IN THE LAB WITH THEOPHILUS TETTEY, PHD

OCTOBER 2025 THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

apples & oranges

Endocrine News delves into the mysteries behind RARE endocrine disorders.

STRING OF CLINICAL PEARLS:
A look at rare clinical cases from *JCEM Case Reports* presented at **ENDO 2025** in San Francisco.

UNINTENDED CONSEQUENCES:
From the pages of the *Journal of the Endocrine Society*, we look at the history of human growth hormone and protein-misfolding diseases.

FOLLOWING UP:
Recently released guidelines present best practices for treating hypoparathyroidism ... with the help of several Endocrine Society members.

STAYING IN CONTROL:
Encouraging clinical trial results for treating Cushing's syndrome

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THE ENDOCRINE SOCIETY IS
THRILLED TO ANNOUNCE AND CONGRATULATE THE

2026 LAUREATE AWARDS WINNERS

FRED CONRAD KOCH LIFETIME ACHIEVEMENT AWARD
Robert M. Carey, MD, MACP

EDWIN B. ASTWOOD AWARD FOR OUTSTANDING RESEARCH IN BASIC SCIENCE
Christopher Kevin Glass, MD, PhD

GERALD D. AURBACH AWARD FOR OUTSTANDING TRANSLATIONAL RESEARCH
Ismaa Sadaf Farooqi, MD, PhD

INTERNATIONAL EXCELLENCE IN ENDOCRINOLOGY AWARD
Rebecca Reynolds, MD, PhD

OUTSTANDING CLINICAL INVESTIGATOR AWARD
Samuel Klein, MD

VIGERSKY OUTSTANDING CLINICAL PRACTITIONER AWARD
Lisa B. Nachtigall, MD

OUTSTANDING EDUCATOR AWARD
Bradley David Anawalt, MD

OUTSTANDING MENTOR AWARD
Patricia Lee Brubaker, PhD

OUTSTANDING SCHOLARLY PHYSICIAN AWARD
Martin Reincke, MD

RICHARD E. WEITZMAN OUTSTANDING EARLY CAREER INVESTIGATOR AWARD
Katrin J. Svensson, PhD

ROY O. GREEP AWARD FOR OUTSTANDING RESEARCH
Alvin C. Powers, MD

SIDNEY H. INGBAR AWARD FOR DISTINGUISHED SERVICE
R. Paul Robertson, MD

AWARDS WILL BE PRESENTED AT ENDO 2026:
THE ANNUAL MEETING & EXPO IN CHICAGO, IL, JUNE 13–16, 2026.

LEARN MORE ABOUT OUR WINNERS AT
ENDOCRINE.ORG/LAUREATE

ENDOCRINE SOCIETY
Hormone Science to Health

Society Membership Offers Many Benefits to Unlock Professional Success

With skill, hard work, and a bit of luck, almost anyone can achieve their career goals. But with the backing of a renowned global organization — filled with the best minds in the field and offering world-class educational and development programs — you can soar to the highest levels of professional success.

Of course, I'm referring to the Endocrine Society and what it can do for our members.

As our annual membership renewal campaign gets underway, now is a good time to underscore the breadth and depth of the Society's offerings — something I have experienced first-hand throughout my own career journey.

I'm a perfect example of how the Society, and its many benefits, can foster a lifetime of professional and personal growth.

I attended my first **ENDO** in 1996, and my involvement with the meeting quickly expanded. Over the years, I've had the opportunity to be involved in everything from chairing sessions and judging posters, to serving as chair of Basic Sciences on the Annual Meeting Steering Committee, and more.

Those **ENDO** experiences led me to engage directly with the Society and serve in various leadership capacities, including as editor-in-chief of our flagship basic science journal, *Endocrinology*, and ultimately as your president today.

I mention this as a reminder to all members that you, too, can tap into the Society's programs. Doing so allows you to make a difference in our field and in your own careers. This holds true whether you're a researcher or a clinician, and whether you're early in your career or a seasoned veteran.

Programs that Benefit Members

As mentioned, the Society has long offered a wealth of programs and activities.

For instance, members enjoy discounts when attending **ENDO** and other educational meetings and programs. Members also receive complementary online subscriptions to four of our scientific journals, and research members receive significant discounts when publishing their research in the Society's peer-reviewed journals.

Our professional growth programs offer opportunities for recognition through awards and grants, as well as the chance to find new job opportunities through the career center and mentorship programs. Members also can help further the field by seeking out leadership opportunities through the Society.

These are just a few of the many benefits of membership. See sidebar for a more comprehensive list.

Member Survey Coming

But like any responsible organization, we're always looking to improve. This month, you will receive a survey to tell us how we can make your membership even more valuable.

The primary objective of this survey is to hear from members about the challenges they are facing now and what they need from the Society.

We also want to hear how satisfied members are with our programs, products, and services. We count on member input to help us evolve our offerings to ensure we're providing exactly what our members need. We would love to hear from you.

> "Our professional growth programs offer opportunities for recognition through awards and grants, as well as the chance to find new job opportunities through the career center and mentorship programs."

Finally, I'll remind you to renew — if you haven't already done so — including through our auto renewal program. Memberships are set to expire on Wednesday, December 31. If you sign up for Auto Renewal, you'll guarantee your membership never lapses, and you can save 20% on next year's renewal when you opt in.

As a veteran scientist and proud member of the Society, I encourage you to dive in, find your people, and have a blast! EN

Carol A. Lange, PhD
President, Endocrine Society

Membership Benefits and Programs

The Endocrine Society offers many benefits and programs that members may take advantage of at all stages of their careers. Below are just a few of them:

Professional Growth:

- Awards and grants
- Career center
- Mentorship opportunities
- Leadership opportunities through committees, task forces, and advocacy
- Visibility through poster presentations
- A curated list of research grant opportunities

Community:

- 10 Special Interest Groups
  - Women's Health SIG launching soon!
- Online EndoForum Community
- Member directory

Knowledge and Research:

- Five Scientific Journals
- *Endocrine News* each month, the leading magazine for endocrinologists
- Center for Learning with CME/MOC credit
  - Just released: On-demand *Updates in Hypothyroidism Treatment - New Evidence for T3 Combination Therapy*
- Podcasts
- **ENDO 2025** Session recordings
  - State-of-the-art endocrinology research
  - Updated clinical skills for more effective diagnosis, management, and treatment of endocrine disorders and related sequelae
  - Updated knowledge and clinical skills in improving patient care
- Clinical Practice Guidelines
  - Two new guidelines were just released:
    - *Primary Aldosteronism*
    - *Preexisting Diabetes in Pregnancy*
- Scientific Statements
- Latest headlines from *Endocrine News*, eNews, and the *Endocrine Briefing* weekly newsletter

Member Discounts:

- **ENDO** meeting registration
- Publishing in our scientific journals
- *Endocrine Reviews* journal subscription
- Complimentary online subscription to four of our scientific journals:
  - *The Journal of Clinical Endocrinology & Metabolism*
  - *Endocrinology*
  - *Journal of the Endocrine Society*
  - *JCEM Case Reports*
- Education and training courses
- Conference recordings
- Store products

Not Apples and Oranges: Rare Endocrine Disorders

While I think every issue of *Endocrine News* is intriguing, this month's issue really piqued my interest because it focuses on the atypical and unusual: rare endocrine diseases. From Cushing's syndrome to hypoparathyroidism and more, we've endeavored to include as many endocrine disorders as possible that might tend to be "off the beaten path," so to speak.

On page 24, Senior Editor Derek Bagley takes us back to San Francisco for a look at the intriguing session stemming from the Endocrine Society journal *JCEM Case Reports* where there were a **"String of Pearls"** presented

during **ENDO 2025**. Make that a string of clinical pearls: unusual cases that often stymie endocrine clinicians but were presented with intrigue as well as solutions for those in attendance. "In the third annual Clinical Pearls from *JCEM Case Reports* the attendees heard presentations from early-career aspiring endocrinologists on the management of Cushing's disease in pregnancy, the presentation and management of metastatic choriocarcinoma-related paraneoplastic thyroid storm, and the management of hypophosphatemic osteomalacia," says JCEM CR Editor-in-Chief William F. Young, Jr., MD. "Each case presentation was followed by a content expert who put the topic into a broader context and expounded on the key pearls that clinicians should take away from the session."

Kelly Horvath takes us on a journey of **"Unintended Consequences"** on page 20 as we look at the history of growth hormone and how it impacted protein-misfolding diseases so many years ago. Originally presented in the pages of the *Journal of the Endocrine Society*, Kelly talked to Alan Rogol, MD, PhD, about exceedingly rare cases of Creutzfeldt-Jakob disease and Alzheimer's disease that occurred when human growth hormone was first administered. Much of the mystery has evolved via treatment with growth hormone extracted from cadavers, the only method available in the middle of the previous century. But as Rogol explains, there was an overwhelming

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need and not enough sources for human growth hormone, so researchers turned to using material from cattle. "It was such a problem that I did my PhD dissertation 55 years ago on the structure of bovine growth hormone because we thought that its active cores might work in humans, which of course seems unrealistic in retrospect," Rogol says. I'm sure you'll be enthralled as I was when you read this fascinating tale.

On page 38, Derek takes us on another trip back to San Francisco and **ENDO 2025** for an examination of new data presented there regarding Cushing's syndrome and one of its pharmacological treatments, osilodrostat. In **"Staying in Control,"** Derek talks to Richard Auchus, MD, PhD, who discusses the results from the LINC rollover study on the long-term safety and effectiveness of osilodrostat in patients with Cushing's disease, which was well-tolerated during extended use. "It turns out that we learned a lot from LINC 3, and we were able to titrate the medication more safely by taking our time and using fewer steps, because the drug is so potent, we didn't really have to go up very high in most people," Auchus says. "Based on the information we learned from LINC 3, we conducted LINC 4 very effectively and really showed a tremendous difference."

Derek takes a deep dive with a look at a new pharmaceutical treatment for hypoparathyroidism in **"Following Up"** on page 34, where he talks to Aliya Khan, MD, who recently served with several other Endocrine Society members on a consensus statement writing group regarding treatment guidelines for this rare disorder. Specifically, palopegteriparatide, which was approved by the U.S. Food and Drug Administration in August 2024 to treat adults with hypoparathyroidism, a malady that is so rare that it only impacts about 0.1% to 0.3% of the population, with the most common cause occurring in 1% to 2% of those undergoing thyroid surgery. Regarding the timing of the consensus statement, Khan says "we felt that we needed to do this because now we actually have an approved drug for hypoparathyroidism, and we wanted to provide information as to when to use it, how to use it, how to start therapy, how to manage therapy."

Despite the array of cases presented in this issue, we barely scratched the surface! Let us know what you think about this issue, and if there are any recommendations for future rare cases we should cover, let us know. You can always reach me at: **mnewman@endocrine.org**.

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

Meet the Endocrine Society's 2026 Laureate Award Winners

The Endocrine Society announced it has chosen 12 leading endocrinologists as winners of its prestigious 2026 Laureate Awards, the top honors in the field.

These professionals have achieved breakthroughs in scientific discoveries and clinical care benefiting people with hundreds of conditions, including diabetes, thyroid disorders, obesity, hormone-related cancers, growth problems, osteoporosis, and infertility.

Established in 1944, the Society's Laureate Awards recognize the highest achievements in the endocrinology field, including groundbreaking research and innovations in clinical care. The Endocrine Society will present the awards to the winners at **ENDO 2026**, the Society's annual meeting, which is being held June 13– 16, in Chicago, Ill.

The Endocrine Society's 2026 Laureate Award winners are:

Robert M. Carey, MD, MACP

Fred Conrad Koch Lifetime Achievement Award

The Society's highest honor, this annual award recognizes lifetime achievements and exceptional contributions to the field of endocrinology. Carey is a professor of medicine and dean emeritus at the University of Virginia School of Medicine in Charlottesville, Va. He is a world-renowned clinical endocrinologist and leader in cardiovascular endocrinology. He is being recognized for his leadership in clinical hypertension, including treating patients, conducting groundbreaking research, and enhancing our understanding of hormonal control of blood pressure. Carey has made major contributions to our understanding of the renin-angiotensin system (RAS), the renal dopaminergic system, and mechanisms of pressure-natriuresis. His studies encompass a combination of cellular and molecular approaches, in vivo animal experiments, and patient-oriented clinical investigation. He is a very active member of the Endocrine Society who has served on many committees and task forces. He was president of the Society in 2008 and is a past recipient of the Distinguished Physician Award and the Outstanding Leadership Award. He is currently a member of the Society's Primary Aldosteronism Guideline Development Panel.

