

JANUARY 2020

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

INTERNATIONAL

AFTERMATH: What Happens After Thyroid Cancer?

We preview an **ENDO 2020** session that details managing thyroid cancer patients and the issues clinicians often face once the cancer is no longer present:

- Hormone replacement therapy: Identifying problems and potential solutions.
- Risks vs. benefits: How intense should observing for tumor recurrence be?
- Radioactive iodine: Addressing the patient's concerns about the long-term consequences.

EYEWITNESS:

Treating patients with thyroid eye disease

MAKING PROGRESS:

A look back at new treatments, therapies, and products from 2019



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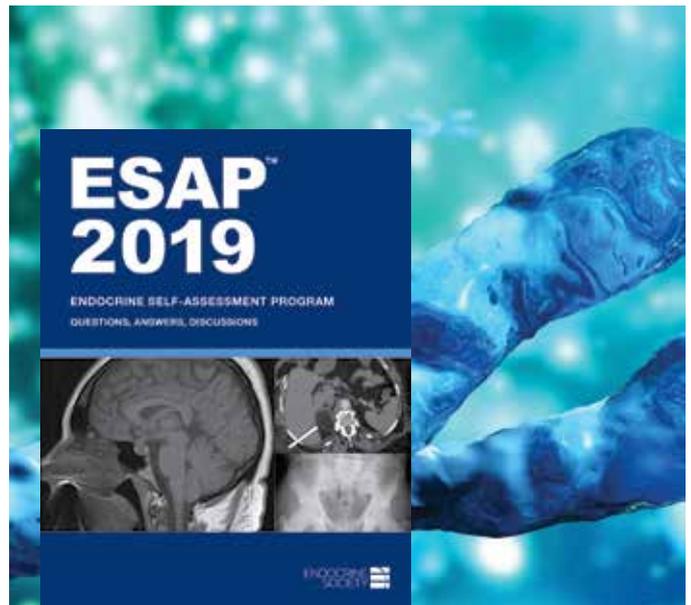
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A very good overview of endocrinology, new diagnostic tools, and treatments using up-to-date research and clinical outcomes.

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18 | 2019: The Year in Review

Endocrine research remains at the forefront of medical breakthroughs — as we showed last month with our cover story “Eureka! The Year’s Biggest Discoveries in Endocrine Science” — which has led to cutting-edge treatment options, therapies, and products. *Endocrine News* reviews some of these new methods to treat a variety of endocrine complications as we kick off a new decade.

BY DEREK BAGLEY

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Endocrine News gets the patient and physician perspective on thyroid eye disease. Patients discuss how it has affected their lives, and clinicians explain the limited treatment choices. However, new options may be on the horizon.

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The challenges of managing thyroid cancer patients include regulating their hormone replacement therapy and monitoring for recurrence. Here, we highlight an upcoming **ENDO 2020** session that details the issues in treating patients post-thyroid cancer therapy.

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BY ERIC SEABORG

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Thyroid Cancer:
What Patients Need to Know

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Keeping Endocrinology in the Public Eye

We live in a world in which members of our community increasingly receive health, research, and policy information from multiple sources, embodying varying degrees of rigor and veracity. As online sources overwhelm the public with health and science information, it becomes increasingly imperative to communicate the value of endocrinology more clearly than ever. The policy makers and influencers making decisions about research funding and clinical resources must understand and be aware that endocrinologists are tackling many serious health issues. These range from major chronic disease epidemics to rare diseases or the health impact of environmental exposures, all of which ultimately impact public health and general well-being.

Media outlets remain an important conduit to raise awareness of the cutting-edge research we conduct and the quality patient care we provide. Through global news coverage, we connect with broad audiences of patients, caregivers, policy makers, research funders, and other stakeholders. The Endocrine Society offers resources to help you communicate the value of your expertise to these audiences.

More than 7,400 news stories mentioned our work in 2019. CNN, BBC News, the *New York Times*, *USA Today*, CBS This Morning, and *TIME* magazine featured us in their coverage. This coverage reached an audience of more than 12 billion unique monthly visitors online and nearly 12 million print readers, TV viewers, and radio listeners worldwide, according to the media database Cision. I have personally experienced this from both sides. For example, work presented by one my trainees at **ENDO 2019** on differences in weight loss with ketogenic diets between male and female animals continues to generate significant media attention. I did not expect this, but this made me realize that many media outlets turn to us and come to our annual meeting to understand the important questions in the field. Our influence in this space cannot be underestimated.

Therefore, the Society actively builds strong relationships with influential health and science journalists to ensure our

messages reach large audiences. When our members address insulin prices, PFAS chemical exposure, and other timely issues on the Hill, our staff invites journalists to attend and interview our experts.

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The Endocrine Society is committed to working with all of our members to ensure that your expertise and thought leadership drives those conversations and continues to raise public awareness of endocrinology from a trusted source.

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Last year, we distributed more than 80 press releases to journalists worldwide on research published in our journals and presented at **ENDO 2019**, among other topics. Moreover, our communications and media relations team drive news coverage with tailored outreach, social media posts targeted to journalists, and media webinars.

For the first time last year, we expanded the number of **ENDO** press conferences to six. To increase the reach beyond journalists who attend the meeting in person, our team webcasts the news conferences to give reporters around the world instant access to our presenters. These news conferences featured the latest research on diabetes, obesity, endocrine-disrupting chemicals (EDCs), bone health, and reproductive health.

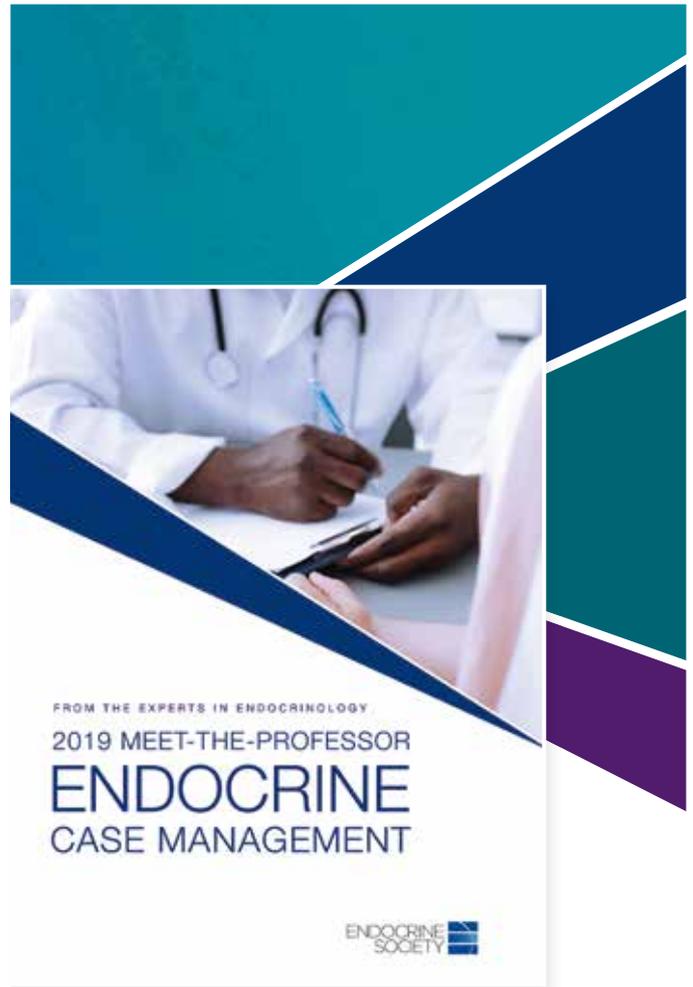
As we embark on a new year, we recognize that endocrine topics such as insulin prices, transgender medicine, and EDC exposure will continue to dominate headlines. Emerging therapies for diabetes, obesity and its complications such as nonalcoholic steatohepatitis (NASH), new diabetes technologies, and access to quality healthcare will continue to generate media interest. The Endocrine Society is committed to working with all of our members to ensure that your expertise and thought leadership drives those conversations and continues to raise public awareness of endocrinology from a trusted source.

Speaking to the news media requires a specialized skillset. To ensure you have the tools you need to elevate your spokesperson capabilities, our media and communications team have generated a video series — 8 Tips for Communicating Science — to advise members on how to become stronger and more effective spokespeople. It only takes 10 minutes to watch the entire series and learn how you can effectively communicate the value of your research. I encourage you to take advantage of this benefit available exclusively to members.

Especially for our trainees, but of relevance across the career spectrum, practicing your pitch is an effective way to improve your interviewing skills. Our media relations staff offers members individual consultations via video call. You can also send the staff a two- to three-minute video of your key messages, and they will respond with advice personalized just for you. Our team is ready to offer advice as you field incoming media requests.

Health and science journalists often have tight deadlines, and it takes the combined efforts of many trained spokespeople to represent the field. If you are interested in serving as a Society spokesperson, don't forget to include that information when you complete your volunteer profile. You also can contact our media relations staff directly at media@endocrine.org. 

E. Dale Abel, MB, BS, DPhil, MD, PhD
President, Endocrine Society



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FROM THE **EDITOR**

JANUARY 2020

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.

Neck & Neck: Thyroid Cancer & Thyroid Eye Disease

Welcome to a new year and a new decade! We're kicking off 2020 with a focus on the thyroid, as you can see from the cover story that is an interesting and often overlooked component of treating thyroid cancer patients. In "Aftermath: What Happens Next After Thyroid Cancer Treatment" on page 32, Eric Seaborg gives readers a preview of a special **ENDO 2020** session on this topic in March in San Francisco that will consist of seven separate sessions. From issues with thyroid hormone replacement therapy and surveillance for disease recurrence to patients' concerns about prolonged exposure to radioactive iodine, this article gives readers a sneak peek at what to expect from this in-depth session.



While it was typical for all thyroid cancer patients to get a neck ultrasound every year after their initial treatment, in low-risk patients it was discovered that when ultrasounds were conducted too much, the scans would pick up lymph nodes that have nothing to do with the cancer thus leading to increased patient anxiety, according to Megan R. Haymart, MD, associate professor of medicine, University of Michigan, Ann Arbor, Mich., who will be one of the speakers at **ENDO**. "It is important that the intensity of the surveillance is tailored to the severity of the patient's disease," she says in the article.

On page 28, senior editor Derek Bagley tackles the topic of thyroid eye disease (TED) in "The Eyes Have It," where he speaks with two patients who have



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Endocrine News® is published 12 times a year by the Endocrine Society, 2055 L Street, NW, Suite 600, Washington, DC 20036
Phone 202-971-3636 • Fax 202-736-9708
www.endocrine.org.

Print ISSN 2157-2089 Online ISSN 2157-2097
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been dealing with TED for many years. Since TED often manifests itself in very obvious ways physically, this can be somewhat off putting for patients. Christine Gustafson, a patient with TED, in Monterey, Calif., discusses how that

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Offering new hope for a longtime endocrine ailment. What better way to kick off a new decade?

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while people are quite kind to her typically, she feels that it was hard for them to look at her. “I just had to stay strong and go forward,” she explains, “and I didn’t know that there was really any hope that I’d ever look normal again.”

That hope has come in the form of a new pharmaceutical called teprotumamab, which has shown promising results in Phase 2 and Phase 3 clinical trials (which Bagley also discusses in “2019: The Year in Review” on page 18) that has shown significant reductions in swelling, proptosis, and diplopia, not to mention overall improvements in quality of life. According to Terry Smith, MD, from the University of Michigan, who was involved in the study, “For the first time we have medical therapy that appears to be highly effective ... in the treatment of moderate to severe active TED” with limited side effects. Smith adds that this new drug could, for the first time, reduce the need for surgery for TED patients.

Offering new hope for a longtime endocrine ailment. What better way to kick off a new decade?

As usual, if you have your own stories to share with the readers of *Endocrine News*, feel free to contact me at mnewman@endocrine.org. 

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



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Endocrine Society, Avalere Health Launch Hypoglycemia Clinical Tools

In December, the Endocrine Society and Avalere Health introduced the first-ever quality measures to help healthcare providers assess how well they identify and care for older adults at greater risk of hypoglycemia — low blood sugar that can be a dangerous complication of diabetes treatment.

A panel of diabetes experts published the quality measures, which focus on outpatient treatment for adults who are 65 and older and have type 2 diabetes, in the Society's *Journal of Clinical Endocrinology & Metabolism*. The panelists relied on their clinical background, measure development

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Hypoglycemia is an area where we can make meaningful strides in improving diabetes care. These first-of-their-kind quality measures will help clinicians better identify patients who are at risk and combat hypoglycemia.
 ”

expertise, and insight into patient perspectives to develop the measure set.

“We convened an expert panel of endocrinologists, primary care physicians, diabetes educators, pharmacists, measurement experts, and patient advocates to ensure that the quality measures reflect a variety of perspectives and a wide breadth of knowledge on hypoglycemia prevention,” says James L. Rosenzweig, MD, of Hebrew SeniorLife in Boston, Mass., who led the expert panel.

An estimated 33% of adults age 65 and older have diabetes, and this age group faces increased risk of developing hypoglycemia. Hypoglycemia can lead to seizures, coma, and even death. The U.S. Department of Health and Human Services identified hypoglycemia as one of the top three preventable and measurable adverse drug events.

“Hypoglycemia is an area where we can make meaningful strides in improving diabetes care,” Rosenzweig says. “Our research has shown a lack of widespread initiatives to address this issue. These first-of-their-kind quality measures will help clinicians better identify patients who are at risk and combat hypoglycemia.”

The quality measures outline key risk factors that raise an individual's chances of developing hypoglycemia and emphasize the importance of people who meet these criteria receiving education to help prevent future episodes.

Key risk factors include:

- Experiencing a hypoglycemic event in which blood glucose levels dropped below 54 mg/dL and required immediate attention within the past year
- Experiencing altered mental or physical status requiring assistance during a severe hypoglycemic event in the past year
- Among individuals who manage their blood sugar with insulin or medicines like sulfonylureas that increase the risk of hypoglycemia:
 - A documented A1c of less than 7% in the past six months, or
 - At least one other relevant chronic medical problem.

The expert panel also recommends that healthcare providers capture information about hypoglycemic episodes where individuals experienced altered mental or physical status requiring assistance within the past year. This information can help clinicians better determine if an individual is experiencing growing unawareness of hypoglycemia over time and identify what kinds of interventions stand the best chance of helping the patient avoid future episodes.

Once medical centers and practices begin using the quality measures, the Society and Avalere hope to use information and data from users to refine the quality measures in the future.

Other authors of the report and recommendations include: Paul R. Conlin, MD, of VA Boston Healthcare System in Boston, Mass.; Jasmine D. Gozalvo, PharmD, BCPS, BC-ADM, CDE, LDE, FAADE, of Purdue University in West Lafayette, Ind.; Stephanie B. Kutler, Endocrine Society; Nisa Maruthur, MD, MHS, of Johns Hopkins University in Baltimore, Md.; Penelope Soli, JD, Avalere Health in Washington, D.C.; Sandeep Vijan, MD, of the University of Michigan in Ann Arbor, Mich.; Amish Wallia, MD, of Northwestern University in Chicago, Ill.; and Robin Fein Wright, LCSW, of Diabetes Sisters in Bolingbrook, Ill.

