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Men's & Health & Testosterone

 New Endocrine Society guidelines detail why hypogonadism patients should be treated when consistently low T levels are tied to symptoms, not what the patient saw on television.

> A closer look at the T Trials shows that testosterone therapy may actually be suitable for older patients with hypogonadism.



ONCE A DAY:

New research may finally achieve the "male pill"

WHY ENDOCRINOLOGY?:

A newcomer's perspective from the bench



Hormone Science to Health

Endocrine

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Shining a Spotlight on Our Field

HEN WE GATHERED TO SHARE THE LATEST in scientific and clinical advances at ENDO 2018, word of these breakthroughs traveled far beyond the plenary rooms and poster hall. BBC News, *The Atlanta Journal-Constitution*, United Press International

wire service, *The Times of India*, *Forbes* and *Newsweek* magazines, *The Scientist*, and thousands of other news outlets broadcast our members' research to the far corners of the globe. Media outlets already have published and aired more than 3,000 news stories about our annual meeting, and the tally continues to grow.

As we seek to broaden understanding of our field among the public, policymakers, and other stakeholders, the media offers an avenue for the Society to position itself as a trusted advisor and advocate — a priority laid out in our fourth strategic plan (SP4). You can volunteer to serve as a

media spokesperson at **endocrine.org/getinvolved**. Through the press, we can communicate the impact of your work to millions of readers and viewers worldwide.

One example of our successful media outreach involves member Stephanie Page, MD, PhD, who presented results from the University of Washington and Los Angeles Biomedical Research Institute's male birth control trial during **ENDO 2018**. Annual Meeting Steering Committee members and

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Hone your communications skills by serving as one of our expert spokespeople. We want to hear from you at **www.endocrine.org/getinvolved**.

staff identified this study as newsworthy, and she discussed the work in a Society news release and at an **ENDO 2018** press conference. The Society's press promotion resulted in Page being interviewed by chief medical correspondent Jon LaPook on *CBS Evening News*, as well as coverage in top-tier

outlets including USA Today, TIME magazine, CNN, FOX News, and WebMD.

Our ENDO 2018 media outreach campaign also featured a poster presented by member Radwa Barakat, BVSC, MSc. Barakat and her colleagues at the University of Illinois at Urbana-Champaign studied how prenatal exposure to the endocrinedisrupting chemical DEHP, found in plastics, could impact fertility in male mice over the course of several generations. A reporter for Great Britain's leading news agency, the Press Association, interviewed her, and the resulting article appeared in

dozens of newspapers throughout the United Kingdom.

To raise awareness of the endocrinology field, our staff is continually reviewing the papers accepted to our journals and **ENDO** abstracts in search of headline-grabbing research. When we share groundbreaking studies in press releases and news conferences, top-tier media outlets take notice. You can see our successes whenever you open your Society e-newsletters. Positive media engagement leads to several benefits for our field, including increased support for scientific research and improved public health literacy.

Just as importantly, media interviews offer our members a chance to shine and advance in their careers. Presenting at one of our press conferences or serving as a spokesperson can add to your resume, and it provides an opportunity to

Presenting at one of our press conferences or serving as a spokesperson can add to your resume, and it provides an opportunity to improve your communication skills.



Stephanie Page discusses her team's research into a promising male birth control pill on the CBS Evening News with Jeff Glor.

improve your communication skills. Our members are passionate about their work, and that shows when they speak to journalists.

To learn more about our media relations program, you can check out our online newsroom or visit **www.endocrine. org/getinvolved** to volunteer to be a spokesperson. Be sure to submit your best work to our journals and to the Annual Meeting Steering Committee for **ENDO 2019**, and next year it could be you on the press conference stage.

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

BY THE NUMBERS

3,015 – News stories mentioning **ENDO 2018** published in March and April*

4.6 billion – Unique monthly visitors to digital media outlets that covered **ENDO 2018**

5.9 million – Print circulation and broadcast audiences of media outlets that covered **ENDO 2018**

40 – Society press releases distributed during the meeting

15 – **ENDO 2018** abstract authors who spoke at Society press conferences

5,653 – Journalists who viewed the press releases through the Newswise wire service

*Figures as of April 18



FROM THE EDITOR



In Pursuit of the Male Pill

E ACTLY TWO YEARS AGO IN ENDOCRINE NEWS WE PUBLISHED a story called "Hard to Swallow" by yours truly on the male birth control pill. At that time, it seemed like the elusive male pill was getting closer to reality based on new research. Now, thanks to a new study that was presented in Chicago during ENDO 2018 in March, science is even closer to making the once-a-day oral contraceptive for men a reality, and it apparently all comes down to a single molecule. In "Within Reach" on

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With this new breakthrough, it appears that one of the main problems with potential side effects has been alleviated via DMAU: "Oral methyltestosterone is hepatotoxic, but DMAU does not contain the methyl group associated with these liver effects," Seaborg writes.

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page 20, Eric Seaborg writes that a safety and efficacy study found that the promising molecule dimethandrolone undecanoate (DMAU) suppresses gonadotropins to concentrations that bring sperm production down to levels known to provide effective contraception without any significant side effects.

The study's co-lead author, Stephanie Page, MD, PhD, professor of medicine at the University of Washington in Seattle, understands quite well that progress is needed; as she said at her press conference in Chicago, "There have been no advancements in male contraception in 300 years." She was referring to the condom, one of only two birth control options available to Endocrine news

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men at the moment. The other, of course, is a vasectomy. In "Hard to Swallow" from 2016, Page lamented the obstacles to a male hormonal contraceptive and stated that there would likely be other types of male contraception created before the pill is a reality, including implant, injection, or a transdermal means such as a patch. "This is due to some of the challenges with oral testosterone delivery," she said in the article, "which include issues of serum half-life ... and some potential side effects."

With this new breakthrough, it appears that one of the main problems with potential side effects has been alleviated via DMAU: "Oral methyltestosterone is hepatotoxic, but DMAU does not contain the methyl group associated with these liver effects," Seaborg writes. "The other main problem has been that testosterone is metabolized so quickly that users would need to take several pills a day. The new formulation overcomes this problem with the addition of undecanoate, a long-chain fatty acid that slows clearance from the body enough to allow a once-a-day pill without damaging the liver or other organs."

The idea that a "once-a-day" male pill could be even closer to fruition caused something of a media firestorm this spring, with Page getting inundated by the media, even appearing on the *CBS Evening News* (see President's Viewpoint on page 4). Indeed, the new data on DMAU is an exciting new discovery. However, men need not queue up in front of the Target pharmacy counter just yet; Page says that even though the study results are a great step forward in developing a prototype of the male pill, "they raise the possibility of a male pill becoming a reality in the next five to 10 years, if the subsequent studies are as promising as we hope."

- Mark A. Newman, Editor, Endocrine News



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WHY ENDOCRINOLOGY?

A Newcomer's Perspective

BY MAIGEN M. BETHEA, DOCTORAL CANDIDATE, Hunter Lab, Graduate Biomedical Sciences, CMDB, University of Alabama at Birmingham, Department of Medicine, Division of Endocrinology, Diabetes & Metabolism, UAB Comprehensive Diabetes Center, Birmingham, Alabama

y first exposure to laboratory research was in the summer of my junior year at my undergraduate institution, Francis Marion University (FMU). My project challenged me intellectually, and despite many difficulties in optimizing experimental conditions, I did not let this factor deter me from learning how to conduct good science and reaching my research aims. I persevered through it, modifying conditions and learning how to improve my efficiency, until I achieved sound data.

It was through this experience in where I learned that science is not definitive, it is a continuum. All of the information I had learned, as well as the skills I had acquired during my undergraduate educational experience, set the basis for my momentum to pursue research diligently and with an open mind. The interconnectedness of all my previous science coursework — chemistry, physics, and cell biology — worked in a synergistic fashion to help me perform my experiments with clarity and vigor. It was very rewarding and fulfilling to utilize knowledge from varying disciplines to achieve my goal. My newfound passion in the lab also allowed me to see that science offered endless possibilities to learn; therefore, I decided to continue the experience of science exploration after graduation.

My journey led me to participate in a two-year NIH-NIGMS sponsored Post-Baccalaureate Research Education Program (PREP) at Wake Forest University to further cultivate the skills needed to enroll in a PhD program. My work at Wake solidified my sincere interest in biomedical research. Currently, I am pursing my doctoral degree in biomedical sciences along with my master's in public health at the University of Alabama at Birmingham. Obtaining these two degrees will give me a unique advantage in that I'll be able to address population-based health questions while using molecular, cellular, and biochemical approaches to solve them. Under the guidance of Chad Hunter, PhD, I was first introduced to the field of endocrinology. My thesis research project investigates transcription factors and co-regulators that govern genes critical to beta cell development and function that could lay the foundation for beta cell replacement therapies and/or novel drug targets for the treatment of diabetes. More specifically, my studies seek to determine the role of a LIM-homeodomain transcription factor named Lhx1 in pancreatic development and function.

Working in Dr. Hunter's lab has provided me with many opportunities to further advance my career as a budding researcher in the field of endocrinology. Since I've been in Dr. Hunter's lab, I've been able to become an active member within the Endocrine Society. In 2016, I was selected as a Future Leaders Advancing Research in Endocrinology (FLARE) fellow. Becoming a FLARE fellow has been a game changer for my career trajectory because it gave me an opportunity to serve the Society and network with experienced and renowned endocrine scientists. As a FLARE intern, I currently serve on the Society's Trainee and Career Development Core Committee (TCDCC). On this committee, I am able to help plan and organize

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

professional development activities for endocrine trainees such as the Early Career Forum (ECF). Additionally, I was able to attend **ENDO 2018** where my abstract was selected for an oral presentation.

My brief affair with this field has proven to be extremely rewarding as well as exciting. My ultimate goal is to work in academia where I can continue to conduct endocrine research. I would like to expose students to the vast

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My brief affair with this field has proven to be extremely rewarding as well as exciting. I would like to expose students to the vast possibilities within endocrinology, through academic mentorship, education, and research training. I know that I will be a great endocrine researcher, filled with passion to conduct impactful science while providing opportunities for future trainees.

