

AUGUST 2017

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

INTERNATIONAL

Where there's smoke, there's **DIABETES?**

A new study uncovers a potential link between secondhand smoke and type 2 diabetes and obesity. While the number of smokers continues to decline, will that have any effect on these other side effects?

BETTER OR WORSE:

More studies link BPA & BPS to endocrine disruption

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COVER STORY

18 | **Innocent Bystanders**

A new study uncovers potential links between secondhand smoke and type 2 diabetes and obesity. Fortunately, the number of smokers is on the decline, but will that reduce rates of diabetes and obesity?

BY KELLY HORVATH

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24 | **No Guarantees**

While bisphenol A is a known endocrine-disrupting compound (EDC), its substitute bisphenol S has been shown to be worrisome as well. Three new studies add more evidence that exposure to these EDCs early in life will likely lead to serious health issues later in life.

BY KELLY HORVATH

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31 | **Basic and Clinical Aspects of Menopause**

A woman's body goes through myriad changes before, during, and after menopause. This article takes a multi-faceted look at these changes, including the effects of obesity, the changes in bone, and the non-hormonal treatments for menopausal bone loss.

BY PAUL S. MACLEAN, PHD, NANETTE SANTORO, MD, MICOL S. ROTHMAN, MD, AND T. RAJENDRA KUMAR, PHD



FROM THE **EDITOR**

AUGUST 2017

Endocrine news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Outside Endocrine Influencers

THIS MONTH'S COVER STORY COMES TO YOU THROUGH A HAZE of secondhand smoke. In "Innocent Bystanders" (p. 18), Kelly Horvath reports on a study that links secondhand smoke to diabetes and obesity, while the actual smokers don't tend to suffer these side effects. According to Theodore C. Friedman, MD, PhD, chief, Division of Endocrinology, Metabolism and Molecular Medicine, Charles R. Drew University of Medicine and Science in Los Angeles, California, and the lead author of the study, smokers could be immune from these possible side effects because of "the hand-to-mouth action of cigarettes, or the effect of cigarettes on the taste buds," smokers tend to be leaner than "secondhand smokers."

From a health disruptor that has obvious repercussions like coughing to those that don't, we take a look at bisphenol A (BPA) and its substitute bisphenol S (BPS) in a variety of recent studies from *Endocrinology* as well as **ENDO 2017** presentations in Orlando. Writer Kelly Horvath once again digs deep into these myriad studies and reports their findings in "No Guarantees" (p. 24). As endocrine disruptors become a more prevalent health risk, studies that examine these compounds and their effects are becoming just as prevalent. In turn, these studies will likely put more pressure on the physicians who treat those who are more harshly affected. "Clinicians who treat patients from particularly vulnerable populations, such as pregnant women and children, can play a greater role in determining potential EDC exposures of patients and in educating patients about minimizing these exposures where possible," according to Lindsey Treviño, PhD, Baylor College of Medicine, Houston, Texas, who presented her study, "Early Life Environmental Exposure Creates 'Super-Promoters' By Developmentally Reprogramming the Epigenome of Genes Associated with NAFLD," at **ENDO 2017**.

In this month's Laboratory Notes article, Glenda Fauntleroy goes "back to the bench" for some basic steps every lab manager needs to consider when his or her lab is in need for an upgrade, whether it's due increased personnel or evolving technology. "Lab Improvement" (p. 38) will provide some preliminary tips before a laboratory is given a makeover. **EN**

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

A NOTE TO READERS

Some of our readers pointed out that June's "Why Endocrinology?" guest column writer has frequently expressed opinions on hypothyroidism and vaccinations that are out of step with current medical thought. *Endocrine News* does not support those views of this guest column writer, and we want our readers to know that moving forward all member submissions will undergo a rigorous vetting process until receiving approval from the *Endocrine News* Editorial Advisory Board. Many thanks for your continuing support of *Endocrine News*, the Endocrine Society, and the science and practice of endocrinology. **Concerns regarding the content of material published in *Endocrine News* should be sent to mnewman@endocrine.org.**

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An endocrinologist and a cardiologist teamed up to create

an entertaining and easily understood method to educate patients. The result is Doctablet, a series of online animations that patients of all ages, backgrounds, and education levels can comprehend and even enjoy.

BY DEREK BAGLEY

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As technology evolves and tech staff expands and contracts, it's key to have a laboratory environment that evolves as well. If you're looking to give your lab space an upgrade, *Endocrine News* has a few helpful hints.

BY GLENDA FAUNTLEROY

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New CDC director named; Society congratulates new FASEB executive director; NIH funding outlook uncertain amid budget battles.

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Our Endocrine Society Family Tree

I HOPE YOU ARE ALL ENJOYING SOME LEISURE time this summer/winter. Research into our personal genealogy is a hobby for many people. As members of the Society, we also have a professional genealogy. This month's letter is about our Society's family tree — our ancestors, current generation(s), and our future progeny! I hope it will stimulate your interest in our past, present, and future.

Who are we?

Your extended Endocrine Society family numbers almost 18,000 and lives in 122 countries. Nearly half of us (40%) live outside the U.S. We are fairly well divided between women and men (42% and 50% respectively, no indicated gender 8%), but we are an “older” group, with a median age of 57 (range 20 to 97). We currently define ourselves further by our primary professional roles and by our primary constituency (Basic or Clinical Science or Clinical Practice) — as shown below:

- Basic Science3,314**
- Clinical Science3,190**
- Clinical Practice..... 10,560**
- Unknown.....582**

It's clear that we are an incredibly inclusive group — and we are united by our endocrine heritage and our commitment to the field. Your elected leadership considers this diversity to be an incredible strength. We are a global force with the power to create and sustain changes needed to better care for our patients and to persevere in asking new research questions in the pursuit of discovery.

We want your leadership to “look” like the entire family, so that opinions and values of our entire membership are considered. To that end, we have steadily increased the number of women, non-U.S. members, people of color, younger folks, and individuals with non-traditional professional roles on our committees and leadership ballots. We strive to represent everyone and to serve each of you in ways that are important to *you*.



Clifford Rosen (Council member), Gary Hammer (SP4 retreat guest), and Genevieve Neal-Perry (Vice President, Basic Science).

Diversity, inclusion, and fairness (for members and patients) emerged as core values at our recent Strategic Plan 4 retreat on June 24 and 25 in Chicago. The retreat was attended by the Council, the SP4 Task Force, as well as 16 guests who represented various aspects of our demographic, as shown in these photographs. As you know, development of a strategic plan allows us to envision the future and to plan around that vision, our core values, and core purpose. I'm thrilled that nearly every proposed vision included “global” concepts including the place of endocrinology at the center of teams providing care; the full range of possible scientific subjects and techniques for research; envisioned partnerships with governments, patients, our sister societies (more family relationships!), and other colleagues; integration of our collective strengths to improve knowledge and care; development of desirable career paths for our younger members; access to care and improved care throughout the world; and emphasis on the fundamental role of science in “grounding” our Society. The Strategic Plan Task Force is



Anthony Hollenberg (Council member), Dale Abel (SP4 Task Force member), and Richard Legro (Secretary Treasurer) at the SP4 Planning Retreat.


“
 It’s clear that we are an
 incredibly inclusive group
 — and we are united by our
 endocrine heritage and our
 commitment to the field.
 ”



Engaged SP4 Planning retreat participants discussing the envisioned future of our field.

working to further develop these ideas, and I look forward to presenting the full plan to you later this year.

We envision a future of promise, in part because of the many challenges that face us in our roles as healthcare providers and investigators. However, I believe that together, our family will meet and conquer these challenges. In looking to the future, we also reflect on our past, and those who came before us. They built the strong foundation on which the Society rests. For those of you who wish to learn more about the Society’s history and contributions, please visit our website at <http://www.endocrine.org/about-us/history>. You will be able to access the Century of Endocrinology Timeline as well as oral and video histories.

Feel free to write if you have any questions about the Strategic Planning Process or suggestions for the Society, at president@endocrine.org. 

— Lynnette Nieman, MD, President, Endocrine Society

Endocrine Society Issues Scientific Statement on Obesity's Causes



A new Scientific Statement issued by the Endocrine Society calls for more research aimed specifically at understanding the underlying mechanisms that make it difficult to maintain long-term weight loss.

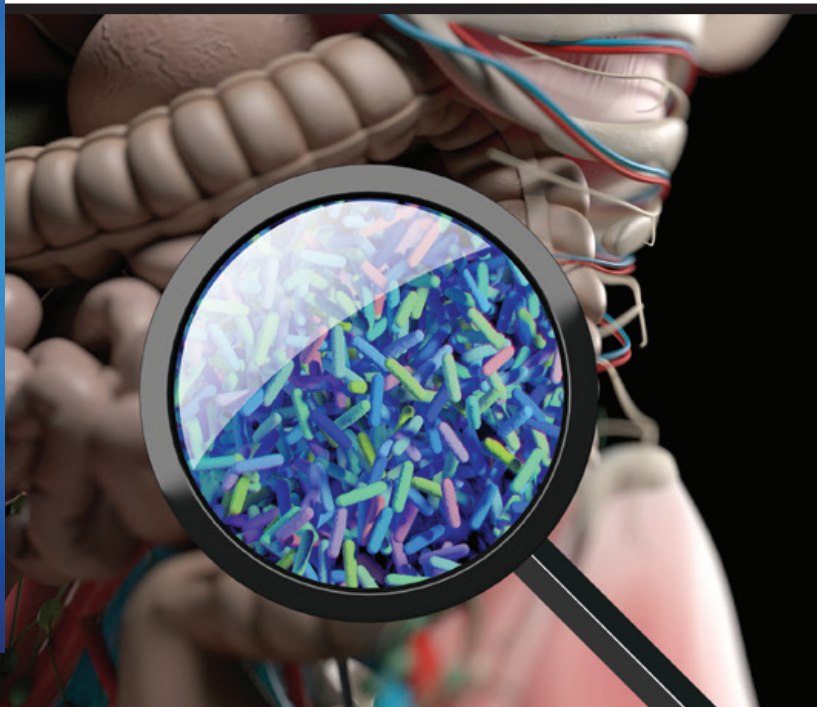
Growing evidence suggests obesity is a disorder of the body's intricate energy balance systems. Once an individual loses weight, the body typically reduces the amount of energy expended at rest, during exercise and daily activities while increasing hunger. This combination of lower energy expenditure and hunger creates a "perfect metabolic storm" of conditions for weight gain.

"Because of the body's energy balance adjustments, most individuals who successfully lose weight struggle to maintain weight loss over time," says Michael W. Schwartz, MD, of the University of Washington in Seattle, and the chair of the task force that authored the Society's Scientific Statement. "To effectively treat obesity, we need to better understand the mechanisms that cause this phenomenon and to devise interventions that specifically address them. Our therapeutic focus has traditionally been on achieving weight reduction. Most patients can do this; what they have the most trouble with is keeping the weight off."

"Healthcare providers and patients need to view this tendency as the body's expected response to weight loss, rather than as a sign of a failed treatment regimen or noncompliance with treatment," he adds.

The Society's statement also calls for additional research into factors influencing obesity:

- ▶ Interactions between genetics, developmental influences, and the environment. Though a substantial portion of obesity risk is conveyed by genes, researchers have not yet been able to identify all of the relevant genes and to understand the nature of their interactions with developmental processes and the environment
- ▶ The effect of endocrine-disrupting chemicals such as bisphenol A on obesity



- ▶ The microbiome, or bacteria in the gut, and its interactions with the endocrine and digestive systems as well as the brain
- ▶ The reasons behind the therapeutic success of bariatric surgery
- ▶ The role that diet composition plays in the development of obesity
- ▶ Biological markers and predictors for diabetes, heart disease, and other conditions that often develop in conjunction with obesity
- ▶ The effects of socioeconomic status on obesity risk
- ▶ Brain imaging to better understand appetite and feeding behavior

Other authors of the statement include: Randy J. Seeley, PhD, of the University of Michigan in Ann Arbor, Mich.; Lori M. Zeltser, PhD, and Rudolph L. Leibel, MD, of Columbia University in New York; Adam Drewnowski, PhD, of the University of Washington in Seattle; and Eric Ravussin, PhD, and Leanne M. Redman, PhD, of Pennington Biomedical Research Center in Baton Rouge, La.

The work was supported by grants from the National Institutes of Health, the National Institute of Diabetes and Digestive and Kidney Diseases-funded Nutrition Obesity Research Centers at the University of Washington, University of Michigan, the Pennington Biomedical Center, Columbia University, and the Russell Berrie Foundation.

