

AUGUST 2018

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

# Endocrine news

INTERNATIONAL

## Out of the ORDINARY:

### A Look at the Research & Treatment of Rare Endocrine Disorders

- How a **Von Hippel-Lindau** patient manages her health and how new research may spare others from this rare genetic disorder.
- New research shows that even when **acromegaly** is successfully treated, follow-up may still be needed.
- A database for pediatric **adrenocortical tumors** has benefitted patients, families, and the physicians who treat them.
- A new treatment for **hypoparathyroidism** has shown promise in a series of longer-term studies.

#### TRENDS & INSIGHTS:

Prostate cancer & androgen receptors; BCG vaccine in diabetes; and more.

#### FROM THE PRESIDENT:

Susan Mandel, MD, previews **ENDO 2019** in New Orleans.

ENDOCRINE  
SOCIETY



Hormone Science to Health

# Endocrine news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

## 2017 – 2019 EDITORIAL ADVISORY BOARD

### Henry Anhalt, DO

Bergen County Pediatric Endocrinology  
Chair, Hormone Health Network  
VP, Medical Affairs, Science 37

### Sally Camper, PhD

Department of Human Genetics  
University of Michigan Medical School

### Rodolfo J. Galindo, MD

Assistant Professor of Medicine  
Mount Sinai School of Medicine

### Christian M. Girgis, MBBS, PhD, FRACP

Royal North Shore and Westmead Hospitals  
University of Sydney, Australia

### Andrea Gore, PhD

Division of Pharmacology and Toxicology  
University of Texas

### Daniel A. Gorelick, PhD

Department of Pharmacology & Toxicology  
University of Alabama at Birmingham

### M. Carol Greenlee, MD, FACP

Western Slope Endocrinology  
Grand Junction, Colo.  
(Faculty for Transforming Clinical Practice initiative [TCPI])

### Gary D. Hammer, MD, PhD

Millie Schembechler Professor of Adrenal Cancer,  
Endocrine Oncology Program  
University of Michigan

### Robert W. Lash, MD

Chief Professional & Clinical Officer, Endocrine Society

### Karl Nadolsky, DO

Diabetes Obesity & Metabolic Institute  
Walter Reed National Military Medical Center;  
Uniformed Services University

### Joshua D. Safer, MD, FACP

Center for Transgender Medicine and Surgery, Endocrinology Fellowship Training  
Boston Medical Center; Boston University School of Medicine

### Shehzad Topiwala, MD, FACE

Endocrinology Department  
SevenHills Hospital, Mumbai, India

### Kristen R. Vella, PhD

Beth Israel Deaconess Medical Center  
Harvard Medical School

### Christina Wang, MD

UCLA Clinical and Translational Science Institute  
Harbor – UCLA Medical Center

## NEWLY UPDATED CPG APP

## Clinical Decisions Made Easy at Your Fingertips

### NOW FEATURING:

- Testosterone Therapy in Men guideline
- SI Unit Converter for international users
- Plus, 37 interactive point-of-care tools, guideline recommendations, patient information, and more



## TO DOWNLOAD VISIT ENDOCRINE.ORG/APP

ENDOCRINE  
SOCIETY

© 2018 ENDOCRINE SOCIETY



## FEATURE

### 18 | Heir on the Side of Caution:

#### How a Von Hippel-Lindau Patient is Managing Her Health

In the two decades since Stacy Lloyd was diagnosed with Von Hippel-Lindau, much has changed in genetic research, treatment, and counseling methods. Thankfully, new methods are evolving constantly to treat, diagnose, and maybe even prevent this rare and often debilitating genetic disorder.

BY DEREK BAGLEY

## FEATURES

### 26 | Aftershocks: Complications After Acromegaly

An **ENDO 2018** presentation that linked essential oils to gynecomastia in pre-pubertal boys caused a bit of an uproar in the spring. The study authors detail what their research means, why certain populations should be mindful of essential oil use, and the importance of future studies.

BY DEREK BAGLEY

### 30 | Hypoparathyroidism: Treatment for an Orphan Disease

While surgery has shown to be the most effective tool in combatting obesity, younger patients are not being offered this option. Providers need to re-evaluate their own biases when treating these patients in terms of how they could improve various quality-of-life factors as well as the young patient's health.

BY ERIC SEABORG

### 36 | Getting the ACT Together: Tumor Database Improves Pediatric Care

The research presented at **ENDO 2018** ran the gamut in terms of breakthroughs in endocrine science. Of particular interest were studies that took a closer look at how offspring could be harmed by endocrine disruptors — specifically BPA and DEHP — while still in the womb.

BY DEREK BAGLEY

#### 2 | PRESIDENT'S VIEWPOINT

**ENDO 2019:** Stimulate Exploration, Enrich Community & Enhance Fundamentals

#### 4 | FROM THE EDITOR

Off the Beaten Pathology

#### 6 | TRENDS & INSIGHTS

*HSD3B1* positively regulated by androgen receptor signaling in prostate cancer; BCG vaccine leads to long-term improvement in blood sugar levels in patients with type 1 diabetes; Broken bones among older people increase risk of death for up to 10 years.

BY DEREK BAGLEY

#### 10 | IN TOUCH

Society sponsors Capitol Hill briefing on transgender health; Barbara Kahn honored by FASEB; Society publishes new practice guideline on treating adult survivors of childhood cancers.

#### 14 | ENDOCRINE ITINERARY

Scientific meetings of interest to endocrinologists from around the world.

#### 17 | DASHBOARD

Highlights from the world of endocrinology

#### 42 | LAB NOTES Q & A FROM THE POND TO THE BENCH

*Endocrine News* talks to 2018 Laureate: Richard E. Weitzman Outstanding Early Career Investigator Award recipient, Gregory Steinberg, PhD, at McMaster University in Ontario about how he first set out to be a scientist as a child, and why a diverse lab is the most effective lab.

BY GLENDA FAUNTLEROY SHAW

#### 56 | ADVOCACY

Endocrine experts influence EU policy meetings; NIH receives increased funding but final outlook uncertain; and Endocrine Society advocates for women's health.

#### 63 | CLASSIFIEDS

Career opportunities

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



Follow us on Twitter:  
@Endocrine\_News

ENDOCRINE  
SOCIETY







## ENDO 2019: Stimulate Exploration, Enrich Community & Enhance Fundamentals

**E** NDO is the Endocrine Society's largest, most visible activity and reflects the breadth, depth, and diversity of endocrine research and clinical practice. Through the years, ENDO has positively impacted me personally and professionally, and I have seen it do the same for countless trainees and colleagues. I suspect I am like you in finding that ENDO offers me so many different enrichment opportunities; it stimulates my curiosity, provides me new knowledge and skills to apply to my practice, and presents me with opportunities to see friends and develop new collaborations.

As president of the Endocrine Society, I am proud to say that our Annual Meeting Steering Committee (AMSC) reflected on what ENDO means to them, and have developed a program designed to **Stimulate Exploration, Enrich Community, and Enhance Fundamentals**. These goals were at the forefront of AMSC planners' minds as they developed an outstanding

scientific and clinical program that showcases leading-edge research and guidance for the most significant clinical challenges in endocrinology. The meeting will feature global perspectives on the science and practice of endocrinology presented by top scientists and clinicians.

A few highlights of ENDO 2019 include:

- A presidential plenary with the director of the National Institutes of Health, Dr. Francis Collins, who will translate whole genome approaches to unraveling diseases;
- Novel plenaries that will examine gene editing and stem cells; novel therapeutic targets in metabolic disease and cancer; insights from the Society's newest inductees into the National Academy of Sciences; big data; senescent cells in aging in disease; and much more;



Annual Meeting Steering Committee members at the May 2018 meeting to plan the program for ENDO 2019




- All new and highly interactive Meet-the-Professor sessions, clinical guidelines presentations, and innovative symposia, all developed with your learning in mind;
- Debates examining what level of hemoglobin A1C we should be targeting as well as if TPO AB or TSH screening should occur for thyroid disease in pregnancy;

“

**I suspect I am like you in finding that ENDO offers me so many different enrichment opportunities; it stimulates my curiosity, provides me new knowledge and skills to apply to my practice, and presents me with opportunities to see friends and develop new collaborations.**

”

- World-class career-shaping information for our clinical and basic science trainees;
- Sessions dedicated to new technologies relevant for endocrine investigation, such as single-cell sequencing, CRISPR, RNAi, and shRNA screens; and big data and bioinformatics for biologists;
- Highly focused learning tracks in reproductive endocrinology, neuroendocrinology, and nuclear receptors that allow you to network with colleagues with similar interests; and
- Expanded opportunities for you to showcase your discoveries and educate your colleagues.

ENDO 2019 provides an opportunity for our community to come together in a vibrant and warm city and continue our personal and professional journeys. Please mark your calendars to be in New Orleans, Louisiana, from March 23 to 26, 2019. If you have any questions or comments, please contact me at [president@endocrine.org](mailto:president@endocrine.org) 

— Susan J. Mandel, MD, MPH, President, Endocrine Society

# MANAGING HYPONATREMIA?

**ure-Na is oral urea made palatable.**

☒ Inpatient ☒ Outpatient

## OUTPATIENT COVERAGE

- ☒ Medicaid\*
- ☒ Medicare Advantage\*
- ☒ Commercial\*
- ☒ VA
- ☒ Indian Health Service
- ☒ Private Pay

\* A PA is typically required.

To speak with a reimbursement specialist about out-patient insurance coverage, please call 1-844-980-9933.

For patients with VA benefits, ure-Na is on the VA National Formulary as UREA 15GM/PKT/PWDR, ORAL.

The use of urea to manage hyponatremia due to SAIDH is guideline supported\*



**ure-Na™**  
*Oral Urea Made Palatable*

For samples of ure-Na please see the sample order section of [nephcentric.com](http://nephcentric.com).

\*The European Clinical Practice Guideline on the management of hyponatremia recommend the use of oral urea as a treatment option in SIADH for moderate to profound hyponatremia. UpToDate also reviews the use of urea as a management option for hyponatremia.

For ure-Na availability outside the USA, please see the International section of [ure-na.com](http://ure-na.com).

