitious steps that we are taking with these journals, in concert with the rest of our impressive family of journals, promise to contribute to greater understanding in science and medicine by facilitating the broad communication of high-quality, authoritative information in endocrine research and clinical care. I thank those mentioned above and the large number of members and staff who have worked on this project thus far — but its ultimate success depends on you, the members of the Society, who contribute articles, read our journals, and share your knowledge with your fellow-members and colleagues. If you have any questions or comments, please do not hesitate to email me at **president@endocrine.org**.

— **Henry M. Kronenberg, MD**, President, Endocrine Society

FROM THE **EDITOR**

Wrapping Up the Year of Endocrinology

AS 2016 COMES TO AN END, WE ARE FINISHING OFF THE ENDOCRINE Society's Centennial year with a month devoted to aging and the endocrine system. To that end, *Endocrine News* is following suit with two articles on very different aspects of aging.

Associate editor Derek Bagley looks at how aging affects patients with diabetes in "I'm Still Here: Diabetes and the Aging Patient" (p. 24). In this article he speaks with David C. Aron, MD, MS, a professor of medicine and epidemiology and biostatistics at Case Western Reserve University School of Medicine in Cleveland, who states that treating older patients with diabetes requires tailored approaches. "The clinician must think in multiple dimensions," Aron says. "While we hold on to our magnifying glasses, we should not forget to reach for the 'minifying' lens which allows one to see a more whole picture."

Eric Seaborg writes about a condition that often accompanies menopause and is somewhat undertreated because patients are too embarrassed to mention it to their doctors. In "Underdiagnosed and Undertreated," Seaborg discusses genitourinary syndrome of menopause (GSM), a condition that many physicians and even fewer patients are aware of. Almost half of all menopausal women will experience the symptoms of GSM but very few will receive appropriate treatment, largely due to their doctors not asking them about it. Risa Kagan, MD, clinical professor of obstetrics, gynecology, and reproductive sciences at the University of California, San Francisco, says that it is up to the physician to ask postmenopausal patients about these symptoms since the diagnosis itself is not difficult. "You often can make a diagnosis even by listening, although you definitely need to do an exam because there is a differential diagnosis," she explains.

We wrap up the Year of Endocrinology with two articles that provide a somewhat comprehensive overview of what took place in 2016 from an endocrine science and treatment perspective. In "2016: A Progress Report" on page 32, Bagley has compiled an exhaustive roundup of some of the new products, therapies and treatments that hit the market this year. From newly approved pharmaceuticals to the latest innovations in technology, we've done our best to cover all the bases in this extensive feature with a generous amount of accompanying photography. But what about research?

Funny you should ask. For the second year in a row we are running "Eureka! The Year's Biggest Discoveries in Endocrine Science." The 2015 edition proved to be so popular that we decided to make this an annual feature (p. 18). Once again, this roundup is put together by Melissa Mapes and she has talked with some of the editors from the Endocrine Society's scientific journals to get their input on new breakthroughs that could very well affect the future of endocrine science for years to come.

As we bid farewell to the Endocrine Society's centennial year, I think we're all excited to see where the next hundred years will take us! EN

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

DECEMBER 2016

Endocrine news

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ENDOCRINE SOCIETY

MEMBERS in the NEWS

Stavros C. Manolagas Receives Middleton Award

Stavros C. Manolagas, MD, PhD, is the recipient of the VA Biomedical Laboratory Research and Development's 2016 William S. Middleton Award from the Central Arkansas Veterans Healthcare System (CAVHS).

Manolagas is the Thomas E. Andreoli, MD, MACP, Clinical Scholar Chair in Internal Medicine, distinguished professor of Medicine, director of the Division of Endocrinology and Metabolism, director of the Osteoporosis and Metabolic Bone Diseases Center, chief of the Endocrinology Section of the Central Arkansas Veterans Healthcare System, and vice chair for research in the Department of Internal Medicine at the University of Arkansas for Medical Sciences (UAMS), Little Rock.

"I am deeply honored to receive the William S. Middleton Award from the U.S. Department of Veterans Affairs Biomedical Laboratory Research and Development Services (BLR&D)," Manolagas says. "For many years I have been collaborating with an outstanding group of co-investigators and I owe a great deal of gratitude to them for this recognition. Since 1960, several members of the Endocrine Society, including three Nobel prize winners, were recipients of this award. I am very humbled to join this distinguished list."

This award recognizes Manolagas' exemplary record of involvement in and service to Veteran's Affairs (VA) and to the biomedical profession as well as his pioneering contributions to the knowledge of the pathophysiologic mechanisms underlying osteoporosis and other metabolic bone disease. Manolagas is responsible for several seminal advances in skeletal biology that have translated into important clinical advances. His discoveries resulted in improved management of chronic kidney disease by the administration of the active form of vitamin D to reduce secondary hyperparathyroidism. His other trademark contributions include understanding the role of sex steroid hormones, including estrogen, in bone biology and the pathophysiology of osteoporosis in both men and women and the development of a treatment for postmenopausal osteoporosis and painful metastatic bone diseases.

The William S. Middleton Award is the highest honor from VA Biomedical Laboratory Research and Development. The award honors a senior VA research scientist in recognition of outstanding scientific contributions and achievements in the areas of biomedical and behavioral research relevant to veterans' healthcare.

NAM
National Academy of Medicine

Endocrine Society Members Elected to the National Academy of Medicine

Endocrine Society members Roger D. Cone, PhD, Hugh S. Taylor, MD, Cheryl Lyn Walker, PhD, and Donald P. McDonnell, PhD, are newly elected members to the National Academy of Medicine (NAM).

The NAM (formerly the Institute of Medicine), was established in 1970 to address "critical issues in health, science, medicine, and related policy." In 2016, the NAM elected 70 new domestic and nine international members, in recognition of major contributions to the advancement of medical sciences, healthcare, and public health.

The Academy has addressed many issues of importance to Endocrine Society members, including testosterone replacement therapy in men, Medicare coverage of routine thyroid screening, and contraceptive research and development.

The Society is encouraged by the election of Endocrine Society members to the NAM and look forward to the impactful work that Cone, Taylor, Walker, and McDonnell will contribute to as members of the Academy.

Endocrinology Gets a New Cover for Its Second Century

January 2017 will mark the launch of the debut issue of the two merged Society journals, *Endocrinology* — publishing for 100 years — and *Molecular Endocrinology* — publishing for 30 years — to create the monthly journal *Endocrinology: Molecular and Physiological Basis of Health and Disease.*

The new *Endocrinology* will publish research papers that provide significant information at the molecular, cellular, tissue, or organismal level of hormone function in the field of endocrinology, offering a single, comprehensive venue that is broad in scope. *Endocrinology* also offers free color online.

Editors-in-chief Andrea C. Gore, PhD, and Stephen R. Hammes, MD, PhD, welcome submissions and proposals for research papers, mini-reviews, and other article types.

For more information on the merger, read the August 2016 article in *Endocrine News*: **endocrinenews.org/magazine-issues/august-2016/**

To view the journal and submit an article, got to **http://press.endocrine.org/journal/endo**

CALL FOR PAPERS

To mark the launch, and to celebrate the centennial of one of its antecedent journals, *Endocrinology* will be publishing three special issues in 2017, focused on the following themes:

Metabolism in Endocrine Health and Disease

Topics include: diabetes, adipose, gut hormones, brain and energy balance, leptin, obesity, reproduction, bone, circadian rhythms, 'omics, kisspeptin, FGFs, nuclear receptors, and GPCRs.

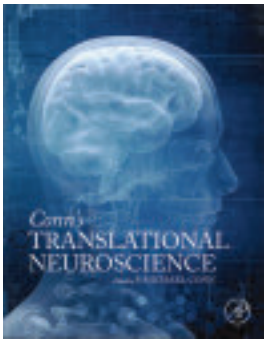
Novel Approaches for Drug Development in Endocrine Disease

Topics include: SERMs, biased agonists for GPCR pathways, pharmacological chaperones to increase receptor expression, antagonist development, and oncology drug development.

Developmental Origins of Endocrine Diseases

Topics include: maternal-fetal endocrinology, sexual differentiation and sex differences, puberty, growth, EDCs, and epigenetics.

Elsevier Publishes New Book by Society Past President P. Michael Conn



Conn's Translational Neuroscience by Endocrine Society past president P. Michael Conn, PhD, MS, was recently published by Elsevier.

Conn, senior vice president for research and associate provost at Texas Tech Health Science Center in Lubbock, served as Society president from 1996 to 1997. One of his major accomplishments while president was the creation of the Hormone Foundation, now known as the Hormone Health Network.

Released on October 11, *Conn's Translational Neuroscience* provides a comprehensive overview reflecting the depth and breadth of the field of translational neuroscience, with input from a distinguished panel of basic and clinical investigators. It alternates scientific and clinical chapters that explain the basic science underlying neurological processes and then relates that science to the understanding of neurological disorders and their treatment.

Chapters cover disorders of the spinal cord, neuronal migration, the autonomic nervous system, the limbic system, ocular motility, and the basal ganglia, as well as demyelinating disorders, stroke, dementia and abnormalities of cognition, congenital chromosomal and genetic abnormalities, Parkinson's disease, nerve trauma, peripheral neuropathy, aphasias, sleep disorders, and myasthenia gravis. This book provides an up-to-date and accessible guide to brain functions at the cellular and molecular level and a clear demonstration of their emerging diagnostic and therapeutic importance.

Prior to his current position Conn, was the director of the Office of Research Advocacy, senior scientist in Reproductive Sciences & Neuroscience, and professor of physiology and pharmacology, cell biology and development, and OB/GYN at Oregon Health & Science University in Portland. Conn and his team identified an underlying biological principle that has dramatically changed scientists' understanding of cellular mutations that result in human disease. He has demonstrated that it is possible to manipulate and redirect the routing of non-functional diabetes, Alzheimer's disease, and cataracts.

Conn also served as an editor of Society journals *Endocrinology* and *The Journal of Clinical Endocrinology & Metabolism* and he adds that this new volume would be a nice addition to the libraries of Endocrine Society members across all constituencies. "The intimacy between the endocrine system and the neurosciences means that this book has much to offer to endocrinologist, both basic and clinical scientists," he says.

Conn's Translational Neuroscience is available at **www.store.elsevier.com** and **amazon.com** with a list price of $165. A Kindle version is available for $132.

Editor's Note: As this issue of *Endocrine News* was going to press, we received late word of P. Michael Conn's passing. We will run a full obituary in the January 2017 issue.

EndoBridge Celebrates Fourth Year in Turkey

The fourth annual meeting of EndoBridge® — co-hosted by the Society of Endocrinology and Metabolism of Turkey, Endocrine Society, and European Society of Endocrinology — took place in Antalya, Turkey, October 20-23, 2016.

The meeting brought together world leaders of endocrinology and 420 colleagues from 29 countries, and was held in English with simultaneous translation into Russian, Arabic, and Turkish. Accredited by the European Accreditation Council for Continuing Medical Education (EACCME), the three-day program included 24 state-of-the-art lectures, 16 interactive case discussion sessions, and poster case presentations covering the full spectrum of endocrinology including diabetes and lipid disorders.

According to Bulent Yildiz, MD, a faculty member at Hacettepe University School of Medicine in Ankara, Turkey, and the founding president of EndoBridge, the conference began on World Osteoporosis Day with the theme, "Love your bones, protect your future." To mark this occasion, numerous lectures on osteoporosis and other bone disorders were presented with over 60 clinical cases in total.

endo bridge®
2016
Bridging the World of Endocrinology

"As usual, we heard inspiring lectures and discussed together several interesting and challenging clinical cases during this year's meeting, but more importantly the meeting again provided a great opportunity for our colleagues from around the world to interact with each other and share their experience and perspectives," Yildiz says. "In an era where bridging becomes more and more important every day, the unique model of EndoBridge® further enhances cross-cultural dialogue, understanding, and collaboration beyond the national borders in the world of hormones."

The fifth annual meeting of EndoBridge® will be held in Antalya, Turkey, October 19 – 22, 2017. Further information is available at www.endobridge.org.

MEMBERS in the NEWS

Laura Vandenberg Honored by the Cornell Douglas Foundation

Laura N. Vandenberg, PhD, an assistant professor of environmental health sciences at UMass Amherst's School of Public Health and Health Sciences (SPHHS) in Amherst, Mass., has been named one of the Cornell Douglas Foundation's 2016 Jean and Leslie Douglas Pearl Award winners for her "outstanding leadership in conducting critical research to identify and address the many issues concerning endocrine disruptors."

The award is accompanied by a $50,000 check to Vandenberg. "This award will allow me to continue to conduct research on endocrine-disrupting chemicals (EDCs) outside of the lab — to use the best laboratory science to better inform chemical safety decision making," she says. "This award offers me the opportunity to continue to advocate for science-based public policies and fight to protect public health."