The statement, “Obesity Pathogenesis: An Endocrine Society Scientific Statement” was published online in the Society’s journal *Endocrine Reviews* at www.endocrine.org/ObesityStatement. The statement will be published in the August 2017 issue of *Endocrine Reviews*.

2017 Vigersky Awards Announced

Manish R. Upadhyay, MD, and Katy J. Brown, DO, are the recipients of the 2017 Harold Vigersky Practicing Physician Travel Award.

Upadhyay is an endocrinologist practicing at Sutter Health in Roseville, Calif. He attended medical school at Maharaja Sayajirao University in India. Brown is an endocrinologist practicing at Providence Health & Services in Missoula, Mont. She attended medical school at Midwestern University in Arizona.

The Vigersky Travel Award was established in 2010 by Society past-president Robert Vigersky, MD, director of clinical and medical affairs for Metronic, to enable U.S. clinicians who do not receive financial support or reimbursement to attend the Endocrine Society’s annual meeting (ENDO) or Clinical Endocrinology Update (CEU).

Endocrine Society Global Outreach Programs Win Association Honors

An Endocrine Society-led global outreach campaign for underserved populations and another program aimed at training the next generation of global endocrine leaders both received American Society of Association Executives (ASAE) 2017 Silver Power of A Awards.

The first Silver Power of A Award went to the EndoCares program. The Society developed this program to provide medical resources, coaching, and education to patients suffering from endocrine-related conditions in underserved areas of the world. In addition, the campaign aims to foster the next generation of endocrinologists and healthcare providers by creating opportunities to further their education and professional network.

In August 2016, the Society launched EndoCares: Diabetes in Lima, Peru. This two-day program — achieved through strategic partnerships with three local organizations: Sociedad Peruana de Endocrinología, Asociación de Diabetes del Peru, and Liga Peruana de Lucha Contra la Diabetes — included a session to educate healthcare providers on diabetes care, a one-day congress for patients with type 2 diabetes, and a one-day type 1 diabetes-focused workshop for patients with type 1 diabetes.

The Society's Global Leadership Academy won the second Power of A Silver Award. Launched at **ENDO 2017**, the Global Leadership Academy was created to provide formal professional leadership training for early career endocrine scientists and practitioners so that they can be leaders in their field, their institutions, and within the Society. This specific cohort is often not provided with this training that is essential to strengthening their leadership capacity and professional development.



STRONGER BY ASSOCIATION

The inaugural program included 30 participants, about half from Peru and the rest hailed from Argentina, Brazil, Japan, Mexico, Myanmar, Serbia, and the U.S. The goal of the Academy is to create a network of leaders, known as “endocrine ambassadors,” who can share their knowledge with their peers and raise the visibility of the profession worldwide. This year’s program was made possible by the support of Sanofi Peru.

The Power of A Awards showcase how associations leverage their unique resources to solve problems, advance industry/professional performance, kick-start innovation, and improve world conditions. The judging committee selected 23 Gold Award winners and 33 Silver Award winners from more than 149 entries.

The winners were selected by the Power of A Awards Judging Committee and are part of The Power of A campaign, which ASAE launched in 2009 to increase awareness about issues that impact associations and to spotlight the expertise and resources available in the association community for policymakers and other key audiences.

ASAE is a membership organization of more than 21,000 association executives and industry partners representing 9,300 organizations. Its members manage leading trade associations, individual membership societies, and voluntary organizations across the U.S. and in nearly 50 countries around the world.





Society Urges European Parliament to Improve Transparency on EDC Criteria

Last month, Member States of the European Union voted in favor of draft criteria to define endocrine-disrupting chemicals (EDCs). The Endocrine Society is extremely concerned that the criteria will fail to identify EDCs that are currently causing human harm and will not secure a high level of health and environmental protection.

Therefore, the Endocrine Society is urging the European Parliament to improve transparency surrounding the process for implementing the criteria and to engage endocrine scientists in further decision-making steps.

The criteria on EDCs cannot be called science-based as it contains arbitrary exemptions for chemicals specifically designed to disrupt target insect endocrine systems that have similarities in humans and wildlife. Previously, the Endocrine Society, the European Society for Endocrinology, and the European Society for Paediatric Endocrinology released a statement strongly objecting to the addition of loopholes in the criteria as they create frameworks where potentially dangerous chemicals cannot be defined as EDCs by law.

The European Parliament will vote on the criteria in the coming months, and the Endocrine Society encourages the Parliament to gather input from endocrine scientists and professional endocrine associations during their deliberations.

Further details regarding the implementation of the criteria still need to be worked out, and the Endocrine Society calls for transparency on how the contributions from endocrine scientists will be given due consideration in the process by European Food Safety Authority, European Chemicals Agency, and the European Commission.

INTOUCH



Endocrine Society Past-President John D. Baxter, MD

Nominations Open for Inaugural Baxter Prize

Scientists and healthcare providers who have demonstrated innovation and entrepreneurship by leveraging endocrine research to improve patient care can now apply for the inaugural John D. Baxter Prize for Entrepreneurship, the Endocrine Society announced today.

The \$50,000 Baxter Prize will be awarded biennially to candidates who demonstrate entrepreneurship through successful business ventures, technology transfer, partnerships with government agencies, or cooperation with mission-based organizations or foundations. The first Baxter Prize will be awarded in 2018 at the 100th anniversary of **ENDO**, the Society's annual meeting.

Individuals and teams of scientists or clinicians are eligible to apply. If a team decides to enter, then one team member must be designated as the lead nominee. Being a member of the Endocrine Society is not required, although membership is strongly encouraged. To apply, or for more information, visit <https://www.endocrine.org/awards/baxter-prize>. The deadline for entries is **September 15, 2017**.

The award was established in memory of Endocrine Society Past-President John D. Baxter, MD, who was a world-renowned scientist known for being the first to clone the human growth hormone gene. During his career, he made many fundamental medical discoveries and translated them into clinical therapies that had far-reaching implications in the fields of biotechnology and genetic engineering, benefiting the health and welfare of patients worldwide. He passed away in 2011.

"In a fitting tribute to Dr. Baxter's legacy, this award will pave the way for innovative thinkers to improve the lives of people who have hormone health conditions," says Endocrine Society President Lynnette K. Nieman, MD. "The Baxter Prize will provide support for deserving entrepreneurs who are changing the endocrinology field."

The Endocrine Society and Baxter's wife, the Hon. Lee D. Baxter, San Francisco Superior Court (ret.), announced the creation of the new award at **ENDO 2016** in Boston, Mass.



Thomas Landefeld Named CSUDH Advisor of the Year

Thomas Landefeld, PhD, professor of biology at California State University, Dominguez Hills, is presented with the 2017 Advisor of the Year Award. He is flanked by CSUDH President Willie Hagan, PhD, (left) and Jordan Sylvestre, president of Associated Students, Inc.




“ Receiving this award is most gratifying as it signifies that I am effectively mentoring students in pursuing their dreams of a career in healthcare.”

Thomas Landefeld, PhD, professor of biology at California State University, Dominguez Hills, was named the university’s Advisor of the Year for 2017.

Landefeld was presented the award at the CSUDH President’s Leadership and Service Awards ceremony earlier this spring. In nominating him, students pointed to his years of dedication in fostering diversity in health fields and serving as faculty advisor for those interested in entering health careers, such as medicine, dentistry, pharmacology, veterinary, physical therapy, or nursing, to name a few. Landefeld does this in his formal role as the advisor to the Pre-Health Society, the university’s largest student organization, but also assists many students outside of the organization who come to him for guidance as well.

As a mentor, Landefeld works one-on-one with students to tailor individualized plans to help them reach their personal and academic goals, and uses his connections with health professionals and doctoral-degree granting institutions to support his students’ growth as undergraduates. Through his efforts, his students get the chance to hear from guest speakers and school recruiters, and take part in a variety of opportunities, from research to conferences and internships — all with the end goal of preparing them for medical school or other graduate programs.

At the event, Pre-Health Society president, Cassandra De Matta thanked Landefeld for his commitment to students, saying, “I cannot emphasize how much he supports us on an individual level but also as an organization as a whole. Because of his leadership, motivation, and commitment for our organization, we have been able to help students find and learn about their health profession aspirations.

“Receiving this award is most gratifying as it signifies that I am effectively mentoring students in pursuing their dreams of a career in healthcare,” Landefeld says of the honor. 

2017 Clinical Endocrinology Update/ Endocrine Board Review

Chicago, Ill.

September 23 – 27, 2017

www.endocrine.org/ceu

www.endocrine.org/ebc

Special discounts are available by registering for both meetings together.



The Chicago Marriott will be the location for the joint meeting of the 2017 Clinical Endocrinology Update (CEU)/Endocrine Board Review (EBR). 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 69th 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 EBR offers a comprehensive mock-exam format with case-based American Board of Internal Medicine (ABIM)-style questions forming the bulk of the presentations. Each section follows the ABIM blueprint for the board exam, covering the breadth and depth of the certification/recertification examination. Each case will be discussed in detail, with the correct and incorrect answer options reviewed. The mock exam appeals to endocrine fellows who have completed or are nearing completion of their fellowship and are preparing to take the board certification exam. Practicing endocrinologists may appreciate the EBR's comprehensive self-assessment of endocrinology either to prepare for recertification or to update their practice.

Reducing the Risk of Preventable Adverse Drug Events associated with Hypoglycemia in the Older Population

Silver Spring, Md., September 12, 2017

The Food and Drug Administration's Center for Drug Evaluation and Research, Professional Affairs and Stakeholder Engagement Staff (PASES) is hosting this one-day public workshop to discuss the importance of individualized glycemic control targets for older patients with diabetes, in order to reduce the risk of serious hypoglycemia, identify and discuss medication safety efforts, discuss future areas of research that could be explored to reduce the risk of serious hypoglycemia, and disseminate the results of this discussion to inform patients, patient advocates, and healthcare practitioners.

www.endocrine.org/fdahypoglycemia

EndoBridge 2017

Antalya, Turkey, October 19 – 22, 2017

Jointly organized by the Endocrine Society, the European Society of Endocrinology, and the Society of Endocrinology and Metabolism of Turkey, EndoBridge will provide a comprehensive

update in the field of endocrinology. This meeting is designed for the clinical endocrinologist. The official language of the meeting is English, but simultaneous translation will be available in Russian, Arabic, and Turkish.

info@endobridge.org

Obesity Week

Washington D.C., October 29 – November 2, 2017

The world's largest obesity-centric conference presents cutting-edge research, medical advances, surgical practices, public policy, and more as it continues to bring together world-renowned obesity experts to share innovations and breakthroughs in obesity treatment.

www.obesityweek.com

19th ASEAN Federation of Endocrine Societies 2017

Yangon, Myanmar, November 9 – 12, 2017

ASEAN Federation of Endocrine Societies (AFES) is an association of seven endocrine societies in Southeast Asia with a conference held every two years. With an extensive program covering a broad array of topics, various networking opportunities,

poster sessions, continuing medical education, updates on new products and technologies at the AFES Expo, keynote speakers, and more, AFES 2017 is a "must-attend" event in Asia and one of the most recognized congresses among the clinicians and researchers in endocrinology.

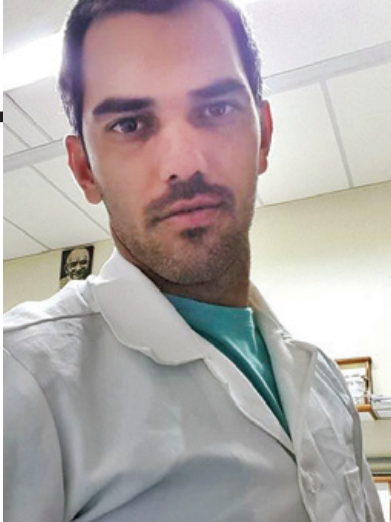
www.afes2017myanmar.com

Translational Reproductive Biology and Clinical Reproductive Endocrinology 2017

New York, N.Y., November 16 – 19, 2017

The objective of this conference is to offer an authoritative 2017 update for reproductive clinicians and researchers, focusing on new translational developments in the field of reproductive biology and physiology, as well as clinically relevant patient-care issues. The conference aims to offer basic scientists and clinicians a unique and intimate framework for interactions and exchanges of ideas around paradigm changes and imminent new developments of significance.

www.afes2017myanmar.com



WHY ENDOCRINOLOGY?

