

OCTOBER 2026

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

Closing Windows of Vulnerability

How early EDC exposure can shape the brain, bones, and hormones — and what can be done now.

TRUST IN THE FEED:

How Sehrish Waheed, MD, turns social media into a tool for stronger patient connections one post at a time

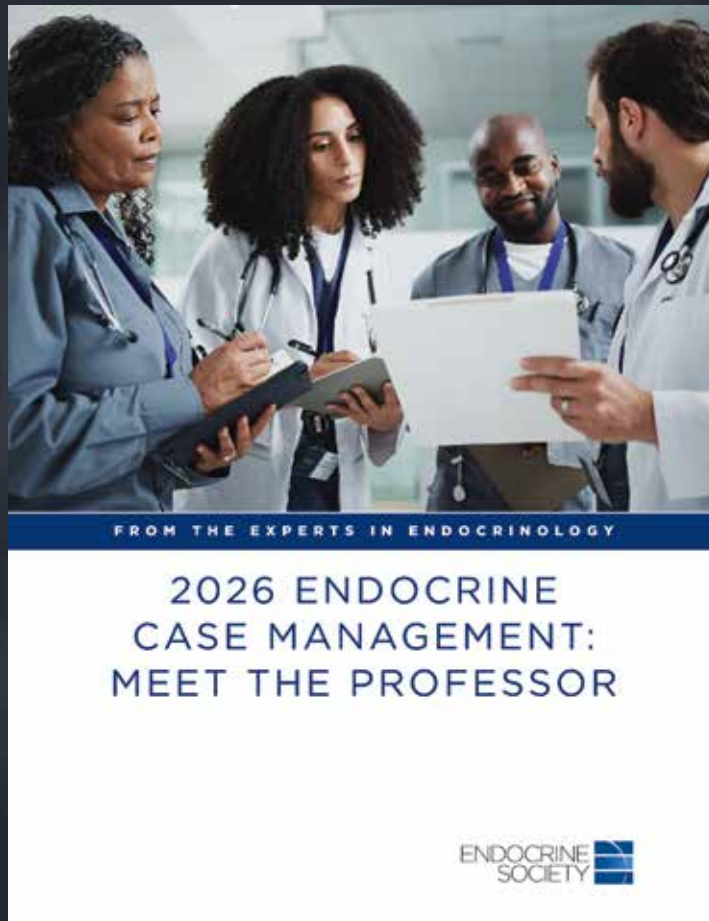
LOW ALP? THINK HPP: Clinical pearls for closing the diagnostic gap in hypophosphatasia

WHERE CARE MEETS

CALLING: Lisa B. Nachtigall, MD, on pituitary care, patient education, and mentoring the next generation

A FAMILY DIAGNOSIS: A look at how one family has been impacted by X-linked hypophosphatemia





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EDC Exposure During Development

Early-life exposure to endocrine-disrupting chemicals may affect brain function, bone development, and hormonal programming during periods of heightened vulnerability. Three studies examine these risks and identify individual, clinical, regulatory, and product-design strategies that may reduce exposure or mitigate consequences.

BY KELLY HORVATH



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A “Family Diagnosis”

X-linked hypophosphatemia can remain undiagnosed across generations when symptoms are mistaken for normal childhood development or ordinary family traits. Here, we look at diagnostic barriers, the importance of testing and genetic counseling, and how identifying one patient can prompt a cascade of family diagnoses.

BY KELLY HORVATH

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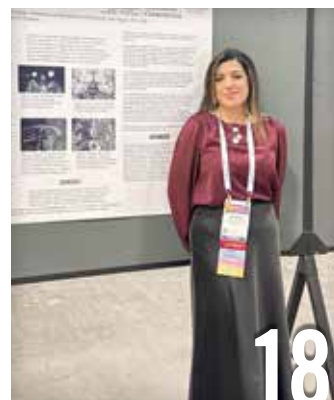
Clinical Pearls in Hypophosphatasia

On behalf of Endocrine Society’s Bone and Mineral Special Interest Group Steering Committee, Anika Anam, MD and Azarmindokht Khosravi, MD, discuss the diagnostic gap in hypophosphatasia (HPP) and preview the SIG’s upcoming October 29 webinar on hypophosphatasia ahead of World HPP Day on October 30, 2026.

BY ANIKA ANAM, MD, AND AZARMINDOKHT KHOSRAVI, MD

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ENDO2027



Mark your calendars for ENDO 2027, taking place June 5–7, 2027, in the beautiful city of Toronto, ON, Canada. The leading global meeting on endocrine research and clinical care will offer a comprehensive education program, vibrant networking events, and cutting-edge innovations. Plan to join us at ENDO 2027 for an unforgettable experience of science, connection, and discovery!



Inaugural EndoForum Live 2027 to Present the Best of Society's SIGs

It's one of my favorite member benefits. The Society's Special Interest Groups – or SIGs as they're affectionately known – bring together peers from around the world who share common clinical, research, or career interests.

Each year, the 12 existing SIGs (see list below) offer a broad range of educational and networking opportunities, including widely attended webinars and lively discussions on EndoForum, our online member-engagement platform.

“

And unlike traditional webinars, where attendees simply listen, EndoForum Live invites you to get involved by asking questions, exchanging ideas, and contributing to meaningful discussions with colleagues across the endocrine community.

”

These events have become so popular, in fact, that our Society staff had the great idea of bringing together some of the SIGs for a full day of integrated programming: thus, the inaugural **EndoForum Live 2027**.

This free, virtual members-only event takes place January 23, 2027, from 9:00 AM to 2:00 PM ET. The programming, designed by each participating SIG, promises something for all attendees, no matter their endocrine specialty.

And unlike traditional webinars, where attendees simply listen, EndoForum Live invites you to get involved by asking questions, exchanging ideas, and contributing to meaningful discussions with colleagues across the endocrine community. All discussions and resources from the event will remain available in EndoForum for further conversations.

Full event details will be coming soon, but here is a sneak peek of some of the topics that will be discussed. Session titles include:

Explore the SIGS

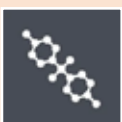
The Society currently has 12 SIGs covering a wide range of subject areas. I invite you to explore the communities and select one or more that suit your interests.



ADRENAL AND PITUITARY SIG: Connect with fellow endocrine experts, from bench to bedside, on the latest in adrenal and pituitary science and clinical care.



BONE & MINERAL SIG: Collaborate and connect with peers on clinical care and research related to bone and mineral metabolism and disorders.



ENDOCRINE-DISRUPTING CHEMICALS SIG: Hear from colleagues on the impact of endocrine-disrupting chemicals (EDCs) and the latest on how we can overcome them.



ENDOCRINE CANCERS SIG: Discuss advancements in understanding and treating endocrine cancers and collaborate with colleagues on the best avenues for care.



ENTREPRENEURSHIP SIG: Share and discuss best practices within the innovation and industry space with other entrepreneurial members of the Society.



MEN'S HEALTH SIG: Join this collaborative community to foster collaboration and advance knowledge in men's health, including male hypogonadism and infertility.



NEUROENDOCRINOLOGY SIG: Collaborate, share, and expand knowledge and practice with neuroendocrinology leaders in the scientific, clinical, and translational arenas.



OBESITY SIG: Participate in obesity education and networking activities, as well as leadership and program development opportunities, including webinars, event meetups, collaborative projects, and more!



ONCOENDOCRINOLOGY SIG: Gain cutting-edge knowledge on the latest advances in cancer care to understand the impact on the endocrine system and long-term treatment options for survivors.



PROFESSIONAL DEVELOPMENT & EARLY CAREER SIG: Accelerate your career by growing your peer network. Find resources and programming designed with the early-career professional in mind.



TRANSGENDER RESEARCH AND MEDICINE SIG: Discover the latest in this evolving field. Connect with scientists, researchers, and clinicians dedicated to advancing transgender research and medicine.



WOMEN'S HEALTH SIG: Engage with researchers and practitioners to exchange ideas, share knowledge, and stay informed on the latest best practices in women's health.

- ▶ Low-Risk Thyroid Cancer
- ▶ Primary Hyperparathyroidism Beyond Calcium: Understanding Skeletal Heterogeneity for Precision Medicine
- ▶ From Puberty to Menopause: Glycemic Management Across Hormonal Transitions in Girls and Women with Diabetes
- ▶ When Cortisol Testing Doesn't Make Sense: Solving the Difficult Cushing Case

▶ Practical Application of AI in Endocrinology

Given the time constraints, it's not feasible to include programming from all SIGs in the 2027 event. Society staff will work hard to ensure that future EndoForum Live events feature sessions from the full range of SIGs.

EndoForum Live is a great opportunity to help shape the future of endocrinology. I look forward to seeing you at this exciting event. ^{EN}

— Nanette Santoro, MD
Endocrine Society President



FROM THE **EDITOR**

OCTOBER 2026

Endocrine news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

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



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All in the Timing

In endocrinology, timing can be everything. The earliest windows of development can shape health for years to come, while a timely diagnosis, a trusted voice, or a committed clinician can alter the course of a patient's life. This issue of *Endocrine News* explores those pivotal moments — and the people working to make them count.

In “Closing Windows of Vulnerability: EDC Exposure During Development,” on page 22, Kelly Horvath examines how exposure to endocrine-disrupting chemicals during vulnerable stages of development may influence brain function, bone development, and hormonal programming. Drawing on three studies, it moves beyond identifying risk to consider practical ways individuals, clinicians, regulators, and product designers can help reduce exposure and lessen its consequences.

In “Building Trust, One Post at a Time,” on page 18, Sehrish Waheed, MD, talks to Glenda Fauntleroy Shaw about how social media can become more than a platform: Used thoughtfully, it can strengthen professional connections, support learning, and help build trust with patients, including those affected by obesity stigma. Her perspective offers an encouraging look at how early-career endocrinologists are shaping both practice and public conversation.

A Focus on Hypophosphatasia

► Ahead of World HPP Day on Oct. 30, we are turning our attention to hypophosphatasia with two articles on this rare disorder. Courtesy of the Endocrine Society's Bone and Mineral Special Interest Group Steering Committee, on page 34 we have a discussion of how persistently low alkaline phosphatase can be an important clinical clue in “Low ALP, Think HPP: Clinical Pearls in Hypophosphatasia” co-written by Anika Anam, MD, and Azarmindokht Khosravi, MD. This piece not only addresses the diagnostic gap, it serves as a preview for an October 29 webinar titled “Hypophosphatasia: From Molecular Mechanism to Clinical Practice.”

► X-linked hypophosphatemia can be overlooked for generations when bone and mobility problems are mistaken for normal development or inherited family traits. “X-Linked Hypophosphatemia: A Family Diagnosis” by Kelly Horvath on page 28 presents one family's

diagnostic experience and emphasizes testing, genetic counseling, and family-wide follow-up. Kelly also highlights one pharmaceutical's company efforts to support families dealing with XL HPP through a family friendly portal.

“

Together, these stories remind us that progress often begins with recognizing a critical window — then having the knowledge, tools, and determination to act.

”

And in “Where Care Meets Calling,” on page 38, our Practice Resources Q&A, 2026 Vigersky Outstanding Clinical Practitioner Award recipient Lisa B. Nachtigall, MD, talks to Glenda about her career and reflects on complex pituitary care, patient education, service, and the enduring value of early mentorship.

Together, these stories remind us that progress often begins with recognizing a critical window — then having the knowledge, tools, and determination to act. I hope this issue informs your work, sparks new questions, and reinforces the many ways endocrinology improves lives. And, as always, feel free to reach out to me for your comments, suggestions, and recommendations: mnewman@endocrine.org.

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

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Meet the 2027 Endocrine Society Laureates

The Endocrine Society today announced it has chosen 13 leading endocrinologists as winners of its prestigious 2027 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 2027**, the Society's annual meeting, being held June 5-7, in Toronto, Ontario, Canada.

The Endocrine Society's 2027 Laureate Award winners are:



Donald Patrick McDonnell, PhD

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. This year's recipient, Donald Patrick McDonnell, PhD, is a professor in the Department of Pharmacology and Cancer Biology at Duke University School of Medicine in Chapel Hill, N.C. Throughout his career, he transformed the field of steroid hormone research by revealing that hormone receptors act through complex, flexible signaling mechanisms rather than simple on/off switches. His discoveries reshaped our understanding of estrogen receptor biology, leading to the development of new targeted therapies for breast cancer, including the approved drug elacestrant (Orserdu™), and uncovering a critical link between cholesterol metabolism, estrogen signaling, osteoporosis, and breast cancer. His pioneering work has had a lasting impact on both basic science and patient care. He's served on several Endocrine Society committees and has won many Endocrine Society awards over the years, including the 2025 Baxter Prize for Entrepreneurship.



JoAnne S. Richards, MS, 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 Edwin B. Astwood, this award recognizes individuals who have made significant

contributions to the field of endocrinology via their outstanding basic science research. JoAnne S. Richards, MS, PhD, is a professor at Baylor College of Medicine in Houston, Texas, who has shaped the field of reproductive endocrinology for more than five decades through groundbreaking discoveries that advanced understanding of ovarian development, ovulation, and ovarian cancer. Her pioneering research identified key hormonal and molecular pathways that regulate ovarian function, including the role of estrogen and luteinizing hormone signaling, and led to the development of innovative mouse models that transformed ovarian cancer research. Her work continues to inform new insights into ovarian health, fertility, and conditions such as polyendocrine metabolic ovarian syndrome (PMOS) [previously known as polycystic ovary syndrome (PCOS)].



Bagher Larijani, MD
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. Bagher Larijani, MD, is a professor of endocrinology and director of the Endocrinology and Metabolism Research Center (EMRC) of Tehran University of Medical Science (TUMS) in Tehran, Iran. He is an internationally recognized leader in endocrinology whose work has advanced diabetes care, endocrine research, and medical education in Iran and beyond. As director of the EMRC, he has championed a multidisciplinary approach to endocrinology, trained generations of clinicians and scientists, and helped bridge the gap between basic and clinical research. His contributions have shaped global efforts to address diabetes, obesity, and other noncommunicable diseases while improving access to comprehensive, patient-centered care.



