

APRIL 2017

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

INTERNATIONAL

Endocrine science is shedding light on various factors that affect vitamin D concentrations in the body. New research reveals how endocrine-disrupting chemicals and certain forms of contraception can impact vitamin D levels.

Let the **SUNSHINE** *in*

STICKER SHOCK:

The burden of the rising costs of diabetes treatments

A CONTROVERSIAL COMBINATION:

Exploring liothyronine to treat hypothyroidism

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Hormone Science to Health

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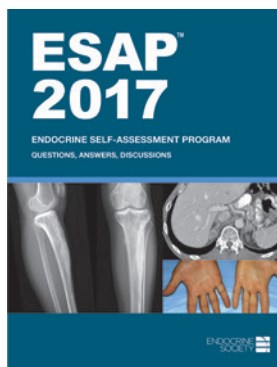
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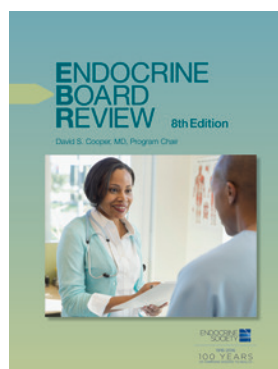
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www.endocrine.org



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Reflections of Memorable Year Full of Landmark Accomplishments

AS I REACH THE END OF MY PRESIDENTIAL term, I am impressed by how much has been accomplished in such a short time. It has been a wonderful experience and a great honor to serve as president of this remarkable society. I was frankly a bit fearful when I started, but quickly found enormous pleasure working with an amazingly engaged leadership, so many active and involved members, and the impressively talented staff. I will highlight just a few of the many accomplishments from this year.

Educational/Scientific Programs

I would like to begin by recognizing and thanking the hard-working and creative members of the Annual Meeting Steering Committee (AMSC). Under the outstanding leadership of its chairs, Gary Hammer, MD, PhD, (overall chair), Carolyn Smith, PhD, (basic science chair), Jack Leahy, MD, (clinical science chair), and Ann Danoff, MD, (physician-in-practice chair), the AMSC has created an outstanding scientific program for ENDO 2017. It's a wonder to see this entire committee working intensely for several long days in a row to fashion a meeting through vigorous debate, thoughtful judgment, and deep experience, followed by a huge effort to make the meeting a reality.

The Clinical Endocrinology Update (CEU) and Endocrine Board Review (EBR) were held last September in Seattle, resulting in the second highest attendance for both activities, following the 2015 record.

Clinical fellowship training programs and trainees are now engaging with the Society's Fellows Training Series (FTS).

This subscription-based platform allows training programs to enroll fellows in a variety of online education resources on numerous topical areas.

Advocacy

The Society's influence and visibility have increased significantly, both domestically and internationally, through our advocacy efforts. Our efforts to influence global policies related to regulation of endocrine-disrupting chemicals (EDCs) have achieved significant impact in 2016.

“The Society's influence and visibility have increased significantly, both domestically and internationally, through our advocacy efforts. Our efforts to influence global policies related to regulation of endocrine-disrupting chemicals (EDCs) have achieved significant impact in 2016.”

One of our top priorities has been advocating for increased funding for the National Institutes of Health (NIH). We held a Hill Day, met with multiple congressional offices, launched online advocacy campaigns, and participated in a leadership role in the broad research community Rally for Medical Research.

We continue to advocate for increased funding and are supporting the March for Science, a global grassroots effort advocating for support of science, support for public funding of research, and support for policies based on scientific evidence.

Our advocacy efforts have also had an impact on NIH policies and research priorities. The update to the Common Rule, which applies to all protections governing human subjects research, included several of our recommendations.

We also have had some important legislative, regulatory, and policy victories in the clinical advocacy area as it relates

to diabetes care. We continue to be a leading advocate for diabetes prevention, coverage, and treatment working closely with the Congressional Diabetes Caucus.

Unexpectedly, we had to advocate for our members and patients impacted by the ongoing restrictions to immigration by the federal government. We are joining with major academic institutions, hospitals, and businesses deeply affected by the new regulations to try to make sure that the interests of our patients and national and international members are acknowledged. We deeply regret that, at this moment, the new restrictions will probably keep some Endocrine Society members from attending ENDO.

Publications

Following extensive survey work and analyses of our current publications, we have embarked on some major changes to ensure the excellence and vitality of all the Society publications. Our basic science journals *Endocrinology* and *Molecular Endocrinology* merged to become *Endocrinology: Molecular and Physiological Basis of Endocrine Health and Disease*, a single, comprehensive, basic science journal for endocrinology. At the upcoming Council meeting we will be considering strategies for strengthening this merged journal. You have probably seen the e-mails with helpful tables of contents of our journals; I've personally found this innovation very useful.

In January, we launched our first new journal in 30 years. *The Journal of the Endocrine Society (JES)* provides rapid peer review and publication of contributions that advance basic science, clinical science, and clinical practice in endocrinology. *JES* is a free, online-only, open-access journal. Starting a new journal is inevitably a daring enterprise, but all the early signs indicate that editor-in-chief Larry Jameson, MD, PhD, and his all-star international editorial group are succeeding in an impressive way.

Global Outreach

This has been one of our busiest and most productive years in our global outreach efforts. Through strategic partnerships with three local organizations in Peru, we successfully launched EndoCares: Diabetes, the Society's first global patient/provider outreach program in Lima, Peru. The program featured provider and patient-education sessions.

“

This has been one of our busiest and most productive years in our global outreach efforts.

”

Last August, we were excited to participate in a joint session at the International Congress of Endocrinology, held in collaboration with the Chinese Society of Endocrinology's annual meeting in Beijing. The Endocrine Society co-hosted the Joint Global Symposium on Obesity with the International Society of Endocrinology and the European Society of Endocrinology. Planning has started for the next joint session during the European Congress of Endocrinology in May 2017, in Portugal.

Another new activity is the launch of our Global Leadership Academy at ENDO 2017 in Orlando. This new program aims to provide training for researchers and clinicians who are between five to 10 years of completion of their formal professional training. The goal is for these individuals to become effective leaders in their own institutions and in organizations around the world.

Other international activities include our participation at meetings in Brazil, India, Mexico, Saudi Arabia, and the United Arab Emirates. This year will be an equally busy year for our international activities as we continue collaborating with endocrine organizations around the world.

In closing, I would like to thank Lisa Fish, my predecessor, for her wisdom and guidance, and wish all the best to my successor, Lynnette Nieman, who has been a big help throughout the year and will be a strategic and visionary leader. I am also grateful to our Council members for their thoughtful and invaluable participation, and to our committee chairs and members for devoting their time and efforts. Finally, I am thankful to the Society staff, in particular the Society's CEO, Barbara Byrd Keenan, for their constant support and partnership. ^{EN}

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



FROM THE **EDITOR**

Welcome to ENDO 2017

IN 2015 WHEN ENDO TOOK PLACE IN SAN DIEGO, CALIF., MORE than a few attendees (from the north and east, especially) commented on how this sunny and mild location was a much-needed antidote to the less-than-kind winter taking place back home. In fact, one Endocrine Society staffer posted a photo as his plane left Reagan International Airport that showed Washington, D.C., seemingly frozen over. The National Mall looked more akin to arctic tundra than it did to one of the country's premier public spaces.

It's two years later and even though we haven't had much of a winter on the East Coast (nobody's complaining), we're all looking forward to descending on Orlando for ENDO 2017 with the thousands of you who have traveled from all over the planet to be a part of the largest endocrinology meeting in the world. While there will be plenty of scientific sessions, ENDO Expo, posters, and more, there will also be a few things that are new this year.

Global Leadership Academy. Debuting on Friday, March 31, the Global Leadership Academy is specially designed for endocrinologists between the five- and 10-year marks in their careers who are looking to gain some vital leadership skills (see InTouch p. 6 for more details).

Two Days of Knockout Rounds. Since it proved to be such a huge success last year, this year ENDO 2017 is going to have two separate sessions of Knockout Rounds where young researchers will have only three minutes — and one slide — to present and defend their scientific findings. Get there early because last year it was standing room only! Saturday (Room WW41A) and Sunday (Room W206) at 2:15 p.m. – 3:15 p.m.

Collaboration Suites. Attendees can reserve complimentary private meeting space for informal gatherings of three to 20 people. These conference rooms are available for 45-minute periods starting on the hour from 8:00 a.m. on a first come, first served basis. Each room has a conference table and chairs, power, projector, and screen. These suites are the perfect place to work on existing collaborations or start new collaborations by inviting ENDO attendees to join you for topical discussions. Reserve your suite at www.endocrine.org/collaborationsuite.

Science Hubs. Located in ENDOExpo, Science Hubs host a wide variety of programs. Whether it's a summary of the top posters or details on the latest Endocrine Society clinical practice guideline, the Science Hubs are the place for you. A full schedule is available via the ENDO 2017 Meetings App.

Collaboration with the American Association of Endocrine Surgeons. On Monday, April 3, more than 500 endocrine surgeons will come to ENDO 2017 for joint sessions ranging from challenging cases to a debate focused on the controversies in thyroid cancer surgery.

This, as they say, is only the tip of the iceberg in terms of all there is to do at ENDO 2017. Can't wait to see you in Orlando! 

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

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Endocrine news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

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

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



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

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

Print ISSN 2157-2089 Online ISSN 2157-2097
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ENDO2017
THE ENDOCRINE SOCIETY'S 99TH ANNUAL MEETING & EXPO

Orlando, Fla., April 1 – 4, 2017

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

www.endocrine.org/endo-2017

19th European Congress of Endocrinology

Lisbon, Portugal, May 20 – 23, 2017

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

www.ece2017.org

American Diabetes Association's 77th Scientific Sessions

San Diego, Calif., June 9 – 13, 2017

The Scientific Sessions offers researchers and healthcare professionals the unique opportunity to share ideas and learn about the significant advances in diabetes research, treatment, and care. Over the course of five days, participants will receive exclusive access to more than 3,000 original research presentations, take part in provocative and engaging exchanges with leading diabetes experts, and expand professional networks with over 13,000 professional attendees from around the world.

www.professional.diabetes.org

Rapid Signaling & Genomic Hormone Action in Health & Disease

Snowmass, Colo., June 11 – 16, 2017

Hormone researchers from around the world will be attending the FASEB Science Research Conference focused on steroid hormone receptors. This five-day event will focus on nuclear and steroid hormone receptor and signaling pathway crosstalk in cancer, metabolism, neuroscience, immunology, and reproduction.

www.faseb.org/src/micro/Site/SteroidHormones/home.aspx

Endocrine Board Review 2017

Chicago, Ill., September 26 – 27, 2017

Unlike other board preparation meetings, the Endocrine Society's Board Review (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.

www.endocrine.org/ebr

Dimensions in Diabetes

Mumbai, India, June 17 – 18, 2017

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 SunPharma, the two-day program brings in eight faculty members to present in-depth lectures on diabetes and its comorbidities.

www.endocrine.org

EndoBridge 2017

Antalya, Turkey, October 19 – 22, 2017

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. 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.

info@endobridge.org

19th ASEAN Federation of Endocrine Societies 2017

Yangon, Myanmar,

November 9 – 12, 2017

ASEAN Federation of Endocrine Societies (AFES) is an association of seven endocrine societies in Southeast Asia with a conference held every two years. With an extensive program covering a broad array of topics, various networking opportunities, poster sessions, continuing medical education, updates on new products and technologies at the AFES Expo, keynote speakers, and more, AFES 2017 is a "must-attend" event in Asia and one of the most recognized congresses among the clinicians and researchers in endocrinology.

www.afes2017myanmar.com

Global Leadership Academy Launches at ENDO2017

THE ENDOCRINE SOCIETY'S 99TH ANNUAL MEETING & EXPO

Cecilia Medina, MD, medical director, Sanofi Peru



When researchers and clinicians get to a certain stage in their careers, often their momentum can grow somewhat stagnant. Their education and much of their training is already behind them so the future can be somewhat uncertain. At this stage in many careers, it is time to assume a leadership role. However, for endocrinology professionals, that path may not always be so clear.

The Endocrine Society's new international initiative, the Global Leadership Academy will provide a helpful guide for these professionals. It will premiere Friday, March 31, in the Orange County Convention Center the day before **ENDO 2017** officially gets under way in Orlando, Fla.

The Endocrine Society's Global Leadership Academy was created to provide formal professional leadership training for endocrinology scientists and practitioners who have reached this uneasy juncture in their careers. Made possible by the sponsorship of Sanofi Peru, this program is geared to those professionals who have completed between five and 10 years of professional training so that young endocrinologists may have the opportunity to improve their "soft skills" that will contribute to their academic and scientific development, according to Cecilia Medina, MD, medical director, Sanofi Peru, who says that "the limited access to such integral initiatives in Peru" inspired the company to play a role in launching the Global Leadership Academy.

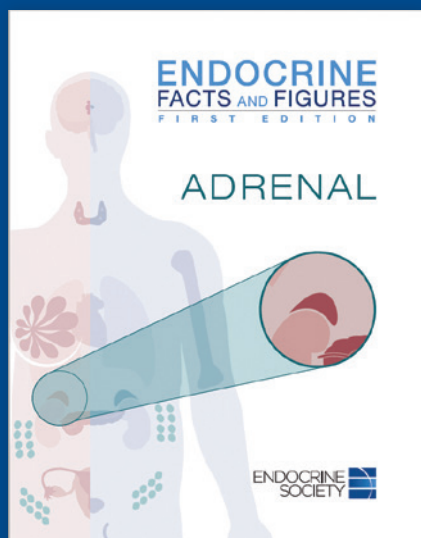
Medina adds that leadership skills for young endocrinologists are important because they "have a key role as leaders of multidisciplinary teams in charge of the management of endocrine diseases. Teams working together need someone who knows how to lead the ship to a good harbor."

