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DUST in the MIND

Could a Home that Can't Pass a "White Glove Test" Lead to Overweight Kids?

From END 2019

A new study presented at **ENDO 2019** seems to indicate that endocrine-disrupting chemicals in household dust could increase the likelihood of obesity in children. However, keeping a clean house may not be a viable solution since many common household cleaners also contain these chemicals.

PILLOW TALK:

More research links sleep to endocrine health

PELLETING PATIENTS:

The problems of customized biodentical hormones



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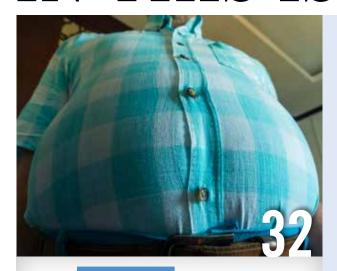
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Introducing New Endocrine Society President, E. Dale Abel, MD, PhD

he Endocrine Society is pleased to welcome its president for 2019 – 2020, E. Dale Abel, MD, PhD who took office March 25, 2019. As chair and department executive officer of the Department of Internal Medicine and director of the Fraternal Order of Eagles Diabetes Research Center at the University of Iowa, his work focuses on cardiovascular complications of diabetes and mechanisms of insulin resistance. Abel is also very involved in mentoring students, research and clinical trainees.

"It's a mix of excitement and a bit of trepidation given the significant responsibilities of the role," Abel says. "With that said, I'm obviously very motivated to serve in this important role."

Abel succeeds Susan Mandel, MD, MPH, as the Society continues its rotation of presidents who represent its core constituencies: basic science researchers, clinical researchers, and clinical practitioners. He credits the support of the past two presidents, Mandel and Lynnette Nieman, MD, as well as the Endocrine Society staff and the Society chief executive officer Barbara Byrd Keenan for bringing him up to speed and preparing him to serve as Society president.

Abel earned his medical degree with Distinction at the University of the West Indies in his native Jamaica (he's the first Jamaican president of the Endocrine Society), before going on to earn his DPhil (PhD) in Physiology at Oxford University as a Rhodes Scholar. He did his residency at Northwestern University in Chicago and fellowship in endocrinology and metabolism at Harvard Medical School and Beth Israel Deaconess Medical Center in Boston.

Abel decided to become an endocrinologist after one of his professors of medicine in medical school inspired him to consider endocrinology as his specialty. Abel says at that time many advancements were being made in receptor biology and the transport of metabolites across cells throughout the body, and this work inspired him to pursue his PhD after medical

school. At Oxford, under Professor John Ledingham, Abel focused his research on insulin resistance and hypertension, which fueled his desire to pursue a career in endocrine research.

He was also inspired by Lewis Landsberg, MD, chair of Medicine at Northwestern to pursue the field in earnest. He found the field to be very intellectually challenging. "I like that," he says. "I like the integrated nature of endocrine circuits." As an endocrine fellow in 1992, Abel says that it became clear to him that the Endocrine Society would be his professional home. He got a trainee membership the next year, and since then, Abel has been involved in myriad aspects of the Society. "I think I've served on almost every committee," he says with a chuckle.

That's a fair assessment. Abel first served on the Minority Affairs Committee, then the Research Affairs Committee (while serving on Scientific Statements Task Forces), the Advocacy and Public Outreach Core Committee, the Strategic Planning Committee for SP3, and many more before being elected to council. In 2012, Abel became the principal investigator of the Society's Future Leaders Advancing Research in Endocrinology (FLARE) program, which provides structured leadership development and in-depth, hands-on training in topics that include scientific communication, networking and negotiating skills, grantsmanship, and lab management. FLARE participants have included junior faculty, basic science, and clinical research trainees from underrepresented minority communities who have expressed a strong desire to succeed in endocrine research careers.

"I've been in continuous service to the Society since the beginning," Abel says. "And what's kept me going is that there are very few organizations that have such tremendous member engagement and a passionate sense of ownership by the membership. We feel like we are doing something that is very important, and that builds very strong loyalty."

As president of the Endocrine Society, Abel's goals are to

guide the implementation of the changes in Society governance should these be approved by members, which he says will increase the relevance of the Society and support the endocrine community to face the challenges of the 21st century. "It will increase the representation and the diversity of our council and board and to reflect members' interests," he says. (See page 19 for details.)

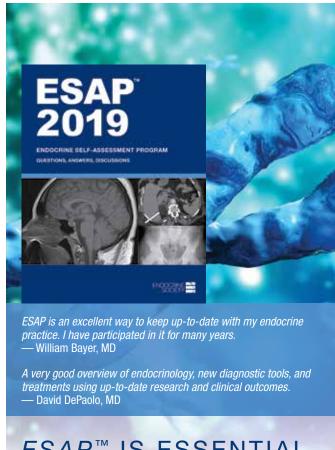
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There are very few organizations that have such tremendous member engagement and a passionate sense of ownership by the membership. We feel like we are doing something that is very important, and that builds very strong loyalty.

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Another of Abel's goals is to increase the outreach by the Society to basic scientists. For instance, the Society has initiated direct outreach and increased collaboration with basic scientists through smaller meetings. He says that he's particularly excited about the Society's global growth and outreach and he hopes that it continues in a way that's both manageable and able to keep up with the needs of a growing membership. He's also looking forward to furthering the Society's impact on the field of endocrinology itself through enhanced educational programs, content, and advocacy for endocrine clinical practitioners and endocrine researchers. "Very importantly, as president, I'll be working closely with our council and staff to strengthen our financial viability to continue to support these programs."

Abel says one of the things that inspires him is his work as a mentor, and as president, he wants to ensure that the Society has the tools to encourage and foster the next generation of leaders. "I think it's important that we focus on members across their professional life cycle," he says. "That way, we ensure we have a well-trained and motivated pipeline to replace the likes of me and others when we move on."



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FROM THE **EDITOR**

Aftermath: Life After ENDO 2019

opefully by the time you receive this issue, your life is as close to normal as possible in the wake of another Endocrine Society annual conference in one of the world's most culturally rich cities, New Orleans! Aside from enjoying some of the most delectable food and drink available on the planet, ENDO 2019 proved to be overflowing with new research in the treatment and science of endocrinology.

However, due to the timing of **ENDO 2019** we are going to feature our annual ENDO wrap up in the May issue, so stay tuned to the May *Endocrine News* for that. Some of the amazing research presented in New Orleans, however, is featured in this month's issue including the cover story "Dust in the Wind" by senior editor Derek Bagley on page 30. New research presented by Chris Kassotis, PhD, at Duke University, seems to indicate the presence of endocrine-disrupting chemicals (EDCs) in common household dust, which in turn lead to a higher incidence of obesity in children who are

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The result has been an increase in the number of patients in endocrinologists' offices with issues caused by elevated levels of testosterone from these customized implants.

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exposed. The researchers wanted to look at children and exposures during more critical periods of development than previous studies had addressed, according to Kassotis. "We hypothesized that an early exposure could potentially be more disruptive to metabolic health than an adult exposure (which we had already demonstrated)," he says.

Bagley also writes about another study presented at ENDO 2019 by Muralidharan Anbalagan, PhD, an assistant professor at the Tulane **APRIL 2019**

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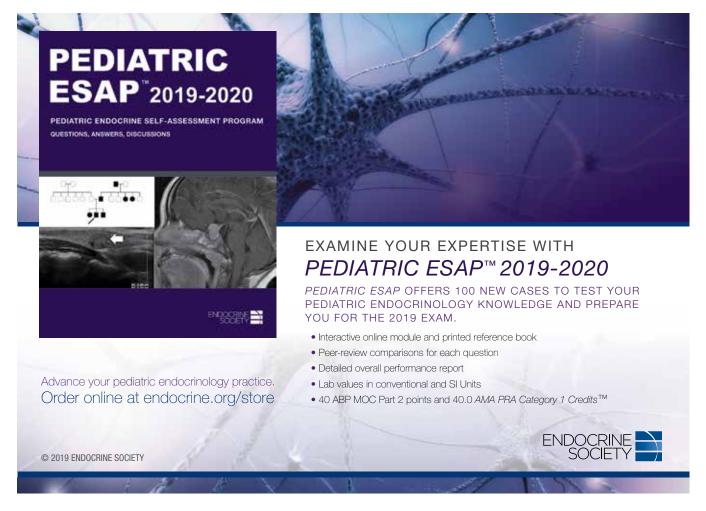
University School of Medicine in New Orleans, that links dim light at night — cell phones, e-readers, televisions, etc. — to the metastases of breast cancer to the bones. In "Pillow Talk" on page 40, Anbalagan says, "If you don't adjust your lifestyle, the circadian disruption by light at night is going to be a huge problem, especially for people who live in large, bright cities as well exposure of lights to night shift workers such as nurses and flight attendants."

On page 44, we take a look at the constant battle to conquer obesity and the possible side-effects weight-loss solutions may have on the patients, some of which have turned out to be positive. Writer Kelly Horvath tackles three very different yet similar studies from the Endocrine Society's *Journal of Clinical Endocrinology & Metabolism* that look at issues surrounding dieting and gastric bypass surgery. In "Gaining Weight, Losing Ground," the topics range from how increased muscle strength is a previously unnoticed benefit of gastric bypass to the impact of weight cycling on people with diabetes, and how, in some cases, mind over matter can have a tangible effect on weight loss.

In "Targeting Patients with Pellets," (p. 34), writer Eric Seaborg takes a critical look at an alarming trend that has been causing more than its fair share of consternation among many endocrinologists of late: the increase usage of custom-compounded biodentical hormones. The result has been an increase in the number of patients in endocrinologists' offices with issues caused by elevated levels of testosterone from these customized implants. What's more, these products are gaining traction through word-of-mouth, anti-aging clinics, and online promotion as "more natural" and "individualized" approaches to correcting "hormone imbalance" compared with FDA-approved hormone replacements.

In anticipation of May's ENDO 2019 coverage, if you have any New Orleans stories you want to share, feel free to email me at mnewman@endocrine.org or tweet at me @Endocrine_News with the #ENDO2019 hashtag. No matter what time of year, ENDO will always be trending!

- Mark A. Newman, Editor, Endocrine News



Stewart Named Editor-in-Chief of The Journal of Clinical Endocrinology & Metabolism



aul M. Stewart, MD, FRCP, FMedSci, executive dean and professor of medicine at the University of Leeds in the U.K., has been named the next editor-in-chief of the Endocrine Society's *The Journal of Clinical Endocrinology & Metabolism* (ICEM).

JCEM is the world's leading peer-reviewed journal for endocrine clinical research and cutting-edge clinical practice information. The journal provides the latest in-depth coverage of new developments that contribute to the understanding, diagnosis, and treatment of endocrine and metabolic disorders.

"I am honored to work alongside such a respected editorial team to lead one of the most prominent journals in medicine and science," Stewart says. "JCEM is internationally recognized for its quality outputs, and I will continue to build on this great reputation to publish groundbreaking and practice-changing research for our ever-growing global readership."

Stewart will succeed R. Paul Robertson, MD, to serve a three-year term beginning January 1, 2020. He currently serves as an associate editor for *Journal of the Endocrine Society*. He has previously served on the editorial boards of JCEM and *Endocrinology* and on the advisory board of *Endocrine Reviews*. He was a former senior editor of *Clinical Endocrinology*.



"I enthusiastically welcome Paul Stewart to the role of editor-in-chief of JCEM," says Society pastpresident Susan J. Mandel, MD, MPH. "Paul's international perspective, combined with his stellar clinical research career and extensive editorial experience, well position JCEM to lead as the premier endocrinology journal."

Stewart is a past member of the Endocrine Society Council and has served on six Endocrine Society committees over recent years. In addition to his role as university executive dean of medicine and health, he is an honorary consultant endocrinologist at the Leeds Teaching Hospitals NHS Trust where his clinical expertise extends to patients with pituitary and adrenal disorders and endocrine hypertension.

He supervises a translational research group that focuses on corticosteroids, specifically cortisol metabolism via 11β -hydroxysteroid dehydrogenases, and his work has led to new discoveries in hypertension, obesity, aging, and polycystic ovary syndrome.

He is a primary investigator within the National Institute for Health Research (NIHR) Biomedical Research Centre in Leeds and an Emeritus NIHR senior clinical investigator. He is a fellow and clinical vice president of the UK Academy of Medical Sciences.

JCEM publishes monthly in print and continuously online; it can be accessed at https://academic.oup.com/jcem.

Council Approves Governance Task Force Recommendations

fter a year of thoughtful deliberation, in March the Governance Task Force (GTF) reported to the Council on ways to enhance our Society's governance — how we organize the Society to get things done. We are thrilled to announce that Council approved these recommendations by unanimous consent and will present the needed bylaws amendments to the membership for a vote of ratification earlier this month.

The field and our members have changed since our last full governance review in 2001. We are now a strong and diverse

global network of 18,000 investigators and practitioners; about half of us live outside of the U.S. We are a unique society made up of leaders with varied professional responsibilities who influence endocrinology from bench to bedside to health policy. The GTF recommendations reflect this evolution and seek to enrich our members' experiences and strengthen our leadership teams and pipeline.

