MARCH 2021

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine news

ENDO 2021

PREVIEW

What You Can Expect at This Year’s All-Virtual ENDO

As this year’s annual conference transitions to online-only for the first time, the world’s leading experts in endocrine science and treatment converge to share the latest scientific discoveries and cutting-edge breakthroughs in patient care.

● On the Right Track: How the many paths of G Protein-Coupled Receptors could lead to treatment breakthroughs in the future

● Opening Arguments: Both sides make their points about using radioactive iodine treatment for hyperthyroidism and its associated cancer risks

● No Place Like Home: How environmental factors impact disparities in obesity treatment

● Lifetime Care: A comprehensive look at treating transgender patients throughout their lives

A CHEMIST AT HEART:
In the lab with Richard J. Auchus, MD, PhD

CRITICAL CARE:
How COVID-19 impacted CGM use in hospitals
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Learn the latest best practices for assessing and treating high cholesterol in patients with endocrine diseases like hypothyroidism, menopause, and Cushing Syndrome.

Guideline Highlights:
- Obtain a lipid panel in adults with endocrine disorders to assess triglyceride levels and to calculate low-density lipoprotein cholesterol (LDL-C).
- Treat adults with type 2 diabetes and other cardiovascular risk factors with a statin in addition to lifestyle modifications, aiming for an LDL-C goal of < 70 mg/dL.
- Consider statin therapy, irrespective of the cardiovascular risk score, in adults with type 1 diabetes who are age 40 years and older, and/or have a history of diabetes of at least 20 years, and/or either microvascular complications, chronic kidney disease in stages 1-4, or obesity.

Read the guideline at endocrine.org/lipid2020
IN THIS ISSUE

18 | Lifetime Care: A Comprehensive Look at Treating Transgender Patients

A relatively new field, transgender medicine will be featured in the ENDO 2021 session, “Transgender Care: A Comprehensive Assessment for a Multi-Faceted Condition,” a live, 90-minute program taking place Sunday, March 21, 2021 at 12:15 p.m. Program co-chair, Stephen M. Rosenthal, MD, and Sabine E. Hannema, MD, PhD, talk to Endocrine News about what attendees can expect from the three varied programs that will each have moderated Q&A sessions with world-renowned experts.

BY DEREK BAGLEY

22 | No Place Like Home: How Environmental Factors Impact Disparities in Obesity Treatment

ENDO 2021 will feature “How Do We Confront Disparities in Obesity and COVID-19 Treatment?” which will have three different programs with individual Q&A sessions on Monday, March 22 at 12:15 p.m. Rebecca E. Hasson, PhD, FACSM, highlights what attendees can expect from her presentation on obesity-related metabolic risk factors caused by one’s environment.

BY DEREK BAGLEY

28 | Plenary Pioneers, Part II: On the Right Track: How the Many Paths of GPCRs Could Lead to Treatment Breakthroughs

At ENDO 2021, the first time the Endocrine Society’s annual conference has gone all-virtual, a live Presidential Plenary on March 20 will feature a pair of presentations on the latest developments in basic tissue engineering. Nobel Prize winner Brian Kobilka, MD, talks to Endocrine News about his session, “Structural Insights into G Protein-Coupled Receptor Activation: Implications for Drug Discovery.”

BY KELLY HORVATH

32 | Critical Care: How COVID-19 Response Could Advance Use of CGM in Hospitals

Several studies have shown the effectiveness of continuous glucose monitoring in treating hospitalized COVID-19 patients with diabetes. As nurses and other healthcare staff enthusiastically accept the use of these devices, a significant cost benefit was also found.

BY ERIC SEABORG

Opening Arguments: Debating the Use of Radioactive Iodine Treatment for Hyperthyroidism

The controversy around the use of radioactive iodine to treat hyperthyroidism will be addressed at this year’s all-virtual ENDO 2021 in the session, “Does the Treatment of Hyperthyroidism Lead to Cancer?” Both sides of this issue give us a preview of what to expect from what promises to be a lively discussion.

BY KELLY HORVATH

4 | PRESIDENT’S VIEWPOINT
A Cause for Celebration in Unprecedented Times

6 | FROM THE EDITOR
ENDO 2021: An Annual Conference From the Comfort — and Safety — of Home

8 | TRENDS & INSIGHTS
Health disparities in diabetes require a broader look at systemic racism; Myriad factors linked to metabolic pregnancy complications; COVID-19 may reduce fertility in men; and New drug shows promise in treating diabetic macular edema.

BY DEREK BAGLEY

12 | ENDOCRINE ITINERARY
Scientific meetings of interest to endocrinologists from around the world

38 | LABORATORY NOTES
A CHEMIST AT HEART
Endocrine News talks with 2021 Outstanding Clinical Investigator Laureate Award recipient Richard J. Auchus, MD, PhD, who reflects on his career, how he became one of the world’s leading experts on steroid-related diseases, and what research his lab is planning in the future.

BY GLENDIA FAUNITEROY SHAW

40 | ADVOCACY
Society to school Congress on obesity; Members virtually advocate on the Hill for research funding; Congress focuses on COVID-19 relief/recovery legislation; and Biden administration weighs in on ACA as SCOTUS decision expected by June.

45 | HORMONE HEALTH NETWORK
Estrogen Fact Sheet

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Hormone Science to Health

2 | MARCH 2021 | ENDOCRINENEWS.ORG
A Cause for Celebration in Unprecedented Times

When my predecessor, then-president E. Dale Abel, MD, PhD, made the difficult but wise decision to cancel ENDO 2020, and then passed me the presidential gavel in our virtual Annual Business Meeting in early April 2020, we had no idea that the pandemic was going to consume the entire year and result in a second virtual annual meeting, ENDO 2021, some 12 months later.

It is within this challenging time that our organization was tested, opportunities were born, and our global leadership became increasingly manifest. I would like to dedicate my last presidential letter to you — our members, my colleagues. As stated in Strategic Plan 4, “We envision a world in which advances in endocrine science, education, and care promote optimal health and well-being.” In spite of the enormous obstacles and challenges we have faced as families, clinicians, scientists, educators, and also as patients ourselves in these unprecedented times, you have led with mission, front and center. Let us celebrate our accomplishments.

Despite our inability to gather, socialize, and learn in person, I am immeasurably proud that our global endocrine community is now all the more connected, united, and inclusive. We have embraced digital care, digital learning, and even digital research exchange as one alternative form of connecting with our scientific and clinical colleagues, and of course, our patients. Obviating traditional barriers such as time and distance, this new normal has propelled us forward and already demonstrated meaningful benefits for our expanding community.

I want to thank past-president Abel, the chairs of the 2020 Annual Meeting Steering Committee (AMSC), and the amazing staff who worked with them to quickly pivot and, in a couple of months, created a virtual conference, the first of its kind. ENDO Online 2020 was a major success, attracting more than 27,000 registrants and 17,000 attendees, the largest event in our longstanding history! The event provided live and on-demand programming and was offered free to all participants, members and non-members alike. In September, we delivered our first ever virtual Clinical Endocrinology Update (CEU) and Endocrine Board Review (EBR) meetings. Collectively, these meetings attracted more than 1,700 global participants, setting records for both meetings.

We are eager to continue embracing this new, virtual world and hope that you will join us for an all-virtual ENDO 2021! Our ENDO 2021 chairs, Felix Beuschlein, MD, Megan Haymart, MD, Jennifer Richer, PhD, and Bulent Yildiz, MD, together with the AMSC members, have created a remarkable program. We will mirror the principal elements of ENDO, including top-flight educational programming, an interactive EXPO center, and plenty of networking opportunities.

In addition to our traditional meetings, our Education and Meetings staff team, working closely with our members, continues creating podcasts, webinars, and multiple educational opportunities on a monthly basis. The global reach of these virtual platforms continues to grow and influence endocrine policy, science, and care.

Our advocacy efforts have not stopped during this pandemic; we have just adapted to continue advocating virtually to help support our researchers and clinicians during these difficult times. Last April, our Government and Public Affairs staff team, organized a virtual Hill Day, which was very well attended since it didn’t require for our members to travel to
Washington, D.C. We continue to advocate for improved physician reimbursement and telehealth flexibilities during the pandemic.

On the Society’s website, we have created online resources of curated links to support our members during this unique time. We have established a virtual environment where members can share resources, ideas, or ask for help. Our new Community Connect platform is facilitating ongoing engagement with members around the globe.

Our Publications department continued its long streak of innovations for journal authors and readers in 2020. In response to lab work shutdowns due to the pandemic, our journals *Journal of the Endocrine Society* and *Endocrinology* promoted Brief Reports (up to 2,400 words) as a vehicle for quickly getting important research findings into the scientific literature.

While nothing is close to “business as usual,” we will continue to be nimble and adapt to the needs of our members, our patients, and the world as we move forward. I firmly believe that our courage and resilience is what is catapulting us through this difficult time, and we are coming out stronger. The flexibility, dedication, and creativity of our members in strong partnership with our talented staff has been exemplary, and the results have been outstanding. In an environment where so many businesses are struggling to survive, we not only have survived this year, but we truly thrived.

I would like to thank those who have advised, supported, and guided me through my presidential year. A special thank you to my colleagues on the Executive Committee: E. Dale Abel, MD, PhD, immediate past-president; Carol Wysham, MD, president-elect; and Dolores Shoback, MD, secretary-treasurer; our board members for their dedication, thoughtful input, and support; and our committee chairs and members, who, partnering with our staff, make things happen. I have to give a special thanks to the executive leadership team of Rob Lash, MD, interim CEO; Krista Kirk, chief of staff and CHRO; and Paul Hedrick, chief financial officer. They have led this organization during challenging times with extraordinary skill and commitment. They have provided the stability, trust, and confidence that has and will continue to serve as a foundation for our culture of inclusion and servant leadership in our field.

