

AUGUST 2021

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

# Endocrine news

## *Next to* **NORMAL** Prediabetes in Older Adults

- ▶ How useful is the concept of “prediabetes” in people over a certain age?
- ▶ While many older adults could be considered to have prediabetes, many will never develop type 2 diabetes.
- ▶ Conflicting messaging is causing confusion among patients as well as physicians.
- ▶ Oral glucose tolerance testing could be a valuable tool for these patient populations.



### CEU 2021 PREVIEW:

Health disparities in treating diabetes

### CEU 2021 PREVIEW:

The challenges of managing Cushing's disease

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Hormone Science to Health

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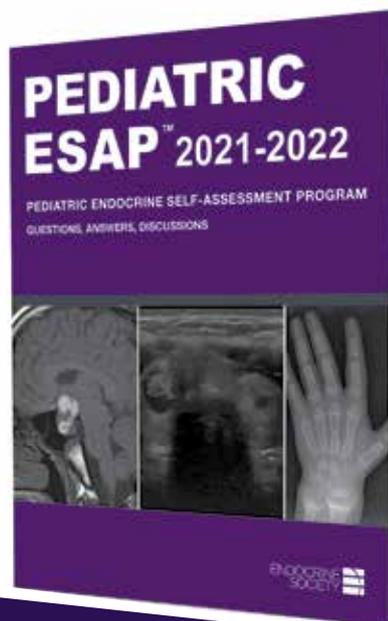
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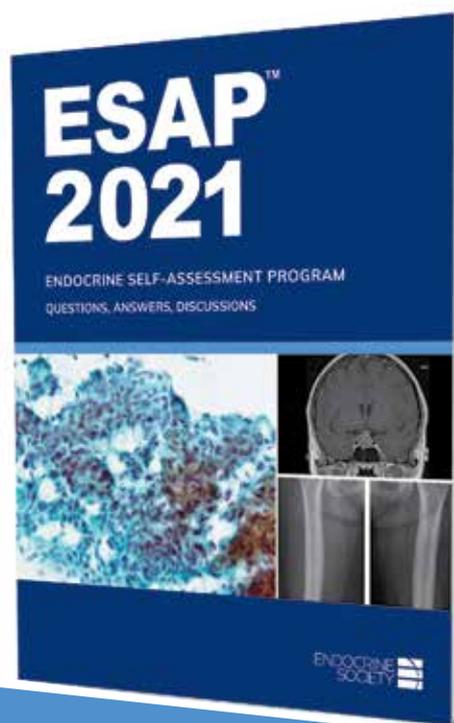
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### How Useful is the Concept of Prediabetes in Older Adults?

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Hormone Science to Health



## Celebrating 100 Years of Insulin

This year marks 100 years of insulin, a discovery that has saved millions of lives by transforming diabetes from certain death to a chronic condition. The field has come so far since 1921 with knowledge of the importance of glycemic control, advances in insulin delivery models, diabetes technology, and type 1 diabetes prevention research. I can only imagine what the next 100 years will bring.

“

The field has come so far since 1921 with knowledge of importance of glycemic control, advances in insulin delivery models, diabetes technology, and type 1 diabetes prevention research. I can only imagine what the next 100 years will bring.

”

Our members have greatly contributed to the advances we see today in diabetes prevention and treatment and are at the forefront of breaking research, including advances in CGM technology, research into beta cell transplants, and a diabetes medication derived from Gila monster venom. Over 26 million people benefit from these therapeutic advances today, and many are enjoying lives free from diabetes' most severe complications.

We're commemorating the discovery with a year-long initiative highlighting insulin's past, present, and future. Our virtual events this fall include a webinar on health disparities in diabetes, a patient roundtable, and a November event during Diabetes Awareness Month to discuss what the next 100 years of insulin will look like.

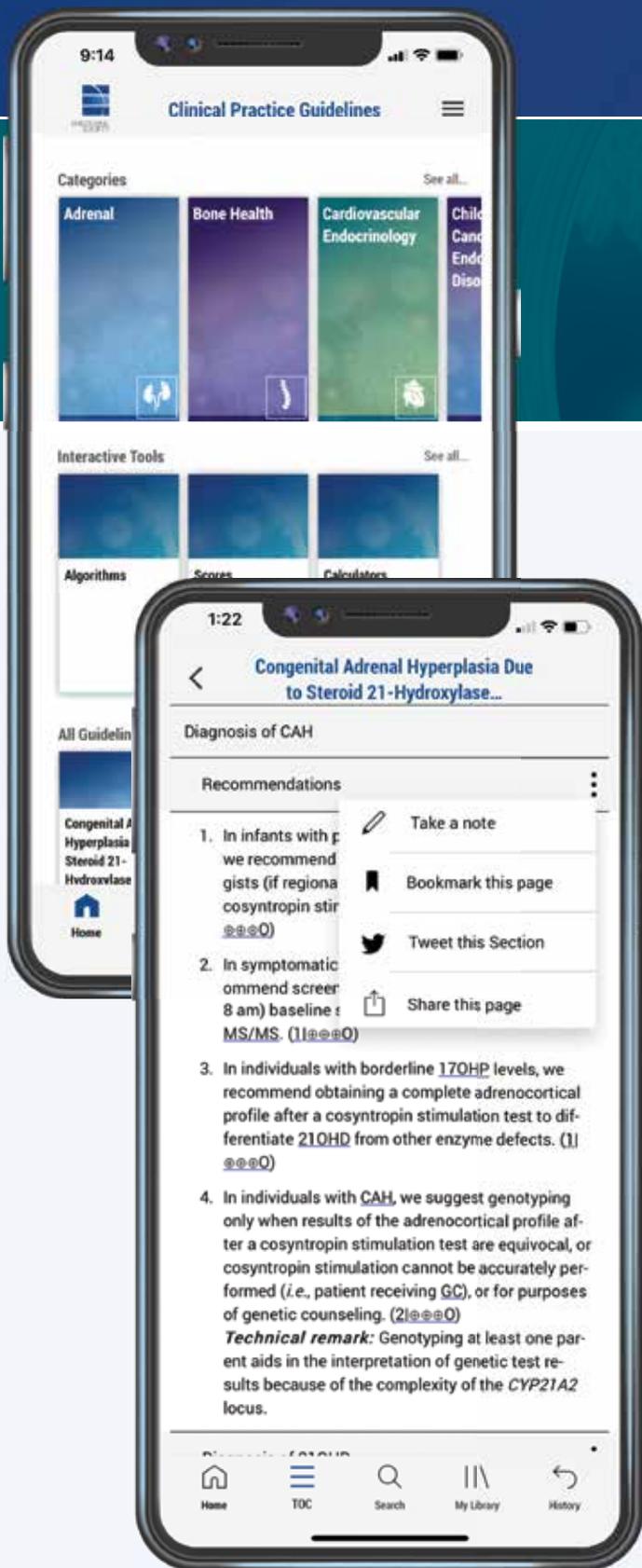
During our health disparities webinar, our experts will cover the historical and present-day racial and socioeconomic barriers to diabetes care and where the gaps are for underrepresented minority communities. Attendees will learn about strategies to work toward equity in healthcare through interventions in education, practices, and policies. Our experts will discuss solutions, including access to affordable insulin and insurance and the need for more training among healthcare providers.

We are holding a patient roundtable moderated by *Endocrine News* to share insights into a day in the life of a person with diabetes. The discussion features a panel of patients — one who has been on insulin for many years and a young adult patient to discuss the transition from pediatric to adult care — along with clinicians who have developed strong patient-provider relationships to deliver the best care possible.

I am most excited about our November event on the future of insulin as diabetes technology is close to my heart. Top researchers and clinicians are coming together to discuss the technology and therapies that will transform the field over the next 100 years. Research into robots that would automate routine tasks and free up clinicians' time, next-generation glucagon, and weekly insulin injections are just a few of the innovative topics being discussed. Our goal is to help both patients and clinicians see what the future of insulin and delivery technology will be to ensure they are as prepared as possible for this ever-changing landscape.

I encourage everyone to join us in celebrating this important milestone for our Society and the field of endocrinology. Let us know how you are celebrating, and visit [www.endocrine.org/insulin100](http://www.endocrine.org/insulin100) for more insulin-related resources for you and your patients. We look forward to seeing you all in the fall and are honored to be a part of this celebration! 🇺🇸

Carol H. Wysham, MD  
President, Endocrine Society



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FROM THE **EDITOR**

AUGUST 2021

# Endocrine news

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

## To Pre- or Not to Pre-: The Confusion Over Prediabetes in Older Adults

**T**his month's cover story wades into the concept of "prediabetes," specifically in older adults. Well, the article doesn't so much wade into the concept as dive in headfirst.

In "Next to Normal" on page 20, Eric Seaborg thoughtfully delves into this classification that is seemingly awash in mixed and conflicting messages. In several older adults classified with prediabetes at baseline, "many were more likely to return to normal glucose levels or die after six years of follow-up instead of progressing to diabetes," says Mary R. Rooney, PhD, MPH, a postdoctoral fellow at the Johns Hopkins Bloomberg School of Public Health in Baltimore, Md., and the lead author of a prospective cohort analysis published in *JAMA Internal Medicine* earlier this year. "Even across all the different definitions of prediabetes, these definitions didn't really capture risk of progression to diabetes well," she adds.

The Endocrine Society's *Treatment of Diabetes in Older Adults: An Endocrine Society Clinical Practice Guideline* recommends following up in older patients designated as having prediabetes with an oral glucose tolerance test. According to Marie E. McDonnell, MD, director of the diabetes program at Brigham and Women's Hospital, Boston, Mass., and a member of the Endocrine Society guideline committee, "The issue is not so much about prediabetes, it is more about not missing diabetes." However, she does note that these patients can benefit from a prediabetes diagnosis because Medicare will cover the costs of a diabetes prevention program. "It might get them free access through Medicare to a lifestyle behavior modification program that will focus on eating well and exercising, and that has benefits way beyond glucose control," she adds. Since these patients could benefit greatly from various lifestyle modifications, McDonnell suggests that a prediabetes designation could actually be beneficial.

As I'm sure anyone reading this is well aware, next month the Endocrine Society will be hosting Clinical Endocrinology Update 2021 (Sept. 10 – 12) and Endocrine Board Review 2021 (Sept. 22 – 24). To give you a preview



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of what you can expect from CEU 2021, we've included a couple of features highlighting two of the sessions taking place once again in an all-virtual format:

- ▶ **Challenges in the Management of Cushing's Disease** — On page 30, senior editor Derek Bagley has conducted a very informative Q&A with this session's speaker Anthony Heaney, MD, PhD, about this condition that continues to confound endocrinologists — and other clinicians as well — due to how often its symptoms mimic a variety of other, more commonplace disorders. Heaney says that he hopes attendees to his session learn that Cushing's disease is one of the most challenging conditions that endocrinologists will ever have to diagnose and treat. "All endocrinologists will encounter patients who might or might not have Cushing's disease," he says. "So, a basic understanding about how to approach such a patient is very helpful to the vast majority of endocrinologists."
- ▶ **Health Disparities in Diabetes** — On page 32, Kelly Horvath speaks to Rocio I. Pereira, MD, about her CEU 2021 session focusing on health disparities, which remains one of the most daunting barriers to delivering care to certain patient populations, many of them affected disproportionately by a number of endocrine conditions. According to Pereira, one of the biggest barriers to care is often the healthcare system itself. "There is bias built into our healthcare system," she explains. "And although sometimes we as individuals might not be able to change that, there are things that we can change as individuals to improve the overall culture of healthcare for our patients and to work with them to overcome those barriers that have resulted from both social determinants of health and societal bias and systemic racism."

For more information about CEU 2021 and EBR 2021, both taking place in September, go to: [www.endocrine.org/ceu2021](http://www.endocrine.org/ceu2021) or [www.endocrine.org/ebr2021](http://www.endocrine.org/ebr2021) to find out more.

If you have any ideas or suggestions for stories you'd like to see in *Endocrine News*, feel free to contact me at: [mnewman@endocrine.org](mailto:mnewman@endocrine.org). 

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



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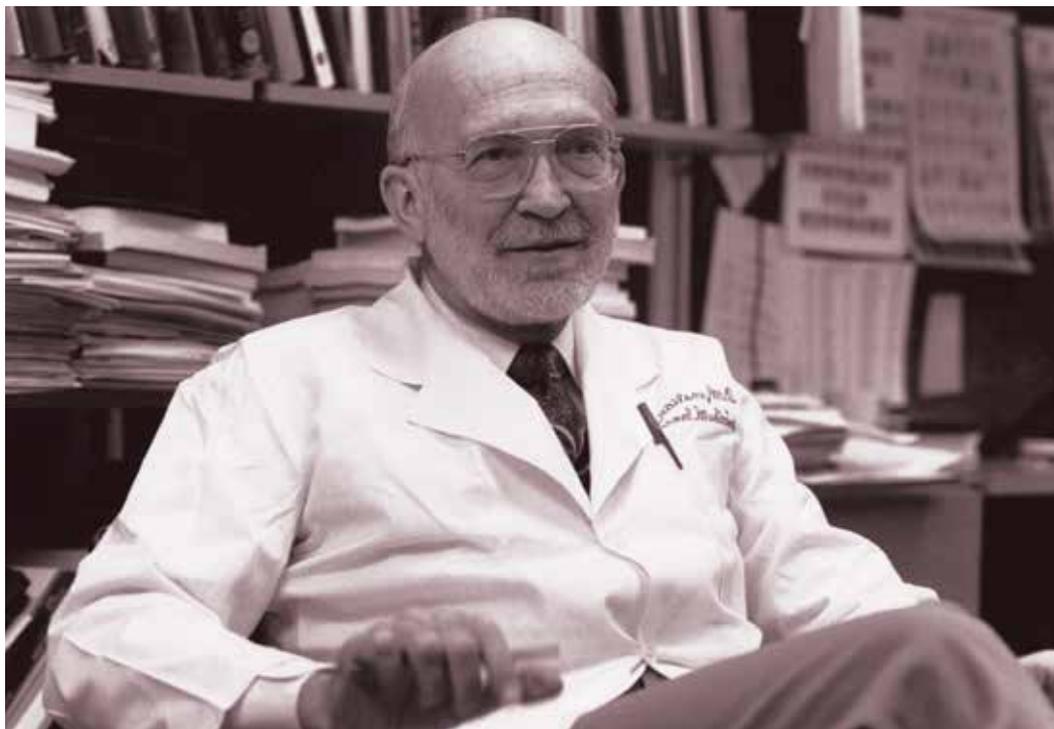


Photo: UT Southwestern Medical Center

## A True Renaissance Man: Remembering Jean D. Wilson, MD

**When Endocrine Society past-president Jean D. Wilson, MD, passed away in June, the sheer volume of accolades and anecdotes that came pouring in made it obvious that he had an enormous impact on the field of endocrinology. Stephen R Hammes, MD, PhD, and Richard J. Auchus, MD, PhD, share their memories of this remarkable man and how he touched their lives and careers.**

**J**ean Wilson, MD, past-president (1990 – 1991) of the Endocrine Society, the American Society for Clinical Investigation, and the Association of American Physicians, died peacefully on June 13 at the age of 88.

Raised in the small town of Wellington on the Texas panhandle, Jean went on to major in chemistry at the University of Texas (Austin). He then attended the fledgling medical school UT Southwestern in Dallas in Quonset huts and temporary buildings with the intention of becoming a medical missionary. After remaining for internal medicine training, he spent two years at the National Institutes of Health (NIH) before returning as a faculty member in 1960, where he remained for the next 60 years. His scientific contributions are best remembered for the discovery and characterization of the 5 $\alpha$ -reductase enzymes, genes, and deficiency syndromes, which culminated in the development of specific inhibitors used clinically for prostate hyperplasia and hair loss.