**Learn more about the use of urea and ure-Na for hyponatremia at [ure-na.com](http://ure-na.com)**



FROM THE **EDITOR**

## Off the Beaten Path: Rare Endocrine Disorders

**T**his month's issue is a first for *Endocrine News*; we're devoting much of our feature well to rare endocrine disorders. Hypoparathyroidism (70,000 patients in the U.S.), acromegaly (<20,000 cases annually), adrenocortical tumors (1 – 2 per 1,000,000) and Von Hippel-Lindau (1 in 36,000 in the U.S.) all get their due in this issue.

Senior editor Derek Bagley writes about the complications that can occur after treatment or even a cure of acromegaly in "Aftershocks: Complications After Acromegaly," on page 36. He spoke with Frederic Castinetti, MD, PhD, who led a French study that discovered a significant proportion

“

**Biological material, including tumor and blood samples from the patient and their relatives, allows us to perform collaborative investigations to understand the biology of the disease and ultimately improve the outcomes for these patients.**

”

of acromegaly patients still had comorbidities even after they had been successfully treated. "Once your job is done and the secretion is controlled, never forget that the comorbidities can still be there," Castinetti says. The study's findings were published in *The Journal of the Endocrine Society* in December 2017.

On page 40, "Hypoparathyroidism: Treatment for an Orphan Disease" by Eric Seaborg discusses a trio of studies that cite the potential for a new treatment that has shown promise in terms of both safety and effectiveness. Seaborg speaks with lead author Dolores Shoback, MD, professor of

AUGUST 2018

# Endocrine news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Editor: **Mark A. Newman**  
mnewman@endocrine.org

Senior Editor: **Derek Bagley**  
dbagley@endocrine.org

Art Director/Production: **Anthony S. Picco**

Art Director/Design: **Catherine C. Neill**,  
**CNJ Creative, LLC**  
www.cnjcreative.com

Prepress & Printing: **The Sheridan Group**  
www.sheridan.com

*Endocrine News* is a registered trademark owned by the Endocrine Society.

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



President: **Susan Mandel, MD**  
president@endocrine.org

President-Elect: **E. Dale Abel, MD, PhD**  
dale-abel@uiowa.edu

Past-President: **Lynnette Nieman, MD**  
Lynnette.Nieman@gmail.com

Secretary-Treasurer: **Richard S. Legro, MD**  
rlegro@hmc.psu.edu

Chief Executive Officer: **Barbara Byrd Keenan, FASAE, CAE**  
bbkeenan@endocrine.org

Chief Communications Officer: **Aaron Lohr**  
alohr@endocrine.org

The mission of the Endocrine Society is to advance excellence in endocrinology and promote its essential and integrative role in scientific discovery, medical practice, and human health.

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

Print ISSN 2157-2089 Online ISSN 2157-2097  
Copyright © 2018 by the Endocrine Society.  
All rights reserved.


- Please send letters to the editor, comments, and suggestions for *Endocrine News*\* to mnewman@endocrine.org.
- Product print and product online display advertising, by Pharmaceutical Media, Inc., contact Joe Schuldner, jschuldner@pminy.com, or John Alberto, jalberto@pminy.com.
- For classified print advertising by Pharmaceutical Media, Inc., Dan Simone, dsimone@pminy.com
- For classified online advertising by endocrineers@endocrine.org

**The statements and opinions expressed in *Endocrine News*\* are those of individual authors and do not necessarily reflect the views of the Endocrine Society.**

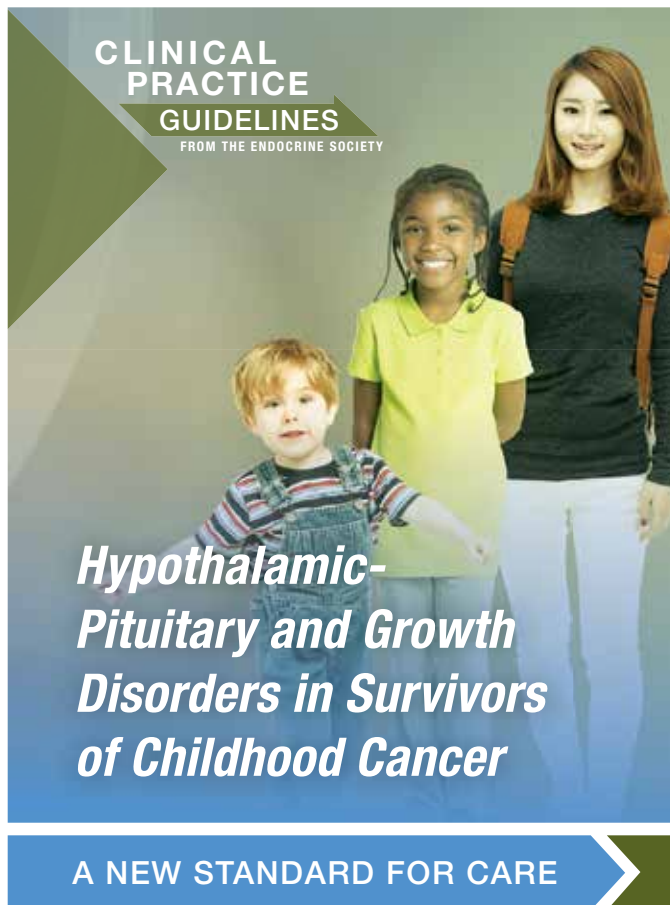
Advertising appearing in this publication does not constitute endorsement of its content by *Endocrine News*\* or the Endocrine Society.

medicine; director, UCSF Training Program in Diabetes, Endocrinology, and Metabolism, University of California, San Francisco, who presented the results of the studies at **ENDO 2018** in Chicago. All three studies center around the use of recombinant human parathyroid hormone (1-84), which was recently approved by the U.S. Food and Drug Administration based on relatively short-term clinical trials. However, longer-term studies show the drug's benefits continue without additional side effects, according to Shoback.

"Heir on the Side of Caution" on page 28 details how Von Hippel-Lindau patient Stacy Lloyd has taken charge of her treatment with the help of her endocrinologist Paul Kopp, MD, from Northwestern University. After giving a Meet the Patient session at **ENDO 2018**, the duo spoke to us about how this rare disorder can not only change the patient's life, but the lives of affected family members as well. Could genetic editing be an eventual "cure?"

A different kind of story takes us into the lab of Emilia Pinto, MD, at St. Jude's Hospital in Memphis, Tenn., to discuss the creation and use of the International Pediatric Adrenocortical Tumor Registry, a database of young patients with this rare condition ("Getting the ACT Together," p. 46). According to Pinto, the registry offers the opportunity to collect clinical and demographic information, familial cancer histories, lab work, treatments, and outcomes. "Biological material, including tumor and blood samples from the patient and their relatives, allows us to perform collaborative investigations to understand the biology of the disease and ultimately improve the outcomes for these patients," she says. 

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



CLINICAL  
PRACTICE  
GUIDELINES  
FROM THE ENDOCRINE SOCIETY

***Hypothalamic-  
Pituitary and Growth  
Disorders in Survivors  
of Childhood Cancer***

**A NEW STANDARD FOR CARE**

Get the latest recommendations on how to diagnose and manage hypothalamic-pituitary and growth disorders commonly found in childhood cancer survivors.

The guideline emphasizes key differences in the testing and treatment of these disorders that are specific to the childhood cancer survivor such as:

- Diagnosis and treatment of growth hormone deficiency
- Treatment of adrenocorticotrophic hormone deficiency

Learn about the importance of life-long screening for earlier detection and better care of these patients.

**READ THE GUIDELINE AT  
[ENDOCRINE.ORG/CPG](https://www.endocrine.org/cpg)**

© 2018 ENDOCRINE SOCIETY

ENDOCRINE  
SOCIETY 





**BY DEREK BAGLEY**  
Senior Editor

# BCG Vaccine Leads to Long-Term Improvement in Blood Sugar Levels in Patients with Type 1 Diabetes, Study Shows

“

**This is clinical validation of the potential to stably lower blood sugars to near normal levels with a safe vaccine, even in patients with longstanding disease. In addition to the clinical outcomes, we now have a clear understanding of the mechanisms through which limited BCG vaccine doses can make permanent, beneficial changes to the immune system and lower blood sugars in type 1 diabetes.**

”

**L**ong-term follow-up of participants in clinical trials of a generic vaccine to reverse advanced type 1 diabetes finds significant clinical benefits, including restoration of near-normal blood sugar levels. Three years after receiving two administrations of the bacillus Calmette-Guérin (BCG) vaccine four weeks apart, all members of a group of adults with longstanding type 1 diabetes showed an improvement in HbA1c to near normal levels – improvement that persisted for the following five years. The study from a Massachusetts General Hospital (MGH) research team – published in *npj Vaccines* – also reports that the effects of BCG vaccine on blood sugar control

appear to depend on a totally novel metabolic mechanism that increases cellular consumption of glucose.

Researchers led by Denise Faustman, MD, PhD, director of the MGH Immunobiology Laboratory, point out that BCG is one of the oldest vaccines in the world. It was used for almost a century to prevent tuberculosis and has been known for more than 30 years to boost production of a cytokine called tumor necrosis factor (TNF), which may be beneficial in autoimmune diseases both by eliminating the autoreactive T cells that attack an individual's tissues – in the case of type 1 diabetes, pancreatic islets –



and by inducing production of regulatory T cells (Tregs) that could prevent an autoimmune reaction. Faustman's team first reported in 2001 that inducing TNF production could cure type 1 diabetes in mice, but since TNF dosing is toxic in humans, clinical trials have utilized BCG for its ability to elevate TNF levels safely.

"This is clinical validation of the potential to stably lower blood sugars to near normal levels with a safe vaccine, even in patients with longstanding disease," Faustman says. "In addition to the clinical outcomes, we now have a clear understanding of the mechanisms through which limited BCG vaccine doses can make permanent, beneficial changes to the immune system and lower blood sugars in type 1 diabetes."

Initial clinical trial results, published in a 2012 *PLOS One* paper, reported that two doses of BCG spaced four weeks apart led to reductions in autoreactive T cells, an increase in Tregs, and what turned out to be a transient increase in insulin production. But by the end of that short, 20-week trial, there was no reduction in HbA1c, the established measure of blood sugar levels over time. An extension and expansion of that trial with long term follow-up, the current results are based on data from 282 human study participants – 52 with type 1 diabetes who participated in the BCG clinical trials and 230 who contributed blood samples for mechanistic studies.