Mirjam Christ-Crain, MD, PhD
OUTSTANDING CLINICAL
INVESTIGATOR AWARD

This award honors an internationally recognized clinical investigator who has contributed significantly to understanding the pathogenesis and therapy of endocrine and metabolic diseases. Mirjam Christ-Crain, MD,

PhD, of the University Hospital Basel in Basel, Switzerland, has transformed the diagnosis and treatment of vasopressin-related disorders through pioneering research that has directly improved patient care worldwide. Her work established copeptin-based testing as the new gold standard for diagnosing arginine vasopressin deficiency (formerly central diabetes insipidus) and introduced innovative treatment approaches for the syndrome of inappropriate antidiuresis (SIAD). By advancing both clinical practice and scientific understanding of these disorders, her research has set new international standards and opened promising avenues for addressing their physical and psychological impacts. She served as an Editorial Board member for the Society's *Journal of Clinical Endocrinology & Metabolism* from 2020-2021.



Rebecca Adochio, MD
VIGERSKY OUTSTANDING
CLINICAL PRACTITIONER
AWARD

This annual award recognizes extraordinary contributions by a practicing endocrinologist to the endocrine and/or medical community.

Rebecca Adochio, MD, is a dedicated endocrinologist, educator, and healthcare leader whose commitment to personalized, compassionate care has improved the lives of patients across Colorado and the surrounding region. As medical director of Colorado Mountain Medical/Vail Health in Avon, Colo., she has expanded access to endocrine care, championed telehealth innovation, and led community education programs focused on diabetes prevention and management. Her exceptional clinical expertise, mentorship and unwavering dedication to patient-centered care have made her a trusted leader in endocrinology and an advocate for advancing health in her community.



Amal Shibli-Rahhal, MD
OUTSTANDING EDUCATOR
AWARD

This award recognizes exceptional achievement as an educator in the discipline of endocrinology and metabolism. Amal Shibli-Rahhal, MD, is a professor of medicine and associate dean for Student Affairs and Curriculum at the

Carver College of Medicine at the University of Iowa in Iowa City, Iowa. She is an innovative endocrinologist and nationally recognized medical educator whose leadership has advanced medical training from the classroom to clinical practice. In her current role, she has championed groundbreaking teaching methods, curriculum development, and learner mentorship, inspiring future generations of physicians, including many who have pursued careers in endocrinology. Her contributions have elevated the role of endocrinologists as leaders in medical education and earned her numerous prestigious teaching and leadership honors. She is currently a member of the Endocrine Society's In-Service Training Exam (ITE) Review Working Group and was previously a member of the Clinical Endocrine Education Committee.



Ghada El-Hajj Fuleihan, MD, MPH
OUTSTANDING MENTOR AWARD

This annual award recognizes a career commitment to mentoring and a significant positive impact on mentees' education and career. Ghada El-Hajj Fuleihan, MD, MPH, is a professor of medicine at the American

University of Beirut in Beirut, Lebanon, and a globally recognized leader in bone and mineral research whose dedication to education and mentorship has transformed clinical and translational research training across Lebanon and the Middle East. Through innovative programs at the American University of Beirut, including the NIH-funded Scholars in Health Research Program, she has trained hundreds of researchers and helped cultivate a new generation of physician-scientists working around the world. Her visionary leadership in medical education, osteoporosis research, and fellowship development has had a lasting impact on endocrinology and strengthened research capacity across the region. She is currently an Editorial Board member for the *Journal of the Endocrine Society* and a Board Representative for the Endocrine Society's Global Engagement Advisory Group.



Anuja Dokras, MD, MHCI, PhD
OUTSTANDING SCHOLARLY
PHYSICIAN AWARD

This annual award recognizes outstanding contributions to the practice of clinical endocrinology in academic settings. Annuja Dokras, MD, MHCI, PhD, is a professor at the University of Pennsylvania in Philadelphia, and

an internationally recognized leader in women's health whose pioneering research and clinical leadership have transformed the understanding and care of polyendocrine metabolic ovarian syndrome (PMOS). She established one of the first multidisciplinary PMOS centers in the United States and advanced research on the long-term health impacts of the condition, including its links to mental health and cardiovascular disease, and played a key role in developing international PMOS guidelines. Through her scientific contributions, advocacy efforts, and mentorship, she has improved care for patients worldwide and helped shape the future of PMOS research and education.



Rafael Arrojo e Drigo, PhD
RICHARD E. WEITZMAN
OUTSTANDING EARLY CAREER
INVESTIGATOR AWARD

This annual award recognizes an exceptionally promising young clinical or basic investigator. Rafael Arrojo e Drigo, PhD, of Vanderbilt University in Nashville, Tenn., is an internationally

recognized endocrinologist whose innovative research has transformed our understanding of thyroid hormone biology, diabetes, and the biology of aging. By integrating cutting-edge technologies across molecular, cellular, and whole-organism systems, he has uncovered fundamental mechanisms that regulate hormone signaling, pancreatic islet function, and metabolic health. His pioneering discovery of "age mosaicism," which revealed how aging is spatially and biologically regulated within tissues, has reshaped scientific understanding of aging and opened new avenues for research into human health and disease.



Shalender Bhasin, MD
ROY O. GREEP AWARD FOR
OUTSTANDING RESEARCH

This annual award recognizes meritorious contributions to research in endocrinology. Shalender Bhasin, MD, is a professor and chief at Brigham and Women's Hospital in Boston, Mass., and a world-renowned leader in reproductive

endocrinology whose groundbreaking research has transformed the understanding and clinical use of testosterone therapy. Through landmark clinical trials and fundamental discoveries in hormone biology, he established key standards for diagnosing and treating hypogonadism, clarified the benefits and risks of testosterone therapy, and advanced the development of new treatments for muscle loss associated with aging and disease. His influential research, clinical guidelines, and leadership have shaped endocrine practice worldwide and improved care for millions of patients. He is currently the chair of the Endocrine Society's Men's Health Special Interest Group and its Testosterone Therapy in Men with Hypogonadism Guideline Writing Committee.



Lauren Fishbein, MD, PhD
SIDNEY H. INGBAR
DISTINGUISHED SERVICE AWARD

This award recognizes distinguished service to the Endocrine Society and the field of endocrinology. Lauren Fishbein, MD, PhD, of the University of Colorado School of Medicine in Aurora, Colo., is an internationally recognized leader in

neuroendocrine cancer research, patient care, and education whose contributions have advanced the understanding and treatment of pheochromocytoma and paraganglioma. Through her extensive leadership within the Endocrine Society, groundbreaking research, and dedication to mentorship, she has strengthened the endocrine community while helping shape the next generation of clinicians and scientists. Her commitment to scientific excellence, patient advocacy, and service has had a lasting impact on both the Endocrine Society and the field of endocrinology. She's held many positions within the Society and is currently serving on the Society's Board of Directors, as a Board Representative for the Society's Advocacy and Public Outreach Core Committee and as an associate editor of *Endocrine Reviews*.



Stephanie Seminara, MD
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. Stephanie Seminara, MD, is a professor of medicine at Harvard

Medical School and chief of the Reproductive Endocrine Unit at Massachusetts General Hospital in Boston, Mass. She also directs the P50 Harvard National Center for Translational Research in Reproduction and Infertility. She is a reproductive endocrinologist and translational investigator who utilizes genetics and novel peptide probes to generate novel insights into sexual maturation and develop new diagnostic tools for reproductive disorders. The focus of her investigative program is the elucidation of hypothalamic pathways that control human reproduction, including the genetic architecture of human puberty and fertility. Seminara treats both men and women with a wide range of reproductive endocrine disorders.

Aliya Khan, MD, FRCP, FACP



OUTSTANDING LEADERSHIP IN
ENDOCRINOLOGY AWARD

This award is presented in recognition of outstanding leadership in fundamental or clinical endocrinology as exemplified by the recipient's contributions and those of his or her trainees and associates to teaching, research, and/or administration. Aliya Khan, MD, FCCP,

FACP, is a globally recognized leader in endocrinology whose contributions have advanced the diagnosis and treatment of complex metabolic bone and parathyroid disorders. Through her leadership in developing international, evidence-based clinical guidelines, pioneering work on novel therapies, and creation of a world-class metabolic bone disease fellowship program, she has improved patient care and trained a new generation of endocrine specialists around the world. Her commitment to education, research, and mentorship has left a lasting legacy in advancing endocrine care on a global scale.

Nominations for the 2028 Laureate Awards will open later this fall.



Zerihun Haile-Selassie, CAE

Zerihun Haile-Selassie Wins 2026 Nonprofit CFO of the Year Award

Endocrine Society Chief Financial Officer Zerihun Haile-Selassie, CAE, has been selected as a 2026 Nonprofit CFO of the Year for his dedication to operational excellence, innovation in finance and management, and exceptional leadership and commitment to improving accountability and financial reporting.

Haile-Selassie won the category for CFO of a large nonprofit association.

“Zerihun’s recognition is a testament to his outstanding leadership, strategic insight and dedication to the Endocrine Society’s mission,” said the Endocrine Society interim CEO Krista Kirk. “His thoughtful stewardship has strengthened our organization and positioned us for continued growth and impact. We are incredibly proud of him and grateful for the expertise, integrity, and vision he brings to our work every day.”

Haile-Selassie provides strategic leadership and oversight of the Endocrine Society’s Finance and Accounting, Information Technology, Publications & Journals, and Innovative Business Development initiatives. Throughout his four years at the Society, he has strengthened its financial stability, advanced strategic growth and long-term planning, and aligned financial stewardship with mission priorities to drive lasting impact. He is recognized as a trusted leader, partner, and mentor within the Endocrine Society and across the boards and committees he serves.

Beyond his executive role, Haile-Selassie is deeply engaged in the broader nonprofit community. He currently serves as chair of FAR (Finance Administration Roundtable), a member of the Board of Directors at GWSCPA (Greater Washington Society of CPAs), a member of the ASAE ForesightWorks Advisory Group, and a member of the Sage Intacct Nonprofit Advisory Council. He also is a 2022–2024 ASAE DELP Scholar, was recognized as a Rising Star for the 2018 Nonprofit CFO Award, and was named one of the top 25 CFOs in Maryland for 2023.

He is a Certified Association Executive (CAE) and a Certified Corporate Board Director (BCBR) from Santa Clara University Leavey School of Business.

NIH Awards Multi-University Team Over \$4M to Improve Women's Health

Backed by a new \$4.6 million award from the National Institutes of Health (NIH), several university researchers are launching a novel project to transform how medications are developed and prescribed for women.

This is the first installment of an award worth up to \$12.8 million over three years. Researchers from Rutgers, Emory, Tulane, University of Colorado Anschutz, Michigan State University, University of Michigan, and University of Utah are collaborating to accomplish this goal, which the lead scientist describes as a moon shot.

“Women experience large shifts in reproductive hormones at several points in their lifespan: puberty, pregnancy and menopause,” said Endocrine Society President **Nanette Santoro, MD**, the E. Stewart Taylor Professor, Department of Obstetrics and Gynecology at the University of Colorado Anschutz. “During reproductive years, women also undergo profound day-to-day changes in reproductive hormone levels, giving them a markedly different endocrine backdrop than men. Using state-of-the-art computational technology to examine how these changes interact with commonly used medications is a critical pathway toward supporting life-course women's health.”

Clinical trials often fail to account for the unique ways female hormones change throughout life — such as during menstrual cycles, pregnancy, birth control use, menopause and hormone replacement therapy. This oversight can lead to treatments that are less effective or cause more severe side effects in women than in men.

To bridge this gap, several researchers are collaborating to build advanced computer models that will predict how a woman's natural hormonal changes affect how medicines move through and act within the body. Their findings are expected to result in stronger research studies, advances in precision medicine and better real-world outcomes for women.

“Developing computational models that provide insights into women's health — including the consequences of disease, efficacy, and side effects of medicines — and integrate age and reproductive cycle stage is a moon shot,” said former Endocrine

Society President **Teresa K. Woodruff, PhD**, the lead investigator on this project, president emerita of MSU and an MSU Research Foundation Distinguished Professor in the Department of Obstetrics, Gynecology and Reproductive Biology at the MSU College of Human Medicine and in the Department of Biomedical Engineering at MSU's College of Engineering. “Our world-class team is taking on this project to enable a generation of healthier women.”

This award is part of a national program, the just-announced **Computational Modeling of Hormone Homeostasis Initiative**, which is a joint effort by the NIH Office of Research on Women's Health and the Division of Program Coordination,



**ENDOCRINE SOCIETY PRESIDENT
NANETTE SANTORO, MD,**

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OBSTETRICS AND GYNECOLOGY
AT THE UNIVERSITY OF
COLORADO ANSCHUTZ**

“During reproductive years, women also undergo profound day-to-day changes in reproductive hormone levels, giving them a markedly different endocrine backdrop than men. Using state-of-the-art computational technology to examine how these changes interact with commonly used medications is a critical pathway toward supporting life-course women's health.”

Planning, and Strategic Initiatives to leverage advancements in computer modeling to deepen the understanding of sex-specific hormonal biology. A total of \$21 million is being awarded to expand national research and high-impact science. The award number is 1OT2OD042764.

Research teams across the country will be developing the next generation of human-based data-driven tools that advance understanding of hormone-related health and improve care for people and communities.

Closing the Gap in Women's Metabolic Health

Metabolic conditions such as obesity, type 2 diabetes, cholesterol imbalances, and thyroid disorders are widespread in women. They also frequently co-occur with reproductive conditions like polycystic ovary syndrome (PCOS).

Because energy metabolism and female reproductive hormones directly influence each other, widely prescribed drugs — including insulin and GLP-1 weight-loss and diabetes medications — can produce different results in women depending on their individual hormone levels.