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possibilities within endocrinology, through academic mentorship, education, and research training. I know that I will be a great endocrine researcher, filled with passion to conduct impactful science while providing opportunities for future trainees. So, when posed with the question "Why endocrinology," I ask, "Why not endocrinology?"

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

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INTOUCH



Wanda Johnson Named **Meeting Professional of the Year**

he Endocrine Society's chief program officer Wanda Johnson won the PCMA Education Foundation's Visionary Award honoring the Meeting Professional of the Year.

A veteran Society employee with more than 20 years' tenure, Johnson leads the Education, Science, and Professional Development Department. Her team is responsible for organizing ENDO, the Society's annual meeting and expo, as well as 25 other educational events each year. ENDO is the world's premier event where scientists and clinicians network and exchange information about groundbreaking advances in the endocrinology field.

"Wanda is passionate about continuous learning and strives to ensure our meetings and events are always the best they can be," says the Society's CEO, Barbara Byrd Keenan, FASAE, CAE. "Her pursuit of excellence spans her Endocrine Society career and is reflected in our award-winning and record-breaking signature events."

Johnson received her award at the PCMA Education Foundation's 2018 Professional Excellence Awards at the Marriott Marquis in Washington, D.C., in May. The Meeting Professional of the Year Award recognizes a PCMA member who exemplifies professional excellence in contributions to their organization, PCMA, and the business events community. With more than 7,000 members and an audience of more than 50,000 individuals, PCMA is the world's largest network of business events strategists.

"It is truly an honor to receive this recognition from my peers in the meetings and events industry," Johnson says. "I'm proud to play a role in organizing events where scientists and clinicians connect. Our work fosters innovation and fuels tomorrow's medical and scientific breakthroughs."

Johnson's work helps ensure that endocrinologists are supported

and valued throughout their careers. She manages the Society's initiatives to promote diversity and inclusion, and to nurture early-career professionals who represent the future of the field.

Johnson currently is leading the expansion of the Society's Clinical Endocrinology Update (CEU), a three-day meeting where experts share the latest advances in the diagnosis and treatment of hormone conditions with clinicians. Building on record attendance in 2017, the Society will hold CEU on both the East and West Coasts this fall for the added convenience of members.

Among her achievements, Johnson oversaw the Society's yearlong celebration of the organization's centennial in 2016. To commemorate 100 years of advances in endocrine science and clinical care, the Society held numerous events and developed a digital timeline highlighting the field's achievements.

Johnson has a bachelor of science degree from the University of Maryland University College in Paralegal Studies/Management Studies. She received her Certified Meeting Professional designation in 1995 and her Certified Association Executive designation in 2009. She was named a fellow of the Alliance for Continuing Education in the Health Professions in 2012.

How Was YOUR CEU Experience? Endocrine News is planning a special issue this summer devoted to CEU and we want to hear from you!

Why did you go? How many times have you been? What was your favorite part? Do you want to share any memorable experiences? Let the editor know about your CEU experiences and email him at: mnewman@endocrine.org.

EBB/CEU



REGISTER

Members in the News:

Gerald I. Shulman Receives ADA's Highest Honor



PhD, is the recipient of the American Diabetes Association's (ADA's) 2018 Banting Medal for Scientific Achievement, the ADA's highest honor.

The Banting Medal recognizes significant, long-term contributions to the understanding, treatment, or prevention of diabetes. Shulman will be recognized with this honor during the ADA's 78th Scientific Sessions, June 22–26, 2018, at the Orange County Convention Center in Orlando, Florida, and will deliver his Banting Medal Lecture, titled "Mechanisms of Insulin Resistance: Implications for Obesity, Lipodystrophy, and Type 2 Diabetes," on Sunday, June 24.

Currently, the George R. Cowgill Professor of Medicine and Cellular and Molecular Physiology at Yale University School of Medicine and co-director of the Yale Diabetes Research Center, Shulman is a Howard Hughes Medical Institute Investigator. He is renowned for his transformative studies examining the molecular mechanisms of insulin resistance in humans, and his work has been vastly important to our knowledge of the origination and development of type 2 diabetes.

Shulman has developed and implemented novel tools to identify the underpinnings of human metabolic physiology, leading to cutting-edge discoveries that have challenged the status quo and stimulated new directions in the field of diabetes research. His groundbreaking application of magnetic resonance spectroscopy made it possible to directly examine intracellular glucose and lipid metabolism in humans, thus providing a dynamic view of intracellular metabolism for the first time. Using this approach, he found that defects in insulin-stimulated muscle glycogen synthesis, due to defects in glucose transport activity, were the major factors responsible for muscle insulin resistance in individuals with type 2 diabetes and prediabetes.



National Institute of Diabetes and Digestive and Kidney Diseases

Attention Endocrine Scientists: NIDDK Seeks New Director

hat better way for the importance of endocrine science and research to have a place at the table than having an endocrine scientist as the new director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) at the National Institutes of Health (NIH)?

The NIDDK is seeking an exceptional investigator with a record of accomplishment in research and research administration to serve as the director, Division of Diabetes, Endocrinology, and Metabolic Diseases. The Division of Diabetes, Endocrinology, and Metabolic Diseases (DEM) provides research funding and support for basic and clinical research in the areas of type 1 and type 2 diabetes and other metabolic disorders, including cystic fibrosis; endocrinology and endocrine disorders; obesity, neuroendocrinology, and energy balance; and development, metabolism, and basic biology of liver, fat, and endocrine tissues. DEM also provides funding for the training and career development of individuals committed to academic and clinical research careers in these areas. The director is the leader of one of the four extramural divisions in NIDDK. The division, that is mandated by the authorizing legislation which created NIDDK, is responsible for maintaining a research program in diabetes, endocrinology, and metabolic diseases.

QUALIFICATIONS REQUIRED:

The qualifications of the director include an MD degree or equivalent, national recognition for leadership in diabetes, endocrinology, and metabolic diseases research, and significant management experience. *Sub specialization in endocrinology is desirable*, but candidates with other training and substantial research accomplishments relevant to diabetes and endocrine and metabolic diseases will be considered.

SALARY/BENEFITS:

The salary for this position is commensurate with qualifications and professional experience. A full civil Service benefits package is available, which includes retirement, thrift savings plan participation (401K equivalent), health, life and long-term care insurance.

HOW TO APPLY:

NIDDK will be accepting applications from May 15, 2018, to June 15, 2018. Please submit a CV and cover letter, to including a vision statement and qualifications for the position, to Camila Torrella at **torrellacm@mail.nih.gov**. For any questions about the position or the application process, please contact Camila Torrella (**torrellacm@mail.nih.gov** or 301-594-7772).

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BY DEREK BAGLEY Senior Editor



The authors of the review also detail some behaviors that explain the connections between chronodisruption (chronic desynchronization of 24-hour rhythms), such as how meal timing can affect weight gain.

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Understanding Circadian Clock May Be Key to Combating Obesity

nderstanding how the circadian clock, as well as key clock proteins, affect the formation and accumulation of adipose tissue could be another front in the battle against obesity, according to a paper recently published in *Endocrine Reviews*.

The review, by Oren Froy, of the Hebrew University of Jerusalem in Rehovot, Israel, and Marta Garaulet, of the University of Murcia, Spain, points out that obesity is a major risk factor for many illnesses, and that obesity - excess fat accumulation in white adipose tissue - has been related to irregular sleep/wake cycles. The central circadian clock is confined to the suprachiasmatic nuclei (SCN) in the anterior hypothalamus, but clock genes that are found in peripheral tissues like the liver and adipose tissue mediate activity of nuclear receptors, enzymes, hormones, and transporters involved in carbohydrate, lipid, and protein metabolism. "Knockouts or mutations in clock genes that lead to disruption of cellular rhythmicity have provided evidence to the tight link between the circadian clock and metabolism," the authors write.

Animal studies have shown that mice with mutated clock genes are obese and develop a metabolic syndrome of hyperleptinemia, hyperlipidemia, hepatic steatosis, and hyperglycemia; mice with deleted *Bmal1* genes were obese, and *Bmal1* deletion led to changes in the expression of hypothalamic neuropeptides that regulate appetite; circadian changes in hepatic Cry1/2 expression led to mice being more vulnerable to high-fat diet-induced obesity that correlated with increased insulin secretion. "Consistent with these findings, genetic polymorphisms in human clock genes have been associated with metabolic alteration," the authors write.

The authors of the review also detail some behaviors that explain the connections between chronodisruption (chronic desynchronization of 24-hour rhythms), such as how meal timing can affect weight gain. Mouse studies showed that changing feeding time led to an increase in weight gain, and in humans, unusual eating times disrupt the circadian system, which can produce adverse health effects. The authors write that the timing of food intake might have a significant role in obesity, weight loss, and glucose metabolism. "For example," the authors write, "mice with adipocyte-specific deletion of *Bmal1* fed a high-fat diet during the light period gained significantly more weight compared to mice fed during the dark period. Thus, disruption of the adipocyte clock leads to obesity without an overall increase in daily caloric intake when mice are fed during the inactive phase."

The review covers many more topics in this area, but the authors note that despite the immense knowledge of how the internal clock affects health, there is still a big gap in this knowledge and clinical practice. "Currently, large-scale epidemiological studies are repeatedly demonstrating that the alteration of the circadian system has an impact on health and is associated with several adipose tissue-related metabolic illnesses, such as obesity, metabolic syndrome, or diabetes. Nevertheless, the success in translating this knowledge to the clinical practice is still limited," the authors write.

Findings: Looking ahead, the authors write that further research is needed into synchronizing these molecular clocks in the different types of adipose tissues with the rest of the body. Understanding the connections among these genetic variants and obesity may help researchers design individual therapies for obesity. "The current knowledge of the presence of an internal clock in the different adipose tissue types, white, brown, and beige, and its connection with key elements in metabolism may help us to achieve a better understanding of adipose tissue function, and to design novel strategies to combat obesity," the authors conclude.