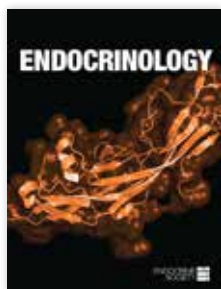
Regular monitoring of clinical trial participants found that HbA1c levels of those receiving BCG had dropped by more than 10% at three years after treatment and by more than 18% at four years. That reduction was maintained over the next four years, with treated participants having an average HbA1c of 6.65, close to the 6.5 considered the threshold for diabetes diagnosis, and with no reports of severe hypoglycemia. Participants in the placebo group and in a comparison group of patients receiving no treatment experienced consistent HbA1c elevations over the same eight-year time period.

In investigating how BCG administration produces its beneficial effects, the research team identified

a mechanism never previously seen in humans in response to treatment with any drug – a shifting of the process of glucose metabolism from oxidative phosphorylation, the most common pathway by which cells convert glucose into energy, to aerobic glycolysis, a process that involves significantly greater glucose consumption by cells. The researchers also found that BCG could reduce blood sugar elevations in mice that were caused by means other than autoimmune attack, raising the possibility that BCG vaccines could also be beneficial against type 2 diabetes.

Mihai G. Netea, PhD, professor in the Department of Internal Medicine at Radboud University Medical Center in the Netherlands, says of this study, "The clinical effects and the proposed mechanism demonstrated are exciting and add to the emerging consensus that the BCG vaccine can have a lasting and valuable impact on the immune system. We know, and this study shows, that BCG vaccination induces epigenetic reprogramming at the chromatin architecture level and functional alterations indicative of a permanent change in immunity. The MGH trials and other, larger prevention and intervention trials underway around the globe may lead to a major shift in the prevention and treatment of infections and autoimmunity." Netea was not involved in the current study.

**Findings:** The MGH team's findings set the stage for further testing of BCG administration, including the FDA-approved phase 2 study currently underway, testing multiple BCG doses in a large group of participants with longstanding type 1 diabetes. That trial is fully enrolled, and there are seven additional BCG clinical trial groups currently recruiting or enrolling at MGH, with a pediatric trial in the planning stages. The MGH BCG clinical trial program is entirely funded by private philanthropy from individuals and family foundations, including the Iacocca Foundation.



“  
Given its critical role in extragonadal androgen synthesis, we sought to directly interrogate the transcriptional regulation of *HSD3B1* in multiple metastatic prostate cancer cell models.  
”

## *HSD3B1* Positively Regulated by Androgen Receptor Signaling in Prostate Cancer

**T**he *HSD3B1* gene is positively regulated by androgens and androgen receptors (ARs), a finding that may play a role in more tailored treatment of prostate cancer, according to a study recently published in *Endocrinology*.

Researchers led by Nima Sharifi, MD, of the Cleveland Clinic in Cleveland, Ohio, point out that prostate cancer requires gonadal testosterone (T) for growth and progression, and advanced prostate cancer initially responds to androgen deprivation therapy (ADT; castration), but cancer treated by this castration results in castration-resistant prostate cancer.

The androgen-synthesizing enzyme  $3\beta$ HSD1, encoded by *HSD3B1*, converts dehydroepiandrosterone (DHEA) to androstenedione (AD), and regulates the rate-limiting step in the conversion of DHEA to the potent androgens T and dihydrotestosterone (DHT). “A genetic variant of *HSD3B1*—1245A>C; rs1047303—results in decreased proteasomal degradation of  $3\beta$ HSD1 and in a strikingly dimorphic shift in DHEA metabolism, likely leading to increased DHT synthesis from extragonadal precursor steroids in metastatic tumors,” the authors write. They go on to write that their previous studies have shown that patients who inherit this *HSD3B1* variant have worse outcomes when undergoing ADT. “This is mechanistically attributable to the ability of tumors harboring the variant to more effectively use adrenal DHEA/DHEA sulfate for tumor androgen synthesis to fuel tumor growth when gonadal T is no longer available because of ADT,” they write.

The researchers wanted to find out how the transcriptional regulation of *HSD3B1* works in



prostate cancer since relatively little is known about this process. “Given its critical role in extragonadal androgen synthesis, we sought to directly interrogate the transcriptional regulation of *HSD3B1* in multiple metastatic prostate cancer cell models,” the authors write.

Using cell cultures and mice, the researchers found that VCaP, CWR22Rv1, LNCaP, and LAPC4 models demonstrate induction of *HSD3B1* upon androgen stimulation for approximately 72 hours, followed by attenuation around 120 hours. “We found that in multiple CRPC models, *HSD3B1* is induced by the synthetic androgen R1881 and that this effect can be abrogated by the AR antagonist enzalutamide,” the authors write. “ $3\beta$ HSD1 protein is also induced, and enzyme functionality was confirmed by measuring flux from DHEA to AD and other downstream metabolites via HPLC. Further, *HSD3B1* mRNA and protein are suppressed in an in vivo VCaP xenograft model after castration.”

**Findings:** The authors note that they were surprised by these results and had actually anticipated the opposite, since T deprivation spurs an increase in compensatory androgen synthesis. “Namely,” the authors write, “we fully expected that AR stimulation would instead suppress *HSD3B1* transcript and potent androgen synthesis from extragonadal precursor steroids.” Still, based on these results, the researchers conclude that *HSD3B1* is unexpectedly positively regulated by androgens and ARs. They go on to write that there are potential clinical implications, such as the use of enzalutamide, a direct AR antagonist, and testing for *HSD3B1*(1245C) germline variant inheritance.



# Broken Bones Among Older People Increase Risk of Death for Up to 10 Years

**B**roken bones among older people increase their risk of death for up to 10 years, according to a new study published in *The Journal of Clinical Endocrinology & Metabolism*.


Researchers led by Jacqueline Center, MBBS, PhD, of the Garvan Institute of Medical Research in Sydney, Australia, point out that older people with broken bones face a higher risk of death, and that risk can stay elevated for years. Hip fractures are known to increase the mortality risk among older people, and this is the first study to identify how long this risk lasts for different fractures. Non-hip fractures contribute to more than two-thirds of all fragility fractures and can include fractures of the femur, pelvis, clavicle, or lower leg. “The extent of any increased mortality risk associated with fractures other than hip and vertebrae remains controversial,” the authors write. “Importantly, no study to date has been conducted to determine long-term excess mortality attributable to individual non-hip fractures accounting for time-related mortality changes, even though these fractures contribute to more than two-thirds of all fragility fractures.”

“A fracture is the starting point for much wider health issues that persist long after the fracture has healed and can ultimately result in earlier death,” Center says. “We tracked the increased risk of death for fractures in different bones and found that they vary. The heightened risk can last for over a decade after a hip fracture, and for most other fractures (apart from distal or minor fractures), the increased risk is for about five years.”



This nationwide, registry-based follow-up study included all individuals in Denmark over the age of 50 who first experienced fragility fractures in 2001 and were followed up to 10 years for their mortality risk.

In the year after breaking a hip, men faced a 33% higher risk of death and women had a 20% higher risk. For femur or pelvic fractures, the one-year excess mortality was between 20% and 25%, respectively. A significant risk of death was still observed 10 years after a person broke a hip and approximately five years following non-hip fractures. “We hypothesized that the more severe fractures were associated with excess mortality, with the length of the excess mortality being fracture type specific,” the authors write. “The study findings are consistent with the hypothesis, suggesting excess mortality was associated with virtually all proximal and lower leg fractures. Excess mortality remained evident for more than 10 years after a hip fracture and for approximately [five] years following a proximal non-hip or lower leg fracture, ranging from [three] years following a rib fracture to about [six to seven] years following a vertebral or humerus fracture.”

**Findings:** “Our findings emphasize just how crucial early intervention is,” Center says. “We need to understand the risk of breaking a bone before the fracture happens and treat that individual accordingly. While intervention after the first fracture is critical, we also need to diagnose those at risk of breaking bones before these major health impacts have occurred.” 



“

The extent of any increased mortality risk associated with fractures other than hip and vertebrae remains controversial. Importantly, no study to date has been conducted to determine long-term excess mortality attributable to individual non-hip fractures accounting for time-related mortality changes, even though these fractures contribute to more than two-thirds of all fragility fractures.

”

# Endocrine Society Hosts Congressional Briefing on Transgender Health

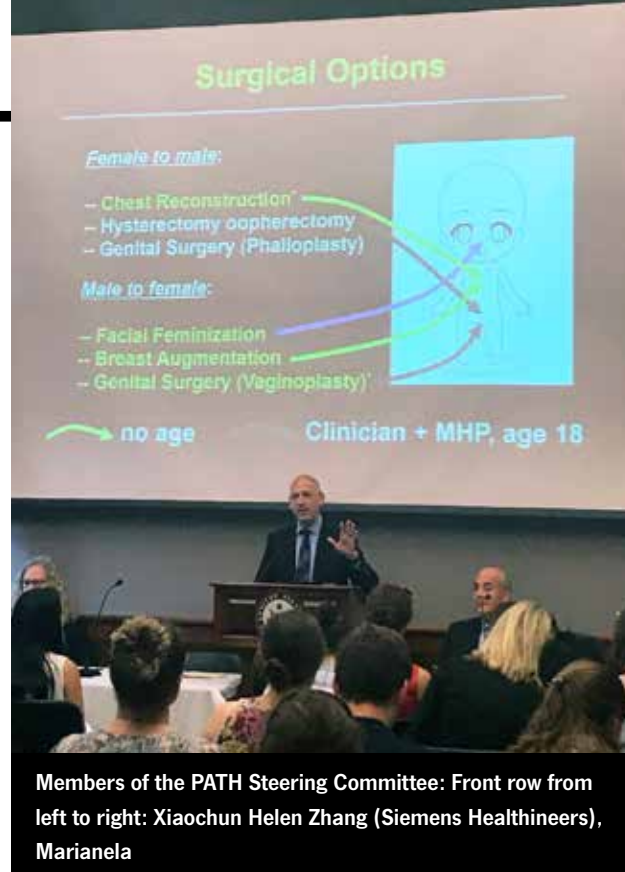
**O**n Monday July 30, the Endocrine Society hosted a congressional briefing entitled “Transgender Health: Meeting Patient Needs Through Research and Improved Access to Care.” The briefing was sponsored by Sen. Cory Booker (D-N.J.).