The work on measures was part of a broader quality improvement effort, the Hypoglycemia Prevention Initiative, which was launched by the Endocrine Society and Avalere Health to study how hypoglycemia could be prevented in older individuals with type 2 diabetes and whether primary care physicians could incorporate diagnostic and preventive services into their workflow. The Hypoglycemia Prevention Initiative is supported by Merck & Co., Inc.; Lilly USA, LLC; Novo Nordisk, Inc.; Sanofi; and Abbott Diabetes Care, Inc.

The manuscript, “2019 Endocrine Society Measure Set for Older Adults with Type 2 Diabetes at Risk for Hypoglycemia,” was published online, ahead of print.

Correa Appointed Diversity Director at University of Arizona College of Medicine



Ricardo Correa, MD, has been named Graduate Medical Education (GME) diversity director at the University of Arizona College of Medicine in Phoenix, where he will chair the newly established diversity and inclusion subcommittee of the GME committee.

The goal of the subcommittee is to help ensure and create practices that focus on mission-driven, ongoing, systematic recruitment and retention of a diverse and inclusive workforce of residents, fellows, and other members of the college community. The subcommittee will also make recommendations to establish policies and procedures related to the recruitment and retention of minorities underrepresented in medicine, as well as medical leadership in accordance with the college’s mission.

Correa is a member of the university’s Diversity Committee and has served in leadership roles to bring the Building the Next Generation of Academic Physicians (BNGAP) conference to the college. In addition, he recently completed the highly prestigious U.S. Presidential Leadership Scholars Program.

Correa serves as the director of the Endocrinology, Diabetes, and Metabolism Fellowship and as an assistant professor of medicine in the Division of Endocrinology. His work and research focus on improving health disparities for underrepresented minorities, including Latinx and the transgender population.

At the national level, Correa is involved with the Diversity Collaborative of the Alliance Academy of Internal Medicine (AAIM), the Diversity group for the ACGME, the International Medical Graduate governing council of the American Medical Association and the Group of Diversity of the AAMC.

An alumni of the Endocrine Society’s Future Leaders Advancing Research in Endocrinology (FLARE) program, Correa is also a member of the Publications Core Committee and the *Endocrine News* editorial board.

MEMBERS
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NEWS

Carolyn Smith, PhD, professor of molecular and cellular biology and chair of the Endocrine Society's Annual Meeting Steering Committee (AMSC), was named dean of the Graduate School of Biomedical Sciences at the Baylor College of Medicine in Houston, Texas.

Smith is also a member of the Dan L. Duncan Comprehensive Cancer Center where her research focuses on the molecular pharmacology of estrogen receptors, regulation of gene expression by transcriptional coactivators and corepressors, tamoxifen resistance in breast cancer, and steroid hormone action in urothelial carcinomas. She has served as the director of the Tissue and Cell Culture Core for the Center for Reproductive Biology and the Department of Molecular and Cellular Biology since 1994.

Smith received her Bachelor of Science from the University of Toronto and her PhD from the University of Western Ontario. She completed her postdoctoral fellowship at Baylor and joined the faculty in 1994. Over the years, she has served in several leadership roles within her program as well as the graduate school, including senior associate dean of graduate education and academic program development for four years before serving as interim dean.

Smith Named Dean of Baylor's Graduate School of Biomedical Sciences

She has published more than 100 papers and been continually funded by the National Institutes of Health (NIH) since 1996, along with support from the American Heart Association, Department of Defense, and the National Space Biomedical Research Program. She has served on numerous study sections for the NIH, Department of Defense, and the American Cancer Society most recently as a member of their Extramural Grants Council.

Within graduate education, her interests focus on the development of academic programs, assessment with the goal of enhancing program effectiveness, and creating an environment that supports the professional development of research students and postdoctoral fellows. Smith has mentored six PhD students and 24 postdoctoral fellows in her laboratory.

"Baylor College of Medicine is a vibrant and dedicated community with outstanding faculty and research programs that provide exceptional opportunities for training graduate students and postdoctoral fellows," Smith says. "It has been my honor to work with the dedicated students, fellows, faculty and staff of Baylor in my prior roles in graduate education, and I am excited by the opportunity to lead and further develop the graduate school's world-class training programs."

Aside from her duties chairing the AMSC, Smith is also on the Society's Scientific and Educational Programs Core Committee, Basic Science Outreach Advisory Committee, and has served in various capacities on a variety of other committees as well as on the editorial board of *Endocrinology* from 2008 to 2011.



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Hormone Science to Health



BY DEREK BAGLEY
Senior Editor



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TSH levels slightly above the reference range should not prompt referral to pediatric endocrinologists unless another basis for clinical concern is present.

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Slightly Elevated TSH Levels Not a Cause for Referral to Pediatric Endocrinologists

Children with thyroid stimulating hormone (TSH) levels slightly above reference range shouldn't be referred to pediatric endocrinologists unless there is another cause for clinical concern, according to a paper recently published in the *Journal of the Endocrine Society*.

Researchers led by Perrin C. White, MD, of the Division of Pediatric Endocrinology at the University of Texas Southwestern Medical Center in Dallas, point out that limited data are available to help primary care physicians distinguish



abnormal lab results that show actual thyroid disease from things like laboratory error or acute illness. “Such information could help primary care practitioners limit referrals to pediatric endocrinologists for evaluation of abnormal thyroid function to those patients likely to require treatment,” the authors write.

The researchers looked at determining the reproducibility of TSH testing in pediatric patients referred to pediatric endocrinologists. They write that they also wanted to identify the threshold TSH levels that would predict presence of antithyroid autoantibodies and inform decisions by pediatric endocrinologists at their institution to initiate or continue treatment with levothyroxine.

The team analyzed data from a retrospective case series of 325 children ages one to 18 years, referred to the endocrinology clinic at a tertiary children's hospital for hypothyroidism. Of these 325 children, 191 were treated, and the treated children were more likely to have higher referral TSH, positive autoantibodies, and abnormal thyroid gland examination findings, according to the authors. “Mild elevations of TSH (5 to 6 mIU/L) were unlikely to be reproduced with repeat testing, to be associated with positive autoantibodies, or to result in decisions by pediatric endocrinologists to treat the patients,” they write.

The authors note that this study did have a few potential limitations, like the fact that the decision by the endocrinologist to treat was subjective and that TSH reference ranges in children have varied in the reported data. “Finally, the decision to continue or start therapy was determined by each individual endocrinologist, and no written standard of care was used,” the authors write. “The present study was undertaken to provide data for such a guideline.”

Findings: Still, based on their findings, the authors conclude: “TSH levels slightly above the reference range should not prompt referral to pediatric endocrinologists unless another basis for clinical concern is present.”

BPA Exposure Leads to Abnormal Estrous Cycle and Folliculogenesis, Mouse Study Finds

Exposure to bisphenol A (BPA), even at environmentally low doses, disrupts the preovulatory luteinizing hormone (LH) surge and leads to abnormal estrous cycle and folliculogenesis, according to a study recently published in *Endocrinology*. This disruption is reversible following adult exposure, but it persists into adulthood after neonatal exposure.

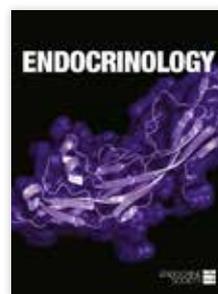
Researchers led by David Lopez-Rodriguez, MSc, at the neuroendocrinology laboratory of Anne-Simone Parent, MD, PhD, (GIGA-Neuroscience), the University of Liege, Belgium, point out that BPA is found in almost everything, even though it has been partially banned in some countries. Humans are exposed to BPA through food and drink, and several studies have implicated BPA in contaminating fetuses and neonates. “Sex steroids play a crucial role perinatally in ‘organizing’ the control of female reproduction,” the authors write. “For that reason, the adult female estrous cycle is altered following exogenous exposure to sex steroids during that vulnerable perinatal period. Therefore, the effects of early exposure to BPA on puberty and reproduction are a matter of concern.”

The researchers note that they have already shown that BPA exposure can delay or advance vaginal opening, through a low or high dose, respectively. For this study, the authors write, they wanted to see whether neonatal exposure to a low dose of BPA could produce persistent disruption of folliculogenesis and estrous cycle that could be consistent with disturbed organization. “We also used the high BPA dose because opposing effects on GnRH secretion and pubertal timing were seen after using the low and the high doses of BPA neonatally,” they write. “Finally, the aim was to evaluate whether adult BPA exposure in similar conditions would produce persistent or transient effects on ovulation and folliculogenesis.”



The team injected one-day-old and 90-day-old rats with either corn oil or BPA (a high dose or a low dose) for 15 days. Neonatal exposure to both doses disrupted the estrous cycle and folliculogenesis, a disruption that persisted into adulthood. Both doses given to adults caused a reversible decrease in antral follicles and corpora lutea as well as a reversible disruption of the estrous cycle associated with a delay and a decrease in the amplitude of the LH surge was also observed, according to the authors. “Although the alterations of estrous cyclicity persist after neonatal exposure, they appear to be transient during adult exposure to BPA,” the authors write. “During 2 weeks of adult exposure to a very low or high dose of BPA, altered estrous cyclicity occurs together with disruption of the late stages of folliculogenesis (antral follicles and corpora lutea). Importantly, all of these effects appear to have disappeared 1 month after stopping the exposure to BPA.”

Findings: “In conclusion,” the authors write, “we show that both adult and neonatal exposure to a very low dose of BPA in the range of nanograms can result in alteration of estrous cyclicity and folliculogenesis.” They go on to write that their findings show that when further evaluating BPA’s effects on the female reproductive axis, very low doses should be used, while including the neonatal period and addressing neuroendocrine and ovarian endpoints.



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Although the alterations of estrous cyclicity persist after neonatal exposure, they appear to be transient during adult exposure to BPA.

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Until this controversy concerning surgical timing is resolved, parents and physicians are left to make surgical decisions for affected children on a case-by-case basis with input from other members of the health care delivery team.
”

Review Examines Optimal Care for Patients with 46,XY Differences of Sex Development

Treating patients with 46,XY differences of sex development (DSD) will require interdisciplinary healthcare teams trained to care for patients and their families, according to a paper recently published in *Endocrine Reviews*.

The review, by Amy B. Wisniewski, of Oklahoma State University in Stillwater, et al., points out that DSD are a heterogeneous group of congenital conditions, and that people with DSD who possess a 46,XY complement can present with variable degrees of virilization of their external genitalia. Conditions labeled 46,XY DSD are complex and widely varied, and there is still much to be learned about these conditions. “The aims of this proposal are to review what is known about prevalence, incidence, morbidity, diagnostic tools and timing, sex of rearing, endocrine and surgical treatment, fertility and sexual function, and behavioral development in affected people,” the authors write.

The authors cover the diagnostic tools like hormonal, imaging, and genetic studies, as well as the prenatal and postnatal diagnostics. Prenatal diagnosis of DSD has increased with the utilization of noninvasive prenatal testing (NIPT) by cell-free DNA analysis of maternal blood to screen for aneuploidy during the first trimester of pregnancy, a test that is 98% to 99% accurate.

Once a newborn is diagnosed with DSD comes the challenging decision of what sex to rear the child. According to the authors, such decisions are based on the understanding that someone’s gender identity might not align with their anatomical sex. Sexual attraction is also difficult to predict. “Such discordance between sex, gender identity, and sexual orientation illustrates the complexity physicians and caregivers face when deciding on a sex of rearing for a newborn with 46,XY DSD,” the authors write. “As older children recognize and reveal their gender identity over time, decisions regarding sex of rearing do not apply to them.”

The authors note that most individuals affected by 46,XY DSD have a deficiency in either androgen production or action as part of their condition, and they will need hormone treatment such as androgen or estrogen replacement. These patients may also opt for surgeries, like masculinizing or feminizing procedures, but there remains some controversy over timing of these surgical procedures. “Until this controversy concerning surgical timing is resolved, parents and physicians are left to make surgical decisions for affected children on a case-by-case basis with input from other members of the health care delivery team.”

The review covers a lot, detailing sexual function of people with 46,XY DSD — their quality of sexual life compared to unaffected adults — and that these patients may seek treatment for infertility, although fertility potential varies depending on the underlying etiology of their condition.

Findings: Treating these patients will require family-centered, interdisciplinary care. The authors write that interdisciplinary care is provided by a team of specialists who work together to provide healthcare for patients and families. In the context of DSD, interdisciplinary care includes nursing, medical specialists, surgical specialists, and mental health, social work, and peer-to-peer support. “Optimally, the team works with a family as soon as DSD is suspected to provide appropriate information during the medical evaluation,” they write.

Treatment of these patients has improved in recent years. However, the authors write, “What remains to be improved is understanding how to talk about DSD, as well as developing evidence-based mental health care, surgical interventions, and fertility optimization.”