Vandenberg is an internationally known expert on the effects of EDCs on development and how environmental exposures in early life can contribute to adult diseases including breast cancer, infertility, and obesity. She uses molecular, genetic, tissue-based, and endocrine tools to investigate such chemicals as bisphenol A and S (BPA and BPS) and others used as plasticizers, in flame retardants and cosmetics.

In addition to laboratory studies, Vandenberg's research has focused on understanding "big picture" issues in the study and evaluation of EDCs. "How do we determine which [compounds] are safe?" she ponders. "How do we identify safe doses? Which are the best endpoints to evaluate effects that are relevant to human diseases? How should endocrinology be incorporated in the risk assessment process? I have been privileged to work at the intersection of several scientific fields including endocrinology, environmental health, and developmental biology."

The Cornell Douglas Foundation is an environmental health and justice advocacy group based in Bethesda, Md. The Jean and Leslie Douglas Pearl Award is given to organizations and to individuals who are dedicated to improving the lives of others and to providing a sustainable earth for future generations. EN

ENDO2017
THE ENDOCRINE SOCIETY'S 99TH ANNUAL MEETING & EXPO

Orlando, Fla., April 1 – 4, 2017

The Endocrine Society holds its annual meeting within arm's reach of the "happiest place on Earth" in Orlando. With over 9,000 attendees, nearly 3,000 abstracts, and over 200 other sessions, it is the leading global meeting on endocrinology research and clinical care. The meeting also hosts other satellite and pre-conference events, such as our Early Career Forum and Hands-On Thyroid Workshops.
www.endocrine.org/endo-2017

Sixth International Conference on Endocrinology

Dallas, Texas, December 5 – 7

This year's annual congress highlights the theme "New recommendations and practical approaches in the treatment of endocrine disorders," which reflects the emerging progress being made in endocrine disease research as discoveries in the lab are translated into treatments in an increasingly targeted and precise manner.
http://endocrinology.conferenceseries.com/

ThyroAlex 4

Alexandria, Egypt, December 16

Fourth Semiannual Thyroid Themed conference to be organized by Endocrinology Unit Alexandria Faculty of Medicine in Alexandria covering thyroid eye disease, arrhythmia and thyroid, brain and the thyroid, update on anti-thyroid drugs embryopathy, and thyroid and diabetes.
Tamer_elsherbiny@alexmed.edu.eg

53rd Annual Clinical Diabetes and Endocrinology

Aspen, Colo., January 21 – 24, 2017

This conference will address multifaceted approaches to management and treatment of type 1 and type 2 diabetes, including both existing and emerging therapeutics; osteoporosis management and treatment; testosterone therapy in men and women; diagnosis and treatment of pituitary disorders; drug therapy for Graves disease; subclinical thyroid disease; adrenal insufficiency management; case studies in obesity and dyslipidemia; and much more.
marlinl@njhealth.org

Keystone Symposium on Obesity and Adipose Tissue Biology

Keystone, Colo., January 22 – 26, 2017

This meeting will bring together cell biologists, biochemists, geneticists, physiologists, drug developers, and clinical researchers, thereby facilitating knowledge exchange and interactions leading to elucidation of better treatments for obesity and diabetes.
info@keystonesymposia.org

2017 Gordon Research Conference on IGF & Insulin System in Physiology and Disease

Ventura, Calif., March 12 – 17, 2017

This meeting will present cutting-edge research on the roles of IGFs and insulin and their signaling pathways in normal physiology and in major diseases. The program will bring together investigators around the globe who are at the forefront of this exciting field to discuss key aspects of the IGF and insulin biology.
cduan@umich.edu

Sex and Gender Factors Affecting Metabolic Homeostasis, Diabetes, and Obesity

Tahoe City, Calif., March 19 – 23, 2017

The goal of this meeting is to fill a need in the scientific community by connecting interdisciplinary groups of scientists who normally would not have an opportunity to interact. This group includes investigators studying sex differences, the role of sex hormones, the systems biology of sex and the genetic contribution of sex chromosomes to metabolic homeostasis and diseases.
info@keystonesymposia.org

19th European Congress of Endocrinology

Lisbon, Portugal, May 20 – 23, 2017

The largest European gathering of endocrinologists and endocrine scientists from around the world converge at this annual meeting with the aim of shaping the future of endocrinology to improve science, knowledge, and health across Europe and beyond.
www.ece2017.org

WHY **ENDOCRINOLOGY?**

Patients Are a Virtue

BY DEENA ADIMOOLAM, MD, Assistant Professor, Division of Endocrinology, Diabetes and Bone Disease, Icahn School of Medicine at Mount Sinai, New York, N.Y.

My inspiration to pursue endocrinology comes from the many personal and professional encounters that I have experienced throughout my career. My academic and professional mentors have molded me into the endocrinologist I am today with their knowledge, compassion, and dedication to bringing out the best in their mentees. The incredible stories that my patients share keep me motivated to be a better doctor every day. The patients that I've met, in every chapter of my life, demonstrate the ever-growing need for physicians to educate and empower the public.

During medical school, I chose to volunteer in a remote village in India where diabetes was highly prevalent. I remember spending many sleepless nights before that trip, familiarizing myself with diabetic drugs and all their mechanisms of action — I even made flashcards with the different types of insulin and their varying pharmacokinetic profiles!

When I arrived in India, much to my disappointment, I quickly learned that my flashcards weren't necessary. The needs of these villagers were complex, and I soon realized that insulin wasn't all that they needed. I met Narain, a 37-year-old farmer with type 1 diabetes who was blind in one eye and on the verge of dialysis. He was diagnosed with type 1 diabetes at age 35, which was the same age he saw a doctor for the first time in his life! He did not understand his hyperglycemic symptoms for years, and thought it was a "natural part of aging." Narain was engaged to be married, but as soon as the diagnosis was made, the wedding was called off. Diabetes affected his health, his life, and his future. Many of the villagers I met had similar stories. They had no education on what diabetes was, nor how to prevent it. I was surprised to be diagnosing individuals in their mid-70s with diabetes for the first time. I spent hours educating the villagers on diabetes, its symptoms, treatment, and prognosis. I was hopeful that through promoting education and awareness, I could make a difference in their lives.

Post medical school, I continued to witness how a lack in health education and awareness leads to poor health outcomes, and it had a profound impact on me. During residency at Yale, I met Lara, a 22-year-old naturopath who presented to the hospital in diabetic ketoacidosis (DKA) — her HgbA1c was 15. She was diagnosed with type 1 diabetes at the age of 18, and despite medical advice to take insulin, she relied on Chinese herbs and a full carbohydrate restriction to treat her condition. When I asked her why she didn't want to take insulin, she answered, "Why do I need it when I don't eat carbs?" Our team educated her on why insulin was necessary to stay alive, and she told us we were the first people in four years to tell her this! She stopped all herbal medications and became a patient I continued to follow in clinic. Luckily she was never admitted for DKA again.

I found the stories of diabetic patients empowering and felt compelled to change their lives for the better through education and spreading awareness. With the mentorship of Dr. Stephen Huot and the Yale Primary Care faculty I discovered new outlets to share the importance of preventative medicine with the community. I worked with Dr. Huot to coordinate health fairs to provide preventative care and disease screenings to thousands of individuals in the community. Throughout residency, I spoke on primary care prevention on the radio and at various events throughout the area. I began to realize the power of media, and started to blog routinely on various health topics. EN

Stay tuned for part two of Adimoolam's "Why Endocrinology?" column in the January issue.

To celebrate 100 years of the Endocrine Society, throughout 2016 *Endocrine News* is running a "Why Endocrinology?" column in each issue. If you'd like to share your story with our readers, contact Mark A. Newman at **mnewman@endocrine.org**.

> "While we hold on to our magnifying glasses, we should not forget to reach for the 'minifying' lens **which allows one to see a more whole picture.**"
>
> **— DAVID C. ARON, MD, MS,** professor of medicine and epidemiology and biostatistics, Case Western Reserve University School of Medicine, Cleveland, in "I'm Still Here: Diabetes and the Aging Patient" on page 24.

FROM THE CENTURY OF ENDOCRINOLOGY TIMELINE

2006:

Clark T. Sawin Memorial Library and Resource Center Established

Through a generous donation by Dr. Clark T. Sawin's widow, Mrs. Leslie Sawin, the Clark T. Sawin Memorial Library and Resource Center was established at the Endocrine Society's national office in 2006. By cataloging and preserving historical endocrine literature and artifacts, the library plays an important role in the Society's mission to support the field of endocrinology. Originally comprised of Dr. Sawin's personal collection of over 6,500 items, the library now holds more than 8,100 items including books, oral histories with leaders in the field of endocrinology, and special collections donated by members and friends of the Endocrine Society.

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

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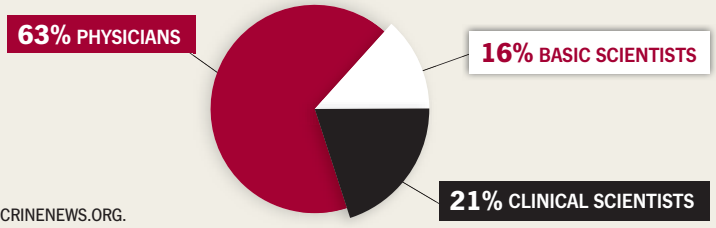

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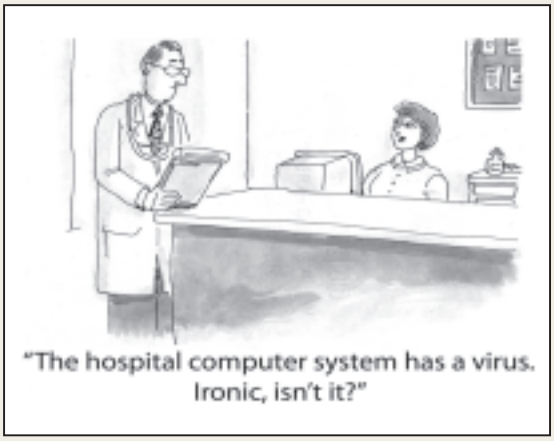

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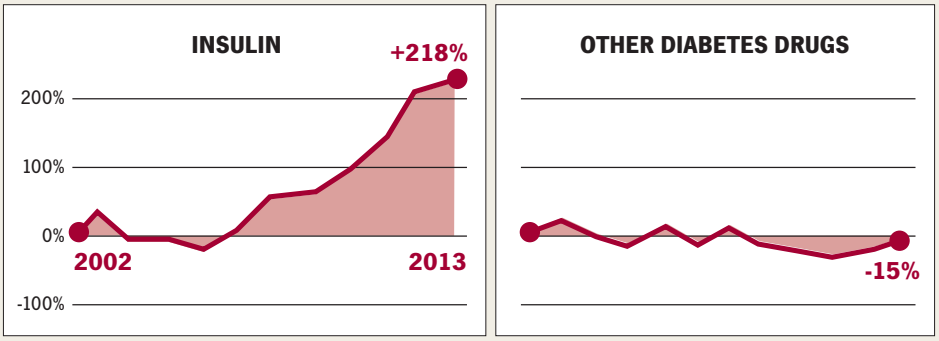
8.9 MILLION

The number of fractures caused by osteoporosis around the world each year, which is essentially a fracture every three seconds.

— SOURCE: *OSTEOPOROSIS INTERNATIONAL*, 2006

Spending on Insulin vs. Other Diabetes Drugs

While spending on insulin per patient has skyrocketed – thanks to price hikes and increased use – spending on other diabetes drugs has stayed roughly the same. (Note: Does not include rebates/discounts).



— SOURCE: *JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION*

BY DEREK BAGLEY

Menopausal Hormone Therapy Improves Bone Health

Women who undergo hormone therapy for menopausal symptoms such as hot flashes may be able to increase bone mass and improve bone structure, according to a new study published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Georgios Papadakis, MD, of the Lausanne University Hospital in Lausanne, Switzerland point out that menopausal hormone therapy (MHT) "was for many years a first-line therapy in the prevention of postmenopausal osteoporosis, a practice supported by observational data." However, there was some controversy over studies showing that the bone benefits of this treatment may be outweighed by other adverse events, such as an increase in breast cancer, coronary heart disease, and stroke. According to the authors, further studies showed promising evidence for reduced risk of adverse events in younger postmenopausal women, as well as for sustained protection against bone loss even in lower doses, which also lowered the other risks. "As a result," they write, "the latest guidelines reestablish MHT as a first-line treatment for the prevention of fracture in at-risk women before age of 60 years or within 10 years after menopause without any mandatory time limit for the duration of treatment."

This new study is the first to show MHT can improve bone structure in addition to bone mass, and that the bone health benefits persist for at least two years after women stop treatment. "When used in the right context, specifically in postmenopausal women younger than 60 years old for whom the benefits outweigh risks, menopausal hormonal therapy is effective for both the prevention and treatment of osteoporosis," says Papadakis.