The funding from Sanofi Peru will be used for the one-day launch workshop on March 31, and will host a cohort of approximately 40 promising future endocrinology leaders. Roughly half of the participants will be from Peru, all chosen by the sponsor, with the rest from around the world who were chosen by various partner societies. Special consideration will be given to candidates who have never attended **ENDO**.

The Academy's goal is to create effective leaders at these professionals' institutions as well as in other organizations around the world. Medina hopes that the young endocrinologists who take part in the program will not only gain new insight but will be able to pass along their knowledge to their peers and become the next generation of thought leaders.

Global Leadership Academy Objectives

- ▶ Provide leadership training for the professional growth of mid-career members;
- ▶ Ensure a rich and diverse pipeline of future leaders in endocrinology; and
- ▶ Build a global network of leaders in endocrine research and practice who will serve as ambassadors of the field.



Endocrine Facts and Figures Publishes Adrenal Chapter

The most recent Endocrine Facts and Figures chapter has been published online and is devoted to the myriad issues that involve the adrenal glands. This chapter presents available data on the epidemiology, cost burden, key trends on diagnosis and treatment, and health outcomes of adrenal insufficiency, Cushing's Disease, and Cushing's Syndrome. The entire chapter can be downloaded in a convenient PDF format.

The final two chapters of Facts and Figures — Cancers & Neoplasias and Reproduction & Development — are undergoing review and should be released for publication this summer.

The mobile-friendly site endocrinefacts.org continues to expand its reach with 30,595 visitors, 36,961 sessions, 75,522 page views, and 370 unique subscribers. In addition, the International Academy of Visual Arts recently recognized the site with the 2016 Silver Davey Award, which recognizes the work of organizations that derive their strength from big ideas.

Society Strengthens Global Partnerships

The Endocrine Society has been diligent in working with international endocrinology organizations, which have helped foster valuable international partnerships while also spreading the Society's message to promote the practice and science of endocrinology.

In December, the Society sponsored a lecture at the Mexican Society of Nutrition and Endocrinology (SMNE) Congress in Monterrey. This was the Society's fourth collaboration by sponsoring a lecture or symposia. Mark Molitch, MD, Feinberg School of Medicine - Northwestern University, Chicago, spoke on behalf of the Society. Additionally, the Society had a booth on the exhibit floor and processed approximately 100 membership renewals or new memberships and product sales. The most popular products sold were Meet the Professor, ESAP, *Diagnostic Dilemmas: Images in Endocrinology*, and the *Endocrine and Metabolic Medical Emergencies* books, as well as orchidometers.

Council member Guillermo Umpierrez, MD, Emory University School of Medicine, Atlanta, Ga., was also an invited speaker and represented the Society in a meeting with the SMNE leadership and Society staff to discuss plans for next year's congress and the Society's continuing collaboration with the SMNE.

For the fifth year, the Endocrine Society participated as a knowledge partner in the Eighth Annual Emirates Diabetes & Endocrine Congress (EDEC) which took place in Dubai in February.

Ten Society members presented to more than 3,700 attendees. Members representing the Society included Henry Kronenberg, MD, PhD, president, Endocrine Society, Massachusetts General Hospital; John Bantle, MD, University of Minnesota; John Bilezikian, MD, Columbia University; Ian Blumer, MD; David Cooper, MD, Johns Hopkins; Michael Irwig, MD, George Washington University; Laurence Katznelson, MD, Stanford University; Stephanie Lee, MD, PhD, Boston Medical Center; Francesco Rubino, MD, King's College London; and Peter Trainer, MD, The Christie Clinic.

Other global Society initiatives in the past year have included working with the European Union to influence the regulations of endocrine-disrupting chemicals and establishing EndoCares in Peru.



The Endocrine Society Reaches a Social Media Milestone

If you follow the Endocrine Society via Twitter (@TheEndoSociety), you may have noticed that as of March 8, we reached a significant milestone with 10,000 followers. This means that aside from the thousands of followers who are concerned and interested in the work the Endocrine Society is doing to advance endocrine science and clinical care, it can further the Society's reach into the hundreds of thousands ... or even millions!

Twitter, Facebook, and other forms of social media are just some of the many ways that the Endocrine Society is getting its message out around the world.

MEMBERS
in the
NEWS

Sathyavani Prabhakar Joins Lahey Hospital & Medical Center



The Center for Medical Weight Loss at Lahey Hospital & Medical Center in Burlington, Mass., recently announced the addition of Sathyavani Prabhakar, MD, to its growing staff.

Prabhakar is a patient-focused physician with professional interest in comprehensive diabetes, weight, and nutrition management. She has a clinical background in diabetes and related complications.

Prior to joining the Center for Medical Weight Loss, Prabhakar spent seven years as a practicing endocrinologist at the Wheaton Franciscan Medical Group in Racine, Wis., in addition to spending two years as an attending endocrinologist at the Diabetes and Endocrinology Center of Western New York in Buffalo.

Prabhakar received her degree in medicine from Stanley Medical College and Hospital in Chennai, India, and completed an internal medicine residency at the Mount Sinai School of Medicine Program in Jersey City, N.J. She also completed a fellowship in endocrinology, diabetes, and metabolism at the State University of New York, Buffalo. She is board certified in internal medicine, endocrinology, diabetes, and metabolism, and is an active member of both the American Diabetes Association and the Endocrine Society.

The Orange County Convention Center
by Songquan Deng/Shutterstock.com



First-Timer Activities at ENDO 2017

THE ENDOCRINE SOCIETY'S 99TH ANNUAL MEETING & EXPO

ENDO 2017 will feature the launch of the first ever “first-timer” activities. The goal of these activities is to orient new attendees to the meeting culture, promote the value of Society membership, and encourage networking between thought leaders in endocrinology.

First-time attendees are encouraged to check out www.endocrine.org/firstendo and be sure to stop by the Membership Counter to pick up a welcome kit and meet at Booth 941 from 2 p.m. to 4 p.m. on Monday April 3, for exclusive perks, networking, and more.

So, if you see an attendee wearing the “first-timer” ribbon or button at ENDO 2017, please give him or her a warm welcome!

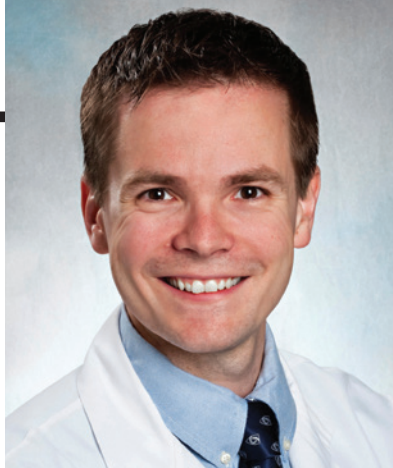


Merck, Pfizer Receive FDA, EMA Filing Acceptances for Diabetes Drugs

Merck and Pfizer announced that the U.S. Food and Drug Administration (FDA) has accepted for review three New Drug Applications (NDAs) for medicines containing ertugliflozin, an investigational SGLT2 inhibitor in development to help improve glycemic control in adults with type 2 diabetes: one for monotherapy, one for the fixed-dose combination of ertugliflozin and JANUVIA® (sitagliptin), and one for the fixed-dose combination of ertugliflozin and metformin.

The Prescription Drug User Fee Act (PDUFA) action date from the FDA is in December 2017 for the three NDAs. Additionally, the European Medicines Agency (EMA) has validated for review three Marketing Authorization Applications (MAAs) for ertugliflozin monotherapy and the two fixed-dose combination products.

These marketing applications to the FDA and EMA are supported by studies in the VERTIS clinical development program of ertugliflozin, including VERTIS MONO, VERTIS FACTORIAL, and VERTIS SITA2, which were first presented at medical congresses in 2016. The full VERTIS clinical development program is comprised of nine Phase 3 trials in approximately 12,600 adults with type 2 diabetes. ^{EN}



WHY ENDOCRINOLOGY?

It Was the Logical Choice

BY OLE-PETTER R. HAMNVIK, MB BCH BAO, MMSc, MRCPI, Assistant Professor of Medicine, Harvard Medical School, and Associate Physician, Brigham and Women's Hospital

As a child, when someone asked “What do you want to be when you grow up?” my answers included gardener, chef, and baker, but never doctor. Later, I wanted to see the world and work as a diplomat. This led me to move from my native Norway to France for high school, where I first became excited about science. My high school biology teacher inspired me to leave diplomacy behind; through the lens of original research studies, he introduced me to cell biology and molecular biology, creating a passion for the scientific method and human biology. Although a career as a PhD researcher tempted me, I was not ready to let go of the human interaction that I had envisioned in a diplomatic career. I therefore decided to pursue medical school, which led me to the Royal College of Surgeons in Ireland.

I love biochemistry and human physiology because an understanding of their underlying principles allows one to make sense of complex clinical scenarios. This also translated into an immediate affinity for the feedback loops, receptors, and metabolic processes of endocrinology. But I also found medical genetics to have a similar logical underpinning, which led me to my first clinical experience in the U.S.: completing an elective in medical genetics at Johns Hopkins Hospital under the supervision of Dr. Ada Hamosh. Although medical genetics was not the path I pursued, I was awestruck by the advanced level of patient care, by the focus on education in the graduate training programs, and the research opportunities in the U.S. I decided to pursue training in the U.S. after medical school.

However, before moving to the U.S., I completed an internship in Ireland. During this time, I had the luck of working with Dr. Christopher Thompson and Dr. Rachel Crowley in the Endocrinology Department at Beaumont Hospital in Dublin. Dr.

Thompson introduced me to the intriguing and variable clinical presentations in endocrinology, and he modeled a rigorous and physiology-based approach to diagnosing and treating endocrine disease. The patients taught me the importance of understanding their subjective disease experience, even if the diagnoses and treatments often rely on objective test results. Dr. Thompson also insisted that all his trainees experience the academic aspects of endocrinology. I was therefore mentored by Dr. Crowley in my first clinical research project, examining the morbidity of craniopharyngiomas, and I served as a tutor for a group of medical students.

“
While I never grew up to be a diplomat, a career as an endocrinologist has allowed me to go to many new and exciting places — if not geographically, then at least intellectually.
”

Eventually, I made it to the U.S., where I started my internal residency training at Brigham and Women's Hospital (BWH). My mind was set on endocrinology as a subspecialty; while I had not had a lot of research experience, I nevertheless had enjoyed learning about research and therefore was planning a career as a clinician-investigator. However, early on I benefitted from the mentorship of Dr. Graham McMahon, who at the time was a faculty member at BWH and had graduated from the same Irish medical school as I had. He has had a successful career as a clinician-educator, and I suspect that he could see my passion for teaching and clinical care rather than research. Although I pursued research training during my endocrinology fellowship, the teaching opportunities afforded to me by Dr. McMahon and my residency program director, Dr. Joel Katz, excited me the most. The opportunity to convey the enthusiasm about endocrinology and patient care that my biology teacher and mentors showed me gave me a new energy and direction. As I wrapped up my fellowship, I realized that the clinician-educator path would be my future.

The field of endocrinology has afforded me multiple valuable


As the Endocrine Society embarks on its second century, *Endocrine News* will continue to tell the stories of how endocrinologists chose this remarkable field. If you would like to share your story with our readers around the world, contact Editor Mark A. Newman at mnewman@endocrine.org.

opportunities. First, due to the non-procedural and outpatient nature of the specialty, it combines well with non-clinical endeavors such as medical education; it is my impression that endocrinologists are heavily overrepresented in medical education positions — including the dean of Harvard Medical School when I started my first faculty position. With this flexibility, it was possible for me to combine clinical practice with several positions within education administration — as the associate program director of the BWH endocrinology fellowship with my mentor, Dr. McMahon, as the program director; as an assistant program director in internal medicine in which I mentored and evaluated internal medicine residents; and in a range of other mentorship and course director roles. Thanks to the flexible nature of endocrine practice, I have also taken on a role as an education editor for the *New England Journal of Medicine*.

Second, I have realized that endocrinologists are on the front lines of one of the civil rights issues of our era, namely the rights of transgender people. We are often the primary providers for transgender people in our role as prescribers of gender-affirming hormone therapy. Of all the patients that I care for,

this is where I think I can make the most difference — both in the actual provision of gender-affirming hormonal therapy, but also in providing a compassionate and caring clinical setting where patients can feel safe, valued, and heard.

Third, my fellowship and early faculty years have overlapped with the rise of cancer immunotherapy, with attendant endocrine side effects. In addition, the cancer survivorship population is increasing in size. I realized that understanding both cancer treatments and endocrine disease would be an asset and thus delved into the cancer literature to understand the endocrine effects — both acute and chronic — of cancer therapies. This allowed me to develop the oncoendocrinology clinic at Dana-Farber Cancer Institute. Through this clinic, I strive to be at the cutting edge of endocrine disease, treating endocrine complications of cancer agents that are still in the clinical trials phase.

While I never grew up to be a diplomat, a career as an endocrinologist has allowed me to go to many new and exciting places — if not geographically, then at least intellectually. And I still garden, cook, and bake in my free time! 