Having not set foot once in the Endocrine Society office this year and instead coercing so many of you to spend numerous hours on videoconferences, I am convinced more than ever that it takes a village. Thank you all. I hope that at some point in the near future we will be able to meet again in person with forever increasing appreciation for your contribution to the Endocrine Society and global endocrine community.

In closing, this has been an amazing year of growth for me, personally, and in parallel for our Society as we continue to serve as global ambassadors for endocrine science and care. I feel honored and humbled to have been given the opportunity to serve this outstanding organization. Thank you for your trust and continued engagement.

Onward and upward!

My best to you all,
Gary D. Hammer, MD, PhD
President, Endocrine Society
In anticipation of the first ever, all-virtual Endocrine Society annual conference, the majority of this month’s issue is devoted to bringing you a few highlights of what you can expect from this year’s ENDO 2021, taking place March 20 – 23. Like a lot of you reading this, I am also very disappointed to not be able to see you all in person in San Diego (especially considering the winter weather that is taking aim at the Washington, D.C., area at the moment!), but I think as you read through this issue of Endocrine News, you will be intrigued, if not thoroughly impressed, by what the Endocrine Society has planned for this year’s event.

“As you read through this issue of Endocrine News, you will be intrigued, if not thoroughly impressed, by what the Endocrine Society has planned for this year’s event.”

Since COVID-19 is the reason we’ll all still be at home and not attending sessions in person, it’s appropriate to feature research on how the virus affects endocrine patients. In “No Place Like Home” on page 22, senior editor Derek Bagley discusses a session by exercise physiologist Rebecca E. Hasson, PhD, FACSM, detailing the impact of environmental factors on treating patients with obesity and COVID-19. Not surprisingly, some of the most detrimental behaviors can begin in children who grow up in poorer neighborhoods that can sometimes be more dangerous. Sometimes a youngster’s only stress reduction is eating sugar-filled foods that can lead to a lifetime of stress eating. And, as expected, obesity.

Bagley turns his journalistic prowess to another ENDO 2021 preview article on page 18 entitled “Lifetime Care: A Comprehensive Look at Treating Transgender Patients,” which delves into the relatively new endocrine field.
of transgender medicine. Based on the “Transgender Care: A Comprehensive Assessment for a Multi-Faceted Condition” ENDO 2021 session, Bagley speaks with program co-chair Stephen M. Rosenthal, MD, and Sabine E. Hannema, MD, PhD, who discuss what attendees can expect from the three varied programs that will each have moderated Q&A sessions. Due to recent controversies surrounding treating younger transgender patients, this session is definitely not to be missed!

Another endocrine controversy takes center stage during ENDO 2021 in the intriguingly named session, “Does the Treatment of Hyperthyroidism Lead to Cancer?” in which two experts will take opposing views on this hot-button topic. On page 24, Kelly Horvath talks to Cari M. Kitahara, PhD, who takes the view that the use of radioiodine does cause secondary cancers, and Brian W. Kim, MD, who will argue that radioiodine in low doses is a safe treatment choice. This live session will take place on Sunday, March 21 from 2 p.m. to 3 p.m. and will be moderated by Bryan R. Haugen, MD.

In the January issue, we ran the article “Plenary Pioneers Part 1: When Engineering and Endocrinology Meet,” that was part of an ENDO 2021 Presidential Plenary session entitled “The Impact of Basic Tissue Engineering and the Basic Biology of GPCRs in Emerging Therapies.” On page 28, we have the second article in the series by Kelly Horvath, “On the Right Track: How the Many Paths of GPCRs Could Lead to Treatment Breakthroughs,” that features Nobel Prize Laureate Brian Kobilka, MD, who discusses his session, “Structural Insights into G Protein-Coupled Receptor Activation: Implications for Drug Discovery.” He talks about the intricacies of GPCRs as drug targets and how a better understanding of GPCR signaling could lead to a remarkable number of breakthroughs in drug design.

These articles barely scratch the surface of what you can expect from ENDO 2021, which as this month’s issue shows, really does have something for everyone. And just because we’re not gathering in person, I look forward to being there with you tuning in to these remarkable presentations.

If you have any comments about the stories in this month’s issue or ideas for topics, please feel free to contact me at: mnewman@endocrine.org.

— Mark A. Newman, Editor, Endocrine News
Poor social conditions caused by systemic racism contribute to health disparities in people with diabetes, according to a paper recently published in *The Journal of Clinical Endocrinology & Metabolism*.

The authors of the paper, Sherita Golden, MD, MHS, of Johns Hopkins Medicine in Baltimore, Md., et al., write that as endocrinologists, the focus has been on the biology of metabolic disease risk, but they ask whether the call to endocrinology is even broader: “Why are we seeing these biological responses leading to higher metabolic disease risk and poorer outcomes in minority populations?”

The authors go on to point out that as a specialty, endocrinologists are well positioned to view the contributing factors and solutions more broadly and enable them to provide public health and policy-level prescriptions to address the structural and institutional racism that continues to plague social as well as medical systems.

Minorities are disproportionately affected by diabetes because of poor social conditions that contribute to negative health outcomes such as poverty, unsafe housing, lack of access to healthy food and safe physical activity, and inadequate employment and educational opportunities. These are known as the social determinants of health and are the result of residential racial segregation and a lack of economic investment in Black communities. Unethical practices and experimentation in minority communities have also caused racial bias in our medical systems and a lack of trust between minority patients and health care providers.

“Traditionally, physicians have focused on the biological contributors to disparities in diabetes, obesity, and other chronic diseases; however, given the bright light shone on health disparities during the COVID-19 pandemic, we need to view the contributing factors and solutions more broadly,” Golden says.

The authors also note how the COVID-19 pandemic has laid bare just how deep and wide these disparities run. There is already a higher prevalence of diabetes among African Americans, but African Americans also have increased exposure to COVID-19. African Americans are disproportionately employed in essential jobs in the service sector, they may face inability to socially distance because of crowded housing, they rely more on public transportation, and the mass incarceration of African American men has led to a higher rates of exposure. “Unfortunately, these complex circumstances have created a scenario in which African Americans who already have a high burden of chronic metabolic conditions that portend a poor outcome are also more likely to contract COVID-19 and die,” the authors write.

To address health disparities in diabetes, the authors recommend health systems implement the National Standards for Culturally and Linguistically Appropriate Services in Health and Health Care. These standards ensure interpretation services are available to all patients and that patient education materials are at a literacy level most people can understand. They also recommend more training among healthcare providers on unconscious bias, anti-racism, and the value of diversity in clinical care settings. Finally, “we must also address poverty-related [social determinants of health (SDOH)] (e.g., food and housing insecurity) by integrating social needs into medical care and using our voices to advocate for social policies that redress SDOH and restore environmental justice,” the authors write.
COVID-19 Infection May Reduce Fertility in Men

In yet another indictment of the COVID-19 pandemic and an example of just how many health outcomes the virus affects, the novel coronavirus may negatively affect sperm quality and reduce fertility in men, according to research published in *Reproduction*. The study indicates that COVID-19 can cause increased sperm cell death, inflammation, and oxidative stress, resulting in lower sperm quality and potentially reducing fertility. These findings provide the first, direct experimental evidence that the male reproductive system could be targeted and damaged by COVID-19, and they suggest that men’s reproductive function should be evaluated after infection to detect and avoid further fertility problems.

While COVID-19 is predominantly transmitted through respiratory droplets that infect the lungs, kidneys, intestines, and heart, other studies have also found that it can infect the male reproductive organs, impairing sperm cell development and disrupting reproductive hormones. These findings suggest that the male reproductive system is potentially vulnerable to COVID-19 infection; however, the effects of the virus on male reproductive function are not clear.

Researchers led by PhD student Behzad Hajizadeh Maleki, of Justus-Liebig-University in Giesen, Hesse, Germany, investigated the effect of COVID-19 infection on male fertility by evaluating markers of inflammation, oxidative stress, sperm cell death, and semen quality. Analysis was done at 10-day intervals for a follow-up time of 60 days, in 84 men with confirmed COVID-19 and 105 age-matched healthy controls. A urology expert determined that all the men were fertile. In men with COVID-19, markers of inflammation and oxidative stress in sperm cells were significantly increased by more than 100% compared to age-matched healthy controls, pathways that facilitate sperm cell death were activated, and sperm concentration was reduced by 516%, mobility by 209%, and sperm cell shape was altered by 400%. This state represents oligoasthenoteratozoospermia, which is one of the most common causes of subfertility in men.

“These effects on sperm cells are associated with lower sperm quality and reduced fertility potential. Although these effects tended to improve over time, they remained significantly and abnormally higher in the COVID-19 patients, and the magnitude of these changes were also related to disease severity,” Hajizadeh Maleki says.

These novel findings add to the current understanding of the disease and reveal that men recovering from COVID-19 may find it harder to conceive, due to abnormally low sperm quality. This suggests reproductive function should be monitored and evaluated by health professionals following infection to detect and avoid more severe reproduction problems in the future.

Hajizadeh Maleki adds, “The results from this study also suggest that the male reproductive system should be considered a vulnerable route of COVID-19 infection and should be declared a high-risk organ by the World Health Organization.”

More extensive studies, with longer follow up, are necessary to validate the conclusions drawn from this study and determine exactly how COVID-19 affects reproduction and fertility in men.
Factors Other than Gestational Weight Gain Linked to Metabolic Complications of Pregnancy

Factors other than how much weight a woman gains during pregnancy may contribute to metabolic complications such as gestational diabetes mellitus (GDM), according to a paper recently published in the Journal of the Endocrine Society.

Researchers led by Fernanda L. Alvarado, MD, of the Mother Infant Research Institute at Tufts Medical Center in Boston, Mass., point out that efforts to reduce complications of GDM by having women decrease excessive weight gain during pregnancy have seen limited success. “Increased [gestational weight gain (GWG)] early during pregnancy has been associated with the development of GDM, but the role of excess GWG in the development of GDM is still unclear,” the authors write.