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San Francisco, California
March 28 – 31, 2020

KEY DATES

ADVANCE REGISTRATION DEADLINE:

February 13, 2020

LAST CALL ABSTRACTS:

Opens January 9, 2020

HOUSING DEADLINE:

March 3, 2020

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www.endocrine.org/endo2020

Miami Thyroid Oncology Symposium

Miami, Florida

March 13 – 14, 2020

Organized by the Miami Cancer Research Center, the 4th Annual Miami Thyroid Oncology Symposium will begin with a course on the essentials of clinical genomics that aims to provide a strong foundation for practicing physicians and help them understand the evolving role of clinical molecular testing. There will be an oral/poster abstract presentation session, followed by an expert panel discussion on the first day, which will provide a platform for young physicians in training and all

academic and practicing physicians to present and discuss their research work and clinical experience.

www.miamicancerresearch.org

Clinical Endocrinology 2020

Boston, Massachusetts

March 21 – 25, 2020

Harvard Medical School has selected more than 40 faculty and outside experts to present up-to-date, evidence-based approaches to endocrine problems. This course will cover many topics including osteoporosis, diabetes, hypercholesterolemia, pituitary tumors, menopause, thyroid abnormalities,

reproductive dysfunction, and a broad spectrum of other clinical problems in endocrinology.

www.endocrinology.hmscme.com

Endocrine Fellows Series: Type 1 Diabetes Care and Management

San Francisco, California

March 24 – 26, 2020

Fellows Series: Type 1 Diabetes Care and Management is a comprehensive conference for adult and pediatric endocrine fellows interested in type 1 diabetes. A preconference event to **ENDO**, the unique and highly sought after program offers an opportunity to learn from leaders

in the field through interactive sessions, small group discussions, and hands-on learning. The curriculum provides comprehensive education not typically taught in fellowship and opportunities to connect with thought-leaders and peers.

www.endocrine.org/meetings-and-events/fellows-conferences/t1d-fellows

The 4th International Symposium on the Calcium Sensing Receptor (CaSR)

**San Francisco, California
March 26 – 27, 2020**

This symposium will bring together basic, translational, and clinical scientists from different disciplines who study the biochemistry, molecular biology, cell biology, physiology, and pathophysiology of the CaSR and clinical disorders of CaSR function. The program will include lectures, oral abstract presentations, poster discussion sessions, and forums for young investigators to meet senior experts.

www.ncire.org/casrsymposium2020



Photo: Dana Fleming/Shutterstock.com

American Association of Endocrine Surgeons 41st Annual Meeting

**Birmingham, Alabama
April 4 – 6, 2020**

The American Association of Endocrine Surgeons (AAES) 41st Annual Meeting will feature symposia on wellness, diversity and inclusion, business in surgery, interesting case presentations, and a new quick shot poster session to allow more presenters to the podium. Additionally, the AAES will again host the Advanced Endocrine Surgery Course as an opportunity to review current standards in management of complex endocrine diseases, while engaging on a personal level with nationally recognized authorities in the field.

www.endocrinesurgery.org

INTERNATIONAL ITINERARY

Diabetes Expo Asia Pacific – Global Summit on Diabetes and Endocrinology

**Bangkok, Thailand
January 27 – 28, 2020**

The theme of the 2020 Diabetes Expo Asia Pacific will be “Novel Advancements in Diabetes and Endocrinology.” The conference will look at various metabolic diseases and their complications including diabetic nephropathy, ophthalmology in diabetics, and diabetes skin complications. Tracks will also look at genetic mechanisms leading to endocrine disease, functional studies of genetic mutations that shed novel insights into the pathogenesis of endocrine disorders, and how the endocrine system regulates interactions with environmental stimuli.

www.diabetesconference.endocrineconferences.com

Groningen Pituitary and Skullbase Symposium

**Groningen, Netherlands
March 4 – 6, 2020**

The Groningen Pituitary and Skullbase Symposium will look into the care and cure of patients with pituitary or skullbase pathology. The conference will focus on various aspects of pituitary and skullbase diseases. A national and international faculty will be present to elucidate on radiology, radiotherapy, endocrinology, surgery, and research topics.

www.gps-symposium.com

17th Biennial Congress of the Asian Association of Endocrine Surgeons – AsAES 2020

**Melbourne, Australia
March 5 – 7, 2020**

AsAES 2020: Controversies in Endocrine Surgery will focus on key areas of endocrine surgery including benign and malignant thyroid disease, parathyroid disease, and management of adrenal pathology. Partnering with the Endocrine Society of Australia – ESA, the symposia will offer a combined multidisciplinary program on Day 2, which will focus on areas of combined interest to both endocrine surgeons and endocrinologists.

www.asaes.com

EMBO EMBL Symposium Inter-Organ Communication in Physiology and Disease

**Heidelberg, Germany
March 15 – 18, 2020**

This symposium will showcase how sophisticated genetic approaches are transforming the understanding of physiology and reveal emerging paradigms of inter-organ communication relevant to metabolic homeostasis and disease. The conference aims to provide a high visibility platform to scientists who use modern molecular genetic tools to discover inter-organ communications to illustrate how much our molecular and genetic understanding of whole-organism physiology has progressed in the past 20 years.

www.embo-embl-symposia.org



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“ Our conclusion strengthens the position that once you achieve a certain level of vitamin D sufficiency, there is no further benefit of pushing the dose higher for bone. **Our study actually raises the possibility that there is harm in pushing the dose higher, which is something that other studies have raised as well.**”

— DAVID A. HANLEY, MD, professor, Departments of Medicine, Oncology, and Community Health Sciences, University of Calgary, Alberta, Canada, discussing how it's possible that when people take more than the recommended amounts of vitamin D, it serves no benefit in the article **“Vitamin D: When Enough is Enough”** on page 42.



Percentage of the likelihood that individuals with hypothyroidism 60 years or older are more likely to die from all causes than those without this condition.

— SOURCE: JOURNAL OF THE ENDOCRINE SOCIETY



25% Percentage of the U.S. veteran population living with type 2 diabetes

— SOURCE: U.S. DEPARTMENT OF VETERANS AFFAIRS



Percentage of young Americans with type 1 diabetes who have attempted suicide, suggesting pediatric type 1 diabetes treatment should incorporate evaluation of suicide risk.

— SOURCE: DIABETES CARE

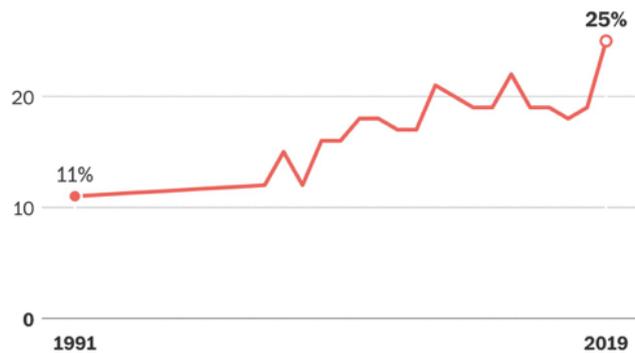
2019:82% vs. 2009:63%

Percentage of covered workers who must meet a deductible before healthcare coverage kicks in.

— SOURCE: HENRY J. KAISER FAMILY FOUNDATION'S EMPLOYER HEALTH SURVEY

Record share of Americans delay treatment due to cost

Percent saying they or a family member put off care for a serious medical condition “because of the cost you would have to pay”



Source: Gallup

THE WASHINGTON POST



3 out of 4

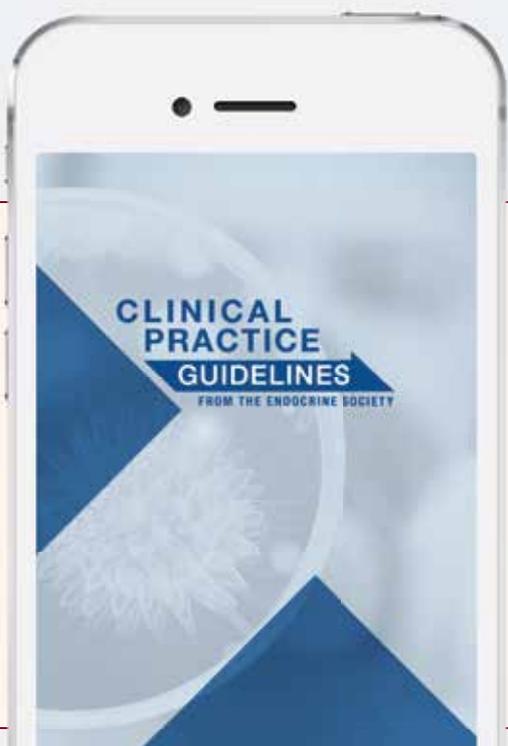
The number of diabetics who don't adequately control the four major factors that increase the risk of serious complications: blood glucose, blood pressure, blood cholesterol, and smoking.

— SOURCE: DIABETES CARE

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2019: The Year in REVIEW

BY DEREK BAGLEY



Endocrine research remains at the forefront of medical breakthroughs — as we showed last month with our cover story “Eureka! The Year’s Biggest Discoveries in Endocrine Science” — which has led to cutting-edge treatment options, therapies, and products.



Endocrine News reviews some of these new methods to treat a variety of endocrine complications as we kick off a new decade.

Calculating Diabetes Complications

Cleveland Clinic researchers have developed a risk calculator that can show patients with type 2 diabetes their risks of developing major health complications over the next 10 years depending on which course of treatment they choose.

Research has shown that weight-loss surgery can help people control their diabetes and improve cardiovascular health. In 2016, the world's leading diabetes organizations recommended in a consensus report that metabolic surgery should be a treatment option for people with type 2 diabetes and obesity. However, few eligible patients undergo the surgery.

To help patients and their physicians better predict the health benefits of usual care versus surgical treatment, Ali Aminian, MD, a bariatric surgeon at Cleveland Clinic, and his research team developed a risk score calculator that provides personalized evidence-based information based on a patient's current health status.

"The calculator can be a useful tool for physicians and

patients with type 2 diabetes and obesity. It shows a patient's risk of heart disease, stroke, heart failure, diabetic kidney disease, and death over the next 10 years with usual care. It also shows how a patient's risk of those adverse events could change after metabolic surgery," says Aminian, who is also lead author of the study.

The calculator — 10-year Individualized Diabetes Complications Risk Scores — was developed in two phases over the course of about two years. In the first phase, an observational study looked at nearly 2,300 patients who underwent metabolic surgery and 11,500 matched patients with similar characteristics who received usual medical care.

The Phase 1 results, published in the *Journal of the American Medical Association (JAMA)* in September, show that weight-loss surgery performed in patients with type 2 diabetes and obesity is associated with 40% lower risk of death and major adverse cardiovascular events than usual medical care. Surgical patients also lost more weight, had better diabetes control, and used fewer medications for treatment of their diabetes and cardiovascular disease than those undergoing usual medical care.

In Phase 2, the researchers used the same group of patients to identify predictors for different health outcomes. Evidence-based models were built and integrated into a risk calculator to estimate the likelihood of coronary heart disease, stroke, heart failure, diabetic kidney disease, and mortality over the next 10 years in patients with type 2 diabetes and obesity with and without bariatric surgery.

“Based on the advice of subject matter experts, our team was able to explore 26 risk factors for the different outcomes, including risk of dying, in that large group of patients,” says Michael Kattan, PhD, chairman of the Department of Quantitative Health Sciences in Cleveland Clinic’s Lerner Research Institute. “We then compared machine learning and traditional statistical techniques to identify the most accurate prediction models for each outcome and built those into the calculator.”

Steven Nissen, MD, chief academic officer of the Heart & Vascular Institute at Cleveland Clinic, adds, “Diabetes can be a devastating disease and combined with obesity, patients are at a high risk for cardiovascular complications. Metabolic surgery is an underutilized treatment for these patients. This calculator can help both physicians and patients quantify the risks and benefits of surgery and make the best decision for treatment.”

The calculator will be accessible on the Cleveland Clinic Risk Calculator Library website and as a smartphone application (BariatricCalc). The second version of the app with additional calculators was released during ObesityWeek 2019.

This study was partially funded by an unrestricted grant from Medtronic. Medtronic had no role in the design, conduct of the study, or reporting of the results.

Pharmaceutical Breakthrough for Thyroid Eye Disease Patients

An integrated clinical trial of teprotumumab showed promise for the treatment of active thyroid eye disease (TED). The results support prior analyses of significant reductions in inflammation, proptosis, and diplopia, as well as improvements in quality of life (QoL). These data were presented at the 89th Annual Meeting of the American Thyroid Association (ATA). This was the first presentation of the pooled analyses and builds on the individual positive results of the Phase 2 and Phase 3 clinical studies. The drug is being developed by Horizon Therapeutics plc.

Teprotumumab is an investigational medicine, and its safety and efficacy have not been established. The teprotumumab Biologics License Application (BLA) was granted Priority Review by the U.S. Food and Drug Administration (FDA) and if approved, teprotumumab would be the first FDA-approved medicine for the treatment of active TED. The Prescription Drug User Fee Act (PDUFA) goal date is March 8, 2020.

“This is the largest placebo-controlled evaluation of active thyroid eye disease to date and an important step toward better understanding the devastating, vision-threatening effects of this disease,” says George Kahaly, MD, PhD, of the Johannes Gutenberg University Medical Center in Mainz, Germany, and lead study author. “These data highlight the urgent need for targeted intervention strategies and illustrate the potential for teprotumumab to reduce the painful and disfiguring symptoms of thyroid eye disease, and importantly, to help improve quality of life.”

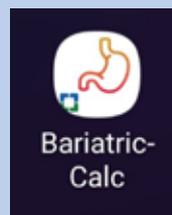
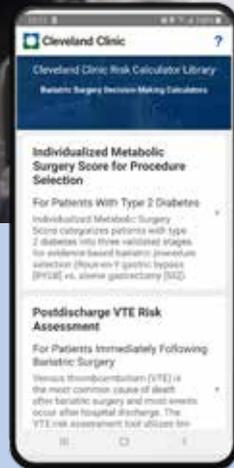
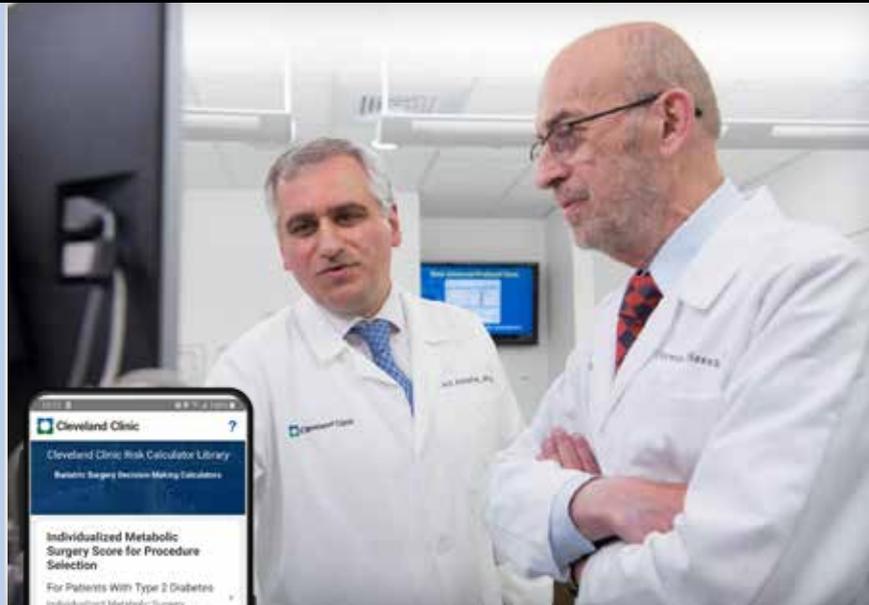
The pooled analysis of the Phase 2 and Phase 3 OPTIC studies presented during ATA represent the experience of 171 patients with recent onset of TED (less than nine months) treated with teprotumumab or placebo every three weeks for a total of eight infusions.

Key study findings include the following:

- **Proptosis:** At week 24, 77.4% of patients receiving teprotumumab experienced a ≥ 2 mm reduction in proptosis, compared to 14.9% of patients receiving placebo ($p < 0.001$). The reduction in average change from baseline through week 24 in proptosis was greater in patients who received teprotumumab (-2.63 mm) than in those who received placebo (-0.31 mm, $p < 0.001$).
- **Diplopia:** The diplopia responder rate, which is defined as the percentage of patients whose diplopia improved one or more grades, was higher with teprotumumab (69.7%) versus placebo (30.5%; $p < 0.001$) in those with baseline diplopia.
- **Quality of Life:** Patients treated with teprotumumab experienced improvements in average change from baseline through week 24 in QoL scores (overall 15.55 vs 5.92, $p < 0.001$), including visual functioning (16.81 vs 6.10, $p < 0.001$) and appearance (13.51 vs 5.78, $p = 0.002$). The GO-QoL scale consists of two subscales to evaluate the quality

“Diabetes can be a devastating disease, and combined with obesity, patients are at a high risk for cardiovascular complications. Metabolic surgery is an underutilized treatment for these patients. This calculator can help both physicians and patients quantify the risks and benefits of surgery and make the best decision for treatment.”