For the past three decades, we have classified members into constituent groups defined by three traditional roles of our members: basic scientist, clinical scientist, and physician-

Members of the Council, Governance Task Force, member guests, and staff participated in the June 2018 Governance Retreat where they provided insight and guidance to inform the Governance Task Force's work.



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in-practice. We have chosen our leaders under a tripartite rotation as well. However, increasingly our professional roles do not fit neatly into a single category. For example, more than half of the respondents to a recent survey indicated that they have an educator role in addition to other responsibilities; others indicated a primary professional role not currently recognized in the constituencies. These members are disenfranchised from serving on our Council. Under the GTF recommendations, we will shift to an expanded "professional profile," which will allow members to selfidentify with multiple professional roles. For example, currently a basic scientist can only choose that role. In the future, a member can identify as a basic scientist without clinical responsibilities or as a basic scientist with educator duties as well, allowing us to better understand our members' professional lives, serve their needs, and assure that our governance is representative of this diversity.

Two of the GTF recommendations are predicted to enhance the value of membership

for everyone. First, we endorse providing leadership development training for all members at all career stages. Training will be aligned to the competencies needed as a member, committee member, committee chair, etc., and will be developed so that it is useful at your workplace and while doing Society work. Second, we will ask you to update your profile to tell us how you want to be involved with the Society. The new expanded professional profile will help us to better match you with meaningful opportunities to volunteer for service.

These expanded profiles also will help us build a highly skilled and diverse Nominating Committee and Council — to be known as the Board of Directors in the future (a term better understood worldwide). The Nominating Committee will be

expanded to 15 members to better represent our entire membership, and the Board will remain unchanged at 15 members. All members will be encouraged to submit nominees to serve on the Board and the Nominating Committee.

The President occupies the highest officer position in the Society. As such, it is important to many Society members, and to the GTF, that it remain an elected position. Thus, the Nominating Committee will continue to slate two candidates for President-elect for members to vote on each year. However, it is equally important to ensure that the Board is effective and strategically balanced. To ensure that the Board reflects our diverse membership, the Nominating Committee will appoint one person to fill each vacant Board seat, without designated seats. With the emphasis on balance, members will be chosen on their leadership attributes, how they represent our diverse membership, and their ability to advocate for and represent the scientific nature and values at the core of our Society.

The Council and GTF believe that these recommendations will improve representation of our global community, educators, and basic scientists without clinical roles.

This is an exciting time for our Society as we enhance our governance structure. We ask that you check your email and vote to ratify the bylaws changes to help grow and strengthen our Society. For more information and to read the full GTF report, please go to endocrine.org/membership/gtf.

— Lynnette K. Nieman, MD, chair, Governance Task Force; E. Dale Abel, MD, PhD, president; Gary Hammer, MD, PhD, presidentelect; and Susan Mandel, MD, MPH, immediate past president

Endocrine Society Hires Experienced Executive as Chief Strategic Partnerships Officer



ichel Y. Farhat, PhD — a seasoned executive with more than 20 years of experience in the pharmaceutical industry — has joined the Endocrine Society as its chief strategic partnerships officer.

In his new role, Farhat will develop and execute a global strategic partnerships strategy. He will identify opportunities to collaborate with stakeholders to provide information and tools for Society members and endocrine patients worldwide. He also will lead the Society's Corporate Liaison Board, which forges partnerships between the Society and senior executives in industry.

Farhat brings extensive experience building strategic alliances and networks of influencers and organizations to this position. He spent the past five years serving as senior director, Patient and Professional Advocacy, for Novo Nordisk Inc. Prior to leading Novo Nordisk's professional advocacy function, he spent 15 years in various medical affairs and professional advocacy roles for Procter and Gamble's over-the-counter brands and pharmaceutical products.

"The Endocrine Society is forming important collaborations that expand access to care, accelerate discovery, and promote public health," Farhat says. "I am honored to have the opportunity to foster these important connections and build new relationships that will be instrumental in our leadership of the global endocrine community."

Farhat has served on boards and committees for the American Academy of Family Physicians, JDRF, the American Heart Association, and other medical industry professional organizations.

"Michel's extensive experience building partnerships and deep understanding of the healthcare industry are valued assets for our team," says Society CEO Barbara Byrd Keenan, FASAE, CAE. "True collaborations are essential for achieving our ambitious goals of unifying and growing the endocrine field. We are delighted to welcome Michel to our team."

Farhat understands Society members' careers as a veteran of academic research. He spent 10 years at Georgetown University Medical Center, where he ultimately became an associate professor. Farhat graduated with his Doctor of Philosophy degree in pharmacology from the American University of Beirut. He is fluent in English, Arabic, and French.

TRENDS & INSIGHTS



BY DEREK BAGLEY
Senior Editor



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AFFs can be devastating, but even under the most pessimistic assumptions, the benefit/risk ratio is highly positive for BPs, particularly during three to five years of use. As understanding of AFFs increases. it is becoming increasingly possible to maximize BP benefits while minimizing AFF risk.

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Review Examines Relationship Between Atypical Femur Fractures and Bisphosphonates

paper recently published in *Endocrine Reviews* covers atypical femur fractures (AFFs) and examines their relationship with bisphosphonates (BPs), as well as prevention of these rare but devastating bone breaks.

The review, by Dennis M. Black, PhD, of the University of California, San Francisco, et al., points out that BPs have been the mainstay in the treatment of osteoporosis since the early 1990s, but by about 2006, AFFs emerged as a potential side effect to these drugs. Organizations like the American Society of Bone and Mineral Research, the European Society on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis, and the International Osteoporosis Foundation released position papers and statements, and the FDA held a hearing on the safety of BPs in 2010. This all eroded patient and physician trust in

these drugs, which led to about a 50% decrease in their usage from 2007 to 2012.

However, AFFs remain extremely rare, and the benefits gained from BPs used when treating more common fractures far outweigh the risks of AFFs. "Under the most likely set of assumptions about AFF risk [relative risk of 1.7 for any BP use], upon treating 10,000 osteoporotic women for three years, 1,000 fractures, including 110 hip fractures, would be prevented while causing only 0.08

AFFs," the authors write. "Stated another way, for one AFF associated with three years of BP treatment, ~1,200 fractures (including about 130 hip and 850 vertebral fractures) would be prevented."

The authors continue by writing that there remains significant controversy between the use of osteoporosis therapies and duration of therapy to the risk of AFFs and about the pathophysiology of AFFs. "This review discusses the current evidence regarding their epidemiology and pathogenesis, clinical implications, and recommendations, and it identifies areas where future research is needed," they write.

The review covers a lot, but the authors write that there seem to be specific risk factors that could put patients at a higher risk for AFFs, including bone geometry, race, and conditions like diabetes. But since the mechanisms for these risk factors aren't well understood, they should be further studied.

Findings: The authors also write that temporary drug holidays after three to five years of therapy are appropriate for BPs in patients at low risk of fracture. In fact, there are some data that show a drug holiday can decrease AFF risk, which means an improved benefit/risk ratio. Still, the

authors write, "[m]ore research about the impact of temporary BP drug holidays on AFF risk is needed."

"In conclusion," the authors write, "AFFs can be devastating, but even under the most pessimistic assumptions, the benefit/risk ratio is highly positive for BPs, particularly during three to five years of use. As understanding of AFFs increases, it is becoming increasingly possible to maximize BP benefits while minimizing AFF risk."



Genetic Studies Provide Possible Mechanistic Link Between Endometriosis and Ovarian Cancer

enetic breakthroughs from three recent whole-exome sequencing studies of endometrial and endometriotic epithelial cells provided some unexpected findings linking endometriosis and ovarian cancer, according to a paper recently published in *Endocrinology*.

The paper, by Serdar E. Bulun, MD, of the Feinberg School of Medicine at Northwestern University in Chicago, notes that while associations between endometriosis and epithelial ovarian cancer have been reported, the mechanisms haven't been well understood.

In this paper, the researchers review and discuss the results from three exome-wide sequencing studies that demonstrated commonly occurring epithelial mutations in PIK3CA and ARID1A in endometriosis that are uniquely shared with clear cell and endometrioid ovarian epithelial cancers. These studies also showed mutations in KRAS that are commonly observed in low-grade serous ovarian cancers are uniquely observed in the epithelial cells of extraovarian endometriotic lesions. "As a further twist," the authors write, "the epithelial cells (a.k.a., glandular cells) in histologically and clinically normal endometrial tissue harbors many driver mutations (e.g., PIK3CA, KRAS) with comparable mutant allele frequencies to those found in ovarian endometriotic epithelium."

The authors go on to write that the stromal cells seem to lack any mutations that would alter protein function, but these endometriotic stromal cells contain numerous epigenetic defects that favor overproduction of E2 and overexpression of the steroid receptor ER β that mediates an intense and E2-induced inflammatory process involving overproduction of cytokines and prostaglandins.

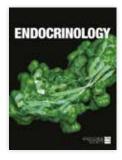
These findings raised some intriguing questions, the authors write, so they set out to provide answers



and a plausible link between epithelial mutations in endometriosis and ovarian cancer initiation. Epithelial mutations in endometriosis driving ovarian cancer makes sense because endometriosis occurs as a result of retrograde menstruation, and these cells can become implanted in ovarian inclusion cysts or extraovarian peritoneal or subperitoneal sites.

As for the non-mutated stromal cells, their widespread epigenetic defects alter gene expression and induce an inflammatory environment. "In addition, massively high concentrations of estrogen in the ovary may exert an additional and direct genotoxic effect on DNA and cause accumulation of additional mutations and malignant transformation in initially mutated endometriotic epithelial cells in an ovarian endometrioma, which may initiate epithelial ovarian cancer," the authors write.

Findings: The authors point out that this focused review only attempts to provide some initial thoughts on the questions the findings of these genetic studies raised. "Developing novel disease models and paradigm-shifting approaches will be essential to providing definitive answers to these challenging questions," they conclude.



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Individuals using statins may be at higher risk for hyperglycemia, insulin resistance, and eventually type 2 diabetes. **Rigorous** preventive strategies such as glucose control and weight reduction in patients when initiating statin therapy might help minimizing the risk of diabetes.

Statins Linked to Higher **Diabetes** Risk



ndividuals who take statins may be at higher risk for developing high blood sugar levels, insulin resistance, and eventually type 2 diabetes, according to an analysis published in the British Journal of Clinical Pharmacology.

Researchers led by Prof. Bruno Stricker of the Erasmus Medical Centre in the Netherlands point out that while there are several epidemiological studies on the association between statins and incident diabetes, most of them lack details. "In this study, we aimed to investigate the association of statin use with glycemic traits and incident type 2 diabetes," the authors write.



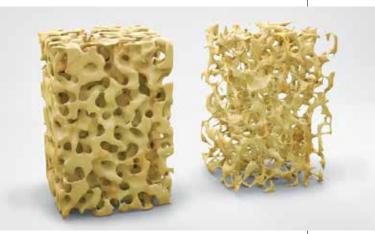
Compared with participants who never used statins, those who used statins tended to have higher concentrations of serum fasting insulin and insulin resistance. Participants who ever used statins had a 38% higher risk of developing type 2 diabetes during the study. This risk was more prominent in individuals with impaired glucose balance and in overweight/obese individuals.

Findings: Based on these findings, the authors conclude: "Individuals using statins may be at higher risk for hyperglycemia, insulin resistance, and eventually type 2 diabetes. Rigorous preventive strategies such as glucose control and weight reduction in patients when initiating statin therapy might help minimizing the risk of diabetes."

"The findings suggest that in patients who initiate statin therapy, preventive strategies such as blood sugar control and weight loss may be warranted for minimizing the risk of diabetes," Stricker says.

Oral Complications Are Rare in Older Women Treated for Osteoporosis

ral complications are rare in women taking medications for postmenopausal osteoporosis, according to a study published in *The Journal of Clinical Endocrinology* & Metabolism.



Osteonecrosis of the jaw (ONJ) is exposed bone in the jaw that is slow to heal (eight weeks or longer, with effective treatment), usually after a major dental procedure. It was first reported in 2003 in patients with advanced cancer receiving high doses of zoledronic acid and denosumab. Rates in cancer patients receiving high doses are around 1% to 2% per year. ONJ is less common in patients with osteoporosis receiving lower doses of these medications (about one case every 10,000 patient-years), yet there is still a lot of concern among dentists and patients. The authors write that "[t] reatment recommendations for ONJ emphasize a conservative approach in mild cases, with escalating strategies based on increasing ONJ stage (including

antibacterial mouth rinses, oral antibiotics, and surgical debridement)."

"Our study covered the seven-year extension of the denosumab pivotal trial. We found dental procedures were common among these patients, but ONJ was rare with only 5.2 cases for every 10,000 patient-years. Not only was ONJ rare, but the 11 cases where the outcome is known have healed," says the study's lead author, Nelson Watts, MD, of Mercy Health in Cincinnati, Ohio. "The ONJ cases typically followed dental extractions or poorly fitting dentures. Of the 212 patients with dental implants, only one developed ONJ, and she

continued denosumab, healed her ONI, and still has the implant."