The authors go on to write that the relationship between GWG and changes in maternal insulin resistance are not well described, and few studies have baseline measures before pregnancy. “Hence, the purpose of this secondary analysis was to examine the relationship between the longitudinal changes in weight/body composition and insulin sensitivity/response and to estimate its impact in women with normal glucose tolerance (NGT) and those who developed GDM,” they write.

The researchers analyzed data from 29 NGT and 17 GDM women, evaluating them for longitudinal changes in insulin sensitivity/response using the hyperinsulinemic-euglycemic clamp and an IV-glucose tolerance test. They found no significant difference in clinical characteristics between women with NGT and those developing GDM. But prior to pregnancy, the women who developed GDM had lower insulin sensitivity levels compared to NGT women. “Changes in body weight contributed to only 9% of the Δ in insulin sensitivity both in women developing GDM and NGT women,” the authors write.

The authors conclude that they found no clinically significant correlation between changes in components of glucose metabolism and weight or body composition from preconception to late pregnancy. “We hypothesize that this low contribution is the main reason why lifestyle interventions during pregnancy targeting maternal weight have not impacted the progression of insulin resistance during pregnancy,” they write.
Late last year, two identically designed global Phase III studies — YOSEMITE and RHINE — met their primary endpoint and showed that faricimab given every eight weeks and at personalized dosing intervals of up to 16 weeks to treat diabetic macular edema (DME) demonstrated non-inferior visual acuity gains compared to aflibercept given every eight weeks.

Farcimab was generally well-tolerated with no new safety signals identified. The studies each have three treatment arms, with participants randomized to receive either faricimab or aflibercept at fixed eight-week intervals, or faricimab at personalized intervals of up to 16 weeks, following a loading phase. Genentech, a member of the Roche Group, is developing the drug.

In a secondary endpoint, across both studies, more than half of participants in the faricimab personalized dosing arms achieved an extended time between treatments of 16 weeks at year one. This is the first time any investigational medicine has achieved this level of durability in a Phase III study of people with DME.

“These positive results show that faricimab has the potential to offer lasting vision improvements for people with diabetic macular edema, while also reducing the treatment burden associated with frequent eye injections,” says Levi Garraway, MD, PhD, chief medical officer, and head of Global Product Development. “We look forward to discussions with global regulatory authorities, with the aim of bringing this potential new treatment option to people with this condition as soon as possible.”

In addition to the YOSEMITE and RHINE studies, the Phase III Rhone-X study is investigating the long-term safety and tolerability of faricimab for the treatment of DME. Farcimab is also being studied in the Phase III TENAYA and LUCERNE studies as a potential treatment for neovascular or “wet” age-related macular degeneration (nAMD), an advanced form of AMD, which can cause rapid, severe, and irreversible vision loss.
The all-virtual {**ENDO 2021**} will mirror the principal elements of {**ENDO**}, including top-flight educational programming, an interactive EXPO center, and networking opportunities. {**ENDO 2021**} is the leading global meeting for endocrinology research and clinical care.

Join us for the most well-attended and valued translational endocrinology meeting in the world. Bringing together leading experts, researchers, and the most respected clinicians in the field, {**ENDO 2021**} represents a convergence of science and practice that highlights and facilitates breakthrough discoveries in the field of endocrinology. Spend time connecting with peers and colleagues, exchanging ideas and information, and getting out in front of the latest trends and advancements in hormone health.

{**ENDO 2021**}'s comprehensive virtual program offers attendees the opportunity to learn about the latest developments in hormone science and medicine from renowned investigators, expert clinicians, and educators from all over the world. You will get inspired by experts and stay at the forefront of scientific discovery and high-quality patient care.

**This year’s program includes:**

- More than 70 live sessions and another 70 sessions accessible on-demand;
- Six plenary sessions including two presidential plenaries on data in endocrine research and the impact of basic tissue engineering in emerging therapies;
- 24 live Meet the Professor sessions and another 20 available on-demand; and
- More than 20 oral sessions and a robust poster hall for accepted scientific abstracts.

www.endocrine.org/endo2021

**IMPORTANT NOTE:** To receive the member rate, your membership must be renewed for 2021 before registering for {**ENDO 2021**}. 
**Miami Thyroid Oncology Symposium**  
**April 9 – 10, 2021**  
**Miami, Florida**  
Organized by the Miami Cancer Research Center, this two-day program offers a course on Thyroid Nodules & Cancer: Cutting Edge Ultrasound and Molecular Diagnostics to provide a foundation for practicing physicians in understanding the evolving role of clinical molecular testing and its integration with the contemporary ultrasound imaging for diagnosis and management of thyroid nodules and cancer.  
https://miamicancerresearch.org/events/symposium

**ACOG Virtual Annual Clinical & Scientific Meeting**  
**April 30 – May 2, 2021**  
ACOG’s 2021 Annual Clinical and Scientific Meeting (ACSM) will take place virtually, April 30 – May 2, to ensure the safety of meeting attendees, our members, and their patients. Cutting-edge research, the latest clinical practice strategies, and extensive engagement opportunities will continue to make this event the premier educational conference for obstetrics and gynecology. This gathering of the leading women’s healthcare experts delivers skill development, best practices in patient care, and the most up-to-date clinical content. The 2021 meeting will allow participants to experience three days of engaging and interactive educational content, centered around the 2021 initiative, “Personalizing Care: A Way to the Future.”  
https://events.jspargo.com/acog21

**Steroid Hormones and Receptors in Health and Disease Conference**  
**May 25 – 27, 2021**  
This FASEB Science Research Conference (SRC) is dedicated to exploring emergent knowledge on rapid and genomic actions of nuclear receptors in health and disease. This year, the conference is jointly organized by FASEB and the International Committee on Rapid Responses to Steroid Hormones (RRSH), which held its first bi-annual meeting in 1998 and has convened in Europe, North America, and Asia. This is the first conference organized by FASEB and RRSH and will be held virtually.  
https://src.faseb.org/shr

**eECE 2021**  
**May 22 – 26, 2021**  
Join colleagues from all over the world for the 23rd European Congress of Endocrinology taking place online on our interactive virtual platform, ESE On Demand. Following feedback from our highly rated online Congress last year, we are introducing enhanced networking features; allowing attendees to connect and collaborate with their fellow endocrine professionals from across the globe. This year, e-ECE 2021’s program will include: plenary and award lectures bringing you excellence in basic and clinical research; 30 symposia sessions from over 90 international speakers; joint symposia with partner societies; Meet the Expert sessions; debate sessions; and more.  
www.ese-hormones.org/

**Plenarenio Diabetes, Obesity, and Cholesterol Metabolism Conference 2021 (PDOC 2021)**  
**May 24 – 25, 2021**  
**Belgrade, Serbia**  
PDOC 2021 will provide the platform for diabetologists, endocrinologists, nutritionists, and other related professionals to present their latest research. It aims for invaluable scientific discussions and contributes to the future innovations and recent trends in diabetes, obesity, and endocrinology and also will bring together an interdisciplinary and global team of research professionals. Keynote and plenary sessions followed by young researchers and poster sessions will allow for widespread participation of attendees at all career stages.  
https://metabolicdiseases.plenarenio.com/

**EndoBridge 2021**  
**Antalya, Turkey**  
**October 21 – 24, 2021**  
EndoBridge® is a unique initiative with the vision of bridging the world of endocrinology. EndoBridge® is co-hosted by the Endocrine Society and the European Society of Endocrinology in collaboration with the Society of Endocrinology and Metabolism of Turkey. The meetings are held in English with simultaneous translation into Russian, Arabic, and Turkish. Accredited by the European Accreditation Council for Continuing Medical Education (EACCME), this three-day scientific program includes state-of-the-art lectures delivered by world-renowned faculty and interactive sessions covering all aspects of endocrinology. EndoBridge® provides a great opportunity for physicians and scientists from around the world to interact with each other, share their experience and perspectives, and participate in discussions with global leaders of endocrinology.  
www.endobridge.org
OPENING Arguments: Debating the Use of Radioactive Iodine Treatment for Hyperthyroidism

BY KELLY HORVATH
This month’s ENDO 2021 is noteworthy not just for being the first-ever all-virtual ENDO conference, but it will also have some fun surprises. One exciting session not to miss is “Does the Treatment of Hyperthyroidism Lead to Cancer?” happening Sunday, March 21, from 2:00 p.m. to 3:00 p.m.

The topic of this debate, whether radioactive iodine used in the treatment of hyperthyroidism leads to secondary cancers, is top of mind for many endocrinologists, given the interest in and even ongoing controversy surrounding it. It has the added benefit of being about something other than COVID-19!

The spark that lit a fire beneath this lively and, until now, entrenched in the scientific literature, discussion was the 2019 publication of “Association of Radioactive Iodine Treatment with Cancer Mortality in Patients with Hyperthyroidism,” in JAMA Internal Medicine, by lead author Cari M. Kitahara, PhD, of the National Cancer Institute, Division of Cancer Epidemiology and Genetics, in Bethesda, Md., and the “Yes advocate” of this star-powered debate.

Not surprisingly, given the widespread use of radioactive iodine in the treatment of hyperthyroidism, this paper has become one of the most cited and discussed papers in the thyroid field. Since its publication, letters to the editor and written responses have opened up the discussion throughout the field. However, this ENDO 2021 debate will bring it live in real time. Offering the opposing argument to Kitahara’s Yes

“[I]t’s generally accepted that if you get to a high enough dose, there is a concern that it may have secondary unwanted side effects including causing other cancers. With that background, the question then becomes, ‘is there an increased risk of secondary cancers if we use radioactive iodine at the low doses that are used to treat hyperthyroidism?’”