The speakers at the briefing consisted of Endocrine Society member Joshua Safer, MD, executive director of the Mount Sinai Center for Transgender Medicine and Surgery in New York City; Rachel Levine, MD, the Pennsylvania’s Secretary of Health and a professor of pediatrics and psychiatry at Penn State College of Medicine; and Karen L. Parker, PhD, director of the Sexual & Gender Minority Research Office, Division of Program Coordination, Planning and Strategic Initiatives of the Office of the Director at the National Institutes of Health in Bethesda, Md.

The briefing was moderated by Robert W. Lash, MD, the Endocrine Society’s chief professional & clinical affairs officer, and was conceived to highlight the evolving approaches of treating transgender patients to members of Congress as well as their staffs. “We were delighted to be able to contribute to the growing awareness of the medical, legal, and public policy issues facing the transgender community,” Lash says. “Our attendees, who were from both sides of the aisle, had the opportunity to



Members of the PATH Steering Committee: Front row from left to right: Xiaochun Helen Zhang (Siemens Healthineers), Mariana



hear national experts discuss how research is informing our understanding of transgender medicine.”

In his presentation addressing an evidence-based approach to transgender medicine, Safer explained to the attendees about the biological underpinning to gender identity. “We are medical providers and scientists who may have hypotheses about medical strategies that may work but who then defer to the actual data when we have it,” he explains. “We provide the best care for our patients when we follow the science.”

Safer further adds that the credibility of the medical and scientific community in the greater community results from our evidence-based, scientific approach. “Our sober, honest interpretation of the scientific data has contributed to a shift in the general community regarding approach to transgender individuals as well.”

At one point, Safer addressed the potential factors that determine gender identity and how these are viewed differently today than they were in the past. “It was widely accepted that gender identity was passive and could be manipulated externally only a decade or so ago,” he explains. “However, despite the lack of understanding of mechanism, the data for a durable biological underpinning to gender identity has shifted the care strategy entirely. Instead of devoting erroneous effort to trying to manipulate gender identity, the accepted establishment care model has shifted to aligning external anatomy with gender identity when medical intervention is sought.”

Parker discussed the research being done at the NIH, specifically research that addresses sexual and gender minority (SGM) research. SGM is an umbrella phrase that encompasses lesbian, gay, bisexual, and transgender populations, as well as those whose sexual orientation, gender identity and expressions, or reproductive development varies from traditional, societal, cultural, or physiological forms, according to her presentation.

“Sexual and gender minorities still ace unequal treatment and are denied equal legal protections causing stress in their daily lives,” Parker says, adding that health disparities include mental and physical risks to due to unequal treatment and lack of access to care.

Levine, who herself is transgender, approached the information from a more personal standpoint and attempted to dispel rumors that the general public – and even some healthcare professionals – may harbor towards transgender individuals. “It’s impossible to hate someone whose story you know,” she says, adding a quote from Yoda from the Star Wars films to illustrate her point: “Fear is the path to the dark side. Fear leads to anger. Anger leads to hate. And hate leads to suffering.”

She also addressed the number of health disparities that affect transgender people citing that at least one-third have experienced a negative reaction from a healthcare provider in the past year and 40% have attempted suicide in their lifetime. This is nearly nine times the average rate in the U.S. of 4.6%. “This is the result of bullying, harassment, discrimination, and violence that leads to these negative outcomes,” she says.

Lash says that it was a special privilege to hear from Levine, “a physician and policy maker whose perspective as a transgender woman called attention to the issues of discrimination and access to care that transgendered men and women still face,” he says. “We hope that sessions like these will help to shape the discussion of this important issue.”

The briefing on the Hill was just another component of the Endocrine Society’s continuing efforts to meet transgender patients’ needs through research as well as improve their access to quality care. As part of its efforts to improve care for transgender people, the Society is advocating for no discrimination by providers or insurance companies; establishing medical intervention as the standard of care; transgender treatment should be covered by insurance; and increased funding for research.

— Mark A. Newman

## Congratulating the 2018 Endocrine Fellows Series Awardees

**C**ongratulations to the 2018 awardees for this year’s Osteoporosis Fellows Series held August 1 and 2 in Santa Fe, N.M. This two-day conference is designed for clinical endocrine fellows in adult and pediatric programs that are looking to update their knowledge of rare bone diseases and clinical best practices.

The faculty will select the top four abstracts presented at the Osteoporosis conference for an additional speaking session at the Santa Fe Bone Symposium, the premier clinical bone conference in the country, which is held August 3 and 4.

### FULL LIST OF 2018 AWARDEES:

1. Ahlam Alzenaidi, MD, Louisiana State University
2. Rachel Arakawa, MD, Columbia University Medical Center
3. Gauri Behari, MD, University of Arizona Phoenix
4. Luis Chavez, MD, University of Rochester
5. Lisa Cruz-Aviles, MD, Yale School of Medicine
6. Kyrmarie Davila, MD, San Juan City Hospital
7. Kristen Gonzales, MD, Mayo Clinic
8. Julie Islam, MD, Scripps Clinic
9. Christina Kwan, MD, California Pacific Medical Center
10. Eli Miller, MD, Temple University Hospital
11. Komal Motwani, MD, Eastern Virginia Medical School
12. Nandini Nair, MD, Columbia University
13. Manav Nayyar, MD, University of Missouri - School of Medicine, Columbia
14. Pilar Ortegon Zambrano, MD, University of New Mexico
15. Mohammed Qureshi, MD, Houston Methodist Hospital
16. Zeb Saeed, MD, Indiana University School of Medicine
17. Nicole Sagalla, MD, Duke University
18. Darius Schneider, MD, PhD, University of Washington
19. Shiksha Sharma, MD, Montefiore Medical Center
20. Rahaf Sultan, MD, Henry Ford Health System
21. Fadwa Sumrein, DO, Rutgers New Jersey School of Medicine
22. Sikarin Upala, MD, University of Chicago
23. Neha Verma, MD, The Ohio State University
24. Noor Yazdanie, MD, Baylor Scott & White Health
25. Adnin Zaman, MD, University of Colorado
26. Maryam Rivaz, MD, University of New Mexico






Barbara B. Kahn, MD

## Barbara B. Kahn, MD, to be Honored by FASEB

**E**ndocrine Society member, Barbara B. Kahn, MD, will receive the 2019 FASEB Excellence in Science Award. Kahn, vice chair for research strategy in the Department of Medicine at Beth Israel Deaconess Medical Center (BIDMC) and the George R. Minot Professor of Medicine at Harvard Medical School, is one of few physician-scientists to receive this award. She leads a highly successful research laboratory that has made seminal contributions to understanding the pathogenesis of obesity and type 2 diabetes.

Awarded by The Federation of American Societies for Experimental Biology (FASEB) – the nation's largest coalition of biological and biomedical researchers, representing the Endocrine Society and other scientific societies and over 130,000 researchers worldwide – the Excellence in Science Award recognizes women whose outstanding career achievements in biological science have contributed significantly to the understanding of a particular discipline through scientific achievements, training of students and postdoctoral fellows, and contributions to the broader scientific community. Award recipients receive an unrestricted research grant of \$10,000.

Kahn has been at the leading edge of research on the molecular and cellular mechanisms underlying type 2 diabetes and the link between obesity and diabetes. She made some of the earliest observations of the dysregulation of glucose transporter gene expression and cellular function in altered nutritional and metabolic states such as obesity and diabetes. The work of her lab has revealed paradigm-shifting insights into how different metabolically important tissues communicate and coordinate responses to metabolic challenges.

A dedicated mentor throughout her career, she's mentored nearly 100 postdocs and students. In her leadership positions at Harvard and Beth Israel Deaconess including as chief of the Division of Endocrinology, Diabetes and Metabolism, she has supported and developed junior faculty. In her role planning scientific sessions for the Endocrine Society and ADA – and as chair of national and international conferences for FASEB and other scientific organizations – she seeks to promote diversity and give junior faculty opportunities in high-visibility positions. 

## New Society Guideline Focuses on Treating Adult Childhood Cancer Survivors

**I**n July, the Endocrine Society issued a Clinical Practice Guideline advising healthcare providers on how to diagnose and treat the endocrine disorders that affect a significant portion of childhood cancer survivors in the U.S.

The guideline, titled “Hypothalamic-Pituitary and Growth Disorders in Survivors of Childhood Cancer: An Endocrine Society Clinical Practice Guideline,” was published online and appeared in the July 2018 print issue of *The Journal of Clinical Endocrinology & Metabolism (JCEM)*. Recent data shows that almost 50% of these survivors will develop an endocrine disorder over their lifetime. The guideline provides recommendations on how to diagnose and manage certain endocrine and growth disorders commonly found in childhood cancer survivors.

Childhood cancer is relatively rare, and due to improvements in treatment and patient care, the current five-year survival rates exceed 80%. It's estimated that by 2020, there will be half a million childhood cancer survivors in the U.S. These survivors face a greater risk of developing serious medical complications, even decades after cancer treatment ends. Endocrine disorders are especially prevalent among this population, often as a result of their previous treatments, particularly exposure to radiation therapy.

“Childhood cancer survivors have a high risk of developing endocrine disorders,” says Charles A. Sklar, MD, of the Memorial Sloan Kettering Cancer Center in New York, N.Y. Sklar chaired the writing committee that developed the guideline. “Our new guideline addresses the growing risk of endocrine disorders among childhood cancer survivors and suggests best practices for managing pituitary and growth disorders commonly found in this population. The guideline stresses the importance of life-long screening of these survivors for earlier detection and optimal patient care.”

Recommendations from the guideline include long-term screening of childhood cancer survivors who underwent radiation therapy to the brain. This population should be

screened for growth disorders, pituitary hormone deficiencies, and early puberty. If a condition is diagnosed, in most instances, clinicians should treat these survivors with the same approaches as other patients who develop endocrine conditions.

Other members of the Endocrine Society writing committee that developed this guideline include: Zoltan Antal of the New York Presbyterian Hospital, Weill Cornell Medical College, and



the Memorial Sloan Kettering Cancer Center in New York, N.Y.; Wassim Chemaïtilly of St. Jude Children's Research Hospital in Memphis, Tenn.; Laurie E. Cohen of Boston Children's Hospital in Boston, Mass.; Cecilia Follin of Skane University Hospital in Lund, Sweden; Lillian R. Meacham of Emory University School of Medicine in Atlanta Ga.; and M. Hassad Murad of Mayo Clinic in Rochester, Minn.