The cross-sectional study is based on data from the OsteoLaus cohort. The cohort consisted of 1,279 women aged 50 to 80 residing in the city of Lausanne, Switzerland. The participants were divided into three categories: 22% were undergoing MHT during the study, 30% were past users, and 48% of women had never used MHT. To measure whether MHT influenced bone health, researchers used dual x-ray absorptiometry (DXA) scans of the participants' lumbar spines, femoral necks, and hips to assess bone mineral density. Based on the lumbar scan image and a well-validated software, Trabecular Bone Score was calculated for each woman, an indice assessing the quality of the underlying bone structure.

Age and body mass index were major factors modifying the results of the study. Other variables assessed included the history of fractures in participants, and the use of supplements such as current or past use of calcium and/or vitamin D. Blood test results for vitamin D levels from 1,204 out of the 1,279 participants were also factored into the study.

> When used in the right context, specifically in postmenopausal women younger than 60 years old for whom the benefits outweigh risks, menopausal hormonal therapy is effective for both the prevention and treatment of osteoporosis."

Findings: The researchers found higher Trabecular Bone Scores in current MHT users compared to past users or women who had never used MHT. All bone mass density values were significantly higher in current users compared to past users or participants who had never used MHT. Past users of the therapy exhibited higher bone mass density and a trend for higher bone microarchitecture values compared to women who had never used MHT. The researchers note that the duration of MHT had no effect on bone health. However, in past users the time since MHT discontinuation seems to be a crucial factor and the protective effects disappear two to four years after treatment withdrawal.

"Women at menopause should take note of this study, because its results can help optimize the use of menopausal hormone treatment in women at risk of osteoporosis," Papadakis says.

Low Blood Glucose Levels in Hospitalized Patients Linked to Increased Mortality Risk

In hospitalized patients, hypoglycemia is associated with increased mortality risk, according to a study recently published in *The Journal of Clinical Endocrinology & Metabolism.*

The paper comes as a coalition of diabetes stakeholders issues a strategic and actionable blueprint to address the deadly threat hypoglycemia poses to people with diabetes. (See the special section on the Endocrine Society's blueprint for managing and preventing hypoglycemia in our November issue.)

Researchers led by Amit Akirov, MD, of Rabin Medical Center in Petah Tikva, Israel, point out that in-hospital insulin treatment is associated with an increased risk of hypoglycemia, which is often asymptomatic due to "hypoglycemia unawareness or altered consciousness associated with acute illness or drug therapy." So in-hospital insulin treatment leads to complications with hypoglycemia, which in turn leads to other complications such as ischemic events and longer hospital stays.

The researchers analyzed data from nearly 3,000 patients with hypoglycemia at a 1,330-bed university-affiliated medical center. They evaluated medical records and the hospital's mortality database to investigate the association between hypoglycemia and mortality in hospitalized patients. They found that for patients with hypoglycemia, almost 32% had died at the end of the follow-up period.

Findings: Mortality risk was higher in insulin-treated patients with moderate hypoglycemia (40-70 mg/dL), compared to patients without insulin treatment with similar glucose values. However, with severe hypoglycemia (<40 mg/dl), the increase in mortality risk was similar with insulin-related and non-insulin related hypoglycemia. Cause of admission did not affect the association between glucose levels and mortality. "Hypoglycemia is common among hospitalized patients with and without diabetes mellitus," says Akirov. "Our findings suggest that hypoglycemia, whether insulin-related or non-insulin related, is associated with short- and long-term mortality risk. These data are a timely reminder that hypoglycemia of any cause carries the association with increased mortality."

Customized Vitamin D Supplements May Benefit Pregnant Women

Individualized supplement doses help protect pregnant women from vitamin D deficiency, according to a study recently published in *The Journal of Clinical Endocrinology & Metabolism*.

The research found vitamin D supplements are less effective at raising vitamin D levels in pregnant women if they deliver their babies in the winter, have low levels of vitamin D early in pregnancy, or gain more weight during pregnancy. Women with these risk factors may need higher doses during pregnancy than other mothers-to-be.

"It is critical for pregnant women to have sufficient levels of vitamin D for the health of their baby," says one of the study's authors, Nicholas C. Harvey, MA, MB, BChir, MRCP, PhD, professor of rheumatology and clinical epidemiology at the University of Southampton in Southampton, UK. "Our study findings suggest that in order to optimize vitamin D concentrations through pregnancy, the supplemental dose given may need to be tailored to a woman's individual circumstances, such as the anticipated season of delivery."

The analysis examined data from the Maternal Vitamin D Osteoporosis Study (MAVIDOS), a multi-center, double-blind, randomized, placebo-controlled trial of vitamin D supplementation in pregnancy. The study examined vitamin D levels in 829 pregnant women who received early pregnancy ultrasounds at one of three United Kingdom hospitals.

Beginning around 14 weeks' gestation, the women were randomized to receive either a 1,000 IU/day dose of a vitamin D3 supplement called cholecalciferol or a placebo. Researchers measured vitamin D levels in the participants' blood prior to the start of the study and again at 34 weeks' gestation.

Participants who received the supplement had varying levels of vitamin D in the blood, even though they received the same dose. Researchers found women who delivered in the summer, who gained less weight during pregnancy and who had higher vitamin D levels early in pregnancy tended to have higher levels of vitamin D in the blood than their counterparts. Women who consistently took the supplement also had higher levels of vitamin D than participants who did not.

Findings: **"Our findings of varied responses to vitamin D supplementation according to individual attributes can be used to tailor approaches to prenatal care," says one of the study's authors, Cyrus Cooper, OBE, MA, DM, FRCP, FFPH, FMedSci, professor of rheumatology and clinical epidemiology at the University of Southampton's MRC Lifecourse Epidemiology Unit. "This work will inform the development of strategies to enhance bone development across generations."** EN

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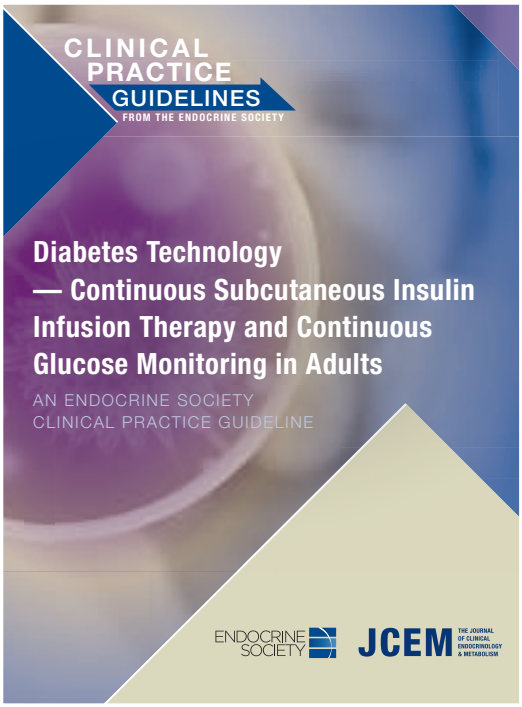

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2016 Eureka

BY MELISSA MAPES

For the second year in a row, *Endocrine News* talks to editors from Endocrine Society journals to get the scoop on the top endocrine discoveries of 2016.

The life work of a scientist requires an enormous amount of patience. "Eureka moments" take years of tireless experimentation and iteration to achieve, which is why impactful discoveries deserve celebration. Over the past year, many important papers have been published in the field of endocrinology — from confirming the essential role of ESR1 in male reproductive health to uncovering the therapeutic potential of corticosterone for congenital adrenal hyperplasia.

This article is a sampling of the research achievements of our community in 2016, as picked by five editors from the journals *Endocrinology* and *The Journal of Clinical Endocrinology & Metabolism* (*JCEM*). While not intended as a comprehensive overview of all major studies, it instead aims to encourage reflection on this year's successes and recognize a few important publications across a handful of endocrine specialties.

Testosterone Under the Microscope

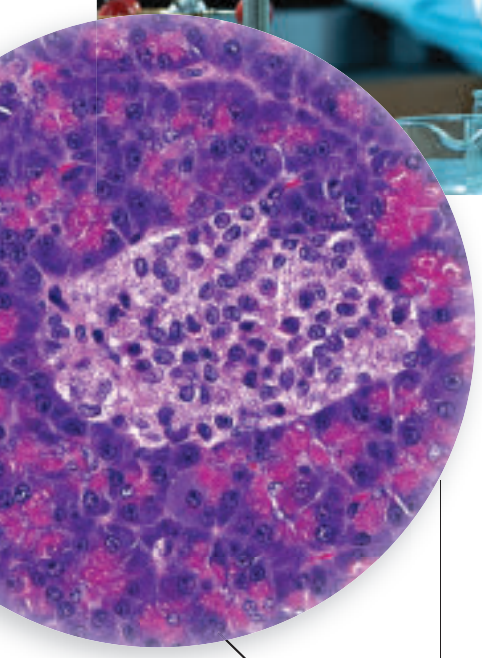
In last year's "Top Endocrinology Discoveries of 2015" article in *Endocrine News*, two reproductive specialists underscored the revelation that testosterone therapy, which is widely prescribed in aging men, lacks solid evidence of beneficial effects. They described the need for more concrete literature on the subject.

Fortunately, the call for more research is leading to important publications in this area. Alvin M. Matsumoto, MD, professor at the University of Washington and an associate editor of *JCEM*, points to the initial publication of The Testosterone Trials in the *New England Journal of Medicine* as a critical step forward.

"In the area of male reproductive endocrinology, I think that this is the most impactful report in the last year," Matsumoto says.

The publication, "Effects of Testosterone Treatment in Older Men" by Snyder, PJ, et al, followed 790 men over the age of 65 with unequivocally low serum testosterone levels for one year as they participated in at least one of three trials: The Sexual Function Trial, the Physical Function Trial, and the Vitality Trial. Half of the participants received testosterone gel, and half received a placebo.

"Versus placebo, testosterone treatment for one year moderately improved sexual function and slightly improved depressive symptoms and mood, but did not improve fatigue or walking distance," Matsumoto explains.



Pancreatic islet tissue samples may become more widely available based on a study that uncovered that human islet isolation for science may be able to accept tissue from donors with a wider cold ischemia time (CIT) window. With more acceptable samples to work with, scientists may be able to further diabetes research at a faster rate.

The sample size was not large enough to draw conclusions about possible negative effects, implying that the jury is still out on testosterone supplementation. The moderately positive effects are not enough to make the case for continued use. Still, there are four additional studies in the queue for publication from The Testosterone Trials — relating to bone health, cognition, anemia, and coronary artery plaque formation — that could sway recommendations for or against the therapy.

The Fairer Sex Steroid

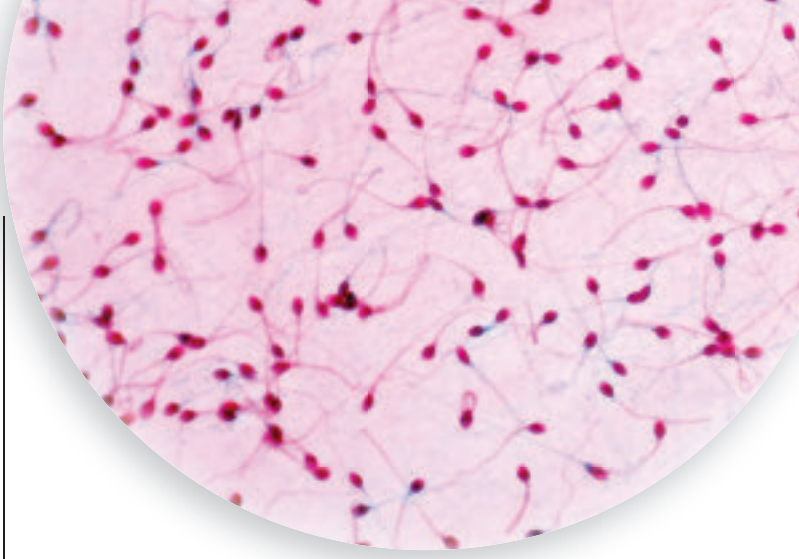
While testosterone supplementation remains under scrutiny, estrogen as a part of male reproductive health is receiving more attention. Gail S. Prins, PhD, professor at the University of Illinois at Chicago and an associate editor for *Endocrinology*, sees the study published in the July issue of that journal, "Membrane-Localized Estrogen Receptor 1 Is Required for Normal Male Reproductive Development and Function in Mice" by Nanjappa, M, et al, as a top discovery in the field of steroids and male reproduction.

"Nearly 20 years ago, *Nature* published an important study about ER (ESR1) and estrogen, identifying for the first time that ERalpha possesses an essential physiologic role in male reproduction by controlling fluid resorption in the rete testis and influencing the fertilization capacity of spermatozoa," Prins says. "Since that time, the molecular pathways involved in ESR1 actions have been shown to be numerous and include membrane-initiated signaling due to ERa localized to the membrane."