— BRIAN W. KIM, MD, RUSH UNIVERSITY MEDICAL CENTER, CHICAGO, ILL.
Precisely quantifying these risks requires a very large study of patients followed for many years, preferably decades. Also, few studies have had information on dose of radioactive iodine administered (administered activity), to assess whether the long-term risks of cancer increase with greater radiation exposure. **Establishing a dose-dependent relationship is important for determining whether an association might be causal.**

— CARI M. KITAHARA, PHD, NATIONAL CANCER INSTITUTE, DIVISION OF CANCER EPIDEMIOLOGY AND GENETICS, BETHESDA, MD.

position is Brian W. Kim, MD, of the Rush University Medical Center, in Chicago, Ill. Bryan R. Haugen, MD, of the University of Colorado School of Medicine in Aurora will moderate this debate, which will no doubt have legions of supporters and detractors on both sides.

Haugen looks forward to the conversation between Kitahara, who is well-published in the area, and Kim, a clinical expert and also knowledgeable in this arena. “Dr. Kitahara’s recent paper has generated some controversy, so it will be good to work through this with two experts,” Haugen says. “We have a really good format set up with each getting introduced and then having 10 minutes to make their case. Each will then follow with five minutes to reflect on what the other said and respond with a rebuttal. After this didactic part, I’ll be fielding questions that have been sent in during the presentation for about 15 minutes, and then we’ll summarize.”

Although he is a scientist as well as a clinician taking care of patients with hyperthyroidism and therefore has personal opinions about this, Haugen says that’s not part of his role here. “My goal is to make sure it’s a good discussion by getting the most common and pointed-at data questions answered. My goal won’t be pushing one side.” Haugen jokes that he has the easiest job among the three participants. The hard work, he says, he’ll leave to Drs. Kitahara and Kim.

**All Too Much**

Even with her more onerous task as one of the debaters, Kitahara says she also looks forward to discussing the research and answering questions from the audience. To back up to how the controversy began in the first place, Kitahara explains that, because ionizing radiation, one of the three main treatment options for hyperthyroidism, is an established carcinogen, greater exposure to it is associated with an increased risk of cancer, yet studies of patients treated for hyperthyroidism have shown inconsistent results regarding associated long-term cancer risks.

However, all the studies on this topic have had important limitations, according to Kitahara. “Precisely quantifying these risks requires a very large study of patients followed for many years, preferably decades. Also, few studies have had information on dose of radioactive iodine administered (administered activity), to assess whether the long-term risks of cancer increase with greater radiation exposure,” she says. “Establishing a dose-dependent relationship is important for determining whether an association might be causal.”

In 2016, Kitahara took over the Cooperative Thyrotoxicosis Therapy Follow-up Study (CTTFUS) of 35,000 subjects who were treated in the mid 20th century. The CTTFUS had not
thus far demonstrated clear evidence of an effect, but Kitahara extended the mortality follow-up by over 20 more years. “Shortly before I came on board, the dosimetry (radiation exposure assessment) component of the study was completed, which allowed us to evaluate, for the first time, risks of death from individual cancer types across levels of absorbed dose to those organs and tissues” she says. “Importantly, the CTTFUS is the largest cohort study on this topic and has followed the patients for mortality outcomes for nearly seven decades.”

Underlying this position is that, in addition to the thyroid gland taking up radioactive iodine during treatment for hyperthyroidism, several other organs and tissues either also take up some of the radiation or are exposed to low-to-moderate radiation coming off the irradiated thyroid gland. “The level at which these other organs and tissues are exposed is high enough that we would expect, in theory, to find a small increased risk of cancer at some of those sites,” Kitahara continues, “so large studies that can precisely and reliably quantify these risks are of great interest to physicians who treat patients with hyperthyroidism, and to the patients themselves.”

Although Kitahara has more to say on the subject, as you’ll see on the 21st, that’s an excerpt of her position at the upcoming debate. So where is the “No advocate” coming from?

Less Is More

Kim agrees that evidence shows that radioactive iodine can increase the chance of developing secondary cancer, but with caveats — namely, that the risk is quite low, while the dose has to be very high to pose even that level of risk, which, granted is sometimes considered necessary for the treatment of thyroid cancer. That, points out Kim, is not what this debate will be about, however.

“Because there is a concern with high doses used for cancer, there is a question about whether the low doses we use for hyperthyroidism might also convey an increased risk of cancer,” Kim explains. “So, it’s generally accepted that if you get to a high enough dose, there is a concern that it may have secondary unwanted side effects including causing other cancers. With that background, the question then becomes, ‘is there an increased risk of secondary cancers if we use radioactive iodine at the low doses that are used to treat hyperthyroidism?’”

Kim says there are several studies on whether low-dose radioactive iodine increases the risk for cancer. “While there are mixed results of these studies, in general, most expert bodies would suggest that low-dose radioactive iodine is safe,” he says. “For example, the American Thyroid Association’s most recent guidelines counsel that it is safe, and other international guidelines suggest likewise.”

This brings us back around to Kitahara’s findings that propose otherwise, but Kim will also present some of the critical feedback of that study (no spoilers here — you’ll have to tune in to learn more).

And this debate is on! 📅
Lifetime CARE:
A Comprehensive Look at Treating Transgender Patients
A relatively new field, transgender medicine will be featured in the **ENDO 2021** session, “Transgender Care: A Comprehensive Assessment for a Multi-Faceted Condition,” a live, 90-minute program taking place Sunday, March 21, 2021, at 12:15 p.m. Program co-chair, Stephen M. Rosenthal, MD, and Sabine E. Hannema, MD, PhD, talk to *Endocrine News* about what attendees can expect from the three varied programs that will each have moderated Q&A sessions with world-renowned experts.

On Sunday, March 21, **ENDO 2021** will feature a session titled “Transgender Care: A Comprehensive Assessment for a Multi-Faceted Condition.” As the name suggests, this session will review the care of transgender persons, from pediatric to adult care, and even as they transition from youth to adult care — patients who need specialized, targeted care, from hormonal management to psychosocial assessment.

The session comes at an exciting but challenging time for transgender patients. While there has been some promising research on the mental health side and the beneficial physiologic outcomes of the current models of care (a paper recently published in the *Journal of the Endocrine Society* by Baker et. al., found that hormone therapy for transgender persons is associated with increased quality of life, decreased depression, and decreased anxiety), some barriers to care exist on the political and legislative fronts — not to mention the already numerous barriers to care transgender patients face day to day.

The United Kingdom’s High Court on December 1, 2020, decided that minors younger than age 16 likely could not give informed consent for pubertal suppression. And while the High Court has granted permission of a coalition of LGBTQ+, youth, reproductive health, and medical organizations — including the Endocrine Society — to intervene in an appeal of its decision, similar legislation is pending in various U.S. states. These measures would restrict gender-affirming care for gender diverse individuals younger than 18 and would criminalize providers following practice guidelines.

After transgender and gender diverse minors start puberty, prescribing hormones to suppress puberty is the recommended strategy if it is desired by the patient and if diagnostic and treatment criteria are met. This treatment, which has completely reversible effects on pubertal development, gives adolescents more time to explore their options.
“This is going to be an exciting symposium,” says Stephen M. Rosenthal, MD, a pediatric endocrinologist, medical director of the Child and Adolescent Gender Center at the University of California, San Francisco, and co-chair of this ENDO 2021 session. “There’s going to be an opportunity to not just listen but directly ask questions to the presenters.”

A Rapidly Growing Field

This is a relatively new and small field, but it’s progressing and growing rapidly. The chance of an endocrinologist caring for a transgender patient rises every day. “More and more people are presenting to pediatric endocrinologists and adult endocrinologists for services related to gender care,” Rosenthal says. “It’s really important to be current on the latest research and outcomes.”

Rosenthal says that in the past two years, there has been a tremendous amount of high-quality research outcomes studies. However, what’s needed now are long-term follow-up studies. “Just by definition, it’s going to be a while before we have those,” he says.

Mental Health Impacts

For now, Rosenthal invites ENDO 2021 attendees to listen to the expert speakers, pioneers in the field of transgender medicine.

The mental health provider that has performed the diagnostic evaluation of the adolescent, and therefore knows about their specific situation and their development, assesses the ability of the adolescent to provide informed consent, together with the multidisciplinary team. We feel that this is more appropriate than involving a court to perform such an assessment.”

— SABINE E. HANNEMA, MD, PHD, AMSTERDAM UNIVERSITY MEDICAL CENTERS, AMSTERDAM, NETHERLANDS

Transgender Care: A Comprehensive Assessment for a Multi-Faceted Condition

March 21, 2021, 12:15 p.m. - 1:45 p.m. (EST)

Attendees will learn about providing treatment to transgender persons focusing on fertility, psychosocial assessment, and transition of care in a program consisting of three separate presentations, which will each be accompanied by a moderated Q&A session.

- Psychosocial Assessment: A Key Component in the Care to Transgender Youth — Thomas D. Steensma, PhD, Amsterdam University Medical Centers, Amsterdam, Netherlands
- Hormonal Management of Gender Dysphoria in Adolescents — Sabine E. Hannema, MD, PhD, Amsterdam University Medical Centers, Amsterdam, Netherlands
- Transition of Care for Transgender Youth — Vin Tangpricha, MD, PhD, Emory University School of Medicine, Atlanta, Ga.

“The panel that has been put together by the Annual Meeting Steering Committee is absolutely superb,” Rosenthal says. “All three of them are internationally recognized experts in transgender care.”