— STEVEN NISSEN, MD, CHIEF ACADEMIC OFFICER, HEART & VASCULAR INSTITUTE, CLEVELAND CLINIC, CLEVELAND, OHIO



Cleveland Clinic's Ali Aminian, MD, (left) and Steven Nissen, MD (right) developed the 10-Year Diabetes Risk Calculator to aid physicians and patients.

of life of patients with TED, including impacts on visual function and self-assessment of appearance. A change of six points is considered clinically significant.

- **Clinical Activity Score (CAS):** At week 24, nearly two-thirds of teprotumumab-treated patients (61.9%) had no or minimal inflammatory symptoms as measured by CAS (described as a CAS of 0 or 1) compared to 21.8% of placebo-treated patients ($p < 0.001$). CAS is a scale used to assess the disease activity of TED and measures the degree of inflammation, including pain, swelling, and redness. The CAS scale ranges from 0 to 7, with a score of 0 representing no signs or symptoms of inflammation.
- In addition, 73.8% of teprotumumab patients versus 13.8% of placebo patients had an overall response at week 24 — defined as the percent of patients with ≥ 2 -point reduction in CAS and ≥ 2 mm reduction in proptosis from baseline.

The majority of adverse events experienced with teprotumumab treatment were graded as mild to moderate and were managed in the trials, with few discontinuations. In the Phase 2 clinical

study, the only drug-related adverse event identified by the investigators was hyperglycemia. Other adverse events included nausea, diarrhea, muscle spasms, hearing impairment, and inflammatory bowel disease in a patient with a recent diagnosis of ileitis and colitis. No deaths occurred during the trial. The safety profile of teprotumumab in the Phase 3 clinical study was similar to that seen in the Phase 2 study with no new safety observations.

“For the first time we have a medical therapy that appears to be highly effective, not just efficacious, effective in the treatment of moderate to severe active TED and that the drug exhibits a very promising side effect profile,” says Terry Smith, MD, of the University of Michigan, who was also involved in the study. “Glucocorticoid steroids are only effective in about half of patients with this disease, and when they’re effective, what they do is to reduce inflammation and swelling — superficial sorts of effects that do not touch the severity of the disease, the proptosis, the double vision, and they are fraught with side effects. Now we have a therapy that may, and the jury’s out on this, but it is the hope that this drug, for the first time, will reduce the need for surgical remediation in the disease.”



“ Glucocorticoid steroids are only effective in about half of patients with [thyroid eye disease], and when they’re effective, what they do is to reduce inflammation and swelling — superficial sorts of effects that do not touch the severity of the disease, the proptosis, the double vision, and they are fraught with side effects. Now we have a therapy that may ... reduce the need for surgical remediation in the disease.”

— TERRY SMITH, MD, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICHIGAN

New Diabetic Kidney Disease Treatment

In September, the FDA approved a new indication for canagliflozin to reduce the risk of end-stage kidney disease (ESKD), worsening of kidney function, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes and diabetic kidney disease (nephropathy) with a certain amount of protein in the urine. The Janssen Pharmaceutical Companies of Johnson & Johnson are marketing the drug as INVOKANA.

“With the approval of these new uses, INVOKANA is now the only diabetes medicine indicated to help type 2 diabetes patients reduce the risks associated with diabetic kidney disease, including hospitalization for heart failure,” says James List, MD, PhD, global therapeutic area head, Cardiovascular & Metabolism, Janssen Research & Development, LLC. “This significant advancement addresses serious unmet needs and could change the trajectory of care for the many millions of patients living with type 2 diabetes and diabetic kidney disease.”

In the U.S., one in three people with type 2 diabetes has diabetic kidney disease (DKD), which multiplies the risk of cardiovascular complications including heart failure and CV death and puts patients on a trajectory to dialysis and kidney transplant.

The new indication is based on results from the Phase 3 CREDENCE study in patients with type 2 diabetes and DKD, which was stopped early because it met the prespecified criteria for efficacy. In CREDENCE, INVOKANA 100 mg demonstrated a 30% reduction in the risk of the primary composite endpoint, comprising end-stage kidney disease (ESKD), doubling of serum

creatinine, and renal or CV death. (There were too few events to evaluate the risk of renal death. INVOKANA is not indicated to reduce the risk of renal death.) Results also showed INVOKANA reduced the risk of secondary CV endpoints, including a 39% reduction in the risk of hospitalization for heart failure. Overall, adverse events and serious adverse events were similar but numerically lower in the INVOKANA group compared to placebo. The rates of diabetic ketoacidosis and genital mycotic infections were numerically higher in the INVOKANA group, as observed in other clinical trials. Additionally, there was no imbalance in lower limb amputation or bone fracture in this trial, and no new safety signals were identified.

“Millions of type 2 diabetes patients around the world have DKD and almost half of them aren’t even aware of it. By the time they are referred to a nephrologist, it is often too late because their disease has progressed to the point where dialysis is inevitable,” says CREDENCE study investigator George Bakris, MD, professor of medicine and director of the Comprehensive Hypertension Center at the University of Chicago. (*Bakris was compensated for his work on the CREDENCE study.*) “For nearly two decades, we’ve been searching for a treatment that can help us intervene earlier to slow kidney disease progression. With the approval for this new indication for INVOKANA, physicians will not only be able to help reduce the risks associated with diabetic kidney disease, but also reduce the risk of hospitalization for heart failure in patients with T2D and DKD.”

And new advancements continue to be made, even as this article goes to press, meaning ever-improving therapies so patients can lead healthier lives. Wonder what’s in store for 2020.



Nasal powder therapy for ages four and older

The FDA Approves Novel Treatments for Severe Hypoglycemia

In July, the FDA approved a nasal powder glucagon therapy for the emergency treatment of severe hypoglycemia that can be administered without an injection. Eli Lilly and Company is marketing the drug as Baqsimi and was featured in the Trends section of the September 2019 issue. The therapy has been approved to treat severe hypoglycemia in patients with diabetes ages four and older.

Baqsimi is a powder administered into the nose and will come in a single-use dispenser that can be given to someone suffering from a severe hypoglycemic episode. “There is no need to reconstitute it by injecting the liquid in the powder vial, dissolving it, then drawing back the liquid in a hurry while the person with diabetes is unconscious or suffering a very low glucose and unable to help himself or herself,” says Grazia Aleppo, MD, FACE, FACP, a professor of medicine at the Feinberg School of Medicine at Northwestern University in Chicago. “This treatment is groundbreaking because anyone will be able to deliver this rescue medicine; the previous injectable needed to be reconstituted and given intramuscularly, and very few people would feel comfortable giving this type of injection to a family member unless they were trained on how to give intramuscular injections.”

Then in August, the FDA approved a ready-to-use, room-temperature stable liquid glucagon for the treatment of severe hypoglycemia in pediatric and adult patients with diabetes ages 2 years and above. Xeris Pharmaceuticals is marketing this new glucagon injection as GVOKE.

The Food and Drug Administration (FDA) last year approved novel and groundbreaking therapies for severe hypoglycemia.

GVOKE is the first glucagon product approved that can be administered via a prefilled syringe (GVOKE PFS) or auto-injector (GVOKE HypoPen) vastly reducing the steps to prepare and administer glucagon in the event of severe hypoglycemia, or dangerously low blood sugar levels. These formats are designed to provide the reliability of a ready-to-use liquid glucagon while making it easier for patients or caregivers to administer quickly and simply. “The advantage of this injection over the other injections is the other injections really required mixing, reconstituting during

a period of tremendous anxiety when a loved one is unconscious and unable to recover from hypoglycemia without any intervention,” says Henry Anhalt, DO, vice president of medical affairs at Science 37 in Los Angeles.

“What we’ve seen over the last two months represents a tremendous advance in the care of people living with diabetes,” Anhalt continues. “We have the nasal glucagon [Baqsimi], and now we have this stable liquid glucagon, so all of these things I think really represents significant advances, and that the

members should be aware that there are options out there that go beyond what they’ve traditionally been using. It’s good time to sort of step back and reevaluate whether there are ways that we can leverage new discoveries towards improving the outcomes in those patients.” EN



Prefilled glucagon injection for ages two and older

BAGLEY IS THE SENIOR EDITOR OF ENDOCRINE NEWS. HE WROTE ABOUT TREATING TRANSGENDER PATIENTS IN THE OCTOBER ISSUE.



TRUST

But **VERIFY:**

The Impact of Erroneous ACTH Assays

BY DEREK BAGLEY

An ACTH assay's accuracy became so concerning that it warranted a paper in the *Journal of the Endocrine Society* that detailed five separate cases. Raising awareness of this rare but serious issue can avoid misdiagnoses that put patients in peril.

Last April, an article appeared in the *Journal of the Endocrine Society* titled, “Assay-Specific Spurious ACTH Results Lead to Misdiagnosis, Unnecessary Testing, and Surgical Misadventure — A Case Series,” which details five cases of patients whose diagnoses or differential diagnoses of Cushing syndrome were confounded by erroneous results from an adrenocorticotropic hormone (ACTH) assay.

The paper, by Loren Wissner Greene, et al., implicates the Siemens ACTH Immulite Assay — widely used in labs across the country — as the problematic test. “Because many high-volume reference laboratories in the United States use this assay, we believe it is critical to inform physicians, especially endocrinologists and endocrine surgeons, of this ACTH assay problem,” the authors write.

The authors also write that as they were compiling the data on the five patients discussed in this paper, multiple other cases were brought to their attention, leading them to believe these five were not isolated or unique cases. “Since 2012, we have been accumulating a series of cases highlighting serious issues with this assay,” the authors write. “The purpose of the present report was to highlight this problem and provide endocrinologists with the clinical context and suggest a corrective course of action.”

A serious issue indeed: This assay has produced falsely elevated results that led to referral of these patients for further expensive and invasive diagnostic procedures, including MRI, petrosal sinus sampling, and even unnecessary surgery before their results were corrected and clarified by other assays and follow-up.

Specious Results

In late 2015, James W. Findling, MD, a practicing endocrinologist in Menomonee

Falls, Wis., contacted Hershel Raff, PhD, about a patient who was referred to Findling with plasma ACTH results done on the Siemens Immulite instrument that did not agree with the results Findling got from his hospital's laboratory that used the Roche Cobas ACTH assay. At that time, Raff's laboratory was using the Tosoh AIA assay, so Findling wanted to see what results the Tosoh would produce. The Roche and the Tosoh methods showed results consistent with the patient's clinical presentation and other laboratory results.

Around this time, Greene, FACP, FACE, MD, MA, of the New York University School of Medicine, had a similar case, so Raff advised Greene to assay her patient's samples on an alternate instrument, and the ACTH results from the alternate assay lined up with the clinical picture. Almost simultaneously, Findling heard from Eliza B. Geer, MD, a practicing endocrinologist at Memorial Sloan Kettering in New York, N.Y., who had two patients with cases similar to the other two patients.

Raff says that they decided to gather these patients for the aforementioned case series published in the *Journal of the Endocrine Society*. Strikingly, as Greene, et al., were working on their paper, another paper was published in *Clinical Biochemistry* by Donegan, et al., titled “Corticotropin hormone assay interference: A case series.” “ACTH assay interference resulted in falsely elevated ACTH concentrations using the Siemens Immulite assay and consequently led to additional unnecessary testing,” the authors of that paper write.

“Erroneous results cause the misdiagnosis of disorders as well as miss critical diagnoses,” Raff says. “As we demonstrate in our paper, lack of diagnosis and misdiagnosis is problematic and unsafe, leading to unnecessary testing, procedures, and even surgery.”

“ We can’t expect clinicians who have limited exposure to Cushing’s, or other hypothalamic–pituitary–adrenal axis conditions, to recognize that a result (like an ACTH value) may not fit with the rest of the clinical picture. **This is challenging even for those of us who see Cushing’s in the clinic every day. Until awareness is raised about the inaccuracies of the Immulite assay, clinicians will not know that they need to ‘trust but verify.’**”

— ELIZA B. GEER, MD, MEMORIAL SLOAN KETTERING, NEW YORK, N.Y.

Potential Safety Issues

Before going further, it should be made clear that the authors of the JES paper are in no way endorsing any particular ACTH assay nor are they looking for any action to be taken against Siemens. In fact, according to Findling and a recent study by Shi, et al., in *Clinical Chemistry* entitled “An Intact ACTH LC-MS/MS Assay as an Arbiter of Clinically Discordant Immunoassay Results,” fewer than 3% of patient samples return erroneous results on the Siemens Immulite assay. Still, inaccurate results can lead to very real complications. “The problem is that that translates into some potential patient safety issues in those patients, even though it’s a small number of patients, particularly if the clinician who has ordered the assay doesn’t appreciate that these studies can be erroneous,” Findling says.

The clinical courses that the authors describe in their case series were markedly altered by erroneous results. Geer says that her two patients, for example, each were thought to have a chronic and potentially incurable diagnosis (occult ectopic Cushing) that turned out to be a condition curable by surgery (Cushing due to an adrenal nodule). “We highlight just a handful of people who have been affected by this problem; undoubtedly there are many people whose clinical course is unknowingly heading down the wrong path because of inaccurate ACTH results as we describe in our paper,” she says.

Greene says that before the situation was clarified in the first patient, this patient sought out medical care and further testing at four different medical institutions. This 21-year-old woman was put through a battery of tests, including three MRIs at two institutions. She underwent unnecessary petrosal sinus sampling that, in turn, had falsely elevated ACTH results, leading to invasive pituitary surgery. When her ACTH samples were analyzed again using a different assay, her ACTH levels were normal. “Additional follow-up data have confirmed that this patient did not have Cushing syndrome,” the authors write.

“When I presented this case at an interdisciplinary pituitary conference, another case from another institution was getting a ‘workup’ including an MRI from another institution,” Greene says. “I have heard about several more cases subsequently, whose workup was misled by this assay.”

Confounding Diagnoses

The authors tell *Endocrine News* that since “Assay-Specific Spurious ACTH Results Lead to Misdiagnosis, Unnecessary Testing, and Surgical Misadventure — A Case Series” was published, they have been contacted a number of times, from very experienced academic endocrinologists, for help clarifying test results that are confounding their diagnoses and overall clinical picture.

Gabrielle Page-Wilson, MD, of Columbia University in New York, a co-author of this paper, says that just last week, an endocrinologist contacted her regarding a patient with persistently elevated ACTH levels previously measured at ARUP Laboratories. The patient had seen a prior endocrinologist and had undergone extensive testing for both Cushing syndrome and adrenal insufficiency, which included multiple lab tests and pituitary imaging. The Immulite assay is prone to interference from heterophile antibodies, which can create both false positive and false negative results and can be blocked by removing immunoglobins.