“Because female hormone levels are constantly shifting, precision medicine allows us to map out these complex interactions,” Woodruff said. “This NIH-backed initiative will create the first computationally driven clinical tool designed to guide medical care across every stage of a woman's life.”

The team will use advanced computational and modeling frameworks to accomplish five main goals:

1. Artificial intelligence will digitize and organize over 40 years of hormone research data, creating a free, publicly accessible database.
2. A standard computer model will map out a normal 28-day menstrual cycle alongside how key organs (like the liver, muscle, and fat tissues) are regulated by hormones to process nutrients.
3. Real-world patient data will expand the standard digital model to account for various groups — such as women going

through menopause or taking birth control — and specific health conditions like diabetes and obesity.

4. Lab-grown organ testing will be achieved by using human-relevant three-dimensional tissue models and mini lab-grown organoids (such as liver, muscle, and ovarian tissue) to inform, test, and verify the computer predictions.
5. Personalized treatment tools for specific medications (including metformin, insulin, and GLP-1 drugs) predicted by the computer models will help doctors better prescribe ideal doses and avoid dangerous side effects.

Public Health Impact

The final open-access computer platform will give healthcare providers practical tools to anticipate drug efficacies, prevent harmful side effects, and tailor prescriptions for female patients. Additionally, the findings will directly inform NIH guidelines, national safety standards, and clinical protocols for testing new treatments.

All computer models and data produced through this NIH initiative will be freely available to researchers and healthcare professionals worldwide upon completion.

Additional researchers include Sudin Bhattacharya, Brian Johnson, Rance Nault, and Timothy Zacharewski from Michigan State University; Shuo Xiao and Jiyang Zhang from Rutgers University; Ariella Shikanov from the University of Michigan; Endocrine Society member Corrine Welt from the University of Utah; Hao Zhu from Tulane University School of Medicine; and Mary Sammel from the University of Colorado Anschutz. 

[EDITOR'S NOTE: The content of this story was provided by Michigan State University's MSU Newsroom.]

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“The Endocrine Society is an organization focused on excellence and committed to fairness and integrity, a trusted source of information, and a hub of professional opportunities that transcend the local politics of one’s individual medical center or university. **There is much value to that, and I think the Society is beneficial to endocrinologists at every stage from the earliest phase of one’s career to the most senior.**”

Lisa B. Nachtigall, MD, the Endocrine Society’s 2026 Vigersky Outstanding Clinical Practitioner Award recipient when asked what impact the Endocrine Society has had on her career in **“Where Care Meets Calling”** on **page 38**,

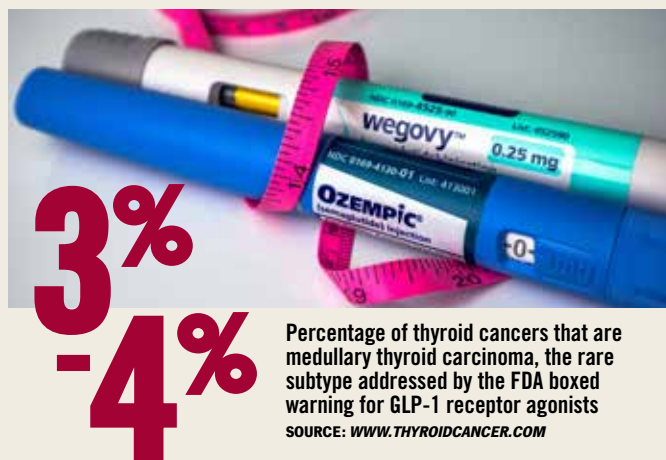
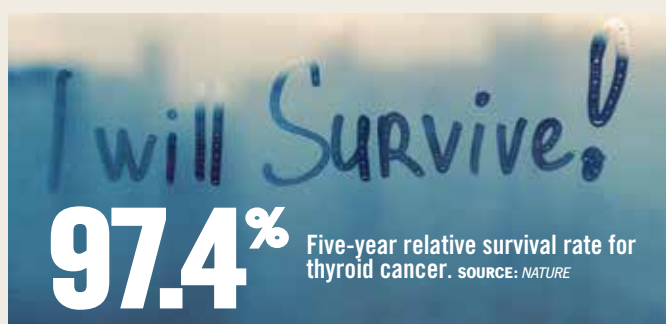
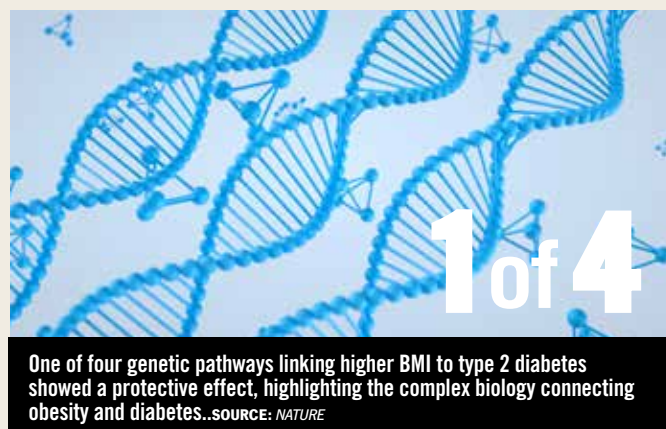


PHOTO: KK Stock/Shutterstock.com



The average annual compensation for U.S. endocrinologists in 2025.

SOURCE: PEW CHARITABLE TRUSTS



<1%

Proportion of primary aldosteronism cases that are actually diagnosed, despite the condition affecting an estimated 5%–20% of people with hypertension.

SOURCE: JAMA





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Epigenetic regulation is mediated through several interrelated molecular mechanisms: DNA methylation, histone modification, ATP-dependent chromatin remodeling, non-coding RNA-mediated regulation, and higher-order chromatin architecture.

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Moving Targets: Epigenetics and Disease Progression in Neuroendocrine Neoplasms

Neuroendocrine neoplasms (NENs) can show up anywhere in the body and can impact any organ system. These tumors originate in diverse sites, according to the authors of a recently published paper in *Endocrine Reviews*, which kind of makes them moving targets.

Authors of the paper, “**Epigenetics and disease progression in neuroendocrine neoplasms**,” led by Madson Q. Almeida, MD, PhD, of the University of Sao Paulo in Brazil, write that although clinical, biochemical, and pathological features have been associated with metastatic potential, the reliable prediction of disease progression and prognosis in NENs remains a major challenge.

The review then discusses epigenetics and how epigenetic regulation is mediated. The authors write: “Epigenetic regulation is mediated through several interrelated molecular mechanisms: DNA methylation, histone modification, ATP-dependent chromatin remodeling, non-coding RNA-mediated regulation, and higher-order chromatin architecture.”

The authors point to the technologies that have given rise to what Almeida and colleagues call “one of the most transformative tools in rare disease diagnostics”: DNA methylation epigenatures that the authors describe as genome-wide methylation patterns that are uniquely and reproducibly associated with specific Mendelian syndromes. “Their utility lies in their ability to serve as a downstream readout of functional disruption in the epigenetic machinery, effectively bridging the gap between genetic variant identification and phenotypic consequence,” the authors write.

Turns out, the authors write, these circulating epigenetic biomarkers are emerging as promising non-invasive tools for early diagnosis,

risk stratification, and disease monitoring. “Epigenetic mechanisms are dynamic and reversible, which makes them good candidates for therapeutic targeting,” the authors write. “The clinical translation of these insights is rapidly evolving.”

The review describes several neoplasms, including pheochromocytomas/paragangliomas (PPGLs), gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs), lung neuroendocrine neoplasms (LNENs), medullary thyroid carcinoma (MTC), and pituitary NETs (PitNETs). It also describes emerging epigenetic therapies, like global DNA methyltransferases inhibitors.

Medications like azacitidine and decitabine block DNMT activity and have been evaluated as a potential treatment for NETs. Pre-clinical studies have indicated that DNMT inhibitors (DNMTi) may have particular efficacy in PPGLs with SDH pathogenic variants and can reduce both proliferation and metastasis. HDAC (histone deacetylases) inhibitors can inhibit cell growth and cell motility. “Pre-clinical studies in GEP-NETs have also shown HDACi to decrease proliferation, inhibit cell cycle progression, and increase apoptosis, as well as increase SSTR2 expression, therefore providing both anti-tumor agent and agent to aid in increasing radioligand expression,” the authors write.

And while these new therapeutic options are promising, the authors write there’s more work to be done. Identifying epigenetic biomarkers across a large, diverse population is imperative. “With sustained technological advances and rigorous clinical validation,” the authors conclude, “the epigenome is poised to transition from a research focus to a cornerstone of precision medicine in neuroendocrine oncology.”

— Derek Bagley

Measuring Up to Cancer: The Association Between the Degree of Hypercortisolism and Metastatic Disease

Adrenal tumor size and the severity of cortisol excess are associated with a higher risk of metastatic disease at diagnosis, according to a study recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Marta Arajuo-Castro, of Hospital Universitario Ramon y Cajal in Madrid, Spain, point out in their article, **“Severity and management of hypercortisolism in patients with adrenocortical carcinoma and overt Cushing’s syndrome,”** that Cushing’s syndrome (CS) due to adrenocortical carcinoma (ACC) is a rare but highly aggressive condition in which excess cortisol may worsen oncological outcomes.

Up to 70% of ACCs are hormonally active, according to the authors. “Several studies have shown that ACC with associated CS is characterized by adverse prognosis, higher recurrence rates, and worse survival than nonfunctioning ACCs,” the authors write.

But there are few data about biochemical outcomes in patients with CS due to ACC – most studies have been focused on survival, the authors note. “The present study aimed to describe real-world management strategies for hypercortisolism in patients with ACC and to provide an overview of the biochemical response achieved with the different medical therapies used in routine clinical practice and to evaluate the association between the degree of hypercortisolism and survival outcomes in patients with ACC-associated CS,” they write.

For this study, researchers included 101 patients with ACC in an international retrospective study to evaluate the prognostic role of baseline hypercortisolism on survival outcomes, including

progression-free survival (PFS), disease-free survival (DFS), and overall survival (OS). “This international study provides clinically relevant evidence on how the severity of hypercortisolism and its management influence survival,” the authors write. “We found that higher baseline cortisol excess was associated with an increased risk of recurrence or progression, supporting its role as a marker of tumor aggressiveness.”

The authors write that several key findings emerged from this study:

- ▶ Adrenalectomy was linked to a high rate of biochemical remission in localized disease and offered partial endocrine control even in cases of metastasis,
- ▶ The severity of hypercortisolism was associated with an increased risk of recurrence/progression,,
- ▶ Although overall survival did not differ by cortisol severity, older age, UFC, hypokalemia, R0 after surgery, and Ki-67 were independent predictors of recurrence/progression and may help refine prognostic stratification.

“Together, these findings highlight the clinical importance of early detection and aggressive treatment of cortisol excess in ACC,” the authors write. “Future prospective studies are needed to better define the prognostic role of cortisol excess severity and to optimize therapeutic strategies for controlling hypercortisolism in this challenging patient population.” ^{EN}

— Derek Bagley



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Future prospective studies are needed to better define the prognostic role of cortisol excess severity and to optimize therapeutic strategies for controlling hypercortisolism in this challenging patient population.

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EARLY CAREER CORNER

Sehrish Waheed, MD¹, Nicholas Vernetti, MD², Samer Nakhle, MD²
Sunrise Health GME Consortium Endocrinology, Diabetes and Metabolism Fellowship, Las Vegas, NV
The authors declare they have no conflicts of interest.

BACKGROUND

Sepio- or S syndrome (SOS), also known as the Mowat-Wilson syndrome, is a rare autosomal recessive disorder characterized by the presence of at least two of the following features: optic nerve hypoplasia, polydactyly, congenital deafness, and midline brain anomalies, such as absence of the septum pellucidum and/or corpus callosum.

INTRODUCTION

We present a case of a young female with primary amenorrhea, absence of secondary sexual characteristics, right-sided vision loss, and hypopituitarism.

CASE DESCRIPTION

A 22-year-old female with a history of generalized seizures presented for evaluation of primary amenorrhea. She had congenital right vision loss. She had never experienced puberty or developed secondary sexual characteristics. She was treated with human chorionic gonadotropin (HCG), gonadotropin and oral contraceptive pills (OCP) for short stature when she was 15 years old for less than two years. She had never undergone a pelvic ultrasound. She denied anorexia or bulimias. She was diagnosed with hypothyroidism in childhood and has been on a stable dose of levothyroxine. Laboratory findings revealed FSH 1.6 mIU/mL (normal: 2.5-8.1 mIU/mL), LH 0.3 mIU/mL (normal: 1.5-16.6 mIU/mL), TSH 0.07 mIU/mL (normal: 0.40-4.50 mIU/mL), T4 2.2 ng/dL (normal: 0.8-1.8 ng/dL). Repeat tests showed TSH 0.02 mIU/mL, thyroid peroxidase antibody (TPO) 110 IU/mL (normal: <9 IU/mL), ACTH 14 pg/mL (normal: 5-20 pg/mL), IGFBP-1 <10 ng/mL (normal: 53-313 ng/mL), DHEAS 5.5 pg/mL, IGFBP-1 <10 ng/mL, prolactin 4 ng/mL (normal: 0-20 ng/mL), cortisol 2.2 mcg/dL (normal: 4-22 mcg/dL), estradiol <2 pg/mL (normal: 23-440 pg/mL). An MRI revealed an abnormal pituitary gland with changes in the right optic nerve.

Degrees of Sepio- or S syndrome (SOS), also known as Mowat-Wilson syndrome. Our patient had all of the components. Patient was started on hydrocortisone and low-dose estradiol/progesterone. Eight weeks after initiating treatment, the patient was seen in follow-up. She reported improved energy levels, had gained a few pounds, and experienced withdrawal bleeding, indicating a response to hormone replacement.



Figure 1. Axial T2-weighted MRI shows choroid plexus cysts (white arrows) and optic nerve hypoplasia (black arrow).



Figure 2. Coronal T1-weighted MRI shows hypoplasia of the right optic nerve (black arrow) and right optic chiasm (white arrow).