Researchers used data from the sevenyear FREEDOM Extension trial to assess information on oral procedures and cases of ONJ in women taking denosumab for postmenopausal osteoporosis. They found 45% of patients had at least one invasive dental procedure, but the overall rate of ONJ was low. ONJ incidence was higher in those reporting a dental procedure.

"Results from this analysis suggest that denosumab therapy may be continued during routine oral procedures and dental care, and that the low risk of ONJ should be weighed against the previously demonstrated fracture prevention benefits of denosumab therapy in women with postmenopausal osteoporosis," the authors conclude.

Findings: "My hope is our study will help patients and oral care providers be better informed about the low risk of ONJ compared to the fracture prevention benefits of antiresorptive therapy in women with postmenopausal osteoporosis," Watts says.



66

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2019 Clinical **Endocrinology** Update/ **Endocrine Review Board**

CEU East: Miami, Florida, **Sept. 5 - 7, 2019**

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

Miami's Intercontinental Hotel will be the location of the 2019 Clinical Endocrinology Update (CEU) East September 5 - 7, and the Hyatt Regency Seattle will be where the joint meeting of the Endocrine Board Review (EBR) and CEU West take place on September 17 - 21. Each year CEU brings together hundreds of endocrine clinicians for a unique learning experience and opportunities to network with expert faculty and colleagues. Attend the 70th CEU to receive the most trusted and clinically relevant information about recent advances in the field of endocrinology. The educational programming at CEU appeals to clinicians at all levels of practice, as well as fellows and other members of the clinical practice team.

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

www.endocrine.org/ceu www.endocrine.org/ebr/2019

> **Early Registration:** Now - August 3, 2019

Society for Inherited Metabolic Disorders (SIMD) 41st Annual Meeting

Bellevue, Washington, April 6 - 9, 2019

The SIMD meeting will feature a half-day joint session with the American College of Medical Genetics and Genomics. Topics discussed include novel inborn errors of metabolism (IEMs) and treatments, diagnosis of IEMs, complementary use of genomics and metabolomics, and a satellite session on cerebral creatine deficiency syndromes hosted with the

Association for Creatine Deficiencies. www.simd.org

Pediatric Endocrine Society Annual Meeting and Pediatric Endocrinology Boards/Pediatric Endocrinology Recertification

Baltimore, Maryland, April 24 - 30, 2019

The Pediatric Endocrine Society (PES) will host the 2019 Board Review Course on April 24 - 26 just prior to the 2019 PES Annual

Meeting and will end in time to attend the PES Committee Meeting on Friday afternoon, April 26th. This unique event is the only course offered by the Pediatric Endocrine Society to provide targeted preparation for the Pediatric Endocrinology Boards and the Pediatric Endocrinology Recertification Exam. It is also an intensive review of pediatric endocrinology for pediatricians and adult endocrinologists. The course utilizes formal didactic sessions, as well as informal question/answer opportunities and social interactions with educational leaders in the field.

www.pedsendo.org

Endocrine and Diabetes Controversies in Adult Primary Care Practice

Brewster, Massachusetts, May 3 - 5, 2019

Endocrine and Diabetes Controversies in Adult Primary Care Practice is intended to provide up-to-date, state-of-the-art continuing medical education for primary care physicians and clinicians who are on the front lines of identifying and managing a wide spectrum of diabetes and endocrine disorders.

http://cmeregistration.hms.harvard.edu/endocrine2019

International Conference on Reproductive Medicine and Biology

Las Vegas, Nevada, May 22 - 23, 2019

The International Conference on Reproductive Medicine and Biology (ICRMB19) provides a global platform for international scholars and researchers to voice their research findings to the world. This conference provides an opportunity for the fertility and medicine industry to learn about current and upcoming issues, explore new developments in culture technology, and interact with others with similar interests. Topics of interest include but are not limited to assisted reproductive technology in vitro fertilization, female reproductive endocrinology, fertility preservation, male reproductive endocrinology, and obesity and metabolism.

www.meetingsint.com

American Diabetes Association 79th Scientific Sessions

San Francisco, California, June 7 – 11, 2019

The Scientific Sessions offers researchers and healthcare professionals an opportunity to share ideas and learn about the significant advances in diabetes research, treatment, and care. Over the course of five days, attendees will receive access to more than 2,800 original research presentations, take part in in-depth conversations with leading diabetes experts, and expand professional networks with colleagues from around the world.

www.professional.diabetes.org

INTERNATIONAL ITINERARY

Keystone Symposia on Immunometabolism and Metaflammation and Metabolic Disorders

Vancouver, BC, Canada, April 14 - 18, 2019

This conference will cover the molecular mechanisms and physiological outcomes of immunometabolic interactions in the context of chronic metabolic diseases. www.keystonesymposia.org/19D6

World Peptide Congress

Tokyo, Japan, April 17 - 18, 2019

The World Peptide Congress will bring together world-class biochemists, scientists, professors, and scholars to concentrate on "Accelerating Current Innovations in Peptide Research." Peptides play important roles in living body systems by controlling, directing, and coordinating inter- and intra-cellular communications and cellular function, and this conference will focus on the latest stimulating patterns and advancements in the field of peptide science.

https://www.meetingsint.com/conferences/peptide

Clinical Diabetes 2019

Osaka, Japan, June 17 - 18, 2019

Clinical Diabetes 2019 is designed to provide an exclusive forum for doctors, dieticians, researchers, scholars, students, and scientists to discuss and learn about the latest advancements, challenges encountered, trends, concerns, applications, and solutions for mitigating diabetes.

https://www.meetingsint.com/conferences/clinicaldiabetes

World Congress on Thyroid Cancer

Rome, Italy, June 20 - 22, 2019

This scientific meeting is organized for experts in the fields of endocrinology and oncology from around the world to share research and ideas to further the understanding of the management of thyroid cancer. The delegates attending this congress lay the groundwork for collaborations and the direction of future thyroid cancer research.

www.thyroidworldcongress.com

9th International Conference on Children's Bone Health

Salzburg, Austria, June 22 – 25, 2019

ICCBH meetings provide an international forum for the presentation and discussion of current basic and clinical science in the field of bone metabolism and bone mass in children, adolescents, and young adults. The conference topics will include bone and mineral metabolism, development, pediatric endocrine practice, among others. (20 CME credits offered.)

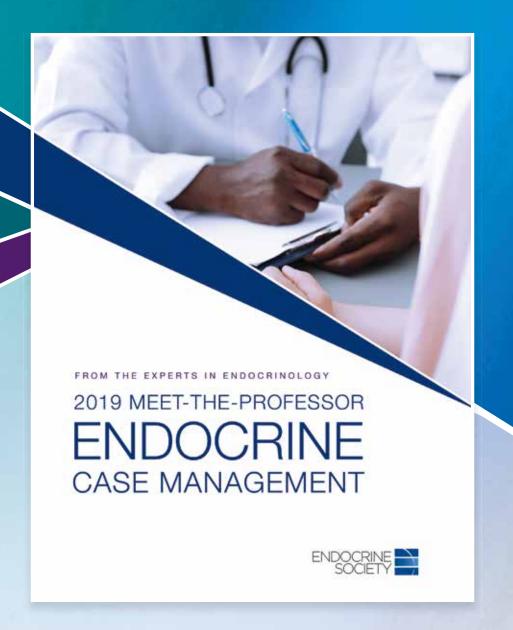
www.iccbh.org

28th European Diabetes Congress

Edinburgh, Scotland, July 17 - 18, 2019

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

www.diabetesexpo.com



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The message patients got was that mainstream medicine hormones are bad, and that message was distorted into: 'Those hormones that doctors give you are bad, but this mom-and-pop shop is compounding this all-natural stuff, and they have not been proven to cause any of those problems.'"

according to NANNETTE SANTORO, MD, Department of Obstetrics and Gynecology, at the University of Colorado School of Medicine in Denver,
 discussing the increase in patients getting biodentical hormones in "Targeting Patients with Pellets" on page 34.

HALL OF PRESIDENTS

Roger Charles Louis Guillemin, PhD

(1986-1987 Endocrine Society President)

Roger Charles Louis Guillemin, PhD, received the National Medal of Science in 1976 and the Nobel prize for medicine in 1977 for discoveries that laid the foundation for brain hormone research.

Guillemin's research has led to treatments for many diseases, including thyroid disease, problems of infertility, diabetes, and several types of tumors. Guillemin was also among the first to isolate endorphins. Additionally, his work with cellular growth factors, in addition to



inhibins and activins, led to the recognition of multiple physiological functions and developmental mechanisms.



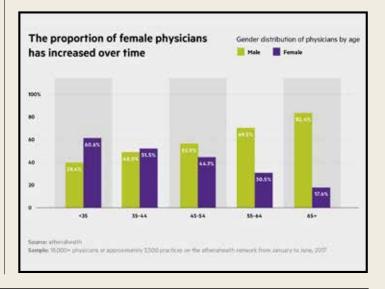
Percentage of transgender patients who postpone care due to fear of discrimination from a healthcare provider – source: MODERN HEALTHCARE

73%

Percentage of Baby Boomers who noticed a health benefit following a vacation.

- SOURCE: AARP, THE MAGAZINE





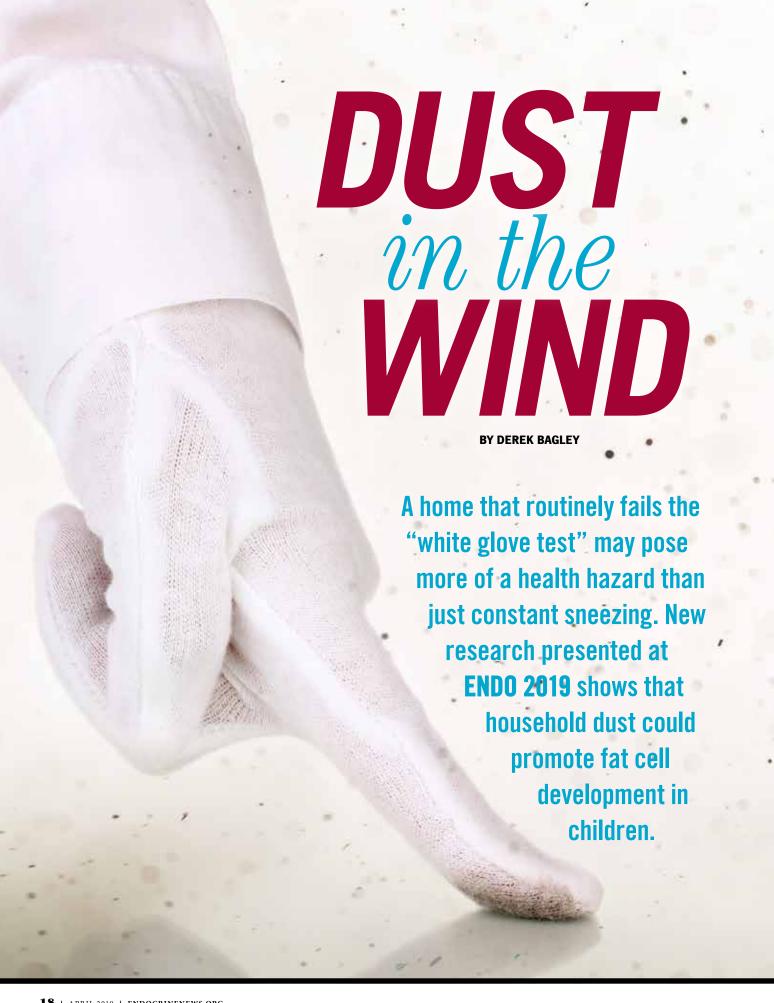


ARE PHYSICIANS BURNED OUT OR DEPRESSED?

45% Burned Out
11% Colloquially Depressed
4% Clinically Depressed

- SOURCE: MEDSCAPI





There's a saying attributed to late interior designer Mario Buatta: "Dust is a protective coating for fine furniture." It's a cheeky statement, to be sure, and it probably started many neat-freaks' eyes twitching, but new evidence shows that not only is house dust unsightly, but it also appears to promote the development of fat cells, even at very limited exposure.



hristopher Kassotis, PhD, of Duke University's Nicholas School of the Environment in Durham, N.C., and his colleagues presented their research at ENDO 2019 in New Orleans, detailing how they investigated the effects of chemicals isolated from dust samples and how they promote growth of fat cells and lipid formation.

Hundreds of chemicals have been measured in indoor house dust by several researchers, including Heather Stapleton, PhD, also of Duke's Nicholas School of the Environment. Stapleton and her colleagues previously showed that many common indoor contaminants in dust can activate the peroxisome proliferator activated receptor gamma (PPARg), often considered the master regulator of fat cell development. "The next obvious question was whether these common contaminants (and house dust) could promote fat cell development in cell models," Kassotis says. "My first project at Duke evaluated a suite of common indoor contaminants, finding that many of these chemicals could promote fat cell development, and that low levels of house dust extracts did as well."