Christopher Kevin Glass, MD, PhD

Edwin B. Astwood Award for Outstanding Research in Basic Science

Originally awarded from 1967 and renamed to honor the scientific contributions of the late Dr. Edwin B. Astwood, MD, this award recognizes individuals who have made significant contributions to the field of endocrinology via their outstanding basic science research. Glass is professor of cellular and molecular medicine and professor of medicine at the University of California, San Diego in San Diego, Calif. He is being recognized for his novel research that uncovered how nuclear hormone receptors and other signal-dependent transcription factors regulate the development and functions of macrophages, which play key roles in immune responses and are major contributors to nearly all chronic diseases. These findings provided evidence that therapeutic targeting of macrophages could inhibit the development of atherosclerosis independent of changes in circulating cholesterol levels.

Rebecca Reynolds, MD, PhD

International Excellence in Endocrinology Award

This award is presented to an endocrinologist who has made exceptional contributions to the field in geographic areas with underdeveloped resources for hormone health research, education, clinical practice, or administration. Reynolds is personal chair of metabolic medicine and dean international at the College of Medicine and Veterinary Medicine, University of Edinburgh in Edinburgh, Scotland. As a physician scientist, her research focuses on women's health in pregnancy and the health of next and future generations, with a particular focus on low- and middle-income countries (LMICs). Her work contributes directly to the discovery of new interventions to improve pregnancy outcomes. She has fostered partnerships between her university and LMICs and leads a teaching program with numerous international students.

Samuel Klein, MD

Outstanding Clinical Investigator Award

This annual award honors an internationally recognized clinical investigator who has contributed significantly to understanding the pathogenesis and therapy of endocrine and metabolic diseases. Klein is the William H. Danforth Professor of Medicine at the Washington University School of Medicine in St. Louis, Mo. He uses a combination of sophisticated basic and clinical science research techniques to address clinically relevant questions in human subjects, which are ultimately directed to improving health and patient care. His research is focused on understanding the cellular and multi-organ system physiological mechanisms responsible for the heterogeneity in metabolic dysfunction associated with obesity, prediabetes, diabetes, and the therapeutic effects of weight loss. He also has conducted important clinical trials that evaluated the efficacy and metabolic effects of weight reduction therapies.

Lisa B. Nachtigall, MD

Vigersky Outstanding Clinical Practitioner Award

This annual award recognizes extraordinary contributions by a practicing endocrinologist to the endocrine and/or medical community. Nachtigall is the clinical director of the Neuroendocrine Clinical Center at Massachusetts General Hospital (MGH) and an associate professor of medicine at Harvard Medical School in Boston, Mass. In addition, she is the director of MGH International Education Programs for the MGB/MGH Endocrine Division, and of the MGH/Harvard Medical School advanced clerkship in clinical neuroendocrinology. She has extensive clinical experience in all pituitary disorders, particularly acromegaly. She is an internationally recognized clinical expert, who speaks nationally and internationally and has published extensively in the field of pituitary care. She has co-founded and directs a visiting scholars program encouraging a pipeline of students and trainees in endocrine. She has been an impactful advocate for patients with rare disorders, including organizing educational programs for patients with acromegaly. She has served on multiple Endocrine Society committees and task forces.

Bradley David Anawalt, MD
Outstanding Educator Award

This annual award recognizes exceptional achievement as an educator in the discipline of endocrinology and metabolism. Anawalt is a professor and vice chair in the Department of Medicine at the University of Washington School of Medicine in Seattle, Wash. He is a world expert in andrology and the diagnosis and treatment of male hypogonadism. He also is a dedicated teacher, known for his ability to convey not only factual material, but a sense of collegiality and joy in learning among his students. He has held numerous service positions with the Endocrine Society and is currently a member of its Endocrine Self-Assessment Program (ESAP™) Faculty Group and CoDI. He's also a regular presenter at **ENDO**, the Society's annual meeting.

Patricia Lee Brubaker, PhD
Outstanding Mentor Award

This annual award recognizes a career commitment to mentoring and a significant positive impact on mentees' education and career. Brubaker is a professor emerita in the Departments of Physiology and Medicine at the University of Toronto in Ontario, Canada. Since 1985, she has had the privilege of mentoring hundreds of post-doctoral fellows and graduate and undergraduate research students. Under her mentorship, she provides her students with a roadmap for success in their chosen careers, and her students have gone on to publish papers in high-impact journals. Many of her undergraduate trainees remain in her laboratory over extended terms, and she has continued to mentor many of her trainees for years post-graduation. She is currently chair of the Endocrine Society's Publications Core Committee and was the associate editor of *Endocrinology*, the Society's basic science journal.

Martin Reincke, MD
Outstanding Scholarly Physician Award

This annual award recognizes outstanding contributions to the practice of clinical endocrinology in academic settings. Reincke is a professor of endocrinology and chair of Medical Department IV at the Ludwig-Maximilians University Hospital in Munich, Germany, a leading institution in German academic medicine. He is an internationally recognized leader in the diagnosis and management of adrenal and pituitary disorders who played a key role in building a large-scale international research consortia to address major therapeutic challenges in patients with primary aldosteronism and Cushing's syndrome. He previously served on the editorial board of *The Journal of Clinical Endocrinology & Metabolism*.

Katrin J. Svensson, PhD
Richard E. Weitzman Outstanding Early-Career Investigator Award

This annual award recognizes an exceptionally promising young clinical or basic investigator. Svensson is an associate professor in the Department of Pathology at Stanford University, and the metabolic core director and affinity group leader at the Stanford Diabetes Research Center in Palo Alto, Calif. Her research focuses on understanding intercellular communication to maintain metabolic homeostasis, with a particular emphasis on secreted signaling molecules and peptides. Her laboratory discovered Isthmin, a secreted protein that regulates insulin independent glucose uptake and lipid homeostasis. Additionally, her group developed computational methods to predict new peptides and ligand-receptor pairs, advancing the discovery of novel endocrine pathways.

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Alvin C. Powers, MD

Roy O. Greep Award for Outstanding Research

This annual award recognizes meritorious contributions to research in endocrinology. Powers is the Joe C. Davis Chair in Biologic Science, professor of medicine and molecular physiology and biophysics, and director of the Vanderbilt Diabetes Center (VDC) at Vanderbilt University Medical Center in Nashville, Tenn. Powers is a physician-scientist who has made fundamental research discoveries revealing how alterations in islet biology are linked to the pathogenesis of type 1 and type 2 diabetes, cystic fibrosis-related diabetes, monogenic diabetes, and post-transplant diabetes. The work of his research group, especially the emphasis on translating research on human islet biology into advancing human diabetes research, has redefined our understanding of islet structure and function and its role in glucose homeostasis and diabetes. Powers has served on several Endocrine Society committees and task forces and is an author of the Society's recent Scientific Statement on type 1 diabetes.

R. Paul Robertson, MD

Sidney H. Ingbar Distinguished Service Award

This award recognizes distinguished service to the Endocrine Society and the field of endocrinology. Robertson is professor emeritus at the University of Washington School of Medicine in Seattle, Wash. He has made numerous scientific contributions to endocrinology over the course of his career with research that improves our understanding of pancreatic islet function in humans, animals, and clonal cell lines. He's served in numerous leadership roles at the Endocrine Society, the National Institutes of Health, and many other scholarly societies and institutes. At the Endocrine Society, he's served as editor-in-chief of *The Journal of Clinical Endocrinology & Metabolism* and *Endocrine Reviews*, and as a member of the Society's Publications Core Committee.

Ismaa Sadaf Farooqi, MD, PhD

Gerald D. Aurbach Award for Outstanding Translational Research

This annual award recognizes outstanding contributions to research that accelerates the transition of scientific discoveries into clinical applications. Farooqi is a clinician scientist at the Institute of Metabolic Science at the University of Cambridge in Cambridge, U.K., who is being honored for her discoveries of fundamental mechanisms that control human energy homeostasis. With colleagues, she discovered the first genes whose disruption causes severe obesity. In pioneering clinical studies, she established that the principal driver of human obesity is a failure of the central control of appetite and that the leptin-melancortin pathway regulates food intake, macronutrient preference, food reward, and body weight. Her research has changed the investigation, management, and treatment of children and adults with severe obesity.

Nominations are being accepted for the 2027 awards cycle until January 20, 2026. Any submissions received after that will be considered for the following year.

Endocrine Society Launches Women's Health SIG

The Endocrine Society is excited to announce its newest Special Interest Group (SIG) focusing on the many endocrine-related aspects of Women's Health.

These SIGs are member-led communities where members from around the globe can connect, share, learn, and collaborate on specific topics in the endocrine world.

The mission of the Women's Health SIG is to create a collaborative community of healthcare professionals dedicated to advancing the quality of care for women. This group will provide a platform for researchers and practitioners to exchange ideas, share knowledge, and stay informed on the latest best practices in women's health. Emphasis will be placed on integrating cutting-edge scientific advancements with well-established, evidence-based approaches.

Joining the Women's Health SIG guarantees that you are the first to know about SIG education and networking activities, as well as leadership and program development opportunities, including webinars, event meetups, collaborative projects, and more.

Join your colleagues to explore the spectrum of women's health issues that demand deeper focus and fresher solutions, from the complexities of menopause to managing osteoporosis, polycystic ovary syndrome (PCOS), and more.

For more information, go to: **www.endocrine.org/our-community/special-interest-groups/womens-health**.

Osteoporosis Treatment Rates Rise, But Millions Still Fall Through Cracks

> The study highlights a crucial disconnect: A fragility fracture should be a wake-up call for both patient and physician to investigate underlying bone health, yet it is frequently not. This underdiagnosis contributes directly to the underuse of medications that could prevent future, and potentially more severe, fractures.

A new study in *The Journal of Clinical Endocrinology & Metabolism* has revealed a concerning paradox in the management of osteoporosis in the United States. While the use of drug therapies for the bone-weakening disease has increased over the past decade, a significant and persistent trend of underdiagnosis means millions of high-risk patients are missing out on vital treatment, leaving them vulnerable to debilitating fractures.

There are two ways osteoporosis is diagnosed: before or after a fracture. The former, or primary prevention, is done via bone density setting (e.g. a T score <-2.5) and the latter, secondary prevention, when a fracture has occurred. Professional societies differ in screening guidelines, but typically bone density testing is recommended for women aged ≥65 years as well as younger postmenopausal women with histories of nontraumatic fractures and risk factors.

"Trends in Osteoporosis Drug Therapy Receipt Among Commercial and Medicare Advantage Enrollees in the United States, 2011 – 2022," a retrospective analysis of over 166 million patient-quarter observations from commercial and Medicare Advantage health insurance data between 2011 and 2022, found a clear split in care. Among women aged 65 and older with an official diagnosis but without a prior fragility fracture, prescription fill rates increased from 36.3% to 50.1%. Similarly, for those with an official diagnosis of osteoporosis who had already suffered a fragility fracture, which is a key indicator of underlying bone disease, the fill rate rose from 30.8% to 43.7%.

This upward trend suggests that once osteoporosis is identified, doctors are increasingly prescribing the necessary medications to prevent future fractures. However, the study's most alarming finding lies in what happens before a diagnosis is made. Researchers found that more than 70% of all patients who experienced a fragility fracture — a clear symptom of bone fragility and a diagnostic criterion of osteoporosis — did not have a corresponding diagnosis of osteoporosis in their medical records. In this case, fewer than one in 11 women received treatment.

This startling statistic points to a systemic failure in the healthcare system to properly screen and diagnose at-risk individuals. As a result, the very patients who most urgently need intervention are often overlooked. The study highlights a crucial disconnect: A fragility fracture should be a wake-up call for both patient and physician to investigate underlying bone health, yet it is frequently not. This underdiagnosis contributes directly to the underuse of medications that could prevent future, and potentially more severe, fractures.

The trend is further underscored by the fact that for patients with fragility fractures but no documented osteoporosis, the use of drug therapy declined between 2011 and 2022, from 9.2% to just 7.4%. This suggests that without an official diagnosis, doctors are less likely to initiate treatment, despite the obvious clinical evidence of bone fragility.

The findings from this study confirm what many bone health experts have long feared: A significant gap exists in patient care that puts millions at risk. To change this trajectory, the authors state that healthcare community must prioritize greater awareness, systematic screening, and timely diagnosis of osteoporosis, especially for anyone who has suffered a fracture. — *Jackie Oberst*

As GLP-1 Prescriptions Soar, Poison Center Study Finds Exposures Are Common But Generally Mild

A new study from a poison control center in Alabama offers a reassuring perspective on the rising number of calls related to popular GLP-1 receptor agonists, such as Ozempic and Wegovy. While exposures to these medications have increased significantly over the past two decades, the research suggests many cases are accidental, associated with mild symptoms, and rarely lead to serious health complications.