Search, Discover, Teach, Repeat

BY LUIZ FERNANDO FONTE BOA, Mestrando na Pós Graduação de Medicina (Endocrinologia - HUCFF); Institute of Biophysics Carlos Chagas Filho-UFRJ, Molecular Radiobiology Laboratory, Cidade Universitária, Rio de Janeiro, Brazil

My relationship with endocrinology actually started before I even knew what endocrinology was; in my family, I had many relatives with hormone-related problems, such as obesity, diabetes, and thyroid disorders. I can still remember asking my mother why she was taking medicine every day. She told me that it was for her thyroid since her body did not produce thyroid hormones. Thankfully, the medication my mother took when I was a child has continued to help her maintain her health to this day.

As is often the case with children, I had forgotten all about my mother's medication and her thyroid condition but was reminded of endocrinology once again when I began my undergraduate degree in biological sciences at University of Itaúna in Brazil. When I was studying physiology, those old dysfunctions finally started to make sense to me, and I could understand these issues a little better.

When I entered the laboratory to prepare for my master's degree in endocrinology at Federal University of Rio de Janeiro, I was stepping into a lab that was well known for endocrine physiology. Here in the lab, I saw firsthand how perfect a field of study endocrinology would be for me. I began to understand how hormones are produced and secreted, as well as their interactions with other hormones and the many other components of the organism.

It was incredible then, and it's incredible now! Each day I want to learn more and more. It's exciting. I chose endocrinology

because I felt a kinship to it, an attraction to the science of it all, and it has always seemed like a perfect, natural fit. I'm also fortunate that I have an advisor and mentor who continues to inspire me: Rodrigo Fortunato, PhD, a physiology professor at Federal University of Rio de Janeiro. I have been continuously amazed by his knowledge of endocrine physiology and his able mastery of the content. Dr. Fortunato is the type of mentor, scientist, and professional I hope to be.

“
I truly believe that the world needs more knowledge about endocrinology and endocrine science. It can only improve the lives and the health for everybody.
”

However, one of my fondest wishes is to be able to communicate my knowledge about the many charms of endocrinology to others. I truly believe that the world needs more knowledge about endocrinology and endocrine science. It can only improve the lives and the health for everybody. I hope one day to be able to communicate such knowledge to the world ... but in the meantime, I will spread this knowledge among my peers and students.

To put it simply, I live, work, breathe, play, and study endocrinology. For me, endocrinology and endocrine science has become not just a field of study, but my life's ambition. It is a life of autocrine, paracrine, and endocrine activity that I never want to live without. After graduation, I intend to continue my research and teaching, either here or somewhere else in the world. To put it simply: I love what I do: Search, discover, teach, repeat. ^{EN}

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

“ I live, work, breathe, play, and study endocrinology. For me, endocrinology and endocrine science has become not just a field of study, but my life’s ambition. I intend to continue my research and teaching, either here or somewhere else in the world. **To put it simply: I love what I do: Search, discover, teach, repeat.**”

— LUIZ FERNANDO FONTE BOA, Mestrando na Pós Graduação de Medicina (Endocrinologia - HUCFF); Institute of Biophysics Carlos Chagas Filho-UFRJ, Molecular Radiobiology Laboratory, Cidade Universitária, Rio de Janeiro, Brazil, discussing his passion for endocrine science in this issue’s “Why Endocrinology?” column on page 12.

FROM THE CENTURY OF ENDOCRINOLOGY TIMELINE

1971:

Diethylstilbestrol (DES) Identified as Transplacental Carcinogen



Diethylstilbestrol (DES) was prescribed to millions of pregnant women, primarily from 1938 to 1971, in the mistaken belief that the drug prevented miscarriage and ensured a healthy baby. Instead, DES harmed the mothers who were prescribed it and children born to mothers prescribed DES are at increased risk of severe health problems, including cancer, infertility, and adverse pregnancy outcomes. The adverse outcome was initially described by Herbst, et al. DES was the first identified transplacental carcinogen, and research continues to examine the effects of DES on offspring, including the effects of DES in the third generation, i.e. the children of men and women exposed to DES in utero.

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

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19%

The increase in “gender confirmation” surgery in 2016 from 2015. Gender confirmation surgery encompasses a number of procedures, including face and chest operations, and is a more inclusive term than “gender reassignment” surgery, which can include reshaping the genitalia.

— SOURCE: AMERICAN SOCIETY OF PLASTIC SURGEONS

600

The number of international units of daily vitamin D recommended for children and adolescents.

— SOURCE: HORMONE HEALTH NETWORK (WWW.HORMONE.ORG)

ACROMEGALY AFFECTS 78 Americans Per Million Per Year



— SOURCE: WWW.ENDOCRINEFACTS.ORG

BY DEREK BAGLEY

Cabergoline Tapering Successful at Maintaining Normal Prolactin Levels in Patients with Macroprolactinomas

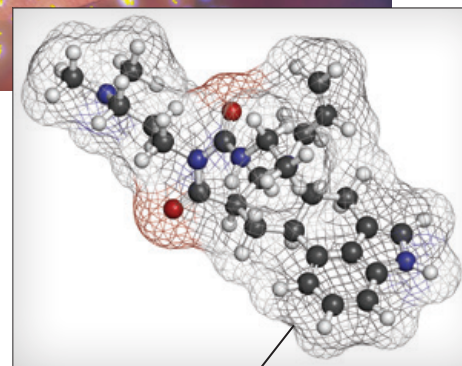
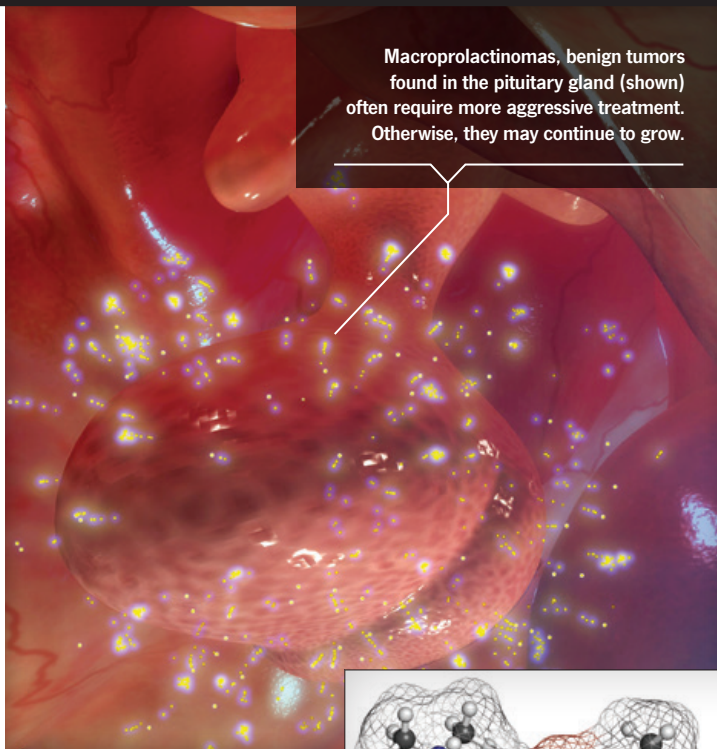
Tapering cabergoline (CAB) levels can still maintain normal prolactin (PRL) levels in patients with macroprolactinomas, according to a study recently published in the *Journal of the Endocrine Society*.

Researchers led by Phillippe Chanson, MD, of Hopital de Bicetre in Le Kremlin-Bicetre, France, point out that CAB is “currently the dopamine agonist (DA) of choice” in treating macroprolactinomas because it’s the most effective drug. They also note that Endocrine Society guidelines recommend continuing DA therapy for a minimum of two years once PRL levels have normalized, and that between 24% and 75% of patients maintain a normal PRL level after DA withdrawal. However, they write, there are few data on the necessary dose of CAB to achieve and maintain normal PRL levels.

The team retrospectively studied 260 patients in two groups: one group whose doctors chose to maintain the CAB dose — the fixed-dose group — and one group whose doctors chose to taper the CAB dose — the de-escalation group. PRL levels normalized in 157 patients, with 84 of these patients tapering their CAB doses, 77 of whom maintained normal PRL levels. De-escalation even worked in patients who required larger doses, so-called “CAB resistant patients.” The authors write that tapering had no negative long-term effect on tumor size.

“A low effective initial dose of CAB seems to be a good predictor of successful subsequent CAB withdrawal,” the authors write. “In our experience, when a very low maintenance dose and/or a long dosing interval has been achieved, complete CAB withdrawal can be attempted. However, lengthy follow-up is necessary, because CAB has a very long half-life.”

Macroprolactinomas, benign tumors found in the pituitary gland (shown) often require more aggressive treatment. Otherwise, they may continue to grow.



Cabergoline drug, chemical structure; Atoms are represented as spheres with conventional color coding: hydrogen (white), carbon (grey), etc.

Findings: Based on these results, the researchers conclude that the CAB dosage to maintain normal PRL levels is lower than the initial dosage used to normalize PRL levels, and that tapering is almost always successful, even in the CAB resistant patients. They go on to write, “This tapering strategy has two potential benefits: It reduces the possible risks associated with long-term CAB exposure, and it identifies patients in whom hyperprolactinemia is likely to recur if CAB is discontinued. Importantly, CAB de-escalation does not result in renewed tumor growth.”



Type 1 Diabetes Organ Donors Show High Rates of Illicit Drug Use and Suicide

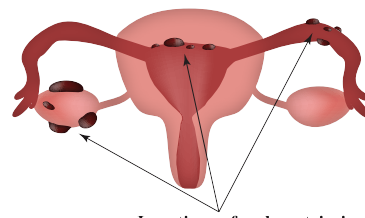
A letter published recently in *Diabetes Care* says that there is a high rate of illicit drug use and suicide in people with type 1 diabetes who donate their pancreases to the Network of Pancreatic Organ Donors with Diabetes (nPOD). This network collects, processes, and distributes these organs to researchers studying diabetes around the world.

Researchers led by Desmond A. Schatz, MD, of the University of Florida Diabetes Institute, reviewed terminal hospital records of 100 people with type 1 diabetes who donated their organs to nPOD, 45% of whom were female and 79% Caucasian. The donors' ages ranged from four to 61, with a mean age of 28. They found that the most common cause of death was anoxia, brought on by drug overdose, myocardial infarction, pulmonary embolism, or cerebral edema. "Deaths due to anoxia coincide with a history of illicit substance abuse in 26% (15/57) of cases, and the majority of individuals had positive toxicology upon arrival to medical care," the authors write.

The researchers also found that eight of the donors had committed suicide, at an average age of 21, with three of the donors under the age of 18 when they committed suicide by either overdosing on their insulin or self-inflicted gunshot wound. The authors go on to write that this suicide rate is similar to the type 1 diabetes registry in the U.K., where 6% of people with type 1 diabetes commit suicide.

Findings: The authors note that there are implicit biases in this small study, but they write, "the high rate of suicide and drug use should continue to spur our energy and resources toward caring for the emotional and psychological needs of those living with type 1 diabetes."

Autocrine Prolactin Associated with Endometrial Cancer Growth, Metastasis, Reduced Sensitivity to Chemotherapy



Locations of endometriosis

Researchers have shown that autocrine human prolactin (hPRL) promotes endometrial tumor growth and metastasis, as well as reduces sensitivity to chemotherapy, leading to worse survival outcomes.

Based on this association, the investigators also point to a possible therapeutic strategy for endometrial cancer (EC). The results were published recently in *Endocrinology*.

The team, led by Peter E. Lobie, MD, PhD, of the National University of Singapore, and Tao Zhu, MD, PhD, of the University of Science and Technology of China in Hefei, note that treating late-stage EC remains a major challenge, with poor response to chemotherapy and low patient survival rate. They have built on earlier studies, which reported elevated serum hPRL levels in EC tumors, by further delineating the functional roles of hPRL in EC progression.

For this study, they show that autocrine hPRL expression stimulated EC cell proliferation, invasion, and migration, and promoted tumor growth and metastatic colonization in xenograft models. "In addition," the authors write, "forced expression of hPRL decreased sensitivity of EC cells to chemotherapeutic drugs (i.e., doxorubicin and paclitaxel), both in vitro and in vivo."

Consistently, they show that depleting hPRL significantly reduced oncogenicity and enhanced the sensitivity to chemotherapy. Therefore, the researchers propose that targeting prolactin signaling could be considered as a viable adjuvant therapy in late-stage EC to improve the response to chemotherapy.

A companion piece written by Felicitas Lopez Vicchi and Damasia Becu-Villalobos, PhD, of the Instituto de Biología y Medicina Experimental Conicet in Buenos Aires, Argentina, concluded that based on the results of this study, as well as existing literature, "patients with endometrial cancer in advanced stages or with chemoresistance could benefit from anti-PRLR strategies used in combination with actual therapies."