“Assay interference was suspected, and I recommended that the provider send a blood sample for ACTH to the Mayo Clinic, where the Roche Cobas ACTH assay is in use, but she was unable to refer the sample to another lab through her practice,” Page-Wilson says. “However, upon treatment of the patient’s plasma sample with polyethylene glycol (PEG), the ACTH level normalized, consistent with the precipitation of interfering immunoglobulins. This is just one of several similar cases underscoring the need to raise provider and institutional awareness of the limitations of the Immulite ACTH assay that

is in common clinical use.” (ARUP Laboratories has since switched from the Immulite to the Roche Cobas ACTH assay.)

Geer, Greene, and Findling describe similar experiences: An endocrinologist reaches out about spuriously elevated ACTH results and is subsequently advised to seek results from alternate or multiple laboratories, which easily clarifies whatever “medical mystery” had been set off by the inaccurate test results. “This situation is dangerous for patients and leads to unnecessary and potentially dangerous workups for them,” Greene says.

Critical Thinking & Clinical Data

In the Discussion section of their paper, Greene, et al., write that endocrinologists are very reliant on specialized test results. But why shouldn't they be? Shouldn't clinicians be able to trust assay results from well-established commercial laboratories? “While no assay is 100% sensitive and specific or immune from confounding interferences, clinical lab tests are generally held to high regulatory standards intended to ensure accuracy, specifically so that providers can feel comfortable trusting the results and using them to guide patient care,” Page-Wilson says. “It is always important for providers to think critically about clinical data, but it is equally important for commercial labs to use assay platforms that minimize the likelihood of unreliable results.”

Diagnosing and localizing Cushing syndrome can be challenging, and it involves the whole clinical picture — clinical presentation, comorbidities, differential diagnosis, lab testing, and finally identifying the primary source of the hormonal derangement, such as pituitary, ectopic, adrenal, etc. “We can't expect clinicians who have limited exposure to Cushing's, or other hypothalamic-pituitary-adrenal axis conditions, to recognize that a result (like an ACTH value) may not fit with the rest of the clinical picture,” Geer says. “This is challenging even for those of us who see Cushing's patients in the clinic every day. Until awareness is raised about the inaccuracies of the Immulite assay, clinicians will not know that they need to ‘trust but verify.’”

What's more, according to the authors, is the fact that in some cases, patients took it upon themselves to pursue further endocrine testing and definitive treatment. “Patients are savvy and smart, and of course they regularly consult Dr. Google,” Geer says. “Patients understandably seek treatment that they believe will help resolve their symptoms. Many people will seek evaluations with multiple practitioners, until they are offered the treatment they are looking for — even if this is the wrong treatment.”

Raff says that there is the general concept that all results on all tests from a clinical laboratory should always be evaluated with the notion that the result could be erroneous for a variety of reasons. He teaches his endocrine fellows to first repeat the test in the same lab if they think the result is incorrect and to make sure that the sample is drawn and processed correctly at the correct time of day and under the correct clinical circumstance (e.g., fasting vs. non-fasting, standing vs. sitting, etc.).

“I also tell them not to ignore an odd result,” Raff says. “It does take time and effort to request that the laboratory refer the sample to another laboratory using a different method but, as our paper references, this is the only way to resolve this problem efficiently.” 



AT A GLANCE

- ▶ The Siemens Immulite ACTH assay has been reported to produce erroneously elevated results, which led to patients undergoing further expensive and invasive treatments.
- ▶ The problem became widespread enough that a paper appeared in the *Journal of the Endocrine Society* detailing five cases in which patients had inaccurate ACTH assay results.
- ▶ The authors of the paper want to raise awareness of this problematic assay among endocrinologists, since misdiagnosis can be dangerous for the patient.

—BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT THE JOY OF INNOVATION IN A CLINICAL PRACTICE IN THE NOVEMBER ISSUE.



The Eyes Have It:

BY DEREK BAGLEY

Endocrine News gets the patient and physician perspective on thyroid eye disease. Patients discuss how it has affected their lives and clinicians explain the limited treatment choices. However, new options may be available soon.

The Effects of Thyroid Eye Disease



Christine Gustafson, of Monterey, Calif., swam a mile a day and biked everywhere she went. When she noticed her heart was racing and that she was losing weight while one of her eyes seemed to be closing shut, she went to her doctor and her doctor asked her whether she'd experienced any anxiety as well. "And I said, 'Oh, you have no idea how much anxiety I have,'" Gustafson says. "Out of the blue, a lot of anxiety."

The doctor tested her blood and called her the next day, telling Gustafson that she needed to see her endocrinologist immediately, that the numbers of autoantibodies that came back from her blood tests were the highest the doctor had ever seen. Gustafson rode her bicycle to her endocrinologist's office, a fact that caused her endocrinologist to doubt the initial blood tests. "She seriously thought they weren't my blood tests," Gustafson says. "She said, 'They get mixed up all the time. There's no way these numbers would be you.'"

When the second tests confirmed the original results, Gustafson was diagnosed with Graves' disease and thyroid eye disease (TED). Gustafson's eye wasn't closing shut; her other eye was opening wider.

Nancy Patterson, of Hendersonville, N.C., was diagnosed with TED 32 years ago, and in those three decades, she has seen no breakthroughs in TED, at least none that benefitted her. "The treatments have been the same," she says. "There is now a great deal more research, but for 32 years there hasn't been [a clinical breakthrough]."

Up to half of Graves' disease patients develop TED, which is a separate condition from Graves', characterized by "bulging" or protruding eyes, staring, and double vision, symptoms that, for now, patients simply have to live with. "The development of the eye disease is a complication that affects patients deeply," says Giuseppe Barbesino, MD, of the Thyroid Unit at Massachusetts General Hospital in Boston. "It is a multifaceted disease. It is really difficult to treat when it happens, and there are many different aspects of the functioning and the well-being of patients that are affected by this condition that sometimes they need to be addressed separately."

“ People were very kind to me, but I know that it was hard for them to look at me. For me, I just had to stay strong and go forward. And I didn't know that there was really any hope that I'd ever look normal again.”

— CHRISTINE GUSTAFSON, MONTEREY, CALIF., PATIENT WITH THYROID EYE DISEASE

“

The development of the eye disease is a complication that affects patients deeply. It is a multifaceted disease. **It is really difficult to treat when it happens, and there are many different aspects of the functioning and the well-being of patients that are affected by this condition that sometimes they need to be addressed separately.**”

— GIUSEPPE BARBESINO, MD, THYROID UNIT, MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

Here, we'll look at how deeply TED affected Gustafson and Patterson, as well as why it's a challenging disease for even endocrinologists to diagnose and treat.

Reaching Out

In the 1990s, Patterson founded the Graves' Disease and Thyroid Foundation as both an outlet for her own suffering with TED, and as a forum for others to share their experience with the disease, to make the experiences less isolating. Patterson says she's heard of patients with TED being misdiagnosed with allergies or pinkeye, up until the physician finally recognizes TED when the patient's eyes are bulging. “There are literally thousands of people I've talked to — over almost 20 years' worth — almost none of them had any hope,” she says.

Barbesino tells of a patient with Graves' disease who was referred to him by an ophthalmologist, whose eyes were protruding. The patient told Barbesino that not only were her eyes “bulging like crazy” but that she was starting to have trouble distinguishing colors, which told Barbesino that the disease was now affecting the patient's optic nerve — one of the worst complications of TED. “This poor lady was losing her vision over a period of a few days, and I wasn't able to give her the treatment that she deserved because no surgeon was available,” Barbesino says. “Of course, we have other medical treatments for her, which slowed down the disease, but she ended up losing a good deal of her vision. This is the most terrible case that you can think of.”

In the 10 years since Gustafson was diagnosed with Graves' disease and TED, she's had six surgeries on her eyes. She's remained hopeful and positive, running her own business and keeping up with her active lifestyle. “But it's really hard because I go to the sports center to swim,” she says. “There's little kids,

they say, ‘Mommy, what's wrong with that lady?’ You know? And it's just like I would feel so funny around kids, just because sometimes I actually scared kids. Like Halloween, I would never answer the door because it frightened kids to look at me.”

Limited Treatment Options

Often, patients with TED can't drive; they can't work. These patients can't even watch television or read, and once the double vision has established itself, surgical treatment is the only option left, Barbesino says. In extreme cases, vision loss can occur as a consequence of optic nerve compression. Part of the problem may be that patients are often treated too late in the disease course. “We have a lot of evidence and indications that early treatment may be more effective, although ultimately, we do not yet have a treatment that is proven to alter the eventual outcome, say two to three years after the onset,” Barbesino says.

According to Barbesino, the main reason treatment management so far has been so disappointing to patients is that physicians are unable to treat the moderate severity forms of TED. Unless visual function is jeopardized, anti-inflammatory treatment has so many side effects that physicians tend not to recommend it, at least in the United States. “We are hesitant to use medications that have a significant side effect profile for this purpose, and that's part of the problem that we see and deal with,” he says.

Compounding the problem is that often patients may think they have a common problem like allergies, or they spend months going back and forth to a general ophthalmologist and they're prescribed eye drops or antihistamines.

Then a light bulb goes off, and someone says, ‘Oh no, this might be thyroid eye disease,’ Barbesino says. “I do warn my patients



with hyperthyroidism of early signs, such as the edema and the irritation, the pain behind the eyes, the double vision, all things that I want them to call me about.”

Patterson says she was on steroids, eye drops, an ice pack. She taped her eyes. “But it’s not like I just had to go home and sit and wait until it went away,” she says.

New Therapies Around the Corner?

Patterson says she started the Graves’ Disease and Thyroid Foundation “before the Internet was invented” because she realized that patients like her were tired of talking about their quality of life, or lack thereof. “Other people who do not have the illness don’t recognize it; it’s not very visible,” she says “And family sometimes get tired of hearing about it, so you tend to withdraw. And to have somebody to talk to, or a group of people to talk to, the thing that comes out most often is support.”

Gustafson says when she found others like her online, she cried. “I thought, ‘Oh my God, there’s somebody else out there,’” she says. Beyond that, Gustafson says she has just tried to carry on. She designs websites, and she’s a photographer who regularly meets with her clients. “People were very kind to me, but I know that it was hard for them to look at me,” she says. “For me, I just had to stay strong and go forward. And I didn’t know that there was really any hope that I’d ever look normal again.”

There is hope on the horizon. The drug teprotumumab has shown promise in Phase 2 and Phase 3 clinical trials. Results support prior analyses of significant reductions in inflammation, proptosis, and diplopia, as well as improvements in quality of life. “For the first time we have a medical therapy that appears to be highly effective, not just efficacious, effective in the treatment of moderate to severe active TED and that the drug exhibits a very promising side effect profile,” says Terry Smith, MD, of the University of Michigan, who was involved in the study presented at the 89th Annual Meeting of the American Thyroid Association. “Now we have a therapy that may — and the jury’s out on this — but it is the hope that this drug, for the first time, will reduce the need for surgical remediation in the disease.”

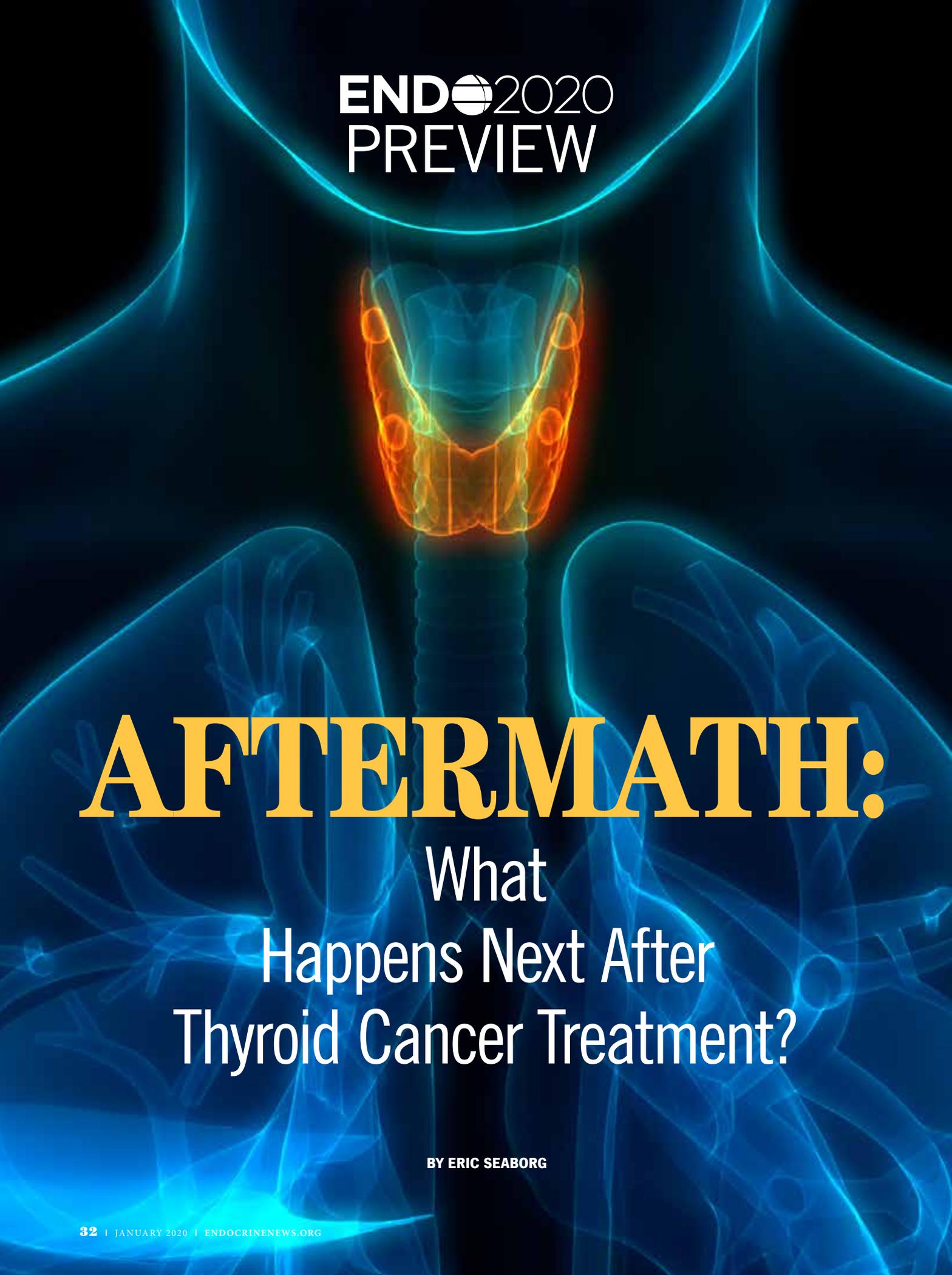
And while the jury is still out on this, Gustafson, Patterson, and Barbesino call for more awareness among the healthcare community, even among endocrinologists. Patterson says that patients should also be aware of what to discuss with their doctors. “The patient’s responsibility is to talk to the doctor in terms that are useful to the doctor,” she says. “It’s much more useful to say, ‘I’m sleeping three hours a night maximum,’ instead of, ‘I’m not sleeping.’ One’s much more factual.”