The Clinical Practice Guideline was co-sponsored by the European Society of Endocrinology and the Pediatric Endocrine Society. The Pituitary Society endorsed the guideline.



## 2018 Clinical Endocrinology Update/Endocrine Board Review

**CEU/EBR East: Miami, Fla.  
Sept. 4 – 8, 2018**

**CEU West: Anaheim, Calif.,  
Oct. 18 – 21, 2018**

[www.endocrine.org/ebr/2018](http://www.endocrine.org/ebr/2018)

[www.endocrine.org/ceu/2018miami](http://www.endocrine.org/ceu/2018miami)

[www.endocrine.org/ceu/2018anaheim](http://www.endocrine.org/ceu/2018anaheim)

**Early Registration: Now – August 17, 2018**

*This year, endocrine clinicians from around the world will have a choice of which CEU they choose. CEU/EBR East will take place in Miami in September, while CEU West will land on the West Coast in October.*

Miami's Intercontinental Hotel will be the location for the joint meeting of the 2018 Clinical Endocrinology Update (CEU)/Endocrine Board Review (EBR) East from September 4 – 8, and the Hyatt Regency Orange County in Garden Grove, Calif., will be where CEU West takes place on October 18 – 21. Each year CEU brings together hundreds of endocrine clinicians for a unique learning experience and opportunities to network with expert faculty and colleagues. Attend the 70th CEU to receive the most trusted and clinically relevant information about recent advances in the field of endocrinology. The educational programming at CEU appeals to clinicians at all levels of practice, as well as fellows and other members of the clinical practice team.

Unlike other board preparation meetings, the Endocrine Society's EBR courses offer a comprehensive mock-exam format with case-based American Board of Internal Medicine-style questions forming the bulk of the presentations. Each section follows the ABIM blueprint for the board exam, covering the breadth and depth of the certification/recertification examination. Each case will be discussed in detail, with the correct and incorrect answer options reviewed. The mock exam appeals to endocrine fellows who have completed or are nearing completion of their fellowship and are preparing to take the board certification exam. Practicing endocrinologists may appreciate the EBR's comprehensive self-assessment of endocrinology either to prepare for recertification or to update their practice.

### 9th International Congress of the Growth Hormone Research and IGF Societies

**Seattle, Washington, September 14 – 17, 2018**

The International Congress of the Growth Hormone Research and IGF Societies will gather researchers and practitioners to provide an opportunity to learn from them and to share data. Initially organized by the GRS, the last several meetings have been jointly hosted by both the GH Research and IGF Societies.

<http://grs-igf2018.com>

### Principles of Critical Care Medicine for the Non-Intensive Care Specialist

**Boston, Massachusetts, September 26 – 28, 2018**

Keeping pace with the rapid changes in evidence-based critical care medicine is a challenge for specialty-trained intensivists; for non-intensivists, the challenge of staying up to date may be overwhelming. This CME course is intended to provide core clinical critical-care skills to healthcare providers who are not trained as intensivists, but whose clinical duties involve taking care of critically ill patients. The focus of this course will be to highlight recent important evidence-based advances in the practice of modern critical care medicine.

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

### Grit for Women in Medicine: Growth, Resilience, Inspiration, and Tenacity

**Truckee, California, September 26 – 29, 2018**

This course is designed to empower women and men in medicine with the skills and resources to remove barriers and bias of women in leadership positions, specifically in healthcare. Leaders in business and healthcare will present evidence-based strategies to promote professional development and enhance personal well-being. Nationally, there is a large number of female clinicians reporting burnout which has a potential effect on patient experience, compliance, and outcomes. This course will address the growing need for improved clinician wellness and development for a gender balanced leadership healthcare team.

<https://gimededucation.mayo.edu/>

### 88th Annual Meeting of the Thyroid Association

**Washington D.C., October 3 – 7, 2018**

This meeting is designed for the community of endocrinologists, basic scientists, internists, surgeons, nuclear medicine scientists, pathologists, trainees, nurses, physician assistants, advanced practice providers, and other health care professionals who wish to broaden and update their knowledge of the thyroid gland and its disorders. A customized educational track will be available to

trainees to enhance their meeting experience.

[www.thyroid.org/88th-annual-meeting-ata/](http://www.thyroid.org/88th-annual-meeting-ata/)

### Magee-Womens Research Summit

**Pittsburgh, Pennsylvania, October 8 – 10, 2018**

Magee-Womens Research Institute at the University of Pittsburgh announces the inaugural Magee-Womens Research Summit. This conference will serve as a premier forum for scientific exchange on topics related to early human development and women's health and wellness across the lifespan.

<https://mageesummit.org/>

### World Congress Insulin Resistance Diabetes and Cardiovascular Disease

**Los Angeles, California, November 29 – December 1, 2018**

Offering three days of CME, the World Congress Insulin Resistance Diabetes and Cardiovascular Disease is a state-of-the-art program featuring distinguished global experts presenting unique topics and lectures on the most innovative clinical research and basic science in cardiometabolic disorders. The Congress is a premier global meeting dedicated to diabetes, obesity, lipids, cardiovascular disease, and energy balance.

<http://www.wcir.org/>



## SPOTLIGHT



### **Obesity Week – The Obesity Society and American Society for Metabolic and Bariatric Surgery Joint Meeting**

**Nashville, Tennessee, October 11 – 15, 2018**

Obesity Week is the largest obesity-centric conference in the world with the broad, comprehensive bench-to-bedside and continuum of care content. This is an international event focused on the basic science, clinical application, surgical intervention, and prevention of obesity. By combining both American Society for Metabolic & Bariatric Surgery (ASMBS) and The Obesity Society (TOS) annual meetings, ObesityWeek brings together world-renowned experts in obesity to share innovation and breakthroughs around the globe. This year, the international conference will focus on the heart, the cardiac component of obesity.

This year's multi-track schedule offers a plethora of options for all attendees including pre-conference courses, hands-on skills labs, and an industry sponsored symposium. Interdisciplinary research, education sessions, and policy programming will focus on the latest breakthroughs in the science of obesity. Conference programming will cover the full interdisciplinary spectrum and features leading experts in their respective fields.

Attendees will have the opportunity to meet face-to-face with over 4,000 surgeons, researchers, physicians, and healthcare professionals from across the globe during the exhibit. Additional networking events offer further opportunities for attendees from all fields to collaborate with others who are part of other leading obesity organizations.

In addition, attendees will enjoy all Nashville, the City of Music, has to offer with a wide variety of dining options featuring Southern fare, endless entertainment in the home of country music, and countless attractions for all ages. Make plans to attend Obesity Week now at [www.obesityweek.com](http://www.obesityweek.com)

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

## INTERNATIONAL ITINERARY

### **Endocrine Society of Australia and The Society for Reproductive Biology Annual Meeting**

**Adelaide, Australia, August 19 – 22, 2018**

Featuring combined international Endocrine Societies, attendance is anticipated to exceed 700 delegates representing a variety of specialties including endocrinology, cell and molecular biology, reproductive biology, gynecology, pharmacology, and rheumatology. Key themes for the meeting include dynamic endocrine testing, transgender endocrinology, endocrine control of reproduction, neuroendocrinology, and a focus on women's health.

[www.esa-srb.org.au/](http://www.esa-srb.org.au/)

### **EndoBridge 2018**

**Antalya, Turkey, October 25 – 28, 2018**

Jointly organized by the Endocrine Society, European Society of Endocrinology, and the Society of Endocrinology and Metabolism of Turkey, EndoBridge will provide a comprehensive update in the field of endocrinology. Held on October 25–28, 2018, in Antalya, Turkey, this meeting is designed for the clinical endocrinologist. The official language of the meeting is English, but simultaneous translation will be available in Russian, Arabic, and Turkish.

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

### **International Conference on Diabetes & Metabolism**

**Dubai, UAE, October 15 – 17, 2018**

This international conference highlights recent advancements related to diabetes and cholesterol metabolism. The scientific sessions emphasize diabetes mellitus, diabetes complications, endocrinology, obesity, metabolic syndrome, epidemiology of diabetes, cholesterol metabolism, lipid metabolism, cardiovascular diseases, hypercholesterolemia, and recent advances in treatments and therapies.

[www.metabolicdiseases.conferenceseries.com/](http://www.metabolicdiseases.conferenceseries.com/)

### **18th International Congress of Endocrinology and 53rd SEMDSA Congress**

**Cape Town, South Africa, December 1 – 4, 2018**

The Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) is hosting ICE 2018 with the 53rd annual SEMDSA Congress. The Program Organizing Committee is currently putting together a stimulating program including cutting-edge academic endocrinology for basic scientists and clinicians.

[www.ice2018.org](http://www.ice2018.org)



# *Endocrine and Growth Survivors of Childhood Cancer*

R CARE



Recommendations on how to diagnose and manage  
growth disorders commonly found in

This guideline emphasizes key differences in the testing  
and treatment of these disorders that are specific to the  
childhood cancer survivor such as:

- Diagnosis and treatment of growth hormone deficiency
- Treatment of adrenocorticotrophic hormone deficiency

It also emphasizes the importance of life-long screening for  
early detection and better care of these patients.

AT  
CPG

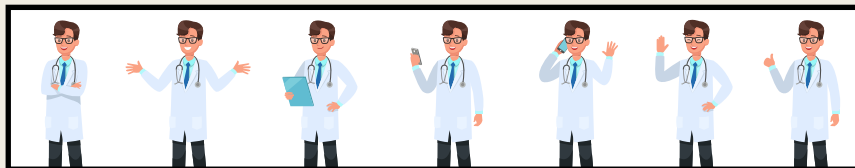
ENDOCRINE  
SOCIETY 

“

“Knowledge is power for patients and enables them to take care of themselves appropriately. Physicians should also go over the plan of care, what’s next, and the necessary surveillance with the patient (and caregiver/family as appropriate) and allow them to ask questions. **Patience is really important at this time, in my opinion.**”

— STACY LLOYD, a Von Hippel-Lindau patient discussing how other VHL patients should empower themselves and take control of their treatment in “Heir on the Side of Caution” on page 28.