Figure 3. Sagittal T1-weighted MRI shows enlargement of the posterior pituitary gland (white arrow) and a small anterior pituitary gland (black arrow).



Figure 4. Sagittal T1-weighted MRI shows a small anterior pituitary gland (black arrow) and a small posterior pituitary gland (white arrow).

DISCUSSION

This patient presented with primary amenorrhea and absence of secondary sexual characteristics, right-sided vision loss, and hypopituitarism. The hormone profile demonstrated pituitary hypopituitarism, including hypogonadotropic hypogonadism, and hypothyroidism. The combination of these endocrine abnormalities points to a diagnosis of a congenital endocrine dysfunction in SOS.

Neuroimaging confirmed lesions between the optic nerves and optic chiasm, further supporting optic nerve hypoplasia. Pituitary gland hypoplasia was also evident on the MRI and was consistent with the diagnosis of a congenital endocrine dysfunction.

The patient's diagnosis of SOS is confirmed by the combination of clinical findings and imaging studies. She reported improved energy levels and experienced withdrawal bleeding, indicating a response to hormone replacement therapy. This case highlights the importance of a comprehensive endocrine evaluation in adult patients with primary amenorrhea and congenital vision abnormalities. SOS should be considered in the differential diagnosis, particularly when multiple pituitary hormone deficiencies are present.

Early diagnosis and multidisciplinary management are necessary to optimize clinical outcomes and quality of life.

CONCLUSION

This case illustrates a clinical presentation of SOS in an adult female with previously unrecognized hypopituitarism. The diagnosis was established through a combination of clinical findings, laboratory tests, and imaging studies. Hormone replacement therapy and vision rehabilitation are essential components of management. Understanding the clinical presentation and endocrine abnormalities in SOS can aid in the diagnosis and management of this rare condition. Further research is needed to elucidate the underlying genetic and molecular mechanisms of SOS and to optimize long-term hormonal and clinical outcomes.

Sehrish Waheed, MD, is ready to discuss her poster during ENDO 2025 in San Francisco, Calif.

Building Trust, one

Early-Career
 Member Sehrish
 Waheed, MD, on
 How Social Media
 Enhances Her
 Practice

BY GLENDA FAUNTLEROY SHAW

post
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 time





Sehrish Waheed, MD

Sehrish Waheed, MD, discusses her use of social media, preparation for the Endocrinology, Diabetes, and Metabolism certification exam, and the professional support she received from the Endocrine Society. She also describes her commitment to building trusting relationships with patients, particularly those affected by obesity stigma.

Last October, Sehrish Waheed, MD, better known as “@NoSugarMD” to her social media followers, was deep in study mode, preparing for the American Board of Internal Medicine (ABIM) Endocrinology, Diabetes, and Metabolism certification Endocrine Board exam.

Like many physicians facing a board exam, Waheed had assembled an arsenal of study materials to help her prepare. One day, she snapped a photo of some of the resources making the process a little easier and shared it on Instagram. Among them were the Endocrine Society’s Endocrine Board Review (EBR) resources, including sample cases, interactive practice exams, and the *Endocrine Board Review* book.

EBR is the Society’s comprehensive board-preparation program designed to help endocrinologists prepare for the exam. But for Waheed, the post was simply a glimpse into the work happening behind the scenes as she prepared for an important milestone in her young career.

Waheed practices at Platinum Hospitalists in Las Vegas, where she joined in August 2025 after completing an endocrinology fellowship at MountainView Hospital in Nevada.

Endocrine News caught up with her to talk about the story behind her social media posts, how she approached studying for the boards, and the Endocrine Society resources she found useful along the way.

***Endocrine News:* You use your social media account regularly as part of your professional life. What do you find most valuable about blogging?**

Sehrish Waheed, MD: I enjoy doing the medicine part, but I also want to make sure I’m adding in a glimpse from my personal life as well. What I think is more helpful, from a medical standpoint, is that it allows me to help patients beyond the exam room. I feel like there’s so much misconception on the internet about basic things I tell my patients, like about PCOS (now officially referred to as Polyendocrine Metabolic Ovarian Syndrome [PMOS]) and checking insulin levels. I like to blog about my personal life because I want to show the human side of being a physician. Medicine can feel very clinical and intimidating, and I think allowing people to see that I’m also a person with a life outside of medicine helps create a sense of connection and makes me more relatable and approachable and I really enjoy it.

***EN:* You did a post last October showing some Endocrine Society materials, such as the Endocrine Board Review book, while you were studying for your board exam. What made the materials you chose most useful to you?**

Waheed: The materials I used from the Endocrine Society included the *Endocrine Board Review*, ESAP (Endocrine Self-Assessment Program), and the

in-training examination questions. I actually started working on questions very early during my fellowship and continued doing them throughout my training. In the particular post you mentioned, I was listening to lectures by Dr. Stephanie Page and Margaret F. Lippincott from the Endocrine Board Review live study sessions from September of the previous year. Those two lectures were extremely helpful. One of them focused on hormonal therapy, a topic that we unfortunately don't get a lot of exposure to during endocrine fellowship. As a result, many of us don't develop strong foundational concepts in that area. Listening to Dr. Lippincott's lecture really helped me better understand and approach women's health questions on the board exam.

EN: What do you hope that other trainees who are studying for the Boards can take away from your posts?

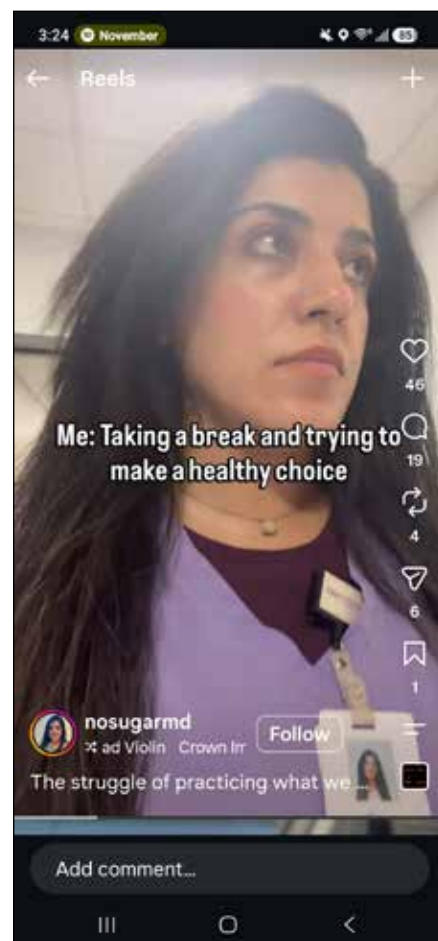
Waheed: If I had to do it all over again, I would recommend starting early. Start working on questions early in

fellowship and keep doing them consistently throughout your training. I think that steady practice makes a big difference when it comes time to prepare for the boards.

EN: What are other ways the Society has supported you in the early part of your career so far?

Waheed: The Endocrine Society has been a tremendous resource for early-career scientists and endocrine fellows. The Endocrine Society meetings, for example, are incredibly valuable because they provide an opportunity to learn about the latest developments in the field.

The mentorship program has also been amazing. During my first year, I had the opportunity to connect with people I never imagined I would have the chance to speak with. Through the program, I was able to gain new perspectives, make new friends, and meet colleagues in the field.





I also had the opportunity to participate in the Diabetes Type 1 and Obesity Fellow Programs, and both were incredibly valuable experiences for me. I was especially excited to be selected for these programs alongside other fellows from across the country. They gave me the opportunity to learn from experts in these areas, expand my knowledge, and connect with other fellows who share similar interests.

One of the things I appreciate most about the Endocrine Society is how genuinely they care about what young endocrinologists are doing. I'm not a big influencer. I only have a few hundred followers but for the Society to notice me and other young physicians, recognize our work, and appreciate what we're doing means a lot. It makes you feel seen and supported early in your career, and that has been really special to me.

EN: You mentioned that blogging is a way to help you connect with your patients. What do you find is the most rewarding part of today's doctor-patient relationship with the patients you see in your practice?

Waheed: For me, it's really about a sense of community. As an early-career endocrinologist, building long-term relationships with my patients is very special to me. I'm still early in my career, but I've already started developing those relationships. Now, some of my patients are coming back for their third visit, and I know what is going on in their lives and how they're doing.

My clinical focus is obesity, and there is so much stigma surrounding obesity. Many of my patients have already been through so much. Being able to give them confidence and let them know that I'm not there to judge them is incredibly important to me.

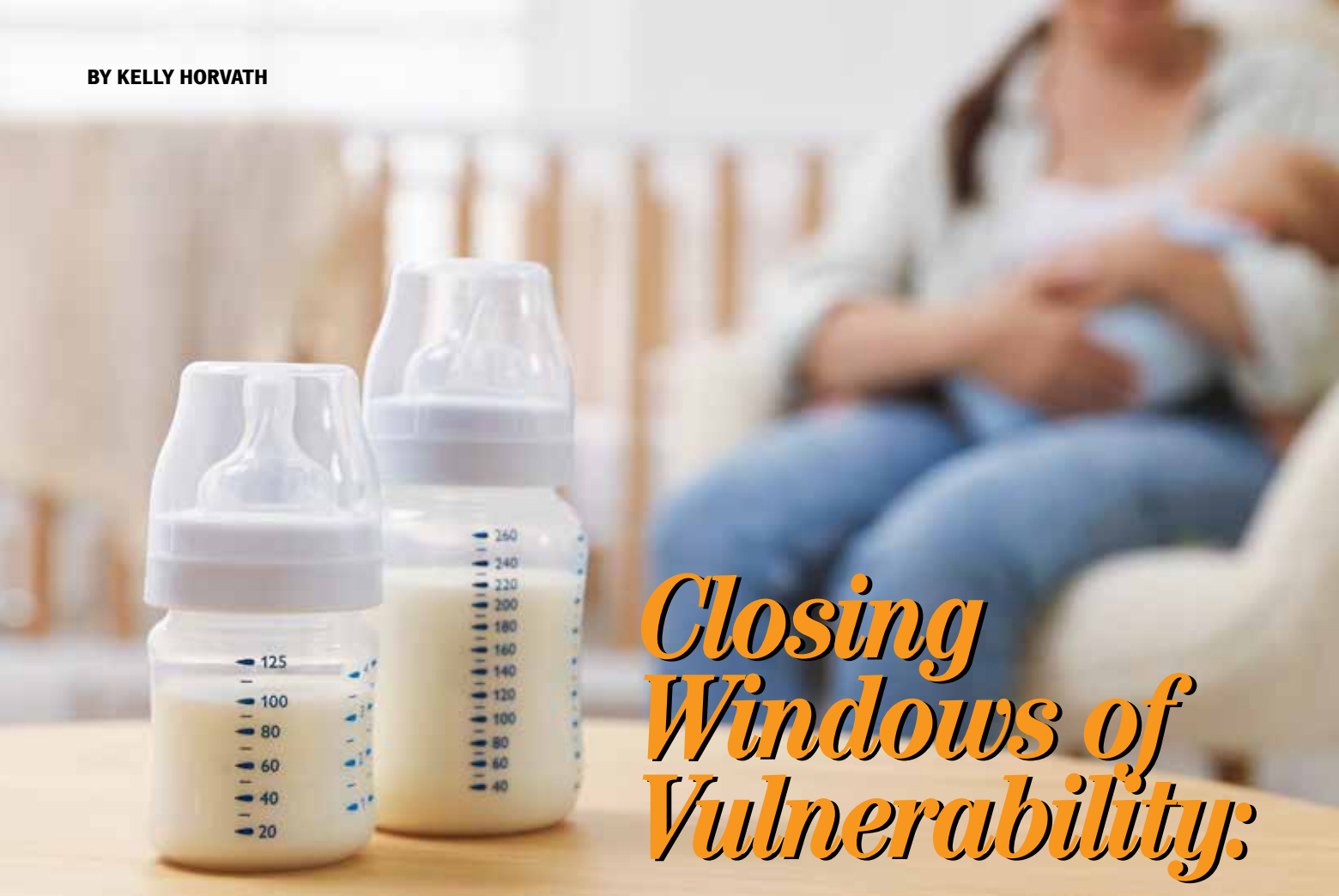
I really appreciate it when my blogging helps patients connect with me on a more personal level. They get to know me as a person, and then, when we're in the exam room, I can focus on treating their medical problems while also listening to them and understanding their experiences.

I think that combination allowing patients to know me as a person while also being there for them as their physician is helping me build meaningful relationships with my patients and give back to my community. **EN**

“One of the things I appreciate most about the Endocrine Society is how genuinely they care about what young endocrinologists are doing. **I'm not a big influencer. I only have a few hundred followers but for the Society to notice me and other young physicians, recognize our work, and appreciate what we're doing means a lot. It makes you feel seen and supported early in your career, and that has been really special to me.**”

— SEHRISH WAHEED, MD, ENDOCRINOLOGIST,
PLATINUM HOSPITALISTS, LAS VEGAS, NEV.

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



Closing Windows of Vulnerability:

EDC Exposure During Development

With October taking a pediatric health focus at *Endocrine News*, this article explores three studies that examine how endocrine-disrupting chemicals (EDCs) interfere with human development and seek ways to ameliorate these exposures.

Despite our growing awareness that EDCs are linked with all manner of adverse human health outcomes, including altered neurodevelopment and associations with obesity and attenuated growth, they continue to be widely used in consumer products, electronics, and agriculture. The studies profiled here demonstrate that early life represents a period of particular vulnerability to EDCs' harms.

Early Phthalate Exposure

In research presented at **ENDO 2026** in June, Osvaldo Juan Ponzo, MD, PhD, professor of physiology at University of Buenos Aires School of Medicine in Buenos Aires, Argentina, demonstrated that mature male rats exposed to the EDC di-

Early-life exposure to endocrine-disrupting chemicals may affect brain function, bone development, and hormonal programming during periods of heightened vulnerability. Three studies examine these risks and identify individual, clinical, regulatory, and product-design strategies that may reduce exposure or mitigate consequences.