This new publication proves that the pathway is vital for ESR1 actions. "Deletion of the membrane component with retention of the nuclear ESR1 signaling results in many similar phenotypes in sperm maturation, rete testis fluid absorption, and so on as observed with the total ESR1 knockout mouse," she continues.

The results indicate that new therapeutic tools could be on the horizon, taking advantage of "a previously underappreciated pathway." The possibilities are far-reaching, and may even include a male contraceptive approach. Further research will determine the clinical potential of tapping into these rapid signaling pathways in the male reproductive tract.

Male Birth Control Shots Show Promise



As Endocrine News reported in June, the ongoing search for the ever-elusive male hormonal birth control method seems to be many years away. However, a new study published in *The Journal of Clinical Endocrinology & Metabolism* this fall revealed that new shots that men can take have been shown to prevent pregnancy in their female partners.

According to Mario Philip Reyes Festin, MD, of the World Health Organization and one of the study's authors, "it is possible to have a hormonal contraceptive for men that reduces the risk of unplanned pregnancies in the partners of men who use it," adding that the findings confirmed the efficacy of this contraceptive method previously seen only in small studies.

The prospective Phase II single arm, multi-center study tested the safety and effectiveness of injectable contraceptives in 320 healthy men ages 18 to 45 who were all in monogamous relationships for at least a year. The men underwent testing to ensure they had a normal sperm count at the start of the study.

The men received injections of 200 milligrams of a long-acting progestogen called norethisterone enanthate (NET-EN) and 1,000 milligrams of a long-acting androgen called testosterone undecanoate (TU) for up to 26 weeks to suppress their sperm counts. The men received two injections every eight weeks. Participants initially provided semen samples after eight and 12 weeks in the suppression phase and then every 2 weeks until they met the criteria for the next phase. During this time, the couples were instructed to use other non-hormonal birth control methods.

The hormones were effective in reducing the sperm count to 1 million/ml or less within 24 weeks in 274 of the participants. The contraceptive method was effective in nearly 96% of continuing users. Only four pregnancies occurred among the men's partners during the efficacy phase of the study.

However, side effects such as depression, acne, injection site pain, muscle pain, and others caused 20 subjects to drop out. Festin says that more research is needed to advance this method so that it can be made widely available as a contraception option. "Although the injections were effective in reducing the rate of pregnancy," he says, "the combination of hormones needs to be studied more to consider a good balance between efficacy and safety."

The Heart and the Hormone

Two articles stand out to Robert H. Eckel, MD, professor at the University of Colorado Denver and an associate editor for *JCEM*. With a background in both endocrinology and cardiology, he pays close attention to scientific developments that overlap across both fields.

The first paper that Eckel highlights is "Cholesterol Lowering in Intermediate-Risk Persons without Cardiovascular Disease" by Yusuf, S, et al. The study, which was published in the *New England Journal of Medicine* in May 2016, set out to evaluate the potential benefits of statins in groups that have been underrepresented in previous trials, such as ethnic minorities and patients with intermediate cardiovascular risk.

After collecting data from 12,705 participants across 21 countries, the authors discovered, "Treatment with rosuvastatin at a dose of 10 mg per day resulted in a significantly lower risk of cardiovascular events (26.5% lower) than placebo in an intermediate-risk, ethnically diverse population without cardiovascular disease."

The other top study, in Eckel's opinion, is "Efficacy and Tolerability of Evolocumab vs Ezetimibe in Patients With Muscle-Related Statin Intolerance: The GAUSS-3 Randomized Clinical Trial" by Nissen, S, et al., published in the *Journal of the American Medical Association* (*JAMA*) in April.

Between 5% and 20% of patients on statins report muscle-related intolerance, meaning a significant population requires an alternative therapy for lowering lipids. This study investigated the effectiveness of two nonstatin therapies — ezetimibe and evolocumab — in adult patients with a history of statin intolerance.

Results demonstrated that evolocumab led to a significantly greater reduction in LDL-C levels after 24 weeks than ezetimibe. However, both drugs saw muscle symptoms in over 20% of participants, and the authors concluded that further testing of long-term effects and safety are needed.

DID OUR PREDICTIONS FOR 2016 HOLD UP?

These are the research trends that we expected to see more of in 2016, based on interviews with editors of *Endocrine Reviews.* Have you seen these topics emerge in your reading? Let us know by submitting your feedback online: mnewman@endocrine.org.

- **Metabolic reprogramming and its importance for understanding hormone action**
- **Stress hormones in regulating cardiovascular function**
- **Sex differences in metabolic homeostasis, diabetes, and obesity.**
- **Genotype-phenotype correlation and inherited predisposition for developing pituitary adenomas**
- **Epigenetic effects during pregnancy and in offspring**
- **Importance of local control of thyroid hormone levels by the types 2 and 3 deiodinases**
- **Mutations that underlie thyroid cancer and development of targeted therapies**
- **Bone's role in the homeostatic mechanisms of the whole body**
- **Chronic exercise and the recently discovered protein, irisin, on skeletal turnover**
- **Free vitamin D rather than total vitamin D evaluations**
- **Treatments for hypophosphatasia**
- **X-linked hypophosphatemia and hypoparathyroidism**
- **Crescent application of new methods for genetic diagnosis, such as gene panel and whole genomic/exomic sequencing**
- **Tools for investigating epigenetic factors, such as DNA methylation and microRNA**
- **Effects of testosterone (and its metabolites) on bone, muscle, brain, prostate, and the cardiovascular system**
- **Male hormonal contraceptives**
- **Relationship between body weight and male gonadal function**

A Bigger Biobank

According to Patricia Brubaker, PhD, FRSC, professor at the University of Toronto and an associate editor for *Endocrinology*, one particular paper from this past year comes to mind — a study that could lead to a greater number of human islet samples for diabetes research.

Generally, the world of research faces more restrictions now than ever, but there are exceptions to the rule. Every so often a finding indicates that the rules can be loosened, which is what Lyon, J, et al, discovered with "Research-Focused Isolation of Human Islets From Donors With and Without Diabetes at the Alberta Diabetes Institute IsletCore" published in the February issue.

This study uncovered that human islet isolation for science may be able to accept tissue from donors with a wider cold ischemia time (CIT) window.

"Through 142 isolations over approximately five years, we confirm that CIT and glycated hemoglobin each have weak negative impacts on isolation purity and yield, and extending CIT beyond the typical clinical isolation cutoff of 12 hours (to ≥ 18 h) had only a modest impact on islet function," the authors state.

With more acceptable samples to work with, scientists may be able to further diabetes research at a faster rate.

Avoiding Adverse Metabolic Effects

Richard Auchus, MD, professor at the University of Michigan and an associate editor for *Endocrinology*, cites "ABCC1 confers tissue-specific sensitivity to cortisol versus corticosterone: A rationale for safer glucocorticoid replacement therapy" by Nixon, M, et al., published in the journal *Science Translational Medicine* in August as one of the most impactful studies of 2016.

"This paper could be revolutionary," Auchus says.

In treating congenital adrenal hyperplasia, the challenge is keeping excess adrenal androgens at bay while attaining sufficient physiological glucocorticoid replacement. The glucocorticoid replacement therapies currently in place — namely cortisol infusions — almost always come with adverse metabolic effects.

This study indicates that corticosterone is a preferable alternative to cortisol. In patients with Addison's disease, adrenal androgens were suppressed at similar levels when treated with cortisol or corticosterone, but corticosterone resulted in fewer negative metabolic outcomes. Thus, development of a pharmaceutical therapy using corticosterone could mean better health for people with congenital adrenal hyperplasia.

The past year has brought endocrinology closer than ever to solving some of the most complex diseases and disorders on the planet, as the studies highlighted in this article clearly demonstrate. Though the journey to discovery is often a long one, the achievements of researchers in 2016 show that the field of endocrine science is not slowing down. EN

MAPES IS A WASHINGTON, D.C.–BASED FREELANCE WRITER AND A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS*. SHE WROTE ABOUT THE IMPACT OF WEARABLES ON PATIENT TREATMENT IN THE NOVEMBER ISSUE.

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ENDOCRINE SOCIETY

Hormone Science to Health

As diabetes patients are living longer, endocrinologists are finding themselves faced with a unique set of treatment challenges not often found in younger patients.

From cognitive function to cultural norms, treating older diabetes patients is much more complicated than ever before.

I'm Still Here:

BY DEREK BAGLEY

DIABETES AND THE AGING PATIENT

During the Endocrine Society's 97th annual meeting in San Diego, Pendar Farahani, MD, MSc, assistant professor in the Department of Clinical Epidemiology and Biostatistics at McMaster University in Hamilton, Ontario, Canada, presented research on the clinical gaps in statin therapy among older patients with diabetes. The study, which analyzed more than 200,000 people in two cohorts – those aged between 65 and 75, and those aged over 75 – found that on average, more than 30% of older patients with diabetes are not utilizing statin therapy, despite needing the medication.

This is a significant and troublesome finding, because, as Farahani says, older individuals with diabetes should by default be on a statin for cardiovascular protection. He explains that he and his team focused on statin treatment because it's well established, and it allowed them to look at real-world data. "Most of the evidence that we have and that we rely on is from randomized, controlled trials," Farahani says. "And if you look at the randomized, controlled trials, most of the time they are not representative of the patient populations we see, especially in elderly."

A subsequent study conducted by Farahani and his team, published last December in *Clinical & Investigative Medicine*, found that these gaps become even wider when factoring in gender. Data show that women are less tolerant of statins, findings that became more apparent as statin doses increased over the years as guidelines evolved. The researchers also found that there was no clinically significant difference in treatment between the 65-75 cohort and the 75-plus cohort, which was surprising because they thought the 65-75 cohort would have been treated more aggressively. "Sometimes we do not change the medication according to the life expectancy and comorbidity of our patients," Farahani says.

Ultimately, these findings point to a larger issue when treating older patients with diabetes. These patients comprise a heterogenous population that continues to grow, as life expectancy increases alongside diabetes rates. And the key to treating them successfully depends on myriad, diverse factors.

PHYSICIAN BIAS

At the surface, there can be a stigma surrounding older patients with diabetes. Bias can play a role as doctors may make assumptions about what these individuals are capable of doing or not doing. Or because these patients tend to have shorter remaining life expectancies than younger patients, their doctors may go with less aggressive treatment options. But according to the U.S. population-based Health and Retirement Study (Blaum et al. *Medical Care* 2010), half of diabetes patients over age 75 are capable of leading active, healthy lifestyles. And an even higher percentage of patients 65 to 75 are still relatively healthy, says Jeffrey Halter, MD, professor emeritus of internal medicine in the Division of Geriatric and Palliative Medicine at the University of Michigan in Ann Arbor. "Age alone shouldn't determine how aggressive the diabetes management goals should be," Halter says.

> **Age alone shouldn't determine** how aggressive the diabetes management goals should be."
>
> — JEFFREY HALTER, MD, PROFESSOR EMERITUS OF INTERNAL MEDICINE, DIVISION OF GERIATRIC AND PALLIATIVE MEDICINE AT THE UNIVERSITY OF MICHIGAN, ANN ARBOR.

Still, diabetes already demands much of patients, and as these patients grow older, they're at greater risk for developing comorbidities. "By virtue of having lived longer these individuals have more time to have accumulated more conditions, so that multi-morbidity is very common in this population," says David C. Aron, MD, MS, professor of medicine and epidemiology and biostatistics at Case Western Reserve University School of Medicine in Cleveland. He goes on to say that having multiple conditions itself brings problems, including interactions between conditions (for example, treating lung disease with steroids makes glycemic control worse), polypharmacy (leading to more drug-drug interactions and adverse events), and conflicting practice guidelines (which are usually designed for people with one condition).

Deena Adimoolam, MD, assistant professor in the Division of Endocrinology, Diabetes and Bone Disease at Icahn School of Medicine at Mount Sinai in New York, describes a particularly dizzying example of what some older patients with multiple conditions exacerbated by diabetes may experience. "Some elderly patients may develop chronic kidney disease," she says. "Chronic kidney disease may lead to impaired ability to metabolize certain diabetes medications which can lead to persistent hypoglycemia. Hypoglycemia in the elderly may predispose them to falls and subsequent fractures, which can be fatal."

Compounding this problem is the fact that many symptoms of hypoglycemia are non-specific, like weakness or confusion. "It may be difficult to identify whether a patient is having symptoms of hypoglycemia versus symptoms of a different medical issue like a cerebrovascular accidents, myocardial infarct, delirium, dementia, and/or seizures," says Adimoolam.

TAILORING TREATMENT

To make matters worse, there's a higher rate of dementia in patients with diabetes, and the reason for this isn't known, although it's under investigation. Halter says that in analysis, patients with dementia had severe hypoglycemia, which he says wasn't a surprise, but it is scary. "Endocrinologists and diabetologists need to be tuned into this problem," he says.

According to Halter, 20% of those who participated in the NIH's Action to Control Cardiovascular Risk in Diabetes (ACCORD) Trial had significant cognitive impairment on testing, even though cognitive issues should have excluded them from the study. "These were missed in recruitment," he says, "and it's one example of the magnitude of the problem."