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— **OLE-PETTER R. HAMNVIK, MB BCH BAO, MMSC, MRCPI**, assistant professor of medicine, Harvard Medical School and associate physician, Brigham and Women's Hospital, on why he chose endocrinology over baking, diplomacy, or gardening as a career in this month's "Why Endocrinology?" column on page 10.

FROM THE CENTURY OF
ENDOCRINOLOGY TIMELINE

2010:

*Nobel Prize in
Physiology or
Medicine Awarded to
Robert G. Edwards*



In 2010, Robert G. Edwards received the Nobel Prize in Physiology or Medicine “for the development of in vitro fertilization.” Edwards believed that in vitro fertilization could be used as a treatment for infertility beginning in the 1950s. He worked systematically to realize his goal. Through his research, Edwards discovered important principles for human fertilization and succeeded in accomplishing fertilization of human egg cells in cell culture dishes. The efforts of Edwards were proved a success when the first “test tube baby” was born on July 25, 1978. In the following years, Edwards and his colleagues continued to research and refine IVF technology and share it with scientists and physicians throughout the world.

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



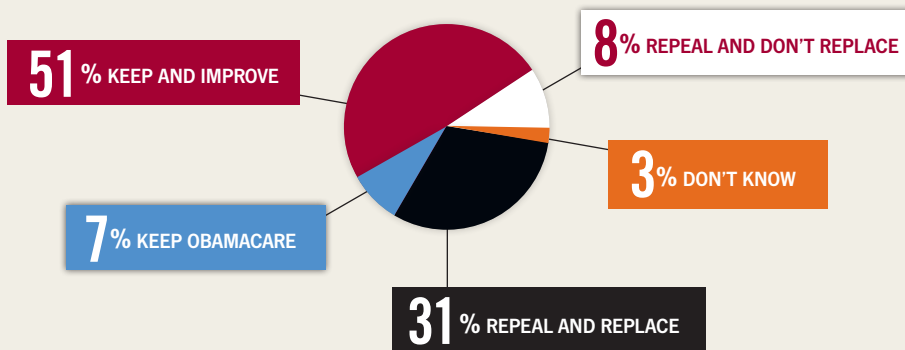
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1.7 million

**The number of
children whose
deaths are linked
to living in polluted
environments.**

— **SOURCE: WORLD HEALTH
ORGANIZATION**

— What the People Want: — **Americans & Obamacare**



— **SOURCE: MONMOUTH UNIVERSITY POLLING INSTITUTE SURVEY CONDUCTED MARCH 2 – 5 OF 801 ADULTS**



BY DEREK BAGLEY

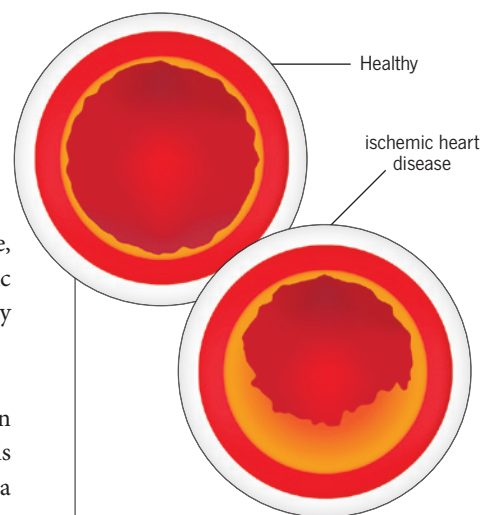
“Metabolically Healthy Obese” People at Higher Risk of Ischemic Heart Disease

In yet another blow to the idea that there are “metabolically healthy” obese people, Danish researchers have found that obesity carries with it a higher risk of ischemic heart disease (IHD), irrespective of metabolic health, according to a study recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Kristine Færch, MSc, PhD, of the Steno Diabetes Center Copenhagen in Gentofte, Denmark, point out that recent studies have categorized some obese individuals as not having an increased risk of obesity-related complications, but obesity remains a major public health concern. “The concept of metabolically healthy obesity has been discussed over the past decade, and the conclusions are ambiguous,” the authors write. So the team set out to determine whether obesity is a risk factor for developing IHD, no matter how metabolically healthy an obese person is.

The team followed 6,238 men and women from the Danish prospective Inter99 study for more than 10 years. They classified the participants according to BMI, as well as four metabolic risk factors. “Metabolically healthy individuals were defined as having zero metabolic risk factors, and metabolically unhealthy individuals as having minimum of one,” the authors write.

Of the participants, 323 developed IHD during the follow-up period. The researchers found that metabolically healthy obese men were more likely to develop IHD than their healthy normal weight counterparts. The women’s results were less pronounced. What’s more, many of the metabolically healthy participants became metabolically unhealthy after five years of follow-up.



Findings: The authors conclude that based on these results, that not only do “metabolically healthy obese” individuals carry an increased risk of IHD, metabolically healthy obesity is also not a permanent state. “In conclusion,” they write, “our results suggest that the metabolically healthy obese phenotype is not a benign condition, and we question the feasibility of denoting a subgroup of obese individuals as metabolically healthy.”

High fat diet-
induced obese and
healthy control
mice



Animal Study Parses Influence of Genes and Environment in Metabolic Disease

By comparing two strains of mice — one that becomes obese and diabetic on a high-fat diet and another resistant to a high-fat regimen — researchers identified genome-wide changes caused by a high-fat diet, according to a study recently published in the *Journal of Clinical Investigation*.

Researchers led by Raymond Soccio, MD, PhD, an assistant professor of medicine, and Mitchell Lazar, MD, PhD, director of the Institute for Diabetes, Obesity, and Metabolism at the Perelman School of Medicine at the University of Pennsylvania in Philadelphia and their team looked at the interplay of genes and environment in two types of white fat tissue, subcutaneous fat versus visceral fat around abdominal organs. The latter correlates strongly with metabolic disease. This visceral fat shows major gene expression changes in diet-induced obesity. The study confirmed this relationship and extended these findings to show that the epigenome in visceral fat also changes on a high-fat diet.

“We focused on the epigenome, the part of the genome that doesn’t code for proteins but governs gene expression,” Lazar says.

The team next treated obese mice with the drug rosiglitazone, which targets PPARgamma in fat to treat diabetes in people. “While the drug-treated obese mice were more insulin sensitive, we were surprised to see that the drug had little effect on gene expression in visceral fat,” Soccio says. “This led us to look at subcutaneous fat, and we discovered that this depot is much more responsive to the drug.”

“These results are clinically relevant and indicate that the ‘bad’ metabolic effects of obesity occur in visceral fat, while the ‘good’ effects of rosiglitazone and other drugs like it occur in subcutaneous fat,” Lazar says.

In particular, the drug-induced changes they found in subcutaneous fat reflected the phenomenon of browning, in which white fat takes on characteristics of brown fat, typically in response to cold exposure or certain hormones and drugs. White fat stores energy, while brown fat dissipates energy by producing heat, mediated by uncoupling protein 1, or *Ucp1*. The most interesting discovery of the study, say the authors, involves *Ucp1*.

They found that rosiglitazone increases *Ucp1* expression in both obesity-prone and obesity-resistant strains of mice. However, in subcutaneous fat of the obesity-resistant mice, *Ucp1* expression was high even in the absence of the drug. “But the real surprise came when we looked at the offspring of obesity-resistant and obesity-prone parents, which have one of each parent’s version of the *Ucp1* gene,” Soccio says.

Findings: The researchers found that the obesity-prone mouse strain’s version of the *Ucp1* gene has lower expression and less PPARgamma binding than the obesity-resistant version. This imbalance shows that the obesity-prone mouse strain’s *Ucp1* is genetically defective, since it is less active than the other strain’s version, even when both are present in the same cell nucleus. In their final experiments, the team asked what happens when browning and *Ucp1* expression are activated using rosiglitazone or exposure to cold, both environmental factors. They found that in both cases, total *Ucp1* expression goes up as expected, but the obesity-prone strain’s defective version of *Ucp1* now reaches equal levels to the obesity-resistant strain’s version. “Importantly, we were only changing the mouse’s environment with a drug or temperature, not the actual DNA sequence of the *Ucp1* gene,” Lazar says. “We propose that this result indicates epigenomic rescue of *Ucp1* expression in subcutaneous fat cells.”

The team is following up the mouse studies using human fat biopsies to figure out the exact DNA sequence differences responsible for variable *Ucp1* expression, both in mice and in humans. The relevance of this study extends even beyond *Ucp1* and obesity. “Many gene variants are thought to exert their effects by ultimately altering gene expression levels, and this study shows that a genetic predisposition to altered gene expression can be identified and then overcome with treatment,” Lazar says. “This is the dream of precision medicine, and hopefully our study is a step in this direction.”



Bread baked with inulin powder

Prebiotics May Benefit Obese Children

Researchers at the University of Calgary in Canada have found that a daily addition of a particular prebiotic fiber prior to dinner may help children feel satiety and eat less. The study was published in the *American Journal of Clinical Nutrition*.

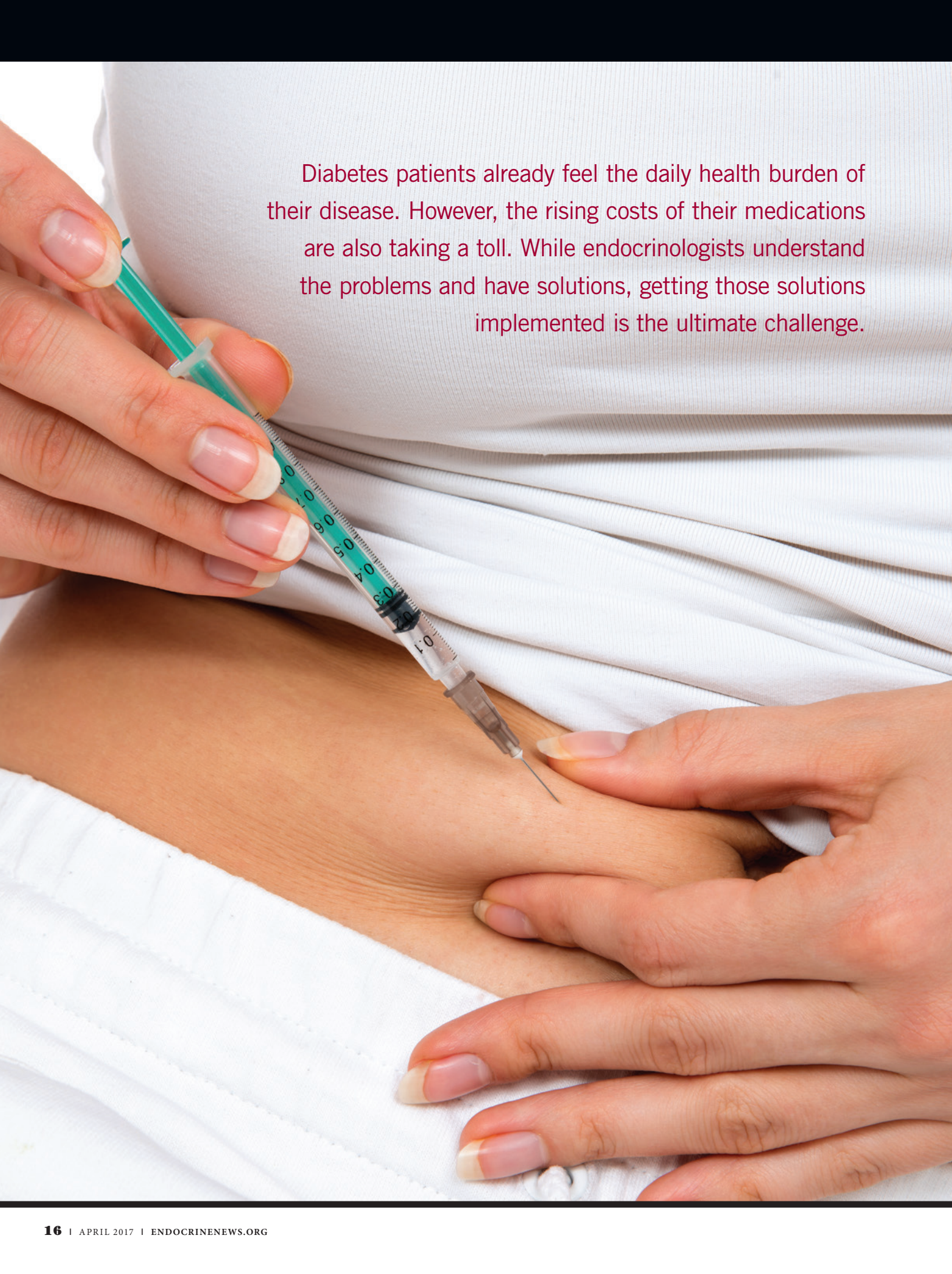
The researchers led by Professor Raylene Reimer point out that studies have shown prebiotics to be effective in improving satiety in adults with overweight and obesity, but studies showing their efficacy in children are limited.

“The results of this dietary intervention study highlight the potential of prebiotic supplementation in the management of pediatric overweight and obesity, with significant improvements in sensations of appetite and marked reductions in energy intake in children 11 – 12 years of age,” says Reimer.

The study conducted was a randomized double-blind, placebo-controlled trial involving 42 overweight and obese boys and girls between the ages of seven and 12. They were randomly assigned to receive eight grams per day of oligofructose-enriched inulin or a maltodextrin placebo for 16 weeks.