“We are usually afraid,” Barbesino says, “of one of our patients calling one Friday afternoon saying, ‘My eyes are swelling. What do I do now?’ It is because we don’t have much to offer them, nor can we predict the course of the disease accurately.” 

AT A GLANCE

- ▶ Up to half of patients with Graves’ disease develop thyroid eye disease (TED), a disease separate from Graves’ that is devastating to patients and often challenging to diagnose and treat.
- ▶ Currently, patients with TED can choose between treatment with poorly effective and poorly tolerated intravenous glucocorticoids, or live with the symptoms, as physicians are often hesitant to intervene until vision changes occur, which is when surgery is the only option available.
- ▶ There have been some recent developments, but until these drugs are brought to market, patients have found ways to cope, such as finding others online who also suffer from TED and can provide support.

— BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT TREATING TRANSGENDER PATIENTS IN THE OCTOBER ISSUE.



ENDO2020
PREVIEW

AFTERMATH:

What
Happens Next After
Thyroid Cancer Treatment?

BY ERIC SEABORG

The challenges of managing thyroid cancer patients include regulating their hormone replacement therapy and monitoring for recurrence. Here, we highlight an upcoming **ENDO 2020** session that details the issues in treating patients post-thyroid cancer therapy.

Thyroid cancer patients generally have an excellent prognosis but require careful management to optimize their care. Some strategies for optimizing this care based on the latest evidence will be covered in a session entitled “You’ve Been Cured of Thyroid Cancer — Now What?” at **ENDO 2020** in March in San Francisco.

For many, if not most, patients, treatment involves a total thyroidectomy. Endocrinologists have a lot of experience with standard levothyroxine (T4) hormone replacement medication. Most patients do well with it, but “a subset do not feel good despite standard therapy. The question is, is it related to the management of their thyroid or not,” says Anne R. Cappola, MD, ScM, of the Perelman School of Medicine of the University of Pennsylvania in Philadelphia. She will speak at the session on dealing with the “unhappy thyroid patient.”

Steps to Better Management

Cappola follows several steps in treating these patients. “The first step is to try to optimize the management with levothyroxine. I begin by making sure they are taking their T4 appropriately and that their thyroid stimulating hormone (TSH) levels are in range. If you are not taking it right, and your levels are not right, then you are not going to feel right, and that is an easy thing to try to stabilize,” she says.

“The second step is to see what else is going on that can be causing those symptoms. If you sit down and talk to the patient, you may find another etiology,” Cappola says. In one case, a patient changed jobs and reported feeling much better — leaving the stress of the previous job alleviated her symptoms. In another case, a patient had slight anemia and was receiving iron infusions. Her CBC results were off, and a hematologist spotted that her lymphocytes didn’t look right — and that led to a diagnosis of chronic lymphocytic leukemia.

A Role for T3?

Only after ruling out other possibilities does she discuss an alternative to the standard therapy, keeping in mind that levothyroxine is the only recommended thyroid hormone replacement therapy in patients with residual thyroid cancer. “There is a small subgroup of patients without residual disease where I consider a therapeutic trial of physiologic dosing of T3,” Cappola says. “I will give a small dose of T3 twice a day. If they don’t feel better, then I stop it. And if they do, I am still not entirely convinced it is not a placebo effect, but it is something that I know how to monitor and it is a small dose, so I feel comfortable with it.”

She says that controlled trials of combination therapy of T4 and T3 vs. T4 plus placebo have found no difference in results between the therapies, but she speculates that there could still be a group of patients who could benefit but that trials have not identified. She also notes that there can be consequences of not taking patients’ concerns seriously because “the internet has answered this question on its own,” and it is easy for a patient to find an “integrative medicine specialist who will hold their hand and say, ‘I can help you. I have the answer.’ I wouldn’t recommend widespread T3, though there are a lot of people out there prescribing a lot of T3.”

Recurrence Surveillance

As in other cancers, a major post-treatment concern is whether remission will last. “The majority of thyroid cancer patients are followed for many years to make sure there isn’t a recurrence of their cancer,” says Megan R. Haymart, MD, of the University of Michigan in Ann Arbor, who will speak on tailoring the surveillance protocol to the needs of the patient.



“ The first step is to try to optimize the management with levothyroxine.... The second step is to see what else is going on that can be causing those symptoms. If you sit down and talk to the patient, you may find another etiology.”

— ANNE R. CAPPOLA, MD, SCM, PROFESSOR OF MEDICINE, PERELMAN SCHOOL OF MEDICINE OF THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PA.

The intensity of the surveillance is changing for many patients as clinicians seek to balance the risks with the benefits, considering that thyroid cancer is generally not as aggressive as many other cancers. “It used to be that after initial treatment, virtually all patients would get a neck ultrasound every year,” Haymart says. “However, for some of our low-risk patients, we found that if you do an ultrasound too often you start picking up lymph nodes that have nothing to do with the thyroid cancer, and it can lead to extra biopsies and to extra patient anxiety. It is important

that the intensity of the surveillance is tailored to the severity of the patient’s disease.”

The severity of a patient’s disease can be determined using the American Joint Committee on Cancer staging system, the American Thyroid Association (ATA) risk stratification system, and the ATA’s response to therapy reclassification system. These systems can help establish current disease status as well as predict survival and likelihood of recurrence — and thus help physicians determine how often to perform a neck ultrasound. “Some low-risk patients may just need one or two ultrasound exams and could then be followed by blood work. If the blood work is reassuring, these patients may not need additional ultrasound exams. Other patients who are higher risk may need closer surveillance with ultrasound evaluation or additional imaging studies,” Haymart says.

Biochemical monitoring of TSH to ensure the thyroid hormone replacement dose is appropriate and for the presence of the tumor marker thyroglobulin may provide all the reassurance needed in

See it at ENDO 2020!
**You've Been Cured of Thyroid Cancer...
Now What?**

Saturday, March 28, 2020, 9:45 AM – 11:15 AM

This discussion on patient-centered care for thyroid cancer survivors will feature seven presentations, including a trainee/early-career abstract presentation, discussion, and a Q&A session.

“ It used to be that after initial treatment, virtually all patients would get a neck ultrasound every year. However, for some of our low-risk patients, we found that if you do an ultrasound too often you start picking up lymph nodes that have nothing to do with the thyroid cancer, and it can lead to extra biopsies and to extra patient anxiety. It is important that the intensity of the surveillance is tailored to the severity of the patient’s disease.”

— MEGAN R. HAYMART, MD, ASSOCIATE PROFESSOR OF MEDICINE, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICH.

many patients. “Thyroglobulin is a very sensitive tumor marker in the majority of patients, with a few exceptions, such as when the cancer is dedifferentiated,” Haymart says.

As more patients have lobectomies instead of thyroidectomies, thyroglobulin tests may be less useful in these patients, who may require more reliance on surveillance with neck ultrasound.

Radioactive Iodine

A third session speaker, Anna Sawka, MD, PhD, associate professor of medicine in the Division of Endocrinology at the University of Toronto, will discuss potential long-term consequences of radioactive iodine treatment — and the concerns that patients commonly express about it.

Patients considering radioactive iodine treatment or thyroid cancer survivors who have received it are often worried about developing another cancer related to their treatment. Sawka will discuss a recently published systematic review and meta-analysis from her group that considered six studies involving more than 11,000 thyroid cancer patients. The study found that the pooled risk ratio for any subsequent malignant neoplasm after radioactive treatment for thyroid cancer, after adjustment for confounders, was 1.16 (CI 0.97–1.39). A secondary meta-analysis in this study found that the risk of subsequent leukemia was increased, although it is relatively rare.

Patients are also often concerned about how treatment might affect future reproduction, so Sawka will review the recent literature on reproductive considerations in both sexes.

The most recent literature and state of the evidence will be a key aspect of this ENDO session — but presenters will also cover the questions that remain to be answered. 

—SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT POST-PRANDIAL GLUCOSE LEVELS IN THE DECEMBER ISSUE.



AT A GLANCE

- ▶ Patients who are unsatisfied with their thyroid hormone replacement therapy need special attention to identify the source of the problem — and potential solutions.
- ▶ As evidence and experience accrue, the intensiveness of the surveillance of thyroid cancer patients for recurrence is being fine-tuned with an eye toward balancing risks and benefits.
- ▶ Patients often have concerns about the potential long-term consequences of radioactive iodine treatment, and it is important to address them.

Vitamin D:

Vitamin D enthusiasts have long promoted high doses to obtain hoped-for benefits, but clinical trials are not finding them.

BY ERIC SEABORG

Clinical trials of high doses of vitamin D are not finding the benefits that some advocates had promoted and are even hinting at some adverse effects.

“The enthusiasm for high-dose vitamin D has certainly outpaced the evidence. And now that we’re getting the results of randomized clinical trials of higher doses, we’re seeing that more is not better, and in many cases is worse,” says JoAnn Manson, MD, DrPH, professor of medicine at Harvard Medical School and principal investigator of the VITAL trial, one of the largest trials of moderate-dose vitamin D.

The accumulating evidence is reinforcing the idea that adequate vitamin D is needed to maintain health, but once a person achieves an adequate level, further increases do not accrue further benefits.

The Bounds of Bone Benefits

The need for vitamin D for bone health is well-established, so researchers at the University of Calgary led by David A. Hanley, MD, and Stephen K. Boyd, PhD, decided to examine the effects of increased doses. In a study published in August in *JAMA*, some 300 healthy adults were randomized to receive daily doses of vitamin D3 for three years at 400 IU, 4,000 IU, or 10,000



When Enough Is Enough

IU. The researchers included the 4,000 IU level because the U.S. National Academy of Medicine and Health Canada consider it to be the tolerable upper intake level.

The researchers assessed participants' tibia and distal radius using high-resolution peripheral quantitative computed tomography, a measure of bone density that is much more sensitive than the standard dual energy x-ray absorptiometry. They hypothesized that higher doses might increase bone density so were surprised when the subjects who received 4,000 IU or 10,000 IU had statistically significantly lower radial bone mineral density than patients who received 400 IU. Those who received the 10,000 IU dose also had lower tibial bone mineral density.

“Our conclusion strengthens the position that once you achieve a certain level of vitamin D sufficiency, there is no further benefit of pushing the dose higher for bone. Our study actually raises the possibility that there is harm in pushing the dose higher, which is something that other studies have raised as well,” Hanley tells *Endocrine News*. “Two studies using huge doses of vitamin D as an intermittent, once-yearly bolus have actually shown an increase in fractures and falls.”

Hanley's group found that participants receiving the 10,000 IU dose had increased levels of a marker of bone resorption known

““ The enthusiasm for high-dose vitamin D has certainly outpaced the evidence. And now that we're getting the results of randomized clinical trials of higher doses, we're seeing that more is not better, and in many cases is worse.”

— JOANN MANSON, MD, DRPH, PROFESSOR OF MEDICINE, HARVARD MEDICAL SCHOOL; PRINCIPAL INVESTIGATOR, VITAL TRIAL



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— DAVID A. HANLEY, MD, PROFESSOR, DEPARTMENTS OF MEDICINE, ONCOLOGY, AND COMMUNITY HEALTH SCIENCES, UNIVERSITY OF CALGARY, ALBERTA, CANADA

as CTx and suppression of parathyroid hormone, which hints at a mechanism by which high vitamin D levels could harm bone density.

Any Role in Diabetes Prevention?

The role of vitamin D beyond bone health is a hot topic in endocrinology, with perhaps the most interest relating to preventing type 2 diabetes — which was the focus of the Vitamin D and Type 2 Diabetes (D2d) study. This trial enrolled more than 2,400 participants with prediabetes and randomly assigned them to receive either a daily dose of 4,000 IU vitamin D or placebo over two-and-a-half years. The subjects were enrolled regardless of their vitamin D blood levels, and the serum 25-hydroxyvitamin D levels of the group that received vitamin D rose from a mean of about 28 ng/mL at baseline to 54 ng/mL at 24 months, whereas the placebo group’s levels remained at a mean of about 28 ng/mL.

The study was powered to detect a 25% lower risk of the participants’ prediabetes progressing to diabetes, but the investigators reported a reduction of 12% in the risk of diabetes, which was not statistically significant. The authors noted that similar trials from Norway and Japan reported nearly identical reductions in diabetes risk.

Anastassios G. Pittas, MD, professor of medicine at Tufts Medical Center and lead author of the D2d study, which was published in August in the *New England Journal of Medicine*, says that he is collaborating with the investigators from the other trials to perform an individual participant data meta-analysis.

“Once we combine all the data, we will have a total cohort of over 4,000 participants and that will allow us to better estimate

the benefit, if any,” Pittas explains. “We are excited about this collaboration because the data suggest that vitamin D supplementation may decrease diabetes risk among persons at risk for diabetes not selected for vitamin D insufficiency by a smaller effect size — 10% to 15% — that none of these trials were individually powered to detect.”

VITAL Signs

The diabetes question may receive a more definitive answer in a few months when more results from the VITAL trial (VITamin D and Omega-3 Trial) will be published. VITAL is a randomized, placebo-controlled trial of 26,000 participants who received 2,000 IU/day of vitamin D, some with and some without an additional supplement of omega-3 fish oil, over five years. Participants were enrolled regardless of vitamin D status at baseline.

Principal investigator Manson noted that the primary outcomes results, published in fall 2018 in the *New England Journal of Medicine*, found that vitamin D did not significantly affect heart attack, stroke, or cancer incidence. However, it was associated with a decrease in cancer deaths that started one to two years after participants began treatment. Manson was also on a team that published a meta-analysis in the *Annals of Oncology* of randomized clinical trials of vitamin D supplementation that found that it did not reduce cancer incidence but significantly reduced cancer mortality.

Correcting Low Vitamin D Levels

In the D2d study, when investigators looked only at participants who had very low vitamin D levels (less than 12 ng/mL) at



baseline, vitamin D supplementation significantly reduced the risk of diabetes — by 62%. “If vitamin D can help prevent diabetes, people with lower vitamin D levels might benefit more than those who already have higher vitamin D levels, so this result is not surprising,” Pittas says. “However, because the D2d study was not designed to examine this question, further research is needed to confirm this observation.”

Manson says that evidence continues to mount supporting the 2011 vitamin D dietary intake recommendations from the Institute of Medicine (now the National Academy of Medicine) that 600 to 800 IU a day would meet the needs of the vast majority of the population. “If you start out with a low vitamin D level, then with even 400 IU a day, and certainly with 1,000 IUs, you’re going to have a very substantial increase in the blood level. After that, higher doses lead to proportionately smaller increments in the blood level,” she says.