One of the symposium speakers, Sabine E. Hannema, MD, PhD, Amsterdam University Medical Centers in Amsterdam, Netherlands, will address the hormonal management in adolescents, as well as counseling prior to treatment and fertility preservation. “In my talk, I will discuss the endocrine treatment recommended for transgender adolescents by current guidelines, i.e., puberty suppression and gender affirming hormone treatment (testosterone for trans boys and estradiol for trans girls),” she says. “I will review the aims of the treatment and show data on the outcome, including effects on psychological functioning. In addition, the safety of treatment will be considered, taking into account effects on bone mineral density and cardiovascular risk factors.”
For transgender adolescent patients, developing secondary sex characteristics associated with their designated sex at birth can be very stressful, which can have a very real and very damaging impact on psychosocial functioning and school performance. It can lead to depression and anxiety. “Puberty blockers are used to stop further pubertal development, alleviate the distress, and improve well-being,” Hannema says. “While puberty is suppressed, the adolescent has time to carefully consider if they wish to pursue further treatment such as gender affirming hormone treatment.”

And while the U.K. and the U.S. mull legislation that could harm transgender patients seeking care, in the Netherlands, where Hannema practices, puberty blockers are available without legal restraints, so transgender patients are able to get optimal care through a multidisciplinary team — through which the adolescents and their providers are able to make the best decisions for the health of the patient. “The mental health provider that has performed the diagnostic evaluation of the adolescent, and therefore knows about their specific situation and their development, assesses the ability of the adolescent to provide informed consent, together with the multidisciplinary team,” Hannema says. “We feel that this is more appropriate than involving a court to perform such an assessment.”

Hannema tells *Endocrine News* that even though puberty blockers are reversible, if adolescents subsequently start gender affirming hormones and choose to undergo a gonadectomy, that will leave them infertile, so her talk will also highlight the importance of fertility counseling as well as some of the challenges that unfortunately await these patients. “Many adolescents are interested in becoming a parent, and they may wish to pursue fertility preservation prior to the start of treatment, although several studies have shown that there are many barriers that adolescents face,” she says.

Recent data have shown that current care models do have a positive impact on mental health in transgender adolescents, so professional societies endorse the treatment recommended in current guidelines. However, according to Hannema, many questions regarding the treatment remain to be answered and deserve further study. “Some people argue that the positive outcomes reported by several studies do not weigh up against possible risks,” she says. “I will show the data that are available on the efficacy and safety of the treatment which support the recommended approach.”

And as the number of transgender patients seeking endocrine care grows, that means that not only will endocrinologists find themselves treating more transgender patients, transgender patients will see more physicians in different specialties for their care. “I hope that after attending the session, people will feel that they have a good overview of the treatment options, the benefits and potential risks, and are aware of issues that deserve special attention when counseling adolescents and their families, and during follow-up,” Hannema says.
How Environmental Factors Impact Disparities in Obesity Treatment
ENDO 2021 will feature “How Do We Confront Disparities in Obesity and COVID-19 Treatment?” which will have three different programs with individual Q&A sessions on Monday March 22 at 12:15 p.m. (EST) Rebecca E. Hasson, PhD, FACSM, highlights what attendees can expect from her presentation on obesity-related metabolic risk factors caused by one’s environment.

ENDO 2021 is only weeks away, but of course the premier annual meeting for endocrinologists has been moved to a virtual platform as the COVID-19 pandemic continues to wrap its tentacles around just about every aspect of daily life. Nothing has been untouched.

These pages have covered just how much the novel coronavirus has upended healthcare and research, and indeed shown how COVID-19 has exposed the stark inequities experienced by communities of color and socioeconomically disadvantaged populations. And now, a session at ENDO will further highlight these problems and provide attendees ways to address this important but extremely delicate situation. “How Do We Confront Disparities in Obesity and COVID-19 Treatment?” on March 22 will feature several presentations from experts talking about disparities in obesity, as well as how the pandemic has affected their efforts.

For her talk, Rebecca E. Hasson, PhD, FACSM, associate professor at the University of Michigan and director of the university’s Childhood Disparities Research Laboratory and Active Schools & Communities Initiative, will focus on how external factors contribute to disparities in obesity. Her presentation, titled “Environmental Determinants that...”
Contribute to Racial/Ethnic Disparities in Obesity-Related Metabolic Risk Factors,” will provide an overview of the different dimensions of psychosocial stress and highlight the psychosocial pathways that contribute to metabolic health disparities in pediatric populations, according to the abstract.

“I’ve done a lot of research over the past 10 years focused on the behavioral factors that increase a child’s risk for type 2 diabetes and obesity and the environmental factors that contribute to unhealthy behaviors that lead to, or directly contribute to, increased obesity, increased insulin resistance, inflammation, and type 2 diabetes risk,” Hasson says.

Impacts of Chronic Stress

Everyone experiences stress from time to time — it’s unavoidable. But when it’s chronic stress, that becomes a problem. Hasson says the body was simply not designed to handle chronic stress repeatedly over a long period of time. The body will maladapt and dysregulate cortisol, which leads to behavioral changes, which affect metabolic health.

“A two-year-old can’t go out for a run. The only stress reduction that they have is, ‘Ooh, that little fruit loop actually tasted good.’ And we know that sugar activates the brain reward system. They really will feel good after they eat some sugar or something sweet, and you can train the brain at a very young age to start stress eating.”

— REBECCA E. HASSON, PHD, FACSM, ASSOCIATE PROFESSOR; DIRECTOR, CHILDHOOD DISPARITIES RESEARCH LABORATORY AND ACTIVE SCHOOLS & COMMUNITIES INITIATIVE, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICH.

How Do We Confront Disparities in Obesity and COVID-19 Treatment?

Monday, March 22, 2021, 12:15 p.m. – 1:45 p.m. (EST)

Attendees will learn about physiological, clinical, social, and behavioral aspects of disparities in obesity and obesity treatment in a program consisting of three separate presentations, all of which will be accompanied by a moderated Q&A session.

- Environmental Determinants that Contribute to Racial/Ethnic Disparities in Obesity-Related Metabolic Risk Factors — Rebecca E. Hasson, PhD, University of Michigan Medical School, Ann Arbor, Mich.
- Race/Ethnicity, Obesity, and COVID-19 — Monica Webb Hooper, PhD, National Institutes of Health, Bethesda, Md.

For those lacking resources to address chronic stress, this cycle is even more severe. There is an old saying: “It’s expensive to be poor.” An adolescent in a low-income house may be stressed about studying for an exam but can’t afford a tutor or take time off from a job to study, which of course leads to more stress. Meanwhile, the parents are worried about keeping the lights on or having enough food to eat. “Then you become food insecure. Minority adolescents experience discrimination in the form of unfair treatment to where you lose out on different opportunities,” Hasson says.

Minorities experience racial discrimination at a rate up to five times more than non-Hispanic whites — another chronic stressor. And now, another thing keeping children up at night is community violence. It’s not a new phenomenon, but evenings punctuated with gunshots or walking through
the neighborhood and witnessing punches thrown can have not just an effect on a child’s psyche, but their metabolic health as well. Hasson and her co-authors in a paper recently published in *Psychoneuroendocrinology* identified a cross-sectional association between community violence and hypothalamic-pituitary-adrenal axis dysregulation in adolescents who were overweight/obese.

“We’ve shown our findings, even in suburban areas, that if a child has heard a gunshot, and they hear it repeatedly, that also has dysregulation in their cortisol responses because now you’re talking about their perceptions of neighborhood safety,” Hasson says.

**Impacts of Global Stress**

One of the main resources a person has to protect against stress and even chronic stress is social support and connectedness — travel or meeting a friend for lunch or a backyard barbecue or a simple hug from a loved one. But of course, those kinds of things have been extremely limited or non-existent during the ongoing pandemic.

Then come the stressors of contracting COVID-19, of losing a job, of the social isolation. “You have this compounding problem and not only are you going through it, but so is

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**AT A GLANCE**

- Environmental factors that cause chronic stress can increase the risk for metabolic disease, especially in minority or socioeconomically disadvantaged populations.

- COVID-19 has compounded this problem, as the usual way to deal with stress — social connectedness — has been severely limited by the pandemic.

- Knowing about the external stressors like community violence that affect patients can help endocrinologists tailor more personalized treatments.

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Exercise has been shown to affect stress response due to its direct and independent effect on cortisol release. Encountering a stressor post-exercise will more likely produce a dampened response.
everyone around you,” Hasson says. “We have this global stressor on top of these individual and community stressors. That’s not even a perfect storm, that’s a tsunami.”

And while adults have turned to other coping skills, children don’t have the same ones, at least ones that are healthy and effective. Children live in an ecosystem, and even if the child doesn’t feel stressed, how the parents respond to stressors can indeed affect the child’s weight. In 2019, Hasson and her co-authors published a paper in the Journal of Obesity that found parents’ exposure and appraisal of stressors related to community safety are associated with increased adolescent obesity in African American youth.

Hasson says that we don’t teach children how to cope with stress, and that children as young as two can start to stress eat. “A two-year-old can’t go out for a run,” she says. “The only stress reduction that they have is, ‘Ooh, that little fruit loop actually tasted good.’ And we know that sugar activates the brain reward system. They really will feel good after they eat some sugar or something sweet, and you can train the brain at a very young age to start stress eating.”

Hasson also implicates things like video games and social media — which also activate the brain’s reward system — as sedentary coping mechanisms that children have turned to, especially as COVID-19 has limited exercise opportunities. “School’s closed, gym’s closed, park’s closed,” she says. “And if you don’t live in a safe neighborhood, you’re not exercising.”

**Kids on the Move**

Hasson and her team have shown that children do enjoy exercise if they get the chance. They tested this theory in the laboratory, offering children the choice of two minutes of activity or two minutes of a video game. The children preferred the activities — Hasson and her team published a paper in *Journal of Physical Activity and Health*, finding that the children’s mood was significantly higher after engaging in activity breaks and the children rated the activities as more enjoyable than video games. “Kids do want to move,” Hasson says. “We just have to give them that opportunity.”

Before COVID-19, Hasson and her team had developed a program for children who were sitting too much in classrooms. They trained teachers to implement five four-minute activity breaks.
I think having a broader understanding of these social factors that shape behaviors and shape health outcomes will help the endocrinologist get a better picture of what they’re dealing with and may help to make their prescriptions a little more precise.”