The researchers found that compared with the placebo, in the age group of 11- to 12-year-olds, their calorie consumption decreased significantly by approximately 113 kcal. The placebo group actually increased energy intake by 137 kcal. They also found that ghrelin was increased by 28% in all of the children in the prebiotic group after 16 weeks compared to baseline levels. The placebo group levels of ghrelin only increased by 8%.

Findings: The authors conclude: “Independent of other lifestyle changes, prebiotic supplementation in children with overweight and obesity improved subjective appetite ratings. This translated into reduced energy intake in a breakfast buffet in older but not in younger children. This simple dietary change has the potential to help with appetite regulation in children with obesity.” ^{EN}



Diabetes patients already feel the daily health burden of their disease. However, the rising costs of their medications are also taking a toll. While endocrinologists understand the problems and have solutions, getting those solutions implemented is the ultimate challenge.

Sticker SHOCK

BY DEREK BAGLEY



AN INCONVENIENT TRUTH ABOUT TREATMENT COSTS

Irl B. Hirsch, MD, professor of medicine at the University of Washington in Seattle runs four half-day clinics a week, treating a large number of patients with diabetes. Eighty percent of his patients have type 1 diabetes, the rest have type 2 diabetes, and 98% of all these patients are on insulin. One of his patients now pays more for her insulin per month than she pays on her mortgage per month. Another patient maxed out his credit cards to pay for his insulin, and he was denied a car loan because of his low credit score.

These examples come at a time of great turmoil in the healthcare system, with providers and insurance companies and Congress all trying to determine who pays for what and who gets what treatment. They come at a time when ill-informed congressional representatives make asinine statements like “patients are going to have to decide whether they want an iPhone or healthcare.” (Just for reality’s sake, an iPhone costs \$700 retail; the newest insulin agonists, like the GLP-1 receptors, cost around \$700 a month, retail. An \$8,400 phone does not exist ... yet.)

But insulin isn’t the only drug patients with diabetes have to take. These patients, and their prescribing physicians, face hurdles when it comes to every kind of diabetes

medication. Hirsch points to drug manufacturers’ co-pay cards as an example of one of these hurdles. “They take away the tiering system,” he says. Where Hirsch practices in Seattle, if a drug is Tier 2, that drug will often generate a prior authorization, “which is the two-word cuss word for endocrinologists,” he says.

“If I’m going to practice evidence-based medicine, I’m going to prescribe Jardiance [empagliflozin] and Victoza [liraglutide] because of their cardiovascular benefits,” Hirsch says. But because those drugs might not be listed on the formulary, or even if there are drugs in this class that are on the list, he has to write a prior authorization. “Writing the prescription is the easy part,” he says. “It’s then convincing the pharmacy benefit manager (PBM) that this is the appropriate drug for that patient. We’re now practicing PBM-based medicine and not evidence-based medicine.”

Haves & Have Not

The global cost of diabetes is now more than \$800 billion a year. In the U.S. alone, the cost is more than \$240 billion a year. And that’s not just direct costs. According to the American Diabetes Association, indirect costs of



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— ROBERT VIGERSKY, MD, MEDICAL DIRECTOR,
MEDTRONIC DIABETES; PAST-PRESIDENT,
ENDOCRINE SOCIETY

diabetes include \$5 billion for increased work absenteeism, \$21 billion for reduced productivity at work, and \$18.5 billion for lost productive capacity due to early mortality.

Diabetes rates, here in the U.S. and around the world, continue to skyrocket. In 2012, 29 million Americans had diabetes, with 1.4 million new cases being diagnosed each year. Millions more have prediabetes. Diabetes is the seventh leading cause of death in the U.S. And many patients with diabetes either reduce the quality of their care or stop compliance altogether because of one reason: cost.

Robert Vigersky, MD, medical director of Medtronic Diabetes and past-president of the Endocrine Society, says that a good doctor-patient relationship is essential to endocrine care, but once some physicians started not appearing on preferred-provider lists, their patients began to relinquish the doctor-patient relationships they had established, in favor of physicians who were on these lists and didn’t cost as much. “That creates a two-tier system,” he says. “Patients who can afford it can get the physician of their choice, and those who can’t are left to find someone on their plan or spend more out of pocket than they did before. It’s very difficult for the patient to navigate the system,” Vigersky continues, “so they often default to what the cost is.”

The cost to treat diabetes effectively has created a system of haves and have nots: Patients who have the least to spend for out-of-pocket charges visit clinics where physicians have the least amount of time to spend with them. These patients also stop taking their medications or take them every other day. Or if certain medications aren’t available to them because of cost or these drugs aren’t on the formulary list, that affects outcomes as well. “These are all barriers to improved results in care of patients with diabetes,” Vigersky says.

Here's how backwards things are: *JAMA Internal Medicine* in January published an article by J. Frank Wharam, et al., titled "Diabetes Outpatient Care and Acute Complications Before and After High-Deductible Insurance Enrollment: A Natural Experiment for Translation in Diabetes (NEXT-D) Study." The authors analyzed data from 12,084 high-deductible health plan (HDHP) members with diabetes who had been enrolled in a low-deductible plan (<\$500) for one year, followed by two years in a HDHP (>\$1,000) after their employers changed plans.

The researchers found that these patients "experienced minimal changes in outpatient visits and disease monitoring after an HDHP switch, but low-income and HSA-eligible HDHP members experienced major increases in emergency department visits for preventable acute diabetes complications." The authors go on to write that these patients had greater concern about out-of-pocket spending than their less vulnerable counterparts, and that they might forgo "expensive scheduled and acute visits [or shift care] to less expensive but potentially less appropriate settings. Such effects might lead to more severe disease by the time of presentation for acute complications."

The cost of diabetes care, it seems, is not without a sense of irony. And the cost is increasing every year. Patients are often on several drugs to treat their diabetes and associated comorbidities, and drug prices continue to rise. "I think everyone knows the huge increases in the cost of insulin that have occurred over the last few years," Vigersky says. "And that has caused some patients to resort to getting insulins that are not as effective."

Insulin:

A Right or a Privilege?

Insulin, of course, is the primary drug used in diabetes care. But it's also a prime example of just how convoluted diabetes care has become. In the U.S., human insulin can be bought over the counter, but analogs still require a prescription. Other countries allow both types of insulin to be sold without a prescription. In other countries, governments negotiate drug prices, rather than leaving that to individual insurance plans. "It really puts us at a disadvantage," Hirsch says.

According to Hirsch, as of 2013, the U.S. and Canada used 12% of the world's insulin, yet those countries generated 52% of the revenue. In contrast, China uses 25% of the insulin in the world, yet that country generates only 4% of the revenue. "That was from 2013," he says, "and the U.S. insulin prices have increased since then."

"This is not a concierge drug," Hirsch says. "This is not a drug that, in my opinion, should only be for the wealthy. It gets back to the premise of the Affordable Care Act. Is healthcare a right or a privilege? Is insulin a right or a privilege? It's my humble opinion that insulin is a right of every American. Nobody should be without insulin therapy. Nobody."



AT A GLANCE

- ▶ Diabetes care is expensive, sometimes so expensive that patients forgo care because of the cost.
- ▶ The system of diabetes care, especially when it comes to insulin, is convoluted and can ultimately be detrimental to patients' health.
- ▶ Endocrinologists have solutions in mind, but they can often be tough to implement.



“ I would invite any government official, whether it’s a senator or congressman, to spend a half day in the clinic with me. **I would like them to see for themselves how my patients struggle.**”

— IRL B. HIRSCH, MD, PROFESSOR OF MEDICINE,
UNIVERSITY OF WASHINGTON, SEATTLE

A Daily Struggle

The cost to treat diabetes has a very real impact on people who need these expensive drugs and treatments just to live. Doctors are coming around to including financial burdens in treatment decisions, but a lot of times their hands can be tied. There are fewer and fewer endocrinologists in private practice; more and more physicians are employed by health plans or other types of care delivery systems in which they have to adhere to a formulary. “You’re constrained by the formulary,” Vigersky says. “You can appeal to the health plan, but the time and cost is really daunting and not feasible for many physicians in practice.”


This is a mess, but what can be done? Diabetes prevention is usually at the top of the list for reducing diabetes care costs, but just days before this issue went to print, the *Journal of the American Medical Association* published a research letter that concluded that many obese Americans have given up trying to lose weight. What’s troubling is that this phenomenon was most common among African American women, who already have a higher risk of developing diabetes. The Diabetes Prevention Program has produced some encouraging preliminary results, but Vigersky says these results still need to be expanded and validated.

As for insulin, Hirsch would like to see the U.S. adopt a system similar to the World Health Organization’s. The WHO has a list of what it calls “essential medicines,” and insulin is on the

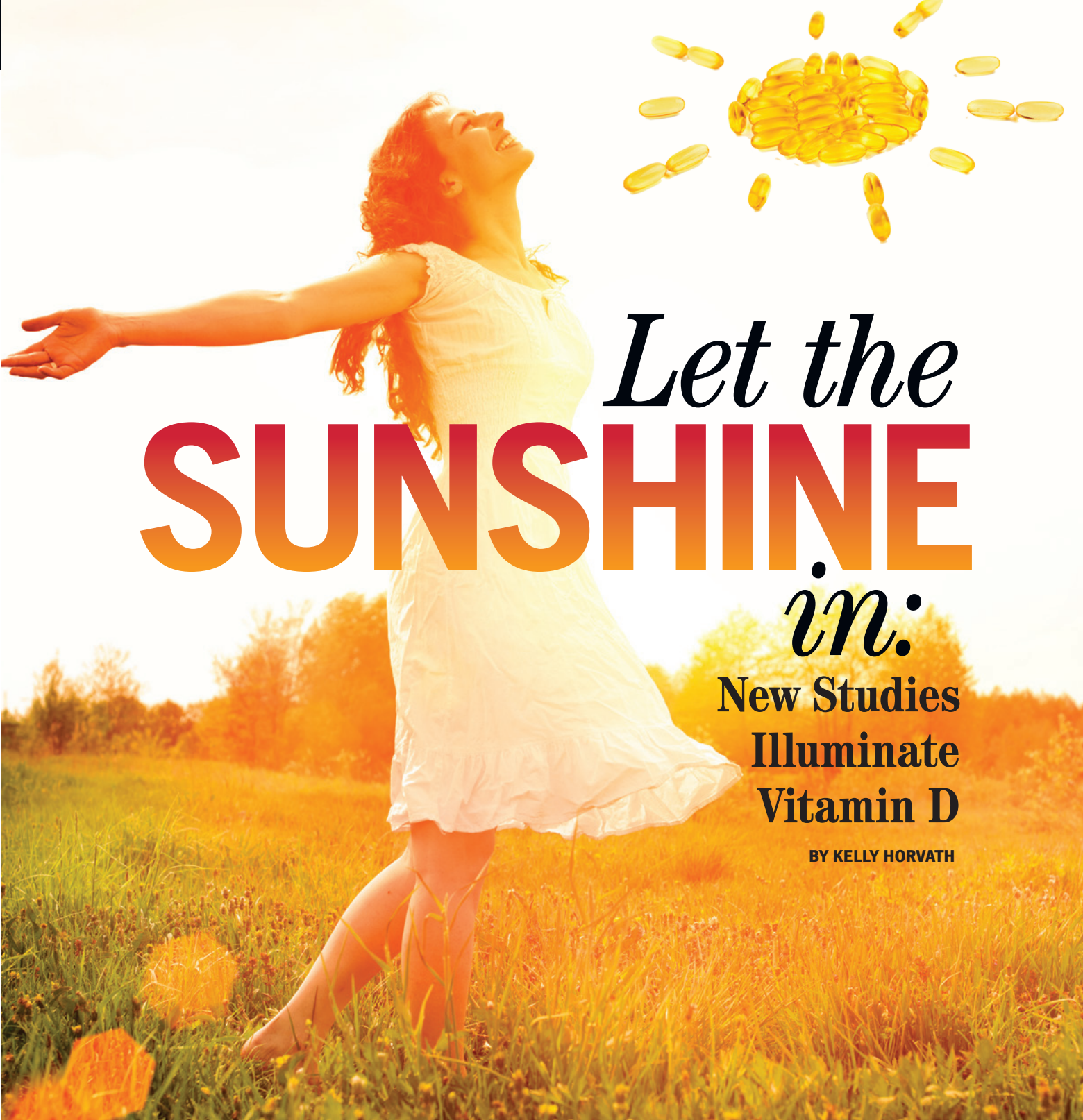
list. “It’s my belief we need to do the same with insulin,” he says. “Maybe not the best and newest and most expensive, but there needs to be a list of medicines that patients can get for a reasonable cost.”

Hirsch’s “dream system” sounds like a simple one, but certainly not an easy one to implement: Along with eliminating the PBM, he says he “would like to see insulin go straight from the manufacturer to the patient at a reasonable cost.”

Healthcare recently has shifted to quality metrics and outcomes, which is a good thing, but Endocrine Society members need to remain active and engaged in this battle for solutions, says Vigersky. “There’s a burden that diabetologists and endocrinologists have that as specialists we will naturally get the patients who are the most challenging,” he says, “and all that needs to be taken into consideration when outcomes are judged.”