(2-ethylhexyl) phthalate (DEHP) during pre- and perinatal development have increased anxiety. DEHP is one of the most commonly used plasticizers globally, used to make certain consumer products (e.g., medical devices, toys, shower curtains, raincoats) more flexible.

As DEHP and its metabolites have been shown to interfere with the reproductive and nervous systems (among others) in both animals and humans, Ponzo and team sought to determine whether γ -aminobutyric acid (GABA) or testosterone was involved in regulating the effects of DEHP on anxious behavior in adult male rats. “In other words,” says Ponzo, “we wanted to investigate whether early-life exposure could induce a lasting ‘imprinting’ effect on the neural structures involved in the regulation of behavior and anxiety. Furthermore, the rising incidence of behavioral and neurodevelopmental disorders in humans together with epidemiological evidence linking exposure to endocrine-disrupting chemicals with adverse neurodevelopmental outcomes, such as the increase in autism, provided an additional rationale for investigating the mechanisms underlying these behavioral alterations.”

The team suspected that GABA and testosterone might remediate some of the harmful effects because of the known interaction between androgenic and GABAergic signaling in the regulation of neural function and behavior. “On the one hand, testosterone can modulate the GABAergic system and may therefore counteract the anxiogenic effects associated with endocrine-disrupting exposure,” says Ponzo. “On the other hand, these endocrine disruptors have an anti-androgenic (i.e., anti-testosterone) effect that induces anxiety; the aim, therefore, was to demonstrate that the competition between testosterone and the anti-androgenic phthalate for the receptor could reverse this behavioral alteration.”

They gave pregnant female rats oral DEHP 30 mg/kg daily, starting with day one of gestation through weaning. At maturity (70 days old), the rats were placed in an elevated plus maze (EPM), which, as its name suggests, is shaped like a plus sign with two open and two closed arms enclosed by high walls. As the EPM test draws on rodents’ natural aversion to open spaces and heights, it allowed the scientists to measure the duration spent in both arms as well as their freezing time (time spent

motionless), head-dipping time (head extended beyond the EPM arms), and stretch-attend posture time (body is stretched forward while the hind limbs remain in place).

The exposed rats not only spent less time in the open arms and more time in the closed arms, compared to controls, they also showed significantly more freezing and stretch-attend time and significantly less head-dipping time, behavior consistent with anxiety. As these behaviors were reversed in those rats who received GABA agonists or testosterone at various pretest time points, the researchers concluded that they are a consequence of neuroendocrine alterations. “This work demonstrates that exposure to EDCs during critical periods of development may have long-lasting consequences for brain function and behavior. Also, the rising prevalence of behavioral disorders in humans — such as anxiety-related issues — appears to be linked, at least in part, to the increasing exposure over recent decades to industrial substances known as endocrine disruptors,” says Ponzo.

PFAS Exposure and Bone Health in Adolescence

In “Per- and polyfluoroalkyl substances and adolescent bone mineral density: assessing periods of susceptibility,” published in *Journal of the Endocrine Society* in March, Jessie P. Buckley, PhD, of the Department of Epidemiology, Gillings School of Public Health at the University of North Carolina in Chapel Hill, N.C., and team sought to identify specific temporal windows during childhood when certain EDCs might exert greater adverse influence on bone mineral accrual.

“Bone health is understudied with respect to how the environment might be causing, or contributing to, lower bone mass accrual during childhood,” says Buckley. What initially led her to study whether per- and polyfluoroalkyl substances (PFAS) might be affecting how children’s bones develop, however, was a bit of an accident. Years earlier while studying body mass index, Buckley noticed something odd: When she looked at height and weight separately, the children with higher EDC exposures had lower stature. “That wasn’t my hypothesis,” she explains, “but it got me thinking about why that would be.” She turned to the animal literature, where EDCs like PFAS are



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Regulatory approaches can reduce exposure across entire populations. This can be helpful for many sources of PFAS that are difficult for individuals to avoid. **Even without regulation, we have seen that consumer choices can impact chemical exposures when individuals use the power of the pocketbook to avoid those chemicals in the things they purchase. If we come at it from multiple angles, hopefully we can move the needle.”**

—JESSIE P. BUCKLEY, PHD, OF THE DEPARTMENT OF EPIDEMIOLOGY, GILLINGS SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL, N.C.

hypothesized to act as obesogens by causing mesenchymal stem cells in bone marrow to differentiate into adipocytes instead of osteocytes, a process mediated by PPAR- γ (peroxisome proliferator-activated receptor gamma). Essentially, some EDCs behave as a PPAR- γ agonist and give it the wrong signal. “If that’s the reason they cause obesity,” she remembers thinking, “then they’re probably also not good for bone health.”

To test this newly emerging hypothesis in humans, Buckley and team used data from a prospective pregnancy and birth cohort called the Health Outcomes and Measures of the Environment (HOME) Study. Pregnant participants were recruited from March 2003 to January 2006, and 218 of their offspring were eligible for Buckley and team’s current study, which required that PFAS be measured in their serum at delivery at ages three, eight, and 12 years as well as completing a bone mineral density (BMD) assessment via dual x-ray absorptiometry (DXA) at age 12.

They specifically looked at four PFAS widely persistent in the environment, found in everything from nonstick cookware to water supplies, including perfluorohexane sulfonic acid (PFHxS), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), and perfluorononanoic acid (PFNA). These four have biologic half-lives in humans ranging from two to nine years and have been detected in human bone tissue. The team wanted to know if serum PFAS concentrations measured at ages eight and 12 years would have stronger associations with lower BMD than the earlier measures, given that peak BMD accrual occurs in early adolescence.

Unfortunately, at least some of their hypothesis proved correct: Higher serum PFOA concentrations were consistently

associated with lower BMD Z-scores at the distal radius. Associations for other PFAS differed by exposure assessment timing, skeletal site, and sex. Fortunately, on the other hand, the team did not have to stop there. “This is a pretty unique cohort,” says Buckley. “They were enrolled as children in the early 2000s, and we’ve been following them ever since. They’re very dedicated participants, and our staff has remained connected with them. Age 12 is at the beginning of a really fast period of bone mass accrual, and we wanted to know if the associations we saw at 12 would still be evident as the kids reached adulthood.” Preliminary findings from a repeat DXA scan at age 18 are showing similar results so far, lending further support to the idea that some periods of growth and development have heightened susceptibility to PFAS’ effects.

These findings appear in “Associations of gestational serum per- and polyfluoroalkyl substances (PFAS) concentrations with late adolescent bone mineral density in the Health Outcomes and Measures of the Environment (HOME) Study,” an abstract published in June in *Environmental Epidemiology* by Singareddy et al., including Buckley.

Buckley remains not only grateful to the cohort for their ongoing dedication to this important work but also hopeful. “Although one solution is to use less PFAS in the future, that doesn’t address the fact that so many people have already experienced PFAS exposure,” she says. This reality prompted a follow-up question: Do protective factors exist? “In a separate study, we found that the associations of PFAS with lower BMD were evident among adolescents with lower calcium intake and physical activity,” Buckley explains. “But we didn’t see an association among those with a more optimal diet or physical activity.”



Two intervention pathways become clear here. One is using less PFAS. Buckley notes that several states (<https://www.saferstates.org/priorities/pfas/>) have introduced policies to reduce PFAS exposure, and awareness is spreading of their dangers. “Regulatory approaches can reduce exposure across entire populations,” Buckley says, “this can be helpful for many sources of PFAS that are difficult for individuals to avoid. Even without regulation, we have seen that consumer choices can impact chemical exposures when individuals use the power of the pocketbook to avoid those chemicals in the things they purchase. If we come at it from multiple angles, hopefully we can move the needle.” The second pathway is accessible now: “More physical activity and better diets are healthy for more than BMD alone and expanding access to safe play spaces and nutritious food would help even those who have already been exposed to PFAS.”

For clinicians, Buckley hopes the team’s work helps broaden the diagnostic lens. “It’s important to think about a person’s environment when trying to understand why their health is a certain way,” she says. She points to practicing endocrinologists who have begun testing patients for PFAS when they suspect high exposure, and a National Academies of Sciences,

Engineering, and Medicine report titled “Guidance on PFAS Exposure, Testing, and Clinical Follow-up.” The larger goal, she says, is “to raise awareness that the environment is important, even for bone health, which I think is under-acknowledged.” She adds that the Endocrine Society has led the way in bringing attention to the potential health effects of EDCs in reports like “EDC-2: The Endocrine Society’s Second Scientific Statement on Endocrine-Disrupting Chemicals.”

“How much bone you accrue during childhood is so important for your lifelong future risk of osteoporosis and fractures in adulthood,” she says. “The lag time between childhood and adulthood makes it hard to do these studies that show the longitudinal link all the way across the life course, but studies like ours are beginning to track the longer-term impacts of early life exposures.” Zooming out, Buckley situates her work inside a much larger exposure problem: “It’s so unfortunate how wide-reaching these effects are,” she says. “Almost everyone in the United States has PFAS in their body. We studied four PFAS, but there are thousands. So, as we move forward, understanding what some of these newer PFAS are doing, and whether they’re also involved in processes that affect bone health and other outcomes, is important.”



“This work demonstrates that exposure to EDCs during critical periods of development may have long-lasting consequences for brain function and behavior. Also, the rising prevalence of behavioral disorders in humans — such as anxiety-related issues — **appears to be linked, at least in part, to the increasing exposure over recent decades to industrial substances known as endocrine disruptors.**”

— OSVALDO JUAN PONZO, MD, PHD, PROFESSOR OF PHYSIOLOGY,
UNIVERSITY OF BUENOS AIRES SCHOOL OF MEDICINE, BUENOS AIRES, ARGENTINA



Preventing EDC Exposure from Breast Milk

Also presented at **ENDO 2026** and published in August in the *European Journal of Endocrinology*, **“Exposure to endocrine-disrupting chemicals in breast milk and infant urine samples: findings from the LIFE-MILCH project,”** illustrates that some of the intervention methods Buckley discussed can actually work in practice.

Maria Elisabeth Street, MD, PhD, associate professor and director of the Division of Pediatric Endocrinology at the University of Parma and University Hospital of Parma, in Parma, Italy, and team undertook a longitudinal study of EDCs in 336 infant–mother dyads enrolled in the LIFE-MILCH project. “After birth, most EDC exposure will occur through feeding. Infancy is a particularly sensitive developmental window and the effects of exposure to EDCs may interfere with hormonal programming with consequences that only become apparent years later,” says Street. The team measured levels of more than 50 different EDCs, including bisphenols (BPA), polycyclic aromatic hydrocarbons, phthalates and metabolites, parabens, polar pesticides, and pyrethroids from samples collected one, three, and six months after birth that confirmed breast milk as a vehicle of environmental exposure. These and other results led Street and team to identify a broader objective: identifying realistic and modifiable sources of exposure while protecting and promoting breastfeeding, which has become the LIFE-MILCH alliance. “Breast milk is the optimal source

of nutrition for infants, and breastfeeding must continue to be strongly encouraged,” she says.

The LIFE-MILCH campaign translates research findings into practical information for three groups: women of childbearing age, pregnant or breastfeeding women, and health professionals, says Street, reaching them through schools, clinics, antenatal classes, and training sessions. Manufacturers are part of the picture too, through monitoring and voluntary agreements to cut EDC contamination in infant products. “The campaign’s effectiveness,” she explains, “is being evaluated through a second round of biomonitoring in mother–infant pairs rather than through awareness measures alone.”

LIFE-MILCH also offers the following reasonable exposure-reduction measures, framed to avoid causing mothers to become anxious or to stop breastfeeding:

- ▶ Use glass, paper, or suitable reusable containers and packaging.
- ▶ Avoid heating food in plastic unless the container is explicitly designed for it.
- ▶ Reduce reliance on canned and heavily packaged food.
- ▶ Follow a varied, balanced diet and wash vegetables and fruit well.



“After birth, most EDC exposure will occur through feeding. **Infancy is a particularly sensitive developmental window and the effects of exposure to EDCs may interfere with hormonal programming with consequences that only become apparent years later.**”

— MARIA ELISABETH STREET, MD, PHD, ASSOCIATE PROFESSOR AND DIRECTOR, DIVISION OF PEDIATRIC ENDOCRINOLOGY, UNIVERSITY OF PARMA AND UNIVERSITY HOSPITAL OF PARMA, PARMA, ITALY



- ▶ Use stainless-steel or ceramic cookware when appropriate, particularly if non-stick surfaces are damaged.
- ▶ Choose personal-care products with simpler ingredient lists and, where possible, products identified as free of relevant phthalates or bisphenols.
- ▶ Limit unnecessary use of fragrances, air fresheners, pesticides, and harsh cleaning products.
- ▶ Ventilate the home regularly and reduce indoor dust.

For clinicians, Street and team's central message is to support breastfeeding. "These results should not be interpreted as evidence against it." Clinicians can ask a few practical questions about food storage, personal-care products, and household chemicals as part of preventive maternal and child health, paired with a clear caution that detection of a chemical does not automatically establish clinical harm in an individual child. Says Street: "Our study primarily identifies population-level exposure patterns. The broader solution requires public-health action, safer product design, continued biomonitoring, and appropriate regulation, alongside individual guidance."

Looking ahead, the team's priority is completing a longitudinal analysis of the full LIFE-MILCH cohort, treating breast milk and infant urine as connected trajectories rather than isolated samples, and studying realistic chemical mixtures rather than single compounds. From there, Street wants to connect exposure to outcomes like growth, adiposity, neurodevelopment, and pubertal timing, while also testing whether the prevention campaign itself measurably reduces exposure. Longer term, the group is moving toward proof-of-concept in vivo mixture studies and work on epigenetic effects in breast milk.