While Jean Wilson's basic and clinical investigation of androgen biosynthesis and action have profoundly

“

My indelible image is still Jean standing in my kitchen with my two small children next to him, as he explained to them how his peanut butter maker worked, followed by the synthesis, not of steroids, but of delicious peanut butter for them to eat. That's just Jean — above all else, he was a caring man who made everybody around him happy.”

— STEPHEN R. HAMMES, MD, PHD, UNIVERSITY OF ROCHESTER MEDICAL CENTER, ROCHESTER, N.Y.

influenced endocrinology, his contributions extend well beyond the laboratory. He cared for the indigent patients of Dallas for decades at Parkland Hospital, both on the inpatient medicine service and the endocrinology clinics. He educated and mentored scores of students, residents, fellows, and junior faculty. His scholarly presence at grand rounds and didactic conferences fostered critical thinking and high standards. His service to professional societies and journals has left a lasting impact on academic medicine.

Most of us remember Jean for his broad interests in the arts and natural sciences. He could tell you, from memory, the prevalence of cryptorchidism in pigs, the reproductive cycle of the platypus, or the reason why male Seabright-Bantam roosters have henny feathering. He was fascinated with birds and became an expert bird watcher, roaming the globe to fill his “bird life list.” After Don Seldin introduced him to opera, Jean became a lover of classical music and musical performances. He would visit Maria New in New York for a week to discuss cases by day, tour museums in the afternoon, and take in opera or a show at night. He was as comfortable discussing sixteenth century paintings as the molecular defects in androgen insensitivity — and he enthusiastically shared his love of art and science with his friends.

I remember being a first-year endocrinology fellow at the University of California San Francisco and sitting in the office of Marvin Siperstein, a giant in diabetes research and chief of endocrinology at the San Francisco VA hospital.

Marvin was explaining to me the importance of strong physician-scientists in medicine. He regaled me with stories about the amazing Jean Wilson, who was a fellow in Marvin's lab at UT Southwestern years before making his seminal discoveries regarding androgen metabolism and actions. Marvin could not say enough positive things about Jean's scientific accomplishments and dedication toward medical research. Fast-forward three to four years later, and I found myself sitting in Jean Wilson's office at UT Southwestern interviewing for a job. I was timidly describing to him my plans to do something radical. I was going to study the novel concept of extranuclear, or nongenomic, steroid hormone signaling — something that challenged one of the very things that Jean had discovered — that steroids signal by modulating transcription. Even more crazy — I was planning to study this in frog oocytes.

I should have known better than to worry. Jean nearly jumped out of his seat and told me that my ideas were wonderful and that the use of a strong, alternative animal model system would be a tremendous asset. That was all I needed, and off to UT Southwestern I went! Little did I know that I would sit in that very office hundreds of times over the next 10 years, as Jean read and edited my papers, advised my research, discussed the previous evening's symphony concert, or talked about the latest opera he saw in New York (in fact, Jean gave my wife and me his box seats to the opera in Dallas — the first of many operas that we attended in person). Jean's passion for training physician-scientists bolstered my desire to try (but of course never completely succeed) to emulate

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Jean knew how to make science truly an adventure .... I hope that we all learn that lesson from Jean, that a life in science is an adventure, not limited to research, and that we should all enjoy the ride, living every day immersed in the totality of experiences that makes us human.”

— RICHARD J. AUCHUS, MD, PHD, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICH.

him, leading me to become a fellowship director and mentor to physician-scientists.

I would not be where I am today without Jean Wilson, and I doubt a week will go by where I will not think of him. But it may not be remembrances of those days in his office, or the lively fellows' conferences at UT, or the steroid synthetic pathways that he (and Rich Auchus!) taught me. My indelible image is still Jean standing in my kitchen with my two small children next to him, as he explained to them how his peanut butter maker worked, followed by the synthesis, not of steroids, but of delicious peanut butter for them to eat. That's just Jean — above all else, he was a caring man who made everybody around him happy.

— *Stephen R. Hammes, MD, PhD*

Jean loved to talk about anything — family, music, science, food. He listened and took an interest in not just my career, but also my life and my person. I could share results with him: results from an experiment or my time in a triathlon, and he would get just as excited. I guess that was the quality of Jean I admired most: He never became too famous or too old to revel in new knowledge, a new baby, new fellows, or seeing and hearing a bird, performance, or a piece of art for the first time.

Jean knew how to make science truly an adventure. The last major project of his career was to show that testosterone, not dihydrotestosterone, is the circulating androgen during male sexual differentiation. He traveled to Australia to work with wallabies as the best model in Marilyn Renfree's group. He painstakingly performed difficult dissections and incubations himself. On return to Dallas, I watched him tediously run and then cut thin-layer chromatography strips, struggling to quantify multiple compounds, a nearly impossible task (“Jean, we have machines that do this better now, called HPLCs...”). His efforts allowed us to (re)discover the alternative or “backdoor” pathway to dihydrotestosterone — and the differences between humans and marsupials, with testosterone being important for the former not the latter! I hope that we all learn that lesson from Jean, that a life in science is an adventure, not limited to research, and that we should all enjoy the ride, living every day immersed in the totality of experiences that makes us human.

— *Richard J. Auchus, MD, PhD*



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**CLINICAL ENDOCRINOLOGY UPDATE (CEU) 2021**

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**BY DEREK BAGLEY**  
Senior Editor



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**We'll soon begin to study satisfaction among patients and clinicians who use this model and evaluate clinical outcomes and quality improvement initiatives, which could lead to broader adoption of CGM and other EHR-connected insulin delivery systems. Integrating CGM data into the EHR is a step in the direction of more efficient and effective diabetes management.**

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## New CGM Links Directly to EHRs

**H**ealthPartners Institute's International Diabetes Center (IDC) recently developed and piloted a process for incorporating patients' continuous glucose monitoring (CGM) data directly into the electronic health record (EHR), improving clinician access to glucose information.

During a presentation at the American Diabetes Association's 81st Scientific Sessions, IDC medical



director Amy Criego, MD, described this process for integrating the data, as well as what this means for the diabetes care management team, including endocrinologists and primary care clinicians in the future.

“CGM data provides a wealth of information. But without easy access, clinicians can't fully leverage this information for their discussion with patients and clinical recommendations,” Criego says. “We demonstrated that there's an effective way for clinicians to both view and track this data over time in the EHR, which we expect will improve how they're able to support their patients.”

IDC partnered with Abbott on this initiative to improve diabetes management by making

FreeStyle Libre CGM data available at the point of care. Clinicians can place an order in the EHR for a patient with diabetes who has agreed to share their CGM data. In real time, the data is transferred from Abbott's cloud-based system, LibreView, via an EHR platform, allowing physicians to automatically view the patients CGM data in their lab results and diabetes flow sheet, and showing time in range and visual alerts for out-of-range values. The Ambulatory Glucose Profile (AGP) report, in PDF format, is also integrated into the EHR and allows clinicians to easily track the patient's glucose trends over time and adjust treatment regimens as needed.

Using this model, clinicians no longer need to log into a separate system to access their patient's CGM data, which should make workflows more efficient and allow more time for treatment discussions.

“More studies are showing the benefits of CGM and validating these tools. The goal now is to make it easier for patients and clinicians to fully realize the benefits of connected diabetes care,” says Endocrine Society member Richard Bergenstal, MD, executive director of the IDC. “We'll soon begin to study satisfaction among patients and clinicians who use this model and evaluate clinical outcomes and quality improvement initiatives, which could lead to broader adoption of CGM and other EHR-connected insulin delivery systems. Integrating CGM data into the EHR is a step in the direction of more efficient and effective diabetes management.”

# Researchers Determine Best Predictors of Acromegaly Remission Following TSS



**T**umor size and random growth hormone concentration at diagnosis are the best predictors for remission of acromegaly after transsphenoidal surgery (TSS), according to a study recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Eva C. Coopmans, MD, of Erasmus University Medical Center in Rotterdam, The Netherlands, point out that TSS is the primary treatment of choice for acromegaly, since it's the only treatment that can provide a cure and results in lower lifetime costs. "Overall, approximately 75% of patients achieve long-term remission, which sometimes takes several years after initial surgery," the authors write. "It is important to identify patients in whom surgical remission is not attainable at an early stage, both to inform patients on expected treatment outcome and to select those who are more likely to need additional therapy."

In this large multicenter study, the researchers analyzed clinical data since 2000 from 282

patients across three tertiary neurosurgical referral centers in The Netherlands. They found that early biochemical remission is best distinguished by maximum tumor diameter at diagnosis and long-term remission occurs more frequently in patients with a lower random GH concentration at diagnosis who harbor a smaller tumor. "Relapse after TSS occurred more frequently in patients who were younger at diagnosis and harbored larger tumors that secrete more GH," the authors write. "This observation confirms and builds upon previous studies, proposing age at diagnosis to be a clinical marker of tumor size and aggressiveness."

The authors go on to write that these predictors can be used to better inform patients on expected treatment outcome and to personalize postoperative treatment and follow-up. "In addition," they conclude, "further optimization of surgical techniques to improve remission rates for patients who harbor large tumors extending laterally into the cavernous sinus is warranted."



“

It is important to identify patients in whom surgical remission is not attainable at an early stage, both to inform patients on expected treatment outcome and to select those who are more likely to need additional therapy.

”



“

The data published in *The Journal of Clinical Endocrinology & Metabolism* demonstrate the potential of tildacerfont to reduce androgen excess without increasing the total daily glucocorticoid dose in patients with classic CAH.

”

## Tildacerfont Evaluated in Two Phase 2 Open-Label Studies

Patients with classic congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21OHD) may benefit from the drug tildacerfont, according to the results from two Phase 2 clinical studies recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Chris N. Barnes, PhD, of Spruce Biosciences (who funded the trial), point out that the current approach to treating CAH is to downregulate the production of excess androgens by administering supraphysiologic levels of glucocorticoids (GC). However, this approach may lead to significant side effects such as stunted growth, obesity, and increased risk of developing type 2 diabetes, cardiovascular disease, osteoporosis, skin toxicities, gastrointestinal disorders, and reduced lifespan, the authors write.

“Tildacerfont (SPR001; LY2371712) is a potent, selective, nonsteroidal, oral, second generation CRF type-1 (CRF1) receptor antagonist that binds to CRF1 receptors in the pituitary gland with high affinity and reduces ACTH secretion,” the authors continue. “When administered to patients with CAH, the reduction in ACTH secretion is expected to reduce overproduction of adrenal cortisol precursors and androgens. By controlling excess adrenal androgens through an independent mechanism, tildacerfont may decrease the clinical symptoms associated with high androgen exposure and allow GC reduction to a dosing regimen nearing physiological levels, thereby reducing the adverse effects of supraphysiologic GCs.”

The researchers conducted two Phase 2 studies to assess the safety and efficacy of tildacerfont in adults with 21OHD. SPR001-201 was an open-label, multi-dose, Phase 2a dose-escalation study that evaluated the ability of tildacerfont

to lower adrenocorticotrophic hormone (ACTH), 17-hydroxyprogesterone (17-OHP), and androstenedione (A4) at doses ranging from 200mg daily to 1,000mg daily in patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency.

SPR001-202 was an open-label, 12-week Phase 2a clinical trial, which assessed the ability of a daily dose of 400mg of tildacerfont to lower ACTH, 17-OHP, and A4 over a 12-week dosing period. SPR001-201 and SPR001-202 comprised the entire Phase 2a clinical development program for tildacerfont in adult classic CAH. In the studies, efficacy was evaluated by changes from baseline in ACTH, 17-OHP, and A4 according to baseline A4  $\leq 2x$  upper limit of normal (ULN), denoted as baseline good disease control, or A4  $> 2x$  ULN, denoted as baseline poor disease control. Safety was evaluated using adverse events and laboratory assessments.

The results of the studies showed that tildacerfont reduced key hormone biomarkers toward normal levels in the baseline poor disease control group, including normalization of ACTH and A4 in 60% and 40% of patients, respectively. In patients with baseline good disease control, these hormones were maintained near or below normal levels. Tildacerfont was generally safe and well-tolerated.

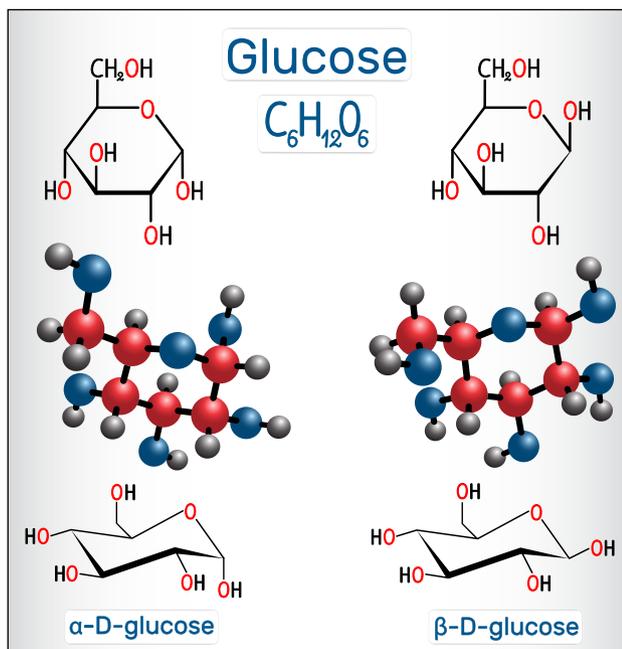
“The data published in *The Journal of Clinical Endocrinology & Metabolism* demonstrate the potential of tildacerfont to reduce androgen excess without increasing the total daily glucocorticoid dose in patients with classic CAH,” says Kyriakie Sarafoglou, MD, associate professor in the Department of Pediatrics – Divisions of Endocrinology and Genetics & Metabolism at the University of Minnesota Medical School, Minneapolis, and first author of the JCEM paper.

# Phase 3 Trial Results Show Promise for Severe Hypoglycemia Treatment

**D** *iabetes Care* recently published results from a Phase 3 trial evaluating dasiglucagon for the treatment of severe hypoglycemia in adults with diabetes. Zealand Pharma is marketing the drug as Zegalogue.

The study found that dasiglucagon administration resulted in a reversal of hypoglycemia (with a median recovery time of 10 minutes) with 99% of trial participants reaching recovery within 15 minutes. “The results of this trial add significantly to the clinical evidence supporting the use of dasiglucagon for the treatment of severe hypoglycemia, and these data build upon the strong clinical data reported throughout dasiglucagon’s clinical trial program in this indication,” says Thomas Pieber, professor of medicine, head of the Division of Endocrinology and Metabolism and chairman of the Department of Internal Medicine at Medical University of Graz, Austria. “This study provides convincing evidence of the potential of dasiglucagon as a treatment that can help patients and their caregivers to address severe hypoglycemia.”

The randomized, double-blind, placebo-controlled multicenter Phase 3 study enrolled 170 adults with type 1 diabetes, each randomized to receive a single subcutaneous dose of dasiglucagon 0.6 mg, placebo, or reconstituted glucagon 1 mg during controlled insulin-induced hypoglycemia. The primary efficacy endpoint was time to plasma glucose recovery, defined as an increase of more than 20 mg/dL from baseline without the need for rescue with



intravenous glucose, in adult patients treated with dasiglucagon versus placebo, with reconstituted glucagon included as a reference.