Machine-Learning Techniques Unlock Hidden Benefit of Weight Loss Interventions for Overweight Patients with Type 2 Diabetes



Losing weight reduces the risk of long-term cardiovascular illness and mortality for the majority of patients with type 2 diabetes, but for a small subgroup, weight-loss intervention can lead to dramatically worse outcomes, according a study published recently in *The Lancet Diabetes & Endocrinology*.

Researchers led by James H. Faghmous, PhD, chief technology officer at the Arnhold Institute for Global Health of the Icahn School of Medicine at Mount Sinai, reanalyzed data from the trial known as Look AHEAD (Action for Health in Diabetes). Using machine-learning techniques, they found that, despite the overall null findings of the trial, 85% of the study sample did experience a clinically meaningful, significant reduction in cardiovascular mortality and morbidity from the trial's intensive weight-loss intervention.

“Our analysis demonstrates that recent advances in machine learning for causal inference can increase the quantity of clinically relevant findings generated from large randomized trials,” says Aaron Baum, PhD, lead economist, the Arnhold Institute for Global Health; assistant professor, Department of Health System Design and Global Health, Icahn School of Medicine at Mount Sinai; and lead author of the study. “As researchers and data scientists, we are always concerned that


an overall study result could mask important disparities in benefit or harm among different types of patients, which is exactly what this study revealed. Being able to identify individuals who could benefit from an intervention is fundamental to patient care.”

The Look AHEAD study enrolled more than 5,000 overweight and obese patients with diabetes with a planned follow-up period of up to 13 years. Its intent was to determine whether modest weight loss through a lifestyle intervention reduced the rate of mortality and serious events like heart attacks and strokes. The trial was halted early by the National Institutes of Health (NIH) after finding no difference in the rates of cardiovascular events between the two groups.

“This research strengthens the role for data science and precision medicine as essential tools that can transform the way healthcare is delivered,” says Prabhjot Singh, MD, PhD, director of the Arnhold Institute for Global Health and Chair of the Department of Health System Design and Global Health, Icahn School of Medicine at Mount Sinai. “Identifying individuals who could benefit from an intervention is crucial for practicing clinicians, while ignoring subgroups who benefit might lead to lack of reimbursement for weight-loss programs, which would neglect vulnerable populations.”

Findings: The team's findings indicated that 15% of subjects had substantially increased risk of cardiovascular events such as heart attack or stroke as a result of weight-loss interventions. This could be the first suggestive evidence of an adverse reaction to what is generally considered a common-sense and innocuous intervention. This subgroup was defined by a combination of two baseline characteristics: mild or well-treated diabetes (HbA1c less than 6.8%) and a negative perception of their health status (SF-36 general health score less than 48). The latter is strongly correlated to depression. This subgroup also:

- ▶ Reported substantially poorer compliance with the exercise portion of the intervention, which is consistent with the importance of assessing patients' readiness for change when recommending behavioral interventions;
- ▶ Experienced less improvement in several intermediate health outcomes, including blood sugar, mental health, and blood pressure.

"This analysis restores my faith in basic common sense," says Ronald Tamler, MD, medical director of the Mount Sinai Clinical Diabetes Institute and co-author of the study. "For the vast majority of people with diabetes, a healthy lifestyle with weight loss carries significant benefits; however, it's not for everyone. Thanks to this work, clinicians can infer which patients will benefit the most from such a lifestyle intervention." 

“ Being able to identify individuals who could benefit from an intervention is fundamental to patient care.”

— AARON BAUM, PHD, LEAD ECONOMIST, THE ARNHOLD INSTITUTE FOR GLOBAL HEALTH; ASSISTANT PROFESSOR, DEPARTMENT OF HEALTH SYSTEM DESIGN AND GLOBAL HEALTH, ICAHN SCHOOL OF MEDICINE AT MOUNT SINAI; AND LEAD AUTHOR OF THE STUDY



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Innocent *bystanders*

BY KELLY HORVATH

A new study uncovers potential links between secondhand smoke and type 2 diabetes and obesity. Fortunately, the number of smokers is on the decline, but will that reduce rates of diabetes and obesity?



The association between smoking and risk factors for respiratory, cardiovascular, and metabolic diseases is widely documented, as are the respiratory and cardiovascular risks for those exposed to secondhand smoke, also known as “passive smoking.”

Potential endocrine disruptions in this latter population, however, were not well studied until a team of researchers from Charles R. Drew University of Medicine and Science in Los Angeles, California, decided to look at what effect secondhand smoke exposure might have on glycemic parameters, on the heels of a recent meta-analysis that demonstrated a link between passive smoking and relative risk of developing type 2 diabetes.

Type 2 diabetes being so strongly associated with obesity begs the question: Are secondhand smoking and obesity interrelated? “I realized that primary smokers may know what they are getting into when they light up, but those exposed to secondhand smoke are innocent bystanders exposed to smoke that may have detrimental effects on their health,” says researcher Theodore C. Friedman, MD, PhD, chief, Division of Endocrinology, Metabolism and Molecular Medicine. “I read some articles in the lay press that the effects of secondhand smoke were exaggerated, which I knew was wrong. I wanted to study the metabolic effects of secondhand smoke to see if those exposed to secondhand smoke have higher rates of diabetes as well as increased body weight.”

Smoking Status

In “Association between Secondhand Smoke and Obesity and Glucose Abnormalities: Data from the National Health and Nutrition Examination Survey (NHANES 1999–2010),” published in *BMJ Open Diabetes Research and Care*, the team analyzed NHANES data from 6,472 participants ages 20 years or older against smoking status (as determined by serum cotinine levels, a byproduct of nicotine known to be an effective measure of exposure to smoking) and response to questionnaires to compare body mass index (BMI), glycated hemoglobin (HbA1c) status, insulin resistance, and fasting plasma glucose level. Exclusion criteria included using tobacco products other than cigarettes (e.g., nicotine gums or patches, chewing tobacco, pipes, etc.) and taking antiglycemic medications.

They stratified participants into non-smokers (2,835), secondhand smokers (1,759), and current smokers (1,878) according to cotinine levels — low, medium, and high, respectively. They next ran those numbers through a second method that incorporated questions about smoking status: Current smokers (1,794) had smoked at least 100 cigarettes in their lifetime and currently smoke (former smokers [1,681] could also be identified according to this method but not by objective cotinine level alone). Secondhand smokers (1,158) had neither smoked at least 100 cigarettes/lifetime nor had smoked in the last five days, had serum cotinine levels of <0.05 ng/mL, and reported having been exposed to cigarettes at home or work or did not report exposure but had serum cotinine levels of ≥ 0.05 ng/mL. Non-smokers (1,839) had neither smoked at least 100 cigarettes/lifetime nor had smoked in the last five days and had serum cotinine levels of <0.05 ng/mL.

Interestingly, although the number of current smokers stayed relatively constant between the two definition methods, the number of secondhand smokers varied considerably, which possibly suggests that some exposure is insidious. Gender and race/ethnicity also played roles, with males and blacks being more likely to qualify as secondhand smokers; likewise, higher alcohol consumption correlated with increased likelihood of being a secondhand smoker, as did lower income level.

Where There's Secondhand Smoke . . .

Results demonstrated that secondhand smoke exposure was associated with higher adjusted levels of insulin resistance, fasting plasma glucose, and HbA1c in addition to higher BMI compared with non-smokers, whereas, somewhat surprisingly, smoking is associated with a lower BMI compared with non-smokers even though smoking confers an increased risk of developing diabetes. Although the detrimental effects of secondhand smoke exposure on glycemic parameters persisted even after adjusting for BMI, they were greatly reduced; therefore, increased weight is mainly responsible for the metabolic disruptions seen in this cohort.



AT A GLANCE

- ▶ **Secondhand smokers had a higher BMI as well as higher levels of insulin resistance, fasting plasma glucose, and glycated hemoglobin than non-smokers, even after adjusting for confounders.**
- ▶ **Although some of the worrisome glycemic parameters in secondhand smokers were due to higher BMI, secondhand smoking is itself a risk for increased BMI.**
- ▶ **Despite current smokers having a lower BMI than non-smokers, their risk for diabetes is nevertheless increased, pointing to smoking — whether active or passive — as being the mediator of some of the negative effects on glycemic parameters.**

“ The decline in secondhand smoke over the years shows that smoke-free laws are working. If this continues, **it may be accompanied by a decline in the rates of obesity and diabetes.**”

—THEODORE C. FRIEDMAN, MD, PHD, CHIEF, DIVISION OF ENDOCRINOLOGY, METABOLISM AND MOLECULAR MEDICINE, CHARLES R. DREW UNIVERSITY OF MEDICINE AND SCIENCE IN LOS ANGELES, CALIFORNIA



Regarding the mechanism by which secondhand smoke increases body weight, Friedman says, “As with most causes of weight gain, it is due to eating more and metabolizing less with less activity, but in this context, it needs to be studied more. It is possible that the hand-to-mouth action of cigarettes, or the effect of cigarettes on taste buds, conditions that are not present for secondhand smokers, may lead to smokers being leaner than secondhand smokers.”

Plans for follow-up studies include determining the effect that secondhand smoke has on body composition, such as whether it leads to increased central obesity. “We will also be trying to address if secondhand smoke is associated with a decline in activity, in an increase in calories, or in a change in food composition,” Friedman adds.

Waiting to Exhale

Potentially good news awaits in that the numbers of secondhand and current smokers declined during the NHANES decade, while the numbers of non-smokers rose. According to the NHANES data, the percentage of participants who met secondhand smoking criteria decreased from 22.3% in 1999 – 2000 to 13.5% in 2009 – 2010. Non-smokers increased from 19.9% in 1999 – 2000 to 38.4% in 2009 – 2010. Public health measures are largely to thank and may reveal continued positive trends.

“The decline in secondhand smoke over the years shows that smoke-free laws are working,” Friedman says. “If this continues, it may be accompanied by a decline in the rates of obesity and diabetes.” To clinicians, he adds, “Advise your patients not to be around secondhand smoke and advocate for more smoke-free laws.” ^{EN}

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HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT PEDIATRIC OBESITY STUDIES IN THE JUNE ISSUE.

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No Guarantees

BY KELLY HORVATH

While bisphenol A is a known endocrine-disrupting compound (EDC), its substitute bisphenol S has been shown to be worrisome as well. Three new studies add more evidence that exposure to these EDCs early in life will likely lead to serious health issues later in life.

Once again, bisphenol A (BPA) is making headlines, and, as always, not in a good way.



Hundreds of epidemiological studies have been published that link BPA, a known endocrine-disrupting compound (EDC) even at very low doses, to health problems affecting all human body systems. Two new studies raise yet more cause for alarm, and a third demonstrates that a commonly used BPA substitute is probably not much better for human health. Collectively, these studies contribute to the burgeoning body of evidence that exposure to EDCs during critical developmental periods predisposes the individual to serious disease.

BPA AND OBESITY

In “Perinatal Exposure to Low-Dose Bisphenol-A Disrupts the Structural and Functional Development of the Hypothalamic Feeding Circuitry,” published in *Endocrinology*, Alfonso Abizaid, PhD, of Carleton University in Ottawa, Canada, and team followed up on existing studies that demonstrated how exposure to BPA in the early postnatal period affects body weight, glucose homeostasis, and liver function in mice to confirm that the metabolic impairments were the result of the exposure rather than a function of their postnatal environment or a certain metabolic phenotype.

“With BPA found in everything from tomato soup can linings, to beer cans, to gas station receipts,” Abizaid says, “it’s vitally important to understand how this and other EDCs affect brain function.” The researchers fed pregnant CD-1 mice a diet of food containing BPA, notably, “at doses lower than levels deemed safe by the U.S. Food and Drug Administration and Health Canada,” Abizaid says. Another cohort of dams was given diethylstilbestrol (DES), and a third chemical-free group represented the control. Offspring were intraperitoneally injected with recombinant mouse leptin, the so-called “satiety hormone,”



“ With BPA found in everything from tomato soup can linings, to beer cans, to gas station receipts, **it’s vitally important to understand how this and other EDCs affect brain function.**”

— ALFONSO ABIZAID, PHD, CARLETON UNIVERSITY, OTTAWA, CANADA

at various time points and then euthanized at different ages for analysis of brain tissue and blood to determine their response to the leptin. As part of the melanocortin system important in energy-balance signaling, a postnatal surge in circulating leptin is thought to encourage the development of projections from pro-opiomelanocortin (POMC) neurons in the arcuate nucleus, a group of cells that are critical for the regulation of feeding and body weight.

Their findings revealed that the BPA-exposed mice had fewer POMC projections and a delayed leptin surge and therefore decreased sensitivity to leptin. Likewise, the leptin surge was blunted in DES-exposed mice. In females only, POMC projections later developed normally with daily injections of supplemental leptin. This implicates BPA as an obesogen, reprogramming the melanocortin system and irrevocably disrupting metabolic homeostasis.