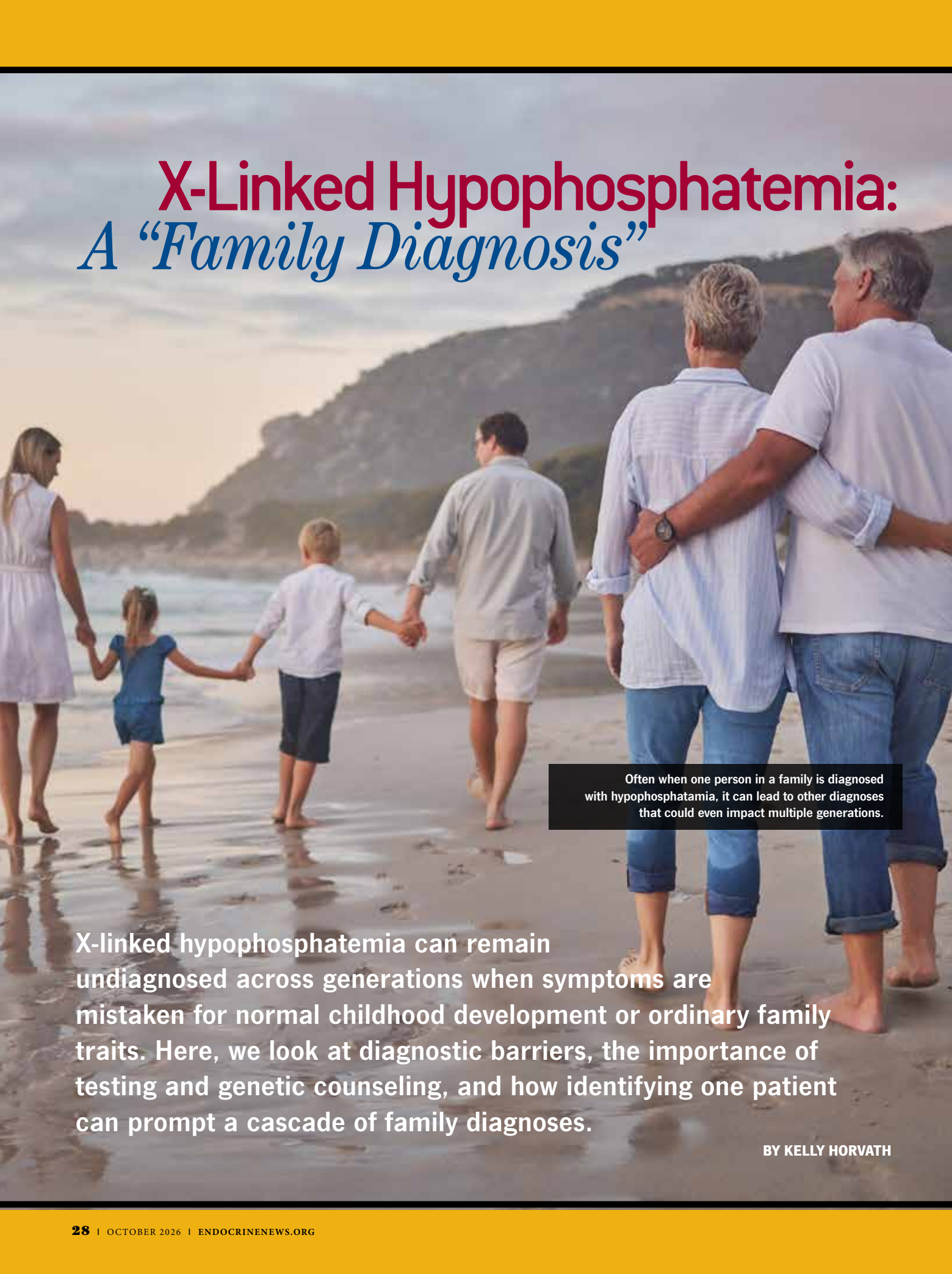
Connecting the Dots

As this research shows, EDCs can affect development during sensitive early-life periods; however, measures exist that may reduce exposure or lessen its consequences. Taken together, these three studies highlight the importance of considering early-life exposure to EDCs as a potential risk factor for later health alterations. ^{EN}

AT A GLANCE

- ▶ The plasticizer di-(2-ethylhexyl) phthalate (DEHP) causes anxiety-like behavioral changes in male rats exposed during pre- and perinatal development, an effect that persists into adulthood, even with cessation of the exposure.
- ▶ In the HOME Study, higher perfluorooctanoic acid levels were consistently linked to lower radial bone mineral density in adolescence, while other per- and polyfluoroalkyl substances showed mixed age- and sex-dependent associations, with overall effect sizes large enough to meaningfully raise fracture risk in children.
- ▶ Investigators confirmed the presence of endocrine-disrupting chemicals (EDCs) in maternal breast milk and infant urine in 336 mother–infant pairs enrolled in the LIFE-MILCH project, findings that prompted creation of a campaign to promote accessible methods to reduce maternal EDC exposure and protect breastfeeding.

– HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. IN THE SEPTEMBER ISSUE, SHE WROTE "MINDING THE GAPS: WHAT HAPPENS WHEN PEDIATRIC PATIENTS WITH PITUITARY TUMORS BECOME ADULTS?"

A photograph of a family of five walking away from the camera on a sandy beach at sunset. From left to right, there is a woman in a white dress, a young girl in a blue dress, a young boy in a white shirt and dark shorts, a man in a light blue shirt and khaki shorts, and an older couple (a woman in a light blue shirt and a man in a white shirt and jeans) walking together. They are all holding hands or walking closely. The background shows the ocean, a rocky coastline, and a cloudy sky with warm sunset colors.

X-Linked Hypophosphatemia: *A “Family Diagnosis”*

Often when one person in a family is diagnosed with hypophosphatemia, it can lead to other diagnoses that could even impact multiple generations.

X-linked hypophosphatemia can remain undiagnosed across generations when symptoms are mistaken for normal childhood development or ordinary family traits. Here, we look at diagnostic barriers, the importance of testing and genetic counseling, and how identifying one patient can prompt a cascade of family diagnoses.

BY KELLY HORVATH

When Emily's seven-month-old daughter Ila began pulling herself up to stand, Emily noticed that her legs were significantly bowed. "You always hear that some bowing under age two is normal," Emily says, "but it just seemed very pronounced."

For the next several months, Emily raised her concerns at Ila's well-child visits, but the pediatrician did not detect anything amiss, telling her that some bowing occurs in up to 95% of children and that Ila would grow out of it. "I thought, maybe I'm blowing this out of proportion," Emily recalls. But by the 15-month appointment, Ila had been walking for a few months, and the bowing was more, not less, prominent. "I really pushed at that visit for more answers," she says, and her persistence finally produced a pediatric orthopedic referral.

During the following nearly two-month wait for the referral appointment, Emily took matters into her own hands, researching online what might explain Ila's condition as well as reaching out to a specialist who studies metabolic bone diseases. "I discovered hypophosphatemia and felt pretty certain that was it," she says. She thought back to her own active childhood and the musculoskeletal issues she experienced. For example, after soccer practice, she would become so stiff during the car ride home that she would have to warm back up just to be able to walk into her house. She also experienced frequent kneecap dislocations and seemed to walk and run at a slower pace than her peers. "I just thought that was my normal," she recalls. "I didn't know that wasn't normal."

When the time came to attend the orthopedic appointment, she was prepared. "I'd found four or five generations of family members who'd had surgeries and knee and joint problems," she explains. Even with that level of support for her hunch, however, the orthopedist reiterated that Ila's bowing was physiologic, an opinion that Emily says "did not hold water for her." Fortunately, just the day before, the specialist she had contacted called and arranged to see Emily and Ila. Emily's instincts were correct, and the diagnosis of X-linked hypophosphatemia (XLH) was confirmed.

Emily calls the whole process her family's "diagnostic odyssey," an unfortunate though certainly apt phrase. According to Mark Eugene Nunes, MD, medical director of Genetics, Genomics, and Metabolism at Intermountain Children's Health in Las Vegas, Nev., having to undertake such an odyssey is far more common than we would like.

Challenges in Diagnosis and Care

Nunes specializes in metabolic bone diseases and offers an important perspective on why identifying these conditions is critical. He uses pouring a driveway as an analogy for understanding the underlying mechanism. "Collagen is like the rebar, the metal grid, and calcium and phosphorus are like the concrete poured over top. If you have no collagen, you're going to have brittle bones; if you have faulty calcium or phosphorus, you're going to have soft bones." Thus, identifying individuals who have low phosphorus, which is necessary for bones and for numerous other biologic functions

“The things you’re not looking for are the things you miss. For a primary care doctor, if you’re not obtaining a serum phosphorus, you’re not going to recognize a low one. For endocrinologists, who are obtaining phosphorus routinely and are more likely to recognize the diagnosis, don’t be afraid to ‘phone a friend’ and ask a genetic counselor for help in making a difference in the lives of four, five, or six of your patient's relatives who are also at risk.”

– MARK EUGENE NUNES, MD, MEDICAL DIRECTOR,
GENETICS, GENOMICS, AND METABOLISM,
INTERMOUNTAIN CHILDREN'S HEALTH,
LAS VEGAS, NEV.



is very important. “It’s extremely important in children,” Nunes continues, “because phosphorus is fundamental for normal growth and development, and it’s important in adults because the bone issues go undiagnosed and unrecognized as well as for the other benefits that correcting abnormally low phosphorus has for a person’s health.”

Yet Emily’s early experience — concern raised, dismissed, raised again — fits a pattern Nunes sees regularly. Part of the problem, he explains, is that routine bloodwork panels will not catch it. Sodium, bicarbonate, and calcium levels are all measured using the same electrode that measures pH, but it cannot measure phosphorus, which requires a special, extra test that adds cost and steps. This means that, “unless you’re checking the serum phosphorus, you’re not going to know it needs correcting,” says Nunes. Unfortunately, primary care clinicians may not even be aware that phosphorus is not on the panel, so educating them is vital: “If they see someone with a high alkaline phosphatase level, which is an indicator of rickets or osteomalacia, one of the tests they should order separately is a serum phosphorus, in addition to the chemistry panel,” he explains.

Another problem contributing to underdiagnosis is mistaking other conditions for XLH, like vitamin D deficiency, which affects a third of the population. It can take a while to see that replacing the vitamin D is not resolving all of a patient’s issues (“the disease process in XLH doesn’t allow conversion of inactive vitamin D into active vitamin D,” explains Nunes) and getting to the root of the problem. Another is skeletal dysplasia, commonly suspected when x-rays demonstrate abnormal-appearing metaphyses. Here, at least, genetic tests may be done, and “you back into the diagnosis of hypophosphatemia because you find a genetic change in the PHEX gene, which is on those skeletal dysplasia panels,” says Nunes. He also explains that XLH is

inherited 80% of the time, while 20% of cases arise from de novo mutations.

Although XLH remains underrecognized, it is nevertheless the most common metabolic bone disease, occurring in about 1 in 20,000 individuals. Nunes says that he sees osteogenesis imperfecta and hypophosphatasia in his clinic more frequently, even though they occur with less frequency within the general population, at 1 in 25,000 and 300,000, respectively.

Nunes also points to a blind spot in how the condition was formerly considered. “We were taught that hypophosphatemia was predominantly a childhood disorder and something you grew out of,” he says. “The idea that there might be adult features of this diagnosis really wasn’t something we understood 20 years ago the way we do now.” These gaps begin to explain why Emily’s own case (and that of some of her relatives) went unrecognized for decades before a specialist connected the dots, and her daughter Ila’s diagnosis brought everything into focus.

Of course, other factors complicate the clinical picture, including transitioning from pediatric to adult care. “Most of the individuals identified in 2026 are children,” explains Nunes, “and they grow up into adults. The old thinking was that treatment stopped once the skeleton was mature. Now we’d like to pass those kids on to an adult practitioner, because the pediatric endocrinologist can’t take care of a 24-year-old with the diagnosis. A lot of the cases coming to an adult endocrinologist are inherited pediatric cases, where the kids have gone through their teenage years and become nonadherent to therapy thinking there aren’t any issues. So, we need a good, warm handoff from the pediatric endocrinologist to the adult endocrinologist for continuity of care.” Nunes cites Vanderbilt University’s Transitions Lab as one that handles this well.

Although bowlegs and short stature in adults were historically considered “family traits” among families, clinical geneticists now recognize it as a possible symptom of heritable metabolic bone disease like XLH, in which correcting the chemical derangement could improve patient quality of life in multiple ways.



“Domino Effect”

Emily recounts how once Ila was diagnosed, “it was kind of like a domino effect through the family tree. This is more widespread than just the two of us.” Her paternal grandmother had begun building an informal family record that Emily later picked up where she left off, cataloguing symptoms across her four sisters and other relatives. Emily’s great-grandfather was never tested, “but it’s safe to say he had XLH due to his very pronounced leg-bowing,” she says. Despite that one of those great-aunts was even treated for bone problems at a specialist hospital in the early 1940s, the notion that this problem was genetic did not occur to their clinicians, so affected family members remained in the dark.

To begin disseminating her findings, Emily used her extended family’s Facebook group. “It put more information out there for everybody to see,” she explains, “and let each relative decide for themselves whether to get tested.” Roughly two dozen living family members now have a confirmed diagnosis, with others clearly affected but never formally tested. This “domino effect,” as Emily called it, is why Nunes considers XLH a family diagnosis, not just an individual one. “About 80% of cases are inherited,” he explains, “and because it’s X-linked, the pattern is predictable: An affected father passes it to all of his daughters and none of his sons; an affected mother can pass it to sons and daughters alike.” Thus, a single pediatric diagnosis can flag other family members from just the pedigree structure and lead to a “cascading diagnosis” throughout the family. Interestingly, families tend to consider their symptoms as a family *trait* rather than a disease process. Nunes describes a family he treated whose great-grandfather had bowed legs, but which did not affect his ability to carry out activities of daily living. This bowing passed, with varying severity, through his daughter, granddaughter, and eventually a great-grandson referred for a suspected skeletal dysplasia. “They didn’t see it as something that stopped mom from working, marrying, or having children. It was just, ‘that’s the way things are in my family.’”