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High Fear of Disease Occurrence, Low Quality of Life Associated with Multiple Endocrine Neoplasia Type 1



atients with multiple endocrine neoplasia type 1 (MEN1) suffer from a fear of disease occurrence that is associated with a lower quality of life, according to a study recently published in *The Journal of Clinical Endocrinology* & Metabolism.

Researchers led by Gerlof D. Valk, MD, PhD, of the University Medical Center Utrecht in the Netherlands, point out that MEN1 is characterized by a lifetime risk of developing primary hyperparathyroidism (pHPT) of almost 100%, a lifetime risk of developing duodenopancreatic neuroendocrine tumors (dpNETs) of more than 80%, and a risk of developing pituitary tumors (PIT) of 70%. The average life expectancy in the Dutch MEN1 population is 73, which is 10 years shorter than the average Dutch population, and since MEN1 develops at a young age, these patients must be intensively monitored.

Fear of cancer occurrence and quality of life have been studied in other hereditary cancer syndromes like Von Hippel Lindau disease, but few studies have addressed these issues in MEN1 patients. "Up to now, it is unclear if having MEN1 leads to psychological distress because of fear of disease occurrence (FDO), thereby potentially affecting quality of life," the authors write.

The researchers sent the Cancer Worry Scale questionnaire (with a score of 14 or higher reflecting a high FDO), the SF-36 Health Related Quality of Life questionnaire, and questions on sociodemographic and medical history to 285 eligible MEN1 patients in the Netherlands, with 227 completing the questionnaires. The mean age of the cohort was 47 years.

Overall, the patients experienced a FDO of 15.1, with 58% reporting a score 14 or higher, and adjusting for age and gender, the FDO scores were negatively associated to almost all SF-36 subscales, the authors write. What's more is that patients had higher FDO scores for their family members than themselves. "MEN1 is a diagnosis that often affects multiple family members, and therefore the high FDO for patients' family members, requires that regular follow up visits should include addressing worries about relatives with MEN1 related problems and psychosocial support should be provided when needed," the authors write.

Findings: Based on these findings, the authors conclude: "The majority of MEN1 patients have fear of disease occurrence for themselves and even more for their relatives. This psychological distress is associated with a lower health-related quality of life. Therefore, in the medical care for MEN1, emphasis should also be placed on fear of disease occurrence and quality of life."



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Taken together. we show that NNT silencing can induce cytotoxicity and impede cell growth in adrenocortical carcinoma cells, as well as sensitize them to chemically induced oxidative stress. Moreover. we have demonstrated how the plasticity of ACC cells can lead to the development of a compensatory molecular response with time.

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Researchers Suggest Novel Treatment Target in Adrenocortical Carcinoma

Researchers may have come across a novel treatment target to treat the rare but aggressive cancer adrenocortical carcinoma (ACC), according to a study recently published in *Endocrinology*.

The researchers, led by Wiebke Arlt and Paul A. Foster, both of the University of Birmingham in the United Kingdom, write that the mitochondrial NADPH generator Nicotinamide Nucleotide Transhydrogenase (NNT) plays a central role within mitochondrial antioxidant pathways, protecting cells from oxidative stress, and mutations that inactivate NNT cause congenital adrenal insufficiency. "Intriguingly," the authors write, "despite the key role of NNT in preserving cellular redox balance and its ubiquitous expression, the adrenal glands are the only affected organ in most patients; this observation suggests a selective sensitivity of the adrenal glands to NNT loss."

The team hypothesized that if they silenced NNT in ACC cells, it would impair the ACC cells' antioxidant capacity and lead to progressive accumulation of reactive oxygen species (ROS), molecular mediators of oxidative stress. This would in turn induce oxidative toxicity and eventually trigger cellular apoptosis. They transiently knocked down NNT in ACC cells and found that "this manipulation increased intracellular levels of oxidative stress; this resulted in a pronounced suppression of cell proliferation and higher apoptotic rates, as well as sensitization of cells to chemically induced oxidative stress," the authors write.

First author and final-year PhD student Vasileios Chortis then generated a stable NNT knockdown model to see what would happen in the long term when silencing NNT in the same cell line. The ACC cells adapted to chronic NNT knockdown and restored their oxidative stress resilience and redox balance, which abrogated the early impact of NNT loss. This was also associated with an increase in oxygen consumption. The researchers were able to observe these pathways through RNA sequencing, during which they observed an up-regulation of genes involved in protein folding and identifying and degrading damaged proteins. Purine and pyrimidine metabolism was activated in these cells, and ribosomal genes were up-regulated. The authors write that "these findings hint at increased protein turnover, involving degradation of damaged protein and acceleration of new protein synthesis. This may represent a key compensatory mechanism against oxidative stress, achieving the timely removal and replacement of irrevocably damaged (oxidized) proteins."

Findings: "Taken together," the authors conclude, "we show that NNT silencing can induce cytotoxicity and impede cell growth in adrenocortical carcinoma cells, as well as sensitize them to chemically induced oxidative stress. Moreover, we have demonstrated how the plasticity of ACC cells can lead to the development of a compensatory molecular response with time and described how changes in polyamine metabolism and [endoplasmic reticulum] protein processing are involved in this process."

READ THIS AND OTHER ENDOCRINE SOCIETY JOURNAL ARTICLES AT HTTPS://ACADEMIC.OUP.COM/ENDOCRINESOCIETY

DASHBOARD

My brief affair with this field has proven to be extremely rewarding as well as exciting. My ultimate goal is to work in academia where I can continue to conduct endocrine research. I would like to expose students to the vast possibilities within endocrinology, through academic mentorship, education, and research training. I know that I will be a great endocrine researcher, filled with passion to conduct impactful science while providing opportunities for future trainees. So, when posed with the question "Why endocrinology," I ask, "Why not endocrinology?"

> — MAIGEN BETHEA, a doctoral candidate in the lab of Chad Hunter, PhD, at the University of Alabama at Birmingham, discussing why she chose endocrine science for her research in "Why Endocrinology?" on page 8.

The average decrease of ambulance calls in areas

- SOURCE: AARP BULLETIN





that operate rideshare services such as Uber or Lyft.

IN 8 The number of women who will develop a thyroid disorder in their lifetime.



"It looks like we've created Super Resistant Rat."

BY THE NUMBERS

TODAY:

Average medical expenditures among people diagnosed with diabetes were

2.3 times

higher than what expenditures would be in the absence of diabetes.

- SOURCE: AMERICAN DIABETES ASSOCIATION

\$36.2 BILLION

The size of the telemedicine industry by the year 2020.

- SOURCE: THE DIABETES COUNCIL

ENDOCRINE ITINERARY



2018 Clinical Endocrinology Update/Endocrine Board Review

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

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

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

Early Registration: Now – August 17, 2018

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

Miami's Intercontinental Hotel will be the location for the joint meeting of the 2018 Clinical Endocrinology Update (CEU)/ Endocrine Board Review (EBR) East from September 4 – 8, and the Hyatt Regency Orange County in Garden Grove, Calif., will be where CEU West takes place on October 18 – 21. Each year, CEU brings together hundreds of endocrine clinicians for a unique learning experience and opportunities to network with expert faculty and colleagues. Attend the 70th CEU to receive the most trusted and clinically relevant information about recent advances in the field of endocrinology. The educational programming at CEU appeals to clinicians at all levels of practice, as well as fellows and other members of the clinical practice team. Unlike other board preparation meetings, the Endocrine Society's EBR courses offer a comprehensive mock-exam format with case-based American Board of Internal Medicine–style questions forming the bulk of the presentations. Each section follows the ABIM blueprint for the board exam, covering the breadth and depth of the certification/ recertification examination. Each case will be discussed in detail, with the correct and incorrect answer options reviewed. The mock exam appeals to endocrine fellows who have completed or are nearing completion of their fellowship and are preparing to take the board certification exam. Practicing endocrinologists may appreciate the EBR's comprehensive self-assessment of endocrinology either to prepare for recertification or to update their practice.

ADA 78th Scientific Sessions

Orlando, Florida, June 22 – 26, 2018 The Scientific Sessions offers researchers and healthcare professionals an opportunity to share ideas and learn about the significant advances in diabetes research, treatment, and care. Over the course of five days, attendees will receive exclusive access to original research presentations, take part in engaging exchanges with diabetes experts, and expand professional networks with attendees from around the world.

https://professional.diabetes.org

Heart in Diabetes

Philadelphia, Pennsylvania, July 13 – 15, 2018 Heart in Diabetes is a unique medical conference bringing together world-renowned clinical leaders in diabetes and cardiovascular disease. The program is designed to evaluate the state-of-the-art clinical data focusing on the management of the heart and kidneys in patients with diabetes. The goal is to align cardiologists, endocrinologists/diabetologists, iridologists, and nephrologists in their understanding and development of appropriate comprehensive clinical management plans for very high-risk patients. www.heartindiabetes.org

2018 Santa Fe Bone Symposium Santa Fe, New Mexico, August 3 – 4, 2018

The Santa Fe Bone Symposium is an annual forum devoted to advances in the science and economics of osteoporosis, metabolic bone disease, and assessment of skeletal health. Presented by the Osteoporosis Foundation of New Mexico, this meeting is for healthcare providers, scientists, and researchers with a special interest in bone disease, and for bone densitometry technologists who seek a high level of knowledge in their field. (*The Endocrine Society's Endocrine Fellows Series: Osteoporosis and Metabolic Bone Conference is held August 1 and 2 in Santa Fe.*)

awards@endocrine.org

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

Seattle, Washington, September 14 – 17, 2018 The International Congress of the Growth Hormone Research and IGF Societies will gather researchers and practitioners to provide an opportunity to learn from them and to share data. Initially organized by the GRS, the last several meetings have been jointly hosted by both the GH Research and IGF Societies. http://grs-igf2018.com

88th Annual Meeting of the Thyroid Association

Washington, D.C., October 3 – 7, 2018 This meeting is designed for the community of endocrinologists, basic scientists, internists, surgeons, nuclear medicine scientists, pathologists, trainees, nurses, physician assistants, advanced practice providers, and other health care professionals who wish to broaden and update their knowledge of the thyroid gland and its disorders. A customized educational track will be available to trainees to enhance their meeting experience. www.thyroid.org/88th-annual-meeting-ata/