In this study, the median time to recovery was 10 minutes for dasiglucagon, compared to 40 minutes for placebo ( $P < 0.001$ ); and 12 minutes for reconstituted glucagon. In the dasiglucagon group, plasma glucose recovery was achieved within 15 minutes in all but one participant (99%), superior to placebo (2%;  $P < 0.001$ ), and similar to glucagon (95%). All patients achieved recovery within the study period after receiving one dose. The most common adverse events reported ( $\geq 2\%$ ) were nausea, vomiting, headache, diarrhea, and injection site pain in adults. <sup>BN</sup>



“

The results of this trial add significantly to the clinical evidence supporting the use of dasiglucagon for the treatment of severe hypoglycemia, and these data build upon the strong clinical data reported throughout dasiglucagon’s clinical trial program in this indication.

”

**ADCES Annual Conference**

**August 12 – 15, 2021**

Association of Diabetes Care & Education Specialists Annual Conference (virtual): All sessions will be recorded and available to access on-demand through Monday, November 8, 2021. We will miss seeing our fellow diabetes care and education specialists, friends, and partners together in Phoenix, but we believe this decision is in the best interest of our collective communities. Over 5,000 people joined us virtually for ADCES20, so we are keeping what worked and improving on the challenges we experienced. The result will be a best-in-class virtual experience for all attendees focused on learning, collaborating, and networking. [www.diabeteseducator.org/annual-meeting/adces21](http://www.diabeteseducator.org/annual-meeting/adces21)

**Heart in Diabetes**

**New York, N.Y.**

**September 10 – 12, 2021**

This CME conference brings clinical leaders in diabetes and cardiovascular disease and practicing clinicians together to improve the care of patients at a high risk of cardiovascular, metabolic, and kidney diseases. This program is designed to evaluate the clinical science aspects of diabetes, obesity, and cardiovascular disease, focusing on the heart and kidney in diabetes. The goal is to develop appropriate, comprehensive clinical management plans aligning endocrinologists, cardiologists, nephrologists, and all other interested clinicians in their understandings of the impact of diabetes and CVD outcome trials on the clinical management of these very high-risk patients.

[www.heartindiabetes.com](http://www.heartindiabetes.com)

**90th Annual Meeting of the American Thyroid Association®**

**Scottsdale, Ariz.**

**September 29 – October 3, 2021**

This meeting is designed for the community of endocrinologists, basic scientists, internists, surgeons, nuclear medicine scientists, pathologists, trainees, nurses, physician assistants, advanced practice providers, and other healthcare professionals who wish to broaden and update their knowledge of the thyroid gland and its disorders.

[www.thyroid.org](http://www.thyroid.org)

**The American Society for Bone and Mineral Research (ASBMR) 2021 Annual Meeting**

**Toronto, Canada**

**October 1 – 4, 2021**

Connect with more than 3,000



**Virtual 2021 Clinical Endocrinology Update/Endocrine Board Review**

**CEU 2021**

**Sept. 10 – 12, 2021**

**EBR 2021**

**Sept. 22 – 24, 2021**

Every year, the Endocrine Society holds Clinical Endocrinology Update (CEU), which brings together hundreds of endocrine clinicians for a unique learning experience.

This year, due to concerns regarding the safety of both attendees and faculty stemming from the COVID-19 outbreak, the Endocrine Society is conducting these sessions in a virtual learning environment.

CEU 2021 offers an opportunity to stay up to date on the newest breakthroughs in clinical endocrinology. Expert faculty deliver a comprehensive three-day program covering a range of clinical practice areas using interactive, case-based learning.

Endocrine Board Review (EBR) is an essential course for endocrinologists preparing to take the boards or practicing physicians seeking an intensive knowledge assessment. The virtual program is designed as a mock exam, with rapid-fire case-based questions emulating the format and subject matter of the ABIM's Endocrinology, Diabetes, and Metabolism Certification Examination. Attendees will have early access to topical on-demand presentations with detailed answer rationale (available in late August).

[www.endocrine.org/ceu2021](http://www.endocrine.org/ceu2021) • [www.endocrine.org/eb2021](http://www.endocrine.org/eb2021)

scientists from around the world for the premier scientific program packed with cutting-edge research in the bone, mineral, and musculoskeletal field. The ASBMR Annual Meeting boasts a variety of educational sessions and poster presentations in four information-filled days. The conference includes hands-on workshops focused on the latest technologies and research tools using model datasets, meet-the-professor sessions, and access to new science, new knowledge, new tools, and new contacts all in one location.

[www.asbmr.org](http://www.asbmr.org)



**Obesity Week 2021**

**November 1 – 5, 2021**

ObesityWeek® is home to the latest developments related to obesity from cutting-edge basic and clinical research to state-of-the-art treatment and prevention to the latest efforts in advocacy and public policy. Present your latest work and stay up to date on the latest advances in the field by attending ObesityWeek®. The overarching theme for ObesityWeek® Interactive will be Pathways to Precision Obesity Care. A key component in the development of precision care for obesity is recognizing and understanding the inherent heterogeneity in both the patterns of development and expression of obesity, and ObesityWeek® Interactive programming will draw specific attention to these topics.

<https://obesityweek.org/>

**Diabetes and Its Complications**

**Livestream**

**November 4 – 6, 2021**

This program provides comprehensive updates, practice recommendations, and the newest evidence-based strategies for the treatment and care of the person with or at risk for diabetes. In addition to state-of-the-art approaches to diabetes management, this course provides comprehensive updates for the prevention, diagnosis, and treatment of diabetes comorbidities and complications.

<https://hmsdiabetescourse.com/>

INTERNATIONAL ITINERARY

**WCO-IOF-ESCEO London 2021**

**London, England**

**August 26 – 19, 2021**

The 2021 World Congress on Osteoporosis, Osteoarthritis, and Musculoskeletal Diseases will take place in London, August 2021, with a very exciting scientific program that will bring together the world's best in the field of musculoskeletal health and disease. The International Osteoporosis Foundation (IOF) and the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO) are thrilled to welcome you in London and hope that this Congress will move the field one step forward on all fronts; from new understanding of bone metabolism and pathology, to new strategies and options in prevention, diagnosis, and treatment.

<https://www.wco-iof-esceo.org/>

**EndoBridge 2021**

**Antalya, Turkey**

**October 21 – 24, 2021**

EndoBridge® is a unique initiative with the vision of bridging the world of endocrinology. EndoBridge® is co-hosted by the Endocrine Society and the European Society of Endocrinology in collaboration with the Society of Endocrinology and Metabolism of Turkey. The meetings are held in English with simultaneous translation into Russian, Arabic, and Turkish. Accredited by the European Accreditation Council for Continuing Medical Education (EACCME), this three-day scientific program includes state-of-the-art lectures delivered by world-renowned faculty and interactive sessions covering all aspects of endocrinology. EndoBridge® provides a great opportunity for physicians and scientists from around the world to interact with each other, share their experience and perspectives, and participate in discussions with global leaders of endocrinology.

[www.endobridge.org](http://www.endobridge.org)

**2021 World Endocrine & Obesity Conference**

**Bangkok, Thailand**

**November 19 – 20, 2021**

Designed as a hybrid conference with both virtual and in-person platforms, the 2021 WEOC will address the complex nature of critical care cases, including their unique physiology, array of procedures, and potential complications. The latest management strategies for challenging clinical problems will be presented and current controversies will be discussed utilizing a variety of educational methodologies.

<https://endocrine.episirus.org>



# DEVIL IN THE DETAILS:

## The Impact of the First Interchangeable Biosimilar Insulin

*When the U.S. Food and Drug Administration approved the first interchangeable biosimilar insulin product last month, many were hailing this as a breakthrough in treating diabetes. The impacts could be immediately felt by people rationing their insulin due to cost as well as long-range effects on future clinical trials.*

Last month, the U.S. Food and Drug Administration (FDA) approved the first interchangeable biosimilar insulin product, indicated to improve glycemic control in adults and pediatric patients with type 1 diabetes and in adults with type 2 diabetes. The FDA granted approval for insulin glargine-yfgn to Mylan Pharmaceuticals Inc., which is marketing the product as Semglee.

Semglee is both biosimilar to and interchangeable with its reference product Lantus (insulin glargine), a long-acting insulin analog. Semglee is the first biosimilar product to get the “interchangeable” designation in the U.S. for the treatment of diabetes. Approval of these insulin products can provide patients with additional safe, high-quality, and potentially cost-effective options for treating diabetes.

An interchangeable biosimilar product may be substituted for the reference product without the intervention of the prescriber. The substitution may occur at the pharmacy, a practice commonly called “pharmacy-level substitution” — much like how generic drugs are substituted for brand-name drugs, subject to state pharmacy laws, which vary by state.

“Biosimilar and interchangeable biosimilar insulin products have the potential to lower costs for patients. Hopefully, this approval will help drive prices down for insulin in the long term. Access to affordable care, and particularly affordable insulin, is a priority in diabetes care,” says Rita Kalyani, MD, associate professor at Johns Hopkins School of

“ Since this is interchangeable by the pharmacist, this means the pharmacist will have the discretion not to use the cheaper insulin. **Admittedly, this is the worst-case scenario, but this is the reason why both clinicians and patients need to be familiar with this new ruling to ensure the best value for this insulin.**”

— IRL HIRSCH, MD, PROFESSOR OF MEDICINE, UNIVERSITY OF WASHINGTON DIABETES INSTITUTE, SEATTLE, WASH.

Medicine. “From a patient perspective, this can help increase access to less expensive alternatives from the pharmacy. However, there will be some individuals that still prefer the brand insulin and there will need to be more education going forward that these two products are, in fact, interchangeable.”

But while on the surface this looks like a wonderful announcement and something that many endocrinologists have been waiting for years to hear, as Irl Hirsch, MD, professor of medicine at the University of Washington Diabetes Institute in Seattle, tells *Endocrine News*, the devil is in the details. Semglee currently costs around \$100 per vial, and while that’s much cheaper than Lantus, that’s still a hefty price tag, especially when you consider Canadians pay around \$30 a vial.

“A bigger concern is whether the [pharmacy benefit managers] will be incentivized not to provide the biosimilar insulin to patients — due to contracting with the pharmaceutical company,” Hirsch says. “Since this is interchangeable by the pharmacist, this means the pharmacist will have the discretion not to use the cheaper insulin. Admittedly, this is the worst-case scenario, but this is the reason why both clinicians and patients need to be familiar with this new ruling to ensure the best value for this insulin.”

There will be some things to iron out — patient and doctor confusion, hesitancy to change medications, etc. — but the hope is that this approval will pave the way for more

interchangeable biosimilars to enter the market and drive prices down. The approval of this new biosimilar is in line with the Endocrine Society’s Position Statement from January, “Increasing Insulin Affordability.” Before Semglee, there were only two biosimilars available, made by Eli Lilly (Basaglar) and Sanofi (Admelog), two of the three insulin manufacturers. “For biosimilars to have an impact on the price of insulin, availability must extend beyond current manufacturers and new companies must be willing to undertake a costly development and strict review process,” the Position Statement authors write.

“ It may allow people who have been rationing their insulin because of cost to stop doing so. This would improve glycemic control in those who are doing so. **I think it will also change the design of trials of new insulins so that they can be designated as both biosimilar and interchangeable.**”

— ROBERT VIGERSKY, MD, CHIEF MEDICAL OFFICER AT MEDTRONIC, DIRECTOR EMERITUS OF DIABETES INSTITUTE AT WALTER REED NATIONAL MILITARY MEDICAL CENTER IN BETHESDA, MD., AND PAST-PRESIDENT OF THE ENDOCRINE SOCIETY.

“This will undoubtedly continue the increase the downward pressure on insulin pricing,” says Robert Vigersky, MD, chief medical officer at Medtronic, director emeritus of Diabetes Institute at Walter Reed National Military Medical Center in Bethesda, Md., and past-president of the Endocrine Society. “Most importantly, it may allow people who have been rationing their insulin because of cost to stop doing so. This would improve glycemic control in those who are doing so. I think it will also change the design of trials of new insulins so that they can be designated as both biosimilar and interchangeable.” 

— BAGLEY IS THE SENIOR EDITOR OF ENDOCRINE NEWS. IN THE JULY ISSUE, HE WROTE ABOUT THE CEU 2021 SESSION ON FATTY LIVER DISEASE.



# NEXT TO NORMAL:

## How Useful is the Concept of *Prediabetes* in Older Adults?

BY ERIC SEABORG

Although more than half of Americans older than age 65 meet criteria for prediabetes, most of them will not progress to developing diabetes. While conflicting messages abound regarding prediabetes, the Endocrine Society recommends an oral glucose tolerance test for those older patients at greatest risk for developing diabetes.

**T**he scientist who helped popularize the term prediabetes now calls that effort a “big mistake.” His concern gained new attention when a recent study found that older adults whose hemoglobin A1c levels put them in the prediabetes category are much more likely to return to normal glycemic levels or die than develop diabetes. The study was one more in a string questioning the value of a diagnosis of prediabetes in this population.

But the Endocrine Society guideline on treating diabetes in older adults notes an often-overlooked aspect of the most common test used in screening for diabetes: As people age, their red-blood-cell life cycles change in ways that can render hemoglobin A1c results unreliable, with results that can mislead in both high and low directions. That's why the guideline suggests following up with an oral glucose tolerance test in patients believed to be at risk for diabetes, according to Marie E. McDonnell, MD, director of the diabetes program at Brigham and Women's Hospital in Boston, Mass., and a member of the Endocrine Society guideline committee. "The issue is not so much about prediabetes, it is more about not missing diabetes," McDonnell says.

## Popularization of the Term

Prediabetes itself does not have clinical consequences, but this distinction can be easily missed in what some call the marketing effort for the condition. Richard Kahn, PhD, was the chief scientific and medical officer at the American Diabetes Association (ADA) in 2001 when the ADA was trying to raise the alarm about the danger signs on the road to developing diabetes.

At the behest of the ADA's head of press relations, Kahn met with other experts who decided to coalesce around using the term prediabetes to replace technical phrases like impaired glucose tolerance and impaired fasting glucose as a way to drive home to the public their concern about the rising threat of diabetes. But the term has since taken on a life of its own that was unforeseeable at the time, says Kahn, who served as the ADA's chief medical officer for nearly 25 years and is now clinical professor of medicine at the University of North Carolina at Chapel Hill.

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“ It is hard to argue against screening for diabetes. **We know that there is a significant number of undiagnosed diabetes in the older adult population, and we know that about a quarter of people over 65 have diabetes.**”

— MARIE E. MCDONNELL, MD, DIRECTOR, DIABETES PROGRAM, BRIGHAM AND WOMEN'S HOSPITAL, BOSTON, MASS.

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The ADA defines prediabetes as an Hb A1c level of 5.7% to 6.4% (with type 2 diabetes starting at 6.5%) or a fasting plasma glucose of 100 to 125 mg/dL (5.6–6.9 mmol/L). With more than 50% of Americans older than age 65 meeting these criteria, the term has become controversial with critics saying the “pre” part is misleading in this population, as evidence has accumulated about the low risk that those with slightly elevated blood glucose levels will go on to actually develop diabetes.

A prospective cohort analysis published in *JAMA Internal Medicine* in February that followed 3,421 adults with a mean age of 76 for a 6.5-year follow-up period highlighted this question about the true level of risk.

“The people who had prediabetes at baseline were actually more likely to return to normal glucose levels or die after six years of follow-up instead of progressing to diabetes,” lead study author Mary R. Rooney, PhD, MPH, a postdoctoral fellow at the Johns Hopkins Bloomberg School of Public Health, Baltimore, Md., tells *Endocrine News*. “Even across all the different definitions of prediabetes, these definitions didn't really capture risk of progression to diabetes well.”

## A Risk Factor Twice Removed

An editorial accompanying the study notes that not only do Hb A1c levels in the prediabetes range pose no risk of complications, but diabetes itself can be controlled. Kenneth Lam, MD, and Sei J. Lee, MD, MAS, both of the University of California, San Francisco, write that it is the “end-organ vascular complications that result from years of poorly controlled diabetes that cause symptoms. Therefore, the modern definition of diabetes is conceptually closer to being a risk factor itself (e.g., something that portends future disease) than an illness (e.g., something that patients experience). Prediabetes, then, is a risk factor twice removed; it is a risk factor for diabetes, which itself may be most accurately described as a risk factor for end-organ vascular disease.”