Again, the reality is that patients are not having to choose between buying an iPhone or investing in their own healthcare. For many patients with diabetes, they’re having to decide whether to buy food or insulin. Make their rent or buy insulin. Miss work because they landed in the hospital with a preventable acute complication, because they couldn’t afford their diabetes medications. “I would invite any government official, whether it’s a senator or congressman, to spend a half day in the clinic with me,” Hirsch says. “I would like them to see for themselves how my patients struggle.” 

BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE THE TWO-PART ARTICLE ON PATIENT-CENTERED CARE THAT RAN IN THE FEBRUARY AND MARCH ISSUES.



Let the **SUNSHINE** *in:*

**New Studies
Illuminate
Vitamin D**

BY KELLY HORVATH

Two recent studies in *The Journal of Clinical Endocrinology & Metabolism* shed light on various factors that affect vitamin D levels in the body. The links between vitamin D and certain forms of contraception as well as how it can be impacted by endocrine-disrupting chemicals have been given a closer look by endocrine researchers.



Because of its wide-reaching implications for the functioning of many body tissues found in cardiovascular, digestive, immune, and reproductive systems, maintaining adequate vitamin D levels is critical for overall human health, especially so for women.

Yet many U.S. women are vitamin D deficient, especially among the African American population. Moreover, getting adequate vitamin D can be difficult for some, as it does not occur in many foods. Two recent studies on vitamin D examine exogenous factors that can influence its levels: one on what can have a negative impact, the other, a positive.

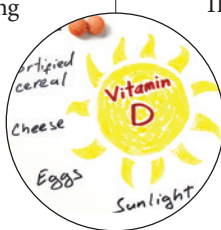
EDCS STRIKE AGAIN

In “Relationships Between Urinary Phthalate Metabolite and Bisphenol A Concentrations and Vitamin D Levels in U.S. Adults: National Health and Nutrition Examination Survey (NHANES), 2005–2010,” published in *The Journal of Clinical Endocrinology & Metabolism*, a team including John D. Meeker, ScD, CIH, and Lauren E. Johns, a PhD candidate at the University of Michigan School of Public Health in Ann Arbor, Mich., took a look at what effect endocrine-disrupting chemicals (EDCs) might have on vitamin D in 4,667 NHANES participants for whom urinary phthalate metabolites, urinary BPA, urinary creatinine, and serum 25(OH)D data were available. “Two previous studies have suggested the potential for

environmental exposure to other EDCs (e.g., pesticides) to alter circulating vitamin D levels in humans,” Johns says. “Phthalates and bisphenol A (BPA) have been shown to disrupt thyroid and reproductive hormones in humans. Because the active vitamin D metabolite in our bodies is similar in structure and function to these other hormones, it is plausible that phthalates and BPA could also impact vitamin D levels in our body through some of the same mechanisms.”

They found that phthalate metabolite levels inversely correlate with total adult circulating vitamin D levels, resulting in a 1.09% decrease. Furthermore, the degree of reduction of vitamin D levels due to environmental exposure to phthalates was sex specific, with stronger associations found in women. BPA level also inversely correlated with vitamin D level, resulting in a 3.71% decrease in women only.

The mechanisms underlying how EDCs act on vitamin D levels in the endocrine system remain largely unknown, but these researchers and others suggest that one possibility is by directly acting on the metabolic enzymes involved in converting inactive vitamin D prohormones to their circulating



metabolites. “It is also possible that phthalates and BPA may indirectly influence circulating vitamin D concentrations through the disruption of calcium homeostasis. BPA in particular has been shown to alter the expression of proteins involved in calcium signaling processes as well as serum calcium levels,” Johns says.

PROTECTING VITAMIN D STATUS

This was the first study to investigate environmental exposure to phthalates (found, for example, in perfumes, hairspray, deodorants, and lotions) and total 25(OH)D, although vitamin D has been investigated in relation to BPA. The findings remain consistent. “While additional studies are required to determine the clinical impact of our findings, the widespread use of these chemicals coupled with the essential role that vitamin D plays in numerous physiological processes in our bodies could mean that the public health implications of these findings may be quite large. It is likely that the downstream clinical outcomes potentially associated with subclinical alterations in circulating vitamin D concentrations are sex-dependent and depend on physiological state (i.e., pregnancy status, adolescence, etc.),” Meeker says.

Once again, the best advice clinicians can give at this point is EDC avoidance when possible. Meeker explains, “Although the widespread use of these chemicals (and their alternatives) precludes complete avoidance of exposure, it may be possible to reduce exposure to some degree by limiting use of plastic-containing products, reducing consumption of heavily processed/packaged foods, and finding more natural alternatives to personal care products.”

NOT SUCH A BITTER PILL

In “Use of Estrogen-Containing Contraception Is Associated with Increased Concentrations of 25-Hydroxy Vitamin D,” also published in *The Journal of Clinical Endocrinology & Metabolism*, a team including Quaker Harmon, MD, PhD, a fellow at the National Institutes of Health’s National Institute of Environmental Health Sciences in Research Triangle Park, N.C., took a closer look at the association between increased levels of circulating vitamin D and estrogen-containing contraceptives found in previous studies, possibly due to alterations in the metabolic pathway of vitamin D. “Previous studies were not able to control for many important variables including time outside,” Harmon says. “We were interested in following up the previous findings in a larger population of young women.”

Measuring serum vitamin D levels from 1,662 African American women ages 23 – 34 in the Detroit area who had been recruited for the Study of Environment, Lifestyle & Fibroids, the researchers found robust support for the association between estrogen-containing contraception and vitamin D levels. Even after controlling for 43 variables, including time outside and supplement use, an independent 20% increase was identified.



AT A GLANCE

- ▶ Environmental exposure to endocrine-disrupting phthalates (metabolites of di[2-ethylhexyl] phthalate) reduces adult circulating total vitamin D levels, particularly in women.
- ▶ Environmental exposure to endocrine-disrupting bisphenol A reduces adult circulating total vitamin D levels in women but not in men.
- ▶ Use of an estrogen-containing contraceptive is associated with a 20% higher serum vitamin D level in African American women of reproductive age.

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SOCIETY

While treatment guidelines are inconclusive about adding liothyronine to levothyroxine to treat hypothyroidism, some patients are convinced that the combination works better for them.



BY ERIC SEABORG

A controversy continues

COMBINATION TREATMENT FOR HYPOTHYROIDISM

YOUR HYPOTHYROID PATIENT COMPLAINS THAT SHE STILL DOES NOT FEEL WELL DESPITE TAKING LEVOTHYROXINE (LT4).

She has been researching on the Internet and has read many accounts from patients in her situation who say that they feel much better when their doctors add another thyroid hormone “called T3 or something ...”

So, you face a dilemma. You have based her treatment on the American Thyroid Association (ATA) guideline that says that levothyroxine (LT4) is the standard treatment. And clinical trials have not found a benefit in adding liothyronine (LT3).

LT4 became the treatment of choice following the discovery that the thyroid primarily makes the prohormone thyroxine (T4), which tissues around the body convert into the active hormone, triiodothyronine (T3). T4 has a half-life of a week or so, while T3's half-life is less than a day. It has worked for most patients to take T4 and let the body do the conversion—except for some 5% to 10% of patients who say it doesn't work for them. Is there a problem in giving them LT3 as well?

Four thyroid experts interviewed by *Endocrine News* all called this combination therapy controversial — but not one of them would refuse to give it a try in an appropriate patient who requested it.

“It is true that levothyroxine has been used for decades and the overwhelming majority of patients are satisfied, but a significant minority are not satisfied,” says Douglas S. Ross, MD, professor of medicine at Harvard Medical School and co-director of Thyroid Associates at Massachusetts General Hospital in Boston. “Why not attempt to mimic normal blood levels with T4 and T3?”



Antonio C. Bianco, MD, PhD, professor of medicine and vice dean of clinical affairs at Rush University Medical Center in Chicago, Ill.

“

It is unquestionable that some patients will tell you that the day they were switched from levothyroxine to combination therapy, ‘a light bulb went on in my brain,’ or ‘I can think again.’ There has got to be something there.

”



Douglas S. Ross, MD,
professor of medicine, Harvard
Medical School; co-director, Thyroid
Associates at Massachusetts
General Hospital, Boston, Mass.

“

There is a problem with using superphysiologic levels of T3, so I don't suggest anyone take extract. But if you provide T4 and T3 at the appropriate ratio, why should that be considered problematic?

”

“It is unquestionable that some patients will tell you that the day they were switched from levothyroxine to combination therapy, ‘a light bulb went on in my brain,’ or ‘I can think again.’ There has got to be something there,” says Antonio C. Bianco, MD, PhD, professor of medicine and vice dean of clinical affairs at Rush University Medical Center in Chicago, Ill.

What the Guidelines Say

Bianco's view is particularly interesting because he co-chaired the task force that prepared ATA's latest hypothyroidism guidelines in 2014, which concluded that LT4 should remain the standard of care: “We found no consistently strong evidence for the superiority of alternative preparations (e.g., levothyroxine-liothyronine combination therapy, or thyroid extract therapy, or others) over monotherapy with levothyroxine in improving health outcomes.” Even among patients who “feel unwell on levothyroxine therapy alone, there is currently insufficient evidence to support the routine use of a trial of a combination of levothyroxine and liothyronine therapy outside a formal clinical trial.”

The European Thyroid Association guideline says that “combination therapy should be considered solely as an experimental treatment” overseen by “accredited internists/endocrinologists, and discontinued if no improvement is experienced after three months.”

The most recently published guideline — from the Italian Thyroid Association in late 2016 — says that combination therapy is “generally not recommended” but a trial “may be considered to improve adherence to treatment or patient well-being.” Perhaps in a concession to reality, it outlines a protocol for combination therapy.

Literature Lacks Evidence

Combination treatment is clearly in use; Bianco estimates that about half the hypothyroid patients referred to him are on it. Much of the interest stems from a tantalizing 1999 study of 33 Lithuanian hypothyroid patients (most of whom were receiving suppressive LT3 doses for thyroid cancer treatment) that concluded that combination therapy “may improve mood and neuropsychological function.” Those findings have proven difficult to duplicate. “Subsequently, there were 10 or 12 studies designed to look at combination therapy in a systematic manner using different ratios of thyroxine to T3. For the most part, none of those studies showed any consistent effect, and four meta-analyses of the literature concluded that there was no consistent benefit,” says James V. Hennessey, MD, director of clinical endocrinology at Beth Israel Deaconess Medical Center.

But the effectiveness of combination therapy remains an open question because of flaws in previous studies and a lack of well-designed, randomized trials, according to Jacqueline Jonklaas, MD, PhD, MPH, associate professor of endocrinology and metabolism at Georgetown University Medical Center, Washington, D.C., and co-chair of the ATA guideline task force: “In the 13 or so combination therapy trials that have been done, the majority only gave the T3 once a day, a few of them gave it twice a day, and that really isn’t enough to maintain nice steady levels of T3.”

Bianco agrees: “When we give combination therapy, we are actually not normalizing serum T3. We are creating pulses of T3. So during a few hours you have a higher level of T3. Then a few hours later, you have a lower level than what you want. Unless we develop a delivery system to provide a steady level of T3, we are not in a position to answer whether combination therapy is better or worse than monotherapy.”

“People have been talking for decades about a time-released T3 medicine,” says Ross. “But that appears to be difficult to make because pharmaceutical companies have not come up with it yet,” despite a potential market of millions of patients. Correct dosing might require taking LT3 several times a day, and for most people compliance would be an issue.

The inability of researchers who design clinical trials to figure out an effective system to administer T3 might give pause to clinicians considering the treatment.

The Ratio Rationale

Ross suggests that a logical treatment strategy is to try to mimic the normal physiological ratio of T4 to T3 of about 14 to 1: “The clinical literature is muddled by the fact that most people who have tried to give T4 and T3 have given way too much T3. There is one study by Escobar-Morales that actually gave the appropriate ratio of T4 and T3. And while the researchers could not demonstrate any physiologic benefit, patients preferred the combination of T4 and T3.”