— REBECCA E. HASSON, PHD, FACSM, ASSOCIATE PROFESSOR; DIRECTOR, CHILDHOOD DISPARITIES RESEARCH LABORATORY AND ACTIVE SCHOOLS & COMMUNITIES INITIATIVE, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICH.

breaks throughout the day. But then the schools closed, so the Michigan state board of education reached out, asking if it was possible to adapt the program for the home environment.

What followed was a Detroit Public Television show available for wide consumption called “Impact at Home” on the Michigan Learning Channel, since almost one-third of children in Michigan don’t have Internet access. Hasson and her team have also been working with a team of school psychologists, health coordinators, and teachers to develop a family engagement toolkit that focuses on resilience. “How do we help parents engage in that conversation?” Hasson says. “Because a lot of parents see that their kids are stressed out, but they don’t really know what to do about it. One is you can move with them. You can think with them, and then you can just be with them.”

Hasson and her team plan to collect data on the initiative, to determine how family engagement is helping build resilience in children, and how exercise is helping children cope with stress. “How was the exercise helping the kids just feel better even if they’re not metabolically improving? But if they’re feeling better, if they’re in a better state, I think that that will transition into engaging in other health behaviors that can change their metabolic health over time,” Hasson says.

Treating the Whole Patient

And these external, environmental factors again speak to the importance of personalized medicine, of treating the whole patient. A question about how many gunshots a child hears in a week might not be on an endocrinologist’s list of questions. Hasson says it’s important to know what’s going on in a patient’s life that may make it more difficult for them to fill their prescription of Metformin or physical activity or to follow nutritionist recommendations. “I think having a broader understanding of these social factors that shape behaviors and shape health outcomes will help the endocrinologist get a better picture of what they’re dealing with and may help to make their prescriptions a little more precise,” she says.

Hasson is an exercise physiologist, and she jokes that of course exercise is the answer to all the world’s problems, but she does point to the fact that exercise does dampen the stress response. “We do know that it has a direct and independent effect on that cortisol release, and so it is elevated during exercise,” she says. “And if you encounter a stressor after you exercise, you will actually have a dampened response.”

But for, say, an adolescent going through puberty — the crucial biological period where children become more insulin resistant — who has low levels of physical activity and high levels of food consumption, the metabolic risk factors are serious. Tack on the fact that this child may live in a lower-resource community and these stressors are even more taxing. “I think focusing on unhealthy eating habits is only giving us half the picture, half the story, and by paying attention to some of these other factors an endocrinologist can really help to move the needle in the right direction for prevention and treatment,” Hasson says.

— BAGLEY IS THE SENIOR EDITOR OF ENDOCRINE NEWS. IN THE FEBRUARY ISSUE, HE WROTE THE COVER STORY ON HOW ENDOCRINE NURSES HAVE BECOME MORE ESSENTIAL THAN EVER DURING THE COVID-19 PANDEMIC.
PLENARY PIONEERS, PART 2:

ON THE RIGHT TRACK:

How the Many Paths of GPCRs Could Lead to Treatment Breakthroughs

BY KELLY HORVATH
At **ENDO 2021**, the first time the Endocrine Society’s annual conference has gone all-virtual, a live Presidential Plenary on March 20 will feature a pair of presentations on the latest developments in basic tissue engineering. Nobel Prize winner Brian Kobilka, MD, talks to *Endocrine News* about his session, “Structural Insights into G Protein–Coupled Receptor Activation: Implications for Drug Discovery.”

Taking place from March 20 to 23, 2021, **ENDO 2021** will offer more than 70 live sessions in addition to another 70 on-demand sessions via a state-of-the-art digital platform that also accommodates interactivity among participants as well as networking opportunities and even a virtual exhibit hall.

One live session you won’t want to miss is “The Impact of Basic Tissue Engineering and the Basic Biology of GPCRs in Emerging Therapies,” a presidential plenary on March 20, from 11:00 a.m. to 12:00 p.m. (EST)

Comprising two talks, this plenary showcases pioneering advances in therapy with “Synthetic Hydrogels as Engineered Niches in Regenerative Medicine,” by Andrés J. Garcia, PhD, executive director, Parker H. Petit Institute for Bioengineering and Bioscience and George W. Woodruff School of Mechanical Engineering Regents’ Professor at the Georgia Institute of Technology in Atlanta, Ga., and “Structural Insights into G Protein–Coupled Receptor Activation: Implications for Drug Discovery,” by Brian Kobilka, MD, professor and chair of molecular and cellular physiology at the Stanford University School of Medicine, Stanford, Calif., and co-recipient of the 2012 Nobel Prize in Chemistry for his work with GPCRs.

In this second of two articles highlighting this plenary session, *Endocrine News* spoke to Kobilka about why G protein-coupled receptors (GPCRs) are such vital conduits for pharmaceuticals, why drug discovery has been so frustrating through the years, and what attendees can expect from his session.

**GPCRs and Drug Discovery**

Having been a pioneer in the structural biology of GPCRs, Kobilka is particularly well suited to share structural insights into GPCR activation. During his presentation, he’ll provide an overview of what GPCRs are, followed by what
has been learned about and from their structures since his trailblazing work more than a decade ago.

As is well known by now since their discovery several decades ago, the GPCR family represents the largest and most versatile group of cell surface receptors, carrying messages from outside a human cell to its interior via the cell membrane. GPCRs, in fact, handle up to 80% of signal transduction across cell membranes.

“The majority of the body’s responses to hormones and neurotransmitters are mediated by GPCRs,” Kobilka says. Cloning of GPCRs, beginning in the 1980s, revealed a common architecture consisting of seven transmembrane helices connected by extracellular and intracellular loops; however, understanding how these helices were arranged in three dimensions would require another 20 years of research by Kobilka and others in the field.

“During my residency in internal medicine, I became very interested in intensive care medicine and in particular the drugs frequently used there. As it turned out, many of these drugs targeted GPCRs. If you wanted to specialize in intensive care medicine at the time, there were essentially two specialties: cardiology or pulmonary medicine,” Kobilka explains.

Kobilka opted to do a postdoctoral fellowship at Duke University because it offered not only a strong clinical cardiology program but also opportunities to do research. Under the mentorship of Robert Lefkowitz, MD, a pioneer in the field of GPCRs and later Kobilka’s Nobel Prize co-recipient, he began studying the β2-adrenergic receptor.

**All Pathways Lead to GPCRs**

Although his fascination developed incidentally, it took hold. “GPCRs are important drug targets because of their central role in normal homeostasis,” Kobilka says. As a result, more than a third of our current pharmaceutics are directed at them. So why, then, have only a very small percentage of the more than 800 known GPCRs been targeted for therapeutics?

This is precisely the tangle Kobilka hopes to start to unravel in his presentation: “I’m going to talk about challenges in drug discovery for GPCRs — why it’s been difficult to obtain drugs that are highly selective and highly efficacious with few side effects. I’ll provide some structural insights into why there have been these challenges and what are the major challenges we face in drug discovery,” he explains.
Clearly, if researchers understand the basic physiology and pathophysiology of GPCRs, they’ll be better equipped to develop new therapeutics that activate or inhibit the receptors, accordingly. So, in 2007, when Kobilka and his colleagues determined the first crystal structures of a GPCR for hormones or neurotransmitters, the search for how these receptors work and how they signal became possible.

In terms of particular challenges, Kobilka says that there are many closely related subtypes — subfamilies within the larger GPCR family. “For example, there are nine adrenergic receptors, and their binding pockets for adrenaline are, in some cases, identical or very similar,” he explains. “As a result, finding drugs that are selective for one over the other has been challenging. Another challenge is that these receptors often signal through more than one pathway, with one pathway providing beneficial effects of the drug, while another pathway might lead to adverse effects.”

This better understanding of the complexities of GPCR signaling is what Kobilka hopes the audience takes away from his presentation and that will perhaps soon lead to breakthroughs in drug design.

— BRIAN KOBILKA, MD, PROFESSOR AND CHAIR OF MOLECULAR AND CELLULAR PHYSIOLOGY, STANFORD UNIVERSITY SCHOOL OF MEDICINE, STANFORD, CALIF.
Several studies have shown the effectiveness of continuous glucose monitoring in treating hospitalized COVID-19 patients with diabetes. As nurses and other healthcare staff enthusiastically accept the use of these devices, a significant cost benefit was also found.
Even amidst the surge in cases, some endocrinologists managed to test CGM for glycemic management of diabetes patients. They found that the devices produced reliable and helpful results with good acceptance by the nurses charged with using them.

After the U.S. Food and Drug Administration issued a policy statement in March 2020 clearing the way for hospitals to use CGM during the pandemic, many endocrinologists seized the opportunity to explore the feasibility and staff acceptance of the technology. The high transmissibility of COVID-19 — with accompanying needs for patient isolation and healthcare worker protection — were strong motivators to lessen the need for bedside glucose measurements, but the results for these objectives were actually mixed.

“Our two major goals last spring were, first, to decrease as much as we could unnecessary exposure of our nursing and physician staff to the virus, and second, to attempt to decrease the burn rate of personal protective equipment, because at that time, there was a looming shortage of PPE,” says Joshua D. Miller, MD, MPH, medical director of diabetes care at Stony Brook Medicine in Stony Brook, N.Y. “We felt that CGM could play a role in limiting the amount of time a nurse had to be in the room with a patient when they otherwise didn’t need to except for checking the blood sugar.”

The ICU vs. the Less Critical

But it didn’t turn out that way at Stony Brook, where Miller limited CGM use to ICU patients. “In the earliest stages of the pandemic, we had much to learn about the impact of COVID-19 on critically ill patients. We found that many patients were so ill that nurses had to go in every hour anyway, to address the ventilator, to address drips, etc. So, while we anticipated nurses being able to decrease the amount of time they would spend in the room, in fact, many were still entering the room frequently. But they weren’t going in to check blood sugars. They were going in to do other things related to the patient’s critical illness,” Miller says.