Other individuals may suffer from depression, and they lose any interest in caring for themselves. "If your elderly patient seems depressed, consider screening them for depression and referring them to a psychiatrist," Adimoolam says. "Depression needs to be treated first before other medical issues like diabetes can be optimized."

Cognitive issues must inform tailored treatment options for these patients. Farahani says he tests cognition for each patient as indicated before starting any treatment plan, as altered cognition, including dementia, will determine the type of care and pharmacotherapy that should be implemented for each patient. "I have seen elderly patients that have been on insulin or other medications with hypoglycemia risk who had mild to moderate cognition issues," he says. "This is important with an aging population."

OVERCOMING CULTURAL DIFFERENCES

What's also important with this aging population when determining a course of treatment is considering cultural challenges and barriers. Older individuals have had many years to establish habits that may be inconsistent with what physicians view as ideal care. "When patients are unwilling to do give up something that from a physician's perspective hinders their care," Aron says, "it is our responsibility to work to come up with the best patient-centered approach."

"Yesterday I had 15 patients from four continents," Farahani says. "When you think about diabetes care, you should include culture as a main component in treatment." He says that one of his patients is an older Italian woman who loves to cook and that's the way she's been living for the last 73 years, so the best approach would be training her on how to change her lifestyle, and give her the appropriate medication.

"In many cultures, food is life and happiness," Adimoolam says. "In many cultures, high carbohydrate foods are a staple and almost impossible to eliminate from the diet. I try to tailor a diabetes regimen based on a patient's preferences for food."

But it's not just cultural differences that can present problems. There can be language barriers; social factors such as stress, food insufficiency, limited finances, or lack of transportation to doctors'

offices; and frustration with the new technology being developed for diabetes care. "The world when radios were made with vacuum tubes is long gone," Aron says. "Now we have apps which present a whole series of challenges not only because of their novelty, but also because of their usability limitations, especially in an aging population with decreasing functional status."

THINKING IN MULTIPLE DIMENSIONS

Of course, this concept of tailoring care for older patients with diabetes is nothing new. But this population continues to grow; people are living longer but diabetes rates continue to skyrocket, so it's important to revisit the issue from time to time. Halter says because we are facing a huge increase in older individuals with diabetes, an important approach is diabetes prevention, and that this population benefits more from lifestyle intervention than younger people.

One of the big challenges in these patients is addressing goals of diabetes management, like a target HgbA1c. These patients may have shot for goals of less than 7% most of their lives, but as they age and might develop other complications, those same goals could put them more at risk for hypoglycemic episodes, which would put them at greater risk of other complications.

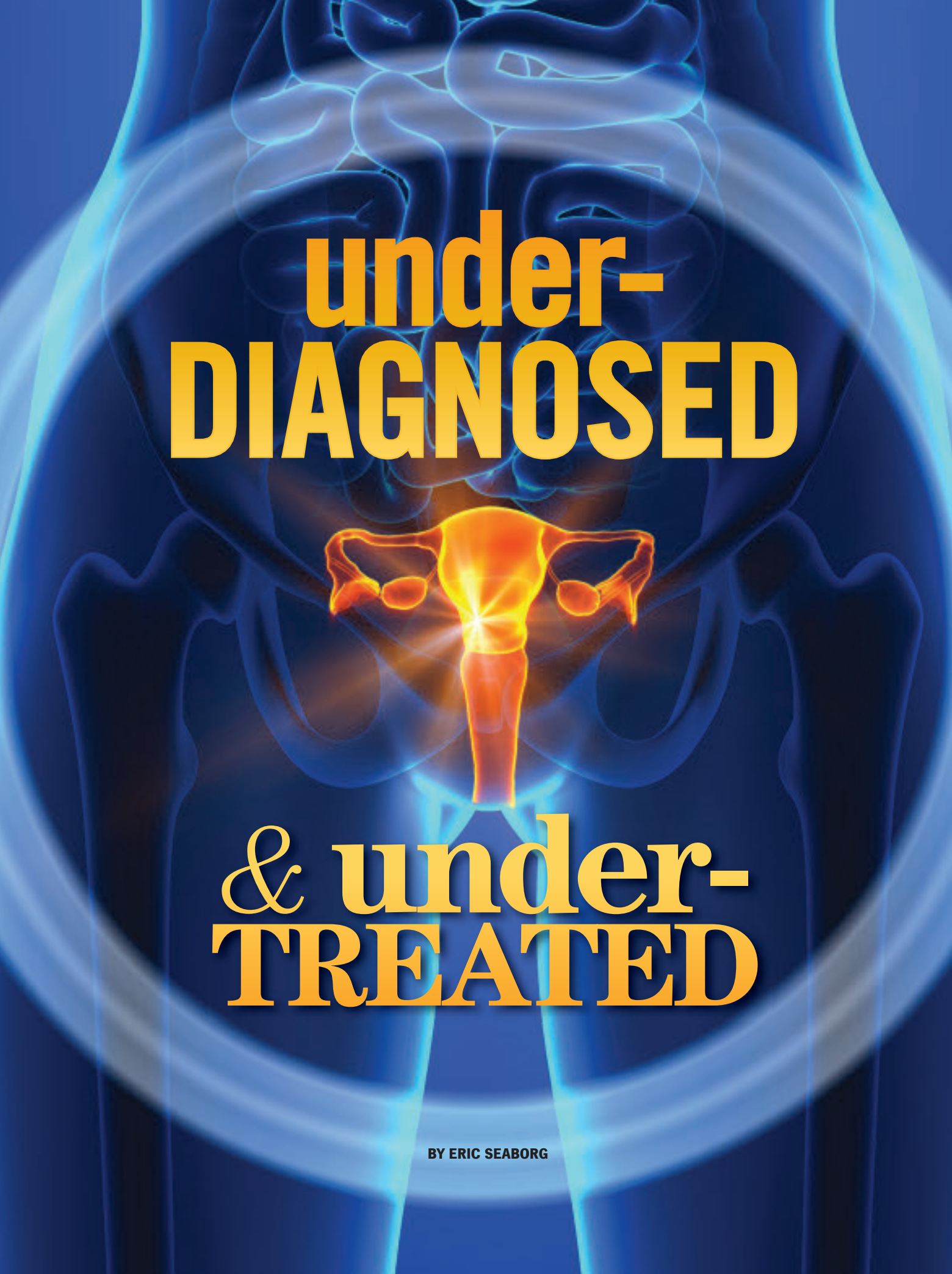
"I find it difficult, especially with my type 1 diabetics, to change their mentality as they age and assure them that a higher HgbA1c might actually be better for them — especially for those with hypoglycemia unawareness and who are at high fall risk," Adimoolam says.

"The clinician must think in multiple dimensions," Aron says. "While we hold on to our magnifying glasses, we should not forget to reach for the 'minifying' lens which allows one to see a more whole picture." EN

BAGLEY IS THE ASSOCIATE EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT HOW PANCREAS DONORS COULD BE THE KEY TO A CURE FOR DIABETES IN THE NOVEMBER ISSUE.

AT A GLANCE

- **Older patients with diabetes comprise an ever-growing population, since people are living longer but diabetes rates continue to climb.**
- **Cognitive issues must be considered along with physical comorbidities when treating older patients with diabetes.**
- **This is a heterogenous group, and treatment of diabetes in these individuals must reflect their diversity.**



under-DIAGNOSED & under-TREATED

BY ERIC SEABORG

Most women have never heard of genitourinary syndrome of menopause. But given its prevalence and progressive nature, many physicians are working to increase attention and treatment.

Some 50% of postmenopausal women will experience the symptoms of genitourinary syndrome of menopause (GSM) at some point, but few women receive treatment — even though safe and effective treatments are available.

The condition is known by several names — including vulvovaginal atrophy — in part because the symptoms resulting from a lack of estrogen can range from sexual discomfort to frequent urinary tract infections. But women do not recognize GSM as "one of the hallmarks of menopause" like hot flashes that they know to talk to their physicians about, says Risa Kagan, MD, clinical professor of obstetrics, gynecology, and reproductive sciences at the University of California, San Francisco.

And sexual function is a topic that women may be hesitant to bring up, says JoAnn Manson, MD, DrPH, a professor at Harvard Medical School and chief of the Division of Preventive Medicine at Brigham and Women's Hospital in Boston: "Women may just not be comfortable talking about the fact that sexual activities are painful for them. People are often embarrassed to bring up subjects like that."

"So if the health-care provider doesn't specifically ask them about these symptoms, it will tend to be missed," Manson says, and surveys show time-pressed clinicians seldom raise the issue. According to some estimates, fewer than 10% of symptomatic women are treated with a relevant prescription product.

FRIGHTENING BOXED WARNINGS

But even when physicians diagnose the condition and write a prescription, many women are scared off by the warnings that the Food and Drug Administration (FDA) requires in the labeling. Package inserts feature a prominent "black box" warning — which critics say is not backed up by evidence — that the products could lead to endometrial cancer, cardiovascular disorders, breast cancer, and dementia. These "class warnings" are included because the products contain estrogen.

Manson is part of a large group of healthcare professionals that has petitioned the FDA to change the labels because the warning is related to systemic estrogen, which these products are not. The systemic estrogens taken in menopausal hormone therapy substantially raise estrogen blood levels. But these are low-dose, locally applied treatments.

"The evidence is that the low-dose vaginal estrogen does not lead to estrogen blood levels that are above the usual postmenopausal range," Manson says. "In that way it is very

WHAT'S IN A NAME?

What if you want to inform the public about a medical condition, but television producers won't let you utter a word in the condition's name?

Public distaste for the "vagina" portion of vulvovaginal atrophy was just one of the tricky issues that led two medical societies to convene a consensus conference to discuss the terminology. The members of the conference agreed that "the term genitourinary syndrome of menopause (GSM) is a medically more accurate, all-encompassing, and publicly acceptable term than vulvovaginal atrophy."

GSM is more accurate because the decrease in estrogen and other sex steroids can lead to changes to a variety of structures: the labia majora, labia minora, clitoris, vestibule, introitus, vagina, urethra, and bladder. Symptoms can include genital symptoms of dryness, burning, and irritation; sexual symptoms of lack of lubrication, pain, and impaired function; and urinary symptoms of urgency, dysuria, and recurrent urinary tract infections.

Following the consensus conference, the boards of directors of both the International Society for the Study of Women's Sexual Health and the North American Menopause Society formally endorsed the new term, and it is being increasingly adopted by other professional groups.

different from systemic estrogen, which leads to several-fold increases in blood levels of estradiol, estrone, or both. There is no evidence of any increased risk of thrombosis or other adverse events such as heart attack, stroke, breast cancer, or dementia, and strong reason to believe otherwise. Studies looking specifically at low-dose vaginal estrogen in terms of breast cancer and other risks have been negative. So we believe that the labeling for low-dose vaginal estrogen should be modified to reflect the evidence."

The levels are so low that the American College of Obstetricians and Gynecologists published a committee opinion in March "endorsing the use of these products in breast cancer survivors if they are unresponsive to nonhormonal over-the-counter lubricants and moisturizers," says Kagan, who is also involved in the effort to change the labeling. The effort has been ongoing for nearly three years with a petition with more than 600 signatures, with no word from the FDA on any impending decisions.

MORE FALLOUT FROM THE WHI

Kagan believes that she and other clinicians are seeing more of the condition because the initial findings of the Women's Health Initiative in 2002 scared many women and physicians away from menopausal hormone therapy. Fewer women are using hormone therapy, and when they do it is for shorter periods at lower doses. "I have women who are in their late 50s, who have vaginas that look like they are 70 or 80 years old," Kagan says.

The problem with the lack of treatment is that unlike hot flashes, which resolve over time, GSM is "a chronic and progressive disorder that if left untreated will only get worse," Kagan says.

CURRENT TREATMENT OPTIONS

For some women, coping with mild symptoms using moisturizers or lubricants may be enough.

But others may need more help — and if the body is breaking down from a lack of hormones, replacing them is not that difficult. "No product works better than estrogen to re-estrogenize the vagina," says Ginger Constantine, MD, president and CEO of EndoRheum Consultants in Malvern, Pa. There are also estrogen receptors in the bladder and the urethra, so conditions such as urgency frequency syndrome also respond to local vaginal estrogen.

There are several effective products on the market: creams that deliver 17β-estradiol (Estrace), conjugated estrogens (Premarin), and estrone (Eastagyn, which is available in Canada, but not the U.S.); a vaginal ring (Estring) that delivers a low dose of 17β-estradiol every day for 90 days; and a suppository tablet (Vagifem) that delivers estradiol.

There is also a vaginal ring (Femring) that delivers a systemic dose of estradiol acetate, and should not be confused with low-dose formulations. Because of the systemic dose, it is approved for the vasomotor symptoms of menopause.