7,120



The number of senior doctors that will be required by UK’s National Health Service hospitals by 2030 to cope with a predicted 47% rise in demand, according to an analysis by the Royal College of Physicians. — SOURCE: THE TELEGRAPH.

## FROM THE CENTURY OF ENDOCRINOLOGY TIMELINE

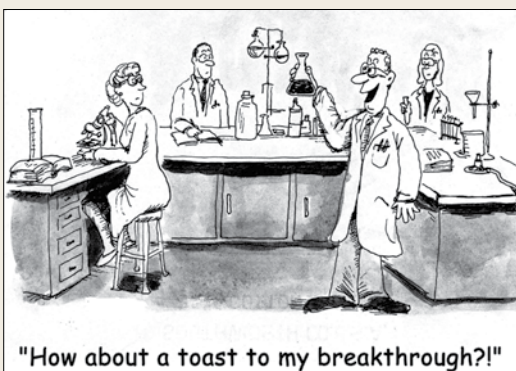
1992



## Polychlorinated Biphenyls Shown to Affect Cognitive Function in Children

Polychlorinated biphenyls (PCBs) were used in a variety of materials through the 1970s before they were banned. However, low levels of contamination in fish and wildlife continued to serve as sources of human exposure.

Jacobson et. al., linked PCB exposure to impairment in cognitive functioning and showed that impairments were predominantly due to developmental, intrauterine exposure, rather than postnatal effects. **For more about the Century of Endocrinology, go to: [www.endocrine.org/timeline](http://www.endocrine.org/timeline).**



## BY THE NUMBERS



15%

The percentage of calories that need to be cut for two years in order to slow the metabolic process that leads to aging and protect against age-related diseases. — SOURCE: CELL METABOLISM

68.5%

Amount of the adult population in the U.S. that suffer from obesity or being overweight.

— SOURCE: ENDOCRINE REVIEWS

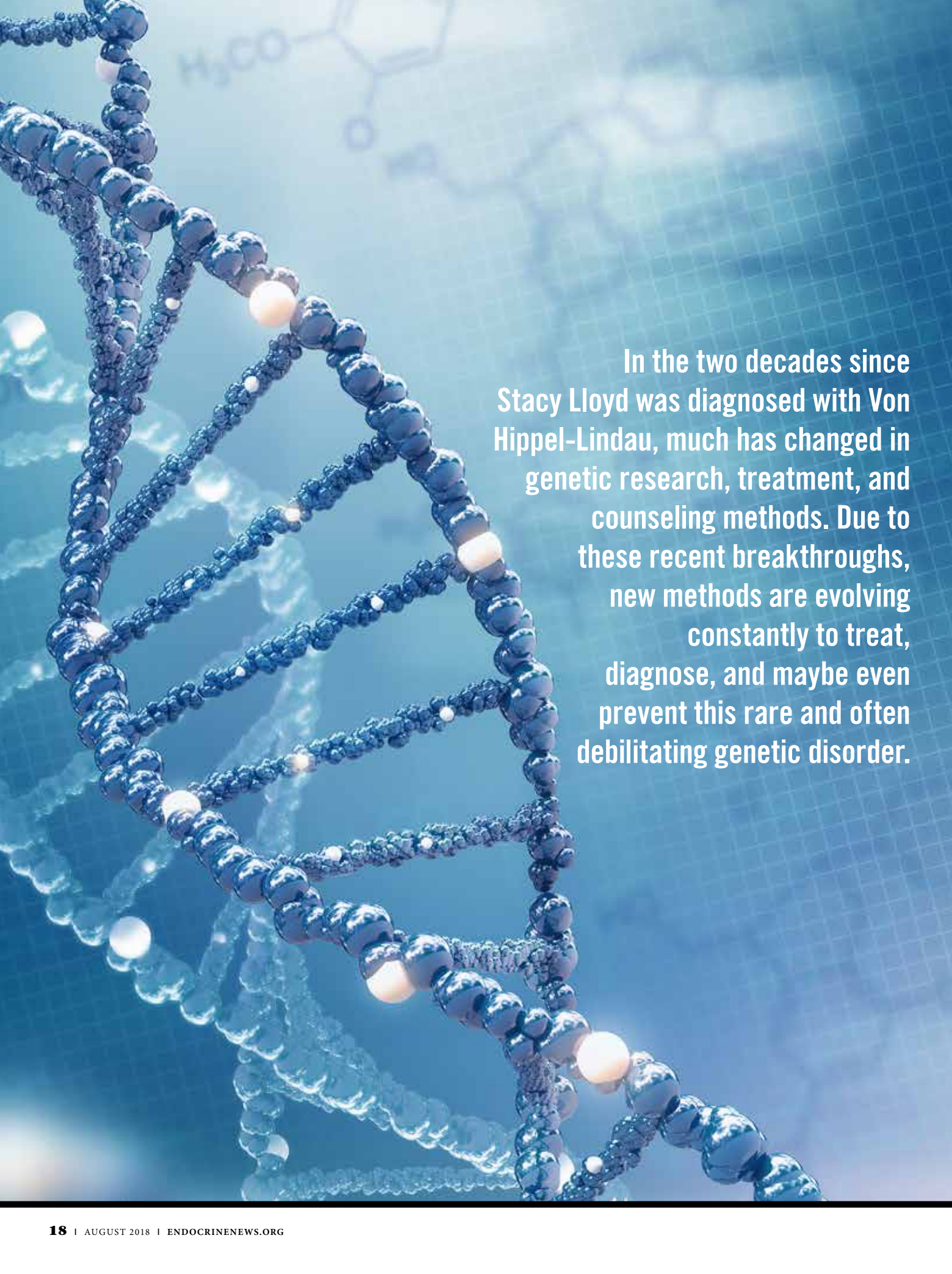


\$327 BILLION

Amount spent treating diabetes in 2017, making it the most expensive chronic disease in the U.S.

— SOURCE: ADA





In the two decades since Stacy Lloyd was diagnosed with Von Hippel-Lindau, much has changed in genetic research, treatment, and counseling methods. Due to these recent breakthroughs, new methods are evolving constantly to treat, diagnose, and maybe even prevent this rare and often debilitating genetic disorder.



## Patient Perspectives

Stacy Lloyd first told her lifelong struggle with Von Hippel-Lindau at **ENDO 2018** in Chicago as part of a Meet the Patient series. She shared the stage with Peter Kopp, MD, from Northwestern University, and together they detailed how Lloyd has been instrumental in managing her own care. Both Kopp and Lloyd were a part of **ENDO 2018** in order to get the story of this rare disease to a wider audience of endocrine professionals, who could easily spend an entire career without ever seeing a patient with Von Hippel-Lindau.

# *Heir on the Side of Caution:* **HOW A VON HIPPEL-LINDAU PATIENT IS MANAGING HER HEALTH**

BY DEREK BAGLEY

---

**T**he morning of June 28, 1996, Stacy Lloyd — 10 years old at the time — was at home and started to feel light-headed and dizzy before she collapsed and had a seizure. She was life-flighted to Children's Hospital of Pittsburgh with a blood pressure of 240/120, and the emergency room physicians didn't know what was wrong with her. They thought she hit her head when she fell.

It wasn't until Lloyd's grandfather spoke up that they knew: He told the doctors that Lloyd's aunt had a tumor removed from her adrenal gland at age 16. "It was like a lightbulb moment in the room," Lloyd says.

Lloyd was diagnosed with a pheochromocytoma and spent the next month at the hospital being stabilized, followed by a 12-hour surgery to remove the pheochromocytoma from her right adrenal gland and a paraganglioma between her aorta and vena cava. Lloyd had

**“ For those already diagnosed, I feel it’s very important to review results in-person (or at the very least over the phone). I’ve had a letter sent to me with imaging results prior to any conversation with the physician. It was scary to read and I wasn’t sure what everything meant, which can lead to anxiety and fear.”**

— STACY LLOYD, PATIENT WITH VON HIPPEL-LINDAU



another surgery three years later after another tumor was spotted on a routine ultrasound, and her physicians diagnosed her with metastases to the bone. “We were quickly referred to the National Institutes of Health,” she says, “where I would officially be diagnosed with Von Hippel-Lindau (VHL) [a rare genetic disease that causes tumors to grow in up to ten different areas of the body]. Since then, I continue to be followed regularly and have annual imaging and lab tests. I have been fortunate to have remained fairly stable over the last 20 years, but continue to monitor the metastatic pheochromocytoma in the bone and watch for new tumors.”

Lloyd now lives in Chicago, and as an adult she has had to take responsibility for and make decisions about her health on her own – like deciding where to seek follow-up and treatment. She is active in the VHL Alliance, a non-profit dedicated to education, awareness, and research for VHL. The Alliance has a list of designated clinical care centers, which pointed her to Northwestern Medicine in 2011. It’s there she started under the care of Peter Kopp, MD, a professor of medicine

in the Division of Endocrinology, Metabolism, and Molecular Medicine at Northwestern, who has a particular interest in genetic endocrinopathies.

Genetics, and how they apply to endocrine disorders, is a rapidly developing field, but it's an area that has fundamentally changed in the last 20 years because physicians and researchers have been able to identify the majority of the genes underlying these inherited disorders. This is good news, but the fact that gene mutations and carriers can be identified opens up a slew of other questions and potential concerns for the involved patients and their doctors.

## Examining the Phenotype's Pedigree

It took three years from the time of Lloyd's first pheochromocytoma diagnosis to her diagnosis of VHL through genetic testing. The average time between the onset of symptoms and formal diagnosis is nine years. "That means we still have some work to do in raising awareness and education around symptoms for both patients and physicians," she says.

The problem is that VHL is such a rare disease that many physicians may not ever see a case. VHL is also a disease that has a huge spectrum of phenotypic manifestations, ranging from very mild to very problematic, according to Kopp. "In Stacy's particular case, she has this unusual finding of widely metastatic pheochromocytoma, which is an endocrine tumor, at a very young age," he says.

Kopp stresses the importance of describing the phenotype in any of these inherited conditions as accurately as possible as the first step to get to a definitive diagnosis. For example, pheochromocytomas can be part of several familial syndromes caused by mutations in distinct genes, or there are various genetic forms of diabetes mellitus. Describing the phenotype accurately requires looking at the pedigree, i.e., the family tree as a whole. "Importantly, for many disorders, mutational analysis can facilitate a definitive diagnosis," Kopp says. Of course, a definitive diagnosis is just the first step. Once a patient tests positive for a genetic endocrinopathy, or any inherited disease, there are many other potential implications.