The study, **"GLP-1 Receptor Agonist Exposures Are Increasingly Common and Generally Associated With Mild Symptoms: A Single Poison Center Experience"** published in *The Journal of Medical Toxicology*, analyzed 152 cases reported to the Alabama Poison Control Information Center between 2006 and 2023. Researchers pulled patient demographics, exposure circumstances, and outcomes from the charts and found that a staggering 91% of these exposures were not intentional overdoses but rather a result of therapeutic or administration errors. A primary culprit, the authors note: patient confusion over how to properly use the pre-filled injection pens.

"A common reason for this error was confusion surrounding how to use pen devices by which these agents are administered," the study's authors write. Patients often believed the pen had malfunctioned after the initial dose, leading them to accidentally administer a second dose before realizing their mistake. This issue alone accounted for 21% of all exposures, highlighting a critical gap in patient education.

The clinical effects reported by patients were largely non-life-threatening. The most common symptoms were gastrointestinal, including nausea, vomiting, and abdominal pain, along with generalized weakness. In a positive finding, most patients — 62% — were able to be safely managed and monitored at home, avoiding the need for hospitalization.

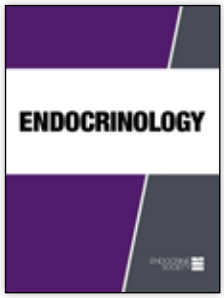
The research also tackles a major concern surrounding these medications: hypoglycemia, or dangerously low blood sugar. The study found this serious side effect to be exceptionally rare. It was reported in only two patients who were taking a GLP-1 agonist alone and in two other patients who were also co-administering insulin, suggesting that GLP-1s on their own pose a minimal risk of severe blood sugar drops.

The study's conclusion points to a clear need for better training at the point of dispensing. With millions of new users unfamiliar with self-injecting medications, the researchers argue that pharmacists and healthcare providers should provide more thorough counseling on pen usage. This simple step could dramatically reduce the rate of therapeutic errors and the subsequent calls to poison control, ensuring patients can safely and effectively use these life-changing drugs.

The authors also suggest that improvements could be made to the pen devices."Opportunity exists to improve how many of these agents are supplied," the authors write. "Providing multi-dose pens and vials may increase the risk for a medication error to occur."

The findings provide valuable data for healthcare providers and patients alike, reinforcing that while caution is necessary, the risks associated with accidental exposure are generally mild. — *Jackie Oberst*

"Patients often believed the pen had malfunctioned after the initial dose, leading them to accidentally administer a second dose before realizing their mistake. This issue alone accounted for 21% of all exposures, highlighting a critical gap in patient education."



How Thyroid Hormones Truly Regulate Your Pulse

For decades, scientists have known that thyroid hormones play a pivotal role in regulating heart rate and other cardiovascular functions. An overactive thyroid, for example, can cause the heart to race, while an underactive one can slow it down. However, new research is revealing that this relationship is far more complex than previously understood, challenging long-held assumptions about the mechanisms at play.

"Thyroid Hormone Receptors in Control of Heart Rate," a recent review article published in *Endocrinology* synthesizes new findings on the individual contributions of two key thyroid hormone receptor isoforms. The research moves beyond the traditional view that the heart's pacemaker channel genes, specifically Hcn2 and Hcn4, are the sole mediators of thyroid hormone's effects on heart rate. Instead, it argues for a more nuanced model that includes both direct action on the heart and indirect effects through the nervous system.

According to the review, the two receptor isoforms — Thyroid Hormone Receptor α (TRalpha) and Thyroid Hormone Receptor β (TRbeta) — each contribute in their own way to the control of heart rate. The article delves into recent discoveries that differentiate the roles of these two receptors, offering a more complete picture of how thyroid hormones exert their influence. While TRalpha appears to be the primary hormone involved in heart rate, knockout studies of this receptor in mice have shown that TRbeta can take over. Similar knockout studies of Hcn2 and Hcn4 also indicate that normal heart rates can occur, suggesting that other genes play a role in thyroid hormone signaling. This is a significant shift in understanding, as it suggests a more intricate regulatory network than a single, simple pathway.

Furthermore, the review explores how thyroid hormones might affect heart rate not just by acting directly on the heart itself, but also by altering the output of the brain's autonomic nervous system. This indirect pathway adds another layer of complexity to the system and opens up new avenues for research and treatment. Understanding this dual mechanism — direct cardiac effects and indirect nervous system modulation — is crucial for developing more precise therapies for conditions related to thyroid dysfunction.

Perhaps most critically, the review also highlights the long-term consequences of thyroid hormone imbalance during a person's developmental stages. It underscores the importance of considering how impaired thyroid hormone action early in life can lead to permanent changes in both the heart and the brain's regulatory centers. This suggests that interventions for thyroid-related cardiovascular issues may need to start earlier than previously thought to prevent irreversible damage.

The research marks a significant step forward in understanding of thyroid hormone's profound and multi-faceted control over the cardiovascular system. By moving beyond a singular focus on pacemaker genes and embracing a model that includes both direct and indirect pathways, scientists are paving the way for more targeted treatments and a better grasp of the lasting effects of thyroid health on our most vital organ. — *Jackie Oberst* EN

"The review also highlights the long-term consequences of thyroid hormone imbalance during a person's developmental stages. It underscores the importance of considering how impaired thyroid hormone action early in life can lead to permanent changes in both the heart and the brain's regulatory centers."

> If people aren't familiar with [tumor-induced osteomalacia], they may not connect the dots and think of that diagnosis. There was a retrospective review of cases that showed that the average time of diagnosis was about three years. **That's three years of this medical uncertainty, poor quality of life, being sent to several different specialists, orthopedics getting scans that are probably unnecessary, treatments that may not work."**
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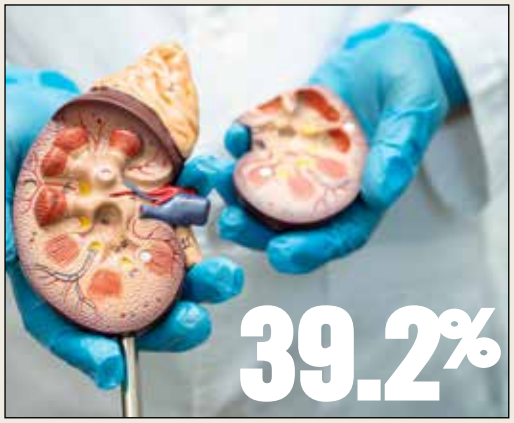
> **Lara McHan, MD,** University of Rochester Strong Memorial Hospital, Rochester, N.Y., commenting in **"String of Pearls"** (p. 24) that details *The Journal of Clinical Endocrinology & Metabolism* Case Reports Clinical Pearls session that took place at **ENDO 2025** in July.



The percentage of U.S. adults aged 18 and older with diagnosed diabetes who also have chronic kidney disease.

SOURCE: US CENTERS FOR DISEASE CONTROL AND PREVENTION

The number of adults in the U.S. who have an endocrine disorder. **SOURCE:** HEALTH.COM

The percentage of Americans who have used GLP-1 drugs for weight loss, with an additional 14% saying they're interested.

SOURCE: *THE BOSTON GLOBE*

The increased percentage by which thyroid cancer prevalence has surged globally since 1990.

SOURCE: *THYROID RESEARCH AND PRACTICE*

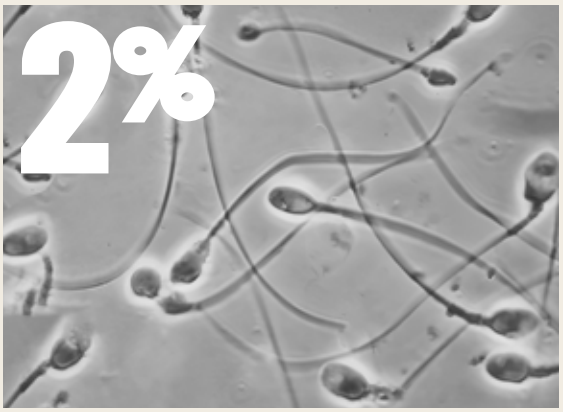
35%

The percentage of Americans who use AI to research health concerns.

SOURCE: DRIP HYDRATION'S AI HEALTH SURVEY

The percentage by which sperm count is declining in men each year as a result of endocrine-disrupting chemicals in plastics.

SOURCE: *THE GUARDIAN*



2025 Clinical Endocrinology Update

CEU 2025
CLINICAL ENDOCRINOLOGY UPDATE

Oct. 23 – 25, 2025/Virtual Only

Join endocrinologists and other healthcare professionals for updates on how to treat various endocrine conditions based on the latest expert guidelines in hormone care. With recent breakthroughs in different areas of the ever-evolving field of endocrinology, staying abreast of innovative practices is essential for optimal patient treatment.

CEU 2025 provides a convenient solution for busy professionals by delivering first-rate education they can immediately implement into their practice. For over a decade, our program has been led by renowned endocrinologists, offering a case-based agenda and evidence-based disease management strategies to equip practitioners with the tools they need to address daily clinical challenges.

CEU is virtual, ensuring accessibility through our online platform. Our expert faculty will cover important endocrinology topics, including adrenal, calcium and bone, diabetes, pituitary, obesity and lipids, female reproduction, male reproduction, transgender care, and thyroid.

With Meet the Professor sessions and a symposium filled with expert insights, this program offers a valuable learning experience for endocrinologists worldwide. Do not miss this opportunity to enhance your knowledge and skills in hormone care. Join us online, and stay ahead in the field of endocrinology!

https://www.endocrine.org/meetings-and-events/ceu-2025

ObesityWeek®

Atlanta, Georgia
November 4 – 7, 2025

The preeminent international conference for obesity researchers and clinicians, ObesityWeek® is home to the latest developments in evidence-based obesity science: cutting-edge basic and clinical research, state-of-the-art obesity treatment and prevention, and the latest efforts in advocacy and public policy. Treating obesity requires multidisciplinary approaches. This is the conference that encompasses the full spectrum of obesity science: from basic science research, to translational research and clinical application, to public policy; from diet, exercise, lifestyle, and psychology to medical and surgical interventions; from pediatric to geriatric to underserved populations. With more than 250 expert speakers presenting the latest research to best practices in clinical care, this conference has it all!

https://obesityweek.org/

Neuroscience 2025

San Diego, California
November 15 – 19, 2025

Each year, scientists from around the world congregate to discover new ideas, share their research, and experience the best the field has to offer. Attend so you can present research, network with scientists, attend sessions and events, and browse the exhibit hall. Join the nearly half a million neuroscientists from around the world who have propelled their careers by presenting an abstract at an SfN annual meeting — the premier global neuroscience event.

https://www.sfn.org/meetings/neuroscience-2025/

ENDOCRINE **ITINERARY**

Lab Manager 2025 Quality & Compliance Digital Summit

Virtual
December 9, 2025

Elevate your lab's quality and standards at the Quality & Compliance Digital Summit on December 9, 2025. Discover how to exceed regulatory expectations and foster a culture of excellence in every aspect of your lab's operations. Attendees will learn how to navigate evolving regulations, implement robust quality management systems, and optimize lab workflows for compliance. This summit is essential for professionals seeking to stay compliant with industry standards, improve lab operations, and ensure the highest quality in their processes. Don't miss this opportunity to elevate your lab's quality and compliance practices.
https://www.labmanager.com/2025-quality-compliance-digital-summit-33204

27th Davidson-Mestman Intensive Course

Miami, Florida
December 10 – 13, 2025

Presented entirely in Spanish, the main objective of this intensive course is to provide physicians with specialized and advanced training in the diagnosis, treatment, and comprehensive management of patients with endocrine disorders, diabetes, and associated cardiovascular diseases, obesity, and endocrine cancers. The program will focus on updating and honing participants' clinical skills, enabling them to deliver cutting-edge, personalized medical care in these specialized areas.
https://www.cursodavidsonmestman.com/

INTERNATIONAL **ITINERARY**

EndoBridge 2025

Antalya, Turkey
October 23 – 26, 2025

EndoBridge 2025 will provide a comprehensive update of recent advances in the full spectrum of endocrinology including diabetes and lipid disorders. The program involves state-of-the-art lectures delivered by world-renowned faculty as well as interactive case discussion sessions. The official language of the meeting is English and simultaneous translation in Arabic and Turkish will be provided. EndoBridge 2025 will bring together leading experts of endocrinology and a diverse and active international scientific community of clinicians and fellows to present and discuss clinical endocrinology topics.
https://www.endobridge.org/