> **Women may just not be comfortable talking** about the fact that sexual activities are painful for them. People are often embarrassed to bring up subjects like that."
>
> — JOANN MANSON, MD, DRPH, PROFESSOR, HARVARD MEDICAL SCHOOL; CHIEF, DIVISION OF PREVENTIVE MEDICINE, BRIGHAM AND WOMEN'S HOSPITAL, BOSTON

An oral tablet, ospemifene (Osphena), is a selective estrogen receptor modulator that has shown efficacy with GSM.

Kagan says that patients ask her which product she recommends, but she does not recommend one over the other because "each woman is different." Some women are comfortable using the ring because they put it in and forget it for three months, but others need to come in to have her nurse practitioner take it out. Women who use creams need to apply them a couple of times a week — and be consistent about the dose.

TREATMENT ON THE HORIZON

Other treatments on the horizon include Prasterone, a suppository capsule containing DHEA that manufacturer EndoCeutics has submitted to the FDA for approval. A decision could come as early as the end of the year.

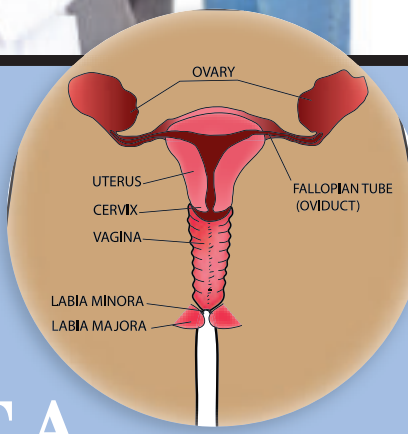
TX-004HR is a vaginal softgel capsule containing 17β-estradiol that has shown promising results in clinical trials. The manufacturer, TherapueticsMD, has submitted a new drug application for TX-004HR to the FDA.

"There still is a lack of recognition of the condition," Constantine says. "If patients realize that these new products have very low doses without systemic absorption, there may be greater acceptability. It may be that the current lack of use of a prescription product is in part because there just is not a product that meets a woman's needs. Maybe some of these newer products will meet that need."

"The obligation is upon physicians to ask postmenopausal women whether they are having these symptoms," Kagan says. The diagnosis itself is not difficult. "You often can make a diagnosis even by listening, although you definitely need to do an exam because there is a differential diagnosis. There are other skin conditions or infections that a patient may have."

But the key to improving postmenopausal quality of life for many women could turn on raising awareness among both women and clinicians of the treatable nature of the condition — and to understand the difference between systemic and local estrogen. EN

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT THE EFFECTS OF DIABETES ON BONE HEALTH IN THE NOVEMBER ISSUE.



AT A GLANCE

- **About half of postmenopausal women will experience genitourinary symptoms such as pain with intercourse and frequent urinary tract infections, but few will receive appropriate treatment.**
- **Warnings on FDA-approved labeling are frightening women away from using effective treatments, even though the evidence does not support the warnings.**
- **Treatments that deliver local, low-dose estrogen and similar products are safe and effective, and do not raise estrogen and estradiol blood levels above the normal postmenopausal range.**

2016: A Progress REPORT

BY DEREK BAGLEY

Endocrine science has been at the forefront of research and treatment for a variety of endocrine disorders. The result is a wide array of therapies, products, and more that came to market in 2016, which *Endocrine News* has compiled here.

This past year was the 100th year of the Endocrine Society and it was not without some exciting breakthroughs, from new devices approved to monitor insulin levels and lifestyle habits in patients with diabetes to promising results in drug trials that could lead to even bigger developments in 2017. Here are a few of the devices, studies, and drugs that made waves in 2016.

> **People with diabetes can often feel embarrassment or discomfort when they need to inject insulin at mealtimes or when snacking. Because patients in the study were empowered to dose discreetly with the OneTouch Via™, they felt encouraged to dose more often – and ultimately, they reported missing fewer doses and better adherence to their treatment regimen."**

The OneTouch Via™ Insulin Delivery

Diabetes Drugs that Reduce CVD Complications, Mortality

The Cleveland Clinic included these drugs – namely empaglifozin and liraglutide – in its top 10 medical innovations for 2017. One of these big announcements at the American Diabetes Association's annual meeting this past year was the results of the LEADER trial, which showed that "In the time-to-event analysis, the rate of the first occurrence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke among patients with type 2 diabetes mellitus was lower with liraglutide than with placebo." The results were published in the *New England Journal of Medicine.*

The OneTouch Via™ Insulin Delivery System

Calibra Medical, Inc., one of the Johnson & Johnson Diabetes Care Companies, presented research at this past year's American Diabetes Association's annual meeting, showing patients who used their OneTouch™ Via — a wearable, on-demand insulin delivery system in development that allows patients to discreetly deliver rapid-acting, or bolus, insulin at mealtimes — missed fewer doses and felt less stress about dosing.

"People with diabetes can often feel embarrassment or discomfort when they need to inject insulin at mealtimes or when snacking. In a social situation, they may choose to miss a dose so they don't have to take themselves out of the moment, but avoiding needed insulin doses may lead to serious health complications over time," says Brian Levy, chief medical officer of Lifescan, Inc. "Because patients in the study were empowered to dose discreetly with the OneTouch Via™, they felt encouraged to dose more often — and ultimately, they reported missing fewer doses and better adherence to their treatment regimen."

A Market Acceptance Evaluation (MAE) study followed 44 patients with a median age of 57 years, who used the OneTouch Via™ patch for 60 days, instead of their bolus injection device (75% pen users and 25% syringe and vial users). Patients responded to insulin usage questionnaires at baseline, then after one, four, and eight weeks. By weeks four to eight, more than half (58% and 52%, respectively) of study participants acknowledged dosing more often than they would with a pen or syringe — with satisfaction rates increasing the longer they used OneTouch Via™. Furthermore, 98% of patients said the patch let them dose discreetly in public, with 88% noting they worried less about forgetting insulin – creating a less stressful disease management experience.

The healthcare professionals who assisted with the study noted that they preferred the OneTouch Via™ over both insulin pens and syringes (75% and 100%, respectively) and would be likely to recommend it to their patients. The doctors also reported that they would start patients on mealtime insulin earlier because of the ease of use of the OneTouch Via™ patch.

Medtronic's MiniMed® 670G System

The U.S. Food and Drug Administration (FDA) this past year approved Medtronic's MiniMed® 670G system, the first Hybrid Closed Loop insulin delivery system in the world.

"This significant milestone represents an important step forward in the management of type 1 diabetes and will improve the quality of life for those living with this chronic disease," says Derek Rapp, president and CEO of JDRF. "We are very encouraged by the speed in which this groundbreaking technology was approved by the FDA, and we are proud of the role JDRF played in achieving this exciting breakthrough. Medtronic and JDRF are committed to ensuring appropriate patient access to this therapy."

"The FDA approval of the world's first hybrid closed loop system is a culmination of many years of hard work and close collaboration with the clinical and patient communities to generate the body of evidence needed to advance this technology for those living with diabetes," says Francine Kaufman, MD, chief medical officer of the Diabetes Group at Medtronic. "We appreciate the unprecedented speed by which the agency approved our PMA submission to help bring this advanced insulin pump therapy so quickly to U.S. patients living with this challenging disease. We are committed to preparing for commercial launch as quickly as possible while ensuring we provide the most successful rollout of this novel therapy."

The system is approved for the treatment of people with type 1 diabetes 14 years of age and older with ongoing studies to expand the indication to additional patient populations.

Medtronic's Partnership with IBM Watson Health

This year, Medtronic, along with its strategic technology partner IBM Watson Health, advanced to the final development stages and revealed the name of a first-of-its-kind cognitive app - SugarWise(TM) with Watson. Relating to a key diabetes concern (sugar) and the intelligence it hopes to deliver (wise), the Medtronic app is designed to assist people in making daily diabetes management easier and potentially more effective.

The first generation of the Medtronic SugarWise app is expected to predict important patterns and trends - based on retrospective analysis of patients' insulin, CGM, and nutritional data - to help people understand how their behavior affects their glucose level in real time. In addition to further advance the capabilities of future generations of the SugarWise app, the companies have revealed new results on hypoglycemia prediction using CareLink data from 10,000 anonymized patients which demonstrated preliminary prediction accuracy of 75% to 86% within a two-to-four-hour window.

Huzefa Neemuchwala, senior director for the Data and Informatics Innovation at Medtronic, explains that he hears from endocrinologists that they can only spend time with their patients for about 1% of their lives, and the other 99% of the time, these patients are "on their own." This new app is a way for clinicians to interact with their patients on a daily basis. "For the endocrinologist," Neemuchwala says, "there is help on the way."

Abbott's FreeStyle Libre Pro System

The FDA approved Abbott's FreeStyle Libre Pro system, a CGM system for healthcare professionals to use with their patients with diabetes.

Eugene E. Wright, Jr., MD, of Duke Southern Regional Area Health Education Center in Fayetteville, N.C., says he finds it challenging to effectively treat his patients with diabetes when it comes to decisions around insulin, nutrition, and medication. "My patients are often out of range, due to inconsistent self-monitoring and insufficient data from traditional glucose meters that are unable to provide a full view of their glucose levels."

"FreeStyle Libre Pro transforms how doctors assess their patients' diabetes," says Jared Watkin, senior vice president, Diabetes Care, Abbott. "This novel technology provides a solution to the ongoing challenge of the need for complete and dependable glucose data. This data is imperative for not only the doctor, but also for the patient to help them achieve optimal health."

MannKind's Promising Results on Affreza, a Rapid-Acting Inhalable Insulin

MannKind Corporation's Afrezza, a rapid-acting inhalable insulin that has demonstrated a faster onset of action and a shorter duration than injectable human insulin in patients with diabetes, helps diabetes patients strike a balance of glucose control while minimizing the risk for hypoglycemic events.

"Afrezza is a rapidly absorbed insulin that happens to be given through inhalation," says Robert A. Baughman, PharmD, PhD, senior vice president of clinical sciences for MannKind Corporation. "It's unique because it's inhaled but also because of whatever pharmacokinetic mechanisms it triggers, it's the fastest."

Baughman and his team conducted a randomized, controlled, six-treatment, six-sequence, six-period crossover dose-response study of three single doses of Afrezza inhalation powder and three single doses of subcutaneous (SC) insulin lispro in patients with type 1 diabetes using the euglycemic clamp technique. They found that Afrezza had a faster onset of action and shorter duration than the SC insulin, meaning patients could take a second dose of Afrezza if needed.

"This is a unique insulin," Baughman says. "Its rapid absorption has a real benefit, its short duration of action has a real benefit, and so if they can find a way to use that with a long-acting insulin, then they can do a much better job controlling it."

Cholestosome™ Oral Insulin Delivery

Another product designed to remove the pain of injecting insulin, this one is still in animal testing. To pack the most insulin into Cholestosome, the researchers at Niagara University conducting these studies determined the optimal pH and ionic strength of the drug-containing solution. They then moved the most promising candidates on to animal testing. Studies with rats demonstrated that certain formulations of Cholestosome loaded with insulin have high bioavailability, which means the vesicles travel into the bloodstream where the insulin needs to be.

Next, the team plans to further optimize the formulations, conduct more animal testing and develop new partnerships to move forward into human trials. They also say Cholestosome may be applicable for delivery of other medications.

Veracyte's Afirma Gene Expression Classifer

At the American Thyroid Association's annual meeting in Denver, Colo., in September, Veracyte scientists presented new data suggesting the potential to enhance the performance of the Afirma Gene Expression Classifier in thyroid cancer diagnosis by combining the test's proven RNA expression-based capabilities with gene variant and fusion information - all on a single, robust RNA sequencing platform. Such enhancements could help to further reduce the number of patients who undergo unnecessary surgery when their thyroid nodules are not clearly benign or cancerous (i.e., indeterminate) following routine cytopathology evaluation.

In the study, company researchers used RNA from 88 thyroid nodule patient samples for which a surgical pathology diagnosis was known to train (with 58 samples) and test (with 30 samples) an enhanced version of the Afirma GEC. Using advanced machine-learning techniques, Veracyte leveraged an RNA sequencing platform to combine the genomic test's RNA gene expression-based algorithm with gene variant and fusion information. The result was an enriched classifier that yielded an overall area under curve (AUC) of 0.88, with a sensitivity of 93% and a specificity of 80%.

"Numerous efforts have been made to diagnose indeterminate thyroid nodules using cancer-associated DNA mutation and fusion information.

Veracyte's Afrirma
Gene Expression Classifer

"Using a powerful machine-learning approach, RNA expression and gene variant and fusion information can be combined into one molecular test that is run on a single RNA-sequencing platform to provide clinically useful information. Ultimately, this should help more thyroid nodule patients avoid unnecessary surgery."