AT A GLANCE

- ▶ **Levothyroxine has been the long-standing standard treatment for hypothyroidism, but a significant minority of patients are dissatisfied with it.**
- ▶ **Although guidelines discourage adding liothyronine to levothyroxine, this combination therapy is not only in use, but many patients prefer it.**
- ▶ **Experts say the controversy over combination treatment can only be resolved with well-designed, randomized clinical trials.**



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ENDOCRINOLOGY IN THE NEWS

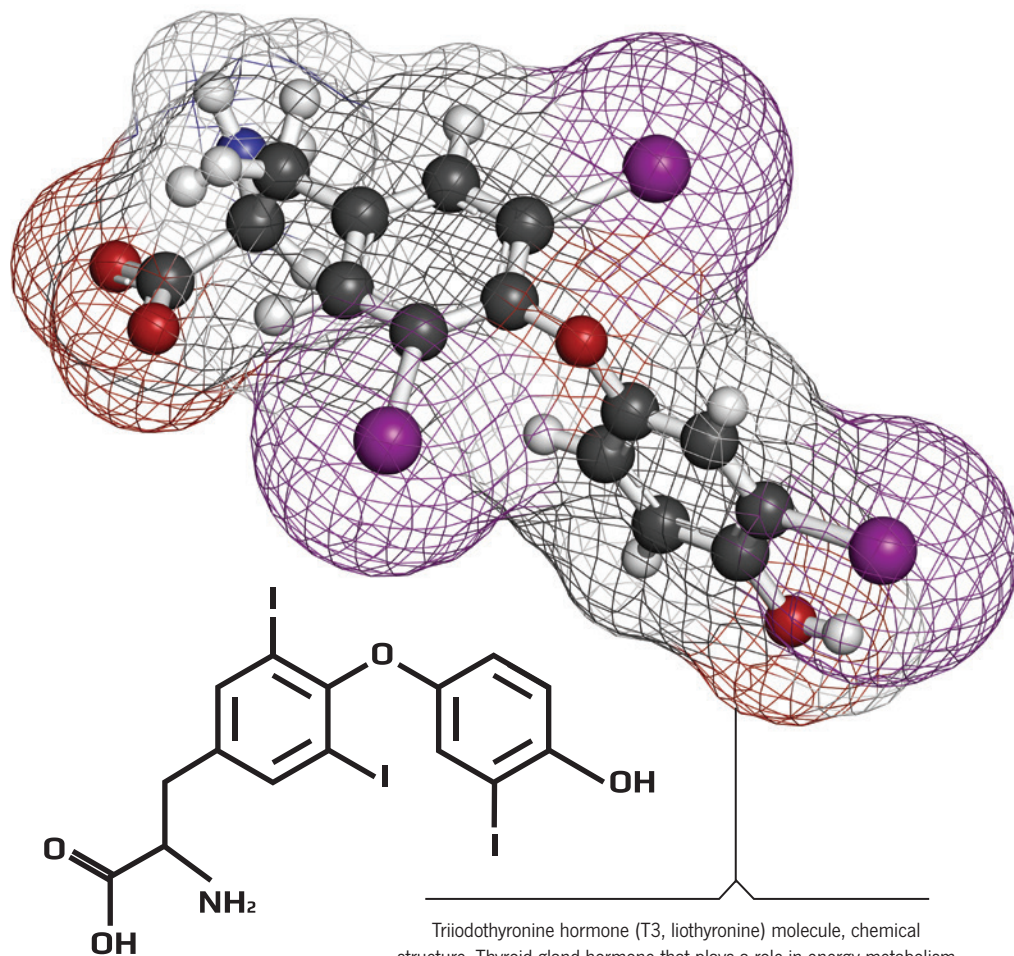
Presidential candidate Hillary Clinton's health became an issue in the campaign when she scaled back some activities when suffering from pneumonia. A condition mentioned in her physician's letters that received less attention was her hypothyroidism. Her physician said Clinton was being treated with the extract Armour Thyroid, which had kept "her thyroid blood tests within normal limits...and stable for many years." The Endocrine Society responded to several press inquiries related to her treatment.

But basing treatment on patients' preferences may not lead to the best outcomes. "T3 has also been used by psychiatrists as adjunctive therapy for depression, so part of this feeling better issue may have to do with the effects of giving too much thyroid hormone," Ross says. "If you give people a little bit too much T4, in general they feel better. Their mental health is better, but their physical health is a little bit impaired. They will complain that they aren't sleeping as well, but they feel better overall and they are less depressed. It may simply be that slightly hyperthyroid people feel better."

The T4 to T3 ratio is one reason why all the guidelines recommend LT4 over thyroid extracts. Extracts from pig thyroid glands are rich in T3, at a T4 to T3 ratio of 4 to 1, which the guidelines say raises safety concerns.

The guidelines also agree that there are some circumstances in which combination therapy should be avoided, such as pregnancy. "The fetus seems to run on maternal T4, rather than T3, and so there is a concern that the fetuses of women taking extract or combination therapy may not have appropriate neurologic development," Ross says.

Another patient population where caution is warranted is the elderly. The ATA guidelines note that "the elderly are more susceptible to the adverse effects of thyroid hormone excess, especially atrial fibrillation and osteoporotic fractures," so T3 peaks could be worrisome.



Triiodothyronine hormone (T3, liothyronine) molecule, chemical structure. Thyroid gland hormone that plays a role in energy metabolism regulation. It is a iodine containing derivative of tyrosine.

In Conclusion ... or Inconclusive

“We just don’t have the data yet to change my mind that adding T3 to T4 actually results in a superior product,” Hennessey says. But he adds: “I see patients on a regular basis who say, ‘I am completely dysfunctional.’ Then someone offers them T3, and the next day they are up performing their activities of daily living as if they have never had thyroid disease. In my opinion, it happens way too quickly for it to actually be thyroid hormone action. But the patients are wedded to it. I tell them that I’m not sure that it was the T3 that did it. But as long as they are not doing any harm by taking too much T3, I am certainly willing to continue to be supportive of their care.”

Ross does not see the harm in trying a different approach when patients are not satisfied with LT4 alone: “There is a problem with using superphysiologic levels of T3, so I don’t suggest anyone take extract. But if you provide T4 and T3 at the appropriate ratio, why should that be considered problematic?” ^{EN}



James V. Hennessey, MD, director of clinical endocrinology at Beth Israel Deaconess Medical Center, Boston, Mass.

“

We just don’t have the data yet to change my mind that adding T3 to T4 actually results in a superior product.

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Jacqueline Jonklaas, MD, PhD, MPH, associate professor of endocrinology and metabolism, Georgetown University Medical Center, Washington, D.C.

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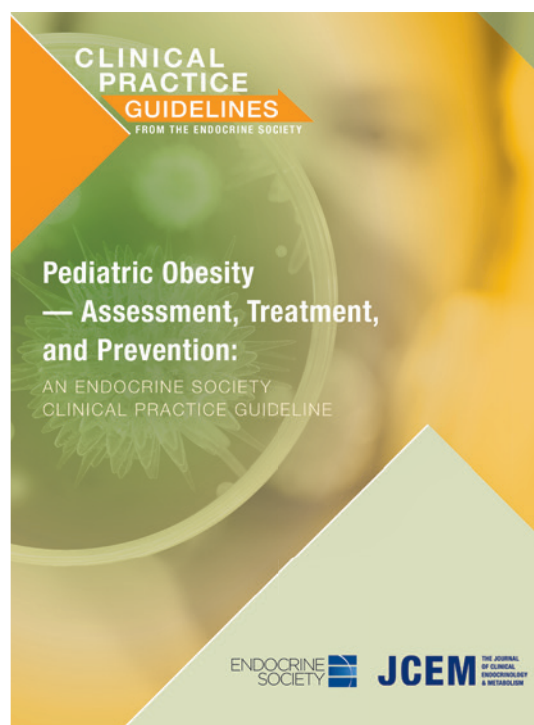
In the 13 or so combination therapy trials that have been done, the majority only gave the T3 once a day, a few of them gave it twice a day, and that really isn’t enough to maintain nice steady levels of T3.

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Cold Cases

BY ERIC SEABORG



A new resource is available for clinicians who have patients with symptoms that make their diagnosis a challenge.

When the patient showed up at a Baylor College of Medicine clinic in Houston with an unusual case of sexual dysfunction, endocrinologist Ashok Balasubramanyam, MD, had a diagnostic ace up his sleeve.

The ace was a new resource for combining data and expertise to solve medicine's toughest cases — the Undiagnosed Diseases Network (UDN) of the National Institutes of Health (NIH) — which came up with a novel explanation for the patient's condition.



A professor in the Division of Endocrinology at Baylor College of Medicine, Balasubramanyam says that Baylor is one of the seven clinical sites across the country selected by the NIH for the network, but that any physician can refer a patient.

Balasubramanyam's patient was a 30-year-old African-American male with a fully developed penis, small testicles, and sexual difficulty such as an inability to have full erections. He had male secondary sexual characteristics that were consistent with his low testosterone levels, and lacked sperm. He had been wrongly diagnosed with "Klinefelter syndrome" when he was 16.

An Unexpected Gene

The patient received a full phenotypic workup and karyotyping, which showed that, despite appearing male, he had two X chromosomes. "XX males are rare but not unknown," Balasubramanyam says. "The reason that they look phenotypically male is almost always because the SRY gene — which until recently was thought to be the principal male sex-determining gene — is somehow transposed onto an X chromosome. So even though they have two X chromosomes, they have the critical gene that makes you a male stuck to one of them."

Although this patient did not have the SRY gene, he did have a mutation on a gene called NR5A1, which is also known as steroidogenic factor-1 because it is powerful in steroidogenesis.

When Balasubramanyam presented the case at the annual meeting of the UDN sites, an investigator from another site said that they had encountered similar patients with the same mutation in the NR5A1 gene. "This is a great advantage of having groups of interested people working in the same field coming together," Balasubramanyam says.

These patients with the NR5A1 mutation presented with a range of phenotypes, including XY females. "Its precise regulation in sexual differentiation remains somewhat unclear, but the literature showed that NR5A1 can be critical for regulating SRY expression, and that mutations in this gene are associated with sexual dysfunction," Balasubramanyam says. "We hypothesize that the location of this specific mutation within the NR5A1 gene appears to work as a kind of 'switch' in the process of sexual development. If there is a single amino acid change at this site against a background of an XX, it gives rise to a male phenotype. But if there is a different amino acid change at the same site against the background of an XY, it appears to give rise to a female phenotype."

Although there is no "cure," the patient is satisfied that he at least has a definitive diagnosis for making his plans for the future and is doing well on testosterone. The Baylor research team is working on "knocking in" the NR5A1 mutation into *drosophila* and mice, to determine the mechanisms by which this switch may regulate the cascade of signals required for full sexual differentiation.

Genesis of the Network

Balasubramanyam says that the UDN is an outgrowth of whole genome or exome sequencing becoming faster and cheaper, which led NIH to look for new ways to harness this new knowledge and combine it with other kinds of emerging data. The UDN has its roots in a predecessor pilot called the Undiagnosed Disease Program (UDP) at NIH that began in 2008. An analysis of the first two years of the UDP found that of 160 patients, diagnoses were made in 39. The diagnoses included two previously undescribed disorders, 23 rare diseases in 28 patients, and nine common conditions.

The success of that program led the NIH to expand it to a full network by committing to spend \$117 million over five years. After a year spent coordinating and setting up procedures, the UDN issued a call for patient applications in September 2016 and by the end of the year had reviewed nearly 900 applications and accepted over 450 patients.

"The network offers an in-depth medical record review for all applicants and an extensive clinical and research evaluation for patients accepted into the study," says Kimberly Splinter, MS, CGC, project manager at UDN's coordinating center at Harvard Medical School. "This evaluation involves numerous tests and procedures, which often occur over the course of a two- to five-day in-person visit at one of the UDN clinical sites. Investigation into

a participant's condition typically does not end there. Additional research often occurs for months and years after the in-person visit is complete and involves a high degree of communication across UDN sites and medical specialties."

In addition to the clinical sites, the network includes two DNA sequencing sites, two model organism screening sites, and a metabolomics analysis site. The model organism sites look for clues in *Drosophila* and zebrafish models by, for example, knocking genes in or out.

The metabolomics core site applies innovative and advanced assay methods to samples sent from UDN's clinical sites for detection and quantitation of metabolites to generate a unique molecular profile for each patient. According to the core's website, its goal is "to integrate metabolomic and genomic data with clinical signs and symptoms, in order to generate hypotheses regarding pathophysiology that can be translated into specific clues regarding the etiology of the undiagnosed disorders being evaluated."

The Power of the Internet

The UDN is also trying to harness the power of the Internet to reach out to both physicians and patients. "We have incorporated an Internet-case finding strategy into the UDN with the goal of identifying patients with the same or similar condition and confirming diagnoses," Splinter says. "We are creating pages on the UDN website that describe the medical history and genetic findings of interested UDN participants. We receive inquiries from people who find these pages and think that they might know someone with the same condition." The UDN website includes articles designed to help physicians and patients make their own searches, such as "Discovering new diseases with the Internet: How to find a matching patient" and "Participant-driven matchmaking in the genomic era."

How to Refer a Patient

"The UDN is interested in evaluating individuals with conditions that remain undiagnosed despite thorough evaluation, ongoing care, and follow-up by a healthcare provider," Splinter says.

When a potential patient is referred to the UDN, a committee vets the application and distributes those accepted among the clinical sites. Patients are often referred to the nearest clinical site, but may be sent to a site with a particular expertise in a condition.

"I would say to any endocrinologist, ... if you find a patient that you have worked up and you cannot nail down the diagnosis, ... please send in the application," Balasubramanyam says.

"We would love to get more physicians, and especially more endocrinologists, involved and enthusiastic about this program. It's potentially a huge benefit for the patients and their families, as well as for clinical science."

ELIGIBLE PATIENTS

Patients must meet certain criteria before they will be considered for study by the UDN

- ▶ Have a condition that remains undiagnosed despite thorough evaluation by a healthcare provider;
- ▶ Have at least one objective finding; and
- ▶ Agree to the storage and sharing of information and biomaterials in an identified fashion amongst the UDN centers, and in a de-identified fashion to research sites beyond the network.

— UDN Clinical Sites —

Baylor College of Medicine, Houston, Texas

Duke Medicine, Durham, N.C., with Columbia University Medical Center, New York, N.Y.

Harvard Teaching Hospitals (Boston Children's Hospital, Brigham and Women's Hospital, and Massachusetts General Hospital) in Boston, Mass.

National Institutes of Health Clinical Center in Bethesda, Md.

Stanford Medicine in Palo Alto, Calif.

University of California, Los Angeles in Los Angeles, Calif.

Vanderbilt University Medical Center in Nashville, Tenn.

Physicians interested in referring a patient can find the application at the UDN website: <https://gateway.undiagnosed.hms.harvard.edu>.