## Genetic Counseling

Lloyd says that a significant percentage of living relatives on her mother's side also tested positive for VHL. Her grandfather passed away in 1996 – the same year as her first surgery to remove the two tumors – from his second heart attack. "We know he carried the gene as my grandmother tested negative," she says. "He likely had a pheochromocytoma (based on what we now know to be common systems) when he passed. I think my grandmother deals with some guilt, and it's just hard for her to watch her children and grandchildren have to deal with something so awful and unpredictable and to be powerless to change or fix it."

# LIFELONG ADVOCACY

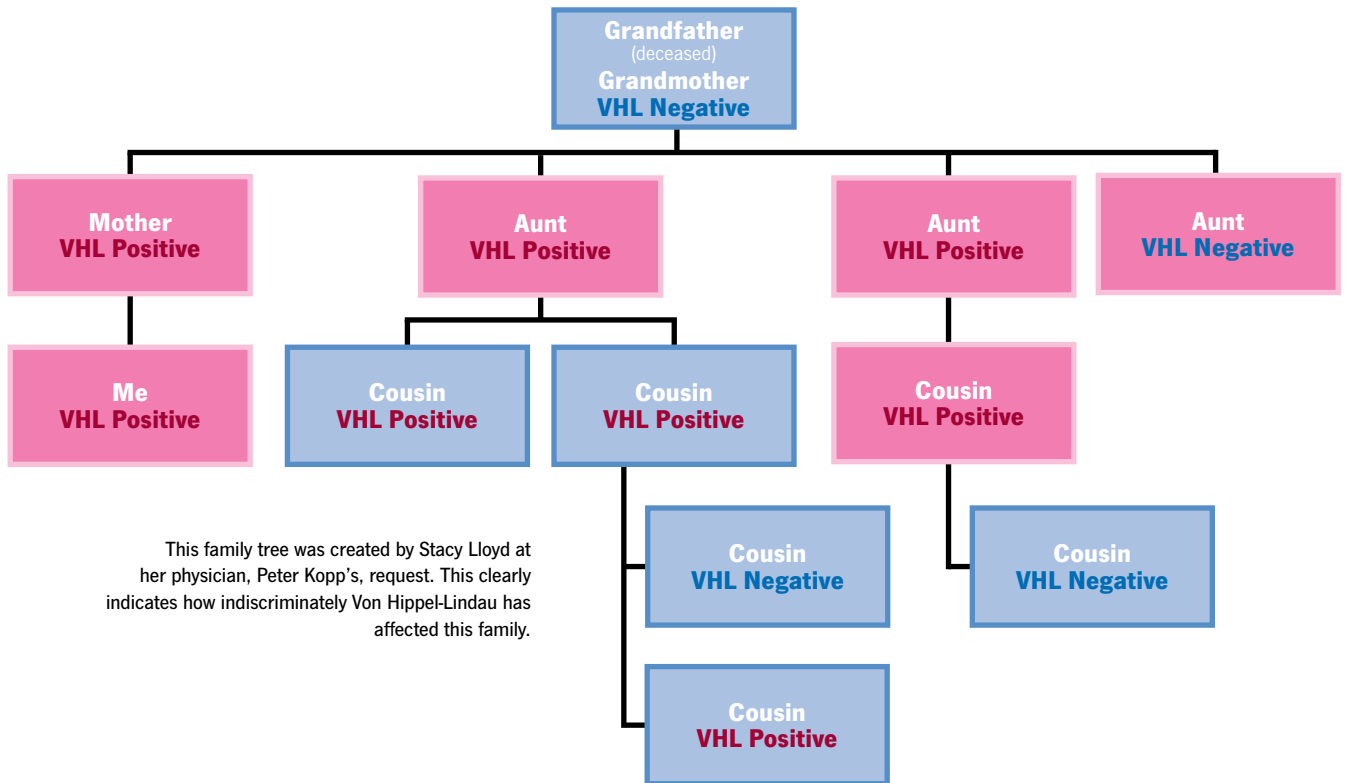
As part of  
Stacy Lloyd's ongoing  
mission to raise awareness  
for Von-Hippel Lindau  
and motivate other  
patients to be the  
best advocates they can  
for their own health,  
she maintains a blog  
about her experiences and  
recently joined the board  
of directors for  
the VHL Alliance,  
a non-profit dedicated  
to improving the quality  
of life for VHL patients  
and their families.



Read Lloyd's blog here: <https://www.passionatepatient.com/>



And visit the VHL Alliance here:  
<https://www.vhl.org/>



These feelings of guilt among family members are not uncommon in these settings, even among family members who test negative for a disease for which their siblings tested positive. “I think they feel it is unfair that their sibling suffers,” Kopp says. “They may not be unhappy that they don’t have to suffer, but they have this feeling that it’s unfair that their sibling or another family member has to suffer.”

A snapshot of Stacy Lloyd (seated, front left) with her relatives at a family gathering. This picture features seven of eight family members with VHL; the eighth had yet to be born, according to Lloyd.

Lloyd says her mother deals with guilt too. Lloyd’s mother also tested positive for VHL and has had a pheochromocytoma removed, but she did not know she had VHL when she was expecting her daughter. “I think it’s just been hard for her to watch me go through so much, especially at a young age,” Lloyd says. “And





she just wishes she could take it all away or switch places with me. I think that's natural for any parent with a child facing any health-related issue."

The diagnosis of an inherited disorder often requires involving the whole family, but so does addressing disease-related feelings, and keeping up on treatments once the diagnosis is made. It can be complicated to deliver a diagnosis of a disease like VHL to patients and their family. Kopp says it should be done with empathy and a thorough explanation of the condition, treatments, implications, and prognosis, but clinicians often lack the time for a thorough discussion. "This is a situation where genetic counselors can be very helpful because they have a good understanding of the phenotype, the mode of inheritance, genetic testing, and the implications of being a carrier. They can often commit the necessary time to cover all aspects, and sometimes are better communicators than physicians who are not specialized in this area," he says.

## A Family Mission

But getting the family together isn't always easy. Kopp says there can be two extremes. One extreme is the family who gets very interested and involved and united, attending clinical visits and educational events together and rallying each other to keep up with their screenings. "It becomes a family mission, if you will," he says.

The other extreme is a family in total denial. "They know that they have a genetic disorder running in their family, and that certain individuals are at

**“ From the other side you could argue, we are making a selection and we are, if you will, breeding the human species to eliminate certain genes. Whether this is acceptable, is a challenging ethical question. Where are the limits? Who defines them?”**

— PETER KOPP, MD, PROFESSOR OF MEDICINE, DIVISION OF ENDOCRINOLOGY, METABOLISM, AND MOLECULAR MEDICINE, NORTHWESTERN UNIVERSITY, CHICAGO



## AT A GLANCE

- ▶ Inherited endocrinopathies, like all genetic conditions, can mean a lifetime of follow-up and family counseling.
- ▶ Genetics, and how they apply to endocrine disorders, has fundamentally changed over the past two decades, allowing physicians and researchers to identify most, if not all, gene mutations.
- ▶ Challenges remain when it comes to treating these patients, from uninterested families to a fragmented healthcare system to physicians who lack training in rare genetic endocrinopathies.



risk, and they simply don't want to address the issue and they walk away and get lost to follow-up," Kopp says.

And this isn't even including potential family members. Lloyd says that her generation is largely more equipped than previous generations with specific knowledge of VHL, its manifestations, and the odds of passing it on, which means they more often will know whether they have VHL before marriage, and that can be a difficult conversation to have with a potential partner. VHL patients never know what to expect – when tumors might appear, when they'll need surgery. And there's a 50% chance they will pass VHL to their offspring.

"So, what do you tell them?" Lloyd says. "At what point in a relationship do you have that conversation? When do you discuss children and the potential to pass it on if having kids is something you want? These are all very personal decisions that each individual patient has to make, but it's certainly not an easy conversation to have. And you have to be prepared for that person to potentially walk away, too."

## Gene Editing

And now that genetic testing is more available, and patients know the risks of passing their conditions on to their children, some ask about the possibility of gene editing. Kopp says genetic editing is in very early stages, and it has been done successfully in only a few instances. However, there is the possibility of pre-implantation testing. "You have an embryo, you test whether the embryo has the mutation or not, and you only take the embryo that doesn't have the mutation," he says. "This can permit a patient to make a selection. And while this is very acceptable for some, it will be unacceptable for others due to ethical concerns."



Indeed, these are very difficult questions, which are influenced by ethical considerations, religious beliefs, and even political views. Kopp says it's important to not view these questions in black and white, but rather to consider that there are a lot of "grays." "I think it certainly will become possible to do gene editing for some of these disorders," he says. "And I think on a positive side note it can alleviate a lot of suffering. It can reduce the frequency of negative genes in certain populations."

"From the other side you could argue, we are making a selection," Kopp continues, "and we are, if you will, breeding the human species to eliminate certain genes. Whether this is acceptable is a challenging ethical question. Where are the limits? Who defines them?" The examples of eugenics also illustrate that such approaches could potentially be abused.

## A Fragmented Healthcare System

Lloyd says she is fortunate to have a supportive family and friends and knowledgeable physicians whom she trusts. She also works in the healthcare industry, which she says has given her access to the best care and the tools to navigate the health system as a patient. But she still sees barriers to quality care for VHL patients, even among her own family members – cost of care, what insurance will cover or whether they will cover VHL care at all, or access to care depending on location. "Those living in rural areas often don't have access to physicians that are knowledgeable about the disease

close to home, so they may not be followed regularly or have to travel far distances to be seen,” she says.

What’s worse, the U.S. healthcare system remains very fragmented, making it difficult to share medical records and coordinate care. “For patients that require care across multiple specialties — like VHL patients — navigating the system and coordinating their care can be extremely frustrating, time-consuming, and stressful,” Lloyd says.

Delivering a diagnosis of VHL, or other genetic diseases, can also be daunting. Some physicians who aren’t trained in this specialty or don’t have access to the patient’s record may deliver the diagnosis and subsequent information poorly. Lloyd was initially told she would never be able to drive or

telling patients what VHL is, all the ways it may manifest, and inform the patient about the different options related to treatment (i.e., surgery, clinical trials, etc.). “Knowledge is power for patients and enables them to take care of themselves appropriately,” she says. “Physicians should also go over the plan of care, what’s next, and the necessary surveillance with the patient (and caregiver/family as appropriate) and allow them to ask questions. Patience is really important at this time, in my opinion.