Because, as Abizaid puts it, “if it happens in animals, it is likely to happen in humans,” his team is in the process of conducting research in humans and to determine if these changes are reversible. “Pregnant humans have enzymes that break down BPA within 30 minutes,” Abizaid says. “But fetuses and newborns do not have these enzymes. We need to understand what BPA is doing to us and make a serious attempt to reduce BPA levels in consumer products as potentially another means to reverse the obesity epidemic.”

BPA'S EFFECTS ON THE DEVELOPING LIVER

In “Early Life Environmental Exposure Creates ‘Super-Promoters’ By Developmentally Reprogramming the Epigenome of Genes Associated with NAFLD,” presented at **ENDO 2017**, a team of researchers led by Lindsey Treviño, PhD, of Baylor College of Medicine in Houston, Texas, sought to identify the molecular causes of the developmental reprogramming they had observed in past animal studies. “Early-life exposure to BPA in rodents leads to the development of non-alcoholic liver disease (NAFLD) in adulthood, a phenotype exacerbated by challenge with high-fat diet,” Treviño says. “However, there is a gap in our knowledge regarding alterations in the epigenome in these models, particularly those alterations that precede overt liver disease and may play a role in modifying disease susceptibility.”

Researchers exposed newborn rat pups to environmentally relevant doses of oral BPA three times over a five-day period and compared their liver tissue either postexposure or during adulthood to control samples. Analysis of liver samples showed increased liver weight as well as increased levels of serum triglycerides, low- and very-low-density lipoprotein, and free cholesterol in BPA-exposed rats, suggesting that BPA had developmentally reprogrammed their livers and predisposing them to a NAFLD phenotype.

“Exposure of developing tissues or organs to an adverse stimulus during critical periods of development can permanently reprogram normal physiological responses contributing to the development of disease later in life,” Treviño explains. “Importantly, different tissues may have very different windows of susceptibility, and epigenomic alterations can persist across the life course (or even across generations).” In rats, five days after birth is one such window for liver.

The team plans to continue examining molecular mechanisms underlying epigenomic changes. “We are also interested in translating these data into humans by examining whether the observed epigenomic changes, and/or associated changes in gene expression, metabolites, and lipids, are also observed in people at risk for NAFLD,” Treviño says. “Even though the direct relevance of our data to human health is still being tested, it is clear that increasing awareness of EDC exposures and their potential health effects is warranted. Clinicians who treat patients from particularly vulnerable populations, such as pregnant women and children, can play a greater role in determining potential EDC exposures of patients and in educating patients about minimizing these exposures where possible.”

“BPA-FREE” IS NO GUARANTEE

In “Regulation of Estrogen Receptor (ER) and BRCA1 By Bisphenol-S (BPS) in Breast Cancer Cells,” also presented at **ENDO 2017**, Sumi Dinda, PhD, of Oakland University School of Health Sciences in Rochester, Mich., and his team investigated whether the bisphenol analogue BPS is a suitable alternative to BPA in many everyday products. BPS is commonly used in products labeled “BPA free” as well as in plastic substitutes and even paper currency.



AT A GLANCE

- ▶ Perinatal BPA exposure affects developmental programming of the hypothalamic melanocortin circuitry in mice, resulting in delayed leptin secretion and lack of response to satiety cues, leading to obesity.
- ▶ Early-life BPA exposure reprograms the developing epigenome to generate molecular “super promoters” responsive to a high-fat diet later in life, resulting in liver impairments and metabolic disease.
- ▶ BPS displays estrogen-like behavior in breast cancer cells, suggesting that it may not be a safer BPA alternative despite its widespread use.



“Clinicians who treat patients from particularly vulnerable populations, such as pregnant women and children, can play a greater role in determining potential EDC exposures of patients and in educating patients about minimizing these exposures where possible.”

— LINDSEY TREVIÑO, PHD, BAYLOR COLLEGE OF MEDICINE, HOUSTON, TEXAS

EDCs interfere with the normal hormonal activity in the body, and bisphenols, specifically, disrupt the proper functioning of estrogen receptors. “Studies suggest BPS induces ER α pathways via its estrogen-mimicking properties in the body, causing increased cell proliferation and resulting in increased breast cancer risk,” Dinda says. “Despite the hope of a safer substitute, studies have shown that BPS exhibits similar estrogenic activity compared to its analogue BPA, due to their structural commonalities.” As most breast cancers are ER positive, and the majority of women who inherit a harmful mutation in the *BRCA1* gene will develop breast cancer, the team sought to elucidate the relationship between ER α , *BRCA1* expression, and BPS for better understanding of breast cancer treatment and prevention.

Exposing two ER-positive breast cancer cell lines to BPS or to an inactive control, they found that BPS behaved like estrogen by increasing protein expression in ER and *BRCA1* after 24 hours. After six days, the BPS-exposed breast cancer cells had proliferated exponentially. When next treated with anti-estrogen agents, the breast cancer cells ceased multiplying.

For oncologists dealing with breast cancer patients, Dinda advises, “be knowledgeable about the potential health risk of BPS since it may cause the cancer to be aggressive due to its interaction with estrogen receptor and *BRCA1* genes.” He and his team are currently conducting additional studies with BPS on breast cancer cells. ^{EN}

HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT A SIDE BENEFIT OF MENOPAUSAL HORMONE THERAPY ON WOMEN'S BONE STRENGTH IN THE MAY ISSUE.

COMING SOON



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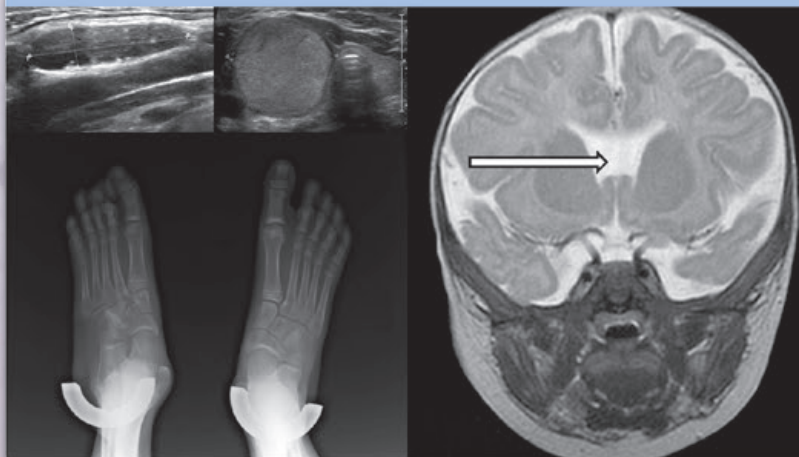
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Basic and Clinical Aspects of Menopause

A woman's body goes through myriad changes before, during, and after menopause. This article takes a multi-faceted look at these changes, including the effects of obesity, the changes in bone, and the non-hormonal treatments for menopausal bone loss.

BY PAUL S. MACLEAN, PHD,
NANETTE SANTORO, MD,
MICOL S. ROTHMAN, MD, AND
T. RAJENDRA KUMAR, PHD



One of the most significant transitions in a woman's life is undoubtedly menopause, the end of the reproductive life, when menstrual cycles no longer occur. The key biochemical event is the cessation of the ovarian output of the female steroid hormone, estrogen. Menopausal transition also initiates a series of events that contribute to the overall process of aging. Osteoporosis, the major bone loss complication, occurs in many post-menopausal women and contributes to frailty and overall diminishing physical strength. Additional biochemical and metabolic changes attributable to loss of estrogen ensue, including neurological, cardiovascular, and musculoskeletal. Estrogen supplementation, commonly known as hormone therapy (HT), to alleviate menopausal symptoms has remained controversial. Several anti-resorptive and anabolic agents are

already available in the clinic for treatment of menopausal bone loss. Several new drugs with different mechanisms of action are also in the pipeline.

In this Tri-Point, a basic scientist describes the bioenergetics aspects of menopause and how obesity affects menopause. Next, a clinician/translational research expert discusses the observational studies on bone changes across the menopausal transition and the long-term trajectories of bone loss, highlighting how critical it is to align the bone curves to the menopausal stage. The epidemiology and the role of factors other than estrogen involved in bone loss will also be discussed. Finally, a practicing clinician discusses non-hormonal treatment options for menopausal bone loss.



Paul S. MacLean, PhD, Professor, Department of Medicine, University of Colorado Anschutz Medical Campus, Anschutz Health and Wellness Center, Aurora

HIGHLIGHTS

Studies in model systems have clearly shown the presence of estrogen receptors in key neural nodes of energy balance regulation.

Menopause is associated with numerous molecular and physiological changes that reduce metabolic function of the liver, lipid accumulation in adipose tissue, and reduced mass and function of skeletal muscle.

Studies with mouse models indicate that elevated levels of follicle-stimulating hormone (FSH) during perimenopausal stage activate osteoclasts and contribute to osteoporosis even in the presence of normal estrogen.

Basic Aspects of Menopause

PAUL MACLEAN, PHD, merges clinical observations with the information garnered from animal (rodent) models to summarize the metabolic consequences of the loss of ovarian estrogen production.

Menopause, Bioenergetics, and Metabolic Health

Menopause is associated with weight gain, increased abdominal adiposity, and a decline in metabolic health that extend beyond bone. Given that estrogen receptors are found in numerous tissues around the body, it is not surprising that the negative consequences of menopause culminate in systemic changes in energy homeostasis and overall metabolic health. The most common approach to model the menopausal transition in animals is surgical ovariectomy. While this model is far from perfect in recapitulating the temporal and hormonal complexities that occur with the natural transition that occurs in humans, it has proven useful in revealing how important ovarian estrogen production is to female physiology, bioenergetics, and metabolic health.

Menopause and Energy Balance

The energy balance equation is a simple juxtaposition of the amount of energy consumed with the amount of energy expended. Any imbalance between these two parameters results in weight gain or loss. In the case of menopause, there is reason to believe that both sides of the equation are affected, favoring a greater consumption of highly palatable foods and a lower level of expended energy. These effects are likely to be mediated, in part, by estrogen's effects in the brain.

Effects on Appetite

Studies in model systems have clearly shown the presence of estrogen receptors in key neural nodes of energy balance regulation. Acting through these receptors, estrogen increases hypothalamic sensitivity, strengthening its suppressive effects on appetite whereas ovariectomy minimizes these suppressive effects of leptin and leads to overfeeding. In human menopause, the story is less clear. Other sex steroids may have stronger, opposing effects on appetite regulation, and food intake in humans is subject to a number of psychosocial and environmental moderators that can often override biological regulators of appetite. Even so, many suspect an effect on the biological control of appetite exists, but that it is too difficult to measure accurately.

Effects on Energy Expenditure

The evidence on the expenditure side of the energy balance equation has been more forthcoming and consistent between species. Both menopause and ovariectomy have been

associated with reduced levels of physical activity. Acutely, the loss of ovarian estrogen production has also been shown to reduce resting energy expenditure. This latter effect may be linked to an enhanced metabolic efficiency, secondary to effects in the brain and a decline in sympathetic tone. Alternatively, this effect may result from the loss of estrogen signaling that occurs in peripheral tissues.

Effects on Peripheral Tissues

Menopause is associated with numerous molecular and physiological changes that reduce metabolic function of the liver, lipid accumulation in adipose tissue, and reduced mass and function of skeletal muscle. Studies in model systems provide evidence that many of these effects are linked to the loss of ovarian estrogen production. In skeletal muscle, ovariectomy suppresses the expression of genes involved in mitochondrial biogenesis, oxidative capacity, and reduces muscle function. In adipose tissues, ovariectomy promotes lipogenesis and adipogenesis. In the liver, ovariectomy leads to the development of hepatic insulin resistance and steatosis. In all of these cases, estrogen replacement resolves the consequences of the surgery. Taken together, these effects enhance the body's ability to take up and store the excess nutrients from the positive energy imbalance in an energetically efficient manner.

The Decline in Metabolic Health

Effects on the brain and key peripheral tissues, therefore, converge to favor overnutrition, deposition of excess nutrients preferentially in visceral adipose depots, pathological ectopic lipid deposition, and the development of insulin resistance. Individual responses to the loss of ovarian function can vary quite dramatically between individuals, as the underlying biology, diet, and exercise levels can significantly moderate outcomes. However, these changes all point to a decline in metabolic health, adding to concerns about bone, which challenge women at this critical transition in life.