Lam agrees with Kahn that the way prediabetes is marketed is questionable. This marketing is highlighted by a website that asks “Could you have prediabetes?” with a “take the test” risk calculator sponsored by the Centers for Disease Control and Prevention, American Medical Association, and Ad Council ([doihavediabetes.org](http://doihavediabetes.org)). A 2016 study in *JAMA Internal Medicine* estimated that the calculator would score 60% of Americans 40 years and older and 81% of those 60 and older as at risk for prediabetes.

This messaging is also present in the ADA’s standards of diabetes care. The standards of care lump the two together under a bold-faced subtitle, “Prediabetes and Type 2 Diabetes.” Yet, the smaller text says: “Prediabetes should not be viewed as a clinical entity in its own right but rather as an increased risk for diabetes and cardiovascular disease.”

“The ADA guidelines specifically state that prediabetes is not a disease, but the marketing around prediabetes strongly suggests that it is a disease,” Lam says.

It is easy to find examples of internists ready to prescribe metformin based on Hb A1c levels in the prediabetes range,

even those barely above normal, *New York Times* health writer Paula Span found in reporting on the February study. The use of drugs in patients with prediabetes contradicts the Endocrine Society practice guideline recommendations for older adults with diabetes, and the guideline notes that the FDA has not approved metformin for prevention. Drug treatment is generally not recommended because the evidence indicates it is not nearly as effective as diet and exercise in prediabetes, particularly in older adults, according to McDonnell. (The ADA

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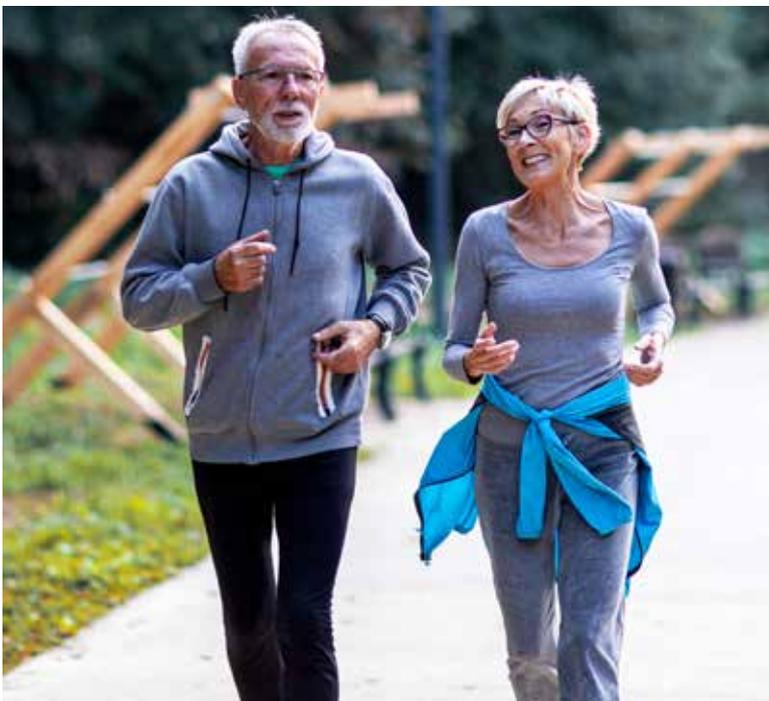


standards say metformin should be considered for prevention, especially in obese patients and those younger than 60 years old.)

The *JAMA Internal Medicine* article is one of a string of studies questioning the relevance of the prediabetes diagnosis in older adults. A 2018 Cochrane Library review of 103 studies found that “because people with prediabetes may develop diabetes but may also change back to normoglycemia almost any time, doctors should be careful about treating prediabetes because we are not sure whether this will result in more benefit than harm.”

## Revised Standards Coming?

The ADA declined repeated requests from *Endocrine News* to comment on how the ADA standards of care treat prediabetes. However, the *New York Times* quoted Robert Gabbay, ADA’s current chief scientific and medical officer, as saying that the professional practice committee will review the recent *JAMA Internal Medicine* study and perhaps adjust the guidelines considering that the risk of older adults of developing diabetes “may be smaller than we thought.”



## AT A GLANCE

- ▶ More than half of older adults meet the criteria for a diagnosis of prediabetes, but most will not progress to developing type 2 diabetes.
- ▶ Clinicians and patients receive conflicting messages about prediabetes. American Diabetes Association guidelines say it “should not be viewed as a clinical entity,” but critics charge that the term’s marketing says otherwise.
- ▶ Hemoglobin A1c levels can be misleading in older adults, so an oral glucose tolerance test can be valuable in identifying which patients are at truly greater risk of developing diabetes, according to an Endocrine Society guideline.

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The people who had prediabetes at baseline were actually more likely to return to normal glucose levels or die after six years of follow-up instead of progressing to diabetes. **Even across all the different definitions of prediabetes, these definitions didn't really capture risk of progression to diabetes well.**

— MARY R. ROONEY, PHD, MPH, POSTDOCTORAL FELLOW, JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH, BALTIMORE, MD.

Gabbay reiterated the often-expressed view that a prediabetes diagnosis is a valuable tool because it can motivate people to try to bring their blood sugar down through the healthy lifestyle choices that everyone should be making. Lam counters that clinicians should not mislead people about their condition or use scare tactics to try to motivate them.

McDonnell notes that glycemia has consequences on a continuum, and that it can still be useful to know that a significant percentage of patients with prediabetes will go on to develop diabetes. She says that clinicians can confirm whether a high Hb A1c is a false flag or whether it indicates “real” prediabetes — or even diabetes.

The Endocrine Society guideline emphasizes that today's older adults can easily live another 20 years. That is plenty of time to develop the complications of diabetes, which appropriate treatment can mitigate.

The Endocrine Society and ADA guidelines both recommend a lifestyle program for prediabetes patients. McDonnell notes that patients can benefit from a diagnosis of prediabetes because it means that Medicare will cover enrollment in a diabetes

prevention program. “It might get them free access through Medicare to a lifestyle behavior modification program that will focus on eating well and exercising, and that has benefits way beyond glucose control,” McDonnell says. Because older adults derive a broad range of benefits from exercise and maintaining healthy body weight, McDonnell suggests that the identification of prediabetes in this group is benign if not beneficial.

## Defining the Parameters

“It is hard to argue against screening for diabetes,” McDonnell says. “We know that there is a significant number of undiagnosed diabetes in the older adult population, and we know that about a quarter of people over 65 have diabetes.”

But the parameters used in the screening can make a big difference, according to a 2020 *BMJ Open Diabetes Research & Care* article that compared the results of using the different cut-offs in the ADA and World Health Organization (WHO) definitions of prediabetes. The authors noted that the “main difference” in the two definitions of prediabetes was the threshold of the glycemic index.

For fasting glucose, the ADA threshold is 100 mg/dL (5.6 mmol/L) whereas the WHO threshold is 108 mg/dL (6.0 mmol/L). The study applied the two definitions to about 9,000 people over age 45 without diabetes from the general population in the Rotterdam Study in The Netherlands. The ADA criteria diagnosed 40% as having prediabetes, compared with 16% using the WHO criteria. Among those classified as having prediabetes, the 10-year risk of developing diabetes was 14% using the ADA definition, compared with 25% using the WHO definition, and lifetime risk was “substantially lower in ADA-defined prediabetes.”

As a geriatrician, Lam notes that the concept of risk — and competing risks — is a key to treating the individual, not the number. The approach when test results indicate prediabetes should be very different in a frail patient in their 80s compared with an obese 65-year-old. <sup>EN</sup>

## RESOURCES

Treatment of Diabetes in Older Adults: An Endocrine Society Clinical Practice Guideline is available at: <https://academic.oup.com/jcem/article/104/5/1520/5413486>

— SEABORG IS A FREELANCER WRITER BASED IN CHARLOTTESVILLE, VA. IN THE JULY ISSUE, HE WROTE ABOUT THE CEU 2021 SESSION DEBATING THE USE OF TESTOSTERONE THERAPY IN FEMALE PATIENTS.



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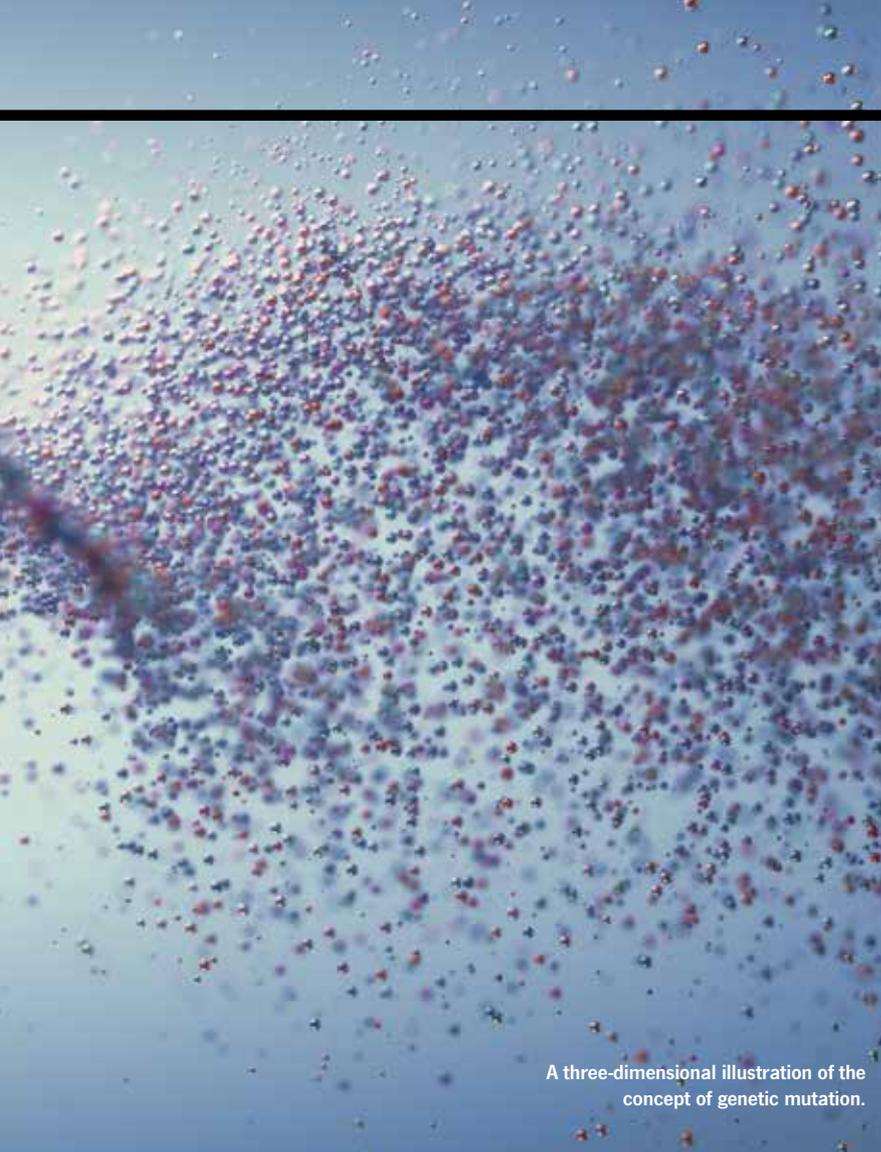
# Unbiased Condition:

## Why Some Men Appear to Have Polycystic Ovary Syndrome

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It is believed that polycystic ovary syndrome (PCOS) can impact up to 10% of women but according to new genetic research presented in March at **ENDO 2021**, it can manifest in men as well. *Endocrine News* talks to the lead researcher, Jia Zhu, MD, about this somewhat surprising revelation as well as how this study could eventually lead to better treatment options for all patients with PCOS.

BY DEREK BAGLEY

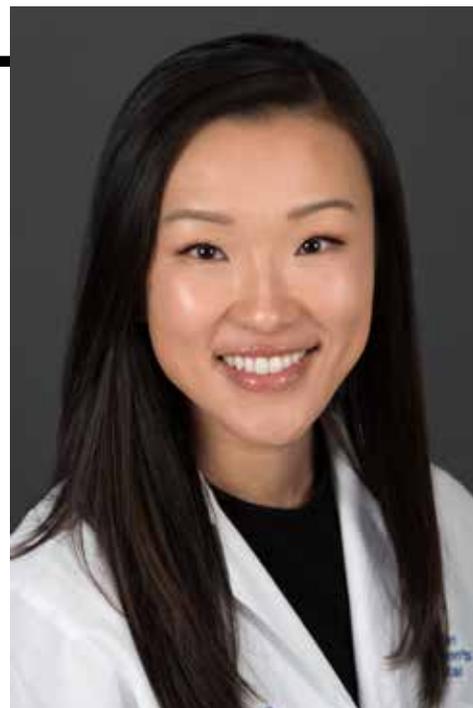


A three-dimensional illustration of the concept of genetic mutation.

**T**he Endocrine Society’s annual meetings always bring new, interesting, and even groundbreaking medical science to the endocrinology community and beyond, and while **ENDO 2021** was all virtual due to the continued COVID-19 pandemic, this year’s annual meeting was no exception. But as with the best of science, answers often bring up more questions.

For instance, polycystic ovary syndrome (PCOS), the heterogenous condition that affects up to 10% of women of reproductive age, has been studied extensively, through physiological and genetic studies, yet the medical community still does not fully grasp what causes PCOS. And now, genetic research presented at **ENDO 2021** suggests men can develop characteristics of PCOS as well. Since men obviously do not have ovaries, these findings point to the fact that PCOS may not depend on the ovaries at all. Again, more questions — and ones that need to be addressed if treatment options are to advance, since the disorder can lead to obesity, diabetes, and cardiovascular disease, which are often life-long conditions.

“We know ovarian-related factors and ovarian-independent factors both play a role, but we don’t know which are the inciting factors, which are the secondary



**“**We know ovarian-related factors and ovarian-independent factors both play a role, but we don’t know which are the inciting factors, which are the secondary consequences, or how they are connected or influence each other. **As a result, the current treatment options for PCOS are limited to management of the symptoms without addressing the underlying causes. The sooner we understand what causes PCOS, the sooner we can develop targeted therapies for PCOS and its counterpart in men.**”

— JIA ZHU, MD, ATTENDING PHYSICIAN,  
DIVISION OF ENDOCRINOLOGY, BOSTON CHILDREN’S HOSPITAL,  
BOSTON, MASS.



“ By demonstrating that genetic risk factors for PCOS are associated with obesity, diabetes, and cardiovascular disease, and male-pattern baldness in men, we show that these genetic risk factors do not require ovaries to result in the characteristics of PCOS. Thus, at least in some cases, the reproductive dysfunction of PCOS may be caused by biological mechanisms common to both men and women.”

— JIA ZHU, MD, ATTENDING PHYSICIAN, DIVISION OF ENDOCRINOLOGY, BOSTON CHILDREN'S HOSPITAL, BOSTON, MASS.

consequences, or how they are connected or influence each other,” says lead researcher Jia Zhu, MD, of Boston Children's Hospital. “As a result, the current treatment options for PCOS are limited to management of the symptoms without addressing the underlying causes. The sooner we understand what causes PCOS, the sooner we can develop targeted therapies for PCOS and its counterpart in men.”