Nevertheless, identifying a heritable diagnosis in one individual may mean being able to make a difference in the lives of the relatives who are also at risk. Recognizing that this sensitive news might be difficult to communicate within some families, Nunes has a suggestion: “I’d say there’s a great role for genetic counselors here; these resources are available to endocrinologists to help sort things out for the family.”

You Miss What You Don’t Look For

Emily, who is an ambassador for pharmaceutical company Kyowa Kirin’s XLH Family Outreach Initiative [see sidebar] program, drew on multiple resources, not to mention her own commitment to advocating for her daughter, to eventually have XLH confirmed across four generations in her family. “So many things can be genetic, or more likely to occur within a family, and it’s worth talking about,” Emily says. This also works in reverse, “When the adult endocrinologist makes the diagnosis in an adult patient, even

AT A GLANCE

- ▶ Many cases of X-linked hypophosphatemia (XLH) remain undiagnosed for a host of reasons, including because they are often attributed to other musculoskeletal conditions, such as physiologic bowlegs that a child will grow out of.
- ▶ Although bowlegs and short stature in adults were historically considered “family traits” among families, clinical geneticists like Mark Eugene Nunes now recognize these as possible symptoms of heritable metabolic bone disease like XLH, in which correcting the chemical derangement could improve patient quality of life in multiple ways.
- ▶ Identifying one person with XLH can reveal previously undiagnosed relatives across multiple generations, an often-overlooked intervention opportunity.

“When the adult endocrinologist makes the diagnosis in an adult patient, even though it might be a brand-new mutation, the patient’s children are certainly at risk. So how do you make sure they get treated? There’s a handoff in the opposite direction that I don’t think we usually think about.”

— MARK EUGENE NUNES, MD, MEDICAL DIRECTOR, GENETICS, GENOMICS, AND METABOLISM, INTERMOUNTAIN CHILDREN’S HEALTH, LAS VEGAS, NEV.

though it might be a brand-new mutation, the patient’s children are certainly at risk. So how do you make sure they get treated?” Nunes asks. “There’s a handoff in the opposite direction that I don’t think we usually think about.”

Nunes has additional, actionable advice for both primary care physicians and endocrinologists. “The things you’re not looking for are the things you miss. For a primary care doctor, if you’re not obtaining a serum phosphorus, you’re not going to recognize a low one. For endocrinologists, who are obtaining phosphorus routinely and are more likely to recognize the diagnosis, don’t be afraid to ‘phone a friend’ and ask a genetic counselor for help in making a difference in the lives of four, five, or six of your patient’s relatives who are also at risk.”

Back to her own family, Emily says, “I feel like it could have been figured out sooner if people had been more open to talking about their health with family members.” In their own ways, Emily, and Nunes, are both working to change that. Meanwhile, Ila is approaching her ninth birthday and doing well, according to Emily. “Having her diagnosis has helped guide our decision-making. For example, instead of soccer, playing a lower-impact sport would be better for her. That’s not to say she can’t ever play soccer, but it helps us think about her health overall. Luckily, she’s not super interested in it anyway.” ^{EN}

Let's Talk About It!

Another solution exists specifically for families with XLH, created by pharmaceutical company Kyowa Kirin that specializes in rare diseases. The company has developed the XLH Family Outreach Initiative to support patients, encourage intra-family communication about XLH, and provide resources such as a digital family tree that highlights inheritance patterns.

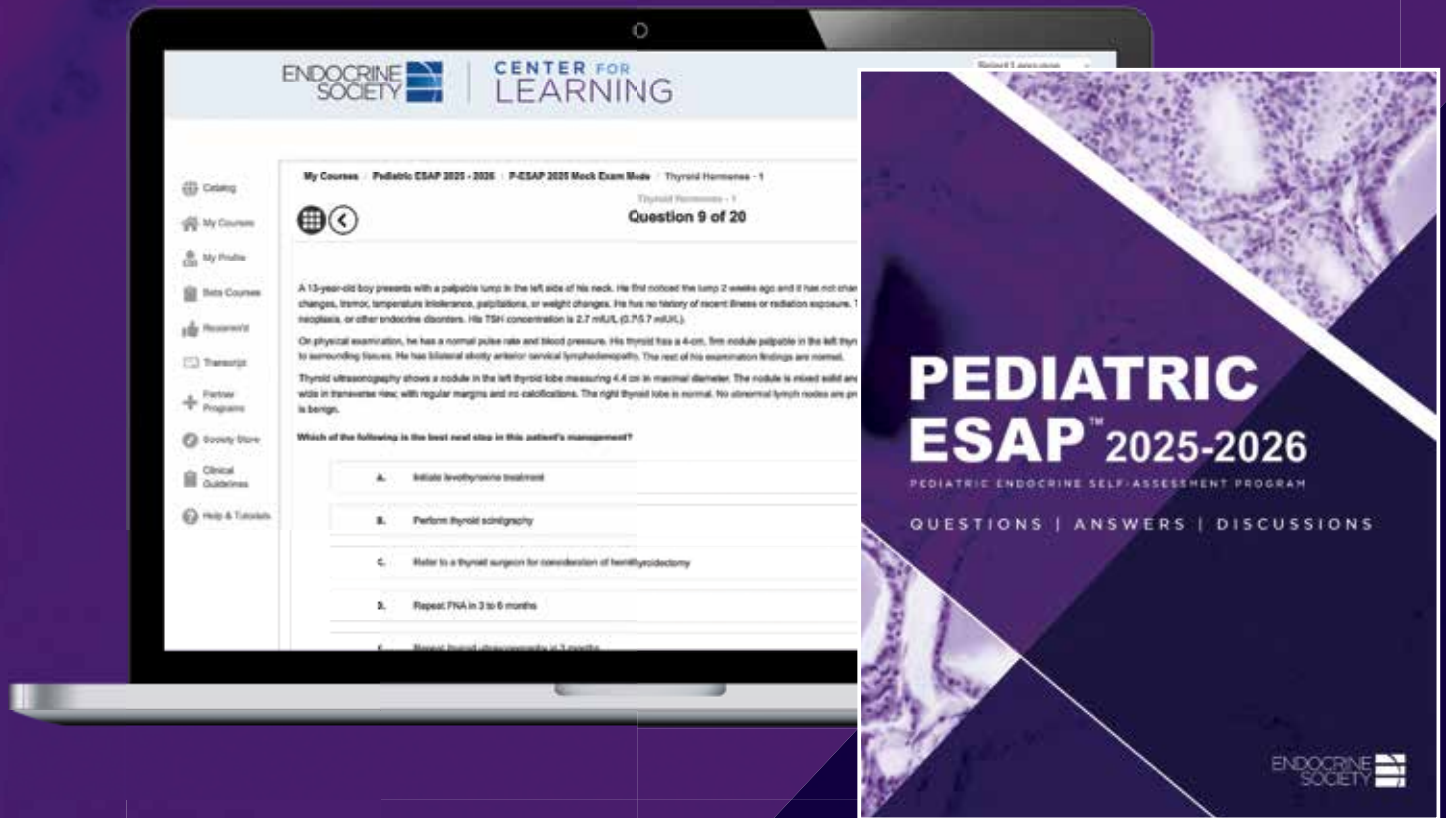
“What continues to strike me about XLH is how much education is still needed, even today,” says Richard Wilson, Kyowa Kirin’s Rare Disease Franchise Head. “It’s remarkable that despite XLH being a genetic condition, many still don’t recognize it within their own family history. We still hear stories of people going undiagnosed as adults, thinking they had childhood rickets or assuming they ‘just had bad bones,’ when in fact it was a hereditary condition affecting multiple generations.”

Wilson describes the outreach initiative as a response to a practical limitation: “While physicians play a critical role in diagnosing and treating the patient in front of them, it may not always be feasible to uncover a broader family history or guide conversations across generations,” he says. “The XLH Family Outreach Initiative helps fill that gap by offering reassurance, clarity and practical tools that support individuals in recognizing the intergenerational signs of XLH, talking with loved ones, and feeling more equipped to advocate for their health.”

Wilson traces this outward-looking approach back to a specific idea embedded in Kyowa Kirin’s culture: Wa. “Wa is a Japanese concept that reflects the spirit of working in harmony—identifying a challenge and coming together, across teams and with the outside community, to work through it collaboratively,” he says. Thinking back to Emily’s “diagnostic odyssey,” this approach clearly makes sense.

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low ALP, think HPP:

clinical pearls
in hypophosphatasia



Asfotase alfa, a bone-targeted recombinant tissue nonspecific alkaline phosphatase (TNSALP), is currently the only approved pharmacologic treatment for perinatal, infantile, and juvenile hypophosphatasia.

On behalf of Endocrine Society's Bone and Mineral Special Interest Group Steering Committee, Anika Anam, MD and Azarmindokht Khosravi, MD, discuss the diagnostic gap in hypophosphatasia (HPP) and preview the SIG's upcoming October 29 webinar on hypophosphatasia ahead of World HPP Day on October 30, 2026.

Persistently low alkaline phosphatase (ALP) can be an overlooked indicator of hypophosphatasia (HPP), a rare inherited disorder that disrupts mineralization of bone and teeth and can affect multiple organ systems. This article outlines diagnostic clues, management precautions, treatment considerations, and an upcoming professional webinar.



Anika Anam, MD



Azarmindokht Khosravi, MD

“ Since HPP affects multiple organ systems, managing HPP requires a multidisciplinary team approach. Not all patients with low alkaline phosphatase levels have HPP. Other medications and conditions that lower bone turnover can lead to a low alkaline phosphatase level. **For example, antiresorptive medications, tamoxifen, hypoparathyroidism, hypothyroidism, Cushing syndrome, and zinc deficiency are associated with low alkaline phosphatase levels.**

A Common Lab Value Hiding a Rare Diagnosis

Alkaline phosphatase (ALP) is included in routine metabolic panels, yet a low alkaline phosphatase level is often overlooked. Hypophosphatasia (HPP) is caused by loss-of-function mutations in ALPL, the gene encoding tissue nonspecific alkaline phosphatase (TNSALP). Without adequate enzyme activity, inorganic pyrophosphate is not converted to inorganic phosphate. Inorganic phosphate is needed to bind to calcium to form hydroxyapatite crystals that mineralize bone and teeth. As a result, pyrophosphate accumulates and blocks normal mineralization of bone and teeth. In HPP, calcium can accumulate in ectopic locations like kidneys or periarticular tissue.

TNSALP is also required for activation of vitamin B6 in the brain. Active vitamin B6 (pyridoxal 5'-phosphate, PLP) functions as a coenzyme for GABA synthesis in the central nervous system. In children, TNSALP deficiency can cause vitamin B6-responsive seizures. Carrier frequency for pathogenic or likely pathogenic ALPL gene variants is approximately one in 341 (0.3%) in a recent large-scale genomic screening of unselected populations (JBMR 2026 <https://doi.org/10.1093/jbmr/zjaf176>).

Diagnostic Pearls and Practical Guidance for HPP Care

HPP is associated with a wide spectrum of severity, ranging from severe life-threatening forms to mild adult-onset disease. Accordingly, HPP is classified into five main types based on the age symptoms first appear: perinatal, infantile, childhood, adult, and odonto (dental only).

HPP commonly affects the musculoskeletal, dental, renal, and central nervous systems. Musculoskeletal symptoms (muscle pain or weakness, bone, and joint pain), renal (hypercalciuria, nephrocalcinosis), dental (abnormal dentition, premature tooth loss), neurologic (fatigue, headache, sleep disturbance) are commonly observed in adults with HPP. HPP is a low bone turnover state; and individuals with HPP are more prone to fractures, particularly stress or atypical fractures.

Quick Tips for HPP

- More than 480 pathogenic or likely pathogenic ALPL variants have been cataloged to date
- Consider HPP when ALP is persistently low, especially alongside stress fractures or atypical fractures, arthralgia, or chondrocalcinosis
- Ask about early loss of primary teeth with intact roots, especially in children
- Avoid starting a bisphosphonate for low bone density before excluding HPP
- Using osteoanabolic agents can avoid oversuppression of bone turnover. If antiresorptive agents are needed, use shortest duration necessary to reduce risk of atypical femur fracture
- Avoid high doses of calcium and vitamin D supplementation due to increased risk of nephrocalcinosis and nephrolithiasis
- Consider referral for genetic counseling given the wide range of inheritance patterns and severity, even within the same family

Individuals with HPP are often misdiagnosed with fibromyalgia, chronic fatigue syndrome, or osteoarthritis. Even when HPP is considered, pitfalls in test interpretation can affect the evaluation. For example, children and adolescents have considerably higher ALP levels compared to adults. Reference ranges differ based on sex, especially during periods of growth and puberty. Measurement of plasma pyridoxal 5' phosphate (PLP), the active form of vitamin B6, and urinary PEA (phosphoethanolamine), which accumulates in HPP tend to be high and can help establish the diagnosis of HPP.

Prognosis and Treatment: A Multidisciplinary Effort

Since HPP affects multiple organ systems, managing HPP requires a multidisciplinary team approach. Not all patients with low alkaline phosphatase levels have HPP. Other medications and conditions that lower bone turnover can lead to a low alkaline phosphatase level. For example, antiresorptive medications, tamoxifen, hypoparathyroidism, hypothyroidism, Cushing syndrome, and zinc deficiency are associated with low alkaline phosphatase levels.

Asfotase alfa, a bone-targeted recombinant TNSALP, is currently the only approved pharmacologic treatment for perinatal, infantile, and juvenile hypophosphatasia. Enzyme replacement improves skeletal mineralization, pulmonary function, hypercalcemia, and muscle strength, with the most pronounced benefit seen in severely affected patients.