SAEM 2025

Buenos Aires, Argentina
November 6 – 8, 2025

The 24th Congress of the Society of Endocrinology and Metabolism (SAEM) will be held at the University of Buenos Aires (UCA) in Puerto Madero, Buenos Aires, Argentina. As has been a feature throughout its history, SAEM offers a first-class scientific program, featuring excellent speakers and the presence of distinguished foreign guests, experts in each discipline. This is a highly valued experience by both trainee and experienced endocrinologists, not only at the national level but also throughout Latin America. SAEM 2025 will cover a wide range of topics of current interest in diagnosis and treatment, such as cardio metabolism, obesity, diabetes, bone metabolism, and other traditional topics. The results of the latest treatments and drugs under investigation will also be showcased.
https://congresosaem.com.ar/

World Endocrine, Diabetes & Cardiovascular Conference (EDCC26)

Bangkok, Thailand
March 6 – 7, 2026

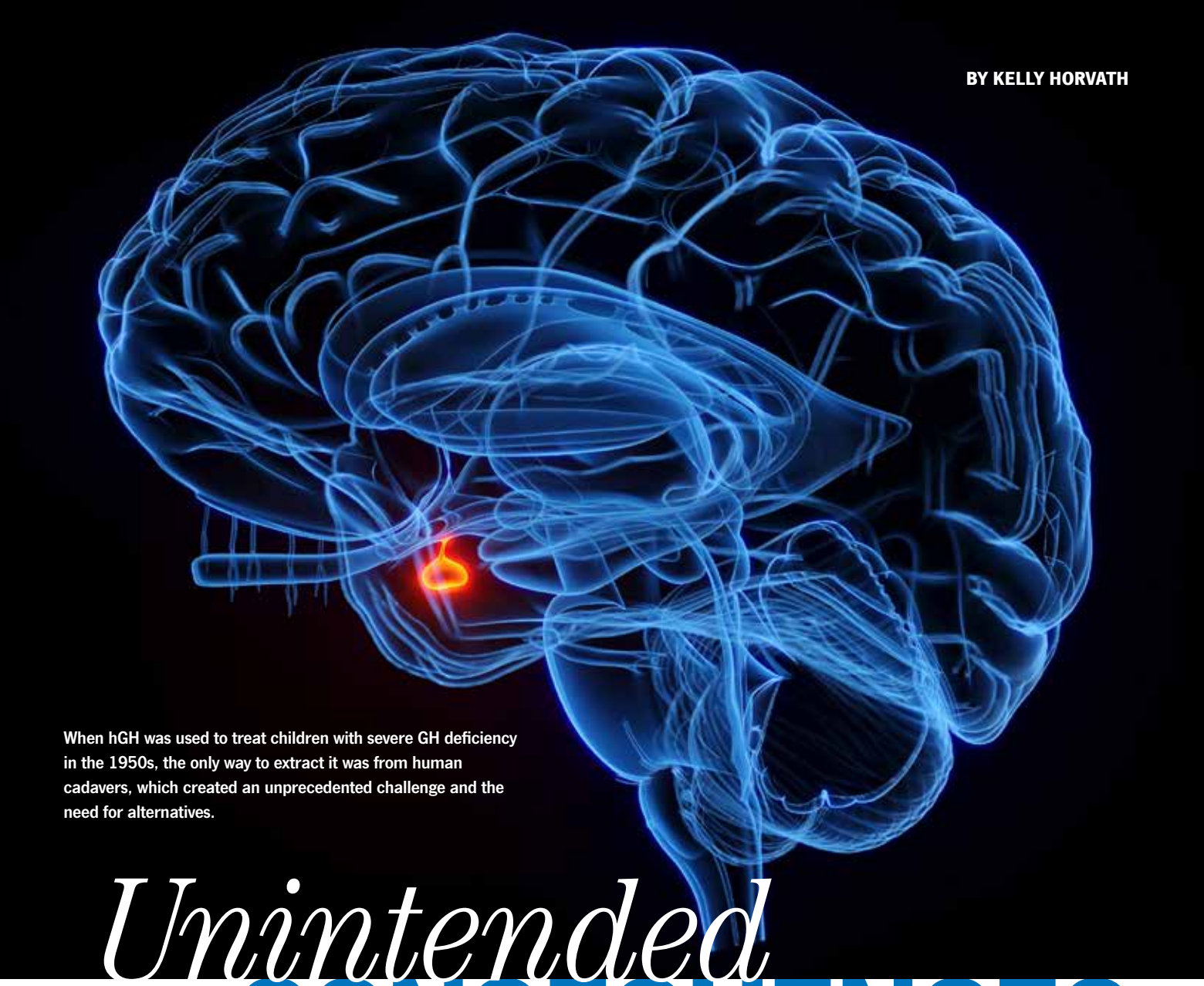
The World Endocrine, Diabetes & Cardiovascular Conference 2026 (EDCC26) will be organized around the theme of "Interdisciplinary Approaches to Endocrine Health." The program includes local and international speakers with inspiring insights to share on advancing endocrinology, diabetes, cardiovascular health, and metabolism quality improvement through patient and family experiences. EDCC26 will feature leading experts, researchers, and healthcare professionals from around the globe and will serve as a platform for the exchange of knowledge, ideas, and insights in the fields of endocrinology, diabetes, obesity, and more.
https://endocrine.episirus.org/bangkok/

ATTD 2026

Barcelona, Spain
March 11 – 14, 2026

The landscape of diabetes care is evolving fast, and the 19th International Conference on Advanced Technologies & Treatments for Diabetes (ATTD) 2026 is where technology, innovation, and research converge to shape the next era of treatment. From AI-driven solutions to the latest in digital health, smart devices, and groundbreaking therapies, this is the conference that defines what's next in diabetes management. Connect with global experts, industry leaders, and visionaries pushing the boundaries of what's possible.
https://attd.kenes.com/

BY KELLY HORVATH



When hGH was used to treat children with severe GH deficiency in the 1950s, the only way to extract it was from human cadavers, which created an unprecedented challenge and the need for alternatives.

Unintended CONSEQUENCES

Human Growth Hormone and Protein-Misfolding Diseases: A Historical Perspective

From the pages of the *Journal of the Endocrine Society*, *Endocrine News* talks with Alan Rogol, MD, PhD, about the rarest of rare cases that involved growth hormone, Creutzfeldt-Jakob disease, and Alzheimer's disease in a tale through time that involves rats, cadavers, and how one treatment evolved through scientific refinement.

Has there ever been a more aptly titled research paper? In "The Unfolding Story of Protein Misfolding Causing Alzheimer Disease in Recipients of Human Pituitary Growth Hormone," published in *Journal of the Endocrine Society* in March, a collaborative research team traces a medical story that spans more than a century — from the early therapeutic hopes of growth hormone (GH) extracted from bovine pituitaries and tested in a bioassay in female rats through the tragic recognition of Creutzfeldt-Jakob disease (CJD) transmission from cadaveric human GH (hGH), to emerging questions about whether Alzheimer's disease (AD) may also be iatrogenically transmissible.

How this paper came together happened almost by chance at a History Committee meeting of the Pediatric Endocrine Society (PES), recalls corresponding author Alan D. Rogol, MD, PhD, professor emeritus of pediatrics and pharmacology at the University of Virginia in Charlottesville, as well as past vice president of the Endocrine Society and then-chair of the PES History Committee. PES Executive Committee member Tandy Aye, MD, from Stanford University brought up Banerjee, et al.'s paper "Iatrogenic Alzheimer's Disease in Recipients of Cadaveric Pituitary-Extracted Growth Hormone," published in *Nature Medicine* in February 2024, that, as the title makes clear, posits that AD may be iatrogenically transmissible. "We thought it would be a good time to remind people about human growth hormone: how it started, how safe it was, how safe it wasn't, and the whole story," Rogol says.

The collaboration that emerged was uniquely positioned to tell this tale. Aye's colleague Darrell M. Wilson, MD (a coauthor of the paper) had been there at the beginning; he and Raymond L. Hintz, MD (also formerly at Stanford) were among the first to see a patient with CJD. In May 1985, Hintz filed a letter with the U.S. Food and Drug Administration explaining that one of his patients who had been treated with cadaveric hGH for 14 years may have contracted CJD as a result. Rogol himself had close connections to Robert M. Blizzard, PhD (also at the University of Virgina), who treated another very early patient who eventually died from CJD. "We had the collective memory of what happened in 1985 as well as what led up to it," Rogol notes.

How It Started

hGH began to be used to treat children with severe GH deficiency in the 1950s; however, access was initially an obstacle. Because GH is species specific, GH from other animals was inactive in humans, so extracting pituitary glands from human cadavers was then the only way to obtain hGH.

This species specificity created an unprecedented challenge and the need to find alternatives, as Rogol's own research illustrates: "So many more children needed to be treated than we had material for," he recounts. "It was such a problem that I did my PhD dissertation 55 years ago on the structure of bovine growth hormone because we thought that its active cores might work in humans, which, of course, seems unrealistic in retrospect."

How Safe It Was

hGH was, of course, believed to be safe. Rogol notes that the only known side effects were reduced efficacy in those who produced antibodies in response to treatment as

"So many more children needed to be treated than we had material for. **It was such a problem that I did my PhD dissertation 55 years ago on the structure of bovine growth hormone because we thought that its active cores might work in humans, which, of course, seems unrealistic in retrospect."**

— ALAN D. ROGOL, MD, PHD, PROFESSOR EMERITUS, PEDIATRICS AND PHARMACOLOGY, UNIVERSITY OF VIRGINIA, CHARLOTTESVILLE, VIRGINIA

well as scoliosis and slipped capital femoral epiphysis, which occur from growing. "That wasn't specific to growth hormone; it was specific to growth promotion," Rogol says.

In 1958, scientists discovered how to purify hGH in greater quantities, and ultimately more than 7,700 children were treated with it. The Hartree-modified Wilhelmi procedure (HWP) added a few more steps to the original procedure pioneered by Alfred E. Wilhelmi, PhD, at Emory University. The modifications by Anne Stockell Hartree, PhD, allowed more efficient extraction of hGH from cadaveric pituitaries, Rogol explains. "It worked perfectly well," he says.

How Safe It Wasn't

The tragedy lay not in the concept but in the execution — specifically, in the purification methods used. CJD is now known to be caused by prions, infectious agents composed of misfolded proteins that can trigger other normal proteins to misfold, creating a chain reaction. Among the multitudes of extracted pituitaries, some would have been contaminated with prions, leading to the development of iatrogenic CJD (iCJD) in more than 200 recipients worldwide.

The cruel irony emerged only decades later when alternative purification methods were developed. To produce purer hGH and therefore fewer antibody-related problems, Albert F. Parlow, PhD, at The Lundquist Institute for Biomedical Innovation at Harbor-UCLA Medical Center, innovated an approach using size-exclusion chromatography, which essentially blocked prions, due to their large size. "That one step, by serendipity, did not permit these prions to go into the final product," Rogol reflects.

Some of the Rest of the Story: Recombinant Growth Hormone

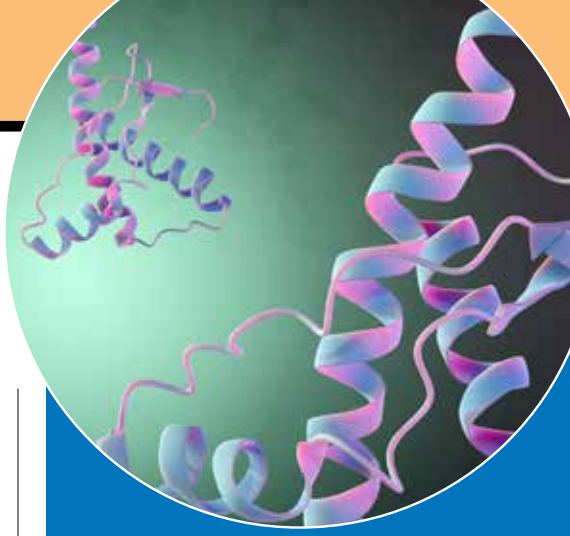
The transition to recombinant hGH (rhGH) brought its own challenges. One company began producing rhGH in the early 1980s in *Escherichia coli*, a revolutionary yet imperfect process, initially. "They would use a centrifuge to remove the bacteria, but some endotoxins and other bug proteins remained, which were quite inflammatory and triggered immune responses," explains Rogol. Nevertheless, the cadaveric hGH extraction method was unsustainable — the pool of children needing treatment was just too large (one pituitary per child per day). "[Wilson] and I lived through this and learned it was really important to get rhGH right because we knew it worked."

By 1985, truly purified rhGH became available, ending the era of cadaveric hormone extraction and its associated risks.