## Typical and Surprising Comorbidities

For this study, Zhu and her team used genetic data from 176,360 men in the United Kingdom to estimate genetic susceptibility for PCOS through an optimized polygenic risk score (PRS). They tested for associations with metabolic disorders (obesity, diabetes, and cardiovascular disease) and male-pattern baldness. “We used logistic regression to calculate odds ratios for dichotomous outcomes by comparing men with high and low PRS (testing a variety of percentile cutoffs) and ANCOVA to compare continuous outcomes across deciles of PRS,” the authors write. “All analyses were adjusted for age, assessment center, genotyping array, and the first 10 principal genetic components to account for ancestry.”

The researchers found that men who had a high genetic risk score for PCOS had increased risk of obesity, diabetes, cardiovascular disease, and male-pattern baldness. The authors write that

the relationship between the PCOS PRS and cardiovascular disease appeared to be mediated by body mass index (BMI). “In contrast, the associations between the PCOS PRS and type 2 diabetes mellitus and hemoglobin A1c remained significant after adjusting for BMI, suggesting independent mechanisms of pathogenesis,” they write.

Zhu explains that one strength of the study was its population size. According to Zhu, to better understand the genetics of complex and common disorders such as PCOS, it is critical to have a large sample of individuals (who can be assessed for even modest effects of genetic factors) and individuals who represent a general population (so the findings can be applied to the population). “The UK Biobank is a tremendously valuable resource to the scientific community and provides a large, population-based cohort to conduct large-scale genomic studies, such as ours,” she says.

“By demonstrating that genetic risk factors for PCOS are associated with obesity, diabetes, and cardiovascular disease, and male-pattern baldness in men, we show that these genetic risk factors do not require ovaries to result in the characteristics of PCOS,” Zhu says. “Thus, at least in some cases, the reproductive dysfunction of PCOS may be caused by biological mechanisms common to both men and women.”



## Familial Traits

The concept of “male PCOS” was proposed 15 years ago, but it remains elusive, and there is no formal clinical definition. Male relatives of women with PCOS can also have features of PCOS, including obesity, type 2 diabetes, cardiovascular disease, and hyperandrogenism or high levels of androgen hormones (such as testosterone). “We already knew from clinical observations that male relatives of women with PCOS had features of PCOS, likely because they shared genetic material with their female relatives,” Zhu says.

In that case, Zhu says she and her team hypothesized and expected to find that genetic risk factors for PCOS would lead to increased risk for these disorders, which they confirmed. “What was particularly interesting to us was the fact that body-mass index (BMI) had a major role in mediating these associations between polygenic risk for PCOS and all outcomes,” she says. “This finding really highlights the major role obesity has in PCOS and its associated comorbidities and provides additional validation that targeting obesity (and its biological pathways) is critical to the management and treatment of PCOS.”

## Dissecting the Biology of PCOS

There is still much to learn about the genetics and underlying biology of PCOS. The ultimate goal is to improve the management and treatment of PCOS for women and the PCOS-like condition in men. Zhu says that clinicians are not quite to the point of being able to use genetic tools like polygenic risk scores in clinical practice to predict risk for the associated features of PCOS. “Until then, we can use these tools to dissect the biology of PCOS as a starting point for future clinical and genetic studies that will continue to pave the way for individualized care for patients with PCOS, including future genetic screening,” she says.

No doubt, more questions will follow and will likely open up more avenues to pursue. In the conclusion to their **ENDO 2021** presentation abstract, the authors write, “Future dissection of these biological pathways will further inform efforts to identify pathological mechanisms underlying PCOS.”

For now, Zhu says she hopes this study will be a kind of lodestar for that work, since clinicians and scientists have expressed interest in this novel genetic approach to validating and characterizing the existence of a male counterpart to PCOS. “Because men do not have ovaries yet can have these features associated with PCOS in women, our work reconceptualizes PCOS as more than a disorder of female reproductive function, but rather a cardiometabolic condition that affects both sexes,” she says. “Future studies of the genetic risk factors for PCOS could help us to better understand the causes and potential treatment targets for PCOS.” <sup>EN</sup>

## AT A GLANCE

- ▶ Polycystic ovary syndrome (PCOS) affects up to 10% of women and has been studied extensively, yet the causes of this disorder continue to elude the medical community.
- ▶ Genetic research presented at **ENDO 2021** suggest men can develop characteristics of PCOS as well, meaning the syndrome may be independent of ovaries.
- ▶ Understanding the biological pathways of PCOS will lead to better treatment options for women and men.

# Challenges in the Management of Cushing's Disease



Anthony Heaney, MD, PhD

(At top) Microscopic image of an adrenal cortical adenoma, a benign tumor of the adrenal gland, which may produce hormones cortisol or aldosterone and lead to Cushing's syndrome or primary hyperaldosteronism.

BY DEREK BAGLEY

Cushing's disease continues to confound endocrine clinicians due to the manner in which it mimics more commonplace disorders. We talk to Anthony Heaney, MD, PhD, about his CEU 2021 session, "Challenges in the Management of Cushing's Disease" and what attendees can expect to learn about this rare endocrine condition.

Cushing's disease is a rare disorder that can often hide behind more common diseases, manifesting as symptoms of conditions that physicians would first point to as the culprit. It can be a challenge just to diagnose, much less treat. Symptoms of Cushing's include obesity, hypertension, and depression, all patient complaints that could easily point to any number of things, so if a patient does have Cushing's, the delay in diagnosis and then treatment only compounds the problem.

For this year's Clinical Endocrinology Update (CEU), Anthony Heaney, MD, PhD, associate professor at the David Geffen School of Medicine at the University of California, Los Angeles (UCLA), and an expert in pituitary tumors, will discuss these barriers to optimal treatment of patients with Cushing's disease during his Meet the Professor presentation, "Challenges in the Management of Cushing's Disease."

*Endocrine News* caught up with Heaney to hear what to expect from his CEU talk.

**Endocrine News:** First off, can you give a little background on your presentation, as well as an overview of what attendees can expect?

**Anthony Heaney:** I plan to use case illustrations to highlight some of the challenges endocrinologists all face in diagnosing and managing a patient with Cushing's disease.

**EN:** Your talk is titled "Challenges in the Management of Cushing's Disease." Can you give an example or a preview of the challenges that you'll cover?

**AH:** As endocrinologists, we face challenges at all stages of Cushing's disease — the diagnosis can be difficult to make, especially in earlier, less frank cases. Locating the site of disease can sometimes be challenging, and the management itself can also be challenging, as although we have some great therapies, they don't always work and recurrence rates in Cushing's disease are quite high.

**EN:** Why is it important for physicians to be aware of these challenging cases?

**AH:** Cushing's disease is one of those diagnoses that is important to consider, and then based on physician index of suspicion, determine which tests and how much testing is needed to either rule it in or exclude it as a cause for a patient's symptoms. We know that the phenotype that we see in Cushing's disease is shared with several other conditions that are much more common, and all endocrinologists will encounter patients who might or might not have Cushing's disease. So, a basic understanding about how to approach such a patient is very helpful to the vast majority of endocrinologists.

**EN:** Are there any new techniques or methods you can share for clearing these hurdles of diagnosing or treating Cushing's?

**AH:** I wish I could answer that with, "Yes, there have been some major breakthroughs," but alas, that would be misleading. We have added some new medical therapies that will be helpful, but no breakthroughs that will really change the situation in my opinion just yet.

**EN:** What do you hope attendees take away from your talk?

**AH:** I hope they take away that Cushing's disease is one of the most challenging conditions that we as endocrinologists diagnose and treat; that there are no perfect algorithms that will easily diagnose every patient; and that a combination of clinical "index of suspicion" and careful, rigorous, and sometimes repeated biochemical testing over time are paramount to helping our patients find help for this disorder. 

“ The phenotype that we see in Cushing's disease is shared with several other conditions that are much more common, and all endocrinologists will encounter patients who might or might not have Cushing's disease. **So, a basic understanding about how to approach such a patient is very helpful to the vast majority of endocrinologists.**”

## CEU 2021

The presentation will be a part of the Clinical Endocrinology Update (CEU) 2021, a comprehensive virtual meeting featuring faculty at the forefront of endocrinology describing the latest advances and critical issues in the field.

Taking place September 10 – 12, each day will feature four hours of live programming, including 36 educational sessions spanning seven topics. All sessions will be recorded and available for viewing 72 hours after they conclude.

Information and registration are available at: [endocrine.org/ceu2021](https://endocrine.org/ceu2021).

— BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. IN THE JULY ISSUE, HE WROTE THE CEU 2021 PREVIEW ARTICLE ABOUT THE SESSION DETAILING WHAT ENDOCRINOLOGISTS NEED TO KNOW ABOUT FATTY LIVER DISEASE.



## Mitigating the Real Culprits of Health Disparities:

Health disparities remain one of the most daunting obstacles to delivering care to a variety of patient populations. We talk to Rocio I. Pereira, MD, about her CEU 2021 session, “Health Disparities in Diabetes,” and about how clinicians can overcome these obstacles to care.

**BY KELLY HORVATH**

**T**his year’s Endocrine Society’s always highly anticipated Clinical Endocrinology Update symposium takes place virtually from Friday, September 10 through Sunday, September 12, where leading experts will present new findings and how these translate to the point of care.

*Endocrine News* is getting an advance peek into one such presentation, from our conversation with Rocio I. Pereira, MD, chief of endocrinology at Denver Health, associate professor of medicine at the University of Colorado, Division of Endocrinology, Metabolism, and Diabetes, and the founder and director of the Vuela for Health lifestyle intervention program for Latino immigrants. Pereira will be discussing healthcare disparities in diabetes.

**Endocrine News:** Let’s start with what got you interested in health disparities in diabetes.

**Rocio “Ro” Pereira:** I started learning about health disparities during my first year of medical school. I was paired with a preceptor who was an internist at one of

the primary care clinics at Denver Health, our local safety-net hospital system. Working at that clinic, I started learning about health disparities, particularly as they relate to diabetes and obesity and realizing that our minority patients — especially Latino and black patients — tend to have more diabetes and their diabetes tends to be less well controlled. This got me thinking about why that is and what we can do about it. I'm a Latina physician and bilingual, so I saw a lot of the Spanish-speaking patients and some of the more recent immigrants. In particular for that population, I realized also that they have a lot of challenges in accessing healthcare.

**EN:** Including language.

**RP:** Including language, exactly.

**EN:** So, you are in a really good position to help them overcome some of those barriers. Tell me a little bit about the session you are going to present at this year's Clinical Endocrinology Update in September.

**RP:** I've been thinking a lot about this presentation because I want it to be actionable. I want to provide useful information for physicians in practice who are seeing patients and wanting to make a change or bring about change and make a difference in health disparities with their patients. I want to be able to give some actionable steps for those physicians.

I'm planning to start with some background to review the current state — the problem with disparities and the prevalence of diabetes in the different populations and then that disparity compared to non-Latino whites.

Next, I'm going to talk a bit about causes and touch on how we as physicians think about first the biology, then the genetics and molecular mechanisms, and then the behaviors that go into all these diseases. We're not really used to thinking about the social determinants of health and how they have the most impact on these disparities.

In the third part, I will talk about best practices in addressing health disparities as an endocrinologist and as a diabetologist in particular. What can we as individuals do in our systems and in our practices to change or encourage change regarding the systemic bias that is built into our systems? But also, as individual practicing physicians caring for patients one on one, what can we do to keep this in the back of our minds and to do the best that we can to address this issue?

**EN:** That sounds wonderful. Which social determinants of health impact diabetes?

**RP:** It's really all of them, and they impact all of healthcare. Food and housing insecurity are probably uppermost, but then there is economic inequity that leads to people not being able to



“ There is bias built into our healthcare system, and although sometimes we as individuals might not be able to change that, there are things that we can change as individuals **to improve the overall culture of healthcare for our patients and to work with them to overcome those barriers that have resulted from both social determinants of health and societal bias and systemic racism.**”

— ROCIO I. PEREIRA, MD, CHIEF OF ENDOCRINOLOGY AT DENVER HEALTH, ASSOCIATE PROFESSOR OF MEDICINE AT THE UNIVERSITY OF COLORADO, DIVISION OF ENDOCRINOLOGY, METABOLISM, AND DIABETES



afford copays for visits or transportation, for example. So, I'll go through the larger categories of the social determinants of health, and then I'll focus on that healthcare piece and what we can do in healthcare.

**EN:** Systemic and individual change. What are some of the key points you're going to make about how to effect those kinds of changes?

**RP:** One key point is that we can all, each of us, do something to address health disparities whether or not we're in a position where we're affecting large systems. There is bias built into our healthcare system, and although sometimes we as individuals might not be able to change that, there are things that we can change as individuals to improve the overall culture of healthcare for our patients and to work with them to overcome those barriers that have resulted from both social determinants of health and societal bias and systemic racism. Things that we can all do are examine processes through an "equity lens" to see where they might not be working for people of color, become more aware of our own biases (we all have them), and use effective communication tools such as motivational interviewing to help us identify non-medical barriers our patients might be facing.

**EN:** This is a very positive message for both clinicians and patients. Clinicians may find new ways to facilitate access to clinical care, and patients will have better outcomes when their access to care improves. What do you hope attendees will take away from your session?

**RP:** I hope that attendees will learn some useful best practices and tools and that they will feel motivated and empowered to work toward culture change to support health equity. <sup>EN</sup>

## CEU 2021

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— HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE THE JULY ISSUE'S COVER STORY DISCUSSING HOW EXPOSURE TO ENDOCRINE-DISRUPTING CHEMICALS CAN HAVE EFFECTS ON THE OFFSPRING AS WELL THE MOTHERS.



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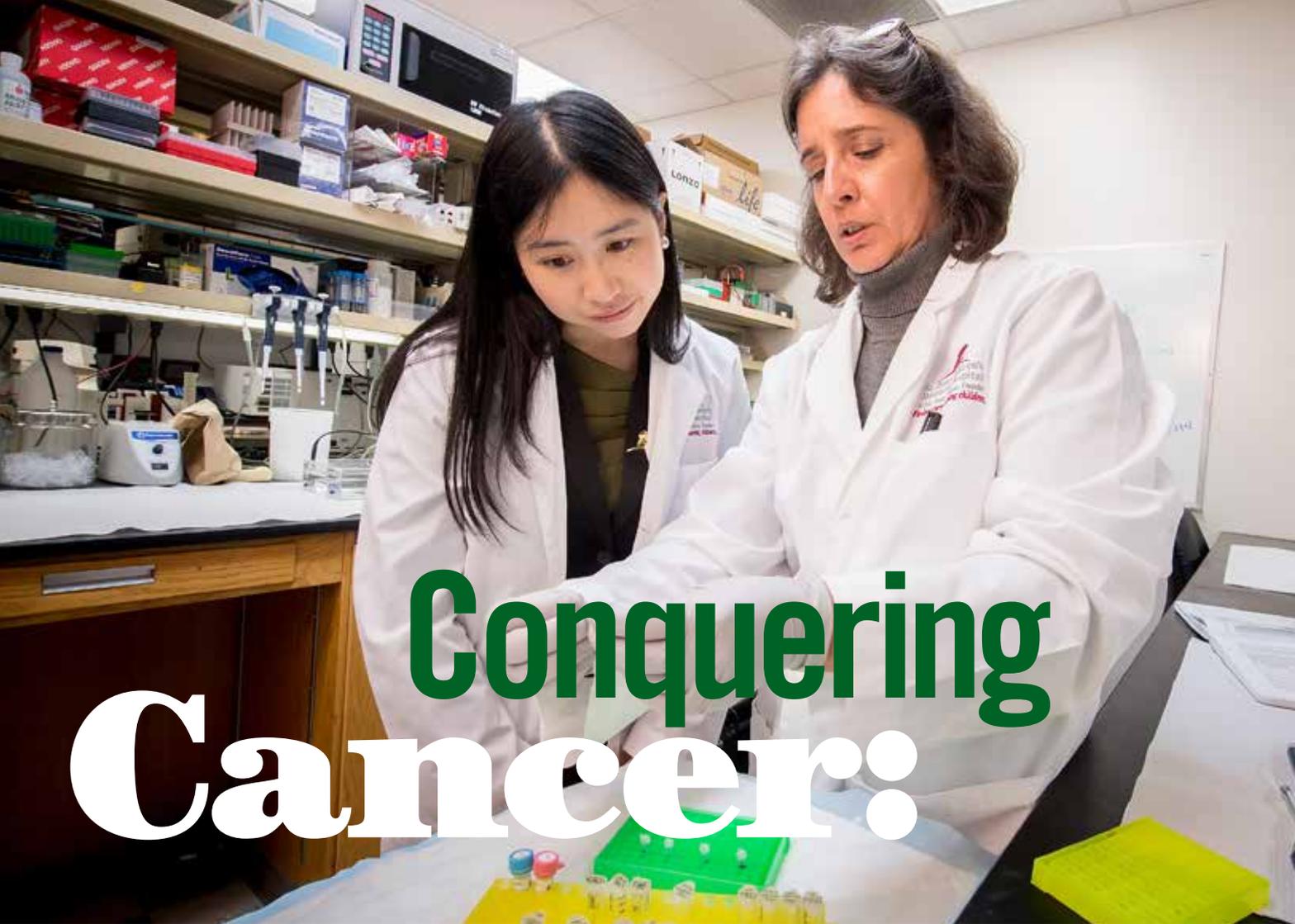
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# Conquering Cancer:

How a Newly  
Discovered  
*Mutation*  
Could Be a  
*Game Changer*  
In Treating  
*Adrenal*  
*Carcinoma*

The discovery of a new mutation could eventually hold the key to treating patients with adrenal carcinoma. *Endocrine News* talks with Emilia Pinto, PhD, a St. Jude's Children's Research Hospital scientist, who hopes that this new finding will raise awareness around the world in families who might be at a greater risk for this rare cancer.