Kassotis and Stapleton, with their colleagues, next explored this association more systematically in a group of adults in a thyroid cancer cohort, evaluating the extent

to which house dust extracts could promote fat cell development in a common cell model and associated this with the metabolic health of adults living in these homes. The researchers recently published their findings in *Science of the Total Environment*.

They found that the extent of fat cell development promoted by the dust extracts was associated with significantly greater thyroid-stimulating hormone concentrations and lower free triiodothyronine and thyroxine in adults living in those homes. The researchers further found a significant and positive association between extent of fat cell development and the body mass index (BMI) of all adults in the study. "These results highlight a contributory role of environmental [thyroid receptor] antagonism as a putative factor in metabolic health," the authors write in their conclusion, "suggesting that further research should evaluate this mechanism and determine whether in vitro adipogenic activity could have utility as a biomarker for metabolic health in residents."

"This suggested that exposures in the indoor environment might play a role in the metabolic health of residents, and we next wondered if this would be more pronounced in children, who may be exposed to these contaminants during a critical window of development," Kassotis says.



Disrupting Metabolic Health

In this current study, Kassotis and his colleagues collected 194 house dust samples from households in central North Carolina, homes inhabited by families who had previously participated in a larger study, and who now had children ages about three to six years old. "Our idea was to look at children and exposure during a more critical period of development than our previous study had assessed. During gestation and early life, precise signaling and levels of hormones are critical to normal development and establishment of regulatory systems," Kassotis says. "We hypothesized that an early exposure could potentially be more disruptive to metabolic health than an adult exposure (which we had already demonstrated)."

The study population demographics reflected those of the Durham, N.C., area — about 40% non-Hispanic white, 40% non-Hispanic black, 20% Hispanic white, and about 55% with a college degree. "Due to their previous recruitment during pregnancy for a previous study, they were perhaps more receptive to another study," Kassotis says, "and participants were most happy about our lab members vacuuming their main living areas – a nice study perk!"

The researchers then extracted the chemicals from dust in the lab and tested their ability to promote fat cell development in a cell model. They found that about two-thirds (125 dust extracts) were able to promote fat cell development, while half (97 dust extracts) promote fat cell proliferation at just 100 micrograms. Children are estimated to ingest between 60 and 100 milligrams of dust each day, according to the Environmental Protection Agency's *Exposure Factors Handbook*.

"Constant Exposure"

But Kassotis here points out that upon further analysis, he and his team did not reveal any striking impacts on child metabolic health, at least not quite the significant impacts they had previously seen on adult health.

Kassotis says that one potential factor in this weaker association may be related to the length of time people had lived in their homes. In the previous study, the adults had lived in their homes for an average of nine years, in contrast to the current study with children in which some of the children had only lived in these residences for several months or years. "That said, we have consistently observed effects of house dust extracts at very low levels, often less than 10 micrograms. In comparison, children are estimated to consume between 60 and 100 milligrams of dust each day, more than 1,000 times this quantity," he says. "While these may seem like low levels, residents are often exposed to these chemicals with great frequency, contributing to nearly constant exposure."

Chemical Imbalance

The results of this current study so far may not have been quite what Kassotis and his colleagues hypothesized, but again, the children haven't had quite the exposure their parents have. And the researchers found several chemicals were significantly elevated in the dust of homes of children who were overweight or obese. So the work goes on.

Kassotis and his colleagues continue to assess the mechanism. He's looking at two potential causative pathways: activation of PPARg and inhibition of thyroid receptor beta (TRb), since



the previous study in adults implicated TRb's role in some of these adverse metabolic effects. "Another path we are still evaluating is the effect of mixtures of contaminants and identifying causative chemicals," he says. "We have measured 111 contaminants in these dust samples, but we suspect that mixture effects of as-of-yet undetermined chemicals are promoting most of the adipogenic activity herein. We have begun to assess that through nontarget analyses, identifying mass spectral signatures present in the samples that are associated with the adipogenic activity and then trying to identify those chemicals."

That non-target analysis has so far found about 35,000 chemicals in the dust of the homes studied, and Kassotis says he hopes this study raises awareness about the vast number of chemicals in the indoor environment. These chemicals come from myriad sources, so Buatta's alleged comment about dust being a protective coating for furniture might not have been that far off the mark after all. But furniture obviously can't experience adverse metabolic effects.

"There are numerous options for reducing these chemicals, from flame retardants to pesticides to plasticizers, etc.," Kassotis says, "and I hope it will allow for more informed decisions from consumers when they make future purchasing decisions."

BAGLEY IS THE SENIOR EDITOR OF ENDOCRINE NEWS. HE WROTE ABOUT THE EFFECT OF SOME ENDOCRINE TREATMENTS ON ADDICTIVE BEHAVIORS IN THE MARCH ISSUE.

AT A GLANCE

- New research shows that chemicals in household dust are implicated in adverse health effects.
- Researchers had previously shown that chemicals in household dust promote fat cell development and inhibit thyroid function in adults, and they are currently studying whether these same effects can be seen in children, who are at a critical stage of development.
- The researchers haven't seen guite as significant an impact in the children as the adults, but the children have had a much shorter duration of exposure, and there's still much work to be done.

Targeting PATIENTS BY ERIC SEABORG With Pellets



Promoted to treat vague symptoms and conditions like "hormone imbalance," custom-compounded bioidentical hormones are increasing in popularity — and problems.



By the time the patient came into the care of endocrinologist Margaret Wierman, MD, she had already had her ovaries removed.

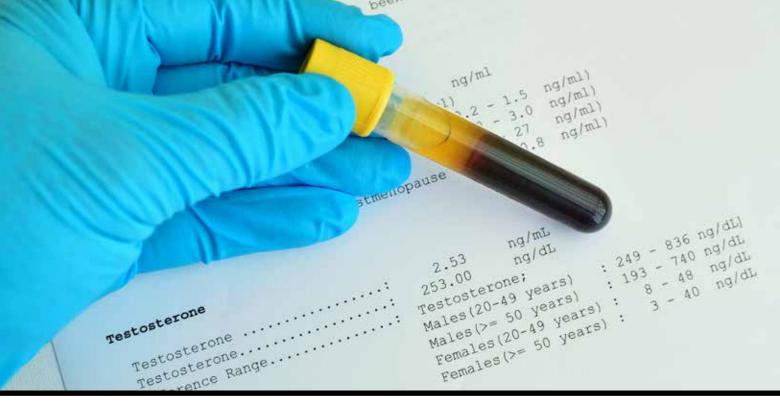
he had presented to the obstetrics and gynecology department with very high testosterone levels and postmenopausal hirsutism that included extra facial hair and male pattern balding. An ultrasound had led to worries about an ovarian tumor, and hence their removal. When her postoperative androgen levels remained elevated, she was referred to endocrinology.

Only when Wierman did an in-depth history did the woman finally reveal that she and her husband had gone to an anti-aging clinic and been implanted with testosterone pellets. "I watched her for over 12 months, as her testosterone slowly fell," says Wierman, who is professor in medicine, OBGYN, physiology, and biophysics at the University of Colorado School of Medicine and chief of endocrinology at the Rocky Mountain Regional Veterans Affairs Medical Center. The patient didn't know to mention the testosterone treatment to earlier providers, perhaps because "she didn't actually know what she had gotten," Wierman says.

The patient had received a treatment known as bioidentical hormone replacement therapy (BHRT)

that is being promoted on the internet, at anti-aging clinics, and by many practitioners. BHRT pellets are subcutaneous implants generally inserted into the hip area and used to treat everything from low libido to hair loss. Hormones may include various estrogens and prohormones such as DHEA or androstenedione, but the most commonly reported problems seem to stem from women given long-term supraphysiologic doses of testosterone, a treatment for which there is no generally accepted medical indication.

Nanette Santoro, MD, E. Stewart Taylor Endowed Chair in the Department of Obstetrics and Gynecology at the University of Colorado School of Medicine in Denver, traces the appeal of this treatment back to a reaction to misleading interpretations of the results of menopausal hormone therapy from the Women's Health Initiative. "The message patients got was that mainstream medicine hormones are bad, and that message was distorted into: 'Those hormones that doctors give you are bad, but this mom-and-pop shop is compounding this all-natural stuff, and they have not been proven to cause any of these problems."



The use of BHRT is spreading via the internet, word of mouth, and even physicians and nurse practitioners. Linda Buckley, MD, an endocrinologist in private practice in the Denver area, says these patients used to present a couple of times a year, but now they are beginning to appear weekly: "We really saw it take off it when the GYNs in the community started using it, because patients were going to their providers with nonspecific complaints like poor libido and decreased energy. We have seen women with testosterone levels of 400 or 500 or 600 ng/dL. They have acne and hair growth, and they are irritable." The normal range is generally less than 50 ng/mL in premenopausal women and less than 20 ng/dL in postmenopausal women.

One of the first of these patients had a history of estrogen-positive breast cancer treated with an ovariectomy and a bilateral mastectomy. Her plastic surgeon recommended BHRT testosterone pellets, apparently unaware that the testosterone can be aromatized into estrogen. "We do everything we can to deplete the patient of estrogen when they have estrogen-positive breast cancers. It was highly alarming to us. We spoke to this plastic surgeon, who made some very erroneous statements," Buckley says.

Wierman had a patient with an enlarging meningioma who had been given pellets containing testosterone, estrogen, and progesterone: "She had levels in the male range of testosterone, which can be converted into estrogens when given at high doses. There are data about these meningiomas growing in response to estrogen and progestins. So it makes you wonder

whether this tumor in her brain grew because of the pellets that she got put inside her."

Santoro had a patient who had testosterone levels close to the male range: "We are going on six months of waiting for her testosterone to come back down to the upper limit of the normal female range." Santoro has also seen aromatase inhibitors being given with the testosterone "to supposedly block the estrogen effect on the breast and make the treatment safe for people with cancer. That is going to very dangerous places, as there are no follow-up data on such treatments that would justify widespread use."

Testosterone in Women

Buckley says that it can be difficult to discover the cause of some women's problems because these "patients were told 'don't tell your endocrinologist that you are doing this. They don't agree with this.' The practitioners make derogatory comments about endocrinologists not being supportive of testosterone replacement in women."

The reason that endocrinologists do not support testosterone treatment in healthy women can be found in "Androgen Therapy in Women: A Reappraisal: An Endocrine Society Clinical Practice Guideline." "We continue to recommend against making a diagnosis of androgen deficiency syndrome in healthy women because there is a lack of a well-defined syndrome, and data correlating androgen levels with specific signs or symptoms are unavailable," the guideline concludes.

Pharmacologic levels of testosterone in women as given in pellets or injections tend to cause a worsening cholesterol profile, high LDL cholesterol, male pattern balding, hirsutism, and acne. They obviously are anabolic, so they may increase muscle mass and decrease fat mass, and at high levels, they may activate 'more energy'— but at what cost?"

— MARGARET WIERMAN, MD, PROFESSOR IN MEDICINE, OBGYN, PHYSIOLOGY, AND BIOPHYSICS, UNIVERSITY OF COLORADO SCHOOL OF MEDICINE; CHIEF OF ENDOCRINOLOGY, ROCKY MOUNTAIN REGIONAL VETERANS AFFAIRS MEDICAL CENTER, DENVER

"We recommend against the general use of T for the following indications: infertility; sexual dysfunction other than hypoactive sexual desire disorder; cognitive, cardiovascular, metabolic, or bone health; or general well-being."

The "Secret Hormone"

The website of BioBalance Health — one company pushing the treatment — contradicts the guideline by calling testosterone a "secret hormone" that is "not acknowledged by the medical community as important to women."

BioBalance describes a condition that "has no official name in the medical world. We have named it Testosterone Deficiency Syndrome (TDS) for women. If you have experienced three or more of these symptoms, you may have Testosterone Deficiency Syndrome: loss of libido, can't sleep, fatigue, hair loss, anxiety, depression, memory loss, weight gain, stubborn belly fat, loss of balance, hot flashes, no motivation, muscle tone loss, arthritis, stamina decrease, [or] sagging skin." The website promises that BHRT can treat these symptoms.

The Hormone Therapy Centers of America website makes similar promises, saying the benefits of BHRT include "calmer, more stable mood; reduced body fat; increased energy levels; higher sex drive; stronger mental clarity; and improved muscle tone and mass" as well as "protection from age-related conditions such as heart disease, cancer, diabetes, Alzheimer's, arthritis, [and] osteoporosis."

Bioidentical hormone replacement therapy (BHRT) pellets are subcutaneous implants generally inserted into the hip area and used to treat everything from low libido to hair loss.

AT A GLANCE

- An alarming number of patients have begun appearing in endocrinologists' offices with symptoms caused by high testosterone levels from custom-compounded bioidentical hormone implants.
- These products are gaining traction through word-of-mouth, anti-aging clinics, and internet promotion as "more natural" and "individualized" approaches to correcting "hormone imbalance" compared with FDA-approved hormone replacements.
- Some practitioners are providing these products in direct contravention of the recommendations of evidence-based clinical guidelines.