World Congress Insulin Resistance Diabetes and Cardiovascular Disease Los Angeles, California, November 29 – December 1, 2018

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

https://www.wcir.org/



Magee-Womens Research Summit Pittsburgh, Pennsylvania,

Bethel

Park

October 8 - 10, 2018 Magee-Womens Research Institute at the University of Pittsburgh announces the inaugural Magee-Womens **Research Summit. This** conference will serve as a premier forum for scientific exchange on topics related to early human development and women's health and wellness across the lifespan. The program will feature top international scientists and thought leaders in the field and will center on three themes - the impact of nine months of pregnancy on 90+ years of health and wellness ("9 90"); sex differences, ("Beyond X and Y"); and "Aging Reimagined." A major event at the Summit will be the awarding of the first Magee Prize, a \$1 million award that will support a two- to threeyear collaborative research program on an innovative transdisciplinary project in the field of reproductive sciences and women's health.

https://mageesummit.org/

ENDOCRINE **ITINERARY**

INTERNATIONAL ITINERARY

16th World Congress on the Menopause

Vancouver, B.C., Canada, June 6 – 9, 2018 This world congress for midlife and global women's health is a multi-disciplinary meeting with an overarching theme of "Dealing with Midlife Health in the 21st Century." The program will cover women's health from pre- to peri-, through postmenopause, with a special focus on the problems of perimenopause and premature ovarian insufficiency. www.imsvancouver2018.com

ThyroAlex 7

Alexandria, Egypt, July 5 - 6, 2018

ThyroAlex is a biannual thyroid disorders-themed conference organized by the Endocrinology Unit, Alexandria Faculty of Medicine, and Alexandria Thyroid Association. The seventh meeting will cover weight changes in thyroid dysfunction, hair disorders in thyroid dysfunction, childhood hyperthyroidism, and thyroid cancer. National, as well as international, speakers will address the audience and workshops will be held on the first day of the conference. www.med.alexu.edu.eg/endounit/

Dimensions in Diabetes

Mumbai, India, July 14 – 15, 2018

This annual program will bring high-quality clinical education to Indian endocrinologists. The goal of the program is to foster relationships with endocrinologists around India while providing a clinical update in the field of diabetes. Supported by Sun Pharmaceuticals, the two-day program brings in eight faculty members to present in-depth lectures on diabetes and its comorbidities.

www.endocrine.org/meetings

9th International Congress of Neuroendocrinology

Toronto, Ontario, Canada, July 15 – 18, 2018 At the ICN 2018, 64 state-of-the-art speakers and eight plenary lecturers will cover the excitement of modern neuroendocrinology from molecules to behavior, across four main themes – metabolism, reproduction, stress, and timing. Highlights include four concurrent symposium sessions, poster sessions with networking opportunities, and top research in neuroendocrinology from around the world. www.icn2018.org

International Conference on Diabetes & Metabolism

Dubai, UAE, October 15 – 17, 2018

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

EndoBridge 2018

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

18th International Congress of Endocrinology and 53rd SEMDSA

Congress

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

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

www.ice2018.org



A new study presented at ENDO 2018 showed that a single molecule that combines androgen and progestin activities appears to be the key to the creation of the elusive daily birth control pill for men.



Both men and women have been wondering what the have shore pormising for stages in understanding the science, that elusive pill is still a few years away.

Exactly two years ago this month, *Endocrine News* ran an article entitled "Hard to Swallow" about the male pill that was seemingly "just around the corner." hat proverbial corner might be closer now, thanks to new research that was presented at ENDO 2018 where researchers unveiled study results that herald a major step forward in the development of a once-a-day male birth control pill.

A safety and efficacy study found that the promising molecule dimethandrolone undecanoate (DMAU) can suppress gonadotropins to concentrations that bring sperm production down to levels known to provide effective contraception — without inducing significant side effects.

Proposed male contraceptives have taken many forms, but the most auspicious approaches combine an androgen with a progestin, and DMAU offers the activities of both in a single molecule.

This general approach parallels the one used for female oral contraception, according to co-lead study author Stephanie Page, MD, PhD, professor of medicine at the University of Washington in Seattle: "Female contraceptives rely on giving women estrogen

66 These promising results are a great step forward in the development of a prototype male

pill. They raise the possibility of a male pill becoming a reality in the next five to 10 years, if the subsequent studies are as promising as we hope."

- STEPHANIE PAGE, MD, PHD, PROFESSOR OF MEDICINE, UNIVERSITY OF WASHINGTON, SEATTLE

plus a progestin, and when you do that, you shut down the body's own production of the hormone. In the case of men, when you give testosterone or other androgen, the brain senses that there is plenty of testosterone in the body, and it shuts down the signals to the testicle for a man to make his own testosterone" by suppressing production of the gonadotropins luteinizing hormone (LH) and follicle-stimulating hormone (FSH) by the pituitary.

"Sexual function, male characteristics, and effects of nonreproductive organs are maintained by the androgen that is part of the contraceptive regime," adds the other lead investigator, Christina Wang, MD, of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center.

The first approaches to male hormonal contraception used testosterone alone, but studies showed that adding a progestin, which also increases suppression of LH and FSH as well as testosterone production by the testes, further lowers sperm production.

DMAU is metabolized to dimethandrolone, which "has very strong binding activity to the androgen receptor, more potent than testosterone. It also binds to the progestin receptor more avidly than testosterone does - about the same as progesterone," Wang says.

Pre-clinical and animal studies have shown that DMAU suppresses gonadotropins, maintains androgenic effects, and inhibits spermatogenesis. Even at very high doses, it has few adverse effects in rats, rabbits, and monkeys, Wang says. A first-in-humans study showed that single oral doses of 200 mg to 800 mg were well-tolerated and reversibly suppressed serum LH.

AT A **GLANCE**

Sex Hormone - Test

12006 [] PROGESTERONE 12007 [] PROLACTIN 12007 [] PROLACTIN 12008 [] TESTOSTERONE 12008 [] TESTOSTERONE

2 mathyROID (intact)

] Serum []

CORTISOL

ESTRADIOL

1001

120031

12004 [

12005 1 LH

10011

INF

31001 3100

- A male contraceptive in any form has been an elusive goal for decades, with approaches involving pills, gels, injections, and implants.
- Most male contraceptive approaches involve supplying an androgen and progestin, and the relatively new agent dimethandrolone undecanoate (DMAU) provides the actions of both, with a half-life long enough to be effective when taken once a day.
- A safety and efficacy study shows that a daily pill based on **DMAU** suppresses production of testosterone, luteinizing hormone, and follicle-stimulating hormone to levels consistent with very low sperm production in long-term studies.



Normal sperm count Low sperm count

66 Female contraceptives rely on giving women estrogen plus a progestin, and when you do that, you shut down the body's own production of the hormone. In the case of men, when you give testosterone or other androgen, the brain senses that there is plenty of testosterone in the body, and it shuts down the signals to the testicle for a man to make his own testosterone."

- STEPHANIE PAGE, MD, PHD, PROFESSOR OF MEDICINE, UNIVERSITY OF WASHINGTON, SEATTLE

The Study Results

The study, presented as an abstract at ENDO 2018, was the second study in men, and focused on safety and efficacy. It enrolled 100 healthy men ages 18 to 50 years to evaluate two capsule-based formulations of the drug, one in oil and one in powder. The double-blind study tested three different doses — 100 mg, 200 mg, and 400 mg — each over a 28-day period. Eightythree participants completed the study, with no one dropping out because of an adverse side effect.

All dosages reduced serum testosterone into the hypogonadal range, with no significant differences between formulations. All but one subject in the 400-mg dosage group had both FSH and LH reduced to below 1 IU/L, concentrations that long-term studies have shown will very likely reduce sperm production to levels that are compatible with effective birth control.

Safety parameters measured included vital signs, hematocrit, liver function, serum lipids, and EKG. The only changes noted were a small decrease in HDL cholesterol, an increase in hematocrit, and a median weight gain of 1.5 to 3.9 kilograms.

Participants reported no change in mood or sexual function using validated questionnaires. Nine subjects (including one in the placebo group) reported a decrease in libido, but all issues resolved by the conclusion of the study.

The endpoints measured hormonal changes but not sperm production because the 28-day length was not long enough to affect the 72-day sperm maturation process. "The next [step] is a three-month study to demonstrate that those changes in hormones actually result in decreases in sperm count, which we anticipate they will," Page says. That study was scheduled to begin in early May. Page notes that the 400-mg dose was very effective, and "200 mg works pretty well, too. We may end up at 300 mg. We are working with doses in this range in this next study" to find the dose that can best suppress sperm production with the fewest side effects.

Other Methods Remain Ahead

This study landed with a splash in the lay press — reflecting the attraction of "the pill" for men — but other approaches to male contraception are actually further along in development, Page says.

The groups at the Los Angeles Biomedical Research Institute and University of Washington have been leaders in studying a once-a-day gel formulation, which could benefit from gel's status as the popular way for American men to receive testosterone. The gel contains testosterone and the potent progestin nesterone. A six-month study in healthy male volunteers found that it reduced sperm



The pill study landed with a splash in the lay press – reflecting the attraction of "the pill" for men – but other approaches to male contraception are actually further along in development, Stephanie Page, MD, PhD says. These include a six-month study of a once-a-day gel formulation and separate studies involving injections and implants.

production to levels consistent with effective birth control in 90% of participants, with minimal adverse effects.

Intramuscular delivery systems involving an injection about every three months or long-acting implants similar to those available to women are also further along in development.

These systems probably received more research attention than pills in recent years because testosterone has been hard to deliver orally.

Overcoming Obstacles

One main problem in developing an oral hormone delivery system has been the danger of liver damage, an obstacle that drugs like DMAU overcomes. Oral methyltestosterone is hepatotoxic, but DMAU does not contain the methyl group associated with these liver effects. The other main problem has been that testosterone is metabolized so quickly that users would need to take several pills a day. The new formulation overcomes this problem with the addition of undecanoate, a long-chain fatty acid that slows clearance from the body enough to allow a once-a-day pill without damaging the liver or other organs.