BY DEREK BAGLEY

Pinto and Catherine Lam, MD, (left) who created the St. Jude Collaborative Rare Endocrine (CoRE) Tumor Referral Clinic that brings patients with adrenocortical tumors and their families to St. Jude for expert consultations with our team (oncologists, endocrinologists, genetic counselor, and biologists).

In Brazil, one in 300 individuals have a single *TP53* mutation – the *TP53*-R337H variant — which is associated with adrenal carcinoma. Most of the carriers of this mutation will never develop cancer, probably going their whole lives blissfully ignorant of terms such as “genetic counseling” or “clinical management.” However, some carriers of this mutation will develop very aggressive tumors and multiple cancers.

Last year, an international group of researchers set out to discover the reason for this highly variable cancer risk, publishing two papers. The first paper, published in *Science Advances*, announced that the investigators had discovered that R337H comes with a second mutation in another gene close by that explains the differences in cancer susceptibility in carriers of the R337H mutation. A second paper, a review article published in *Cancer*, highlighted the contribution of *TP53*-R337H research to help better understand cancer predisposition in Brazilian individuals and families.

“The *TP53* gene is the most studied tumor suppressor gene in cancer biology, and so far, there are currently no therapies that target the p53 pathway,” says Emilia Pinto, PhD, of St. Jude’s Children’s Research Hospital in Memphis, Tenn., and lead author of the papers. “This second mutation modifies that activity of other p53 variants and will be of grand interest in the cancer genetics field.”

## Identifying a Variant

After completing whole genome sequencing of pediatric adrenocortical tumors (the results of which were published in *Nature Communications* in 2015), Pinto looked at the germline DNA of those adrenocortical tumor (ACT) patients harboring the *TP53*-R337H variant to determine the common DNA sequence in chromosome 17 around *TP53* locus shared among carriers. “As the *TP53*-R337H variant retains functionality in laboratory assays and animal models, and alone didn’t explain the cancer phenotype in carriers, the idea was to verify the presence of additional polymorphisms or variants that act as a potential *TP53* modifier and alter p53 function and thus impact cancer risk,” she says.

It was here that Pinto and her team — a group of researchers from Brazil, Spain, France, the UK, Michigan, Pennsylvania, Maryland, and Tennessee — identified the variant E134\* in the tumor suppressor *XAF1*, associated with the *TP53*-R337H, a compound mutant haplotype responsible for a greater risk of sarcoma and subsequent malignancies. Pinto says that some of the genes in the p53 pathway contain functionally significant single nucleotide polymorphisms

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“ The *TP53* gene is the most studied tumor suppressor gene in cancer biology, and so far, there are currently no therapies that target the p53 pathway. This second mutation modifies that activity of other p53 variants and will be of grand interest in the cancer genetics field.”

— EMILIA PINTO, PHD, ST. JUDE’S CHILDREN’S RESEARCH HOSPITAL, MEMPHIS, TENN.

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## Impact of IPACTR

Pinto and her team at St. Jude's Hospital have been able to study these rare cancers in young patients thanks to their International Pediatric Adrenocortical Tumor Registry (IPACTR), a database created more than 30 years ago to better treat not just the pediatric patients but their families as well. Since about half of the patients with adrenocortical tumors have germline *TP53* mutations, the IPACTR has helped identify a pathway for tumor growth in the other half of patients.

"The registry offers the opportunity to collect clinical and demographic information, the family history of cancer, laboratory information, details of treatment practices, and outcome data for children and adolescents with adrenocortical tumors," Pinto told *Endocrine News* for a 2018 feature on the IPACTR. "Biological material, including tumor and blood samples from the patient and their relatives, allows us to perform collaborative investigations to understand the biology of the disease and ultimately improve the outcomes for these patients."

When physicians, healthcare providers, or parents ask St. Jude's physicians about how to manage a child's adrenocortical tumor (ACT), they are invited to participate in the IPACTR. The tumor is histopathologically reviewed and then genetic counseling is offered to the patient and relatives if the patient is *TP53*-positive, all free of charge. The findings from the registry have allowed for more personalized and targeted approaches to treating children with adrenocortical tumors, and the St. Jude's team hopes other healthcare systems develop similar models to study more rare diseases.

(SNPs) that alter the signaling response by this protein, and the identification of the XAF1-E134\* variant only adds to the complexity and potential interface involving two tumor suppressor genes.

"It's possible that each SNP in the p53 pathway may have a modest impact on cancer risk and progression, but collectively has the potential to impact cancer risk, progression, and the efficacy of radiation and chemotherapy," Pinto says. "We are in the beginning to understand the impact of these variants, and more studies are necessary to establish the formulas for cancer risk from the interaction among all these SNPs."

## A European Heritage

Even though pediatric ACT is a rare condition, in Brazil, occurrence of this cancer is 10 to 15 times higher than the rest of the world. Around 50% of patients with ACT are carriers of the germline *TP53* variant, which means pediatric patients diagnosed with ACT is a referral for *TP53* testing, as well as for initiating a germline *TP53* and cancer predisposition program, particularly in services where the lack of structured oncogenetic practice precludes the identification of families with high cancer risk, Pinto tells *Endocrine News*.

"Oncologists, pediatricians, endocrinologists, genetic counselors, and healthcare providers need to recognize that *TP53*-R337H exists alone or is associated to the XAF1-E134\* variant," Pinto says. "Recognizing the constitutive haplotype in carriers of the p.R337 variant is of importance to stratify carriers into high- and low-risk categories and thereby guide physicians in counseling, targeted prevention, and earlier detection of tumors to improve outcomes. As this finding is new, it needs to be incorporated in the clinical practice and be affordable and accessible to everyone who can benefit from it."

For a little background, researchers believe the *TP53*-R337H mutation originated in a single person (the founder) and was passed down through the generations. According to Pinto, the most common ancestor for this mutation is European, probably from Spain or Portugal, since the researchers identified families in those countries with this variant. When the investigators ran a simulation analysis, they estimated the age of this haplotype to be about 577 years, in line with Europeans colonizing Brazil. "Today, one in every 300 individuals in southern and southeast Brazil are carriers of the p.R337H variant," Pinto says. "It's important to note that not all carriers will develop cancer, as we know that this variant is of low or moderate penetrance. In this way, individuals will pass this variant along and the mutated gene becomes more prevalent."

## Familial Screening

Pinto points out that all p.R337H carriers share an identical and small DNA sequence encompassing the *TP53* gene, but a subset of these ACT patients shares a more extensive DNA sequence in this chromosome that includes not only the *TP53* p.R337H variant but also a mutation in *XAF1*, another tumor suppressor gene. “That means, some carriers of the *TP53* p.R337H variant are also carriers of another mutation in close proximity of *TP53*,” she says. “In the presence of this genetic variant in a patient, physicians and healthcare providers will be able to offer screening in additional family members and a surveillance protocol to carriers in order to detect cancer early, when they might be easier to treat.”

There’s still much work to be done — the discovery of the *XAF1*-E134\* variant came 20 years after the identification of the *TP53*-R337H variant in Brazilian carriers. Researchers are aware that there may be additional factors among Brazilians that modulate the cancer phenotype in carriers of the *TP53*-R337H variant, such as genetic or environmental factors, or both. Pinto says that for basic scientists, it will be important in future studies to determine which of those extenuating factors act to modulate cancer risk in these carriers, since again, not all of them will develop cancer.

And for Pinto, this work is personal. She hails from Brazil and received her PhD in physiopathology from the University of São Paulo, Brazil, in 2005. She says she wants to call attention to what’s happening in her home country and to raise awareness in the international medical community to address families with a high risk of cancer and refer them to consolidated services of genetic counseling for a detailed assessment of cancer predisposition pattern.

“A founder mutation in a tumor suppressor gene that exists in one out of every 300 individuals with such diversity in cancer phenotype has a lot to teach us and others in the field. It’s a unique situation of a hypomorphic *TP53* variant widespread in a population,” Pinto says. “Due to the high prevalence of this variant already present in different areas of Brazil, Europe, and the U.S., genetic screening should be considered in families from this geographical region that match the clinical definition of any syndrome with multiple inherited tumors.”

Pediatric cancer is a sentinel for cancer predisposition, Pinto says, and the presence of a germline mutation could imply cancer risk in family members, so for now, she says her team will continue to study *TP53*, since adrenocortical tissue is particularly sensitive to subtle alterations in that gene. “In addition,” she says, “we need to consider the sum or the contribution of each SNP in p53 itself and p53 pathway to establish cancer risk in carriers, and this is particularly important in Brazil due to widespread R337H variant.” 



## AT A GLANCE

- ▶ One in 300 Brazilians carry a mutation associated with adrenal carcinoma, but their cancer risk is highly variable.
- ▶ Researchers have discovered a secondary mutation, close to the first, that may explain this difference in cancer susceptibility.
- ▶ The discovery of this new mutation could help clinicians target treatment or even prevention, but more work needs to be done.

— BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. IN THE JUNE ISSUE, HE WROTE ABOUT HOW TWO COMMUNITY HOSPITALS WERE SUCCESSFULLY IMPLEMENTING INPATIENT DIABETES MANAGEMENT SERVICES.

# We Belong: Imposter Syndrome and How to Remedy It



**S**ome of the most well-known and accomplished famous people in the world have talked about experiencing imposter syndrome, including Michelle Obama, Starbucks CEO Howard Schultz, actress Natalie Portman, and former director-general of the World Health Organization Margaret Chan, who is quoted as once saying, “There are an awful lot of people who think I’m an expert. How do these people believe all this about me? I’m so much aware of all the things I don’t know.”

What is imposter syndrome, and what can you do if you deal with it?

## Defining the Imposter Issue

Neither a mental health or a psychological diagnosis, imposter syndrome is instead “a set of feelings and perceptions that can lead to effects on behavior,” says Maureen Gannon, PhD, the associate dean for faculty development and professor of medicine at Vanderbilt University Medical Center in Nashville, Tenn.

Believing you aren’t good enough is a serious issue that can follow people for a lifetime unless they work on getting it under control. It can manifest as feeling like you don’t measure up to your peers, or that you’re not really a competent and highly trained professional, or that it’s only a matter of time before others realize just how little you know.

Ignoring these feelings can lead to stress, anxiety, and gastrointestinal problems, Gannon adds. “If you are so worried all the time that people will regret hiring you, you will be stressed out,” she adds.

Imposter syndrome is not a lack of confidence, either. Instead, it stems from feeling different, particularly in people whose socioeconomic, racial, or other backgrounds

Imposter syndrome – the belief that you do not belong or that you are not good enough – is more common than people think, especially in the medical field. *Endocrine News* spoke to experts on this dilemma who discuss common solutions to get past these feelings of self-doubt.

BY CHERYL ALKON

differ from those around them. Maybe your parents were elementary school teachers and you're the first in your family to go to medical school, and your classmates all appear to be from families filled with physicians. Imposter feelings can also occur when experiencing transitions, such as moving from college to medical school, or into a new residency, or from residency to an early-career position.

"You come from a different world than where you find yourself now," Gannon says. "It's that you feel you don't really belong in this environment, particularly if you don't see others who came from the background you came from."

The intense training required to become a physician can compound feelings of imposter syndrome, says Gail Gazelle, MD, a former hospice physician, a part-time assistant professor of medicine at Harvard Medical School, and an expert on physician burnout and imposter syndrome. She offers a free guide to dealing with imposter syndrome on her website.

"What we learn in our training is that if we aren't perfect, we are a failure," Gazelle says. As a physician, "you learn early on that we have to stack up well, not just with peers but in all specialties. We become hyper focused on what we think others are doing well, and we are always comparing ourselves to others. This magnifies the difference of the cycle of perceived inadequacy, and this fuels imposter beliefs."

In coaching more than 500 physicians over the past decade, Gazelle says she has never met a doctor who hasn't admitted to feeling like an imposter in some way. "I teach at Harvard Medical School and every single one feels like an imposter," she says. "Everyone is at the top of their game. At an elite institution, you can feel like it, and at a smaller name place, you can also feel that way because 'I'm not at Harvard.' It's really a mental trap."

When your whole identity is shaped around being "the smart one," and you've been told at an early age that your worth is in being smart, imposter feelings can surface if you experience a challenge on a board exam or during teaching rounds, Gazelle says.

“You may not be the best endocrinologist in your state, city, or country, but perhaps you are good enough and that’s okay. You’ve got to survive the marathon of this career. **The more your mind gets caught in the berating, the less stamina you will have to weather the marathon of being a physician.**”

— GAIL GAZELLE, MD, ASSISTANT PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL, BOSTON, MASS.

"You may not be the best endocrinologist in your state, city, or country, but perhaps you are good enough and that's okay," she adds. "You've got to survive the marathon of this career. The more your mind gets caught in the berating, the less stamina you will have to weather the marathon of being a physician."

## How It Hurts

Imposter syndrome can limit a person's career opportunities as well as his or her self-esteem. If you are always worried about making a mistake or disappointing someone because you feel you do not measure up, "you can set a lower bar for yourself and you may not reach the pinnacle of your career that you could have achieved," Gannon says.

This may mean not asking for the lab space you need to perform your best work, or not negotiating for a higher salary or better job benefits. "That fear and stress of trying to be perfect can really be a barrier to career advancement," Gannon adds. "Instead, learning how to overcome such feelings and to recognize that everyone makes mistakes will help you be more proactive in your own career."

Also, perfectionism does not help. "This is the fear that in order to feel like you do belong, you have to be perfect,"

Gannon explains. “You feel like you can’t make any mistakes or you’ll be found out that you don’t belong here. People who tend to be perfectionists feel like their failures will define them, will make people regret they hired them, or got an opportunity in leadership, or leading a committee, or giving a presentation, or rising up in leadership ranks.”

Feeling like an outside influence helped you gain an advantage, rather than relying on your own intelligence, expertise, or knowledge, leads to feeling like you are always waiting to be uncovered as a fraud.