More of the Rest of the Story: What Does This Have to do with Alzheimer's Disease?

Because AD is another protein-misfolding disease (of amyloid-beta and tau), and because recent research has suggested that AD may be transmissible from a host to a recipient mouse — as well as the recent observation that tau

In the early 1980s, one company began producing rhGH in *Escherichia coli* using a centrifuge to remove the bacteria, but some endotoxins and other bug proteins remained. However, by 1985 when truly purified rhGH became available, the era of human cadaveric hormone extraction and its associated risks came to an end.



Creutzfeldt-Jakob disease is caused by prions, infectious agents composed of misfolded proteins that can trigger other normal proteins to misfold, creating a chain reaction. Among the multitudes of extracted pituitaries, some would have been contaminated with prions, leading to the development of iatrogenic CJD (iCJD) in more than 200 recipients worldwide.

protein can behave like prions — the question has arisen as to whether patients who received hGH could develop AD in a manner similar to how younger members of the cohort developed CJD (as reported in Banerjee, et al.). Infection happens not from bacteria or viruses but from the "chain reaction" of misfolding that prions cause and, possibly amyloid-beta and tau proteins. When the autopsy reports of eight people who were treated with hGH and developed CJD demonstrated that four of them also had amyloid-beta and tau proteins consistent with AD in 2015, the question took on new urgency.

"I don't have enough knowledge to be in any particular camp," Rogol acknowledges, "but the statistics are such that to me it is very likely." Not only did half of the above-mentioned eight patients develop AD, but an additional four patients had AD-consistent biomarker and/or imaging findings — the oldest of these patients was 57 years old. Experts like Ellen Leschek and colleagues at the National Institutes of Health in Bethesda, Md., who have followed CJD cases from the beginning, however, believe there are simply not enough data to draw conclusions as well as because possible alternative explanations for AD development existed in the patients in question. "The difference between us and [Leschek's] group is that we are relatively more certain," Rogol explains. "We're not that far different; she's more skeptical, but she's also more knowledgeable."

Enduring Questions

For Rogol, the critical questions about potential hGH-transmitted AD are temporal: "Do these people get Alzheimer-like conditions 10, 20, or 30 years earlier than they otherwise would have?" Additionally, he wonders about disease progression: "Might Alzheimer disease have a different trajectory — from good to bad to worse more quickly — if you got it this way? So, both earlier onset and potentially different symptom trajectory are probably the crux of whether it has been transmitted by growth hormone."

The role of genetics adds another layer of complexity. Animal experiments have shown that genetic susceptibility matters enormously. "If you put Alzheimer and non-Alzheimer brain bits into a genetically susceptible rat, the susceptible rat gets Alzheimer disease on one side, but nothing on the other. If you put them into a genetically non-susceptible rat, nothing happens on either side," Rogol explains.

We will soon have a more complete genetic signature that reveals susceptibility, such as from genes like APOE ε4. What can clinicians do now? "The take-home message is that anybody who had been treated with cadaveric growth hormone and is at risk probably ought to be followed. You don't need to worry about somebody else getting this," Rogol says. Research into the use of human tissue from one individual to another should continue, he emphasizes, given this sobering lesson about unintended consequences, with nothing but the purest of intentions. EN

– HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT THE REMARKABLE AI RESEARCH PRESENTED AT **ENDO 2025** BY THE ELANGOVAN SIBLINGS IN THE SEPTEMBER ISSUE.

AT A GLANCE

- Human growth hormone (hGH) contaminated with prions that was extracted from cadaveric pituitaries and used to treat growth hormone deficiency caused Creutzfeldt-Jakob disease (CJD) in more than 200 recipients.
- Recent studies suggest that eight of these patients developed Alzheimer's disease (AD) or showed biomarker and imaging findings consistent with the disease, suggesting possible transmission through contaminated hormone preparations similar to how CJD was transmitted; amyloid-beta and tau proteins were detected in the preparations.
- Experts remain divided on whether sufficient evidence exists to confirm iatrogenic AD transmission, but none would disagree that surveillance of former hGH recipients must continue nor that further research into protein misfolding disease transmission mechanisms is needed.

The *JCEM Case Reports* Clinical Pearls session at **ENDO 2025** featured three presentations of rare endocrine cases that could answer questions for endocrinologists who could be treating patients with similar symptoms, possibly triggering further investigations that might lead to optimal outcomes.

String of PEARLS

A Look at Rare Clinical Pearls from *JCEM Case Reports*

BY DEREK BAGLEY

The audience for the third-annual *JCEM Case Reports* Clinical Pearls session at **ENDO 2025** in San Francisco, Calif., was much bigger than the first session convened for **ENDO 2023** in Chicago, Ill. That first session in Chicago took place soon after the journal *JCEM Case Reports* launched in late 2022, so it sort of made sense that it was relegated to one of those small rooms on an upper floor. This time in San Francisco, the *JCEM Case Reports* Clinical Pearls session commanded a full theater, and the theater was filled: a testament to the interest of endocrinologists wanting to learn about challenging cases and the the eureka moments that led to optimal care.

When the open-access journal *JCEM Case Reports* (JCEM CR) was announced, Editor-in-Chief William F. Young, Jr., Tyson Family Endocrinology Clinical Professor and professor of medicine, Mayo Clinic College of Medicine and Science, Mayo Clinic, Rochester, Minn., told *Endocrine News* that the editors are looking for case reports on common endocrine disorders with unique — diagnostic, ethical, management — challenges; on rare endocrine disorders that present in a different way; recognition of a new association with an endocrine tumor; or other endocrine diagnosis.

These sessions at **ENDO** aim to highlight those challenges. Young has spoken before about how case reports can lead to a link between two unusual findings that could lead to further investigation. "In the third annual Clinical Pearls from *JCEM Case Reports* the attendees heard presentations from early-career aspiring endocrinologists on the management of Cushing syndrome in pregnancy, the presentation and management of metastatic

choriocarcinoma-related paraneoplastic thyroid storm, and the management of hypophosphatemic osteomalacia," Young says. "Each case presentation was followed by a content expert who put the topic into a broader context and expounded on the key pearls that clinicians should take away from the session."

Successful Medical Management of Cushing's Disease in Pregnancy

Angeliki Theodorou, MD, of the Division of Endocrinology in the Department of Medicine in the Memorial Sloan Kettering Cancer Center in New York, N.Y., presented two case studies she and her mentor Eliza B. Geer, MD, wrote for JCEM CR, two pregnant women with recurrent Cushing's disease (CD), a rare disorder that carries many diagnostic and therapeutic challenges.

No drug to date has been approved to treat CD in pregnancy, and surgery is usually the first option for treating Cushing's, but many pregnant women are not candidates for surgery. How serious CD is in pregnancy can even be tricky to detect. "Cushing syndrome in pregnancy itself presents high risk for both mother and the fetus, including fetal loss, gestational diabetes, preeclampsia, and fetal growth restriction," Theodorou says. "Cortisol normally rises during pregnancy, making it difficult to use the standard non-pregnant reference ranges to assess disease severity."

In the two cases Theodorou and Geer write for JCEM CR, they describe using metyrapone, a drug that has not been approved by the U.S. Food and Drug Administration for pregnant women. Theodorou says that this choice wasn't made without careful consideration. "In these cases, metyrapone was chosen, but it introduces concerns such as potential increases in blood pressure and hypokalemia, which require careful monitoring," she says. "Metyrapone also raises theoretical concerns for fetal virilization by increasing androgen levels, and also neonates must be monitored for adrenaline sufficiency and stress-dose glucocorticoids should be considered during labor."

Theodorou goes on to explain that metyrapone at the time was the most commonly used agent in other similar case reports without any significant adverse events. Other agents used in pregnancy were cabergoline and ketoconazole. "However, cabergoline was mainly administered in patients with prolactinomas, and it's not also effective in cortisol levels," she says. "And ketoconazole has known teratogenic and androgenic effects. Other treatment options were not available or not used at the time, so metyrapone was the most reasonable choice."

So, to the two cases: The first case is that of a 31-year-old woman with recurrent CD who gave birth to twins while on metyrapone. Uneventful pregnancy, healthy twins at 37 weeks. But postpartum she developed hypertension but resolved spontaneously, and she remained on metyrapone. The second case involves a 29-year-old woman with recurrent CD since adolescence, who conceived naturally on metyrapone. But postpartum, she developed preeclampsia, which required temporary antihypertensive therapy.

"Although we had in mind that cortisol levels naturally increased during pregnancy, the clinical well-being of both mother and fetus were taken into account for these decisions. **This example shows that each case should be evaluated separately, always having in mind the clinical well-being of the mother and the fetus."**

— ANGELIKI THEODOROU, MD, DIVISION OF ENDOCRINOLOGY, DEPARTMENT OF MEDICINE, MEMORIAL SLOAN KETTERING CANCER CENTER, NEW YORK, N.Y.

The two cases, while similar, also speak to the importance of tailored medicine. In the first case, the woman required a lower dose of metyrapone, while in the second case, the woman required a higher dose. Theodorou says that in the first case, metyrapone doses were decreased when urinary cortisol excretion was repeatedly in normal range — the non-pregnant normal range. But in the second case, doses remained unchanged with cortisol values above the upper limit. "Although we had in mind that cortisol levels naturally increased during pregnancy, the clinical well-being of both mother and fetus were taken into account for these decisions," she says. "This example shows that each case should be evaluated separately, always having in mind the clinical well-being of the mother and the fetus."

Current guidelines for women with persistent or recurrent CD who want to conceive suggest bilateral adrenalectomy before conception, and again, some pregnant women might not be candidates for surgery, so Theodorou and Geer agree that it's essential to have comprehensive discussions with each patient about the potential risks and benefits of all treatment options. "And if surgery is not an option, metyrapone is a viable option for managing Cushing," Theodorou says. "However, it requires careful monitoring, and those adjustments, and of course, management, should be individualized."

A Case of Metastatic Choriocarcinoma-Related Paraneoplastic Thyroid Storm

Nidhi Gupta, MD, a second-year internal medicine resident at Baylor Scott and White, Temple, Texas, presented a case she and her co-authors wrote on thyroid storm due to gestational trophoblastic disease (GTD) with metastatic choriocarcinoma — a rare but potentially life-threatening endocrine emergency. A woman with molar pregnancy and metastatic choriocarcinoma presented with thyroid storm (Burch-Wartofsky point scale of 45) a few weeks after the evacuation of GTD.

Gupta had already seen a patient with a similar presentation, who passed away after much more severe complications. "But this patient we could save, and she did very well," Gupta says.

Gupta goes on to say that this patient was herself very sick, presenting with thyroid storm — a very deadly emergency — while also being treated for cancer. The patient's T3, T4, and [human chorionic gonadotropin (HCG)] levels were high while her TSH was significantly suppressed. "When she came in thyroid storm, it was more than 900,000 mIU/mL," Gupta says. "In a normal non-pregnant lady, it should be less than five mIU/mL. She was in very severe range, and this was all because of the cancer — metastatic choriocarcinoma, the cancer spread to her lungs, to her brain."

The team stabilized the patient and controlled the thyroid storm, starting her on propylthiouracil, an esmolol infusion drip, and IV fluids. "After that, we transitioned her to methimazole because the dosing is less frequent, and then it causes less impact of toxicity once the patient came out of the thyroid storm," Gupta says.

Then there came the challenge of chemotherapy. Choriocarcinoma had been diagnosed a month earlier, and biopsy results and CT scans showed metastatic lesions. Gupta and her team followed the multidisciplinary approach — endocrinologist, OB/GYN, oncology, intensivist — and they even reached out to other experts internationally. "It was an extensive chemotherapy regimen started in the ICU itself after we did the stabilization and anti-thyroid medications were given," Gupta says. "Combining these two diseases, the cancer and the thyroid storm, and timing the medications. That intricate thing was very important. It was all done by experts from our institute. And they also went out of their way to reach out to more experts so that the things are managed appropriately and in a timely manner."

However, the team suspected that the patient's cancer had low-grade resistance to the chemotherapy, prompting a hysterectomy 113 days after the initial presentation. The surgery was successful, and the patient had three more rounds of chemotherapy. "And at six months she was absolutely all right," Gupta says. "She was asymptomatic; her functional status is absolutely normal. Her thyroid function test normalized with HCGs in the normal non-pregnant range. Everything became good for her, and in the follow-up, she's doing well. There's no recurrence of relapse, which is a good thing. And all the metastatic lesions, they all resolved with the chemotherapy."

Gupta stresses that this was a team effort. The whole multidisciplinary team and even international experts came together to save this patient's life, even amidst financial challenges and insurance hurdles. A happy ending, almost.