"These promising results are a great step forward in the development of a prototype male pill," Page says. "They raise the possibility of a male pill becoming a reality in the next five to 10 years, if the subsequent studies are as promising as we hope."

- CHRISTINA WANG, MD, LOS ANGELES BIOMEDICAL RESEARCH INSTITUTE, HARBOR-UCLA MEDICAL CENTER, LOS ANGELES, CALIF.

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT THE ENDOCRINE SOCIETY'S LATEST CLINICAL PRACTICE GUIDELINE ON TREATING PATIENTS WITH HIRSUTISM IN THE APRIL ISSUE.

Under Scrutiny:



A CLOSER LOOK AT THE T TRIALS



The seven simultaneous studies within The Testosterone Trials show that testosterone therapy may be suitable for older men with hypogonadism.

BY KELLY HORVATH

n December, *Endocrine News* featured "*Eureka!*," a compendium of Endocrine Society journal editors' top picks for ground-breaking research published in 2017. Alvin M. Matsumoto, MD, professor at the University of Washington; associate director of geriatric research, education, and clinical center at the VA Puget Sound; and an associate editor of *The Journal* of *Clinical Endocrinology & Metabolism* (JCEM), was one participant in that article, citing several related papers on male reproductive endocrinology to which he contributed. The vast scope of these studies and their farreaching collective impact merit a closer look.

The Testosterone Trials

Taking place from 2010 through 2014, The Testosterone Trials (T Trials) were seven coordinated double-blind, placebo-controlled studies conducted simultaneously. They consisted of 788 total men ages 65 years abd older with reduced libido, energy, or mobility and serum testosterone concentrations <275 ng/dl on at least two

666 The middle-aged to older individual who does not feel as energetic as he was at age 20 begins to wonder whether his testosterone is low, and a lot of press and testosterone clinics popping up around the United States feed off of that particular complex. As a result, prescriptions of testosterone have skyrocketed, particularly since the advent of a testosterone gel that is easier to administer than the injections that were previously the only formulations available."

— ALVIN M. MATSUMOTO, MD, PROFESSOR, UNIVERSITY OF WASHINGTON, SEATTLE; ASSOCIATE DIRECTOR, VA PUGET SOUND GERIATRIC RESEARCH, EDUCATION AND CLINICAL CENTER; ASSOCIATE EDITOR, THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM occasions, allocated to receive either 5 g daily of testosterone gel (AndroGel 1%) or placebo gel for one year.

Testosterone levels decrease as men age and are associated with various symptoms like those found with testosterone deficiency. However, the knee-jerk response to exogenously replenish serum testosterone has led to conflicting results, which had thus far been based mostly on observational data from chart reviews and databases. The T Trials were an attempt to set the record straight on benefits that testosterone administration actually confers as well as what it does not do, at least in the short term.

"Before these trials, there really were not any well-designed studies that looked at the major outcomes of interest in testosterone treatments of older men. We tried to make up for the limitations of previous studies that were not large enough and trials that included individuals with normal levels as well as low but not unequivocally low levels," Matsumoto explains. "The T Trials only studied individuals with unequivocally low testosterone levels repeatedly as well as symptoms and signs that were consistent with testosterone deficiency. Previous trials did not really look at all the spectrum of potential outcomes that are relevant to older individuals."

The first three studies were in older men with decreased sexual function, physical function, and vitality and were published collectively in the *New England Journal of Medicine* in 2016. In this study, serum testosterone was increased to levels

commensurate with those of men younger than 40. Researchers found that sexual activity and desire increased as did erectile function in the testosterone compared to the placebo-treated group. Less significant increases were seen in walking ability and distance as well as improvements in mood and depressive symptoms.

The subsequent four studies were published individually in 2017 and focused on cognitive function, bone density, anemia, and cardiovascular function. Published in *JAMA*, one year of treatment with testosterone gel did not significantly improve cognitive function in 493 participants with age-associated memory impairment compared with placebo, using a battery of tests that measured verbal memory, visual memory, executive function, and spatial ability.

Published in *JAMA Internal Medicine*, the investigators found that testosterone administration significantly increased bone mineral density and estimated bone strength, as assessed by quantitative computed tomography, more in trabecular than peripheral bone and more in the spine than the hip of 211 participants in the T Trials.

Also published in *JAMA Internal Medicine*, the T Trials investigated whether testosterone would have an effect on anemia in 126 men and found that it increased hemoglobin in those with unexplained anemia as well as those with anemia from a known etiology.

Finally, using coronary computed tomographic angiography, the T Trials investigators showed that testosterone treatment significantly increased coronary artery noncalcified plaque volume in 138 participants, also published in *JAMA*. This finding was concerning, but larger, long-term studies are needed to assess the effect of testosterone treatment on cardiovascular events.

Although not involved in the T Trials, two Endocrine Society experts in male reproductive endocrinology also weighed in. Richard Auchus, MD, PhD, from the

AT A GLANCE

- The T Trials showed that testosterone administration had short-term benefits on sexual function, bone density, anemia, and some aspects of mood and depressive symptoms; it did not show any effect on cognitive function, and it showed an increase in the amount of plaque in coronary arteries.
- Evidence from the T Trials provides a strong rationale for testosterone replacement therapy in older men with low serum testosterone concentrations and unexplained anemia or osteopenia.
- For healthy, nonobese, European and American men, ages 19 – 39 years, the harmonized reference range for total testosterone is 267 to 916 ng/ dL; with this range, hypogonadism can be accurately diagnosed.

The Testosterone Trials

Taking place from 2010 through 2014, The Testosterone Trials were seven simultaneous doubleblind, placebo-controlled studies of almost 800 total men over the age of 65 years and have been detailed throughout medical literature:

- Snyder PJ, et. al. Effects of Testosterone Treatment in Older Men. N Engl J Med. 2016 Feb 18;374(7):611-624.
- 2. Resnick SM, et. al. Testosterone Treatment and Cognitive Function in Older Men with Low Testosterone and Age-Associated Memory Impairment. *JAMA*. 2017 Feb 21;317(7):717-727.
- 3. Roy CN, et. al. Association of Testosterone Levels with Anemia in Older Men: A Controlled Clinical Trial. *JAMA Intern Med*. 2017 Apr 1;177(4):480-490.
- Snyder PJ, et. al. Effect of Testosterone Treatment on Volumetric Bone Density and Strength in Older Men with Low Testosterone: A Controlled Clinical Trial. JAMA Intern Med. 2017 Apr 1;177(4):471-479.
- Budoff MJ, et. al. Testosterone Treatment and Coronary Artery Plaque Volume in Older Men with Low Testosterone. JAMA. 2017 Feb 21;317(7):708-716.
- 6. Travison TG, et. al. Harmonized Reference Ranges for Circulating Testosterone Levels in Men of Four Cohort Studies in the United States and Europe. *J Clin Endocrinol Metab*. 2017 Apr 1;102(4):1161-1173.

University of Michigan Hospitals in Ann Arbor and an associate editor of *Endocrinology*, says, "the T Trials were very difficult to recruit for and had a complicated design, looking at a lot of outcomes, so I commend the investigators for undertaking them. The bottom line is, they confirmed what we already thought, but we now have high-quality evidence to back up what we teach and how we treat patients."

Bradley Anawalt, MD, from Seattle's University of Washington Medicine/Harborview Medical Center and University of Washington Medical Center and an associate editor of JCEM says, "the T Trials will have several important effects for clinical care and future research. The data identified new groups of older men who are likely to benefit from testosterone replacement therapy and provide a strong rationale for replacing testosterone in older men with low serum testosterone concentrations and unexplained anemia or osteopenia."

Questions Answered . . .

"The T Trials, for me, have been a 20-year goal in life in academic medicine," Matsumoto says. "They showed benefits on sexual function, bone density, anemia, and some aspects of mood and depressive symptoms. They did not show any effect on cognitive function but did show an increase of the amount of plaque in coronary arteries. Thus, they are the first short-term outcome studies that have been done in this area large enough to make some actual conclusions that can help clinicians."

According to Peter J. Snyder, MD, from the University of Pennsylvania School of Medicine in Philadelphia and the principal investigator of the T Trials, the T Trials' results demonstrate that increasing the testosterone levels of older men with low testosterone to those levels of young men has clear, though modest, benefits. "If a trial of a much larger number of men followed for a much longer period of time quantitates the risks of this treatment, the benefits the T Trials have demonstrated should greatly influence the decisions of physicians as to whether or not to prescribe testosterone to older men with low testosterone compared to young men," he says.

"The problem is, most of the prescriptions are for individuals that do not meet Endocrine Society criteria for a diagnosis of hypogonadism," Matsumoto says. "The middle-aged to older individual who does not feel as energetic as he was at age 20 begins to wonder whether his testosterone is low, and a lot of press and testosterone clinics popping up around the United States feed off of that particular complex. As a result, prescriptions of testosterone have skyrocketed, particularly since the advent of a testosterone gel that is easier to administer than the injections that were previously the only formulations available." 6 In aggregate, the T Trials have provided information that is useful for clinicians and patients, and these studies should stimulate a greater public interest and federal government investment in research on the benefits and risks of testosterone replacement therapy for men with reproducibly low serum testosterone concentrations and symptoms or signs of androgen deficiency."

— BRADLEY ANAWALT, MD, UNIVERSITY OF WASHINGTON MEDICINE/HARBORVIEW MEDICAL CENTER; UNIVERSITY OF WASHINGTON MEDICAL CENTER, SEATTLE; ASSOCIATE EDITOR, THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

Auchus agrees: "Just like with anything in medicine, there are plusses and minuses that need to be taken into account. But the increases in vitality and physical function being perpetrated by 'testosterone mills' were convincingly shown to be no different than with placebo."

... and Others Remain

"In aggregate, the T Trials have provided information that is useful for clinicians and patients, and these studies should stimulate a greater public interest and federal government investment in research on the benefits and risks of testosterone replacement therapy for men with reproducibly low serum testosterone concentrations and symptoms or signs of androgen deficiency," Anawalt says.