The message patients got was that mainstream medicine hormones are bad, and that message was distorted into: 'Those hormones that doctors give you are bad, but this mom-and-pop shop is compounding this all-natural stuff, and they have not been proven to cause any of these problems."

NANETTE SANTORO, MD, E. STEWART TAYLOR
ENDOWED CHAIR, DEPARTMENT OF OBSTETRICS
AND GYNECOLOGY, UNIVERSITY OF COLORADO
SCHOOL OF MEDICINE, DENVER

The BioTE Medical website promises to correct another problem unknown to most of medical science called "hormone imbalance": "Many women will experience a hormone imbalance and not even realize it. Symptoms can range from subtle to debilitating and are often masked by medications that are prescribed for anxiety, depression, insomnia, weight gain, and more." BioTE Medical claims it provides individualized treatment that "studies have shown improvements in menopause, depression, anxiety, low sex drive, osteoporosis, heart disease, PMS, and many other conditions."

The literature review performed as part of the guideline-writing process did not find these studies. Instead, Wierman, who chaired the guideline committee says the review failed to document the benefit of high physiologic doses of a testosterone patch except for a subset of women with hypoactive sexual desire disorder where the medication increased satisfying sexual events by one per month and improved libido. They suggested a short-term trial for these women with hypoactive desire disorder could be considered, but with careful monitoring. The drug, however, was later denied approval by the FDA because of concerns regarding cardiovascular safety and risk for breast cancer. Thus, there are currently no FDA-approved formulations of testosterone for women.

"Pharmacologic levels of testosterone in women as given in pellets or injections tend to cause a worsening cholesterol profile, high LDL cholesterol, male pattern balding, hirsutism, and acne. They obviously are anabolic, so they may increase muscle mass and decrease fat mass, and at high levels, they may activate 'more energy'—but at what cost?" Wierman says.

Compounding Interest

The unreliability of the custom-compounding process for creating the pellets is another area of concern. The Endocrine Society scientific statement on compounded bioidentical hormones says:

- "There is a general lack of standardization and quality control regarding how custom-compounded bioidentical hormones are produced and administered, leading to the possibility of overdosing, underdosing, or contamination.
- "No evidence supports the popularized notion that custom-compounded bioidenticals have fewer risks when compared with Food and Drug Administration (FDA)-approved hormone treatments.
- "The [widely available] FDA-approved bioidentical hormones produced in monitored facilities demonstrate a high quality of safety and efficiency in trials; therefore, there is no rationale for the routine prescribing of unregulated, untested, and potentially harmful custom-compounded bioidentical HTs."

The companies that market BHRT offer misleading — and obtuse — statements about their relationship with the FDA. The website of a cardiologist in the Charlottesville, Va., area who offers BioTE Medical's product as part of her "wellness" practice says: "Although Synthetic hormones (HRT) are FDA approved, the FDA cannot approve or patent natural pellet therapy (BHRT) because it's (sic) consists of natural occurring substances. For example, water cannot be FDA approved or patented."

BioTE itself says that its "hormones are compounded in one of two pharmacies in the United States that are licensed FDA outsourcing centers and are held to strict standards."

However, the FDA says that "compounded BHRT products are not FDA-approved, which means these products have not undergone an FDA assessment of quality, safety, effectiveness, and bioavailability."

High Out-of-Pocket Costs

BHRT treatment is not cheap. The BioBalance Health website warns that insurance is not likely to cover the average annual cost of \$1,536, but that patients will "save money on copays for the medications you will no longer need for blood pressure, cholesterol, dry eyes, osteoporosis, and anxiety/depression; save your marriage if health and sex are points of contention; [and] prevent Alzheimer's disease and dementia—better than the expensive long-term care insurance."

The websites turn this high cost to their advantage by using it to recruit more physicians to offer the treatment after receiving training from the company. BioBalance Health says

RESOURCES

- Androgen Therapy in Women: A Reappraisal:
 An Endocrine Society Clinical Practice Guideline
 https://academic.oup.com/jcem/article/99/10/3489/2836272
- Compounded Bioidentical Hormones in Endocrinology
 Practice: An Endocrine Society Scientific Statement
 https://academic.oup.com/jcem/article/101/4/1318/2804494

physicians can "start a new practice or use your existing one to create an additional revenue stream of over \$250,000 the first year for virtually no additional costs."

The Hormone Therapy Centers of America site asks: "What other procedures or services have you investigated lately that allow you to realistically add \$250,000 a year to your practice for an investment of \$2,500?"

The lucrative possibilities may be tempting some practitioners: One Colorado OB/GYN practice reportedly dropped its obstetrics work in order to focus solely on supplying BHRT pellets. A clinician at a different practice began offering pellet treatment to avoid losing patients to competitors who did.

Medical Community Pushes Back

Wierman, Santoro, and Buckley are all pushing back against the use of BRHT by encouraging the Endocrine Society to become more active and approaching their state medical board.

"The medical community is engaging directly with the FDA," according to Stephanie Kutler, director of policy and advocacy programs at the Endocrine Society. At the behest of the Endocrine Society leadership, Society experts joined several other professional associations on a recent conference call with the FDA organized by the North American Menopause Society to present "evidence to support our position that bioidentical hormones should be more closely regulated by the FDA and only prescribed when clinically necessary," Kutler says.

The Society welcomes a recent announcement that the FDA has commissioned a study by the National Academies of Science, Engineering, and Medicine to examine the scientific evidence relating to the clinical utility, safety, and effectiveness of BHRT products and plans to have some member experts engage with the study task force.



While insufficient sleep has been shown to have a litany of adverse endocrine effects, a new study presented at **ENDO 2019** revealed the possible dangers of dim light exposure at night that could cause breast cancer to metastasize to the bones.

BY DEREK BAGLEY

n 2019, sleep is becoming a precious commodity. The Centers for Disease Control and Prevention (CDC) report that more than a third of adults in the U.S. get less than the recommended amount of sleep per night, while a study by the RAND Corporation concludes that this lack of sleep costs the U.S. \$411 billion a year.

But it's not just the money lost to productivity that's the problem. Both the CDC and the RAND Corporation declared lack of sleep a public health concern, and both organizations have offered recommendations for improving sleep: Set consistent sleep times, exercise, limit the use of electronic devices before bedtime, and so on. Simple solutions but not always easy ones.

Indeed, insufficient sleep has well documented adverse health effects. And endocrinologists are discovering and documenting even more of these effects. A 2015 Journal of Clinical Endocrinology & Metabolism article showed that even one night of wakefulness can

lead to alterations in epigenetic and transcriptional profile of core circadian clock genes in key metabolic tissues. And now, a new study presented at **ENDO 2019** in New Orleans further reveals endocrinology's role in sleep health.

Muralidharan Anbalagan, PhD, an assistant professor at the Tulane University School of Medicine in New Orleans, La., at **ENDO** showed for the first time in a mouse study that exposure to dim light at night — no more than the light sneaking in under a door — may contribute to the spread of breast cancer to the bones, a growing problem in a society where smart phones twinkle throughout the night and streetlights bathe people's windows in that warm yellow glow.

Night Shift

In 2014, Anbalagan working with the Tulane Circadian Cancer Biology Group headed by Steven M. Hill, PhD, and David E. Blask, MD, PhD, published a paper in *Cancer Research* titled "Circadian and melatonin disruption by exposure to light at night drives intrinsic resistance to tamoxifen therapy



in breast cancer." In that article, the authors pointed out that disruption of circadian rhythms from night shift work or disturbed sleep-wake cycles may lead to an increased risk of breast cancer and that light exposure at night suppresses the nocturnal production of melatonin that inhibits breast cancer growth. (The World Health Organization has designated night shift work involving light exposure as a "possible human carcinogen.")

During that previous study, animals exposed to dim light at night showed increased tumor growth, and they developed a resistance to tamoxifen, a drug used to treat breast cancer. "Strikingly," the authors concluded, "our results also showed



AT A **GLANCE**

- Insufficient sleep is associated with a number of adverse health effects. and endocrinologists play a key role in determining these effects.
- A new study presented at ENDO 2019 shows that dim light exposure at night can promote breast cancer metastases to bones.
- Researchers are studying a potential mechanism for these metastases, as well as a promising new therapeutic target to inhibit or suppress the progression of bone cancer spreading to the bones.

that melatonin acted both as a tumor metabolic inhibitor and a circadian-regulated kinase inhibitor to reestablish the sensitivity of breast tumors to tamoxifen and tumor regression. Together, our findings show how [dim light exposure at night]-mediated disturbances in nocturnal melatonin production can render tumors insensitive to tamoxifen."

More than 150,000 U.S. women had breast cancer in 2017 that metastasized, according to an estimate from the National Cancer Institute. When breast cancer spreads, it often goes to the bones, where it can cause severe pain and fragile bones.

"Since breast cancer metastasizes to bone and melatonin has a bone protecting effect, I planned to do this [current] study," Anbalagan says. He presented his team's findings from the current study, "Disruption of the Circadian Melatonin Signal by Dim Light at Night Promotes Bone-lytic Breast Cancer Metastases," last month in New Orleans.

In this preliminary study funded by the Louisiana Clinical and Translational Science Center (LACATS) in collaboration with Louisiana Cancer Research Consortium (LCRC) and Tulane Center for Circadian Biology, the researchers created a mouse model of bone metastatic breast cancer. They injected estrogen receptor-positive human breast cancer cells that have a low propensity to grow in bones into the tibia of female mice. Like humans, the mice used in this study produce a strong nighttime circadian melatonin signal. All mice were kept in the light for 12 hours each day. One group of three mice was in the dark the other 12 hours, which helped them produce high levels of endogenous melatonin. Another group spent 12 hours in light followed by 12 hours in dim light at night, which suppressed their nocturnal melatonin production.

X-ray images showed that mice exposed to a light/dim light cycle had much larger tumors and increased bone damage compared with mice kept in a standard light/ dark cycle, he reported. "Our research identified the importance of an intact nocturnal circadian melatonin anti-cancer signal in suppressing bone-metastatic breast tumor growth," Anbalagan says.

Too Plugged In?

There are dozens of factors that contribute to sleep loss in this modern, fast-paced society: caffeine use, alcohol use, stress, screen time, shift work. But while this new research indicated nighttime dim light exposure in the promotion of breast cancer metastases, the study also revealed a possible and promising therapeutic target for treating breast cancer and preventing its spread to the bones. The researchers write in their ENDO 2019 presentation abstract that patients with metastatic breast cancer are treated with doxorubicin (Dox), a form of chemotherapy that itself can promote bone damage. "Multiple studies demonstrate adverse/toxic effects of Dox on bone including suppressed osteoblast differentiation and



decreased bone volume," Anbalagan says. "Children treated with Dox are reported to suffer bone damage leading to increased fracture risk. These adverse effects heighten the concern for patients receiving Dox as a part of their therapy."

However, the Tulane University Circadian Cancer Biology Group found that by using Dox in circadian alignment with melatonin in the mice, they saw reduced tumor growth in bone, reduced bone erosion, and promotion of formation of new bone. "Successful use of this chronotherapeutic use of Dox and [melatonin] in clinical trials increasing efficacy in preventing or suppressing breast cancer metastasis to bone while decreasing toxic side effects of doxorubicin would provide a revolutionary advancement in the treatment of bone metastatic breast cancer and decrease the morbidity and mortality associated with breast cancer metastasis to bone," the authors write.

And while melatonin can be bought over the counter, Anbalagan says that natural melatonin is better. Still, he recognizes that can't always be the case. "It's always better to have natural melatonin signaling through sleeping in dark, but most of the time it is not realistic," he says. "So it is better to take a melatonin supplement to restore the circadian rhythm."

Anbalagan says the next steps for his team will be expanding this study and exploring the mechanisms to reveal the key players involved in promoting breast cancer and the involvement of melatonin receptors. For now, it's just a matter of recognizing that the circadian system is extremely important for overall health. "Circadian disruption by light at night is not only a risk factor in cancer, but also in metabolic diseases like diabetes," he says.

"I think in today's plugged-in world, it is really a huge problem," Anbalagan continues. "If you don't adjust your lifestyle, the circadian disruption by light at night is going to be a huge problem, especially for people who live in large, bright cities as well exposure of lights to night shift workers such as nurses and flight attendants."

If you don't adjust your lifestyle, the circadian disruption by light at night is going to be a huge problem, especially for people who live in large, bright cities as well exposure of lights to night shift workers such as nurses and flight attendants."

— MURALIDHARAN ANBALAGAN, PHD, ASSISTANT PROFESSOR, TULANE UNIVERSITY SCHOOL OF MEDICINE, NEW ORLEANS, LOUISIANA



According to recent studies published in *The Journal of Clinical Endocrinology & Metabolism*, researchers are getting a better understanding of obesity and the continuing efforts to combat it. While the bad news is that there are a variety of side effects, the good news is that not all of the side effects are negative.