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT A VARIETY OF NEW OPTIONS TO TREAT OBESITY IN THE MARCH ISSUE.

Five Ways to Lower Your Pipettes Costs

BY GLENDA FAUNTLEROY



They are one of the many necessities you need to keep your research on track. But the omnipresent pipettes can also be one of your lab's biggest costs if you're not careful. *Endocrine News* has assembled some tips to keep those costs down, while you keep your research going.

Unexpected and ongoing excessive costs are common complaints from staff charged with managing pipettes in the laboratory. While pipettes are only one segment of the wide inventory of equipment used in today's labs, they can make up a large part of necessary annual budgets.

Whether you have ten pipettes or a thousand, managing your laboratory's pipettes can be an arduous process. Pipettes that are poorly maintained, for instance, can lead to costly errors — errors that can reach in the hundreds of thousands of dollars, according to a recent white paper published by TTE Laboratories, a Hopkinton, Mass.-based pipette calibration and repair service provider.

To help reduce the number of errors made in your laboratory and lower your pipette costs, follow these five steps:

► **Commit to employee training.**

User errors with pipettes account for as many as 70% of pipette errors made in today's laboratories, according to the white paper. Different levels of user skill and awareness can lead to pipette measurement variability, which can greatly affect test accuracy and hamper confirmation of results. Help eliminate user error by contracting with one of the leading pipette service companies to provide instructions to your staff on the proper pipetting techniques. Service companies offer a range of training options including online webinars or one-on-one hands-on coaching and guidance. When choosing a provider company, ask whether their training program provides a detailed analysis of before and after performance data.

► **Take proper care.**

Proper use and maintenance of your important instruments creates lasting savings. Pipettes that are misused or dropped should be taken out of service and repaired right away. "In our experience, customers who hold their employees accountable by assigning specific pipettes to particular assays, technicians, or even locations see the fewest problems," reports TTE Laboratories.

► **Calibrate on schedule.**


Timely calibration is one of the most important things you can do to maintain costs. Choose a service provider that adheres to proper calibration guidelines. How often your pipettes should be calibrated depends on your application and how frequently the pipette is being used. The American Society for Testing and Materials (www.astm.org) recommends calibration that contains quarterly control checks of 10 data points and monthly verification checks of four data points. Using a reputable service provider will guarantee fast turnaround on your calibration service to keep your laboratory up and running with minimal down time. Be sure to get your calibration service done right and on time.

“Whether you have ten pipettes or a thousand, managing your laboratory's pipettes can be an arduous process. Pipettes that are poorly maintained, for instance, can lead to costly errors — errors that can reach in the hundreds of thousands of dollars.”

► **Do your research before you replace.**

Pipettes can be expensive to replace. Hold back on buying pipettes based on price or brand loyalty alone, suggests TTE Laboratories. Lab managers should do enough research to learn about pipettes that have the lowest costs to own instead of buying the same instruments repeatedly. The costs of ownership include services, repair, and risk of drifting inaccuracy and imprecision that leads to potential assay failure. New models are being regularly introduced to the market that include excellent features that prevent errors, downtime, and repairs. Even the most trusted brands could have chronic repair problems and hidden expenses. Add these following points to your checklist of considerations: a long history of durability and performance, comfort in use, and modern features, such as a volume-lock mechanism.

► **Use validated pipette tips.**

Without the appropriate tip, a pipette is useless. Although they are cheaply sold in bulk and are meant to be disposable, tips greatly affect the accuracy of your pipettes. They are not meant to be universal and can widely vary in performance and quality. Have your service provider evaluate your tips to be sure they are validated to your specific pipette. If validating means paying more for the proper tips, do not hesitate to find a supplier willing to work within your budget. 



Representative Paul D. Ryan (R-WI),
Speaker of the House



Congress Moves Forward with Repeal of the Affordable Care Act

Republican lawmakers in the House of Representatives introduced the American Health Care Act (AHCA) in early March to repeal pieces of the signature legislation of the Obama administration, the Affordable Care Act (ACA) also known as “Obamacare.”

At the core of the new proposal is a belief that consumers will accept fewer benefits and guarantees as long as they have lower costs and the freedom to forego coverage if they want. While President Obama’s 2010 healthcare law broadened coverage for the poor and the sick, Republicans now are focused on reducing regulations, which they believe will reduce costs for everyone.

Despite significant concerns voiced by the Democrats, consumer groups and the AARP, as well as conservative members of the Freedom Caucus, the Republican leadership plans to move the draft legislation through the House voting process before Easter. If passed by the full House of Representatives, the legislation will be sent to the Senate with the goal of having it signed into law by the president before Memorial Day.

Passage of the AHCA is just one piece of the Republicans’ plan to address the Affordable Care Act. Congress is working closely with Health and Human Services Secretary Tom Price to make further administrative changes that would eliminate or alter

portions of the ACA, such as the recently released insurance market stabilization rule. Additional legislation beyond the AHCA is being considered by the House to make changes to malpractice and antitrust regulations and wellness programs.

The AHCA would leave several of the ACA’s more popular insurance reforms in place, including elimination of the preexisting conditions exclusion, coverage of adult children up to age 26 on their parents’ plan, and capping out-of-pocket expenses. It also would maintain the prohibition on lifetime and annual limits. The Society is advocating for continuation of these provisions as part of its health system reform priorities.

The proposed legislation, however, would also make several controversial changes, including removing the individual mandate requirement, eliminating the essential benefit requirements, and shifting the healthcare law’s current focus on helping lower-income people.

The most reviled policy from Obamacare for Republicans is its mandate that most people buy insurance. Republicans, reflecting the views of many voters, despise the mandate and have vowed to kill it. However, it is inextricably linked to the law’s most popular provision — prohibition on insurance company practices to discriminate against consumers with pre-existing conditions. Our concern stems from the notion that if consumers know insurance companies will not raise

prices because an individual is sick, why would healthy people buy insurance? They could simply wait until they got sick, sign up for coverage, and potentially drop off again after receiving treatment. The result would be no mix of healthy and sick people to balance the costs, but mostly sick people seeking services. The Republicans' compromise so far is to keep the pre-existing conditions protection, but only for consumers who have maintained health insurance for some period of time. They argue that even without a mandate there would be a strong incentive for Americans to pay for coverage. In contrast, opponents argue that there is a myriad of scenarios where personal or financial hardships could force someone to go uninsured for a short period of time, leaving them with no way to purchase affordable, comprehensive coverage for the foreseeable future.

Another change in the Republican proposal is the relaxation of the ACA's essential benefit requirements. Obamacare listed 10 categories of services that insurers must cover like maternity care, hospitalization, and preventive services as a minimum for acceptable coverage. Republicans want to eliminate those minimum standards. They say requiring lots of benefits drives up prices and healthy people do not want to pay for services they are confident they will not need.

Other proposed changes would shift the healthcare law's focus on helping lower-income people.

The legislation would transition the ACA subsidies for lower-income Americans to discount premiums to tax credits adjusted by age rather than by income and geographic location. The Republican proposal would reduce by 36% the average tax credits available to people who do not get insurance through their jobs, Medicare, or Medicaid. Although no official estimates of the number of individuals covered under the AHCA have been released, independent analysis from the S&P Global Ratings estimates that up to 10 million people would lose coverage.

The ACA allowed states to expand Medicaid eligibility to nearly all low-income individuals with incomes at or below 138% of poverty, resulting in new coverage for millions of people. Under the Republican proposal, states would be able to continue to enroll adults in the expansion through 2020, when enrollment would be frozen. Anyone who transitioned off the program after that would not be brought back on with the same higher federal payments. States that did not accept

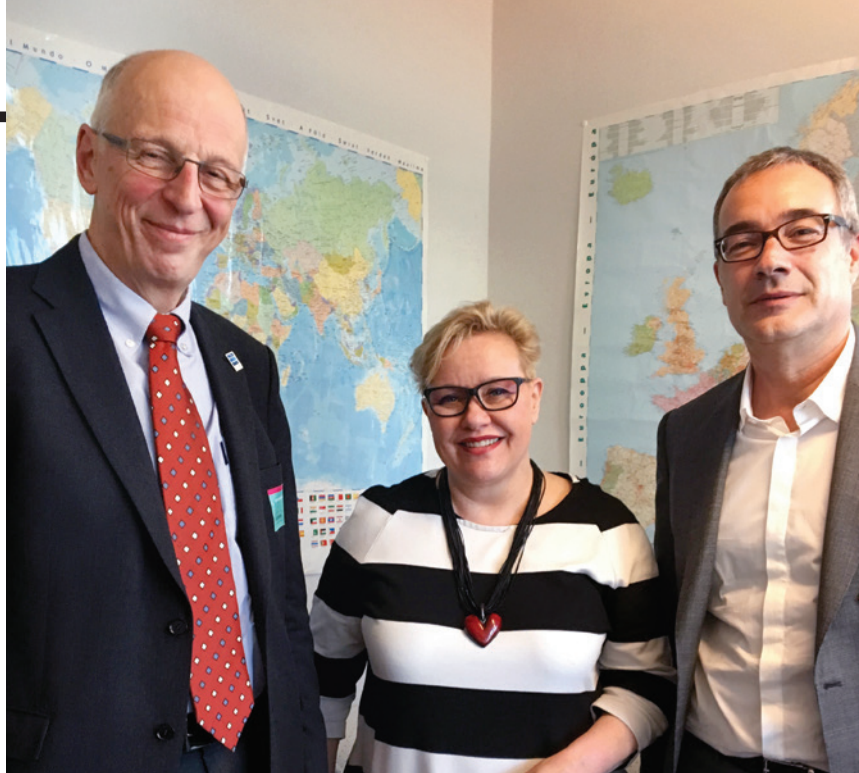
the expansion would get some money to help stabilize their markets. While some conservative lawmakers say that this plan is too generous, Democrats argue many people will lose Medicaid coverage they depend on.

Although Republicans have an aggressive timeline for consideration of the AHCA, there are still hurdles that must be overcome. House Democrats have signaled that they will not vote for the bill, meaning that House leadership must hold the fragmented Republican caucus together for the legislation to pass. Members of the Freedom Caucus have already signaled reservations with the approach being taken as they believe that it establishes a new government welfare program. If and when the bill overcomes these obstacles to clear the House, it will face other hurdles in the Senate where the Republican majority is narrower. With only 52 Republicans in the Senate, the leadership must have support from the entire caucus, and many Republican senators have already signaled concerns with the legislation.

The Endocrine Society has shared with Congress and the administration core principles we believe must be incorporated into any proposal: access to affordable and adequate health insurance, maintenance of the Prevention Fund and preventive services, protection of women's healthcare, and healthcare delivery models that include coordinated care. We have also identified specific provisions of the AHCA with which we have concerns. To see our letters to Congress outlining the Society's positions, please visit www.endocrine.org/advocacy-and-outreach/letters-and-alerts.

TAKE ACTION: We encourage all U.S. members to join the Society's advocacy campaign alerting Congress to our priorities and concerns about the health reform proposal. Please visit www.endocrine.org/advocacy to send a letter to your congressional delegation. You need only to provide your address and our online system will provide a letter template and direct the email to the proper offices.

Endocrine Society Meets with EU Policymakers to Discuss EDC Criteria



As part of the Endocrine Society's Global Endocrine Disrupting Chemicals (EDC) initiative, the Society has engaged with lawmakers in the European Union to ensure that policies governing decisions involving EDCs are based on the latest endocrine science. On March 8 and 9, members of the Endocrine Society's European Union Endocrine Disrupting Chemicals Task Force from France, Spain, Italy, Belgium, and the United Kingdom traveled to Brussels for a series of meetings with EU policymakers, including 17 Members of the European Parliament (MEPs). The meetings came at a critical time, as the European Commission recently released further revisions to proposed criteria to define EDCs in the context of applicable EU laws.

The European Union has struggled for nearly half a decade to identify workable criteria for EDCs. The current proposal uses the World Health Organization's definition for EDCs, but introduces modifications to this option that result in a very narrow definition that will prevent effective regulation. In addition, the latest proposal includes provisions that would exclude pesticides because their chemicals are designed to interfere with the endocrine system of non-human organisms. During the meetings, the Society's representatives discussed the latest science on EDCs, why the proposed criteria would not protect public health, and how the criteria would instead create further confusion if implemented in their current construction. The Endocrine Society has consistently advocated for a set of criteria that would rank EDCs in multiple categories based on available scientific evidence. This option would allow for new data to be incorporated as more studies are published.

Endocrine Society members Jean-Pierre Bourguignon, MD, PhD, (Belgium) and Angel Nadal, PhD, (Spain) meet with Finnish Member of the European Union Sirpa Pietikainen (center) on March 9 to discuss EU policy criteria for endocrine-disrupting chemicals.

Policymakers at the meetings shared their thoughts on the positions of member state governments regarding the criteria and on the anticipated outcome of the current debate. They also made suggestions on how the expertise of endocrinologists and endocrine scientists can be effectively incorporated at different steps before and immediately following adoption of the criteria. Although at the time this article was written, the final text of the criteria is uncertain, so it is clear that the Endocrine Society has influenced the debate and our members will continue to be valuable contributors as the process for implementing the criteria moves forward. Regardless of how the final criteria are written, the Society will continue to advocate for policies that will protect public health from harms due to EDC exposures and seek opportunities to contribute to EU regulatory decisions involving EDCs.