> It's like a puzzle. You require a high index of suspicion because the pregnant patient comes in at six weeks of gestation, and then you end up managing a thyroid storm, and removing her uterus. It's a lot. **And then you learn from your senior, from the attending, everybody in the hospital, all the experts. And that's how you grow."**
>
> — NIDHI GUPTA, MD, SECOND-YEAR INTERNAL MEDICINE RESIDENT, BAYLOR SCOTT AND WHITE, TEMPLE, TEXAS

"The only sad thing is she has lost her uterus," Gupta says. "She's 38 years old, but she has one living child. We could save her life, and she is able to take care of her family. She's doing well, and everything is normal. She has not recurred; she follows up with the OB/GYN, oncology, and endocrinology. They just saw the thyroid function test, and she's doing fine with that."

Gupta says that she's excited to see more challenging cases like this one, and she's planning to apply for a fellowship in endocrinology when she finishes her residency.

"It's like a puzzle" Gupta says, "You require a high index of suspicion, because the pregnant patient comes in at six weeks of gestation, and then you end up managing a thyroid storm, and removing her uterus. It's a lot. And then you learn from your senior, from the attending, everybody in the hospital, all the experts. And that's how you grow."

Two Cases of Improved Bone Mineral Density

Lara McHan, MD, previously of the University of Rochester Strong Memorial Hospital in Rochester, N.Y., now a combined Med-Peds endocrine fellow at the University of Washington/Seattle Children's Hospital, Seattle, Wash., presented two cases of patients with fibroblast growth factor-23 (FGF23)-mediated hypophosphatemia who had low bone mineral density (BMD) at diagnosis and remarkable improvements in BMD with treatment. The first patient is a 43-year-old man who suffered years of progressive pain and multiple fractures. He was diagnosed with tumor-induced osteomalacia (TIO), a rare cause of FGF23-mediated hypophosphatemia, after imaging identified a subcutaneous left flank mass.

McHan says that one of the main challenges for this case is how rare a TIO diagnosis is. She says there are only about 1,000 cases documented in the literature, and it's not something that is taught in medical school. "If people aren't familiar with TIO, they may not connect the dots and think of that diagnosis," McHan says. "There was a retrospective review of cases that showed that the average time from symptom onset to diagnosis of TIO was about three years. For patients, that's three years of medical uncertainty, poor quality of life, seeing several different specialists, being misdiagnosed, and often receiving unnecessary or ineffective treatment."

This patient took longer to finally get a diagnosis of TIO. He had seen multiple specialists and had joint injections to manage the pain. The specialists weren't able to figure out what was going on, and the patient had multiple fractures and surgery on both sides of his hip. "If we're able to diagnose this earlier, we can prevent some of these irreversible skeletal complications that come with a diagnosis of TIO," McHan says.

Once the TIO diagnosis was made, surgeons excised the tumor, which resulted in rapid symptom improvement. McHan and her co-author and mentor Marilyn Augustine, MD, also of the University of Rochester, write that the patient experienced a 96% increase in lumbar spine (LS) BMD after surgery.

> If people aren't familiar with [tumor-induced osteomalacia], they may not connect the dots and think of that diagnosis. There was a retrospective review of cases that showed that the average time from symptom onset to diagnosis of TIO was about three years. **For patients, that's three years of medical uncertainty, poor quality of life, seeing several different specialists, being misdiagnosed, and often receiving unnecessary or ineffective treatment."**
>
> — LARA MCHAN, MD, COMBINED MED-PEDS ENDOCRINE FELLOW, UNIVERSITY OF WASHINGTON/SEATTLE CHILDREN'S HOSPITAL, SEATTLE, WASH.

The funny thing is that the patient had noticed the mass in his left flank years ago, but he just thought it was a little nodule. "It wasn't painful, never bothered him, didn't think anything of it. But then to realize that was the cause of these symptoms I think was interesting. Now he's doing really well, and his quality of life is great after treatment. By removing the tumor, he's essentially cured and just gets regular follow-up."

The second patient is a 48-year-old nonverbal man with autism and intellectual disability who had months of progressively declining mobility, presumed pain, and multiple fractures. McHan is trained in adult and pediatric medicine, so she had some experience with patients who can't voice what's wrong with them. She explains that when you have a patient who has intellectual disability and is nonverbal, you really can't rely on them to be your historian. "The history and physical exam are such important components to thinking through differential diagnosis and work up and eventually getting to what the problem is," she says. "It's really necessary to rely on caregivers in these cases to recognize new symptoms."

This patient lives in a group home and had been really active, but the staff started to notice he was sitting around more than usual and seemed to be in pain. He was admitted to the hospital and had to have surgery, but McHan says that expedited his workup when endocrine was consulted for his fracture history. He was found to have low phosphorous — something that endocrinologists are trained to test for. "We know that phosphorus is important in bone health and routine laboratory testing doesn't include phosphorus," McHan says. "If you have a patient coming in to a general provider for evaluation of nonspecific symptoms such as fatigue, weakness, and pain, they are probably not thinking to check a phosphorus. But when they are evaluated by an endocrinologist, phosphorous is part of the work-up for low BMD."

The patient was diagnosed with FGF23-mediated hypophosphatemia. McHan and Augustine write that the patient has had multiple scans over several years, but no FGF23-secreting tumor has been identified.

He has been maintained on medical treatment with phosphorous and calcitriol with improvement in functioning and 48% increase in LS BMD. "He got better pretty quickly with medical management," McHan says. "But I do wonder how long before that insult of not being able to ambulate — was he maybe having pain, weakness, fatigue that just went unrecognized because he couldn't voice those concerns? So, it is a challenge in these patients. And I am grateful that he had good caregivers who were able to notice that there was a change in his activity and demeanor."

"This is the third time we have hosted Clinical Pearls from JCEM CR, and the number of attendees is increasing each year," Young says. "The concise and intriguing case presentations are outstanding, and the astute clinical pearls from our content experts are a real treat. We are already planning for the fourth edition at **ENDO 2026** in Chicago in June!" EN

– BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT THE RELATIONSHIP BETWEEN TYPE 2 DIABETES AND LIVER DISEASE, AND HOW ENDOCRINOLOGISTS CAN TAKE THE LEAD IN TREATMENT IN THE AUGUST ISSUE.

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ENDOCRINE SOCIETY

BY GLENDA FAUNTLEROY SHAW

As an eager student in his native Ghana, Theophilus Tettey, PhD, saw firsthand how classroom theories had real-world implications. Now, as a researcher at the National Cancer Institute, he hopes to one day create a laboratory that thrives on working across disciplines while providing a welcoming environment for up-and-coming scientists.

connecting Mechanisms *to* Medicine

Q&A with Theophilus Tettey, PhD

At his PhD graduation, Tettey (second from right) is pictured with (from l to r) Ronald (Ron) Conaway, PhD, his PhD co-mentor at the Stowers Institute for Medical Research (SIMR); Leanne Wiedemann, PhD, his third-party monitor during his PhD; and Joan W. Conaway, PhD, his official PhD co-mentor and vice provost and dean of basic research at UT Southwestern.

Growing up in Ghana, West Africa, Theophilus Tettey, PhD, stood out as an exceptional student from an early age. Ghana's educational system steers high-performing students toward math and science, and teachers quickly recognized his remarkable potential. Yet, it wasn't until his undergraduate years at the University of Ghana, Legon, that his true passion for science ignited — sparked by a final-year course on the biochemistry of hormones.

Today, Tettey is a research fellow at the Laboratory of Receptor Biology and Gene Expression in the Center for Cancer Research at the National Cancer Institute (NCI). He joined the lab of Gordon Hager, PhD, in 2020 after earning his PhD at the Stowers Institute for Medical Research in Kansas City, Mo. At the Stowers Institute, Tettey's research uncovered a novel role of the histone chaperone FACT, a protein strongly linked to aggressive cancers, in RNA promoter-proximal pausing. His current work continues to probe similar mysteries.

Theophilus Tettey, PhD

"I want to create a lab that not only generates high-quality science but also trains the next generation to think across disciplines — from molecular mechanisms to translational models. **By combining genomics, chromatin biology, and in vivo systems, I hope to position my lab at the intersection of discovery and application, where insights from basic biology can be turned into strategies that improve patient outcomes."**

— THEOPHILUS TETTEY, PHD, RESEARCH FELLOW, LABORATORY OF RECEPTOR BIOLOGY AND GENE EXPRESSION, CENTER FOR CANCER RESEARCH, NATIONAL CANCER INSTITUTE, BETHESDA, MD.

> Experiencing both the classroom theory and its real-world implications side by side made a lasting impression. I realized that endocrinology wasn't just an academic subject — it was a framework for understanding how multiple systems of the body communicate, and how disruptions in that communication contribute to disease. **That connection between mechanism and medicine was what sparked my commitment to the field."**
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Tettey in the lab at the National Cancer Institute at the National Institutes of Health.

Endocrine News spoke with Tettey to learn more about he first fell in love with the endocrine specialty and his experiences as a rising, young investigator.

***Endocrine News:* When did you know the endocrinology specialty would become your life's work?**

Theophilus Tettey, PhD: The turning point came during my final year as an undergraduate at the University of Ghana. I took a course called biochemistry of hormones, and for the first time I saw how hormones function as the body's master regulators — coordinating stress responses, metabolism, growth, and reproduction. At the same time, I was interning at the Noguchi Memorial Institute for Medical Research, where I was studying immune responses to malaria in children. Experiencing both the classroom theory and its real-world implications side by side made a lasting impression. I realized that endocrinology wasn't just an academic subject — it was a framework for understanding how multiple systems of the body communicate, and how disruptions in that communication contribute to disease. That connection between mechanism and medicine was what sparked my commitment to the field.

Tettey strikes a pose with the ENDO sign at ENDO 2024 in Boston, Mass., in June 2024.

EN: What is your current research focus in Hager's lab?

Tettey: In the Hager lab, I study how mutations in the glucocorticoid receptor influence hormone signaling at both the molecular and organismal level. To do this, I combine genomics, molecular biology, and advanced imaging tools such as number-and-brightness microscopy and single-molecule tracking to observe receptor dynamics in living cells. These approaches allow us to see, in real time, how hormone receptors move, engage chromatin, and recruit cofactors to regulate gene expression. In parallel, I apply genomics and chromatin biology to map how these molecular events translate into changes in transcriptional programs across the genome.

Alongside the cell-based work, I also use genetically engineered mouse models to understand how specific receptor mutations affect whole-body physiology, from stress hormone regulation to development. By bringing together live-cell imaging, genomic profiling, and in vivo models, my research aims to connect single-molecule events with systemic outcomes. Ultimately, this integrated approach provides insight into why certain hormone receptor mutations cause resistance to therapy and how we might design strategies to restore function.

EN: Does any of your current research deal with what would be considered rare endocrine disorders?

Tettey: We recently completed a study of a family with glucocorticoid resistance, a rare endocrine disorder caused by a novel NR3C1 gene mutation. It leads to glucocorticoid insensitivity, HPA axis hyperactivity, hypertension, androgen excess, and poor cortisol suppression. Our work could also inform eventual treatments. We created the first patient-derived NR3C1 CRISPR knock-in mouse model, which mirrors the patient phenotype and provides a preclinical tool to test therapies such as selective glucocorticoid receptor modulators, gene editing, or targeted small molecules aimed at restoring function and reducing symptoms.

EN: How did you first get connected with the Endocrine Society?

Tettey: My first connection was through the FLARE Award in 2024, which gave me the opportunity to attend the **ENDO** meeting and present my work. Being there, surrounded by clinicians and basic scientists working on different aspects of endocrinology, was inspiring. It showed me how discoveries in the lab directly connect to human health, and it made me feel part of a larger scientific community.

EN: You're in the early stages of your career as an investigator. Where do you see yourself in five or 10 years?

Tettey: I see myself leading an independent research program that connects hormone biology, genomics, and advanced imaging with questions directly relevant to human disease. My focus will be on understanding how stress and hormone signaling reshape the genome and contribute to disorders such as cancer and endocrine resistance.

Equally important to me is building a team environment where young scientists can thrive. I want to create a lab that not only generates high-quality science but also trains the next generation to think across disciplines — from molecular mechanisms to translational models. By combining genomics, chromatin biology, and in vivo systems, I hope to position my lab at the intersection of discovery and application, where insights from basic biology can be turned into strategies that improve patient outcomes.

EN: That segues into the current challenges facing scientists. How do you and your colleagues stay motivated and focused on your goals?