FSH Is a New Player in Bone Resorption

Studies with mouse models indicate that elevated levels of follicle-stimulating hormone (FSH) during peri-menopausal stage activate osteoclasts and contribute to osteoporosis even in the presence of normal estrogen. Indeed, null mice lacking either the FSH ligand or its cognate FSH-receptor are bone-loss protected. Moreover, recent studies indicate that a neutralizing antibody against FSH prevents bone loss as well as adiposity in mice. The efficacy of this antibody to prevent bone loss in peri- and post-menopausal women will be worth testing in the future.

“ Given that estrogen receptors are found in numerous tissues around the body, it is not surprising that the negative consequences of menopause culminate in systemic changes in energy homeostasis and overall metabolic health.”



Clinical Aspects of Menopause

NANETTE SANTORO, MD, says that women attain their lifetime peak of bone mass at about age 35, and thereafter, bone is lost. The rate of bone loss is slow in the premenopausal years and accelerates in the post-menopause period. Prior studies of women based on age indicated that bone loss increased around age 45, but little additional clarity could be provided to the trajectory.

Transmenopause and Bone Mineral Density

More recently, SWAN, the Study of Women's Health Across the Nation, a longitudinal, observational study of women traversing menopause, has made the pattern of bone loss much clearer. By following 2,000 women through the menopause, and performing dual energy X-ray absorptiometry (DEXA) bone mineral density (BMD) assessments annually, SWAN clearly showed that peri-menopausal bone loss does NOT begin until women develop prolonged amenorrhea of >60 days. This is consistent with the “late” menopausal transition, which is close in time to a woman's final menstrual period. Looking more closely at the relationship of bone loss to the timing of the final menstrual period, bone loss for any individual woman begins about one year before her final menstrual period. The initial “rapid” phase of bone loss lasts for the -1 to +2 years surrounding the final menstrual period, called the “transmenopause.” Over 10 years, women lose 10.6% of their lumbar spine BMD and 9.1% of their femoral neck BMD; 7.4% and 5.8%, respectively, are lost during the “transmenopause.”

Ethnicity and Bone Loss

Rates of bone loss vary by race/ethnicity, with African-American women being least prone and Chinese and

Japanese-American women most prone to bone loss. Women of higher bone mass index (BMI) also lose bone more slowly. In one study using high-resolution peripheral quantitative CT scanning of bone in 100 African-American and 173 white women, cortical area, thickness, and bone volume were all greater in African-Americans. Such an analysis helps to explain the lower rate of fracture in this group.

Markers of Bone Resorption

Markers of bone resorption follow similar curves. Some women have a trajectory of bone loss that is faster than others due to factors that are not completely understood. For example, it is unclear why bone loss accelerates as estrogen declines in the perimenopause, but then the process slows for most women. It has been hypothesized that hormones other than estradiol are involved. In animal studies, high FSH exposure appears to result in bone loss, but a human study using FSH suppression with a gonadotropin releasing hormone agonist plus aromatase inhibition did not show any differences in markers of bone resorption between women with and without three months of FSH suppression. It is possible that the concomitant use of aromatase inhibition influenced these findings. Higher estradiol and lower FSH are associated with less bone loss at most, but not all, stages of the menopausal transition.

Bone Markers Other than Reproductive Hormones

To address factors other than reproductive hormones that might influence bone loss after menopause, SWAN examined the relationships between commonly used anti-hypertensives, anti-depressants, and antacids on BMD. Similar to prior studies, the use of thiazide diuretics was



Nanette Santoro, MD,
Professor and E. Stewart Taylor Chair of Obstetrics & Gynecology, University of Colorado Anschutz Medical Campus, Aurora

HIGHLIGHTS

The initial “rapid” phase of bone loss lasts for the -1 to +2 years surrounding the final menstrual period, called the “transmenopause.”

Rates of bone loss vary by race/ethnicity, with African-American women being least prone and Chinese and Japanese-American women most prone to bone loss.

Hormone therapy with estrogen or estrogen plus progesterone for women who have a uterus offers effective treatment of symptoms and also prevents bone loss.



Micol S. Rothman, MD, Associate Professor of Medicine and Radiology University of Colorado Anschutz Medical Campus Associate Practice Director, Endocrine Clinic, University of Colorado Hospital Clinical Director Metabolic Bone Program

HIGHLIGHT

Bisphosphonates remain the mainstay of osteoporosis treatment as they are widely available and inexpensive with proven fracture benefit at multiple sites.

Teriparatide is currently the only anabolic agent approved for the treatment of post-menopausal osteoporosis. This is an analog of human parathyroid hormone with proven fracture efficacy for vertebral and non-vertebral fractures.

Deciding when to treat menopausal bone loss must be individualized based on the patient's fracture risk and preferences.

associated with less annualized bone loss at the hip and spine. No association of angiotensin-converting enzyme inhibitors or beta blockers with bone loss was observed. Unlike other studies, which have suggested that selective serotonin reuptake inhibitors antidepressants and proton pump inhibitors or H2 receptor antagonists are associated with bone loss, none of these agents were related to more rapid bone loss or lower bone density in women who took them in SWAN.

Hormone Therapy: Risks and Benefits

Women report the worst menopausal symptoms beginning in the late menopause transition and extending into the early post-menopause. Hence, hormone therapy with estrogen or estrogen plus progesterone for women who

have a uterus offers effective treatment of symptoms and also prevents bone loss. Recent data evaluating long-term hormone use, as well as 13-year post-stopping outcomes from the Women's Health Initiative confirm that the risk-to-benefit ratio of hormone therapy for symptomatic women is MOST favorable for those who are within 10 years of their FMP and age 60 or younger. Thereafter, risks begin to accrue that make hormones a less favorable option. In such instances, other bone-specific drugs make the most sense for women with low bone density or those at exceptional risk for osteoporosis.

Therapeutic Options for Menopause

MICOL S. ROTHMAN, MD is a practicing clinician and the clinical director of the Bone Program at the University of Colorado School of Medicine.

She says that although National Osteoporosis Foundation guidelines suggest bone mineral density screening with DXA for osteoporosis should begin at 65 for most women, those over 50 with additional risk factors for osteoporosis or fractures should undergo BMD testing earlier. If a woman's risk is high enough to warrant pharmacologic therapy, there are currently several non-hormonal options for treatment with additional agents likely be approved soon.

Non-Hormonal Therapies for Osteoporosis

Non-hormonal treatment therapies for post-menopausal osteoporosis include the anti-resorptive agents bisphosphonates and denosumab, as well as the anabolic agent teriparatide. Bisphosphonates remain the mainstay of osteoporosis treatment as they are widely available and inexpensive with proven fracture benefit at multiple sites. They can be given orally in weekly or monthly intervals or in patients with GI or malabsorptive conditions. Bisphosphonates are generally well tolerated. The most common side effects are GI upset and joint pain, but there have been recent concerns raised about rare but serious side effects of these medications such as osteonecrosis of the jaw and atypical femoral fractures. Additionally, these medications will remain in the bone even after treatment has stopped. This allows for the possibility of a "drug holiday" with ongoing fracture protection from the medication.

Antibody-Based Drugs

Denosumab, a monoclonal antibody to RANK-L, is also approved for the treatment of post-menopausal osteoporosis. It is given as a subcutaneous injection every six months. The Fracture Reduction Evaluation of Denosumab in Osteoporosis Every 6 Months (FREEDOM) trial showed robust vertebral, non-vertebral, and hip fracture reduction in post-menopausal women with osteoporosis after three years of treatment. Reported effects include hypocalcemia (which should be corrected prior to initiation of therapy), skin infections, and dermatitis as well as the same rare side effects of bisphosphonates. The mechanism of action is different than bisphosphonates, and at the end of six months the medication is no longer in the patient's system. Therefore, the same "drug holiday" cannot be implemented. There have been recent reports of rapid onset vertebral fractures after stopping denosumab, including several in younger women. The mechanism is unclear, but strong consideration should be given to treating with another agent if denosumab is stopped.

Parathyroid Hormone Analogs

Teriparatide is currently the only anabolic agent approved for the treatment of post-menopausal osteoporosis. This is an analog of human parathyroid hormone with proven fracture efficacy for vertebral and non-vertebral fractures. It is well tolerated, but quite expensive and must be given as a daily subcutaneous injection. Side effects include lightheadedness, GI upset, arthralgias, and hypercalcemia. It should be noted that in animal studies, there were reports of juvenile rats developing

“ While menopausal hormone therapy can be used as an anti-resorptive, it carries a separate set of risks and benefits, including increased risks of breast cancer with combined estrogen plus progestin and venous thromboembolism with oral estrogen.”



osteosarcoma after treatment, but now, with over 10 years on the market, there has been no evidence of a higher incidence of osteosarcoma in humans. Nonetheless, teriparatide should not be prescribed to patients with baseline elevated risk for osteosarcoma. As with denosumab, teriparatide will lose its efficacy after it is stopped and must be followed by another medication to “extend the anabolic window” and stop ongoing resorption.

Selective Estrogen Receptor Modulators

While menopausal hormone therapy can be used as an anti-resorptive, it carries a separate set of risks and benefits, including increased risks of breast cancer with combined estrogen plus progestin and venous thromboembolism with oral estrogen. Although this is generally a safe treatment for women who are within five to 10 years of their final menstrual period, the risks of menopausal hormone therapy increase beyond that age, especially for women with a uterus who must take estrogen plus progestin. Selective estrogen receptor modulators (SERMs: raloxifene and bazedoxifene) can also be used as anti-resorptives. Raloxifene will not relieve menopausal symptoms, but bazedoxifene, which contains a SERM plus conjugated equine estrogens, can relieve common menopausal symptoms and inhibit bone resorption. Both of these compounds have the advantage of an anti-proliferative effect on the breast. Raloxifene has been shown to reduce vertebral fractures as well.


Personalized Treatment Options

In the clinic, deciding when to treat menopausal bone loss

must be individualized based on the patient’s fracture risk and preferences. There are situations in which bone mineral density is low at the time of transition where one might advocate for several years of early bisphosphonate therapy to prevent the typical menopausal bone loss. There may also be a role for treatment in post-menopausal women with low bone density who are stopping estrogen, again to prevent the expected decline in BMD. However, most women will be screened and treated later in life, and medication should be then initiated depending on BMD and overall fracture risk at that time. In addition to the currently approved therapies, there may be new options approved before the end of 2017 including abaloparatide (a PTH-rp analog) and romozosumab (an inhibitor of sclerostin) for treatment of osteoporosis in post-menopausal women.

Conclusions

In this Tri-Point article, we have provided the basic concepts and the essential clinical features of menopause including metabolic and energetics aspects.

We further provided clinical insights into bone loss in post-menopausal women and potential therapeutic options. More efficacious and safe drugs for post-menopausal women are on the horizon. Hopefully, these drugs will soon be available in the market. 

ACKNOWLEDGEMENTS



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Anne Cappola, MD, ScM, Perelman SOM, University of Pennsylvania, Philadelphia, also helped in the review and editing of this article.

Oversight and guidance for the Tri-Point series is provided by the Endocrine Society’s Research Affairs Core Committee.

Toon Therapy

An endocrinologist and a cardiologist teamed up to create an entertaining and easily understood method to educate patients. The result is Doctablet, a series of online animations that patients of all ages, backgrounds, and education levels can comprehend and even enjoy.

BY DEREK BAGLEY

A lack of quality time with patients is a problem in endocrinologists' offices — and indeed in most physicians' offices — that's growing more and more pronounced. This is especially concerning when a healthcare provider has to explain a complicated disease like diabetes, and even more so if these patients live in underserved communities or if English is their second language.

Chris Palmeiro, DO, MS, an endocrinologist practicing in Kingston, N.Y., partnered with Jose Taveras, MD, a cardiologist practicing in the Bronx, to address this problem in a unique way. The two met when they worked together as chief residents of internal medicine and realized their passion for educating patients. Now the two physicians have turned that passion into Doctablet — a free online resource that helps both healthcare professionals and their patients learn about diabetes and a host of other issues. Doctablet uses short, animated videos and informative illustrations so patients can be educated in a more entertaining and less time-consuming way.

"[Doctablet] was really born out of the medical office," Palmeiro says. He explains that the idea behind Doctablet was twofold: One was to better serve communities where they felt they had to explain things in a clear but also a simple message, for a more low-literacy patient population. "So we wanted to create something fun, interesting, and there wasn't quite that resource," he says.