Hanley says: “Studies in Canada indicate that 20% of the population may not have the 20 ng/mL blood level that the National Academy of Medicine concluded would indicate adequate vitamin D for bone health in 97.5% of healthy Americans and Canadians, but the low-dose supplement of 400 IU used in our study would probably protect that 20%.”

The Role of Obesity

Manson is intrigued by the idea that a person’s body mass index (BMI) may influence the efficacy of vitamin D supplementation. When the D2d results are stratified by BMI, participants with a BMI of less than 30 kg/m² experienced a 30% kg/m² reduction in risk for developing type 2 diabetes, whereas those with a BMI above 30 experienced no risk reduction.

The VITAL trial found a 24% reduction in cancer incidence in normal-weight participants, but no reduction among those with a BMI of 27 or above. These findings raise the possibility of reduced bioactivity, or of vitamin D resistance akin to insulin resistance, among people with a high BMI. Manson believes these interactions warrant further study.

As studies of vitamin D supplementation knock down the belief of some patients that “if some is good, then more is better,” Pittas notes that endocrinologists are accustomed to the effect of dosages: “Much more of something may not even be neutral, but may be detrimental. In endocrinology, we are all about balance.” ^{EN}

AT A GLANCE

- ▶ Although some advocates have maintained that higher doses of vitamin D could bring myriad benefits, clinical trials are finding little to no benefit from raising levels above sufficiency.
- ▶ Vitamin D is crucial to bone health, but some trials have found that very high levels could be counterproductive.
- ▶ Some trials of vitamin D’s role in preventing type 2 diabetes have reported small — but not statistically significant — effects, and some researchers believe larger-scale studies could reveal a benefit.

— SEABORG IS A FREELANCER WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT POST-PRANDIAL GLUCOSE LEVELS IN THE DECEMBER ISSUE.



Finders, Keepers: Cultivating and **Retaining Patients**

As more and more patients want their physicians to be “partners” in managing their health, there are simple and unique steps you can take that will keep your patients happy, healthy... and loyal.

BY CHERYL ALKON

Being the go-to endocrinologist for your patients with common endocrine issues such as type 1 or type 2 diabetes or Hashimoto’s thyroiditis ensures that you will oversee patient care for a population that typically needs ongoing prescriptions, medical tests, and regular oversight.

But these days, patients want physicians they can consider partners in their healthcare — and someone they can work with to help them make better health choices. What they don’t want is a doctor who is perceived as being arrogant, close-minded, or outdated. Such perceptions will increasingly turn patients away and push them elsewhere for medical care. With that said, what attributes are important for endocrinologists to show that help maintain patient loyalty?

Be Attentive

Patients are more than their endocrine diagnoses, and listening to their whole stories, rather than identifying their most obvious symptoms, helps show who they are as whole people, not just “overweight type 2s” or “brittle type 1s.”

“When you have a chronic undiagnosed disease, you want someone who will spend the time and work with you,” says Ted Chan, the chief executive officer of CareDash, an online doctor review site based in Cambridge, Mass., that aims to be “the TripAdvisor of healthcare,” per Chan.

Similarly, pay attention to more than just the endocrine symptoms. Are there familial, economic, or other reasons that explain some health complaints? “Most patients want to feel heard and are seeking a meaningful relationship with their provider,” says Io Dolka, MS, chief care advocate of Seattle, Wash.-based GreyZone, LLC, a consultancy company that works with a network of physicians to help patients with complex health issues get diagnoses and answers when they haven’t been able to do so on their own. “If patients feel their endocrinologist understands them as a person, and their personalities match, a strong bond can form,” she says.

Be Flexible and Understanding

Diabetes management in particular involves many decisions about how to achieve blood glucose control. Thyroid conditions can require daily medication adherence, which involves both taking the medication and remembering to fill the prescription in a timely manner.

“There are medical guidelines and then there is real life,” Dolka says. “We would all love for patients to adhere to their A1c goals and specific diets, measure their blood sugar when they should, and report any issues promptly.” But there are many reasons why it’s hard to do so, she notes, such as socioeconomic factors, health literacy, and patient engagement, and a physician who can identify roadblocks and try to help clear them — rather than point out shortcomings — is more likely to be appreciated by, and hopefully followed by, a patient.

“Many people feel they are a person first and a patient second,” Dolka says. “A strict physician who scolds the patient for failing to follow instructions is not someone the patient wants to return to see.”

Accuracy and Managing Online Resources

In the internet age, patients google their doctors and then look at every website that has reviews of that physician, Chan says. “From our perspective, we can see how important it is for doctors to manage their bio, their web presence, the accuracy, and even their phone numbers.”

For an endocrinologist in a smaller practice, it can be a lot of work to regularly update and maintain a web presence, Chan notes. “But if your phone number is wrong on CareDash, or your data is not right across the web, you are likely to be

missing out on appointments,” he says. “I wish there were a better way to pick doctors, but at the end of the day, people are looking at reviews. If you aren’t managing that, you are missing out on patients.”

Accuracy also applies to disease management. Similarly, patients want physicians who can effectively help them manage their conditions. But if patients feel their physicians aren’t offering helpful insight, they won’t maintain a relationship. “If you ultimately fail to help the patient bring the condition under control, sooner or later they will look elsewhere for care,” Dolka says.

Open to Patient Input

Besides searching for their physicians online, patients are collaborating online in Facebook support groups and other forms of social media. Many have no patience for physicians who don’t seem to listen to them or take patients’ personal experience with disease management seriously.

“Patients these days are more and more empowered,” Dolka says. “They access the internet, talk to others like them in dedicated online communities, and quickly can become experts in their own condition. Endocrinologists who are open to patient input from their own experience, or advice coming from others in their communities, and are willing to try things outside the box, will win patients in every corner. Patients are constantly seeking those who are willing to experiment with them to find customized solutions.”

Physicians who respect the internet’s influence in patient empowerment are those who will be better able to attract and retain patients as well as learn from them.

“These days, especially with younger patients, if a physician has the opinion that looking for a doctor using Google is bad, s/he will clash with that patient,” Dolka says. “It’s important to find common ground with those patients, especially the ones who are smart, read about medical trials or studies, and who are challenging them. It’s hard to be challenged, and doctors don’t have time to read and they’re running from one patient to the next, but these patients make them better. It’s a valuable thing to be open to.” 

— ALKON IS A MASSACHUSETTS-BASED FREELANCE WRITER WHO IS THE AUTHOR OF THE BOOK, *BALANCING PREGNANCY WITH PRE-EXISTING DIABETES: HEALTHY MOM, HEALTHY BABY*. SHE WROTE ABOUT THE BENEFITS OF TELEHEALTH IN THE OCTOBER ISSUE.

BY GLENDA FAUNTLEROY SHAW



If you thought moving your home was stressful, wait until you have to move your lab! We share some tips from someone who has been there, moved that.

Time to **MOVE:** The Challenges of Lab Relocation

Moving companies may be the only ones who like moving. The packing, unpacking, and setting up in a new place can give anyone months-long anxiety.

When the move in question is a laboratory filled with extremely costly equipment and years of research data, a relocation can be exponentially more stressful. The good news, however, is that with careful planning and the support of a dedicated team, principal investigators (PIs), and lab managers can successfully meet the challenge of moving to a new institution with as minimal disruption as possible.

A Job for Experts

One of the most challenging aspects of orchestrating a lab move is first simply figuring out what needs to be done and how to go about doing it. Because each laboratory move is unique — involving different staff, institutions, and instruments — even speaking with colleagues who have previously moved is unlikely to reveal all the issues that can arise.

With so many things that can go wrong, something as important as an office relocation should not be left to chance. Hiring an expert relocation company is usually the first step in the process after a move is confirmed.

“Typically, there are companies that move labs. However, there are additional considerations that are associated with lab moves, including biohazard, chemical safety, and delicate expensive equipment,” says Glenn Rowe, PhD, of the Division of Cardiovascular Disease at the University of Alabama at Birmingham.

Rowe knows the trials of relocating all too well. He has helped set up three labs during his more than 20 years of academic research, including his own lab at the University of Alabama at Birmingham in November 2014.

Companies that specialize in lab moves can suggest the best way to transport different pieces of equipment and research materials (for instance, using overnight air or generator trucks). They can determine whether the move will require special equipment such as cranes. But as Rowe points out, a single moving company may not be able to handle the entire move alone.

“Some of [the lab materials] have specific state requirements and federal requirements, especially when crossing state lines,” he says.

State and federal regulations require specific packaging, labeling, and permits for hazardous chemicals and infectious agents. If your chosen mover doesn’t have the experience or necessary permits to move materials such as animals or hazardous cargo, they should be able to coordinate with a third-party shipper.

The relocation company will also need to fully understand the environment of the lab you are moving into early in the process, according *Lab Manager*:

- ▶ Are the proper mechanical and electrical systems in place?
- ▶ Has the IT department set up computer and printer connections?
- ▶ Can your cryogenic freezer (loaded with years of research specimen) be plugged in as soon as the movers arrive at the new space?
- ▶ Are water and gas connected?

“Ideally, you have a lab manager in the origin location who can help coordinate and someone at the destination location who can help, too, but the real logistics really fall on the PI and his people,” Rowe says.

A List of To-Dos

In addition to the physical task of packing and moving the lab, a PI has a host of other challenges to consider, including:

- ▶ **Minimizing the lab’s “down time” between the move:** “Figuring out where stuff is best suited in the new space takes some time,” Rowe advises. “Downtime can be anywhere from three months to a year before you’re back to being fully functional.” Depending on the stage of the PI and/or the size of the lab, working on unfinished papers and grants are good things to do during that period, he adds.
- ▶ **Moving your people:** Postdocs and lab technicians have to make a difficult decision whether to stay at the original institution or move with the lab. It’s important to have one-on-one conversations with each person about their specific options and how your move affects their future educational and career plans.

Rowe’s final words of advice for managers planning for an upcoming move?

“Have a plan in place. Don’t ignore the small stuff and be realistic. Moves are not easy and anything can go wrong.” ^{EN}



Congress Strikes Deal for Fiscal Year 2020 Appropriations

After months of bargaining and numerous stalemates, the House of Representatives and Senate reached agreement on Fiscal Year 2020 appropriations just before funding expired on December 20. The deal also provided a “Christmas Tree” legislative vehicle for various policy measures.

The spending deal was divided into two packages of individual bills covering funding for every federal agency. Funding for the National Institutes of Health (NIH) and other health programs was included in an eight-bill spending package (HR 1865) of mostly domestic programs. A separate four-bill package (HR 1158) contained the Defense, Commerce-Justice-Science, Financial Services, and Homeland Security measures.

In a big win for the Endocrine Society advocacy, the domestic funding bill included record funding for the NIH, which will receive \$41.7 billion, a \$2.6 billion or nearly 7% increase over last year. We strongly advocated for the last year for at least a \$2 billion increase for the NIH. We conducted multiple Hill Days, visits to congressional offices, educational briefings, and online “grassroots” campaigns. We also provided testimony

to the Appropriations Committees discussing the value of NIH research and advances in endocrine-related research, and we joined with other research organizations in a rally for medical research.

In addition, the spending measure carries numerous other policy initiatives that could not pass on their own. It extends funding for several healthcare programs, including the Special Diabetes Program, through May 22, 2020, which is intended to create pressure for a Memorial Day deal on comprehensive legislation to reduce prescription drug prices and crack down on surprise out-of-network medical billing. Both of those efforts ran out of steam in the past few weeks as the House and Senate could not agree on details. It is often difficult to enact legislation during an election year, so having a deadline for popular health programs could be a crucial factor driving momentum for any healthcare legislation in 2020.

A bipartisan drug pricing measure (HR 965), which lawmakers have been pushing for years that would make it easier for generic drug companies to access samples of brand-name drugs, was



Participants gather for 2019's Rally for Medical Research, one of many such activities spearheaded by the Endocrine Society to raise awareness about the importance of medical science and research, specifically endocrinology.

also included in the deal. Lawmakers hope other provisions could lead to lower prices for insulin, an issue we have kept before Congress all year.

Republicans and the White House got some other health-related wins in the spending agreement. For example, the final legislation did not include additional family planning funds or policy riders that would loosen abortion

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In a big win for the Endocrine Society advocacy, the domestic funding bill included record funding for the NIH, which will receive \$41.7 billion, a \$2.6 billion or nearly 7% increase over last year.

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restrictions. Republicans also touted the removal of gun control-related policy language sought by Democrats, though the latter secured \$25 million to research gun violence.

The border wall battle, which led to a 35-day government shutdown in late December 2018 and early January 2019, was defused in part by an agreement to largely keep the status quo, along with no additional restraints on the president’s “transfer authority” to shift prior funding to the wall-building effort. Republicans also preserved White House flexibility to build barriers in more places than the fiscal 2019 spending measure allowed.

As this issue of *Endocrine News* goes to press, President Donald Trump is expected to sign the bill, although its funding is significantly higher than his original budget request.

In January, when Congress returns from its holiday recess, an impeachment trial is expected to begin in the Senate, which will last weeks and distract senators from legislative business. However, we will begin our advocacy for fiscal year 2021 funding and continue efforts to call on Congress to address insulin pricing and further extend SDP.

Endocrine Society Advocates European Union Lawmakers About EDCs

On December 3 – 4, following the 2019 European Union (EU) elections and with the installment of the new European Commission, the Endocrine Society brought members from seven EU Member States to Brussels to meet with policy makers and urge them to take action on endocrine-disrupting chemicals (EDCs). A full day of meetings began with a briefing for Members of the European Parliament on the latest science about the health effects of EDCs.

Swedish Member of Parliament (MEP) Jytte Guteland sponsored the briefing and shared her experience having her blood tested to discover the levels of EDCs already in her body. Endocrine Society members Barbara Demeneix, PhD, DSc, and Remy Slama, PhD,

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The Endocrine Society brought members from seven EU Member States to Brussels to meet with policy makers and urge them to take action on endocrine-disrupting chemicals.

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were invited to describe findings from their report to the Parliament earlier in the year summarizing the scientific evidence for EDC-related harms and calling on policy makers to address regulatory gaps that result in exposures to EDCs. Bjorn Hansen, executive director of the European Chemicals Agency (ECHA), and Christina de-Avila, head of Sustainable Chemicals Unit in the Directorate-General for the Environment, participated in the briefing to give

The Endocrine Society delegation presents the European Union's newly installed Commissioner for the Environment, Oceans and Fisheries, Virginijus Sinkevičius, a certificate of appreciation for prioritizing endocrine-disrupting chemicals. Pictured are Endocrine Society members Remy Slama, PhD; Barbara Demeneix, PhD, DSC; Josef Koehle, PhD; Neil Skakkebaek, MD, PhD; Jenny Visser, PhD; Linda Fryklund, PhD; Evanthia Diamanti-Kandarakis, PhD, MD; Leonides Duntas, MD, PhD; Anne Caufriez, MD, PhD; Georges Copinschi, MD, PhD; and Marc L'Hermite, along with Endocrine Society staff Joseph Laakso, PhD, director of science policy, and Mila Becker, JD, chief policy officer, presenting the certificate to Sinkevičius.



attendees an overview of the progress ECHA and the Commission have made toward the regulation of EDCs, such as exploring class-based approaches to categories of EDCs. Following an open discussion where MEPs had the opportunity to ask questions of the gathered scientists, Slovakian MEP Martin Hojsik delivered closing remarks with a strong call to action.