The potential for cardiovascular harm, in particular, is concerning and will be investigated in upcoming longer-term studies mandated by the U.S. Food and Drug Administration to be undertaken by a consortium of pharmaceutical industry partners. Without the T Trials, which were originally recommended by an Institute of Medicine committee to pave the way in the short term, a long-term safety trial may not have been possible. Although the seven T Trials do help answer some interim questions, others loom large: "The important thing to remember about the trials," Matsumoto says, "is that participants' consistently low testosterone levels were not due to any kind of structural or disease process within the hypothalamic–pituitary– testicular axis. That is, there were no apparent causes other than age itself. So, is there such a thing as age-related hypogonadism or testosterone deficiency?"

That's where the final paper that Matsumoto cited for landmark research in 2017 may come in.

Rising to the Occasion

Published in JCEM, a study that was a joint initiative by the Endocrine Society, the Partnership for Accurate Testing of Hormones (PATH), and the Centers for Disease Control and Prevention (CDC) aimed to standardize a reference range for testosterone levels so that low levels could be differentiated from normal ones, and practitioners could more accurately diagnose hypogonadism. By defining the normal reference range as well as ensuring the accuracy of testosterone assays, this study provides a tool for clinicians considering prescribing testosterone.

This joint initiative analyzed the serum testosterone levels in 9,054 healthy, nonobese men from four epidemiologic studies: the Framingham Heart Study, the European Male Aging Study, the Osteoporotic Fractures in Men Study, and the Sibling Study of Osteoporosis. The levels were cross-calibrated in the CDC Clinical Reference Laboratory and harmonized reference ranges computed for men of a variety of ages. For men ages 19 – 39 years, the reference range was 267 to 916 ng/dL, and the lower limit of the range decreased in older age groups.

The reference range established in this study is really quite a coup. "In most hormone assays, there really have not been any reference ranges established in this large a population," Matsumoto says. "For testosterone, this is the first one to be generated." The virtue of having this harmonized reference range is that values from each study were calibrated to a CDC benchmark to overcome variations that might occur among other assays.

"With this standardization, any laboratory that has a testosterone assay standardized and certified through the CDC can use this large reference range to determine whether a testosterone level is normal or low," Matsumoto says. "Moreover, testosterone values would be more comparable between different laboratories."

HORVATH IS A BALTIMORE-BASED FREELANCE WRITER AND A FREQUENT CONTRIBUTOR TO *ENDOCRINE NEWS*. IN THE FEBRUARY ISSUESHE WROTE ABOUT THE HIGHER RISKS FOR CARDIAC EVENTS IN MIDDLE AGE IN ADULTS WHO WERE OBESE CHILDREN.

According to an updated clinical practice guideline from the Endocrine Society, treatment of hypogonadism should be limited to patients with symptoms tied to consistently low testosterone levels.

n the face of endless television advertisements advising men to "talk to your doctor about low T," a new Endocrine Society clinical practice guideline recommends that clinicians should limit therapy to patients who experience real symptoms and have repeated test results documenting consistently low testosterone levels.

Direct-to-consumer advertising about "low T" is associated with more testosterone testing, increased prescriptions for testosterone, and even increased initiation of therapy without testing, according to a study published in *JAMA* in 2013. The number of men older than age 40 prescribed treatment for "low T" tripled in the first decade of this century, as the delivery systems proliferated to include topical gels, skin patches, pills, and injectables. "Recent surveys indicate that many men are prescribed testosterone treatment without an appropriate diagnostic workup or monitoring plan," says Shalender Bhasin, MD, professor of medicine at Harvard Medical School and chair of the panel that wrote the guideline. "Some men receiving testosterone therapy do not have adequately documented hypogonadism, while others who have hypogonadism are not receiving the needed treatment."

The guideline is particularly timely because in the past three years several significant clinical trials published results that added greatly to the evidence base. Those results did little to change the recommendations from the previous version of the guideline but bolstered the evidence underlying them, Bhasin notes. Lab Test Testosterone

Since the last edition of the guideline in 2010, more accurate testosterone assays have become widely available through the spread of liquid chromatography tandem mass spectrometry techniques.

Diagnostic Assays Improve

EDTA blood () Clotted blood

Result

1.35 (Low)

Since the last edition of the guideline in 2010, more accurate testosterone assays have become widely available through the spread of liquid chromatography tandem mass spectrometry techniques that are benchmarked to the Centers for Disease Control and Prevention's hormone standardization program.

"In the area of diagnosis, the new guideline places greater emphasis on the use of accurate assays for measuring testosterone and the use of rigorous reference ranges to determine whether the testosterone levels are low or normal," Bhasin says. "The guideline also emphasizes that low levels should be confirmed by repeated testing, because testosterone levels vary over time and because of measurement variation."

About 30% of men who have a testosterone result in the hypogonadal range have normal concentrations when they are retested. "Testosterone concentrations exhibit significant diurnal and day-to-day variations and may be suppressed by food intake or glucose," the guideline notes. "Therefore, clinicians should measure total testosterone concentrations on two separate mornings when the patient is fasting."

In men whose test results indicate androgen deficiency, the guideline recommends additional diagnostic evaluation to ascertain whether the deficiency is primary (of testicular origin) or secondary (related to the pituitary or hypothalamus). This distinction can be made by measuring serum luteinizing hormone and folliclestimulating hormone concentrations and is important because patients with secondary hypogonadism might have disorders of the pituitary gland or hypothalamus that require management in addition to testosterone treatment.

6 6 Recent surveys indicate that many men are prescribed testosterone treatment without an appropriate diagnostic workup or monitoring plan.
Some men receiving testosterone therapy do not have adequately documented hypogonadism, while others who have hypogonadism are not receiving the needed treatment."

- SHALENDER BHASIN, MD, PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL

Testing, Not Screening

The guideline recommends against routine screening of the general population for hypogonadism because many older men have low testosterone levels but experience no symptoms. Testosterone levels decline naturally with age, so the notion of countering the decline by taking testosterone to raise it to its previous levels may appeal to some men. But the panel recommended against treating older men who have low testosterone levels but no symptoms because taking testosterone involves uncertain risks.

"The short-term risks of testosterone treatment are relatively low. The most frequent side effect is an increase in red cell mass or hematocrit, which is a manageable side effect. The real concern relates to our lack of understanding of the long-term risks of cardiovascular events and prostate cancer," Bhasin says.

There have been no randomized controlled trials that were large or long enough to determine these risks, but they are still concerning. "There is general agreement that testosterone doesn't cause prostate cancer, but testosterone treatment is associated with greater risk of detection of prostate problems, including the greater risk of prostate biopsy and diagnosis of a subclinical prostate cancer. That is a nontrivial risk of testosterone treatment," Bhasin says.

Shared Decision Making

Given the many uncertainties, the guideline emphasizes shared decision making on treatment. "If a patient has severe symptoms, he may view the uncertainty of

AT A GLANCE

- Encouraged by direct-to-consumer advertising, many patients are seeking testosterone testing. Only those who are symptomatic and have consistently low results on a reliable testosterone assay should be offered testosterone replacement therapy, according to a new Endocrine Society guideline.
- Many symptoms of hypogonadism are nonspecific and subjective, which has led to both overtreatment and undertreatment.
- Because the long-term benefits and risks of testosterone treatment remain unclear, the guideline emphasizes shared decision making tailored to individual circumstances.

Testosterone Therapy in Men with Hypogonadism:

AN ENDOCRINE SOCIETY CLINICAL PRACTICE GUIDELINE "Testosterone Therapy in Men with Hypogonadism: An Endocrine Society Clinical Practice Guideline" was published in the May issue of *The Journal of Clinical Endocrinology & Metabolism* and is available online at https://www.endocrine.org/ testosteroneCPG.

NDOCRINE JURNAL SOCIETY JURNAL OF CLIMICAL SOCIETY SOCIETY

666 Testosterone treatment is being overused, underused, and inappropriately used. The guideline is intended to facilitate appropriate diagnosis and treatment of men who can benefit from testosterone treatment and to optimize the benefit-to-risk ratio."

- SHALENDER BHASIN, MD, PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL long-term risks differently than another person who has very mild symptoms," Bhasin says. "Different people may weigh these uncertainties of risks and benefits differently depending on their unique situation. There may be some benefits in men who have clearly low testosterone levels and significant symptoms, such as sexual dysfunction, anemia, or osteoporosis."

The diagnosis may not be clear-cut because symptoms can be nonspecific and subjective. They include reduced sexual desire and activity, decreased spontaneous erections, decreased energy, decreased self-confidence, depressed mood, poor concentration and memory, sleep disturbance, mild unexplained anemia, and reduced muscle bulk and strength. The guideline suggests that in symptomatic men 65 years or older with consistently low testosterone concentrations, clinicians should "offer testosterone therapy on an individualized basis after explicit discussion of the potential risks and benefits. We suggest that when clinicians institute testosterone therapy, they aim at achieving testosterone concentrations in the mid-normal range with any of the approved formulations."

Undertreatment Also a Concern

Bhasin says the guideline may help with another population because, despite the worries about overuse, there are also some hypogonadal patients who could benefit from testosterone treatment but are not receiving it because they have not been diagnosed or are being treated suboptimally.

"Many of the symptoms of hypogonadism are nonspecific and have significant overlap with aging-related symptoms. Another reason for this undertreatment is that in primary care, issues of men's health have not received the emphasis that they deserve," Bhasin explains. "For instance, men with Klinefelter syndrome have very small testes, and a testicular exam would give away the diagnosis right away. But they can go through life without ever getting a testicular exam. Often, when men complain of the nonspecific symptoms associated with hypogonadism, they can be dismissed, so the diagnosis can be missed. It is paradoxical that it should be so given the very rapid growth of testosterone prescriptions."

"Testosterone treatment is being overused, underused, and inappropriately used. The guideline is intended to facilitate appropriate diagnosis and treatment of men who can benefit from testosterone treatment and to optimize the benefit-to-risk ratio," Bhasin says.