But the main thing that drove them to work on this project, Palmeiro says, is that they saw the time between the physician and the patient dwindling. For Palmeiro and Taveras, a big part of medicine is education, and they've honed techniques over the years to help better explain things to their patients: stories,

DOCTABLET



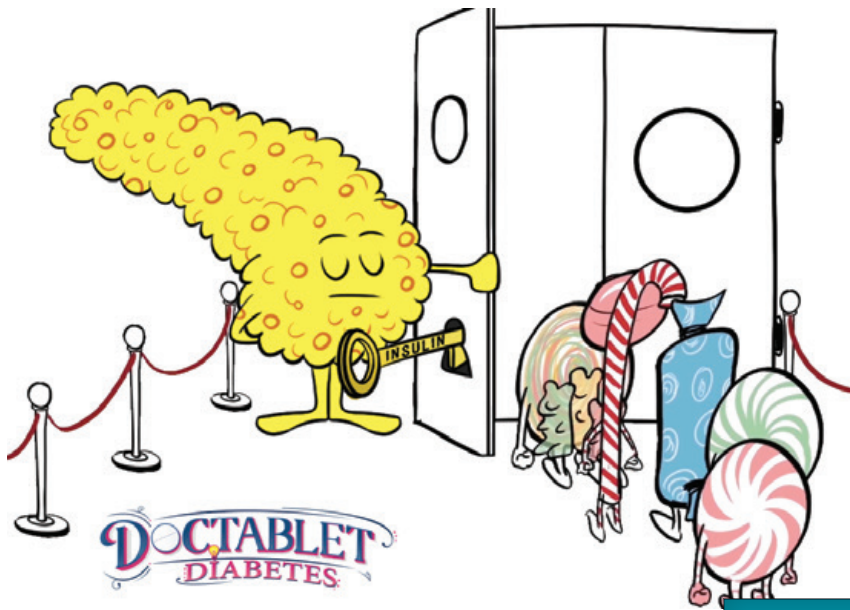
analogies, and so on; they wanted to recreate that part of the visit with Doctablet.

By Doctors, For Patients

The project comes along at a time when a recent survey showed that many adults with diabetes are unaware of their increased risk for serious illnesses. Diabetes and obesity rates continue to climb. A recent report showed that one-third of the world is now overweight, and the U.S. leads the way. "It's the right time," Palmeiro says, "being that this is such a growing field — in endocrinology and cardiology, there's a lot of overlap. Our videos and lessons are serving in that arena because they're such common problems."

In the beginning, Doctablet's videos and illustrations focused mainly on cardiometabolic issues, but the posts have since expanded to cover a wide range of health topics, from nutrition to sleeping problems to dealing with doctors. "We're doing some stuff on adrenal work now, some stuff on osteoporosis," Palmeiro says. "We really are expanding in endocrinology and heart. We're working on an initiative to do something for heart failure. We're focusing on niche underserved communities right now."

For the purposes of this article, let's focus on diabetes. Palmeiro points out that a lot of people with diabetes can't always feel their disease, and it's one thing to explain diabetes to a patient in an office setting, but it's a completely different thing to make sure that patient understands exactly what's going on. Research shows that most patients don't read the handouts they take home from their doctors' offices, or if they do, they may not understand what they're reading.



“ It’s the right time, being that this is such a growing field — in endocrinology and cardiology, there’s a lot of overlap. Our videos and lessons are serving in that arena because they’re such common problems.”

One of Doctablet’s animated videos depicts a steam engine chugging along, representing the pancreas. The train emits puffs of smoke, representing insulin. The video shows the train running along a plain, with small puffs of smoke, representing the pancreas functioning normally, but when the train struggles to climb a steep mountain, the engine kicks into overdrive and the puffs of smoke become bigger and bigger. The train doesn’t slow down at first, and the passengers are unaware of the effort required to maintain the speed. “The videos that we’re doing,” Palmeiro says, “we’re trying to explain simple things like ‘You may not feel diabetes but your pancreas is working overtime.’ The passengers on board, they feel fine, they don’t notice anything, but the train is working. That’s a good example of what pre-diabetes is. And obesity, the high insulin levels those patients have — the pancreas is working overtime and can burn out pretty early. Teaching those lessons to people, I think goes a long way, earlier on in the course, rather than later.”

Plain Language

All of Doctablet’s content is written by physicians. Palmeiro says they have several collaborators who are healthcare providers, and when thinking about a post or video, they try to think of things that they’ve encountered in their offices. For example, Doctablet produced a video about understanding the A1C test. “We have patients who have had diabetes for 20 or 30 years, and they don’t understand what the A1C test is,” Palmeiro says. “It came to the point where I was teaching the same thing about the A1C over and over and trying to find an analogy that worked. And that’s where the video started. They all start in the office.”



Jose Taveras, MD



Chris Palmeiro, DO, MS

The challenge, Palmeiro says, is writing the content in “plain language” — a seventh- or eighth-grade reading level. Just writing a long sentence can push the reading level to ninth or tenth grade. So the idea was to tell stories using animation and illustration. The scripts are written in English and Spanish, with illustrations in mind. Illustration ideas go to a panel of illustrators and animators based around the world. Videos are voiced over by professional voice actors, and Doctablet has even used professional comic book illustrators and animators to create animated graphic novels. Healthcare providers work closely with the authors and illustrators to make sure they get the messages across clearly. “I’ll work with the author of the script if I haven’t written it, for ideas and feedback, so that we make sure that we’re teaching a lesson,” Palmeiro says.

“The creative process is my area of expertise,” he continues. “That’s the part that I love. I like to make boring things fun.” ^{EN}

BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT THE HIGHLIGHTS OF ENDO 2017 IN THE MAY ISSUE.

Lab Improvement

As technology evolves and tech staff expands and contracts, it's key to have a laboratory environment that evolves as well. If you're looking to give your lab space an upgrade, *Endocrine News* has a few helpful hints.

BY GLENDA FAUNTLEROY



It is not uncommon to outgrow your laboratory space. A new work function may change your equipment needs, new staff additions require more space, or you have taken to stacking boxes on much-needed counter space because your current storage is non-existent. This marks the time to consider a redesign of your laboratory.

Planning a lab redesign can be a big undertaking. If you have ever remodeled a room in your home — or watched any show on HGTV — you know there are many points to consider to be sure the new space best fits your needs. When it comes to designing your new lab, never leave safety off of the list, while keeping the following items in mind:



Know your “wants”

Before contacting an architect or design firm about your lab redesign, be sure of what you want from your lab. A lab design is not cookie cutter — different labs require different things. Determining the specifications of the design involves incorporating many attributes, including: how many people will use the lab (and what materials or processes will be used), how many people will work in the space and in what role, and how much space is needed (and don't forget about how many electrical outlets you'll need!). It is also important to consider space accommodations for workers who are shorter or taller than average or have physical or sensory challenges, whether temporary (e.g., pregnancy) or permanent.

Think safety

Any design architect will be sure to discuss the lab safety requirements of your new space. There are many features that are critical: biosafety cabinets, fire protection and detection systems, emergency showers and eye wash stations, easy access, well-marked exits, and proper ventilation. Ventilation systems should control the temperature and keep the space comfortable. Also, when hazardous materials are being used, ventilation systems should include features such as chemical fume hoods to control possible exposure and capture contaminants in the laboratory air.



“ Designing a space with some built-in flexibility can allow you to include features that lab users might not need now, but could come in handy later.”



Improve layout and furniture

Designing the overall layout of your new space should consider separate areas for lab work, personal desk space, meeting space, and eating areas. Some labs use different flooring, for example, to make a visible separation between lab and non-lab space. When choosing work surface stations, choose chemical-resistant, smooth, and easily cleanable material. Also include ergonomic features such as adjustability, appropriate lighting, and equipment layout.

Add closets, drawers, and more closets

Adequate storage always ranks high on the list for any redesign, at work and at home. For lab spaces, hardwood or metal shelving for cabinets is preferred. But while simple cabinets may be fine for electronics, storing lab chemicals usually requires more complex storage spaces. For instance, hazardous materials should be stored and used in lab areas away from heavy traffic flow and ventilation sources that can disrupt airflow. Including plenty of storage space in a redesign can also increase the safety of your lab. Eliminating stacks of boxes in aisles or on top of counters gives workers ample space to work and move around, which can increase efficiency and reduce accidents. You will also need space for the different types of waste collection containers needed for your lab. These may include sharps, laboratory trash, recyclable containers, medical waste, and radioactive waste.

Be flexible

The type of research your laboratory does may change some time in the future. Grant funding, personnel changes, and equipment acquisition are just a few things that can dramatically change your lab five years down the road. Designing a space with some built-in flexibility can allow you to include features that lab users might not need now, but could come in handy later, such as moveable workbenches. The more flexible you and your design team make the plan, the less need for future major structural changes. Work with staff members from multiple departments at your institution to get wide buy-in on your plan — from environmental health and safety staff, researchers, and engineers — to best anticipate how your lab might change in years to come. ^{EN}

Sources: “Health and Safety Design Considerations for Laboratories,” *Lab Manager*; “Five Ways Effective Laboratory Design Impacts Health, Safety, and Productivity,” Harvard T. H. Chan School of Public Health.

FAUNTLEROY IS A CARMEL, IND-BASED FREELANCE WRITER AND A REGULAR CONTRIBUTOR TO ENDOCRINE NEWS. SHE WROTE ABOUT THE LAX REGULATIONS WITH SPERM BANKS IN THE JUNE ISSUE.

NIH Funding Outlook Uncertain Amid Big-Picture Budget Battles



The Endocrine Society has been encouraged by the significant increases in funding for the National Institutes of Health (NIH) in fiscal years (FY) 2016 and 2017. However, further steady and sustainable increases in funding are needed to undo damage caused by years of flat funding prior to 2016. At the time this article was written, several issues complicate the budget outlook for the NIH as we look toward FY 2018, beginning in September.

The overarching issue facing the House and Senate budget committees is the Budget Control Act (BCA), which places austere caps on overall funding levels for defense (\$549 billion) and nondefense (\$516 billion) discretionary funding in FY 2018. Absent a budget deal similar to the ones negotiated in 2013 and 2015, sequestration imposed by the BCA would result in severe cuts, impacting all federal agencies, including the NIH, National Science Foundation (NSF), Centers for Disease Control and Prevention (CDC), and other agencies that support endocrine research and public health. Further complicating the budgetary picture is the need to increase the ceiling on the U.S. government debt, which is set to hit the debt limit sometime in mid-October.

Despite the uncertainty surrounding the prospects of a budget deal, the House of Representatives is moving forward with the budget and appropriations process. House Budget Committee Chairwoman Diane Black (R-TN) is proposing a budget resolution that would significantly raise discretionary spending on defense to \$621.5 billion, while reducing nondefense discretionary spending to \$511 billion. If enacted through the appropriations process, this imbalance would force appropriators to make further cuts to agencies that are funded through nondefense discretionary appropriations, including the NIH and the NSF. However, the

budget resolution is unlikely to move forward as written, given that it violates the current sequester cap of \$549 billion for defense. Moreover, the Senate, which would also need to vote on an overall budget resolution, has not yet indicated its position on topline spending levels for defense or nondefense discretionary spending.

Meanwhile, on July 10, the House Appropriations Subcommittee on Labor, Health, and Human Services and Education (LHHS) proposed an appropriations bill that provides \$35.2 billion for the NIH, or an increase of \$1.1 billion above the FY 2017 level. However, because the overall allocation for the LHHS Subcommittee is reduced by \$5 billion relative to FY 2017, other important agencies such as the CDC would face severe cuts in the bill. While the prospects of the bill moving forward are unlikely, given the other budget issues and limited time for consideration of all 12 appropriations bills in both the House and the Senate, the increase for the NIH in the House LHHS Subcommittee indicates that it remains a high priority for Congress.

Because of the uncertainty surrounding the budget process, there is a considerable chance of at least a short-term Continuing Resolution (CR) to fund the government and allow Congress to work on a budget deal and/or the debt limit through September and into October. However, the prospects of a government shutdown are not insignificant, as it is unclear where the Trump administration's budgetary priorities lie and whether there are circumstances in which they might veto an appropriations bill. The Endocrine Society will join other biomedical research advocates to call on Congress to raise the austere spending limits imposed by the BCA and work toward steady, sustainable increases in funding for the NIH.



Brenda Fitzgerald, MD

Brenda Fitzgerald Named CDC Director

On July 7, Health and Human Services Secretary Tom Price announced that Brenda Fitzgerald had been selected as director of the Centers for Disease Control and Prevention (CDC).

Fitzgerald is an obstetrician-gynecologist who served as the commissioner of the Georgia Department of Public Health. In that capacity, Fitzgerald served on an advisory council on childhood obesity where she helped to develop public-private partnerships to address growing rates of the disease in the state of Georgia. The council's program Georgia SHAPE launched in 2012 and has received more than \$57 million to promote healthy eating and physical activity in the state. The program also encouraged elementary schools to incorporate 30 additional minutes of exercise.