In contrast, Rush University Medical Center in Chicago had a very different experience by using CGM with a different patient population, according to Rasa Kazlauskaite, MD, MSc, associate professor of medicine there. Kazlauskaite avoided using CGM on the most critically ill patients and achieved savings by focusing on those less ill. By the time 34 patients had completed treatment in her study, rough calculations showed that Rush had saved $1,400 on PPE sets and 43 nursing work days just in the time saved in donning and doffing PPE.
Which System to Use

Kazlauskaite and Miller both used the Dexcom G6 sensor because it is a true CGM that transmits readings automatically, has a short warm-up period, and requires no calibration, making it simple to learn. Miller taped the Dexcom receiver to the window next to the nurse’s station, making it easy to read and transfer readings to the patient’s electronic health record for the 30 to 40 patients involved in his study.

Archana Sadhu, MD, director of the system diabetes program at Houston Methodist in Texas, also did a pilot study of COVID-19 patients with a history of diabetes admitted to the ICU, placing six patients on the Medtronic Guardian Connect and five on the Dexcom G6.

The primary outcomes of the study were the feasibility and accuracy compared with fingerstick tests, with secondary outcomes being reliability and nurse acceptance. “Both systems were feasible and reliable with good nurse acceptance,” Sadhu and colleagues wrote in a paper published in the *Journal of Diabetes Science and Technology*.

Monitoring Trends

The CGMs did not replace fingerstick measurements entirely, and Sadhu compared them with a cardiac monitor: “They are ideal to monitor the trend and alert you when something is going wrong, but you are not going to intervene just based on that. You are going to confirm with other data. So, if the CGM shows a worsening trend, then we would confirm it with a blood glucose test, and then use the blood glucose reading as we usually do to adjust the insulin. We were able to monitor the glucose trends with the CGM outside the patient’s room and reduce the number of blood glucose tests by 33%. So, I think it was a wonderful compromise of ensuring patient safety while minimizing healthcare workers’ risk.”

But Miller says the increased information from the constant readings went well beyond the data from fingersticks. “It is not as if we were making insulin changes every day, we were making them every few hours. This gave us a better tool to use against the virus in patients with diabetes. So, having that data outside the patient’s room on the units was really vital,” Miller says.
A year from now, the silver lining in all of this is that COVID-19 will have rapidly advanced the cause for inpatient use of CGM.”

— JOSHUA D. MILLER, MD, MPH, MEDICAL DIRECTOR OF DIABETES CARE, STONY BROOK MEDICINE, STONY BROOK, N.Y.

Kazlauskaite notes that awareness of the trend lines allowed physicians to change insulin doses sooner than reliance on fingersticks would have allowed, heading off potential danger.

Scalability and Acceptance

In all three cases, these were pilot studies that were not immediately scalable for general use because of the intense involvement of the endocrinologists. For example, Sadhu was at the bedside of every patient; Kazlauskaite asked each patient for permission to place the sensor. Each institution had to adjust to issues such as entering the information into its electronic records system. And they are all large hospitals with institutional methods and memories for dealing with patients with diabetes.

Although the need for nurse training is often cited as a hurdle to the use of CGM in hospitals, every study found that nurse acceptance was not only very high, but many nurses were quite enthusiastic, even when faced with implementing a new technology in the midst of the challenges of a pandemic.

Continuous glucose monitors were used successfully in several test studies on hospitalized COVID-19 patients with diabetes.

The monitors led to great savings in the use of personal protective equipment and nursing time in non-critically ill patients, but not in ICU patients.

Nursing and other staff adapted well to the use of the devices and were often enthusiastic in their acceptance — despite the challenges of trying new technology during a pandemic.
“If you rewind decades to when the first commercially available point-of-care fingerstick devices came out, there was a learning curve,” Miller says. “Nurses needed to understand what fingersticks were all about and how the machines worked.”

Despite the challenges, the key takeaway from all three hospitals was that CGM provided accurate, reliable, and helpful data on the glycemic status of patients.

“A year from now, the silver lining in all of this is that COVID-19 will have rapidly advanced the cause for inpatient use of CGM,” Miller says. He foresees the technology taking off in more normal times “when you can take the time to educate, to socialize, and to really inform nursing staff and other allied physician staff about the role CGM can play in the inpatient management of diabetes in the hospital.”

— JOSHUA D. MILLER, MD, MPH, MEDICAL DIRECTOR OF DIABETES CARE, STONY BROOK MEDICINE, STONY BROOK, N.Y.
Continuous Glucose Monitoring
Connecting the Dots

CGMs help with:
• Understanding glucose trends so you can manage eating, exercise, and medication
• Providing more comfort at night and managing hypoglycemia
• Understanding the importance of taking medication and timing of medication

Whether you treat patients with type 1 or type 2 diabetes, this expert-crafted guide will help guide patients in finding the perfect CGM. Visit hormone.org/cgmguide or scan the QR code below to learn more.
Torn between a career in chemistry or medicine, as Richard J. Auchus, MD, PhD, neared the end of his MD-PhD program and needed to choose his residency, he asked some recent graduates, “Who works on steroids?” That would be endocrinologists, he was told, and so began his pursuit to combine his love for both chemistry and endocrinology.

Auchus is now a professor of internal medicine and pharmacology at the University of Michigan in Ann Arbor, Mich., and his pioneering science has transformed fundamental principles of steroid biosynthesis. Endocrine News caught up with the winner of the Endocrine Society’s 2021 Outstanding Clinical Investigator Laureate Award to learn more about how that career choice long ago led to this moment.

Endocrine News: What did it mean to you personally to receive the 2021 Outstanding Clinical Investigator Laureate Award?

Richard J. Auchus: It took some time to wrap my head around what this event meant. First, I thought about my mentors and the guidance they have provided over the years. Second, I remembered all the people in my laboratory and clinical investigation programs who carried out the work. Third, there are all the other people who supported you during your career, your family, your sponsors, the participants in the studies, and the university leadership.

As scientists, we conduct our research because we have this burning curiosity to discover the unknown and to make the world a better place. You have to enjoy the ride, the process of discovery, the struggles and setbacks, the insights that lead to solutions, and of course the day when you look at the data and know something that nobody else has ever known before. When I look over the prior recipients, I am humbled to be on the same list as these luminaries in endocrinology. Awards and recognition from your peers are great, but I am even more thankful for my colleagues and the people I work with who have made the discoveries possible.

EN: You’re recognized as the world’s foremost authority on steroid-related diseases. How did steroid biosynthesis become the pinpoint of your research?

RJA: As an undergraduate at MIT, I majored in chemistry, although I thought that I would ultimately pursue a career in medicine. When I studied biochemistry, I became even more fascinated with enzymes, which are nature’s reagents for making molecules. What could be more important than applying the principles of organic reactions to the molecules of life? I spent my last year in Christopher Walsh’s laboratory studying the mechanism of a
strange chemical reaction for a bacterial enzyme. When it came time to choose chemistry or medicine, I just could not part with either, so I enrolled in the MD-PhD program at Washington University, mainly to work with Doug Covey in pharmacology. Doug synthesized the first aromatase inhibitors and was the perfect thesis mentor. He is an organic chemist who made molecules to study enzymes and to manipulate biology — and he happened to focus on steroid metabolizing enzymes. So, I learned about steroid biosynthesis pathways, nomenclature, and analysis. I did some of the first NMR experiments using a human enzyme, placental estradiol dehydrogenase (17β-hydroxysteroid dehydrogenase type 1).

It was a magical time when I was able to get a sense of how one can merge science and medicine in the physician-scientist role.

During my clinical training, I took an interest in pituitary, adrenal, and gonadal disorders, saw a lot of those patients as I still do, and went to my first Endocrine Society meeting in 1992. During fellowship, I learned molecular biology with Suzanne Fuqua and the breast cancer group at the University of Texas Health Science Center in San Antonio, and this prepared me for my postdoc with Walter Miller at University of California, San Francisco, who cloned several of the genes encoding the human steroidogenic enzymes. With Walt, I was able to incorporate molecular genetic tools into my work on steroid metabolism and develop my independent program.

I am blessed to be able to combine my basic and clinical research interests into an integrated program that has been exciting and rewarding, and I would like to think that we are significantly moving the needle in both areas.

**EN:** Can you share your lab team's major research goals for 2021?

**RJA:** We’ve launched pivotal trials of new treatments for 21-hydroxylase deficiency. We hope to finally get some better options available to endocrinologists for these patients who struggle with the long-term complications of current treatment regimens. With my colleagues, primarily Adina Turcu and Anand Vaidya, we will expand the biochemistry of primary aldosteronism using steroid mass spectrometry as my contribution.

In the laboratory, we are completing some long, detailed experiments with the kinetics of P450 17A1 (steroid 17-hydroxylase/17,20-lyase), the main enzyme we study. We also hope to start experiments to probe the dynamic behavior of P450 17A1 if the pandemic restrictions begin to abate. Finally, we have begun some very interesting comparative biochemistry experiments with P450 11B1 and P450 11B2, which are the 11-hydroxylase and aldosterone synthase enzymes. These enzymes are 93% identical, but only P450 11B2 makes aldosterone, and not very efficiently at that, and we are trying to understand the secrets of how this unique chemical reaction occurs.

You see, I am still a chemist at heart, and I think like a chemist, but I have to understand that chemistry in the context of human biology and endocrinology.

— RICHARD J. AUCHUS, MD, PHD, PROFESSOR OF INTERNAL MEDICINE AND PHARMACOLOGY, UNIVERSITY OF MICHIGAN, ANN ARBOR, MICH.