BY KELLY HORVATH



Tith rates of obesity in the U.S. remaining at staggeringly high levels, scientists are hard pressed to discover the most effective medical interventions to combat this disease. According to the Endocrine Society Facts and Figures Report on Obesity, 35.1% of U.S. adults are obese, defined as a body mass index (BMI) score of ≥30 kg/m². That's more than one in three adults who face any number of comorbidities, increased mortality, and reduced quality of life as well as increased risk of metabolic syndrome, which is itself a major risk for developing such chronic conditions as cardiovascular disease and diabetes. Worldwide, 13% of adults are obese, according to the World Health Organization, but this number has nearly tripled in the past 40 years. In three studies published in *The Journal of Clinical Endocrinology & Metabolism* within the past six months, researchers take up arms against this mighty foe.



Mind Over Matter

In "Application of Mindfulness in a Tier 3 Obesity Service Improves Eating Behavior and Facilitates Successful Weight Loss," the study's first author, Petra Hanson, MBCHB, BSc, MRCP, AFHEA, a research fellow and PhD student at Warwickshire Institute for the Study of Diabetes Endocrinology and Metabolism at University Hospitals Coventry and Warwickshire, in Coventry, U.K., and team add mindfulness, the practice of fully attending to the present moment, to the armamentarium.

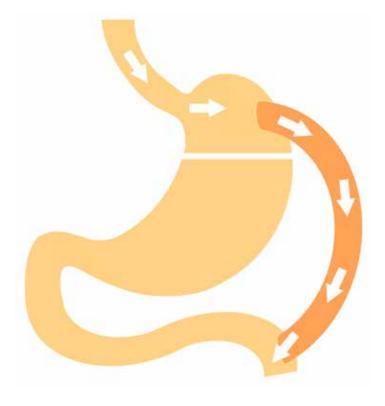
Given the success of the application of mindfulness in a wide variety of clinical contexts in the past 30 years, the team surmised that in patients with potentially problematic eating habits, becoming

...mindfulness techniques can improve eating behavior and facilitate weight loss in patients with obesity attending specialist weight management services. Mindfulness taught in such a setting can also improve patients' confidence and ability to manage weight in the long term. It is a very scalable intervention that can be applied to everyone."

— PETRA HANSON, MBCHB, BSC, MRCP, AFHEA, RESEARCH FELLOW, PHD STUDENT, WARWICKSHIRE INSTITUTE FOR THE STUDY OF DIABETES ENDOCRINOLOGY AND METABOLISM, UNIVERSITY HOSPITALS COVENTRY AND WARWICKSHIRE, COVENTRY, U.K.

more aware of these harmful habits as well as more aware of what is being consumed could help patients lose weight and develop an overall healthier approach to food. To date, most weightloss programs emphasize diet and exercise, and relapses among participants into former habits of poor food choices and low physical activity are rampant. Studies of mindfulness and weight loss, meanwhile, are scant.

The team recruited 53 participants with a BMI >35Kg/m2 and age >18 years to attend four 90-minute group sessions every two weeks for eight weeks at a Warwickshire weight management clinic, 33 of whom completed the series. The focus of the series was on behavior change rather than weight loss, and, as such, training sessions in mindfulness techniques were offered as part of the overall approach. Strategies taught included how to eat mindfully rather than mindlessly in addition to how to practice self-compassion — avoiding excessive self-criticism and instead invoking self-confidence to overcome health barriers.





Participants provided self-reported eating behavior and body weight at the start of the trial and again on completion. After six months, participants who completed the mindfulness training series had lost an average of 6.7 pounds, as compared to about two pounds among the patients who skipped two or more sessions. A retrospective control group comprised 33 participants who attended the group sessions but were not taught how to implement mindfulness techniques; these patients received what is considered "standard care" at the clinic currently and lost significantly less weight on average — about half a pound. Notably, the program's focus on behavior change also produced favorable results, as participants demonstrated significantly less "fast foodism," which the researchers define as eating considerably more fast food than fresh food.

"Our study has shown that mindfulness techniques can improve eating behavior and facilitate weight loss in patients with obesity attending specialist weight management services," Hanson says. "Mindfulness taught in such a setting can also improve patients' confidence and ability to manage weight in the long term. It is a very scalable intervention that can be applied to everyone."

Bypass Surgery Flexes Its Muscles

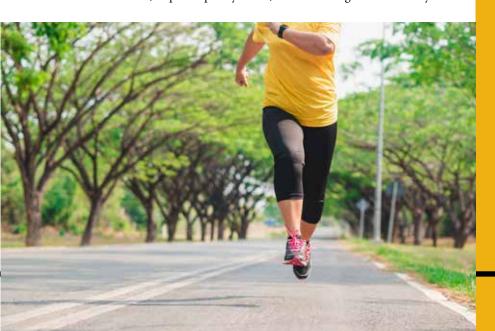
A second study uncovers previously unknown benefits of a common weight-loss surgical procedure. Roux-en-Y gastric bypass (RYGB) surgery anastomoses a small, egg-sized part of the stomach directly to the jejunum so that most of the stomach and the duodenum are bypassed when food is eaten. Thus, the new stomach can hold a considerably smaller amount of food, and considerably less fat is absorbed with the duodenum

out of the picture. For extremely obese patients (BMI \geq 40 kg/mg²) and obese patients with serious comorbidity, such bariatric surgery procedures promise substantial weight loss as well as reduction of obesity-related risk factors and comorbidities. A purported side effect, however, is that patients experience a potentially detrimental and ongoing loss of muscle that can result in long-term skeletal muscle insufficiency, metabolic impairment, and the inability to maintain a physically active lifestyle.

The new study finds that the impact of RYGB on muscle may be misunderstood, however. In "Changes in Lean Mass, Absolute and Relative Muscle Strength, and Physical Performance After Gastric Bypass Surgery," Diana Alba, MD, of the University of California in San Francisco, and team took baseline measurements of fat versus lean mass, handgrip strength, and physical activity and performance (indicated by chair stand time, gait speed, and 400-meter walk time, tests that are valid, reliable, and sensitive to change) in 47 study participants about to undergo RYGB with BMI $44 \pm 8 \text{ kg/m}^2$. They measured changes in these indices at six and 12 months post RYGB.

At 12 months preoperatively, all participants had lost a significant amount of weight, a mean of $30\% \pm 7\%$. Absolute muscle strength decreased at a mean of 2.6 \pm 5.4 kg, a rate that was driven by women versus men; however, relative muscle strength, defined as absolute handgrip strength/BMI and as absolute strength/appendicular lean mass (ALM) — also known as "muscle quality," progressively increased after 12 months, as did gait speed, while time to complete five chair stands and to walk 400 meters decreased in both biologic sexes.

Notably, body composition changes were steepest in the first six months postoperatively, and researchers posit that early interventions, such as perioperative and postoperative resistance training exercises, might help to maintain lean mass, improve quality of life, and avoid long-term disability.



AT A GLANCE

- Applying mindfulness techniques to eating behavior resulted in behavior change and accelerated weight loss in a study of 33 obese patients in Warwickshire, U.K. Participants lost an average of 5.7 pounds more than patients who did not complete the program and consumed more fresh food (as opposed to fast food).
- In a longitudinal study of 10 men and 37 women undergoing RYGB at a San Francisco hospital, patients experienced substantial 12-month postoperative declines in lean mass and absolute muscle strength, but the decline in absolute muscle strength was offset by relative muscle strength (handgrip strength/BMI or absolute strength/ALM) increases as well as by clinically and statistically significant improvements in physical performance parameters (gait speed, 13% faster; chair stand time, 19% faster; and 400-meter walk time, down from 5.3 to 4.4 minutes).
- Higher body-weight fluctuation was independently associated with increased mortality in a Korean community-dwelling population regardless of biologic sex and obesity and smoking status; however, obesity conferred a protective effect on incident diabetes mellitus in obese participants for whom a loss of weight would help to prevent diabetes mellitus.



Weight cycling has the tendency for people to lose weight then gain it back, sometimes gaining more weight than they originally lost.

Health Benefits of Weight Cycling Outweigh Adverse Effects in Obesity

In the third study, the news is not all good — neither is it all bad, and we'll take it. To get the bad news out of the way first, of the millions of people every day who start a diet to lose weight, only a small percentage succeed in keeping the weight off one to five years later. This is at least partly due to the typical diet and feast response, in which the dieter regains the weight lost if not more, then starts another diet — weight cycling.

The upshot is, according to Alba, "Besides reducing body weight and obesity-associated comorbidities and mortality, RYGB significantly improves a person's relative muscle strength and physical performance." The improvement in physical performance is perhaps due to biomechanical changes that RYGB brings about. Although the decline in absolute muscle strength that is a known side effect of bariatric surgery is therefore an incomplete picture, strategies to address the associated loss of lean mass should be part of ongoing research.

Some blame psychology as the basis underpinning the cycle, that hinges on the negative feelings the dieter experiences — deprivation from food restriction, shame, — and disappointment from giving in to the increased desire for tempting foods. To relieve the negative feelings, the dieter eats even more, and the cycle begins anew. But there is undeniably a biochemical explanation to body-weight fluctuation as well. When weight is lost, hunger hormones like ghrelin kick in, while satiety hormones like leptin take a back seat. In addition to this homeostatic feedback mechanism, fat cells are programmed to maintain their size and will overstore fat to reverse any shrinkage.

"Besides reducing body weight and obesity-associated comorbidities and mortality, RYGB significantly improves a person's relative muscle strength and physical performance."

- DIANA ALBA, MD, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO



The benefits of exercise to lose weight are many, especially an increase of lean muscle mass.

As despairing as this tale of woe is, the health repercussions can be downright tragic. In "Body-Weight Fluctuation and Incident Diabetes Mellitus, Cardiovascular Disease, and Mortality: A 16-Year Prospective Cohort Study," Hak C. Jang, MD, PhD, professor, Seoul National University College of Medicine and Seoul National University Bundang Hospital

in Seongnam, South Korea, and team suggest that weight-cycling actually produces harmful changes in body composition by exchanging lean mass for fat mass. As they show, fat mass is reduced more than lean mass during dieting, but lean mass does not increase as much as fat mass when weight is regained.

The team collected health-related outcomes every two years for 16 years in 3,678 Korean participants from the Korean Genome and Epidemiology Study, designed to evaluate noncommunicable disease and related risk factors. "In the 16-year prospective cohort study, we found higher weight cycling was associated with increased risk of all-cause mortality," Jang says.

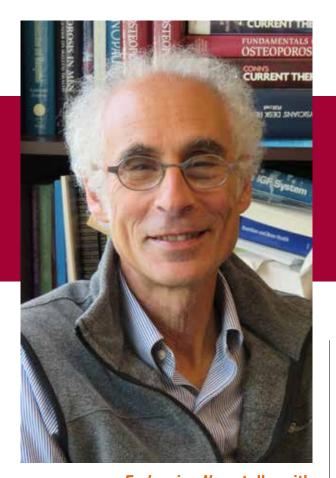
An individual's body-weight fluctuations were calculated by "average successive variability (ASV)," and those with a high ASV of body weight were more obese, had higher blood pressure levels, and demonstrated increased insulin resistance at baseline than those with a low ASV of body weight. A one-unit increase in ASV of body weight was associated with increased mortality in participants with high cardiovascular risk as well as in healthy participants.

As for diabetes mellitus risk, and this is where the news gets a bit brighter, that depended on both the presence of obesity and the degree of bodyweight changes. Diabetes was positively associated with the ASV of body weight in the subgroup whose baseline BMI was $<25 \text{ kg/m}^2$, but negatively associated in subjects with BMI $\ge 25 \text{ kg/m}^2$.

"People with obesity who experienced more weight cycling were less likely to develop diabetes," Jang says. Thus, for obese participants, the beneficial effect of losing weight on diabetes prevention may outweigh the adverse effects of weight cycling.



 HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT THYROID CANCER AND HEART DISEASE IN THE FEBRUARY ISSUE.



Endocrine News talks with Clifford Rosen, MD, chair of the guideline writing committee that created the latest Endocrine Society Clinical Practice Guideline on Pharmacological Management of Osteoporosis in Post-Menopausal Women.

Clifford Rosen, MD

n March, the Endocrine Society issued a Clinical Practice Guideline on treating post-menopausal women with osteoporosis. Titled "Pharmacological Management of Osteoporosis in Post-Menopausal Women: An Endocrine Society Clinical Practice Guideline." The guideline was published online and will appear in the May 2019 print issue of *The Journal of Clinical Endocrinology & Metabolism*.

Clifford Rosen, MD, director, Center for Clinical and Translational Research at the Maine Medical Center Research Institute in Scarborough, is the chair of the writing committee that authored this guideline. He shared his thoughts with *Endocrine News* about how he hopes this guideline will improve patient care and patients' confidence in the treatment they receive as well as how this guideline improves on other guidelines on this topic.

ENDOCRINE NEWS: What was the main reason for the publication of the osteoporosis in postmenopausal women guideline — what drove the decision and why now?

CLIFFORD ROSEN: There is a considerable gap in the treatment of osteoporosis. Most women will not take antiosteoporosis therapies despite their efficacy, and those that do often stop. Hence the rate of hip fractures has leveled off and may actually be increasing. In addition, bone density screening has declined precipitously. These changes are likely due to the perceived risks versus benefits of treating osteoporosis.