Treatment requires frequent subcutaneous injections, typically three to six times per week, and long-term data in adults remain limited. These factors, together with medication side effects and the cost and burden of ongoing injections, make careful patient selection important. Not every patient with a mild, adult-onset form of hypophosphatasia needs enzyme replacement; the

decision should weigh disease severity against the demands of therapy. Monitoring during treatment tracks skeletal, growth, respiratory, and motor function outcomes. Serum alkaline phosphatase rises substantially, often into the thousands, so it cannot be used to titrate dosing. Instead, clinicians should follow serum PLP, calcium, phosphorus, PTH, renal function, and urinary calcium, along with periodic renal and ophthalmic imaging to screen for calcifications.

The Time to Think HPP Is Now

As awareness of HPP grows and diagnostic tools improve, more patients stand to benefit from earlier recognition and treatment. This World HPP Day, and at the SIG's upcoming webinar, we hope you will join us in spreading the message: low ALP, think HPP. ^{EN}

Anika Anam, MD, is assistant professor of medicine in the Section of Endocrinology, Diabetes, and Metabolism at the Yale School of Medicine, New Haven, Conn.

Azarmindokht Khosravi, MD, is associate professor of medicine and clinical director of the Metabolic Bone Disease Program in the Division of Endocrinology, Diabetes, and Metabolism at Cedars Sinai, Los Angeles, Calif.

SAVE THE DATE: Bone and Mineral SIG Webinar on HPP

The Bone and Mineral Special Interest Group is hosting an exciting webinar, "Hypophosphatasia: From Molecular Mechanism to Clinical Practice," on **Wednesday, October 29, 2026**, just ahead of World HPP Day.

The webinar brings together three speakers whose expertise spans the full arc of HPP science, from the molecular biology of TNAP with José Luis Millán, PhD, through translational research bridging bench and bedside with Lothar Seefried MD, to clinical practice with Kathryn Dahir, MD.

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Where Care Meets Calling



Q&A with Lisa B. Nachtigall, MD

Lisa B. Nachtigall, MD, discusses receiving the Endocrine Society's 2026 Vigersky Outstanding Clinical Practitioner Award, her work in complex pituitary disorders, and her efforts to advance endocrinology through patient education, professional service, and early mentorship.

Lisa B. Nachtigall, MD, has built her career around the kind of medicine that extends far beyond the exam room: caring for patients with complex endocrine disorders, advocating for those with rare diseases, and helping inspire the next generation of endocrinologists. In recognition of her extraordinary contributions to clinical practice and the endocrine community, the Endocrine Society selected Nachtigall as a 2026 Laureate recipient of the Vigersky Outstanding Clinical Practitioner Award.

As medical director of the Mass General Brigham Pituitary Center and an associate professor of medicine at Harvard Medical School, Nachtigall has extensive expertise in pituitary disorders, particularly acromegaly. But her impact reaches well beyond her clinical practice. She has organized educational programs for patients with acromegaly, served on numerous Endocrine Society committees and task forces, and co-founded and directs a visiting scholars program designed to introduce students and trainees to endocrinology early in their careers.

BY GLENDA FAUNTLEROY SHAW

Endocrine News caught up with Nachtigall to discuss what continues to excite her about clinical endocrinology, the challenges facing practitioners and their patients, and why she believes exposing young people to the specialty early can make all the difference.

Endocrine News: What did hearing news of the Laureate recognition mean to you?

Lisa B. Nachtigall, MD: This was a career highlight for me. I was thrilled and honored. I felt recognized and valued, in an especially meaningful way, given my passion for the field and the high esteem I hold for the Endocrine Society. With so much talent in endocrinology, I understand how competitive it is to receive such an award.



Lisa B. Nachtigall, MD

EN: As clinical director at Mass General Brigham, what changes in clinical practice are you most excited about, and where do you think we still have the most work to do?

Nachtigall: New effective drugs are exciting. In obesity and metabolic dysfunction, GLP-1s are particularly transformative and their emerging potential role in other diseases beyond obesity, such as inflammatory disorders, is evolving.

Other new targeted therapies designed based on the knowledge of receptor signaling are useful in practice. For example, within my field of expertise, we now have a new oral therapy paltusotine that is easy for patients with acromegaly and works very well in tumors that express the somatostatin receptor type 2 (SST2). Setmelanotide, approved for hypothalamic obesity (HO), targets the melanocortin-4 receptor (MC4R). Both of these new drugs target G-coupled protein receptors.

And while the new drugs are exciting, it's frustrating when we can't get access for patients due to the expense and insurance issues. Prior authorization is a



Nachtigall (left) with her husband, Robert Flaumenhaft, MD, PhD, chief, Division of Hemostasis and Thrombosis, Beth Israel Deaconess Medical Center/Harvard Medical School; and her mother, Lila Nachtigall, MD, a professor of ObGyn at NYU, a menopause expert, and a longtime member of the Endocrine Society, at ENDO 2026 in Chicago, Ill., in June.



“ It is rewarding when patients remember what you say beyond the visit and when they tell me my words become a mantra that they carry through each day. I also love diagnosing functioning pituitary tumors based on clinical history and when patients improve after remission of Cushing disease or acromegaly. They are grateful, and it is gratifying to care for them longitudinally, often over decades.”

— LISA B. NACHTIGALL, MD, MEDICAL DIRECTOR, MASS GENERAL BRIGHAM PITUITARY CENTER; ASSOCIATE PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL, BOSTON, MASS.

limitation and burden where much improvement is needed — a thorn in many specialty practices. Getting the medications approved for our patients is complicated and time consuming for both patients and doctors. In our practice, we are fortunate to have a designated full-time person who just handles prior authorizations; this makes all the difference.

EN: Throughout your career, what has been the most rewarding moment, not necessarily the biggest achievement, but the moment that reaffirmed why you chose this path?

Nachtigall: It is rewarding when patients remember what you say beyond the visit and when they tell me my words become a mantra that they carry through each day. I also love diagnosing functioning pituitary tumors based on clinical history and when patients improve after remission of Cushing disease or acromegaly. They are grateful, and it is gratifying to care for them longitudinally, often over decades.



Nachtigall (second from right) with (l to r): MGH endocrine fellows Manasi Malik, MD, PhD; Afkera Daniels, MD, PhD; Bridget Gosis, MD, PhD; Nachtigall; and Janet Lo, MD, clinical director of the MGH Lipid and Metabolism clinic, associate professor of medicine, Harvard Medical School.



Nachtigall (right) with MGH Neuroendocrine Visiting scholars (l to r) Kevin Bode MD, James Flaumenhaft, MD, PhD student (HMS lab tour guide), and Dennis Nyano, MD.

EN: You've co-founded and currently direct a visiting scholars program encouraging a pipeline of students and trainees in endocrinology. What is the most common message that you use to encourage potential students into pursuing the specialty?

Nachtigall: I try to offer a window on real-life practice in a pituitary center and let them hear the patients' stories from the patient's perspective. I do not try to persuade them to the field, but rather, expose them to highlights and interesting cases and research that stems from the bedside to bench. The longitudinal relationships and multidisciplinary model of a pituitary center has its own draw.

I direct three different programs that involve visitors coming to our center. One is an international program, which includes students or professors who seek to learn more about the pituitary field. The international program attracts physicians and trainees from different cultures and we learn from them, too. There's a second program at Harvard, an advanced clinical clerkship, in neuroendocrine for Harvard medical students. The program that is most unique and critical for the pipeline is our Visiting Scholars program that caters to students from diverse backgrounds who are early career, from the second year of college through medical school. Some haven't applied to medical school yet, but they're interested in learning about it. So, our program gives them very early exposure to the field, and many have gone on to practice endocrinology or a related specialty. I remember one student, especially, as she was one of the first in the program, who pivoted to endocrinology saying, 'I thought I wanted to go into the ER, but I love that your patients know you so well for so many years.' That has stuck with me.

EN: How important has the Endocrine Society been throughout your career?

Nachtigall: The Endocrine society has been a critical part of my career.

Starting with my oral presentation as a fellow in 1996, I recall the excitement and rigor associated with my first scientific talk to national experts at the international meeting that year in San Francisco. Thereafter, I attended ENDOs for 30 years as they reliably offer the highest quality of endocrine education and innovative scientific content. I always learn something new and meet someone new at the annual meeting. The Endocrine Society meetings and committee work connected me with colleagues who have become friends and collaborators, inspired me to grow as an endocrinologist and enabled learning from educators and investigators outside of my home institution.

The Endocrine Society is an organization focused on excellence and committed to fairness and integrity, a trusted source of information, and a hub of professional opportunities that transcend the local politics of one's individual medical center or university. There is much value to that, and I think the Society is beneficial to endocrinologists at every stage from the earliest phase of one's career to the most senior.

EN: Practicing medicine can be all-consuming. What's your favorite way to unplug when you step away from the hospital?

Nachtigall: I like urban hikes, coastal walks, and trails near water. I love the ocean and being outdoors. Exploring with family and friends is the best! 

Endocrine Society Rallies for the NIH



(above) Among attendees at the Rally for Science at the office of Rep. Michael Guest (R-MS) are Endocrine Society member (and a member of the APOCC) Damian Romero, PhD (far left); Rebecca Osthus (American Physiological Society) and Society member Elise Gomez- Sanchez, PhD (fourth from left).

(left) Pictured (l to r) are Matt Ryan (Policy Fellow at Research!America), Endocrine Society member and FLARE fellow, Lydia Agnew, and Sophia Kaska, PhD, the Endocrine Society's manager of Science Policy and Research Affairs.

On September 17, members of the Endocrine Society joined advocates from around the country to call on Congress to provide increased funding for biomedical research as part of the 13th annual Rally for Medical Research. During the meetings, our members helped to raise the profile of endocrine research and reinforce the urgent need to increase funding for the National Institutes of Health (NIH) and protect it from administration proposals that would undermine the agency's ability to fund meritorious scientific research.

The Rally is a high-profile event on the Capitol Hill involving hundreds of meetings with congressional offices over the course of the day. The Endocrine Society once again provided a large contingent of members from important states and districts for the event. This year's event was critical, as the NIH not only faces funding challenges but also is under threat from a proposed rule issued by the Office of Management and Budget (OMB) that would place political considerations above merit-based scientific review for the selection and administration of grants. The rule would also

HOW YOU CAN PROTECT RESEARCH

The NIH urgently needs additional funding, but the agency also needs to be able to spend money in the way that Congress and taxpayers rightly expect. ***We encourage all members of the Society to share our message by sending a letter to your Representative and Senators through our online campaign. Please visit endocrine.org/advocacy/take-action and click on our New NIH Campaign.*** Taking action will take only a minute of your time and will have a real impact!

impose restrictions and barriers on the dissemination of scientific information through publications and conferences.

During the meetings with Congressional offices, Rally participants reinforced the following important messages:

- ▶ Appreciation to Congress for providing consistent bipartisan support for the NIH and urged it to provide it with at least \$51.3 billion in 2027.
- ▶ An urgent call on Congress to intervene and permanently block the proposed OMB rule from being finalized or going into effect.

Since the Rally, there was a meeting at the White House to discuss the proposed OMB rule and the White House discussed issuing an Executive Order to implement the proposed rule's policy changes. Several members of Congress, however, intervened, but it is not clear what the White House may do. Consequently, it is more important than ever that all congressional offices hear from their constituents about the need to urge the administration to withdraw the proposed rule and prevent the enactment of any policies that undermine a federal grant system grounded in scientific merit, transparency, and stability.



Society Submits Comments on the Medicare Physician Fee Schedule Proposed Rule

On September 11, 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 2027.

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, if finalized, would result in a 2.5% increase for the endocrinology specialty, but would also result in an overall decrease of 2.5% to the conversion factor for all physicians. Congressional intervention is necessary to update the conversion factor, and the Society continues to urge Congress to pass legislation providing an annual inflationary update to the MPFS tied to the Medicare Economic Index (MEI) that would override the rule.

The Society commented on several provisions in the rule that are important to endocrinologists. CMS has proposed creating a new practice expense equipment item for Fine Needle Aspiration (FNA), ER130 ("Fine Needle Aspiration portable ultrasound"). The Society advocated for this update to the practice expense inputs for FNA services and we worked with other medical societies to push for this change at the CPT and RUC.

The Society supports this change which is an important win for endocrinologists who perform FNAs. CMS has also proposed deleting the recently created G2211 complex care code and creating a new modifier code (MOD1) to take its place. The modifier,

when appended to an appropriate E/M code, will increase payment by 16% of the value of the reported E/M CPT code. However, we are deeply concerned about the impact this will have on work RVUs, particularly for endocrinologists and other physicians who practice at larger hospital systems and universities.

This proposed change would result in a loss of work RVUs for those who practice at larger systems. In our letter, we urge the agency not to finalize this proposal and to keep the G2211 code. Finally, we are asking CMS not to finalize a proposal that would reduce payment when using a Modifier 25 code under certain circumstances when being billed for an E/M visit.

The Endocrine Society staff worked closely with the Clinical Affairs Core Committee (CACC) to draft our comments. We thank the committee for their feedback and collaboration on this important issue. The final rule is expected to be released by early November at the latest.

You can read the letter we submitted at: endocrine.org/advocacy/society-letters.



Kim Schrier (D-WA)

Representative Kim Schrier to Serve as Diabetes Caucus Co-Chair Starting in January

Representative Kim Schrier will replace Representative Diana DeGette (D-CO) when the new Congress convenes in January 2027 after DeGette lost her re-election earlier this year. Representative Gus Bilirakis (R-FL) will continue to serve as the Republican co-chair of the Caucus. Schrier is the only pediatrician serving in Congress and the only representative with type 1 diabetes. She was diagnosed with type 1 diabetes when she was 16 years old.

The Society has a longstanding partnership with the Congressional Diabetes Caucus, and we work closely with the co-chairs on a wide range of issues impacting endocrinologists and the patients they treat living with diabetes. These issues include insulin affordability and funding for the Special Diabetes Program.

We are grateful to Representative DeGette for her leadership and accomplishments on diabetes issues during her time in Congress. We look forward to working with Representative Schrier on these priorities in the next Congress and know she will make important contributions to legislation aimed at better prevention, increased research, and better treatment of diabetes. ^{EN}

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