However, research is increasingly showing the limitations of this approach in clinical practice because such gene alterations are found in both cancerous and benign patients," says Giulia C. Kennedy, PhD, Veracyte's chief scientific officer, who presented the new data. "We believe that our study is the first to show that, using a powerful machine-learning approach, RNA expression and gene variant and fusion information can be combined into one molecular test that is run on a single RNA-sequencing platform to provide clinically useful information. Ultimately, this should help more thyroid nodule patients avoid unnecessary surgery. Efforts are already underway to apply this approach to a larger study cohort."

Medtronic's Enlite Sensor for Use with the iPro2 Professional Continuous Glucose Monitoring

The FDA announced approval of Medtronic's Enlite sensor for use with iPro2 Professional CGM system. The Enlite sensor is a disposable glucose sensor that can be worn up to six days and provides better comfort.

Like a holter monitor for cardiovascular care, the iPro2 Professional CGM system records a patient's glucose levels 24 hours a day for up to six days. Used intermittently, the iPro2 system provides physicians with insights into how the nutrition plan, medication regimen and daily activities affect glucose levels of people with diabetes, enabling them to know more about their patients' glucose profile in less time and helping them to make more informed decisions regarding diabetes management. Sharing advanced insights enables patients to understand the relationship between their glucose levels and lifestyle choices. In addition, the iPro2 system delivers decision support for diabetes care providers through an algorithm-based, one-page Pattern Snapshot report that enhances their ability to quickly identify and address key problem areas.

"Both physicians and people with diabetes need easy-to-use systems which can provide actionable information. The new Enlite sensor is easy to insert and comfortable to wear. Having six days of patient data permits robust pattern analysis for more accurate decision support," says Robert Vigersky, MD, medical director, Non-Intensive Diabetes Therapies at Medtronic. "With the insights and reports provided through professional CGM, patients can be shown the factors that are driving glucose fluctuations, so together with their doctor they can develop a plan to improve glucose control."

The Ava Bracelet

The Ava bracelet is the first fertility-tracking device to identify the fertile days during a woman's cycle in real time. An FDA-approved Class One medical device, the Ava bracelet was proven in a recently concluded clinical study at the University Hospital of Zurich to detect an average of 5.3 fertile days per cycle with 89% accuracy. The year-long study was conducted under the leadership of Prof. Brigitte Leeners, a world-renowned expert on the mathematical modeling of menstrual cycles.

"Women spend so much time and emotional energy trying to accurately track their cycles, often using multiple methods in tandem," says Leeners. "Timing intercourse around ovulation is critical for conceiving, but the current options for doing so are inadequate. We're long overdue for a device like Ava that detects the fertile window precisely and easily."

Each night, Ava's sensors collect three million data points around physiological parameters including pulse rate, breathing rate, sleep quality, heart rate variability, temperature, and more that correlate with the rise in reproductive hormones estradiol and progesterone. With this information, Ava detects a woman's entire fertile window.

"After a lifetime spent trying to avoid pregnancy, couples who begin trying to conceive often don't realize how difficult it can be to get pregnant. For most women, there are only about six days per month where there is any possibility of conceiving, and only three days per month where it is likely," says Ava Science CEO and co-founder, Lea von Bidder. "Even under the most favorable conditions — a young, healthy couple having frequent unprotected intercourse — there is only about a 25% chance of getting pregnant in a given month."

The RESECTR for Uterine Polyp Removal

Keith Isaacson, MD, a gynecology and reproductive endocrinology surgeon at Newton-Wellesley Hospital in Newton, Mass., this past year became the first physician in the world to use a new tissue resection device to successfully remove a uterine polyp.

"We need safe, accurate, and effective medical devices to perform uterine polyp resection," says Isaacson. "The RESECTR is a simple manual surgical instrument that allowed me to target and efficiently remove the polyp during this procedure. It provides a benefit to patients in that the entire polyp can

EDITOR'S NOTE: INCLUSION IN THIS ARTICLE DOES NOT DENOTE A RECOMMENDATION OR AN ENDORSEMENT BY *ENDOCRINE NEWS* OR THE ENDOCRINE SOCIETY. THIS IS SIMPLY TO SERVE AS AN OVERVIEW OF SOME OF THE BREAKTHROUGHS IN TREATMENT METHODS, PRODUCTS, AND THERAPIES THROUGHOUT 2016.

> **We want everyone with diabetes worldwide to become more engaged in their diabetes management, eat the right foods, take their medications, and lower their blood glucose levels. Now, with One Drop | Mobile on Android, they can."**

be removed under direct visualization in a very short period of time without the risk of bleeding or uterine perforation."

Electromechanical tissue resection systems typically involve complex capital equipment to power rotating blades inside a long cannula. These cutting blades are attached to expensive disposable hand-pieces that often result in reduced physician control and feel for the procedure.

Clinicians control RESECTR positioning, tissue aspiration, and cutting with one hand. Proprietary RESECTR cutting blades spin clockwise and counterclockwise each time the physician squeezes the device handle allowing them a new level of control and feel during actuation.

Dynavax's Promising Results for Its HEPLISAV-B

Dynavax Technologies Corporation announced preliminary results from a Phase 3 trial demonstrating that HEPLISAV-B [Hepatitis B Vaccine, Recombinant (Adjuvanted)] provided a significantly higher rate of seroprotection than Engerix-B®, an approved hepatitis B vaccine, in adults with type 2 diabetes.

The Phase 3 trial, HBV-23, was a randomized, observer-blinded, active-controlled, multi-center study that compared two doses of HEPLISAV-B with three doses of Engerix-B in adults age 18-70. Among the over 8,000 randomized participants, there were 1,144 adults with type 2 diabetes of whom two-thirds had diabetes for five years or more. Demographics consisting of age, sex, and race were generally similar between the two treatment arms.

Results showed that HEPLISAV-B provided seroprotection in 90.0% of participants with diabetes compared with 65.1% for Engerix-B – a statistically significant difference of 24.9%. Larger differences were observed in participants age 60-70, with HEPLISAV-B demonstrating an 85.8% rate of seroprotection compared with 58.5% for Engerix-B. For participants with a body mass index greater than or equal to 30, HEPLISAV-B demonstrated an 89.5% rate of seroprotection compared to 61.4% for Engerix-B.

In the total trial population, the rates of adverse events, serious adverse events, and deaths were similar between the HEPLISAV-B and Engerix-B groups. All adverse events considered to represent potential immune-mediated disorders were reviewed by an independent, blinded Safety Evaluation and Adjudication Committee, which classified these events as not related to vaccination.

Pfizer's SOMAVERT Treatment for Acromegaly

SOMAVERT is designed to specifically block the effects of excess growth hormone in acromegaly. This new preparation offers the same formulation and dosing options as before, with a simplified preparation using a prefilled syringe.

The 10-mg, 15-mg, 20-mg, 25-mg, and 30-mg vials of SOMAVERT are available to provide patients with a wide range of dosing options. This treatment is designed for patients whose acromegaly wasn't controlled with surgery or radiation.

The At Home™ Viniferamine® Diabetic Skin Care Kit

Created by D. Elizabeth McCord, PhD, FAPWCA, The At Home™ Viniferamine® Diabetic Skin Care Kit was designed to improve the quality of skin care for diabetes patients at home.

The Diabetic Skin Care Kit and other kits were designed by McCord to facilitate transitions between hospital care and home care. These hospital-grade skin care products have been improving patient skin care for millions in care facilities and they are now available and accessible to individuals with diabetes for use at home.

One Drop | Mobile, Now for Android

An award-winning diabetes management solution delivered entirely via mobile app, available on iOS since April 2015, One Drop | Mobile was announced this past year for Android users. Since launch, One Drop | Mobile users from over 190 countries worldwide have logged over 1,500,000 user sessions and contributed over 85,000,000 health-related data points. Together, the One Drop community's data is being used to provide meaningful data-driven health insights to all people with diabetes.

"We want to bring the same simple, gorgeous, useful, data-driven experience that we deliver to iOS users to everyone on the Android platform. We want everyone with diabetes worldwide to become more engaged in their diabetes management, eat the right foods, take their medications, and lower their blood glucose levels," says Jeff Dachis, Founder and CEO of One Drop. "Now, with One Drop | Mobile on Android, they can." EN

The 11 Best Apps for Laboratory Research

You might have made hotel reservations or downloaded music from your smart phone or tablet, but now you even have the ability to conduct your research from the palm of your hand.

BY MELISSA MAPES

The mobile era has arrived — smart phones and tablets have taken over many day-to-day activities, from ordering takeout to scanning digital boarding passes at the airport. So why not leverage these tools to make lab research easier as well?

Plenty of medical research apps have flooded the market over the past six years or so, but not all have delivered on promised functionality, making some scientists wary of their worth. However, a handful of mobile apps have risen in popularity and demonstrated practical benefits for lab work. Based on user ratings and recommendations from real researchers, here are the top 11 smart device programs for scientific lab work.

Cell Imaging HD

For projects involving fluorescence microscopy, this app allows researchers to locate and visualize reagents, fluorescent dyes, and protocols. It's specifically designed for research involving cell biology and syncs with nearly all major microscope systems.

CloningBench

From finding the right competent cell to identifying the best Anza restriction enzyme, CloningBench offers tools to help guide important decisions in cloning research. Its features include a molar quantities calculator, gene size estimator, bacterial growth timer, and more.

PCalc

PCalc is one of the highest-rated scientific apps in the mobile sphere. Whether you're an engineer or endocrinologist, this app's extensive toolkit of unit conversions and notation features — amid a long list of other calculating abilities — will replace those Texas Instruments dinosaurs in no time. There's also an Apple Watch version for those who like to crunch numbers on their wrist.

Hivebench

As all researchers know, the lab notebook is the magnum opus of every experiment. It has to be detailed, organized, and precise for a study to be successful. Hivebench seeks to replace the paper notebooks of yesteryear with a mobile version that allows you to securely collaborate with your team and increase efficiency.

Evernote

Similarly, Evernote is widely used by professionals across a wide range of fields, from business to politics to science, to take notes and stay organized. Unlike Hivebench, it was not designed with lab research specifically in mind. However, it is simple to use and available across multiple devices.

Fluorescence SpectraViewer

Fluorescence SpectraViewer is the mobile extension of ThermoFisher's online tool for plotting and comparing spectra. It translates configurations into a simple, printable format that can be shared via email. Researchers can compare up to five emission and five excitation filters per plot on this mobile interface.

JuiceSSH

This "secure shell" client allows researchers to remotely monitor and control systems from a mobile terminal window. It can start and stop automated laboratory tasks from anywhere, and is especially useful for checking in on big computational projects like genome assemblies. Researchers are also able to make emergency interventions faster — saving countless hours of "clean up" time.

PubChase

The PubChase app keeps the latest in biomedical publications at your fingertips. Users can search the entire database of literature, in addition to receiving customized recommendations and saving articles to read later. It's PubMed on your smartphone, anytime you want to use it.

BioGene

BioGene is a quick reference tool for looking up the genes frequently used in medical research. From zebrafish to yeast, scientists can get the pertinent details about the genes appearing in relevant publications — a great complement to literature apps like PubChase and Docphin.

Docphin

Awarded "Best App for Doctors" and "Best App for Medical News & Journals" by Apple Inc. in 2015, Docphin is a robust app for tracking and organizing the latest publications in specific topic areas. It's easy to create alerts for specialties and diseases, and the app will send you an individualized email every week with an overview of the hottest new studies in your field. With the ability to subscribe to your preferred journals and share collections of articles with peers, users can curate the most interesting literature and help keep colleagues up-to-date.

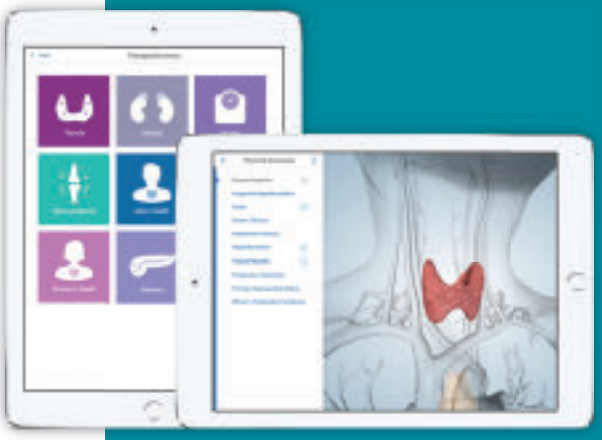
ResearchKit

Rather than a singular app, Apple's ResearchKit is an open source platform that allows scientists to build customized mobile applications for their studies. It doesn't calculate unit conversions or provide publications; the purpose is actually gathering participant data. Researchers can track and monitor participants through their iPhones, making it much easier to recruit and enroll eligible individuals. Currently, the platform has been used to develop apps for studies related to postpartum depression, diabetes, and much more.

New applications for science are coming out all the time, so it is a good idea to keep an eye on the iTunes and Android app stores for emerging tools that might save time, increase accuracy, and add to your knowledge base, all right from your smart device. There is little to lose by trying out these technologies, especially because many of them are free or very low cost.