The Endocrine Society looks forward to working with Fitzgerald to address critical public health issues like diabetes and obesity and to continue the work the agency has done to promote prevention programs nationwide.




FASEB

Federation of American Societies
for Experimental Biology

Endocrine Society Congratulates New FASEB Executive Director

In July, Frank J. Krause, Jr., CAE, will join the Federation of American Societies for Experimental Biology (FASEB) as its new executive director. Krause joins FASEB after serving as the Chief Operating Officer of the American Geophysical Union (AGU), where his responsibilities included strategy, publications, meetings and talent pool programs, financial operations, and the technology and project management office.

The Society has been a FASEB member organization since 1999 and works with the Federation to address science policy issues on behalf of our members. As a FASEB member organization, we are part of a strong collective voice to more effectively advocate for biomedical researchers. Krause joins FASEB at a critical time; steady, sustainable increases for the National Institutes of Health are vitally important to endocrine researchers, and ongoing budget battles threaten to derail significant progress made over the past two years.

The Endocrine Society congratulates Krause on his new leadership of the Federation, and we look forward to working with him to advance science policy and research funding issues that are critical to the biomedical research enterprise. 

Change lives. Start with your own.

Aspirus is a nationally recognized, physician-driven health system based in Wausau which is located in the center of Wisconsin. The care we give to others is the reason Aspirus is thriving and unifying in spite of national health care changes.

There's a simple reason you chose a career in Endocrine Medicine. We invite you to practice it here:

- Join our Endocrinologist and three Nurse Practitioners who practice 100% outpatient consultative endocrinology
- Collaborate with a dedicated and experienced support team, including Certified Diabetic Educators
- Flexible scheduling
- Large referral area that includes 20 counties, willingness to do outreach is preferred
- Potential teaching opportunities available through the Aspirus Wausau Family Medicine Residency program and the Medical College of Wisconsin both onsite
- Above average compensation package that includes income guarantee and production bonuses
- Other incentives: potential for residency stipend, loan repayment of up to \$200,000 and sign-on bonus options
- J1 and H1-B visa possibilities
- We pride ourselves on excellence: Aspirus Wausau Hospital recently received recognition as one of the 100 Best Hospitals in America for 2016
- EPIC EMR used throughout the system



Endocrinology Opportunities Wisconsin \$75,000 Sign On Bonus



Details at www.aspirusproviderops.org

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

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Endocrinologist Opportunity

Ready for a new lifestyle at the beach?

Plant your roots in our sand! **Beebe Healthcare** is a progressive, not-for-profit community health system with a 210-bed hospital and a planned multi-million expansion. Beebe has numerous satellite locations throughout coastal southern Delaware.



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

About the Endocrinologist Opportunity:

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

About Beebe Healthcare:

- Repeatedly recognized with national awards
- Progressive and growing quickly, with high patient satisfaction, and quality of care
- Cardiac surgery, interventional cardiology, cancer center with radiation, 256-slice CT, 3.0T MRI, PET Scan, 3D mammography, and hyperbaric chambers
- 375+ providers on staff; 48,000+ Emergency visits
- Margaret H. Rollins School of Nursing

About the area:

- Nationally ranked family-oriented beaches and boardwalks by *Parents Magazine*, *National Geographic*, *Travel and Leisure*, and *American Profiles*
- Exceptional quality of life and the environment is smart, progressive and safe
- Public and private school options
- Low taxes and no sales tax; low cost of living
- Close to Philadelphia, Baltimore, DC, and NYC



Email cover letter and CV to Marilyn Hill, Director of Physician Services, mhill@beebehealthcare.org • www.beebehealthcare.org

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

This is not visa sponsored opportunity.

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

HORMONES AND ENDOCRINE DISRUPTING CHEMICALS

WHAT YOU NEED TO KNOW

The endocrine system is a network of glands and organs that produce, store, and secrete hormones. When functioning normally, the endocrine system works with other systems to help maintain the body's health. Endocrine disrupting chemicals (EDCs) are substances in the environment (air, soil or water supply), food sources, personal care products, and manufactured products that may interfere with the normal function of your body's endocrine system.

WHAT ARE EDCS

EDCs, a broad category of compounds used in consumer products, electronics and agriculture, have been associated with a diverse array of health issues. These non-natural chemicals or mixtures of chemicals can mimic, block, or interfere with the way the body's hormones work.

They have been linked to human health issues related to **sperm quality, fertility, abnormalities in sex organs, endometriosis, early puberty, nervous system function, immune function, cancers, breathing problems, metabolic issues, obesity, heart health, growth, neurological and learning disabilities**, and more.

Exposure to EDCs can happen anywhere and come from the air we breathe, the food we eat, and the water we drink. EDCs can also enter the body through the skin and by transfer from mother to fetus (across the placenta) or mother to infant (via breast feeding) if a woman has EDCs in her body.

Examples of EDCs include **bisphenol A (BPA), phthalates, pesticides,** and pollutants such as **dioxin** and **polychlorinated biphenyls (PCBs)**.



COMMON EDCS

Some common EDCs and their uses include the following:



Pesticides

Example EDCs: DDT, Chlorpyrifos, Atrazine, 2,4-D, Glyphosate



Children's Products

Example EDCs: Lead, Phthalates, Cadmium



Industrial Solvents or Lubricants and Their Byproducts

Example EDCs: PCBs and Dioxins



Plastics and Food Storage Materials

Example EDCs: BPA, Phthalates, Phenol



Electronics and Building Materials

Example EDCs: Brominated Flame Retardants, PCBs



Personal Care Products, Medical Tubing

Example EDCs: Phthalates, Parabens, UV Filters



Anti-Bacterials

Example EDCs: Triclosan



Textiles, Clothing

Example EDCs: Perfluorochemicals

Visit hormone.org for more information.

Additional Editing by Heather Patisaul, PHD,
NC State University



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EDCS FACTS

EDCs often disrupt the endocrine system by mimicking or interfering with a natural hormone. These “hormone mimics” can trick the hormone receptor into thinking the EDC is the hormone, which can trigger abnormal processes in the body.

Studies support a link between EDCs and harm to human health, but the cause-and-effect relationship is not yet fully understood. Still some EDCs are known to pose a threat to people who have excessive exposure to them.

WHERE ARE EDCS

- Industrial chemicals can leach into soil and groundwater and then make their way into the food chain and build up in fish, animals, and people
- Consumer products such as plastics, household chemicals, fabrics treated with flame retardants, cosmetics, lotions, products with fragrance, and anti-bacterial soaps
- Pesticides, fungicides, or industrial chemicals in the workplace

The best way to avoid exposure is to check labels and avoid products with known EDCs.

DID YOU KNOW?

A developing fetus or infant is more vulnerable to the effects of EDCs than an adult because organ systems are still developing.

Of the hundreds of thousands of man-made chemicals, it is estimated that about 1,000 may have endocrine-acting properties.

Global production of plastics grew from 50 million tons in the mid-1970s to nearly 300 million tons today.

Source: Endocrine Society Introduction to EDCs, A Guide for Public Interest Organizations and Policy Makers

AVOIDING EDCS

Even if some health effects are not fully proven, taking precautions is wise. Become familiar with EDCs to which you and your family may be exposed. Try to avoid unnecessary, preventable exposure to EDC-containing consumer products. Experts suggest avoiding microwaving food in plastics to avoid leaching of EDCs into food, choosing personal care products and cleaners that are unscented, and replacing older non-stick pans with newer, ceramic-coated ones. These precautions are especially important if you are pregnant or planning a family.



RESOURCES

Research on EDCs is growing, so watch for new information on products to help your family's health. Learn more from the following:

- National Institute of Environmental Health Sciences: niehs.nih.gov
 - Pediatric Environmental Health Toolkit: psr.org/resources/pediatric-toolkit.html
- Environmental Working Group: ewg.org

Patients have questions. We have answers.

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



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FROM THE ENDOCRINE SOCIETY

Endocrinologists

The Mount Sinai Health System is currently seeking full time Endocrinologists in Manhattan, Queens, Brooklyn, Staten Island, Westchester and Palm Beach County Florida. The ideal candidate will play an instrumental role in ensuring excellent patient care, quality outcomes, and satisfaction. In addition, we would like to showcase an ambitious and talented physician who is fully committed to ambulatory medicine and the mission of Mount Sinai Health System. Clinical, Academic and Hybrid positions available!

The chosen candidate will be part of a department that is considered to be a leader in the field of diabetes treatment. As a community leader, you will have the opportunity to partner with the Mount Sinai Diabetes Center, the Friedman Diabetes Center at Mount Sinai Beth Israel, our Diabetes Alliance, and even pioneer our Livongo project - a completely new approach for diabetes management that combines the latest technology with personalized coaching.

Position Description:

- Provide care in both high-functioning ambulatory and hospital settings
- University affiliated and community based practice
- Share care responsibilities and coverage with other team members
- Collaborate with multi-specialty practice colleagues as an integral part of a world-class health system
- Benefit from the educational, research, and clinical programs of a nationally ranked Medical School
- Opportunity to apply for a faculty appointment with The Icahn School of Medicine
- Significant opportunities for leadership and career development
- Additional support staff

Position Qualifications:

- Medical Degree from an Accredited University
- New York Medical License
- Board Eligible or Board Certified in Endocrinology
- Some Experience preferred
- Committed to Mount Sinai and the communities we serve
- Excellent communication, bedside manner, and organizational skills
- A strong work ethic and desire to participate in a team-oriented, performance-driven Health System

About the Mount Sinai Health System?

The Mount Sinai Health System is an integrated health system committed to providing distinguished care, conducting transformative research, and advancing biomedical education. Structured around seven hospital campuses and a single medical school, the Health System has an extensive ambulatory network and a range of inpatient and outpatient services—from community-based facilities to tertiary and quaternary care.

The System includes approximately 7,100 primary and specialty care physicians; 12 joint-venture ambulatory surgery centers; more than 140 ambulatory practices throughout the five boroughs of New York City, Westchester, Long Island, and Florida; and 31 affiliated community health centers. Physicians are affiliated with the renowned Icahn School of Medicine at Mount Sinai, which is ranked among the highest in the nation in National Institutes of Health funding per investigator. The Mount Sinai Hospital is in the "Honor Roll" of best hospitals in America, ranked No. 15 nationally in the 2016-2017 "Best Hospitals" issue of U.S. News & World Report. The Mount Sinai Hospital is also ranked as one of the nation's top 20 hospitals in Geriatrics, Gastroenterology/GI Surgery, Cardiology/Heart Surgery, Diabetes/Endocrinology, Nephrology, Neurology/Neurosurgery, and Ear, Nose & Throat, and is in the top 50 in four other specialties. New York Eye and Ear Infirmary of Mount Sinai is ranked No. 10 nationally for Ophthalmology, while Mount Sinai Beth Israel, Mount Sinai St. Luke's, and Mount Sinai West are ranked regionally. Mount Sinai's Kravis Children's Hospital is ranked in seven out of ten pediatric specialties by U.S. News & World Report in "Best Children's Hospitals."

Please specify job number of interest and send CV to:

Alex Cano
 Director Physician Recruitment
 Mount Sinai Health System
alex.cano@mountsinai.org

The Mount Sinai Health System is an equal opportunity employer. We promote recognition and respect for individual and cultural differences, and we work to make our employees feel valued and appreciated, whatever their race, gender, background, or sexual orientation.



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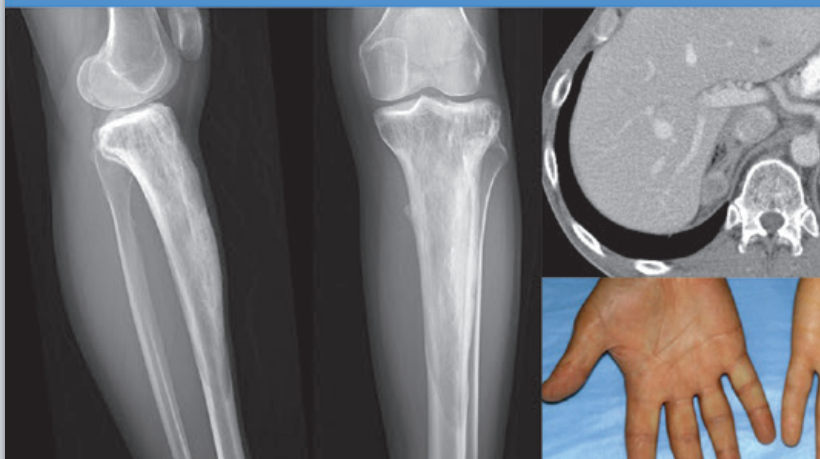
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