Endocrine Society Participates in March for Science; Join Us in Advocating for Support of Science


“The mission of the March includes raising awareness ‘about the very real role that science plays in each of our lives and the need to respect and encourage research that gives us insight into the world.’”

— ENDOCRINE SOCIETY MEMBER JOANNA SPENCER-SEGAL, MD, PHD IS A MEMBER OF THE STEERING COMMITTEE FOR MARCH FOR SCIENCE

On April 22, 2017, scientists from around the world are planning marches to celebrate many ways science has profoundly improved people’s lives. The March for Science event will provide opportunities for scientists from all disciplines to elevate their level of civic engagement and amplify how science serves society, accelerates medical progress, and creates a better world for the next generation. The Endocrine Society is supporting this event, but also encouraging its members to call on policymakers to support science, support public funding of research, and support policies based on scientific evidence.

Endocrine Society member Joanna Spencer-Segal, MD, PhD is a member of the Steering Committee for the March for Science. She explains that the mission of the March includes raising awareness “about the very real role that science plays in each of our lives and the need to respect and encourage research that gives us insight into the world.”

Many of the goals and messages of the March for Science are consistent with the long-standing advocacy priorities of the Endocrine Society, such as celebrating science and supporting federal funding of scientific research. The Society has developed an online toolkit (www.endocrine.org/marchforscience) to facilitate participation in advocacy activities. The online toolkit provides information on where marches will take place, how to get involved, how to contact policymakers, and a sample letter template. Even if you cannot attend the March in Washington, D.C., or one of the other marches around the world, it is even more important for Endocrine Society members to contact elected representatives and policymakers to share the messages about the importance of science. In addition, for those Endocrine Society members who will be attending ENDO 2017 in Orlando, we encourage you to visit the Endocrine Society Booth to pick up an information card with links to our online toolkit. March for Science “Support Hormone Science” T-shirts and buttons will also be available at the Endocrine Society Store.

The long-term success of the March for Science will depend on the consistent engagement of scientists and others supporters of biomedical research in advocacy. The Endocrine Society will continue to provide members with opportunities to advocate for funding for the National Institutes of Health and other endocrine priorities. For more information on how to get involved with our research advocacy efforts, please visit www.endocrine.org/advocacy. 

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- Above average compensation package that includes income guarantee and production bonuses
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Details at www.aspirusprovideropps.org

Contact Jamie Sitko at Jamie.Sitko@aspirus.org or 800.792.8728

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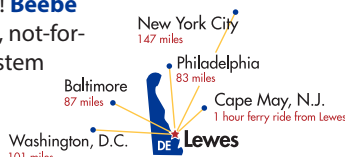
Endocrinologist Opportunity

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Plant your roots in our sand! **Beebe**

Healthcare is a progressive, not-for-profit community health system

with a 210-bed hospital, a planned multi-million dollar expansion, and numerous satellite facilities throughout coastal Delaware.



One main hospital location in Lewes, with additional surgery center and outpatient campuses around Southern Delaware. A short drive from major East Coast destinations.

About the Endocrinologist Opportunity:

- Endocrinologist BC/BE
- Excellent opportunity working with an established practice and Beebe's Diabetes Management Dept.
- Employed within Beebe Medical Group, a multi-specialty hospital network
- Base salary plus incentive and comprehensive benefits package
- This position offers operational support so you can focus on medicine

About Beebe Healthcare:

- Repeatedly recognized with national awards
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- Margaret H. Rollins School of Nursing

About the area:

- Nationally ranked family-oriented beaches and boardwalks by *Parents Magazine*, *National Geographic*, *Travel and Leisure*, and *American Profiles*
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Email cover letter and CV to Marilyn Hill, Director of Physician Services, mhill@beebehealthcare.org • www.beebehealthcare.org

c/o Beebe Medical Group Administration • 1515 Savannah Road, Suite 102 • Lewes, DE 19958

This is not a visa sponsored opportunity.

Beebe Healthcare is a non-smoking and fragrance free system.

HORMONES AND ERECTILE DYSFUNCTION

WHAT YOU NEED TO KNOW

The endocrine system is a network of glands and organs that produce, store, and secrete hormones, which are really important in maintaining a healthy sex drive. Hormones play a big role in men's health, affecting energy, weight, mood, sex, fertility, and much more. Low blood testosterone (male sex hormone) concentrations can result in a lower sex drive and even erectile dysfunction. This is a condition in which a man may have trouble getting or keeping an erection.

WHAT IS ERECTILE DYSFUNCTION






Erectile dysfunction (ED), or **impotence**, is the inability to consistently get or keep an erection (hard penis) long enough to have satisfactory sex.

While it's perfectly natural to notice a gradual decrease in **libido** (sex drive) as you age, the degree of decline varies. Men generally maintain some interest in sex well into their 60s, 70s, and beyond. If you're concerned about loss of sex drive, especially if it happens suddenly, you should consult your doctor. He or she can do a physical exam and request lab tests to determine the cause.

COMMON CAUSES

The most common causes of ED are underlying health problems that affect blood vessels and blood flow in the penis. These include hardening of the arteries (atherosclerosis), diabetes, obesity, smoking, high blood pressure, and high cholesterol.

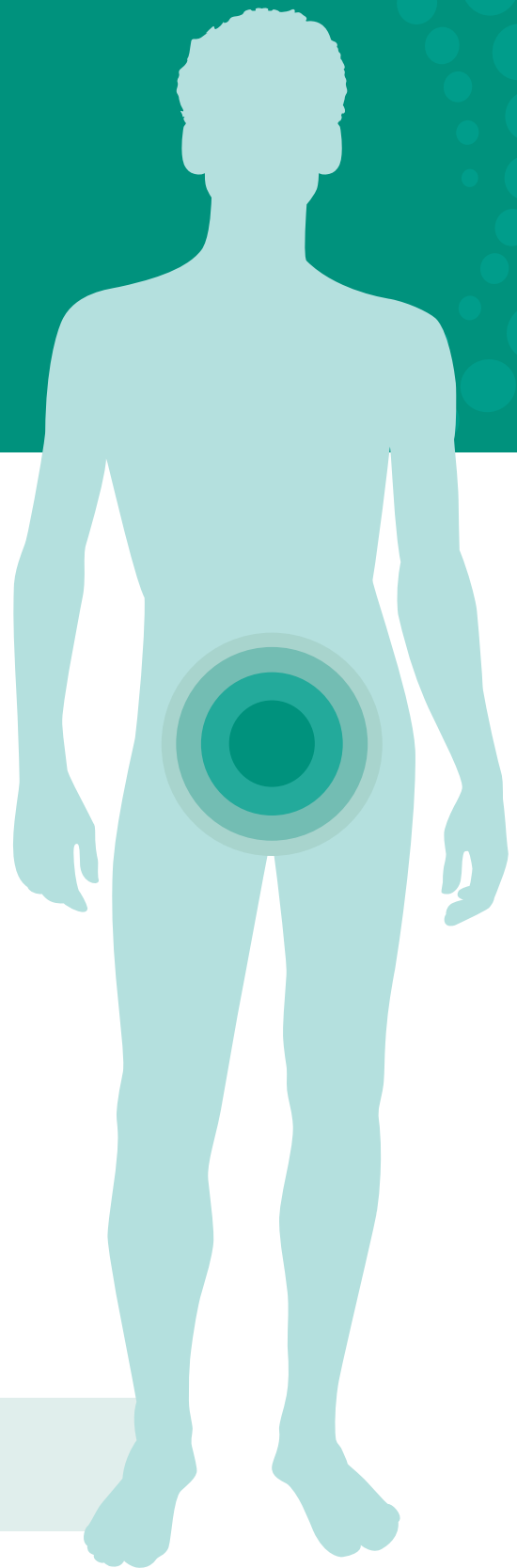
Other common causes of ED may include:

-  Depression or stress
-  Anxiety or fear of sexual failure
-  Decrease in blood testosterone due to an endocrine disorder
-  Medications (antidepressants, sleeping pills, and drugs to treat high blood pressure, pain, or cancer)
-  Alcohol and illegal drugs

Even if ED has a physical cause, emotional factors may make the condition worse.



Don't be embarrassed. It's worth it to have an open and honest discussion with your doctor about your loss of sex drive or erectile dysfunction. A healthy sex life is part of a healthy life in general.



Visit hormone.org for more information.

Additional Editing by Bradley D. Anawalt, MD,
University of Washington



Hormone Health
NETWORK®
Keep your body in balance

DID YOU KNOW?

While it is true that older men may not get “turned on” as quickly, they should still be able to get and keep an erection and enjoy sex.

- Researchers estimate that ED affects as many as 30 million men in the United States.
- About 12 percent are younger than age 60.
- About 30 percent are age 70 or older.

Source: National Institutes of Health

Complications of ED may include:

- Unfulfilled sex life
- Emotional problems, including depression, anxiety, and low self-esteem
- Loss of intimacy with partner, causing a strained relationship
- Inability to get partner pregnant

DIAGNOSIS

Your doctor will carefully evaluate your medical history, including a history of sexual function, medications, illnesses, emotional changes or injuries that could be causing your ED. He or she may also give you a physical exam, schedule lab work like a urinalysis and blood tests, or ask you mental health questions.



TREATMENT

If you only have ED “every once in a while,” you may not need treatment. If your doctor diagnoses you with ED, then the options to treat it will depend on the cause and may include medicine, lifestyle changes, therapy, devices, and other options.

4 QUESTIONS TO ASK YOUR DOCTOR

- Could my ED be caused by another condition?
- Are any of the medications I’m taking making it worse?
- What are the pros and cons of your recommended treatment?
- Are there lifestyle changes I might make to improve my condition?

LIFESTYLE CHANGES THAT MIGHT HELP

- Quit Smoking
- Limit or stop drinking alcohol
- Increase physical activity
- Stop illegal drug use



Patients have questions. We have answers.

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



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FROM THE ENDOCRINE SOCIETY

Endocrinologist



Ochsner Health System in New Orleans is seeking **BC/BE ENDOCRINOLOGISTS** to join our expanding team that includes seven Endocrinologists, seven Advanced Practice Clinicians, and five Certified Diabetes Educators.

Opportunity details:

- Leadership opportunities available.
- Flexible call schedules.
- Sign-on bonuses and relocation assistance.
- Clinical practice opportunities include serving as investigator on diabetes clinic trials; US guided thyroid FNAs, as well as CGMS, thyroid US and Bone Density interpretation.
- Opportunity to engage in mentoring our four endocrinology fellows, as well as internal medicine residents and medical students on rotation.

Ochsner Health System is southeast Louisiana's largest non-profit, academic, multi-specialty, healthcare delivery system. Coordinated clinical and hospital patient care is provided across the region by Ochsner's 30 owned, managed and affiliated hospitals and more than 60 health centers. Ochsner employs more than 1,000 physicians in over 90 medical specialties and subspecialties and conducts over 600 clinical research studies. Ochsner is the only Louisiana hospital recognized by U. S. News & World Report as a "Best Hospital" across three specialty categories caring for patients from all 50 states and more than 80 countries worldwide each year. Our medical school, the Ochsner Clinical School, in partnership with the University of Queensland in Australia, enrolls 130 medical students each year. For more information, please visit our website at www.ochsner.org.

New Orleans is one of the most exciting and vibrant cities in America. Amenities include multiple universities, academic centers, professional sports teams, world-class dining, cultural interests, renowned live entertainment and music.

Interested physicians should email CV to profrecruiting@ochsner.org or call 800-488-2240.
Reference # NOEND-8

Sorry, no J-1 visa opportunities exist.

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Please visit us at booth #633 at the Endo Expo 2017 in Orlando!

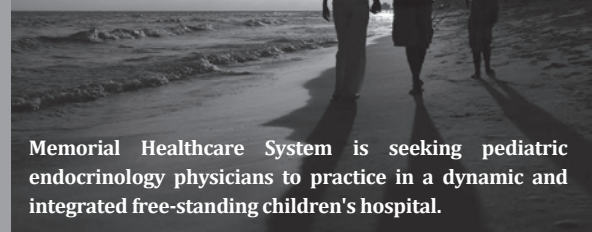
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U.S. News & World Report

Physician Career Opportunities in South Florida



Memorial Healthcare System is seeking pediatric endocrinology physicians to practice in a dynamic and integrated free-standing children's hospital.

Located in South Florida, Memorial Healthcare System is one of the largest public healthcare systems in the United States.

South Florida offers an urban/suburban lifestyle with an abundance of cultural and recreational amenities. With its miles of beautiful beaches, top-rated golf courses, museums and world-class dining, South Florida offers an excellent quality of life. In addition, Florida has **no state income tax**.

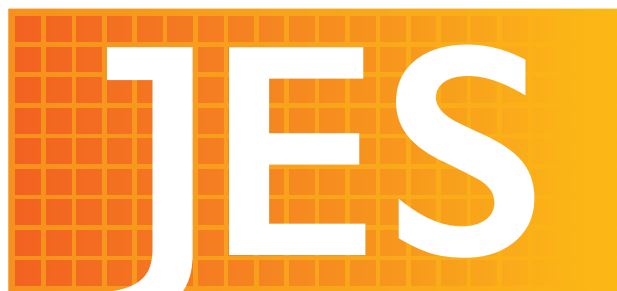
Available positions include:

- Medical Director, Pediatric Endocrinology
- Pediatric Endocrinology (Staff) - Palm Beach, FL

To submit your CV for consideration, please visit memorialphysician.com.

[visit memorialphysician.com](http://visit.memorialphysician.com)

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