If the trend continues, researchers could find their work lives substantially enhanced, both in terms of efficiency and the ability to run experiments remotely. What if you could control all the systems of your study from an iPhone? And collect participant data with a fraction of the in-person hospital visits? Undoubtedly, mobile apps for medical research have the potential to be life-changing for scientists and patients alike. EN

MAPES IS A WASHINGTON, D.C.–BASED FREELANCE WRITER AND A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS*. SHE WROTE ABOUT THE IMPACT OF WEARABLES ON PATIENT TREATMENT IN THE NOVEMBER ISSUE.



EMPOWERING PATIENTS WITH APPS

As all clinicians know, educating patients is key to successful, sustainable care. That's why the Endocrine Society launched the Hormone Health Network's "Journey through the Endocrine System" app. This interactive tool teaches users about the essential elements of the human endocrine system to help them better understand the complex processes of their bodies. With 3D visualizations and fly-through animation, patients get an inside-out look at organs, glands, and endocrine disease states and conditions.

The app includes links to further resources on hormone.org, and can be downloaded via the iTunes store: https://itunes.apple.com/us/app/endocrine-societys-hormone/id1086807348?mt=8

AMA Considers Policies Impacting Endocrinology

The American Medical Association (AMA) recently held its interim meeting of the House of Delegates (HOD), which is the policy-making body of the AMA. The Society's delegates — Vineeth Mohan, MD, Amanda Bell, MD, Palak Choksi, MD, and Robert Vigersky, MD — represented the interests of endocrinologists in the debates surrounding issues that impact the practice of medicine. Discussion of new AMA policy included a range of issues relevant to endocrinologists, including compounding hormone therapies, infertility benefits, and drug pricing. A resolution introduced by the American Association of Public Health Physicians and co-sponsored by the Society called on the AMA to support efforts to set a national goal to eliminate lead exposures in pregnant women and children by 2030 and ensure that no child has a blood lead level >1 µg/dL. It also offers policy changes to reduce lead exposure and remediate current and potential new sources of lead exposure. The resolution is based on the Project TENDR (Targeting Environmental Neuro-Developmental Risks) consensus statement, which the Society has endorsed. The Endocrine Society's delegates also worked closely with the delegates from the American Association of Clinical Endocrinologists, American Society for Reproductive Medicine, and American Association of Endocrine Surgeons during the meeting on issues of importance to endocrinologists.

Society Influences Policy to Improve Care of Chronic Diseases

The Endocrine Society is engaged with the U.S. Senate Finance Committee Working Group on Chronic Care, providing recommendations on policy changes aimed at improving the care of people with chronic conditions. The Working Group released a discussion draft of the Creating High Quality Results and Outcomes Necessary to Improve Chronic (CHRONIC) Care Act in October, proposing policy changes to promote better-coordinated care for seniors with multiple chronic health conditions and to empower doctors and patients to work together to improve the health of the whole person. We support many of the provisions that we believe would benefit patients, such as specific benefit design and supplemental benefits for Medicare Advantage plans, expanded access to telemedicine services, and ability for Medicare Advantage plans to offer incentives to beneficiaries who receive certain services. The discussion draft also calls for a study by the Government Accountability Office on obesity medications and medication synchronization programs. We expect that a final bill will be introduced before the end of the year. Additional information on the CHRONIC Care Act will be included in *Endocrine Insider.*

EVAN EL-AMIN / SHUTTERSTOCK.COM

What Do the U.S. Election Results Mean for the Endocrine Society?

What, specifically, do the U.S. election results mean for the Endocrine Society? It is too soon to tell, but what happens in the next few months will be crucial. We will play a role in sharing and advising the Trump transition team on our priorities. We will continue to advocate for endocrinology in Congress with old friends and new. We will continue to engage in partnerships to move our work forward and link to both seasoned and new leaders who care about our healthcare system and biomedical research. We will reach out to the contacts we have in the Trump transition team to learn more about their priorities, their plans, and how the Endocrine Society can play a role in the future.

What is becoming more clear is that there will be several important healthcare-related policy issues at the top of the new administration's and Congress' agenda. This will include: a repeal and replacement of President Obama's healthcare overhaul legislation; budget resolutions including funding legislation for the National Institutes of Health (NIH); children's health insurance legislation; child nutrition standards; and Food and Drug Administration (FDA) user fees. This is in addition to defense and security issues, immigration, tax reform, and several constitutional issues.

We will continue to share the information we are gathering about the new Congress and administration and we will keep members updated on what we are learning, doing, and planning for the future.

In the meantime, the Congress is back in Washington for a "lame duck" session to wrap up unfinished work from this year. We strongly encourage you to join our online advocacy campaign urging all senators and representatives to finish work on the 2017 budget (even those who were not re-elected or are retiring). If the Congress does not act soon, the NIH will not receive the $2 billion increase recommended by the Senate Appropriations Committee this summer and its funding will remain at the current level. If they don't do it now, the entire negotiating process starts all over again next year.

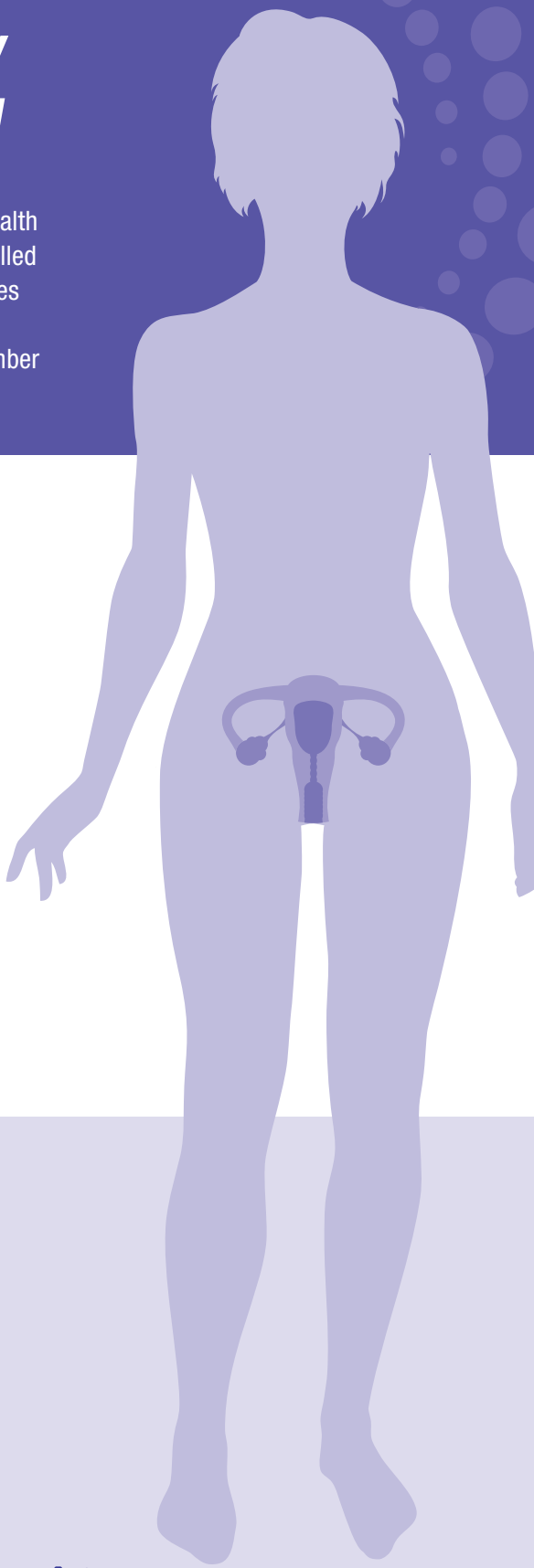
Simply visit **www.endocrine.org/advocacy** to send an email to Congress before December 9 and forward this message to your friends and family. It only takes a minute of your time, but will make a big difference in influencing elected officials.

Society Joins FDA Network of Experts

The Food and Drug Administration (FDA) has created a Network of Experts to provide information on issues under consideration by the FDA to supplement existing knowledge and expertise within the Centers. The Network of Experts is a vetted network of partner organizations and their member scientists and clinicians who can provide FDA staff with rapid access to expertise. The program is designed to broaden staff exposure to clinical and scientific viewpoints, but not to provide external policy advice or opinions. The Society has recently joined the Network, and as a member, we may reach out to you to serve in this capacity and ask for your engagement as we support the work of the FDA on endocrine topics. Interested participants will be asked to fill out a simple conflict of interest form, and, if selected, will be asked to participate on a brief conference call (20-60 minutes on average). Although we will reach out to members based on their self-identified areas of expertise, please contact Stephanie Kutler, director, Quality Improvement (skutler@endocrine.org) if you wish to be included in a standing list of experts or would like to update your areas of expertise on the membership application. EN

HORMONES AND VAGINAL ATROPHY
WHAT YOU NEED TO KNOW

The endocrine system is a network of glands and organs that produce, store, and secrete hormones. These hormones are very important for a woman's health especially during the years when she might become pregnant. Sometimes called "the change," menopause is the time, around age 50, when a woman's ovaries produce fewer hormones and she stops having a monthly period. Menopause takes place gradually over four or five years. A woman may experience a number of uncomfortable symptoms during this time, including vaginal dryness.



WHAT IS VAGINAL ATROPHY?

Vaginal atrophy, also called **VVA** or **vulvovaginal atrophy**, is a condition in which the lining of the vagina becomes thinner and drier. The updated term for this condition is genito-urinary syndrome of menopause (GSM). It can lead to a number of vaginal and urinary tract problems, especially for older women during and after menopause.

A drop in **estrogen**, a female sex hormone, causes the vagina to become dryer and more fragile. This is the leading cause of vaginal atrophy. A drop in estrogen levels may occur:

- During **perimenopause** (the years leading up to menopause)
- After **menopause**
- When breastfeeding
- When taking certain medications
- If you smoke
- After surgical removal of both ovaries
- After radiation therapy for ovarian or uterine cancer
- As a side effect of breast cancer treatment

SYMPTOMS

You may have no symptoms at all. Or you may have:

- Vaginal dryness, itching, or irritation
- Burning feelings in the vagina
- Discomfort or pain during sex
- Light bleeding after sex
- Burning sensation when you urinate
- Frequent or strong urges to urinate
- Urinary incontinence (the loss of bladder control)

Visit hormone.org for more information.

Additional Editing by JoAnn E. Manson, MD, PHD,
Harvard Medical School

Hormone Health NETWORK®
Keep your body in balance

Vaginal atrophy is not only a nuisance. It can cause vaginal and urinary tract infections. It can also have an adverse emotional effect on you and your sexual partner.

DID YOU KNOW?

Sexual activity is a very important part of overall health. The vaginal dryness often associated with vaginal atrophy usually becomes worse with a lack of sexual activity. Sex stimulates blood flow in the vagina and aids in the production of vaginal fluids. So, sex actually keeps the vagina lubricated and healthy.

About 50% of post-menopausal women experience vaginal atrophy symptoms, including irritation and dryness

Only about 7% seek treatment at the first sign of symptoms

1 in 4 women with vaginal atrophy report that it has a negative effect on other areas of their life, including sleep, sexual health, and general enjoyment

Source: National Center for Biotechnology Information

DIAGNOSIS

Vaginal atrophy is often unreported because women think it will just go away on its own. It usually will not and tends to be progressive. Therefore, if you think you may have vaginal atrophy, it's important to talk with your healthcare provider. He or she can diagnose it very quickly during your next pelvic exam. Remember, vaginal health is very important to your overall health!

TREATMENT

For many women, non-prescription (over-the-counter) treatments can help, especially if symptoms are mild. Your healthcare provider may recommend vaginal lubricants or vaginal moisturizers that you can use, especially during sexual activity.

Prescription treatments include low-dose estrogen therapies, including:

- Estrogen cream — placed in the vagina at bedtime
- Estrogen ring — a soft, flexible ring inserted into the vagina every 3 months
- Estrogen tablet — inserted into the vagina with a disposable applicator
- Systemic estrogen — also known as hormone therapy, available in a pill, patch, gel, or spray form
- An oral non-estrogen medication called ospemifene

Depending on the treatment, there may be health risks that you'll want to discuss with your healthcare provider.

4 QUESTIONS TO ASK YOUR DOCTOR

- Is my condition temporary or long-term?
- Are there non-prescription (over-the-counter) treatments that might help?
- What are some other ways to treat my condition?
- What are the risks and benefits of my treatment options?

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**.

The development of this resource was made from the generous support of our sponsor TherapeuticsMD.

Hormone Health NETWORK® FROM THE ENDOCRINE SOCIETY

Now in its 75th year and still the most cited endocrinology journal in the world.

"Endocrinologists publish in JCEM because of its reputation, its impact factor, and its large readership. In addition, I particularly like the format of the different types of articles, including special features and hot topics in translational endocrinology."

— Stephen Lafranchi, MD
Doernbecher Children's Hospital, Oregon Health & Science University

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