“In a lot of cases, people will feel like they got to that opportunity because of something that happened outside their control,” Gannon explains. “If you got a full scholarship because of family, economic, or a certain percentage of people need to be female, you may think ‘am I the best person, or am I only here because I’m a woman or because of outside influences, not necessarily because of skills and expertise. How did I get here? Did I get here because my parents had no money?’”

## Coping with Imposter Syndrome

Both Gannon and Gazelle have a lot of advice on how to live with — and maybe overcome — imposter syndrome and its tendencies:

- ▶ Write a list of all your accomplishments and successes, Gannon says. Don’t use adjectives or qualifiers; be objective. “If your best friend saw that list, what would you say to that person?” Gannon asks. “Look at the data; what have you accomplished?”
- ▶ Consider the concept of creative visualization, as detailed in the book of the same name by Shakti Gawain. “It helps you visualize how you want to be in your career and things you do in life,” Gannon says. “For example, you can visualize how you get up and do a presentation: You are clear. The audience is nodding their heads and getting what you are saying. When you get there, you feel like you’ve almost done it already. Doing these sorts of exercises is very helpful,” she says.
- ▶ Focus on meditation and examining your thinking patterns, which can help you recognize that thoughts are just that — thoughts. “Our minds are very good at

spinning stories about all kinds of things; largely about ways we aren’t good enough,” Gazelle says. “It’s just a mental story — nothing more. With mindfulness, we get to think, ‘What are minds about? Is it even true that I’m an imposter?’ So much of staying out of burnout and building resilience is mindfulness: paying attention to what is going on right now and doing it with less judgement. The core of what we need to do is to shift mental patterns that do not serve us.”

- ▶ Learn from your mistakes and know that everyone makes them. Particularly when working with trainees or mentees, it is important to be honest about when people make a mistake or fail, Gannon says. “Talk about, ‘How did we overcome it?’ This helps others learn that everyone makes mistakes. This is how we grow. You don’t have to be perfect to have success in this career.”
- ▶ Focus on your strengths and make a daily list of three good things that you did that day. “This shifts us from feeling like, ‘I’m never good enough’ to ‘what did I miss today,’” Gazelle says.
- ▶ Give honest feedback. “In a place where everyone gets a trophy, how do you know if you did a good job? People have a hard time internalizing their accomplishments,” Gannon says. “When you tell someone without feeling that they did a good job, they will excuse it and brush it off. But if we get better at giving constructive feedback, it will help others with gaps in their skill set to see what they can work on. That way, when you tell someone that was great without reservation, they will believe you.”
- ▶ Similarly, do not try to qualify or brush off praise others give you. “When you get a compliment, say thank you,” Gannon advises.
- ▶ Remind yourself that all you can do is be good enough, and try your hardest. “It takes a lot of reminders,” Gazelle says.

“You don’t have to live this way, like you’re an imposter,” Gazelle says. “You don’t have to live with the constant accusation of yourself that you’re not measuring up.” <sup>EN</sup>

— ALKON IS A MASSACHUSETTS-BASED FREELANCE WRITER WHO IS THE AUTHOR OF THE BOOK, *BALANCING PREGNANCY WITH PRE-EXISTING DIABETES: HEALTHY MOM, HEALTHY BABY*. SHE WROTE ABOUT FINDING THE TIME FOR COLLABORATION IN THE JULY 2021 ISSUE. .

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# Banish **BURNOUT**

A new survey reports that over 40% of endocrinologists are suffering from burnout. *Endocrine News* looks at the causes and offers some potential solutions to help ease this stress and focus on the “joy in work.”

BY GLENDA FAUNTLEROY SHAW

**T**he past year was tough for everyone, most especially for those in healthcare. *Endocrine News* has chronicled endocrinologists around the globe who immediately switched from providing normal care to treating COVID-19 patients, or offering virtual e-visits from home, or pausing critical laboratory research. Did all of these uncertain changes take a toll? How are endocrinologists faring on feelings of burnout?

In the *Medscape Endocrinologists Lifestyle, Happiness and Burnout Report 2021*, 43% of respondents reported being burned out, depressed, or both — and the number is climbing. About seven in 10 who were burned out thought it was severe enough to have at least a moderate impact on their lives. And a surprising 15% said burnout was so severe that they are considering leaving medicine for good.

## What’s Bothering You?

Employee burnout happens when a person’s physical, emotional, and mental resources are spent. The leading causes of endocrinologist burnout, according to the *Medscape* survey were:

- ▶ Too many bureaucratic tasks: 69%
- ▶ Too little compensation or reimbursement: 51%
- ▶ Spending too many hours at work: 31%
- ▶ Increasing computerization of practice: 31%

Burnout, of course, can lead to many negative consequences such as decreased patient satisfaction, increased errors, and high turnover. The personal risks of burnout of stress and depression are also staggering.

When *Medscape* asked what endocrinologists are doing most to cope with burnout, exercise and talking with family and friends topped the list. But in the workplace, there are many initiatives managers can initiate to support their employees and help alleviate overwhelming feelings of burnout.

## Managers Can Bring the Joy

“The primary advice I give managers dealing with employees who express feelings of being overwhelmed or burned out is to first *ask* what the employee thinks he or she needs to feel less stressed,” advises Nikki Rogers, owner of NBenét HR Consulting. “This may be different by individual.”

“For example, it could be the ability to take a ‘real’ uninterrupted vacation, adjust their work schedule, or perhaps gaining clarified objectives to help them prioritize the most critical work and eliminate non-value-added tasks,” Rogers continues. “The manager should seek to understand what each employee needs and be as flexible as they can to accommodate.”

In a 2020 perspective article in *The Journal of Clinical Endocrinology & Metabolism*, the authors offered that by focusing on “joy in work,” managers can also reduce burnout among endocrinologists. They framed joy in work by four key principles: meaning, camaraderie, choice, and equity:

- ▶ **Meaning:** Spend some hours (20% of work duties is advised) focusing on a project, interest, or activity that you find meaningful, such as community outreach, leading educational initiatives, becoming a mentor, or caring for a specific demographic of patients.
- ▶ **Camaraderie:** Are team members engaged with each other? Eating together is cited as special time that allows employees to share details about work or home life and ease stress. Allow for and plan time for shared team meals.
- ▶ **Equity:** When employees feel the rules of an organization are fair and unbiased, they suffer less burnout. Meetings with an open forum to address perceived inequities can help bring change.



- ▶ **Choice:** Having a say in providing solutions to the organization or team gives staff a feeling their voice has power. Managers can allow for choice by openly asking employees for their opinions and feedback. Use newsletters or bulletin boards to showcase ongoing efforts that arise from staff input.

## Find Stress Relievers

The bottom line to alleviate some of the workplace burnout is to engage in efforts that are known to relieve employee stress. More tips from human resources experts include:

- ▶ Hold short “walk-and-talk” outdoor meetings twice a month for a change of scenery.
- ▶ Try work-from-home Wednesdays. One thing the pandemic shutdown proved is that there is plenty of tasks that can be completed at home. Let team members rotate a different Wednesday at home to decompress.
- ▶ Ask for honest feedback on your management skills. Managers can be the biggest factor in employee stress. If your people skills need a tune-up, request time from your organization’s leadership to attend management training.

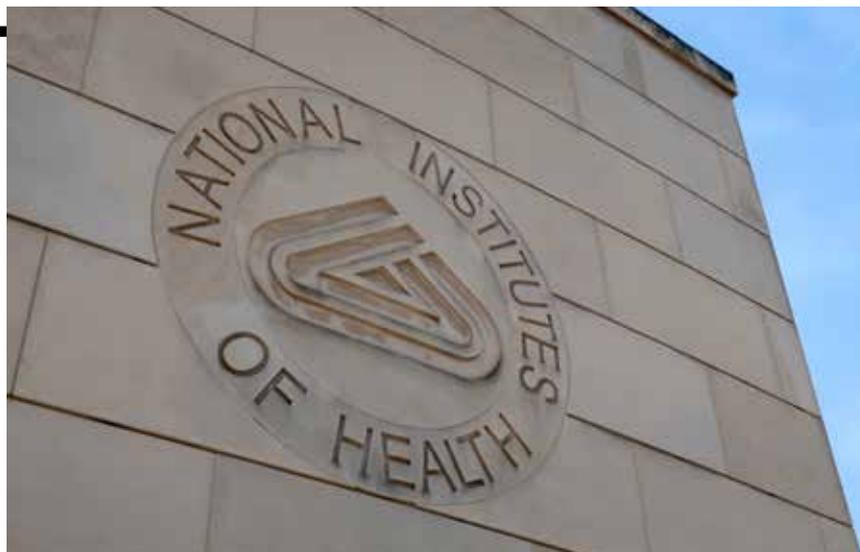
Athansisos Bikas, PhD, of Brigham and Women’s Hospital in Boston and one of the Society’s 2021 Early Investigator Award winners, says these stress reliever tips definitely resonate with him.

“Leaving work physically can be a huge relief,” he says. “I really like the idea of the ‘walk-and-talk’ outdoors meetings. Another potential solution would be a picnic with music every Thursday or Friday just so people can socialize with each other and get their minds off of work. I cannot stress enough how important uninterrupted vacation time is for clinicians, with time away from [electronic medical records].” <sup>EN</sup>

**Eating together is cited as special time that allows employees to share details about work or home life and ease stress. Allow for and plan time for shared team meals.**

– FAUNTLEROY SHAW IS A FREELANCE WRITER BASED IN CARMEL, IND. SHE WRITES THE MONTHLY LAB NOTES DEPARTMENT.

## Endocrine Society Priorities Included in Appropriations Legislation Advancing in House



Last month, the House of Representatives advanced the fiscal year 2022 Labor, Health, and Human Services and Education (LHHS) appropriations bill, which provides funding for the National Institutes of Health (NIH) and several other Society priorities. We were extremely pleased to see a base appropriation for the NIH that was consistent with our request of approximately \$46 billion, or an increase of ~\$3.5 billion. The total request for the NIH was \$49 billion and included \$3 billion directed specifically to a new agency called the Advanced Research Projects Agency for Health (ARPA-H). While the bill passed the full House Appropriations Committee by a party line vote of 33 – 25, representatives from both parties enthusiastically supported the substantial increases for the NIH included in the legislation.

Photo: DCStockPhotography/Shutterstock.com

In addition to a significant increase in funding for biomedical research, the report accompanying the legislation included text that the Endocrine Society advocated for during our Research Hill Day. This “report language” identifies congressional priorities that agencies are expected to address in the coming year. In a section on COVID-19-related research priorities, the report notes the difference in severity and outcomes for COVID-19 between female and male patients due to sex and gender influences, including for patients with long-term symptoms following infection. To better understand how sex differences are implicated in the severity of the COVID-19 pandemic, the committee encouraged the institutes and centers of the NIH in coordination with the NIH Office of the Director and Office of Women’s Health Research to support research that studies how sex as a biological variable impacts short- and long-term outcomes due to infection with COVID-19. Other Endocrine Society priorities, such as support for the Diabetes Prevention Program, improving pediatric reference ranges, and research concerning climate and health and polycystic ovary syndrome (PCOS) were also included.

The House passed its version of the LHHS appropriations bill the last week of July. The Senate, however, still has not come to an agreement on its version of this funding bill and several others and it is expected that action will be stalled until September, and that there is a strong likelihood that it will not be able to pass a final funding bill by September 30, 2021, the end of the fiscal year. If that is the case, Congress will pass a Continuing Resolution to keep the federal government operating at this year’s funding levels, erasing any increases. Consequently advocacy supporting passage of a final funding bill with increases for the NIH and other Endocrine Society priorities is critical.

### Take Action

Endocrine Society members need to urge their congressional delegation to take action so that these proposed increases for the NIH can become a reality through the Society’s online advocacy campaign ([endocrine.org/takeaction](https://endocrine.org/takeaction)). Now really is the time to let your representative and senators know how important it is to support research funding. Taking action is easy, quick, and effective. Our campaign will provide you with a template email and direct it to your elected officials.

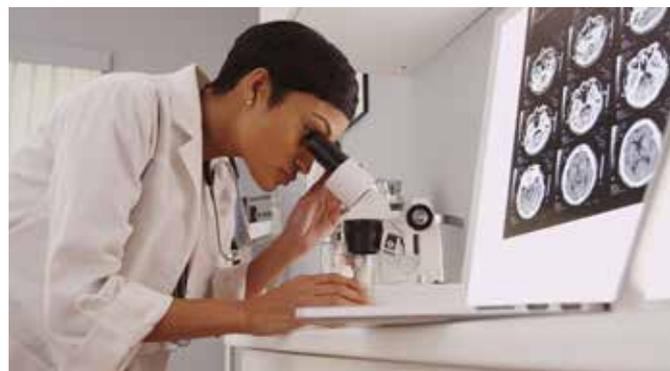
When President Joe Biden's budget for fiscal year 2022 was introduced this summer, many biomedical research advocates took note of a new line item that would direct \$6.5 billion over three years to a new Advanced Research Projects Agency for Health (ARPA-H) to be housed at the National Institutes of Health (NIH). While we were enthusiastic about the prospect of a significant new funding stream dedicated to important problems in biomedical research, there still are many open questions about how the new agency would operate and intersect with researchers and projects already funded by the NIH.

The Biden administration, as well as the NIH and the Office of Science and Technology Policy (OSTP), have shared some concepts reflecting their overarching vision for the program, which will borrow from the model used by the Defense Advanced Research Projects Agency (DARPA). However, they recognize that stakeholder engagement and mutual understanding will be critical to the success of this endeavor in the long run. In July and August, the NIH and OSTP convened a series of meetings to hear from the community about our priorities and potential concerns. Congressional sponsors of authorizing language for ARPA-H also issued a Request for Information (RFI) with a series of questions for stakeholder input. The Endocrine Society has been engaged early and throughout the process as ARPA-H takes shape. Our Research Affairs and Advocacy and Public Outreach Core Committees met in June to discuss the ARPA-H proposal and respond to the RFI. We were also invited to present our perspective at two meetings with the NIH and OSTP to discuss research opportunities that ARPA-H might be able to address.

In our letter to Congress, and during the meetings with the NIH and OSTP, we urged ARPA-H leadership to avoid implementing features that would limit the pool of participating researchers, such as onerous administrative requirements. We also shared opportunities in endocrine research, including cancer, diabetes, and environmental health that would benefit from a new funding model and with project objectives similar to DARPA. Importantly, we argued that funding decisions at ARPA-H should avoid excessive overlap with NIH projects, and that they need to preserve and grow the paylines for investigator-initiated basic and clinical research through regular annual appropriations. We strongly advocated that the NIH should not be required to contribute significant financial resources to ARPA-H projects. Finally, we urged leadership to design ARPA-H to incorporate diverse perspectives, with particular attention to groups that have been historically underrepresented in biomedical research, throughout the planning and execution of projects.

There is still a long road ahead for ARPA-H to become law, but our members will stay involved to ensure that this new program helps advance our Society's research and public health priorities. We will share new developments in *Endocrine News* as we learn more, and we encourage members to also explore the NIH ARPA-H events page (<https://www.nih.gov/arpa-h>) for additional information and opportunities to share your perspective.

## Endocrine Society Discusses ARPA-H with Congress, NIH, and OSTP



“

There is still a long road ahead for ARPA-H to become law, but our members will stay involved to ensure that this new program helps advance our Society's research and public health priorities.

”

# Congress Considers Drug Pricing Legislation to Help Pay for Growing List of Legislation

## Endocrine Society Continues to Advocate for Insulin Affordability

Congressional leaders are continuing to discuss legislative options to address the rising cost of prescription drugs and the Endocrine Society continues to be one of the most vocal advocates urging Congress to address insulin affordability this year.