Nine MEPs attended the briefing, along with staff from other MEP offices representing multiple political parties, reflecting the increased attention that EDCs are receiving as a result of consistent pressure from the Endocrine Society and other stakeholders. The gathered policy makers at the briefing were keenly interested in hearing the perspectives of our expert scientists and clinicians and learning about how EDCs affect different body systems, such as the intestinal microbiome. They also wanted to hear more about the evidence linking EDCs to specific diseases, including cancer.

Following the briefing, we went to the European Commission offices to meet with the newly installed Commissioner for the Environment, Oceans and Fisheries, Virginijus Sinkevičius. Our members reiterated the strong scientific consensus on the health effects of EDCs, including effects on fertility, cancer, and thyroid biology. We encouraged the commissioner to prioritize action on EDCs early and often during his term, and he welcomed our input and advice on how the EU could continue its leadership role in regulating EDCs.

Throughout the meetings, we reminded policy makers of the important accomplishments that EU legislators

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The gathered policy makers at the briefing were keenly interested in hearing the perspectives of our expert scientists and clinicians and learning about how EDCs affect different body systems, such as the intestinal microbiome.

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made during the previous term to identify and regulate EDCs. We encouraged them to maintain momentum, specifically by advancing legislative proposals to close existing regulatory gaps for EDCs in consumer products such as cosmetics and food packaging materials. We were encouraged by two recent developments in the EU. The European Green Deal, presented by European Commission President Ursula von der Leyen on December 12, includes a call for legislative changes that would reflect rapidly developing science on the risks posed by EDCs. The Joint Research Centre also launched a “fitness check” to consider whether the existing legislative landscape is sufficiently fit-for-purpose to regulate EDCs.

We welcome the inclusion of EDCs in the Green Deal and will work closely with our expert members to develop a comprehensive response to the fitness check. We also plan to keep pressure on EU policy makers to take action on EDCs in 2020.

Congress Takes Steps Toward Cosmetics Reform

Before Congress adjourned for the holidays, the House of Representatives was able to advance legislation that reflected some Endocrine Society priorities related to EDCs.

On December 3, Rep. Frank Pallone (D-NJ) introduced the Cosmetic Safety Enhancement Act (HR 5279), which would give the U.S. Food and Drug Administration (FDA) additional authority to regulate harmful chemicals found in personal care products. We were pleased that the legislation is consistent in many aspects with our positions on cosmetics reform, including a strong safety standard and providing the FDA the ability to issue recalls when necessary to ensure the safety of personal care products. HR 5279 is also consistent in many respects with a bill in the Senate also supported by the Endocrine Society, the Personal Care Products Safety Act (S 726), introduced by Dianne Feinstein (D-CA) and Susan Collins (R-ME).

We have been a strong advocate for cosmetics reform, given that some cosmetics and other personal care products may contain harmful EDCs. We are encouraged by continued progress on legislative reforms and look forward to working with Congress in the new year to ensure that consumers are protected from harmful EDCs in the products they use on a daily basis. 



Lab Partners: Helpful Hints to Bring a Lab Into Your Practice

COMPILED AND WRITTEN BY COURTNEY CARSON

Bringing laboratory testing in-house is a growing trend as physicians are finding numerous benefits over outsourcing. While outsourcing is still ideal for some practices, more and more providers are finding that the additional revenue stream, increased patient satisfaction, a stronger collaboration between the pathologist and clinician, and other positive results make an in-house lab the best option.

In-house endocrinology labs can be equipped to perform simple and advanced diagnostic procedures ranging from thyroid aspiration biopsies to hormone level testing. If

you're considering making the move, here is a roundup of some of the key items to get started.

Rules and Regulations

Before doing anything else, a practice should be fully educated on the requirements for housing a lab. All lab testing is overseen by the Centers for Medicaid and Medicare Services (CMS) in the U.S., through the Clinical Laboratory Improvement Amendments (CLIA). The CLIA outlines the federal rules, technical knowledge, and additional state requirements online at: www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/.

One Step at a Time

Where does a practice start once it has made the decision to move forward with in-house testing? The

Commission on Office Laboratory Accreditation (COLA) has created a manual that lays out a step-by-step guide for a start-up lab. COLA also offers clinical laboratory accreditation, education, and consultation.

www.cola.org



▲ Leave It to the Experts

Lab facility planners can ensure a lab not only features the required equipment, they also work to create a layout that best suits the practice needs. These planners, known as interior lab architects, work with physicians and clinical staff as a collaborative team to develop facilities that will enhance scientific discovery and client productivity through the creation of optimal laboratory environments.

One company that specializes in lab planning is HERA Laboratory Planners based out of Atlanta, Ga. HERA's architects are also science planners, who have a deep understanding of trends, issues, and best practices that shape laboratory environments.

www.herainc.com



◀ Space Out

Empty space isn't a luxury found in most medical practices. So when setting up an in-house lab, focusing on products that save space is a must. One such product is Spacesaver, just as its name suggests. This compact cold storage system is designed based on the allotted space and is unique to each practice. By putting shelving on wheels, the storage is a mobile solution that opens up even more space in the lab.

www.spacesaver.com

▼ Right on Time

Accurate and quick diagnosis is crucial in improving patient outcomes. In-house testing — through the use of analyzers, instruments, and reagents at the point of care — also assist in disease state management. The Afinion™ 2 Analyzer makes it fast and easy to test quantitative determinations of HbA1c, lipid panels, and more. The analyzer is designed to enable simple and fast on-the-spot testing, regardless of the sample type, which may be whole blood, plasma, or urine. The rapid results allow for on-the-spot adjustment of therapy, fewer follow-up visits, and enhanced compliance through teachable moments between healthcare providers and patients with chronic conditions, including diabetes and metabolic syndromes.

www.abbott.com



▶ Proper Sendoff

Lab tests represent 2% of medical costs but affect up to 70% of treatment decisions, so this decision is not one to take lightly. While increased revenue generation, faster treatment decisions, and quicker medication adjustments may seem like bringing lab testing in-house is a no-brainer, there are a multitude of challenges that can come along with this decision, ranging from lab licensing requirements to personnel qualifications and the need for additional staff, not to mention the high start-up costs. Continuing to send off lab tests is the ideal situation for certain practices.

Consider whether or not bringing testing in-house will dramatically improve the quality of patient care. If that answer is yes, it may be time to bring the lab to the patient instead of sending the patient to the lab. 

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Endocrinologist

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EMPLOYER: University of Alabama Health Services Foundation, PC

TITLE: Clinical Assistant Professor

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CONTACT: Julia Embry, Manager, HR
University of Alabama Health Services Foundation, PC
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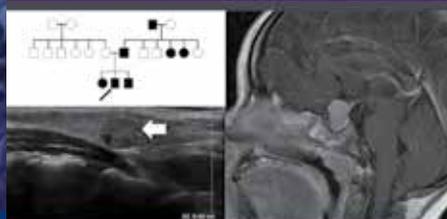
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THYROID CANCER

WHAT YOU NEED TO KNOW

Thyroid cancer is the most common form of cancer in the endocrine system, which includes the glands that produce hormones in your body. Cancer occurs when lumps, or nodules, grow in the thyroid gland. These nodules are not usually cancerous, but if they are, they can be treated effectively. Rarely, they can be life threatening.

Visit hormone.org for more information.



The thyroid gland is a butterfly shaped gland at the front of the neck. It uses iodine, a mineral found in some foods and in iodized salt, to make hormones that help your body. The thyroid hormones control your metabolism and affect your weight and your brain function as well as maintaining your heart, skin, hair, and intestines.



THYROID NODULES

— CELLS IN THE THYROID THAT FORM A TUMOR

- More than 90% are not harmful, but some can be cancerous
- Fewer than 1 in 10 nodules is cancerous
- Signs of thyroid cancer include a swelling or lump in the neck
- Your doctor can detect nodules with a “neck check.” Cancer is confirmed with a fine needle biopsy or by testing a nodule removed by surgery.



THYROID CANCER DOESN'T ALWAYS HAVE SYMPTOMS

See your doctor if you notice:

- a lump or swelling in your neck
- a hoarse voice
- difficulty swallowing
- neck or throat pain
- a swollen lymph node in your neck

Additional editing by Alan P. Farwell, MD, Chief, Section of Endocrinology,
Diabetes and Nutrition Director, Endocrine Clinics Boston Medical Center
Sources: American Cancer Society and National Institutes of Health



Hormone Health
NETWORK®
FROM THE ENDOCRINE SOCIETY

CANCER DIAGNOSIS

Tests that examine the thyroid, neck, and blood are used to detect (find) and diagnose thyroid cancer.

TYPES OF THYROID CANCERS

- **Papillary:** the most common (80% of cases); slow growing; may develop in one or both lobes of the thyroid gland; and may spread to lymph nodes in the neck.
- **Follicular:** the 2nd most common; found more in countries with lack of iodine; grows slowly and is highly treatable.
- **Medullary:** less common; more likely to run in families; more likely to spread to lymph nodes and other organs.
- **Anaplastic:** very rare and very aggressive; quickly spreads to other parts of the neck and body.

THYROID CANCER IS THE #1 FASTEST GROWING CANCER IN THE U.S.

(IN BOTH MEN AND WOMEN)

New cases per year: 62,450



Occurs nearly 3 times more often in women than in men. Can occur at any age (including in children). Seen most often in women in their 40s and 50s and men in their 60s and 70s.

2 out of 3 cases occur in people younger than age 55.

...Age, gender, and exposure to radiation can affect the risk.

YOU ARE AT GREATER RISK IF YOU:

- Are between ages 25 and 65
- Are a woman
- Are Caucasian
- Have a family member who has had thyroid disease
- Have had exposure to radiation, especially as a child. The radiation exposure could come from exposure to a nuclear reactor accident (Chernobyl, Fukushima) or from radiation treatments for another cancer. Indeed, the radiation risk for thyroid cancer at this time is greatest for survivors of childhood cancer who were treated with high dose radiation.



TREATMENT

Doctors remove the thyroid gland and the nodules within it with a surgical operation. Your doctor may also provide a one-time treatment with a radioactive iodine pill that you swallow. This is a single dose and not like radiation used in other cancers. You will need to be on thyroid hormone therapy for the rest of your life. If your cancer is quite advanced (less than 5% of patients), your doctor may provide chemo therapy.

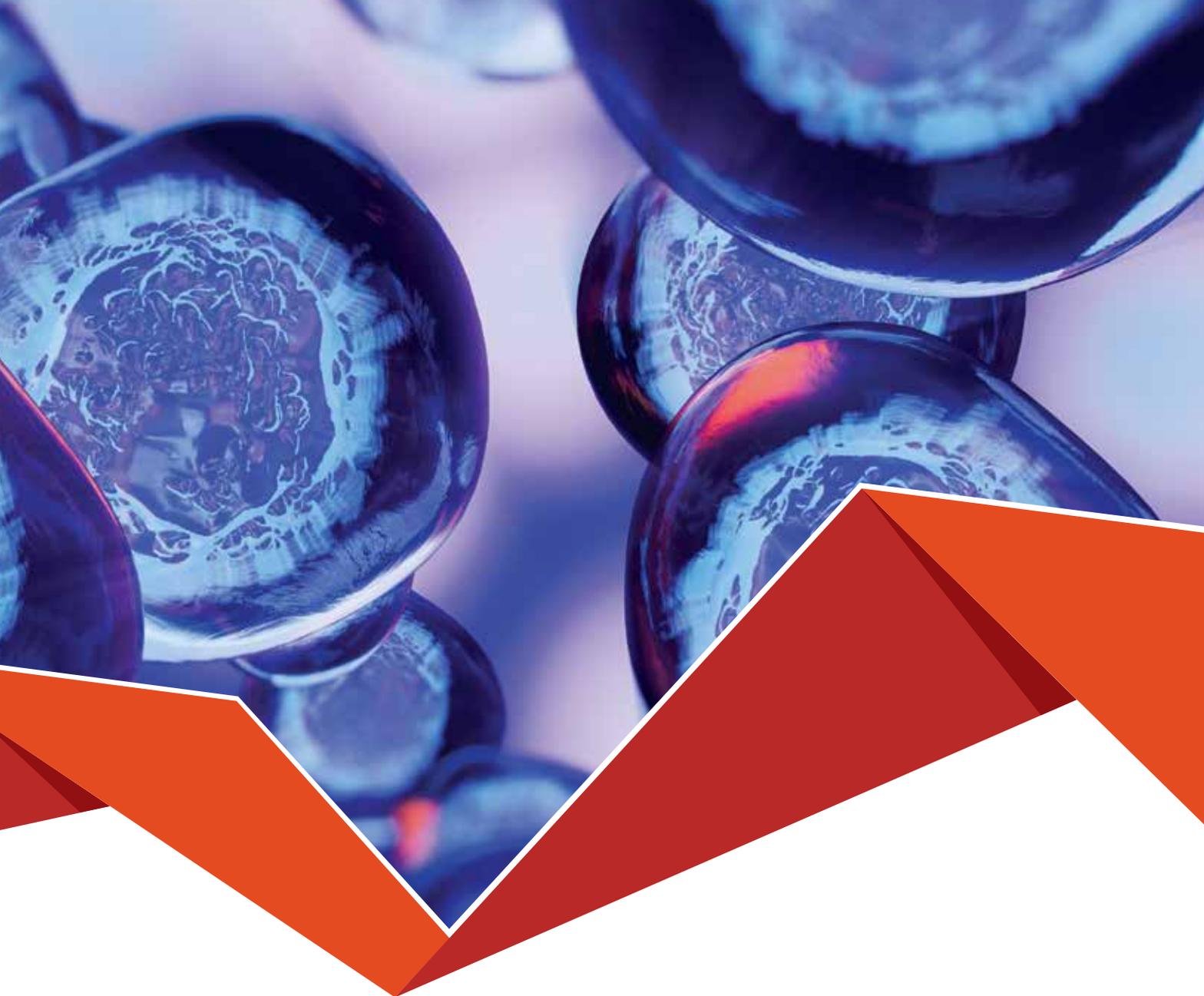
With any cancer diagnosis, look to your family, friends, and healthcare providers for more support.

Patients have questions. We have answers.

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



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Accepted abstracts will be published in a supplemental issue in the *Journal of the Endocrine Society* (JES).

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