EN: What are your hopes for the impact of the guideline on endocrine standards of care for postmenopausal women with osteoporosis?

It is our firm belief that the knowledge gained from reading these guidelines will not only improve patient care but provide confidence in treatment."

CR: By pointing out the therapeutic efficacy, we hope that more providers will engage their patients in shared decision making. It is essential that endocrinologists in particular will be active participants in this process since most of the osteoporosis treatment approaches have been directed at endocrinologists. Notwithstanding, it is our firm belief that the knowledge gained from reading these guidelines will not only improve patient care but provide confidence in treatment.

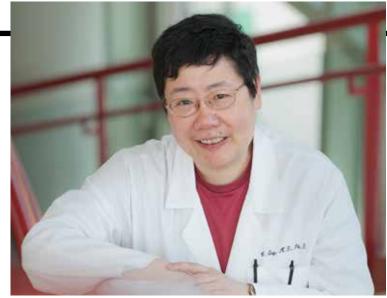
EN: How do you expect other medical specialties to be affected by the guideline writing committee's recommendations?

CR: We think others will embrace the guidelines for diagnosing and treating osteoporosis. Of course, there are other guidelines and recommendations, but [the new Endocrine Society guidelines] are evidence-based, and the result of three years of work to define the optimal approaches to osteoporosis therapy.

EN: What are the key take-home messages for patients in this guideline?

CR: The current treatments are effective, and the risk:benefit assessment often falls toward a significant benefit rather than harm. But once again, it is important to note that efforts to engage patients in their treatments require time, knowledge, and patience. We acknowledge that patient care is not an exact science, and these recommendations do not fit every individual but rather provide a framework for care.





Heir Conditioning

Charis Eng. MD, PhD, from the Cleveland Clinic. discusses her research of tumor suppressor genes, endocrine neoplasias, and why an accurate family history is so important to determine when a cancer screening should be performed.

he American Cancer Society's Medal of Honor recognizes individuals who have made the most valuable contributions in saving more lives from cancer. One of the 2018 recipients, Charis Eng, MD, PhD, of the Cleveland Clinic in Ohio, is no stranger to the endocrine community and was honored for her study of tumor suppressor genes and the understanding of hereditary predisposition and treatment for several types of cancer, including those endocrine-related.

Endocrine News spoke with Eng to learn more about the work that earned her Medal of Honor accomplishment.

Endocrine News: What were your first thoughts when you heard about your Medal of Honor for Clinical Research?

Charis Eng: It was a tremendous honor, and I had all sorts of emotions flooding in and asking, "Can this be true?" It was such a lovely surprise because with a lot of these awards, the intended recipient helps put in the nomination, but I didn't with this one. And so, someone anonymously nominated me, and that is the greatest surprise of all.

EN: A simple explanation of your research is that humans have about 24,000 genes and about six bad ones that can predispose us to serious illness. The goal is to screen for these genetic mutations and identify a patient's cancer risk. Your lab is creating a roadmap for patients to alert them of their increased risk so they can make better decisions about their health and lifestyle. How close are patients to being able to get a roadmap of their predispositions?

BY GLENDA FAUNTLEROY SHAW

CE: Let's step back. We already have a roadmap if only clinicians have the time to take a good family health history. A good family history can provide that first inkling of, "Could I be at increased risk of something that's running in my family?" The truth of the matter, of course, is that non-genetic clinicians

Thyroid cancer research is prolific but not prolific enough, because if you look at thyroid cancer as a whole versus all the other endocrine neoplasias, the knowledge is far behind."

don't have the time. The family health history is sacrificed because clinicians are sitting in front of a patient who has other illnesses that might need immediate care. So, of course that's the problem — it's reactive medicine versus proactive medicine.

But, because of mine and others' research, there are now 59 clinically actionable genes and soon to be 71, that are in the American College of Medical Genetics and Genomics guidelines. The guidelines say that if incidentally any of these are found, whether as a screen or in research, they have to be confirmed in a CLIA/CAP-certified lab in the setting of genetic counseling, and these have to be actioned.

And since I study endocrine neoplasias, I have defined the risk of various endocrine neoplasias. For example, I am most known for finding the PTEN gene, which when altered leads to a very high risk of breast, thyroid, endometrial, and other cancers. I name those three because they are the highest risk, and they are "endocrine organs." So, if there's an alteration in the PTEN gene, it's an 85% lifetime risk of female breast cancer. It's a 35% lifetime risk of thyroid cancer and an 28% risk of endometrial cancer, and endometrial cancer is normally about a 1% - 2% risk. But because of our research, we know when the age of risk begins and how high the risk is in a lifetime.

So, this is where this type of research can be translated to practice guidelines. We know when to begin clinical screening or enhanced surveillance because it is starting earlier and more often. For instance, we've found that the youngest onset of thyroid cancer associated with germline *PTEN* alterations is six years old. And so, the original practice guidelines were, "We could start screening in the teens." And when our research came out, we said, "No, we cannot." And our study, replicated twice independently, formed the basis of altered practice guidelines. So, the moment the doctor finds a *PTEN* mutation, you begin thyroid ultrasounds annually immediately upon that genetic diagnosis, so this is how our work has changed practice.

EN: You're also the editor-in-chief of the journal *Endocrine-Related Cancer*. Regarding submissions, what's the more prolific area of research now?

CE: I would say thyroid cancer research is prolific but not prolific enough, because if you look at thyroid cancer as a whole versus all the other endocrine neoplasias, the knowledge is far behind. Not because we're not good — I think there are some of the greatest minds studying thyroid cancer, but it's just such a complex field that it's taking a very long time. And until very recently, the funding bodies have said, "Nobody dies of thyroid cancer. We don't care." And that's not true because when it's advanced thyroid cancer, you're wringing your hands and wondering, "Now what?" and there's no recourse. So, I think more people need to work harder.

EN: Can you share more about the team at your Eng Lab?

CE: I started the lab at the Dana-Farber Cancer Institute in 1995, and it was just me and four other people. I've been at the Cleveland Clinic for 13 years where I founded the Genomic Medicine Institute and its clinical components. We have the most comprehensive practice of medical genetics and genomics in the country. My lab runs anywhere from 12 to 18 people, and it swells in the summer when I take summer medical or undergraduate students, and even high school students, because I believe strongly in having a pipeline of our next generation.

Read more about Dr. Eng's research at www.lerner.ccf.org/gmi.

Electronic Office Managers

COMPILED AND WRITTEN BY COURTNEY CARSON

From an app that allows doctors to communicate with patients via videoconferencing to a program that manages issues that impact a practice's financial and operational performance, the inclusion of medical software is allowing providers to focus on the health of the patient, rather than getting caught up in the health of their practice.

Most healthcare providers did not get into the healthcare industry to spend time ensuring the business side of their practice runs smoothly. No matter how skilled the surgeon or knowledgeable the physician, a practice cannot run as it should without the proper business model in place. And today, those models almost always revolve around medical software. From electronic medical records to automated billing systems, we have included a roundup of some of those software systems vital for a practice to run as efficiently as possible.



◆ athenahealth

Cloud-based athenahealth "lets doctors be doctors" by providing a suite of services to manage medical records/electronic health records (EHR), revenue cycle, patient engagement, care coordination, and population health. The EHR offers a homepage that allows users to review the daily schedule and patient information, manage orders, and view incoming lab results. The billing module, which can be used in tandem with the EHR or on its own, features a patented and continuously updated rules engine. Athenahealth also includes Epocrates, the mobile medical reference app which has been named the number one app in "Taking the Pulse" U.S. Physicians Survey 2010-2018.

www.athenahealth.com

► NextGen Healthcare

NextGen Healthcare offers solutions for electronic health records (EHR), practice management, and more. Suitable for ambulatory practices of all sizes, NextGen enables users to coordinate patient care while complying with healthcare reform demands such as the Merit-based Incentive Payment System (MIPS), population health, and other value-based care requirements.



www.nextgen.com



► Allscripts Practice Management

A comprehensive practice management and revenue cycle management solution, Allscripts Practice Management includes appointment and patient flow, collections, claims, denial management, and transaction management. This software system can help address all aspects of the revenue cycle from eligibility verification through patient collection, while enabling practices to monitor, track, and respond to issues that impact the financial and operational performance.

www.allscripts.com

▶ eClinicalWorks

eClinicalWorks (eCW) integrated electronic health record (EHR) and practice management solution provides technology through each step of the patient care delivery process. eCW device integration allows for structured data capture and trend analysis, while customizable documentation options assist clinicians across multiple specialties. Patient information ranging from patient demographics to billing to upcoming appointments are accessible in one place at the Patient Hub creating a more seamless approach to viewing important information on everyone being treated in the practice.

www.eclinicalworks.org





◆ Cerner Specialty Practice Management

A front and backend solution for the healthcare sector, Cerner Specialty Practice Management offers its services primarily to small and mediumsized practices. Offering cloud-based and on-premise options, Cerner's features help practices manage self-pay accounts and processes involved with insurance reimbursement, including a real-time check for ensuring that ineligible claims are not processed.

www.cerner.com

► EpicCare

Aimed to meet the needs of large hospitals and healthcare systems, Epic Systems' EpicCare includes dashboards that combine and display clinical and financial metrics, as well as customizable templates, a patient portal, and e-prescribing features. EpicCare features a platform that allows doctors to communicate with patients via video and allows patients to view medical information, message doctors, schedule appointments, and manage medical history via a personalized portal.

www.epic.com





► AdvancedMD

A software suite for independent practices, AdvancedMD incorporates a plethora of features that work together to automate practice workflow. These tools include practice management, electronic health records, patient engagement, telemedicine, rooming, reputation management, financial analytics, and business intelligence reporting. Unifying business, clinical, and patient software, this medical office software is cloud-based and tailored to all roles within the independent practice.

www.advancedmd.com

Endocrine Society Applauds New Call to Action in European Union to Address EDCs



Endocrine Society member Barbara Demeneix, PhD (far right) presented at an educational briefing for Members of the European Parliament last May to explain the danger of exposure to endocrine-disrupting chemicals (EDCs). She and Endocrine Society member Remy Slama, PhD, authored a new report calling for action on EDCs in the EU.

n Wednesday, March 20, the European Parliament released a report on "Endocrine Disruptors: from Scientific Evidence to Human Health Protection." The European Parliament commissioned the report, which was authored by Endocrine Society members Barbara Demeneix, PhD, of Muséum National d'Histoire Naturelle in Paris, France, and Rémy Slama, PhD, of INSERM (National Institute of Health and Medical Research), in Grenoble, France.

The report summarizes scientific knowledge regarding the health effects of endocrine-disrupting chemical (EDC) exposure and demonstrates that EDCs pose a serious threat to the health of citizens around the world currently and for future generations. Areas of consensus among the research community are highlighted so that policy makers appreciate how the science has advanced in recent decades to draw connections between EDC exposure and health risks such as obesity, neurodevelopmental disorders, and reproductive health problems.

Importantly, Demeneix and Slama propose specific actions to address the threat of EDCs consistent with the Endocrine Society's recommendations. For example, they call on the European Union to develop a set of coordinated regulations governing all types of EDCs in order to minimize human exposure. Currently, chemicals are often regulated as separate classes depending on their use, resulting in a fractured regulatory landscape for EDCs. They also identify research priorities that, with additional investment, will help accelerate the identification and appropriate regulation of new EDCs.

The Endocrine Society applauds the European Parliament and Profs. Demeneix and Slama for introducing this important and valuable resource for regulators, policy makers, and other stakeholders around the world. We strongly support the recommendations articulated in the report to better protect public health, and we will continue to work with the European Parliament and European Commission to advance these recommendations and develop a comprehensive strategy on EDCs in the EU.

For more information about the Endocrine Society's position on EDCs in the European Union and our scientific statement on EDCs, please visit www.endocrine.org/edc.

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President Trump Releases FY 2020 Budget Proposal with Cuts for NIH

n Monday, March 11th, President Donald Trump released his FY 2020 budget proposal, which proposes to slash funding for the National Institutes of Health (NIH) by \$4.7 billion in FY 2020, to \$34.4 billion, a 12% cut from the current funding level of \$39.1 billion.

While this proposal for NIH is not likely to become law, as Congress ultimately writes spending bills that the White House can approve, it is important as a starting point for congressional negotiations, represents the third year in a row President Trump is proposing a significant cut to NIH's budget, and sets up another contentious appropriations debate.

President Trump's FY 2020 budget proposal for the NIH is a 180-degree turn from this past September when Congress passed the Labor-HHS-Education Appropriations bill on time, providing the NIH with a \$2 billion or 5.4% increase (from \$37.1 billion to \$39.1 billion) for FY 2019. Since FY 2016, Congress has increased funding for the NIH by 30%, which underscores the fact that members of Congress have been very supportive of medical research, including making the NIH a national priority, for each of the past four years.

In spite of this support for the NIH by Congress, we are facing some challenges, in particular is the fact that the statutory spending caps currently in place for FY 2020 will result in a \$55 billion in cuts to non-defense discretionary spending unless Congress acts to raise the caps.