As this issue of *Endocrine News* goes to press, the path forward for passing legislation to lower drug costs was unclear, but it was increasingly being discussed to help offset the costs associated with the growing list of social legislation President Joe Biden and the Democrats hope to pass this year. Congress was preparing a Budget Resolution that would include measures to reduce patient spending on prescription drugs.

Congressional leaders have sought our feedback on policy options. We met with Majority Leader Chuck Schumer's (D-NY) office and the Senate Finance Committee staff, both of whom asked us to weigh in on possible options to address this issue. The political obstacle for the Democrats is how to hold their party together because some progressives are looking for regulation of price while some moderates are seeking other measures to control consumer costs. Senate Finance Committee Chair Ron Wyden (D-OR) has been negotiating with lawmakers for weeks

on a new drug-pricing bill that falls somewhere between House Democrats' sweeping government price negotiation bill, H.R. 3, and the bipartisan bill he crafted with Sen. Charles Grassley (R-IA) last Congress that would slap inflationary rebates on drug makers but not give the government power to negotiate prices.

“

The path forward for passing legislation to lower drug costs was unclear, but it was increasingly being discussed to help offset the costs associated with the growing list of social legislation President Joe Biden and the Democrats hope to pass this year.

”

Wyden is said to be looking at a version of drug price negotiation that does not rely on foreign prices as the gauge and that ratchets back the number of drugs for which prices would be negotiated.

The Endocrine Society has stressed that action is needed urgently. We expressed that government negotiation is the best solution for lowering the price of insulin. However, we also shared that rebate reform would be an effective option to lower the cost of insulin for consumers and may be the more feasible way to address this problem in the current Congress. We continue to share our position statement on access to affordable insulin with policy makers. Our statement includes both a recommendation for price negotiations and a recommendation to lower the cost of insulin by passing the rebate savings directly to the consumer at the point of sale. The Society also conducted a virtual Hill Day during the week of July 19 for our clinician members so that they could meet with targeted congressional offices and discuss the importance of insulin affordability.



## Endocrine Society Conducts Virtual Hill Day for Clinician Members

**I**n July, the Endocrine Society conducted a virtual Hill Day for our clinician members to discuss two top legislative priorities: affordable access to insulin and expansion of telehealth coverage.

The Hill Day, which was held during the week of July 19, gave Society members an opportunity to talk with lawmakers and congressional staff about the high price of prescription drugs focusing specifically on insulin affordability. We urged Congress to pass legislation lowering the cost of insulin and have highlighted the urgent need to address this ongoing crisis this year. Society members also spoke with lawmakers about expanding access to telehealth services after the public health emergency ends.



We called on Congress to pass legislation to permanently relax the originating site requirement and geographic restrictions, which will ensure that patients can receive telehealth from home. We also urged Congress to pass legislation that would direct the Centers for Medicare and Medicaid Services to make coverage and payment of telephone-based (audio-only) services permanent.

The Hill Day was another example of how the Endocrine Society influences legislation and educates and advocates for policies that impact our members and their patients.

## CMS Releases Proposed 2020 Physician Fee Schedule

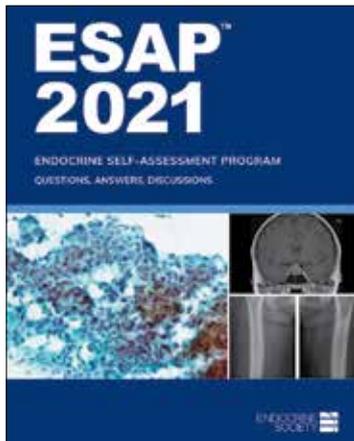
**T**he Centers for Medicare and Medicaid Services (CMS) released the proposed rule for the 2022 Medicare physician fee schedule July 15.

The Endocrine Society staff is analyzing and developing a summary of the 1,700+ page proposal and will distribute detailed information about the rule and our comments to the proposal. We note that the proposed rule would make

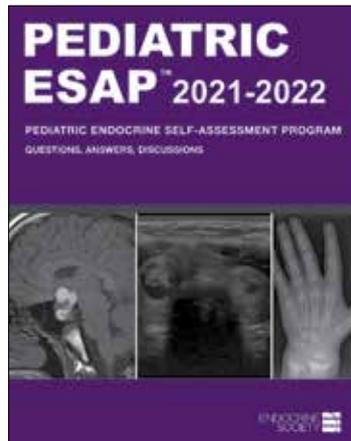
changes to the Medicare conversion factor and implement other policy changes that will lead to cuts for several medical specialties. CMS, however, estimates that the impact of these changes for endocrinologists would result in a 2% increase. We will conduct a session on the impact of the rule on endocrinologists and answer participants' questions during the upcoming CEU on September 12. <sup>EN</sup>

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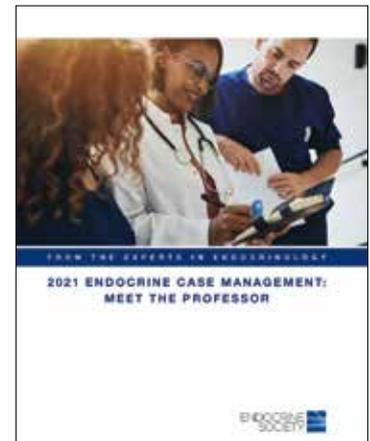
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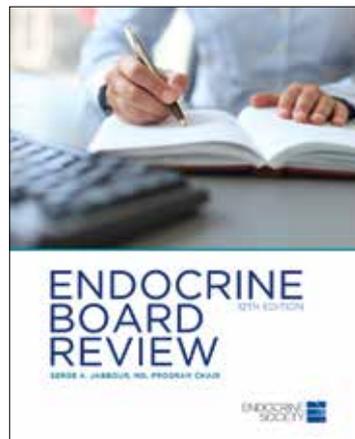
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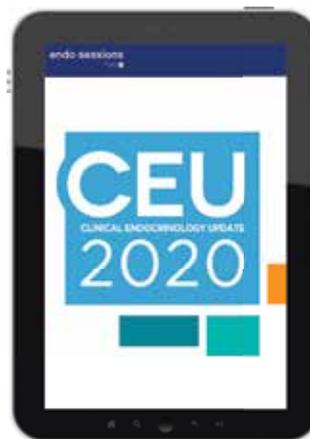
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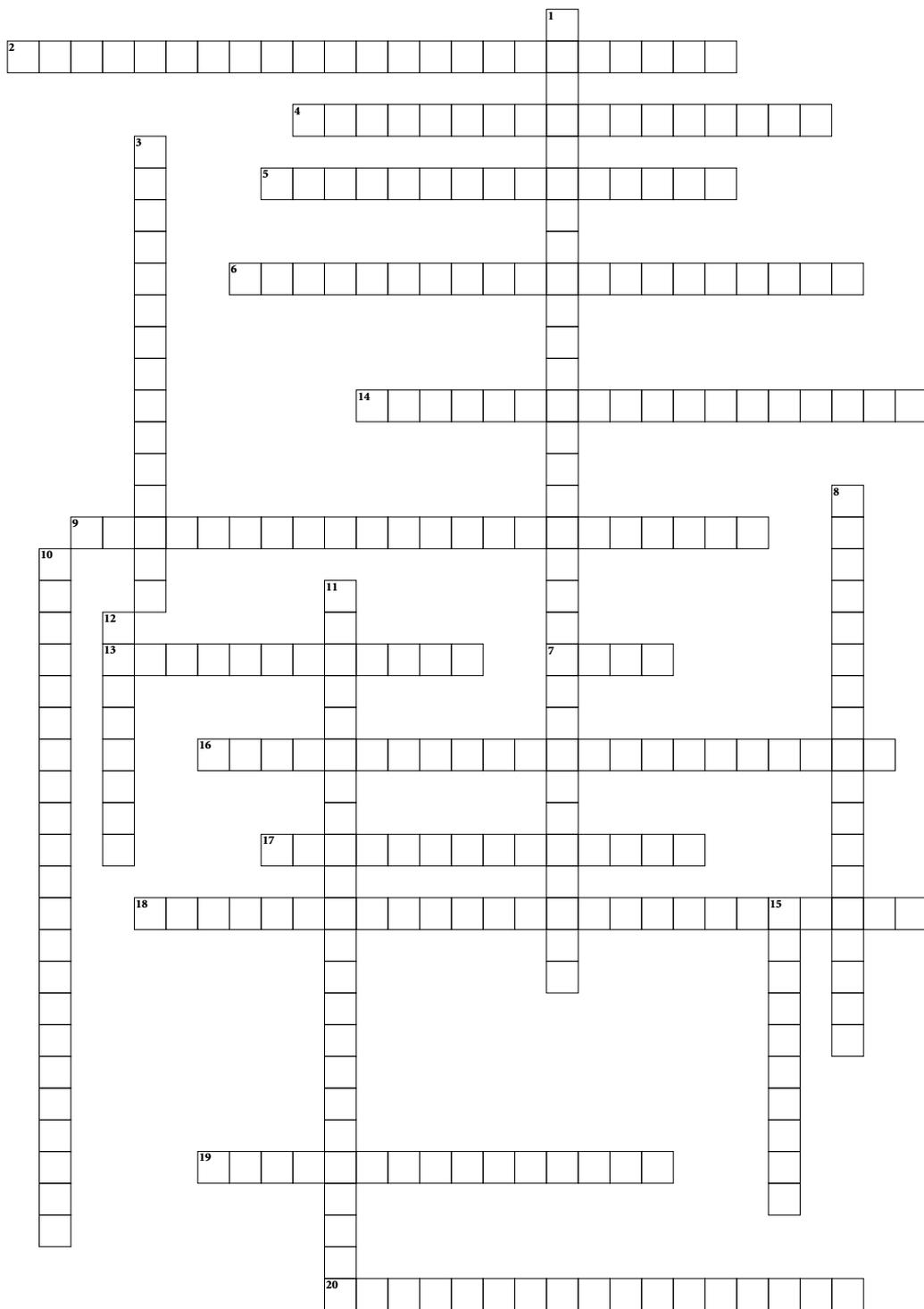


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# RARE DISEASE AWARENESS



### ACROSS

2. A genetic bone disease that is developed when the mineral phosphorus is wasted into urine.
4. A rare condition that leads to frequent urination and excessive thirst.
5. Acute adrenal failure or Addisonian crisis and damage to the adrenal cortex are the primary symptom linked to this condition.
6. More than 175 distinct diseases affecting fewer than 200,000 Americans at any given time.
7. This rare pediatric condition limits the body's ability to produce insulin, and is developed as a result of single gene mutations, monogenic.
9. Newborn babies who are born with an underactive or absent thyroid gland.
13. A rare cancer that is the most common type of cancer that arises in bones, distinguished by the production of unhealthy or immature bone by the malignant cells.
14. Conditions that have these features may or may not be ambiguous, but fall within a group of Disorders of Sex Development (DSD).
16. Often referred to as brittle bone disease, this rare and variable genetic disorder is caused by a mutation in a gene that affects bone formation, structure, and strength of bones.
17. A rare genetic condition that occurs when a female infant is born with a missing or changed X chromosome.
18. Dysgenesis or a thyroid that has developed but cannot make thyroid hormone because of a 'production line' problem, or dysmorphogenesis. This condition can also occur as a syndrome that affects other organs and tissues in the body.
19. A benign tumor causes the pituitary gland to produce too much ACTH.
20. When the immune system mistakes parts of the body as being foreign or 'non-self' and mounts an immune response against the body's healthy cells, tissues, and organs.

### DOWN

1. An inherited genetic disorder that prevents the body from digesting fats. Patients are either unable to make lipoprotein lipase or have a broken form of it.
3. An exogenous or endogenous disorder with physical and mental changes that result from having too much cortisol in the blood for a long period of time.
8. A condition in which the body does not have enough parathyroid hormone (PTH) causing the body to secrete low levels of calcium in the blood.
10. When the body makes abnormal antibodies that attach to normal insulin receptors on your cells and blocks the good effects of insulin.
11. A malignant, or cancerous, tumor that starts in the adrenal glands and presents in bimodal pattern, in the very young in the first decade of life and again in adults.
12. Almost every cell contains receptors for this hormone, and patients with primary AI have a hard time producing this hormone.
15. Pituitary adenoma can create too much GH and IGF-1 creating this rare condition.



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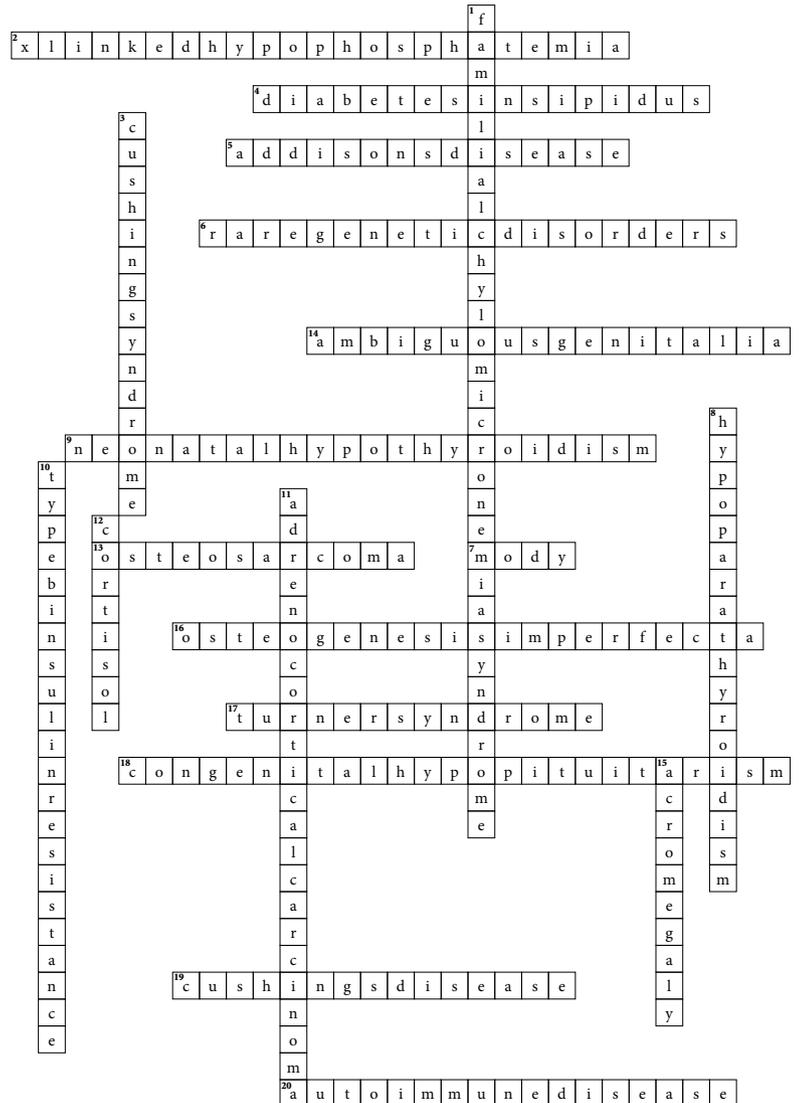


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## ACROSS

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4. DiabetesInsipidus
5. AddisonsDisease
6. RaregeneticDisorders
7. Mody
9. NeonatalHypothyroidism
13. Osteosarcoma
14. AmbiguousGenitalia
16. OsteogenesisImperfecta
17. TurnerSyndrome
18. CongenitalHypopituitarism
19. CushingsDisease
20. AutoimmuneDisease

## DOWN

1. FamilialChylomicronemiaSyndrome
3. CushingSyndrome
8. Hypoparathyroidism
10. TypeBInsulinResistance
11. Adrenocorticalcarcinoma
12. Cortisol
15. Acromegaly



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