"The updated Endocrine Society guidelines on testosterone therapy for men are important and timely," according to Bradley Anawalt, a professor of medicine at the University of Washington who reviewed the guideline but did not serve on the committee. "The authors made their recommendations based on a comprehensive review of the literature including new studies such as the recently completed U.S. Testosterone Trials. The guidelines emphasize a balanced, patient-centered approach to treatment and monitoring." **666** Testosterone concentrations exhibit significant diurnal and day-today variations and may be suppressed by food intake or glucose. Therefore, clinicians should measure total testosterone concentrations on two separate mornings when the patient is fasting."

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT HIRSUTISM TREATMENT GUIDELINE IN THE APRIL ISSUE.

⁻ SHALENDER BHASIN, MD, PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL

Q&A: Daniel J. Drucker, MD, Editor-in-Chief,

Endocrine Reviews

Endocrine News caught up with new *Endocrine Reviews* editor-in-chief, Daniel J. Drucker, MD, to find out what direction he plans to take the journal and what readers can expect under his leadership, and why he believes "if it ain't broke, don't fix it."

BY MARK A. NEWMAN

eginning July 1, Daniel J. Drucker, MD, will become the new editor-in-chief of the Endocrine Society's peer-reviewed journal *Endocrine Reviews*.

Drucker is professor of medicine and the Banting and Best Diabetes Centre-Novo Nordisk Chair in Incretin Biology at the University of Toronto, and a senior scientist at the Lunenfeld-Tanenbaum Research Institute, Mt. Sinai Hospital in Toronto, Ontario, Canada.

A Fellow of the Royal Society, London, Drucker's discoveries have been recognized by numerous scientific and medical societies. He has been honored with the Endocrine Society's Clinical Investigator Award, the American Diabetes Association's Banting Award, the Claude Bernard Award from the European Foundation for the Study of Diabetes, the Manpei Suzuki International Prize, the Rolf Luft Award from the Karolinska Institute, and the Harrington Prize for Innovation in Medicine. Drucker's laboratory studies the molecular biology and physiology of gut hormones, with a focus on the glucagon-like peptides. Drucker's scientific studies have identified multiple novel mechanisms of hormone action, enabling the development of new drug classes for diabetes, obesity, and intestinal failure.

Outgoing editor-in-chief Leonard Wartofsky,

MD, MACP, professor of medicine, Georgetown University, Washington, D.C., had nothing but praise for his successor: *"Endocrine Reviews* has had the highest impact factor of all endocrine journals for many years," he says. "Dan Drucker has had an illustrious career as a clinician investigator, and I could not think of a more capable successor to me as editorin-chief. I am sure that the journal will flourish even further under his guardianship."

Endocrine News caught up with Drucker to find out what fans of *Endocrine Reviews* can expect from his leadership and where he hopes to take the journal in the future.

ENDOCRINE NEWS: Editors-in-chief endeavor to put their own stamp on their respective journals. What is your vision for the future of *Endocrine Reviews*?

DANIEL J. DRUCKER: When something is not broken, don't make up reasons to fix it. However, there are small changes that we can affect to make the journal even more attractive. Evolving flexible journal formats, faster and more responsive

communication with authors, seamless integration with the Endocrine Society publications platforms, while continuing timely dissemination of the best in endocrine science. The editorial board hopes to make its mark through an enduring legacy of quality, while being responsive to adaptations in the way we communicate science.

EN: In looking at the other peer-reviewed publications in this space, what do you feel sets *Endocrine Reviews* apart from the other journals?

DJD: I have great respect for our competitors in the space. A major strength of our journal is the academic editorial board and our daily interaction with real endocrine scientists, basic and clinical. We live the life and are on top of what is hot and what is not. Collectively, we have a broad network of colleagues and interests. We are also easy to reach — have an idea for a review, just email us, or chat with us at meetings. We are your Endocrine Society colleagues, and we would be thrilled to listen to your ideas and suggestions.

EN: Do you expect to be inviting reviews similar to the length, format, and style to those currently being published?

DJD: The new team of editors has expanded the format options to include shorter more concise reviews. For many of us, either authors or readers, there are few topics that can't be summarized within a 4,000-word format. We will

⁶⁶ "A major strength of our journal is the academic editorial board and our daily interaction with real endocrine scientists, basic and clinical. We live the life and are on top of what is hot and what is not."

– Daniel J. Drucker, MD

retain the longer format option and listen to feedback as our style evolves.

EN: Will you be expanding the scope of the journal's subject matter to include topics that may have not been represented in the past?

DJD: The nature of science is the dynamic flow of regular new information. Some fields and topics change slowly, others are exploding with weekly new insights. We will maintain an open mind in regard to new topics, yet we are aware, as a general review journal, that some new topics might just be a bit too narrow and specialized for our audience.

EN: You've been an active user of Twitter before taking on *Endocrine Reviews*. How do you plan to use this platform as editor-in-chief?

DJD: I use Twitter to expand my information-gathering capabilities and to take the pulse of what kind of science

and topics are generating excitement among colleagues. Simultaneously, I will highlight papers within my own areas of interest. As the Endocrine Society increasingly embraces the use of more social media channels, I suspect Twitter will be one of many ways that we engage in the publication conversation and highlight topics of interest in *Endocrine Reviews* and related Endocrine Society publications.

Endocrine Reviews publishes comprehensive, authoritative, and timely review articles balancing both experimental and clinical endocrinology themes. The

journal features Essential Points summaries for each article and professionally prepared illustrations that can be downloaded for presentations and teaching. The journal's Impact Factor ranks among the top of the more than 100 journals in the "Endocrinology & Metabolism" category of Clarivate Analytics' Journal Citation Reports. Reports can be found online at https://academic.oup.com/edrv.

Dan Drucker has had an illustrious career as a clinician investigator, and I could not think of a more capable successor to me as editor-in-chief. I am sure that the journal will flourish even further under his guardianship."

> – Leonard Wartofsky, MD, MACP, professor of medicine, Georgetown University, Washington, D.C.

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A sample of how active Drucker is on Twitter even *before* he takes over the reins of *Endocrine Reviews*.

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Society Brings Researchers to Capitol Hill to Advocate for NIH Funding

Hill Day participants Henry Anhalt, Heidi Vanden Brink, Manesha Taya, and Margaret Eckert-Norton meet with Rep. Tom Reed (R-NY) (middle) to discuss diabetes research.

66 Participating in Hill Day made me realize how important both science communication and advocacy are in order to advance discovery and innovation."

> - HEIDI VANDEN BRINK, BSc, MSc, RDMS, PhD candidate at Cornell University

Springtime in Washington, D.C., always includes cherry blossoms; bus loads of tourists visiting the national monuments, memorials, and museums; and groups who come to Capitol Hill to advocate on issues Congress is considering. The Endocrine Society is no exception.

On May 10, we brought a diverse group of members who conduct research to Washington for a Researcher Hill Day. Because Congress is currently considering funding for fiscal year 2019, which begins October 1, this was a strategic time to bring endocrine researchers to town to share our funding request and educate congressional offices about the value of endocrine-related research. Participants included members from the Advocacy and Public Outreach Core Committee (APOCC), the Research Affairs Core Committee (RACC), Council, participants from the Early Career Forum at ENDO 2018, and participants in the Society's Future Leaders Advancing Research in Endocrinology (FLARE) program. All the participants — whether this was their first time visiting their member of Congress or they have been regular participants in Society advocacy activities — found the experience valuable.

"Participating in Hill Day made me realize how important both science communication and advocacy are in order to advance discovery and innovation," says Heidi Vanden Brink, BSc, MSc, RDMS, PhD candidate at Cornell University and an Early Career ENDO 2018 attendee who took part in the Hill Day. "It was incredibly insightful to meet with congressmen and their staff to understand their roles in advancing science and healthcare and emphasized to me how imperative it is to be able to speak fluently with non-scientists about the relevance of research in our daily lives."

What Happens During a Society Hill Day?

"Members of the Society that attend Hill Day have the opportunity to gain understanding of how the legislative body of government works and how funding is appropriated," says Henry Anhalt, DO, vice president of Medical Affairs at Science37 and Endocrine Society Council Member. "The experience begins with a very comprehensive orientation and identification of the key issues we are advocating for and how to communicate them. In addition, members have the opportunity to meet with their representatives and establish relationships with staffers that will endure past the day itself. Lastly and most importantly, members get to see up close and personal how the Society advocates for us, our scientific endeavors, and the patients we care for."

Participants gathered at the Endocrine Society Headquarters

first thing in the morning for a breakfast briefing led by Society Government and Public Affairs staff. There, they went over the materials for Hill Day, talking points for their visits, and what to expect. Then, armed with state-specific fact sheets about how funding from the National Institutes of Health (NIH) is used and some additional hand-outs provided by the Society, they broke into small groups accompanied by Society staff and headed for Capitol Hill. Throughout the day, participants visited between six to eight congressional offices with their group, which included their Senate delegation and their representative's office. Some groups had the opportunity to meet with the representative or senator, but most met with the congressional staff in the office who work on health issues. Visits to congressional offices are quick - about 15 to 30 minutes — plus time to take a photo and tweet out to the member of Congress, so our participants had to carefully hone in on their messages and get down to business.

"When members of the Endocrine Society participate in Hill Days and advocacy campaigns, we become the voice of over 17,000 clinicians and researchers and the endocrine patients who need our help," says Research Hill Day participant Margaret Eckert-Norton, PhD, assistant director and associate professor at St. Josephs College, and chair of the Endocrine Society Advocacy and Public Outreach Core Committee. "We

66 When members of the Endocrine Society participate in Hill Days and advocacy campaigns, we become the voice of over 17,000 clinicians and researchers and the endocrine patients who need our help."

> MARGARET ECKERT-NORTON, PhD, assistant director and associate professor at St. Josephs College

know that endocrine disorders such as diabetes, infertility and thyroid problems impact millions of individuals and their families. Reminding our policy makers about the science behind the issues supports evidence-based decisions. Through interaction with our representatives, member advocates help promote funding and legislation to facilitate research and improve health outcomes."

What Did We Ask For?