Tettey: I focus on what I can control — advancing projects, sharing results, and building collaborations — while also maintaining balance outside the lab. Time with family and hobbies such as soccer, chess, or playing guitar gives me the energy and perspective to return ready to tackle the next challenge. EN

– SHAW IS A FREELANCE WRITER BASED IN CARMEL, IND. SHE IS A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS* AND WRITES THE MONTHLY LABORATORY NOTES COLUMN.

A new pharmacological treatment could provide hope for hypoparathyroidism patients

FOLLOWING UP

Approved a little more than a year ago by the U.S. Food and Drug Administration, palopegteriparatide was lauded by a panel of experts from around the world in a recently published consensus statement on hypoparathyroidism treatment. Aliya Khan, MD, FRCP, FACP, talks to *Endocrine News* about what this means for these patients' treatment options, quality of life, and other pharmaceuticals on the horizon.

BY DEREK BAGLEY

In August 2022, Aliya Khan, MD, FRCP, FACP, professor of clinical medicine at McMaster University in Ontario, Canada, shared the good news of the molecules that were being investigated and in development to treat hypoparathyroidism — an often-debilitating disease that robs quality of life, impacting both physical and psychological aspects of everyday life. That good news came on the heels of the 2022 Global Hypoparathyroidism Guidelines, which Khan co-authored.

By 2024, Khan was able to share stories of patients who had participated in Phase 3 clinical trials investigating the drug palopegteriparatide: an operating room nurse who had a total thyroidectomy and developed hypoparathyroidism, thoughts so muddled she had to go on disability; a construction worker whose dream was to build houses but was bedridden; a young patient whose calcium was so low he had seizures and was hospitalized time and time again with kidney stones.

On August 12, 2024, the U.S. Food and Drug Administration approved palopegteriparatide for use in adults with hypoparathyroidism. The drug is a sustained release prodrug of active parathyroid hormone (PTH [1-34]) administered once daily. Ascendis Pharma funded the trial and markets the drug as TransCon PTH. The medication is also sold under the brand name Yorvipath.

This past June, Khan and her co-authors published updated recommendations titled "Best Practice Recommendations for the Diagnosis and Management of Hypoparathyroidism" in the journal *Metabolism*. The new recommendations, convened by an international panel of experts, builds upon the 2022 Global Hypoparathyroidism Guidelines through a structured, consensus-based process. These updates provide practical guidance regarding evaluation and management based on new findings and provide a framework for improving patient care, monitoring protocols, and the use of PTH replacement therapy with palopegteriparatide for chronic hypoparathyroidism.

One surprising result that revealed itself during this guideline-writing process was the improvement in renal function. "The degree of improvement in kidney function was phenomenal," Khan says. "What we have seen in patients who have been treated with this medication is it's a life-changing event."

> It was not expected that this would have such a huge impact on kidney function. And we feel that it's probably multiple factors. We know that palopegteriparatide drops the urine calcium, **and a high urine calcium is detrimental for kidney function, but we're also getting these patients off their active vitamin D and their calcium supplements."**
>
> — ALIYA KHAN, MD, FRCP, FACP, PROFESSOR OF CLINICAL MEDICINE, MCMASTER UNIVERSITY, ONTARIO, CANADA

"We felt that we needed to do this because now we actually have an approved drug for hypoparathyroidism, and we wanted to provide information as to when to use it, how to use it, how to start therapy, how to manage therapy," Khan says.

Lessons Learned

Until fairly recently, patients with hypoparathyroidism were treated with active vitamin D and calcium, but that treatment can increase the risk of long-term complications because it can further elevate phosphate, which can cause calcium and phosphate to deposit in the brain, behind the eyes, and in the kidneys, which can cause nephrocalcinosis, with the whole renal parenchymal calcifying.

Khan again touts the benefits of palopegteriparatide over the conventional therapy mentioned above. She says that patients are able to come off their calcitriol, they're able to reduce their calcium supplements to 600 milligrams or less, and they're able to have a significant improvement in quality of life.

One surprising result that revealed itself during this guideline-writing process was the improvement in renal function. "The degree of improvement in kidney function was phenomenal," Khan says. "What we have seen in patients who have been treated with this medication is it's a life-changing event."

Khan says that patients who started palopegteriparatide had improvements in kidney function by five, 10, or even 14 mils per minute. "It was not expected that this would have such a huge impact on kidney function," she says. "And we feel that it's probably multiple factors. We know that palopegteriparatide drops the urine calcium, and a high urine calcium is detrimental for kidney function, but we're also getting these patients off their active vitamin D and their calcium supplements.

"Not only is palopegteriparatide helping them, it also has vasodilatory effects, so it may be helping the kidney, but also getting them off the conventional therapy and is preserving and improving renal function," Khan continues. "And that was a very important lesson to learn."

Quality of Life

And of course, quality of life is a huge concern for these patients. After participating in that Phase 3 trial investigating palopegteriparatide, the

PHOTO: Shidlovski/Shutterstock.com

operating room nurse returned to work; the construction worker reported that he was building his fifth house; the young patient's kidney stones vanished.

The mental health components of these treatments can't be overlooked. "In the questionnaires, one of them was SF-36, that evaluates overall well-being and function and also the hypoparathyroidism patient experience scale, and what we found was a significant improvement in quality of life," Khan says. "This would also include improvements in anxiety, in symptoms of depression, in overall well-being. This was really a game changer."

Individualized Medicine

The authors of the new recommendations write that they are intended to guide individualized, decision making across diverse patient populations and clinical contexts. "The recommendations address practical clinical concerns including postsurgical risk assessment, genetic evaluation in nonsurgical [hypoparathyroidism], comprehensive management of complications, sick day protocols, dose titration with PTH therapy, transitioning between conventional therapy and PTH, as well as considerations for pregnancy, lactation, and care of children," the authors write.

Khan says that these recommendations were endorsed by 25 international societies — an international working group that represented several major endocrine societies around the world. According to Khan, during a one-day meeting at the Parathyroid Summit, the writing group reviewed and discussed all of the complications of hypoparathyroidism and came up with recommendations for management. "We addressed pregnant women, we addressed children, we addressed adults," Khan says. "We have specific recommendations for children and specific recommendations for pregnant women, because there are changes that happen during pregnancy."

For example, the breast and the placenta produce parathyroid hormone-related protein (PTHrP), which then causes increase in endogenous calcitriol. "Now this pregnant woman has her own PTHrP and 125-D, so her requirements for calcitriol may change, but she also has a developing fetus," Khan says. "The requirements may increase, or they may go down, or they may stay the same. The only way we'll know is if we monitor these people very closely. And we recommend that in a pregnant woman, that we check the lab profile every three to four weeks to make sure that we're keeping that calcium normal."

"Because in pregnancy, if we run the calcium high, the baby's parathyroid glands won't develop," Khan continues. "And if we run the calcium low, then the baby's parathyroid glands become overactive. And so it's important that we run that calcium normal, and it can be a changing target during the woman's pregnancy."

Looking Ahead

Khan and her co-authors also point to emerging therapies to treat hypoparathyroidism. The drug eneboparatide — currently in Phase 3 clinical trials — is also a long-acting PHT, PHTrP analogy, and Khan says this molecule has also been shown to be of tremendous benefit in hypoparathyroidism.

For now, Khan says that palopegteriparatide is a major advance in currently available treatments, but the future is looking bright. "We are very enthusiastic that this option is available, and we expect to have other options in addition with eneboparatide. There are other options that will become available over the next five years. But right now, the fact that we can achieve improvements in renal function, quality of life, normalize urine calcium, and serum calcium, and normalize phosphate, it's huge." EN

– BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT THE RELATIONSHIP BETWEEN TYPE 2 DIABETES AND LIVER DISEASE, AND HOW ENDOCRINOLOGISTS CAN TAKE THE LEAD IN TREATMENT IN THE AUGUST ISSUE.

A recent clinical trial reveals encouraging news for a Cushing's disease treatment.

Staying in CONTROL

A poster from **ENDO 2025** showed that osilodrostat provides sustained clinical benefits in Cushing's patients who experienced positive outcomes by the end of the treatment period. Richard Auchus, MD, PhD, discusses how the data reinforce the drug's use, which was well-tolerated for extended periods.

BY DEREK BAGLEY

Not that long ago, the only way to treat Cushing's disease was through surgery. This isn't news to anyone reading this. But many patients with Cushing's — especially after long-term illness — become too sick for surgery. Risk of blood clots, infections. And then there's the myopathy that might not be resolved.

During **ENDO 2025** in San Francisco, Calif., Richard Auchus, MD, PhD, a professor of internal medicine in the Division of Metabolism, Endocrinology and Diabetes at the University of Michigan in Ann Arbor, presented encouraging findings from the LINC rollover study on the long-term safety and effectiveness of the medication osilodrostat in patients with Cushing's disease.

The study demonstrated that osilodrostat — an 11β-hydroxylase inhibitor — provides sustained clinical benefits, with the majority of patients continuing to experience positive outcomes by the end of the treatment period. The data reinforce existing evidence of the favorable safety profile of osilodrostat, highlighting its well-tolerated nature during extended use. The study reported low discontinuation rates due to treatment-related adverse events, and no new safety concerns were identified. The results come from the LINC study — a series of Phase 3 trials studying osilodrostat.

"This is a very potent inhibitor of 11β-hydroxylase and aldosterone synthase," Auchus says. "It's quite effective in treating cortisol excess. And it is, I think, now the most popular cortisol synthesis inhibitor that's used."

Durable Effects

Even when patients with Cushing's have surgery, there's no guarantee of a cure. Auchus tells *Endocrine News* of a patient he treated who had surgery, but Cushing's didn't resolve, so the patient entered the LINC study and remained on osilodrostat for seven years through the extension phase. He was imaged periodically and the tumor returned, but this time, surgery did the trick. "We were able to cure him," Auchus says. "And I don't think it was that unexpected because that's what we saw in the course studies, that the effects [of osilodrostat] are durable."

Auchus explains that sometimes there is no choice but to treat people with medication preoperatively in order to get these patients' cardiovascular and musculoskeletal status in a state where they can survive the surgery. "Even the skin thinning causes the wounds to tear," he says. "If you rehab them for a period of time with medical therapy, then they have less risk of having complications when they go to surgery."

Staying in Control

According to Auchus, osilodrostat was developed as an aldosterone synthase inhibitor, but the selectivity over 11β-hydroxylase, two enzymes that are 93% identical, was not

Richard Auchus, MD, PhD

> I like to tell people normal is normal. We want people not to just be okay, we want them to be normal, **and how can we use these tools in the best way to make people as close as possible to where they should be without the disease?"**
>
> — RICHARD AUCHUS, MD, PHD, PROFESSOR, INTERNAL MEDICINE, DIVISION OF METABOLISM, ENDOCRINOLOGY & DIABETES, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICHIGAN

high enough for it to be administered for treating hypertension without affecting cortisol, so the drug was repurposed for treating Cushing's, and the trials began.

LINC 3 was a randomized withdrawal trial in which all participants were put on osilodrostat with the primary endpoint being the loss of control during that randomized withdrawal period. Auchus says that the FDA wanted a placebo-controlled trial as well, so LINC 4 became the first placebo-controlled trial from the beginning that was ever done for Cushing's.

"It turns out that we learned a lot from LINC 3, and we were able to titrate the medication more safely by taking our time and using fewer steps. Because the drug is so potent, we didn't really have to go up very high in most people," Auchus says. "Based on the information we learned from LINC 3, we conducted LINC 4 very effectively and really showed a tremendous difference."

Researchers are now on to LINC 6, a long-term efficacy trial for people who have been on osilodrostat long term. "It's all about the long-term safety and efficacy," Auchus says. "And the thing about osilodrostat that was borne out both in the core studies from LINC 3 and LINC 4, the extension phase, and even from LINC 6, is that when people are controlled, they don't escape control, they stay in control."

The Work Continues

For now, osilodrostat is dosed twice a day, although Auchus says there are researchers looking at whether the drug can be taken just once a day, or even switching up dosing depending on the severity of the

disease. "The urinary free cortisol is the primary endpoint, but cortisol is supposed to follow a circadian rhythm," he says. "Now, just getting the urinary free cortisol to normal may not be good enough, so people are experimenting with asymmetric dosing."

"By giving it once daily, you start to emulate the circadian rhythm and sleep improves," Auchus continues. "As we get these new tools and we show that they are safe and effective, now it's time for us to use them more effectively and to try to do even better than just normalizing the urinary free cortisol."

Auchus says that when he was a fellow, there were no drugs to treat Cushing's, no interest even from the industry. There is, of course, interest now. Osilodrostat was approved by the FDA in 2020. (Recordati Rare Diseases, Inc., markets the medication as ISTURISA®.) And while osilodrostat is promising, Auchus is careful to say it's just like any other medication; it can have serious side effects. For example, Auchus says, osilodrostat is so potent that you can easily overtreat people and cause adrenal insufficiency.