— FAUNTLEROY SHAW IS A FREELANCE WRITER BASED IN CARMEL, IND., AND A REGULAR CONTRIBUTOR TO ENDOCRINE NEWS.

"You have to enjoy the ride, the process of discovery, the struggles and setbacks, the insights that lead to solutions, and of course the day when you look at the data and know something that nobody else has ever known before.”
Obesity has been a crisis in the U.S. for decades, and unfortunately it continues to impact millions of Americans. According to Centers for Disease Control and Prevention (CDC) data, approximately 42.4% of adults in the U.S. are obese, which has resulted in an estimated $147 billion in medical costs. There is also an alarming connection between obesity and COVID-19. People with obesity contracting COVID-19 are more likely to be hospitalized and placed in intensive care than those who are not obese.

The Endocrine Society has engaged in many efforts over the years related to obesity education, prevention, treatment, and research, including policy-related activities to inform policy makers about obesity.
inform policy makers about obesity. We have advocated for funding for research, Medicare coverage for obesity treatment, and for support for prevention programs at the CDC.

As Congress begins to develop its legislative agenda for 2021, we believe this is a critical opportunity for the Society to share our expertise on this important topic. This month, the Society will publish an Obesity Playbook to educate members of Congress and their staff on the issue of obesity. This playbook, which the Society plans to release during Obesity Awareness Week, will contain a variety of resources for legislators and staff on this topic. This will include national and state-by-state facts and figures about obesity and its cost to show the extent of the problem across the country; information about the state of the science on obesity; and details about the impact of COVID-19 on people with obesity.

The playbook will also include policy options and recent legislative proposals to address obesity. We will also provide a list of obesity experts who are members of the Society. We also plan to host a virtual briefing for congressional staff on obesity later this year. We believe that this education initiative will result in members of Congress being better informed to make policy decisions on obesity and support future legislative proposals by the Society.

Each year in March, members of the Endocrine Society come to Washington, D.C., to discuss the importance of federal funding for biomedical research with their representatives and senators as part of the Endocrine Society’s annual Researcher Hill Day. Although the COVID-19 pandemic has changed how we conduct advocacy, it has not diminished the need to engage with policy makers as they make important funding decisions that will affect the bottom line for the National Institutes of Health (NIH) and other research funding agencies in the coming year.

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Our request to lawmakers is straightforward; for the coming fiscal year (FY), we are urging Congress to provide the NIH with a funding level of at least $46.1 billion, or a $3.2 billion increase over the FY 2020 program level. This will allow the biomedical research enterprise to keep pace with inflation and give the Institutes and Centers the ability to respond to new scientific opportunities. We also are advocating for language in the accompanying congressional appropriations report to support research that will help us understand how sex differences are implicated
in the severity of the COVID-19 pandemic. Specifically, to encourage the NIH to support research that studies how sex as a biological variable impacts short- and long-term outcomes due to COVID-19 infection.

In addition to the annual appropriations process, legislation has also been introduced in Congress that would provide supplemental funds to help research labs recover from the pandemic and restart their work. In February, the Research Investment to Spark the Economy (RISE) Act was introduced; this bill would authorize an additional $25 billion in funds for research agencies, including approximately $10 billion for the NIH. The RISE Act enjoys bipartisan support, and the Endocrine Society has endorsed the bill to help support the research workforce during the pandemic and recovery.

With so much at stake over the coming weeks, the advocacy of Endocrine Society members remains critical in our efforts to improve the outlook for biomedical research funding. We hope that you will add your voice — even if you cannot participate in our virtual Hill Day this month — by taking action in one of the Endocrine Society’s online advocacy campaigns, which you can find at: https://www.endocrine.org/advocacy/take-action.

Congress Focuses on COVID-19 Relief/Recovery Legislation

Last month, the U.S. House of Representatives and Senate agreed to a 2021 budget resolution, setting into motion the budget reconciliation process.

Reconciliation is a budget process that allows legislation to pass the Senate by a simple majority rather than the 60 votes commonly needed. It is a tactic to pass controversial legislation affecting spending and revenue quickly. Democrats will use the reconciliation process to attempt to pass a sweeping $1.9 trillion COVID-19 relief package developed by President Joe Biden that many Republicans oppose.

Now that the budgetary framework is set, lawmakers will focus on the details. The process works as follows: 12 committees in the House of Representatives have been directed to draft portions of the bill, which will be submitted to the Budget Committee. The Budget Committee will then combine them into one legislative vehicle. Next, the legislation will move to the House floor for a vote governed by specific rules and then, once passed, sent to the Senate where Democratic leadership has prioritized passing the legislation by the time expanded unemployment benefits expire March 14.

In addition to unemployment benefits, the House package includes measures to expand Medicaid and eliminate Medicaid drug rebate caps, multiple measures to boost vaccine dissemination to states, and many other Democratic health priorities such as: testing and contact tracing, genomic sequencing, data modernization, expanding the public health
workforce, ACA exchange upgrades, and substance abuse treatment.

The Endocrine Society has continuously advocated for provisions to be included in COVID-19 relief packages that would benefit researchers, physicians, and patients, including:

- Emergency supplemental funding for the National Institutes of Health to fund COVID-19-related research and provide recovery for research;
- Increased access to personal protective equipment;
- Sustained support for funding for core public health infrastructure and workforce;
- Expanded coverage of telehealth; and
- Protection against drug price increases, particularly for insulin.

We will continue to apprise members of developments.

As Biden Administration Weighs in on the ACA, SCOTUS Decision Expected Between March and June

Shortly after taking office, the Biden administration told the U.S. Supreme Court it should uphold the Affordable Care Act (ACA), changing the federal government’s position in a high-profile lawsuit the justices heard last year. President Joe Biden’s position was not unexpected; he had campaigned on expanding the 2010 healthcare law and criticized former President Donald Trump for backing the Republican state officials who sought to overturn it.

The previous administration had argued that the law should be overturned because the law’s requirement that most people have health insurance coverage no longer carried a financial penalty. The Supreme Court had previously cited the penalty as a reason for upholding the law in 2012, saying Congress had the power to levy taxes. The lawsuit came after Republicans effectively ended the so-called individual mandate in 2017 by zeroing out the penalty most Americans faced for not having insurance coverage as part of a tax overhaul, a change that took effect in 2019. A group of Republican state officials then sued, saying the law was no longer constitutional because the coverage requirement would no longer bring in federal revenues.

The Trump administration agreed and argued before the Supreme Court in November that the law should be overturned because of the change. The Biden administration now argues that if the justices find that the mandate is no longer constitutional, the mandate provision is severable from the rest of the law, meaning that if the Supreme Court strikes down the provision, the rest of the law would stand. The Biden administration is not asking for a supplemental briefing to follow up the November oral arguments.

The Supreme Court is expected to issue a ruling sometime between this month and when its term ends in June. The Endocrine Society joined an amicus (friend of the court) brief to provide the Court with information concerning the impact of severability and about the importance of the law in providing access to care.
CARE FOR YOUR CAREER

Join us at our Virtual Career Fair to make connections with recruiters, share your resume and LinkedIn profile, and discuss career opportunities, all from the convenience of your computer or mobile device.

Registration is complimentary and required to participate.

APRIL 1, 2021  5:00–8:00 PM EDT
REGISTER FOR FREE TODAY: ENDOCRINE.ORG/VCF
HOW DOES ESTROGEN WORK?

The ovaries, which produce a woman's eggs, are the main source of estrogen from your body. Fat tissue and your adrenal glands, located at the top of each kidney, make small amounts of this hormone.

WHAT DOES ESTROGEN DO?

Estrogen are a group of hormones that play an important role in the sexual and reproductive development in women. Men have estrogen too but in smaller amounts.

WHY IS ESTROGEN IMPORTANT?

Estrogen helps bring about the physical changes that turn a girl into a woman. This time of life is called puberty. These changes include:

• Growth of the breasts
• Growth of pubic and underarm hair
• Start of menstrual cycles
• Helps control the menstrual cycle and important for child bearing

In women and men estrogen helps control:

• sexual desire
• erectile function
• lipid metabolism
• brain function
• bone health
• skin health

THE THREE TYPES OF ESTROGEN

<table>
<thead>
<tr>
<th>Estradiol</th>
<th>Estriol</th>
<th>Estrone</th>
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<tbody>
<tr>
<td>the most common type in women of childbearing age.</td>
<td>the main estrogen produced during pregnancy.</td>
<td>the only estrogen your body makes after menopause.</td>
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Estrogen levels change throughout the month. They are highest in the middle of your menstrual cycle and lowest during your period. Estrogen levels drop at menopause.

THE LOWS OF ESTROGEN

WOMEN. The most common reason for low estrogen in women is menopause or surgical removal of the ovaries. Symptoms of low estrogen include:
- Menstrual periods that are less frequent or that stop
- Hot flashes (suddenly feeling very warm) and/or night sweats
- Trouble sleeping
- Vaginal dryness and thinning

Some women get menstrual migraine, a bad headache right before their menstrual period, because of the drop in estrogen.

MEN. Low estrogen in men can cause excess belly fat and low sexual desire.

THE HIGHS OF ESTROGEN

WOMEN. Excess estrogen can lead to these problems, among others:
- Weight gain, mainly in your waist, hips, and thighs
- Menstrual problems, such as light or heavy bleeding
- Worsening of premenstrual syndrome (PMS)
- Fibrocystic breasts (non-cancerous breast lumps)
- Fibroids (noncancerous tumors) in the uterus
- Mood swings
- Feeling depressed or anxious
- Breast swelling and tenderness
- Low sexual desire
- Fatigue

MEN. High estrogen in men can cause:
- Enlarged breasts (gynecomastia)
- Poor erections
- Infertility
- Loss of sex drive
- Erectile dysfunction (ED)
- Dry skin

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.

Editor: Subbulaxmi Trikudanathan, MD, MRCP University of Washington Medical Center