Our Hill Day participants focused on asking Congress to support \$39.3 billion for the NIH in FY 2019. This number was developed by the broad research community, including other medical societies, research organizations, universities, and patient advocacy groups so that we all would go to Congress with the same "ask" and not fall into the trap of pitting one disease group against another. While the \$39.3 billion figure sounds very large, it actually represents a realistic request that would continue the NIH's funding trajectory. Since 2003, the NIH has lost 22% of its spending capacity because of budget cuts, sequestration, and inflation. Since 2017, Congress has begun to make up for years of flat funding by providing a \$2 billion increase in FY 2017 and \$3 billion in FY 2018. Our request would provide a \$2 billion increase for the NIH's base plus additional funding for the 21st Century Cures Initiative in FY 2019 and would continue to help close the gap between current funding and constant dollars.

In addition to our funding request for the NIH, we also shared recommendations for language to be included in the Appropriations Report that will accompany the funding bill. We recommended language that asks the NIH director to expand research on PCOS beyond reproduction to include other comorbidities such as diabetes, heart disease, and mental health. We also recommended language that asks the NIH to examine the effect of increasing the current modular budget cap to reduce administrative burden on grant writers and reviewers.

How You Can Help Share Our Funding Request

Our Hill Day group was able to visit close to three dozen congressional offices. Every office was receptive and supportive but agreed that it was important to "keep up the noise" lest members of Congress forget about the value of biomedical research and the danger of funding cuts.

We will continue to follow up with Congress but urge all U.S. members to join our online advocacy campaign at **www. endocrine.org/takeaction** to tell your member of Congress to support \$39.3 billion for the NIH. Taking action is quick and easy. Simply click on the campaign, provide your zip code, and our software will direct an email to your congressional delegation.

If you are interested in participating in an Endocrine Society Hill Day, please contact **govt-prof@endocrine.org**. We will be taking a group of clinician members to Capitol Hill on October 1 - and we are planning another researcher Hill Day on September 13.

"Advocacy drives positive change to improve the lives of patients, physicians, and populations," says Hill Day participant Joshua Joseph, MD, assistant professor of medicine, Ohio State University Wexner Medical Center and former FLARE Fellow. "Telling our personal stories and the stories of our patients through advocacy is one of the most critical endeavors of an endocrinologist."

Policy Makers Focus on Rising Drug Prices: U.S. Senate Addresses Rising Insulin Costs, President Trump Releases Drug Pricing Blueprint

n May 8, the Senate Special Committee on Aging held a hearing to discuss the skyrocketing cost of insulin, which has tripled in the past 15 years, and how to reduce costs through federal policy changes. In her opening statement, Senator Susan Collins (R-ME), who is also co-chair of the Senate Diabetes Caucus, stated that:

"The rising cost of insulin presents a barrier to care for a growing number of Americans with diabetes. We have heard stories from people across the country who have had to ration or skip doses altogether to make their insulin supply last longer. Some have sought medication from other countries, while others have turned to the black market. Still others have raised funds for their insulin using the Internet. These measures can result in major risks that can compromise health and even life."

At the hearing, William Cefalu, MD, chief scientific, medical, and mission officer of the American Diabetes Association, testified about the financial burden of insulin costs on patients and called on transparency across the supply chain to better understand the key contributors to this growing problem. Given the trend toward high-deductible plans, out-of-pocket costs for insulin are cost prohibitive and many individuals have had to take drastic measures to access this lifesaving drug. An example comes from a father of a type 1 diabetes patient, Paul Grant, who testified that he has used credit cards to afford his son's insulin and has even borrowed from friends when the costs were prohibitive; he now purchases insulin from a pharmacy Canada.

Jeremy Greene, MD, PhD, a professor of medicine and the history of medicine at Johns Hopkins University, testified that the top barrier for medication adherence among his patients was the lack of affordability, in part because no generic exists

Members of the Senate Special Committee on Aging at a hearing to discuss the rising cost of insulin on May 8.

even though insulin has been around for nearly 100 years. In a survey of people living with type 1 diabetes, more than half rationed insulin monthly, weekly, or daily due to cost. These individuals were more likely to come from low-income households, have variable insurance coverage, and have more uncontrolled blood sugar levels. Greene further stated that more than one-quarter of life-threatening hospitalizations for diabetes in U.S. inner-city minority patients could be contributed to the lack of insulin affordability.

Addressing the rising cost of insulin is a top priority for the Endocrine Society, which has been working with the Congressional Diabetes Caucus for more than a year on potential solutions. Last year, the Caucus requested information from the Society on the impact of insulin pricing

ADVOCACY

on patients with diabetes. The Society responded with several recommendations, including:

- Integrating formulary and cost information into electronic health records;
- Including insulin on preventive drug lists;
- Ensuring patients receive rebate benefits at point of sale; and
- Making patient assistance programs more accessible and less restrictive.

After receiving these recommendations, the Congressional Diabetes Caucus expanded its inquiry, requesting additional information from manufacturers, pharmacy benefit managers, and insurers. They also issued a request for information into whether value-based contracting could be applied to insulin. The Caucus is expected to release a white paper later this summer with its key findings.

In the days following the Senate hearing on insulin pricing, President Trump also announced his long-awaited plan to address high drug costs in a blueprint called, "American Patients First." The proposal outlines policies to promote competition, get generics to the market faster, lower fees to "middlemen," improve bargaining power in Medicare Part D drug plans, and block foreign countries from negotiating drug prices. While there is no timeline for implementation, initial reactions to the proposal were lukewarm given the lack of specificity and the likelihood of many of the outlined policies to be enacted.

The Endocrine Society will continue to work across the supply chain to mitigate the impact of rising drug costs on patients with endocrine conditions. We are submitting testimony to the record on rising insulin prices to the Senate Aging Committee and will provide feedback on President Trump's drug pricing proposals. Additional information on the Society's work can be found at **endocrine.org/insulin**.

NIH Launches "All of US" Research Program

n May 6, the National Institutes of Health (NIH) officially launched the "All of Us" Research Program with a series of events nationwide. All of Us is an ambitious project to establish a research cohort of one million or more people living in the U.S., with the ultimate goal of accelerating research and improving health. By enrolling so many participants, the NIH hopes to empower researchers with data at quantities that will allow better detection of associations between environmental and biological exposures and a wide variety of health outcomes. Some of the specific scientific opportunities include identifying individual differences in drug responses; discovering biological markers that signal increased disease risk or protection; and creating a platform to enable trials of targeted therapies.

RESEARCH PROGRAM

The program was conceived as part of the \$250 million Precision Medicine Initiative, announced by President Obama in the 2016 State of the Union address and subsequently written into appropriations bills as specific set-asides in the NIH budget. The Endocrine Society provided comments to the NIH during the development of the cohort study to recognize the unique data needs and pressing research questions of endocrine scientists. For example, we encouraged the NIH to collect data on the hormonal status of the cohort, assess fertility history, and examine exposure to endocrine-disrupting chemicals (EDCs). We anticipate that collecting and linking this data to electronic health records will allow researchers to improve our understanding of how hormones may contribute to disease susceptibility and therapeutic responses and empower researchers to more effectively and efficiently develop therapies for rare diseases.

The NIH is eager to work with research participants as partners in this effort, and it is engaging many different communities across the country. We encourage members of the Endocrine Society to explore opportunities to learn more and get involved in this exciting program by visiting **allofus.nih.gov**.

ADVOCACY

Endocrine Society Participates in EDC Briefing at the European Parliament

s regulators in the European Union continue to implement criteria for the identification of endocrine-disrupting chemicals (EDCs) in the context of biocides and pesticides laws, the Endocrine Society is staying engaged to provide advice and guidance to policy makers on this important subject. On May 24, Pavel Poc, Member of the European Parliament, hosted a briefing at the European Parliament about EDC priorities and next steps for policy makers. Barbara Demeneix, PhD, DSc, BSc, was invited to speak at the briefing as a representative of the Endocrine Society.

During her presentation, Demeneix described the scientific evidence that links EDCs to adverse health outcomes such

as obesity, diabetes, reproductive disorders, cancer, and neurodevelopmental disorders, and discussed the unique characteristics of EDCs that challenge conventional regulatory approaches. The variety of hormonal pathways impacted by EDCs, and the breadth of potential sources beyond pesticides and biocides calls for better public health protection and continued action on EDCs worldwide. She closed by sharing recommendations in the Endocrine Society's updated Position Statement on EDCs in the European Union, specifically that a new EU Strategy on EDCs is required, and more research is needed to develop additional public health protections.

The term of the European Commission and Parliament is set to expire this summer, so the briefing offered a chance to assess progress made by the EU and whether current actions are sufficient to address the significant public health challenge from EDCs. Although progress has been made on the implementation of the criteria, current legislative and regulatory policies fall far short of what the Endocrine Society views as appropriate action to reduce public exposure to EDCs and minimize serious harms due to EDCs. We will continue to engage EU institutions in the coming years to improve and expand upon current EDC priorities to protect public health.

You can see the Society's revised position statement on EDCs in the European Union and additional information about EDCs at **endocrine.org/edc.**

Endocrinology/Metabolism Clinician Educator

The Division of Endocrinology, Metabolism and Molecular Medicine at Northwestern University Feinberg School of Medicine seeks a full-time non-tenure-eligible Clinician-Educator at the rank of **Assistant Professor, Associate Professor, or Professor.** Responsibilities include providing direct inpatient and outpatient care and consultation, as well as the potential for a clinical leadership role on the academic medical center campus. Division faculty are expected to teach graduate students and provide leadership and mentoring to our Endocrinology Fellowship Program.

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Please reply to: Dr. Ruth Weinstock, SUNY Upstate Medical University, Department of Medicine, Room 353 CWB, 750 East Adams Street, Syracuse, NY 13210.

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Help patients find the right path

The OneTouch Verio Flex® meter and the OneTouch Reveal® mobile app make testing more meaningful® for your patients.

ColorSure[®] **technology** shows if your patients' results are in or out of range. Plus, optional wireless connectivity with the **OneTouch Reveal**[®] **mobile app** helps your patients manage diabetes on the go and over time.

Recommend the OneTouch Verio Flex[®] meter today.

* Compared to a meter without a color range indicator and a paper logbook.

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