Still, the drug seems promising for patients with Cushing's disease — people who can't sleep or have myopathy so bad they can't climb stairs or even sometimes lift themselves off the floor. So, the work continues. Several drugs are still being studied or in development. "I think it's great for patients, but I think we are going over a very short period of time to using off-label kind of seat-of-the-pants things to using highly effective drugs," Auchus says. "But now it's like, how can we do even better than that? Because I like to tell people normal is normal. We want people not to just be okay, we want them to be normal, and how can we use these tools in the best way to make people as close as possible to where they should be without the disease?" EN

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Endocrine Society Rallies for Medical Research

Endocrine scientists take the Capitol by storm! We thank our members and Pediatric Endocrine Society members who came to Washington to participate in the Rally for Medical Research and visited their congressional delegations to share the value of NIH research and the need to protect its funding. Pictured above: (front row, l to r) Maigen Bethea, Jeanie Tryggestad, and Christy Foster; (back row, l to r) Ronald McMillan, Lee Kraus, Dolores Lamb, Alvin Powers, Damian Romero, and Monica Laronda.

As this issue of *Endocrine News* goes to press, the U.S. House of Representatives and Senate are not close to agreement on an appropriations bill that would fund the Department of Health and Human Services, the National Institutes of Health (NIH), and other federal health agencies for fiscal year 2026, which begins on October 1. Consequently, a partial federal government shutdown appears likely.

Congress is required to fund the federal government by September 30. In September, with the funding deadline looming, Democrats and Republicans could still not agree on final funding numbers and were at odds over specific policy provisions that included adding funding for security for the White House, Supreme Court, and Congress in the wake of violent incidents; extending tax subsidies for people who obtain health insurance from the Affordable Care Act; and restoring cuts to Medicaid. On September 19, the House passed a short-term funding bill to continue funding the NIH and other health agencies (as well as other parts of the federal government), but the Senate could not pass the House-passed, Republican-led measure. The Senate subsequently tried to pass a Democratic alternative, but that failed as well. Then, both chambers recessed until October 1 leaving no time to negotiate a compromise.

Funding for the NIH is a top priority of the Endocrine Society. As a result of our advocacy, the bills that were under development in both the House and Senate stripped away harmful provisions including arbitrary caps on indirect costs, imposing a massive restructuring of the NIH, and forward funding of grants.

In September, the Society ramped up its advocacy to urge Congress to protect the NIH and complete the appropriations process. On September 18, the Endocrine Society joined over 400 scientific, medical, and patient advocacy organizations to rally for medical research and visit congressional offices and to urge them to protect NIH funding. We also launched a new online advocacy campaign to amplify our Hill Day message. In addition, we led a group of over 70 scientific, medical professional, and patient advocacy organizations in urging Congress to protect the NIH.

“Funding for the NIH is a top priority of the Endocrine Society. As a result of our advocacy, the bills that were under development in both the House and Senate stripped away harmful provisions including arbitrary caps on indirect costs, imposing a massive restructuring of the NIH, and forward funding of grants.”

We will keep our members informed. Please visit **www.endocrine.org/advocacy/take-action** for the latest updates.

Endocrine Society Submits Comments on the Medicare Physician Fee Schedule Proposed Rule

The Endocrine Society submitted comments to the Centers for Medicare and Medicaid Services (CMS) regarding the Medicare Physician Fee Schedule (MPFS) proposed rule for Calendar Year 2026. This rule, which is published annually, updates the payment policies and payment rates for Part B services furnished under the MPFS. This year's rule has an increase of approximately 3% for endocrinology, but that increase is negated by other policies in the rule that put downward pressure on physician payment. Our letter encourages CMS to work with Congress to develop solutions to provide long-term sustainability to the MPFS. The Society has urged Congress to pass legislation providing an annual inflationary update to the MPFS tied to the Medicare Economic Index (MEI).

The rule includes a proposal to change the methodology for the allocation of indirect practice expense (PE) within the physician payment formula, which would decrease the portion of the facility PE relative value units (RVUs). The Society urged CMS not to finalize this proposal and expressed concerns about how this would impact our members in private practice and our members who practice in larger institutions but still incur indirect costs such as paying rent and other costs associated

with billing and scheduling. The rule also proposes to reduce the work RVUs for non-time-based services provided by physicians. The agency argues that this proposal is necessary because the onset of medical technology has automatically improved efficiency. We also urged CMS to not finalize this proposed change noting that because of the onset of various diabetes technologies including continuous glucose monitors (CGMs) and insulin pumps, endocrinologists need more time to analyze and review diabetes-related data at each patient visit.

The rule also includes a Request for Information (RFI) on the prevention and management of chronic disease. We expressed

TAKE ACTION

Endocrine Society Continues Advocacy to Support the Treat and Reduce Obesity Act (TROA)

The Endocrine Society is urging members of Congress to cosponsor the Treat and Reduce Obesity Act (TROA). This legislation would allow Medicare to cover FDA-approved anti-obesity-medications (AOM), which are scientifically proven to be effective, and to expand access to Intensive Behavioral Therapy (IBT) for Obesity, which is an effective lifestyle intervention for treating obesity.

The Society has endorsed this legislation, and it is critical that your senators and representatives hear from you about the importance of cosponsoring TROA. Endocrine Society members are encouraged to take action to share the importance of cosponsoring this legislation. Visit **www.endocrine.org/advocacy/take-action** to join our campaign.

our concerns about the ongoing obesity epidemic and urged the agency to find ways to remove barriers in accessing obesity treatment and care including intensive behavioral therapy (IBT). We also commented on proposed changes to the Medicare Diabetes Prevention Program (MDPP) supporting the agency's proposal to expand virtual care options for beneficiaries with prediabetes. The Endocrine Society staff worked closely with the Clinical Affairs Core Committee (CACC) to draft our comments.

MAHA Commission Releases Strategy Focused on Children

The Make America Healthy Again (MAHA) Commission released the Make Our Children Healthy Again Strategy on September 9. The MAHA Commission is tasked with investigating and addressing the root causes of America's escalating health crisis, with a focus on childhood chronic diseases. The strategy outlines 120 initiatives focused on factors like diet, environmental contaminants, lack of physical activity, and "overmedicalization" to align with Secretary of Health and Human Services Robert F. Kennedy Jr.'s policy priorities and strengthen private-sector collaboration.

The strategy report has drawn mixed reactions from researchers and public health advocates who note that its goals stand at odds with other recent administration moves such as cuts to food assistance, Medicaid programs, scientific research, and Kennedy Jr.'s push for changes in vaccine policy. Many also noted that while they agree that the rise in chronic diseases must be addressed, the strategy report offered few details or specific legislative efforts.

Several topics and proposals in the MAHA strategy focus on policy issues of importance to the Endocrine Society. Some examples of where the report is consistent with Endocrine Society policies and areas where we disagree are below.

- Regarding chemicals, we were pleased to see that the strategy references the importance of cumulative/mixture exposures, which often are not accounted for in regulatory strategies. It also is consistent with our view that childhood is a uniquely sensitive life stage, including endocrine disruption, and it cites the Endocrine Society's Scientific Statement on Endocrine-Disrupting Chemicals (EDCs). The strategy report also notes the health effects of phthalates and bisphenols. However, the strategy report argues against regulation of pesticides and fails to note that federal funding of science is the best way to gather unbiased results.

- In sections focused on childhood behavior and the "overmedicalization" of kids, the strategy report highlights the connection between nutrition/physical fitness and obesity and diabetes. It also proposes to increase oversight of direct-to-consumer advertising violations related to prescription drug advertising laws and notes that this will include social media influencers and telehealth companies, an issue the Society has also raised concerns about. However, the strategy report also repeats inaccurate information about vaccines, which the Society has joined with other medical professional societies to protect. EN

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- The Business of Healthcare
- Identifying Your Natural Leadership and Communication Styles

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Spend a year serving on one of the Endocrine Society's governance committees. Interns gain firsthand leadership experience and help shape the Society's programs.

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Connect with accomplished clinicians, build lasting relationships, and receive guidance for your career growth.

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ENDOCRINE SOCIETY

In the Comfort Zone

Emerging technologies and innovative equipment are prioritizing comfort in endocrine laboratories, enhancing both efficiency and staff well-being.

COMPILED AND WRITTEN BY COURTNEY CARSON

Endocrine labs demand intense focus and precision, but long hours at the bench can lead to fatigue, strain, and reduced efficiency. Today's lab equipment manufacturers are addressing these challenges with innovative products designed to improve ergonomics and overall comfort. Here, we take a look at some of the products helping scientists and technicians perform at their best while protecting their health.

BioGrip by BioFit

BioGrip by BioFit aims to reduce strain and improve focus by bringing ergonomic seating to technical workspaces. This chair features antimicrobial, chemical-resistant materials with seamless edges for easy cleaning. Height, tilt, and back adjustments allow users to maintain proper posture for hours at microscopes, benches, or computer stations. Glove-friendly controls mean adjustments can be made without disrupting sterile protocols.
www.biofit.com

QX600 Droplet Digital PCR System

Repetitive pipetting can lead to thumb and wrist injuries, but Eppendorf's PhysioCare Concept pipettes — including the Research Plus and Move It series — help minimize these risks. An ergonomic shape supports a natural grip, while an innovative spring system reduces pipetting forces by up to 50%. These pipettes also feature clear volume displays to reduce errors during sensitive testing of high-volume workflows.
https://corporate.eppendorf.com

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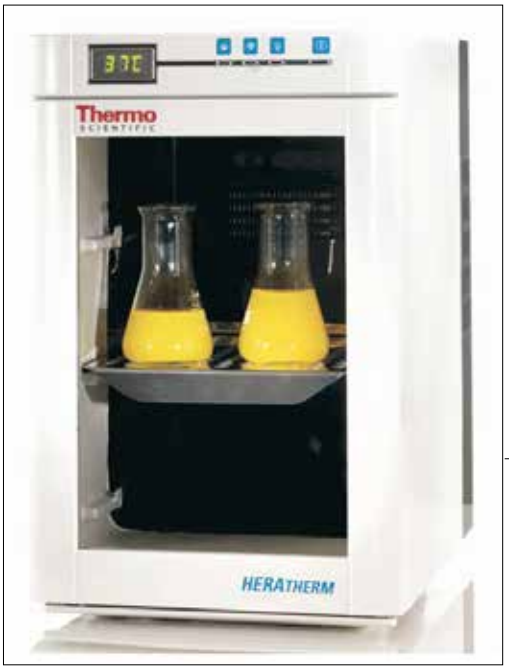

Thermo Scientific Heratherm Compact Microbiological Incubators

The Heratherm Compact Microbiological Incubators from Thermo Scientific integrate user friendly design with advanced performance. Highlights of this incubator include intuitive touch-screen controls and noise-dampening features designed to promote quieter, more efficient workspaces. This incubator offers clear displays to reduce eye strain and ergonomic handles to enhance operator comfort, while the compact footprint saves valuable bench space in busy labs. **https://www.thermofisher.com**

OHAUS Frontier 5000 Series Microcentrifuges

In high-focus laboratory settings, excessive noise can be a major distraction. The OHAUS Frontier 5000 Series Microcentrifuge addresses this challenge with exceptionally quiet operation and advanced vibration control. In addition, its sleek, space-saving design makes this centrifuge a welcome addition to a crowded lab environment, while intuitive, user friendly controls aim to minimize strain allowing technicians to work more efficiently. **https://us.ohaus.com**

LED Task Lighting with Adjustable Color Temperature

Visual strain is another hidden challenge in the lab. Featuring cooler tones ideal for detailed pipetting and warmer settings for data review, LED task lighting from Luxo offers adjustable brightness and color to match specific tasks. Flexible arms and compact bases allow precise positioning to reduce glare and minimize eye fatigue, creating an environment that supports comfort and accuracy over extended periods of time at the bench. **https://glamox.com/luxo**

Comfort in the lab goes far beyond personal well-being — it plays a vital role in accuracy, safety, and the quality of results. By equipping endocrinology labs with modern, ergonomically designed tools like these, teams can work more efficiently and precisely, creating an environment where researchers excel in their efforts to provide patients with the most advanced treatment options available. EN

– CARSON IS A FREELANCE WRITER BASED IN BIRMINGHAM, ALA., AND HAS BEEN PROVIDING *ENDOCRINE NEWS* WITH VARIOUS TRAVELOGUES, ENDOGEAR COLUMNS, AND MORE FOR SEVERAL YEARS.

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