This situation underscores how important it is going to be for the research advocacy community to come together to urge Congress and the president to raise the spending caps for FY 2020, especially if we hope to see the NIH continue to receive a robust, sustained, and predictable funding increase in FY 2020. Consequently, it is critical for Endocrine Society members to join our campaign to increase funding for the NIH and raise the caps. Please visit www.endocrine.org/takeaction to lend your voice to this important issue.

If Congress and the president are unable to negotiate a deal over the next six or so months to raise the spending caps for FY 2020, sequestration (automatic budget caps) will kick in at the start of FY 2020 (October 1, 2019), which could result in the NIH's budget being cut by 9%.



Endocrine Society Urges Congress to Address Rising Cost of Insulin

ince the beginning of the year, Congress and the Trump administration have stated that addressing rising drug prices is a top priority. Congress has conducted several hearings, including hearings to investigate causes for increasing drug prices, reducing barriers to market competition, and the role of pharmacy benefit managers (PBMs).

The Endocrine Society has visited with many congressional offices to share our concerns about the impact of rising insulin prices on people with diabetes, describe how endocrinologists face this issue every day with their patients, and provide some recommendations on ways to address this crisis that we developed through focus groups with our members. While all drug prices are important, we have urged Congress to prioritize insulin because of its special circumstances: 1) It is a drug 7

Endocrine Society Podcast on Insulin Affordability

Listen to the Endocrine Society Podcast on insulin affordability with Alvin Powers, MD, from Vanderbilt University and the Endocrine Society's chief professional and clinical affairs officer, Rob Lash, MD.

https://www.endocrine.org/podcast



million people use; 2) It is a drug that people use to survive, and if they do not have access to it or have the appropriate amount they can have serious complications and die; and 3) It is a drug that was created almost 100 years ago, and its patent was sold for \$1 dollar so that patients would not have a financial barrier, so there is no reason patients are experiencing access to it today. We have advocated that all stakeholders in the drug supply chain have a role in reducing costs. This includes drug manufacturers that set price, PBMs that create the rebate system, and physicians that need to know how to work with their patients to prescribe the insulin that will meet their patients' needs and resources.

These recommendations are described in our position statement on Increasing Insulin Affordability (www.endocrine.org/ advocacy/priorities-and-positions/increasing-insulinaffordability) and include:

- Creating greater transparency across the supply chain to understand rising insulin costs;
- Limiting future list price increases;
- Limiting cost-sharing to a co-pay. In addition, NPH and regular insulin should be available at no cost to the
- Passing along rebate to consumers without increasing premiums or deductibles;
- Improving patient assistance programs so they are less restrictive and expanded to include more accessible and easier to complete applications that can be used for multiple programs (e.g., a common application);
- Training healthcare providers to use lower-cost human insulins (e.g., NPH and regular), so they can prescribe as appropriate; and
- Including up-to-date formulary and real-time price information in electronic medical records.

As a result of our efforts, the Endocrine Society was invited to testify before the House Energy and Commerce Committee Subcommittee on Oversight and Investigations at a hearing on April 2 looking at the impact of rising insulin prices. Read our testimony at www.endocrine.org/advocacy/policycommunications.

Endocrine Society Takes to Capitol Hill in Support of Research Funding

Past-president Susan Mandel, MD (right), with Endocrine Society members Shana McCormack, MD (center), and Lori Raetzman, PhD, visited their congressional delegations during our Researcher Hill Day. Other groups of endocrine researchers fanned out across Capitol Hill to deliver our message to increase NIH funding, raise the current spending caps, and renew the Special Diabetes Program.



t is springtime in Washington, D.C., which means in addition to the annual Cherry Blossom Festival, it is also the time of year when Congress considers funding for federal programs. Capitol Hill is crowded with school groups, tourists, and hundreds of organizations who visit to advocate for funding for their programs. Hallways are crammed with advocates from farmers to veterans to environmental groups to health and research organizations.

The Endocrine Society conducted its Researcher Hill Day February 28. We brought Society members who are basic scientists or clinical investigators to Washington, D.C., for a day of meetings with members of Congress. The focus of our Researcher Hill Day was to advocate for critical research-related issues:

Our asks to Congress were:

- ▶ \$46.1 billion for the National Institutes of Health (NIH) in fiscal year 2020;
- ► An increase in the current statutory spending caps that must be raised to avoid significant cuts to the NIH; and
- ► Renewal of the Special Diabetes Program.

Armed with these messages, our members visited close to 40 congressional offices and met with representatives, senators, and congressional staff. Spring is a critical time to advocate for these priorities as Congress is starting the appropriations process that will determine agency budgets for the next fiscal year. While the issues that we advocate for generally enjoy strong bipartisan support, research and public health programs are threatened as the funds available for non-mandatory programs are at risk of being cut. In addition to these visits, the Society submitted appropriations testimony for the record (www.endocrine.org/advocacy/policy-communications).

Take Action

Society members are encouraged to join our online advocacy campaign to urge their members of Congress to support research funding.

Please visit www.endocrine.org/contactcongress

THE MOST VALUABLE PRACTITIONER

If you are dealing with a hormonal condition such as diabetes or thyroid disease, your primary care doctor may recommend that you see an endocrinologist.

Here are the top 5 reasons why you should schedule an appointment.

AN ENDOCRINOLOGIST IS...

A specialist who has thoroughly studied the endocrine system and hormonal conditions. They will know the best possible treatments for you, even when typical treatments have not worked in the past.

YOUR CASE IS UNIQUE.
Your endocrinologist will combine biochemistry, cell biology, and genetics to unravel mysteries for your unique care needs and help you pursue all treatment options. Non-traditional

patients absolutely need the help of an endocrinologist to treat their hormonal conditions.

3 ASK FOR A DOCTOR WHO IS AWARE OF NEW DEVELOPMENTS IN HEALTH CARE.

Endocrinologists are knowledgeable and up to date on evolving hormonal conditions and treatments. They are even on the front lines of top civil rights issues of our era, namely the rights of transgender people. Patients who visit an endocrinologist will have access to the newest hormone and surgical therapies.



An endocrinologist communicates with your primary care doctor and other healthcare professionals to ensure that hormone imbalance is restored. If you are struggling with a hormonal condition, it is great to have a second option to ensure your health is the best it can be.

Since the 19th Century understanding hormones have been a center of many medical conditions. Endocrinologists are trained to think outside of the box as well as search for non-traditional diagnoses and help to restore hormone balance within the body's systems.

MEDICAL DETECTIVES.



Follow us: @HormoneHealthN

YOUR ENDOCRINOLOGIST AND PRIMARY CARE PHYSICIAN ARE A TEAM

76%

of family physicians follow the recommendations of **endocrinologists** with little to no changes.

60%

of primary care physicians say endocrinologists are a valuable source of information about new diabetes products.



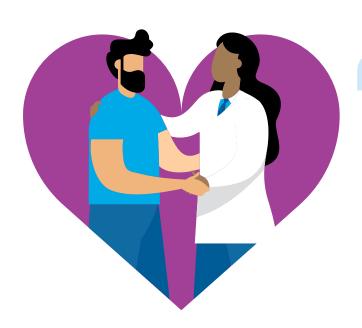
MORE THAN 30

Every year, primary care physicians seek more than 30 consults from endocrinologists.

Topic areas include diabetes and obesity, thyroid, women's health, cardiovascular, bone health, and growth.

NEW PRODUCTS

Most primary care physicians are more likely to adopt new products earlier if recommended by an endocrinologist.



WHY ENDOCRINOLOGY?

"As I begin my early career in endocrinology, my goal remains the same—to provide a better future for patients in the community and abroad, where medical complications and emergencies can be prevented with education, guidance and compassionate care."

Deena Adimoolam, MD

Icahn School of Medicine at Mount Sinai, New York, NY

Patients have questions. We have answers.

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ENDOCRINOLOGY CLINICAL INVESTIGATOR/SCIENTIST

The Division of Endocrinology, Diabetes, and Metabolism at Penn State Health Milton S. Hershey Medical Center, Penn State College of Medicine (Hershey, PA) is seeking an NIH-funded Clinical Investigator/Scientist with a focus on basic/clinical diabetes related research to join an expanding Diabetes program. A highly competitive departmental and institutional start-up package will supplement the candidate's extramural support to strengthen and expand the candidate's ongoing research with the goal of developing novel scholarly initiatives within the division and the institution in the field of diabetes. Joint appointments in Basic Science Departments are anticipated.

The Harrisburg-Hershey area includes the state capitol, a population of 500,000 and offers an excellent combination of low cost of living, excellent schools, cultural activities and attractions that bring millions of visitors each year. We're conveniently located within a short distance to major cities such as Philadelphia, Pittsburgh, NYC, Baltimore, and Washington DC.

Appropriate candidates must possess a MD, MD/PhD or foreign equivalent, NIH funding, the ability to obtain a medical license in the Commonwealth of Pennsylvania.

Qualified applicants should contact:

Andrea Manni, M.D.

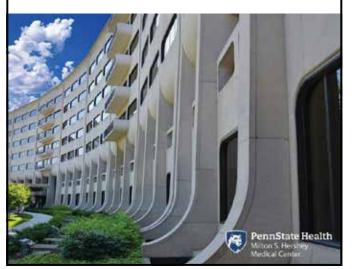
Professor and Division Chief of Endocrinology Diabetes, and Metabolism

c/o Heather Peffley, PHR, FASPR

Physician Recruiter Penn State Health

hpeffley@pennstatehealth.psu.edu

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ENDOCRINOLOGY PHYSICIAN

The Division of Endocrinology, Diabetes, and Metabolism at Penn State Health seeks to fill a junior faculty clinical position. This is a fixed- term position for a **BC/BE Endocrinologist** at the **Assistant Professor** rank. While the primary focus of this position is in patient care, candidates are also expected to participate in teaching and scholarly activities. Candidates will join an academic department, dedicated to education, innovation, leadership and work among highly qualified, friendly colleagues who foster excellent networking opportunities.

Located in a safe family-friendly setting of central Pennsylvania, our local neighborhoods boast a reasonable cost of living whether you prefer a more suburban setting or thriving city rich in theater, arts, and culture. Known for home of the Hershey chocolate bar, Hershey's community is rich in history and offers an abundant range of outdoor activities, arts, and diverse experiences. We're conveniently located within a short distance to major cities such as Philadelphia, Pittsburgh, NYC, Baltimore, and Washington DC. We're proud of our community involvement and encourage you to learn more about our organization.

Appropriate candidates must possess a MD, DO, or foreign equivalent and be board certified/eligible in Internal Medicine and Endocrinology. Candidates should be energetic and highly motivated.

Qualified applicants should upload a letter of interest and CV at: <u>http://tinyurl.com/pj45tup</u> Ref Job ID#954

For additional information, please contact: Andrea Manni, M.D.

Professor and Division Chief of Endocrinology Diabetes, and Metabolism

c/o Heather Peffley, PHR FASPR

Physician Recruiter

hpeffley@pennstatehealth.psu.edu

The Penn State Health Milton S. Hershey Medical Center is committed to affirmative action, equal opportunity and the diversity of its workforce. Equal Opportunity Employer – Minorities/Women/Protected Veterans/Disabled.





Employed Endocrinologist Physician Opportunity Chicagoland Area

We understand the need to balance work with a healthy personal life style. Come join a well-established physician practice that lives by this philosophy. We are growing and looking to add more providers.

Position Highlights

- Well established opportunity 30 minutes from downtown Chicago
- 30 minute commute each way during rush hour from downtown Chicago
- Access to an abundance of cultural activities and world renowned museums that only a world class city can offer
- Private Group Partnership setting and hospital employee
- Collegial group of system physicians eager to provide mentorship and support in developing physician practices
- Healthcare system undergoing explosive growth and expansion in virtually all physician service lines

Job Requirements

- Full-time/permanent position with inpatient and outpatient practice
- Board Certified/Board Eligible required. Although subspecialty interest are encouraged, with the opportunity to design practice around personal goals.
- Unique work structure conducive to utilizing all your skills
 1 in 3 call rotation
 - Office Locations in Munster, IN and East Chicago, IN
- EMR system utilized in Inpatient & Outpatient settings

 EPIC fully integrated HIMSS Stage VII
 (Only 5% of hospitals in country are at this level of sophistication)
 - Easy to use; support department available

Benefit Packages

- Highly competitive salary offers (Negotiable MGMA guidelines)
- Medical/Dental/Vision insurance plans available
- 403B opportunities including employer match
- Exceptional CME funds
- Licensure reimbursement: license, CSR, DEA, Dues/ Subscriptions
- Flexible time off
- Contract bonuses off RVU's
- Sign-on bonus (negotiable)
- Relocation reimbursement (negotiable)

System Details

- Well established not-for-profit 3 hospital system
- Nurse practitioner support in both inpatient and outpatient settings
- Some of the most favorable malpractice laws and regulations in the country

For additional information, please contact Alan Kumar, MD and Jennifer Malinowski via email at: alan.kumar@comhs.org and ilmalinowski@comhs.org



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