“For those already diagnosed, I feel it’s very important to review results in-person (or at the very least over the phone). I’ve had a letter sent to me with imaging results prior to any conversation with the physician. It was scary to read and I wasn’t sure what everything meant, which can lead to anxiety and fear.”

“This ‘advice’ might sound silly or ridiculous because this should be the norm in healthcare,” Lloyd says, “but in a time where we are seeing many healthcare organizations looking to cut costs and physicians having to see more and more patients with fewer resources, patient-physician interactions can suffer.”

The physicians involved in the diagnosis, surveillance, and therapy of patients with rare inherited disorders do need appropriate training and expertise, which are not always part of traditional training. Consultation with an expert in the field, a medical geneticist, or a genetic counselor is often indicated. “This can be helpful for diagnostic purposes, the identification of management issues, the determination of genetic risk in relatives and offspring, as well as for appropriate psychological support,” Kopp says. <sup>(1)</sup>

walk at prom. But, she points out this was 20 years ago, and there have been many developments in subsequent decades. Her personal awareness, education, knowledge of surveillance guidelines, and resources have greatly expanded.

Based on her own experiences, Lloyd’s advice is: At the time of diagnosis, healthcare providers should be direct in





A blue-tinted profile of a human head facing left. Inside the head, the brain is depicted with glowing blue lines representing neural pathways. A specific area in the center, representing the pituitary gland, is highlighted in a bright red color. The overall image has a medical and scientific feel.

# AFTER SHOCKS:

A French study published in the *Journal of the Endocrine Society* reveals myriad complications that many acromegaly patients face after they've been successfully treated. Lead researcher Frederic Castinetti, MD, PhD, discusses his research and why follow-up may still be required once a patient is "cured."

BY DEREK BAGLEY





# Complications AFTER Acromegaly

**L**ast December, a paper appeared in the *Journal of the Endocrine Society* (JES) that shined a light on problems that patients with acromegaly might face – even after their acromegaly was successfully treated by surgery and/or medication.

A team led by Frederic Castinetti, MD, PhD, of the French Reference Center for Rare Pituitary Diseases HYPO (Aix-Marseille University and La Conception Hospital, Marseille, France), examined data from 130 patients whose acromegaly had been controlled and even cured, looking to find just how many of these patients might still suffer from major metabolic comorbidities like diabetes and hypertension.

Acromegaly is rare, affecting an estimated three or four million people a year. And it's slow-moving; the time it takes to accurately diagnose acromegaly is five to 10 years, which provides ample time for any number of comorbidities to arise. "As a rule," Castinetti and his team write, "[comorbidities] are already present at the time acromegaly is diagnosed."

Castinetti and his team found that a significant proportion of their study participants had lingering comorbidities even after their acromegaly had been controlled – 27% for altered glucose tolerance or diabetes, 39% for hypertension, 34.3% for hypercholesterolemia, and 13.3% for hypertriglyceridemia.

Castinetti and his team wrote in the JES paper that these results were expected, but these numbers may come as a surprise to other physicians and researchers. *Endocrine News* caught up with Castinetti to talk about this study and what it means for those treating this complicated disease.

**ENDOCRINE NEWS:** First off, tell me about the origins/impetus of this study.

**FREDERIC CASTINETTI:** For many years, the main focus in terms of management of acromegaly (or any other secreting pituitary tumors, such as in Cushing's disease), has been the control of hypersecretion. This is why the majority of the studies focused on surgery and antisecretory drugs. Some studies focused on the comorbidities of acromegaly and showed that growth hormone (GH) hypersecretion led to comorbidities such as diabetes and hypertension.

In a French multicentric study, we had shown\* that about a fourth of patients with acromegaly were lost to follow-up. The majority of the patients lost to follow-up are the ones who are in remission, and we just thought it would be interesting to check whether, despite remission of acromegaly, these patients still needed to be followed for their comorbidities. In other words, would these comorbidities persist even in patients cured for a relatively prolonged period? This was a way for us to emphasize the need that these patients be followed for a long-term period (even if they were cured).

**EN:** I found this part at the beginning interesting: "The overall diagnosis delay is usually [five] to 10 years, which allows for

\*Further reading: "Patients lost to follow-up in acromegaly: results of the study," by Delemer B., Chanson P., Foubert L., Borson-Chazot F., Chabre O., Tabarin A., Weryha G., Cortet-Rudelli C., Raingeard I., Reznik Y., Reines C., Bisot-Locard S., Castinetti F.; *Eur J Endocrinol.* 2014 Apr 19;170(5):791-7



Castinetti and team, from left to right: M. Sahnoun, MD, protocols supervisor; H. Buhagiar, hospital stay coordinator; I. Pellegrini, psychologist; Prof. T. Brue, endocrinologist and head of the department; Castinetti; C. Rochette, MD, endocrinologist and assistant; I. Morange, MD, endocrinologist; F. Albarel, MD, endocrinologist, in charge of the Reference Center for Rare Pituitary Diseases. Not pictured: T. Cuny, MD, endocrinologist; M. Vermalle, MD, endocrinologist; M. Foglietta, hospital stay coordinator.

the installation of a number of comorbidities. As a rule, these are already present at the time acromegaly is diagnosed.” Can you tell me a little more about that?

**FC:** Physicians are not very good at early diagnosis of acromegaly. During all this period of latency (and undiagnosed acromegaly), GH excess has the time to lead to comorbidities, and it is likely that the longer the delay to

diagnosis, the higher the risk of persistent comorbidities after acromegaly remission/cure.

**EN:** You write that there is still a debate on the persistence of comorbidities after control of hypersecretion. Can you give me the broad strokes of this debate?

**FC:** What we wanted to say was that some teams still did

“ The majority of the patients lost to follow-up are the ones who are in remission, and we just thought it would be interesting to check whether, despite remission of acromegaly, these patients still needed to be followed for their comorbidities.”

— FREDERIC CASTINETTI, MD, PHD, OF THE FRENCH REFERENCE CENTER FOR RARE PITUITARY DISEASES HYPO, AIX-MARSEILLE UNIVERSITY AND LA CONCEPTION HOSPITAL, MARSEILLE, FRANCE

**“We wanted to warn physicians of the need of persistent follow-up of such patients with acromegaly: Once your job is done and the secretion is controlled, never forget that the comorbidities can still be there.”**

— FREDERIC CASTINETTI, MD, PHD, OF THE FRENCH REFERENCE CENTER FOR RARE PITUITARY DISEASES HYPO, AIX-MARSEILLE UNIVERSITY AND LA CONCEPTION HOSPITAL, MARSEILLE, FRANCE



Frederic Castinetti, MD, PhD

not take precisely into account the risk of persistent comorbidities after the cure/remission of acromegaly. But I guess now we cannot say that there is still a debate. Of note, there has been a recent paper by Moises Mercado's team, published in [*The Journal of Clinical Endocrinology & Metabolism*], that showed roughly the same results we showed (i.e., persistence of

diabetes and hypertension in patients with acromegaly cured or in remission).

**EN:** It's interesting that the rate of diabetes is actually higher in controlled or cured patients than in the general population.

**FC:** We could say that a body that has been exposed to an excess of GH secretion keeps a kind of memory of these negative effects. Altered glucose metabolism due to GH hypersecretion could thus persist despite normal GH levels, possibly because the organism is not anymore able to correctly adapt its blood glucose.

**EN:** You write about the discrepancies in findings and say that “probably suggests that other modifying factors modulate the overall risk of diabetes in patients with acromegaly.” Can you speak a little more to that?

**FC:** The thing is that diabetes is not only linked to GH hypersecretion. We did not have the data about familial cases of diabetes. And we know that in this population, the familial history of diabetes increased the risk of diabetes independently of the GH status.

**EN:** You write that your group only focused on controlled patients. What was the reasoning behind that?

**FC:** It is very easy to understand that patients with persistent GH hypersecretion have an increased risk of diabetes. But it is less obvious in patients with no persistent GH hypersecretion. We wanted to warn physicians of the need of persistent follow-up of such patients with acromegaly: Once your job is done and the secretion is controlled, never forget that the comorbidities can still be there.

**EN:** Why do you think this kind of follow-up hasn't been evaluated in international guidelines?

**FC:** As previously mentioned, this issue is now becoming more and more recognized. It is likely that the future guidelines will take into account these points and the follow-up of patients after the cure/remission.

**EN:** This part struck me as well: “This is a highly relevant issue, as about a fourth of the patients have been found to be lost to follow-up after control of hypersecretion.”

**FC:** In our previous study (ACROSPECT Study), we showed that about a fourth of patients were lost to follow-up. The reason is obvious: when, as a patient, you understand that your disease (acromegaly) is cured, you think you do not need any follow-up.

**EN:** What would you want Endocrine Society members and others who might read this article to take away from your findings?

**FC:** Keep an eye on your patients with acromegaly, even if they are cured or are in remission. Persistent comorbidities are not infrequent and observed in roughly 25% of cases even when GH secretion is normal. **EN**

# Hypoparathyroidism: **TREATMENT FOR AN ORPHAN DISEASE**



Due to its rarity, hypoparathyroidism was the last endocrine disorder to have a replacement hormone. New studies reveal positive results for the safety and efficacy of a promising new treatment.

**BY ERIC SEABORG**





**H**ypoparathyroidism was the last endocrine disorder to have a replacement hormone available for treatment. Just three years ago, the U.S. Food and Drug Administration approved recombinant human parathyroid hormone (1-84) — or rhPTH (1-84) — under the trade name Natpara. The European Union followed suit in 2017, where the drug is called Natpar.

Those approvals were based on relatively short-term clinical trials, but more treatment information has accumulated in the years that the drug has been on the market. Longer-term studies now show that the benefits of rhPTH (1-84) continue over the long-term without the development of additional side effects, according to Dolores M. Shoback, MD, of the University of California, San Francisco, who was lead author of a five-year efficacy and safety study released as an abstract at **ENDO 2018**.

Although the new findings are heartening, standard treatment for hypoparathyroidism continues to be oral calcium and activated vitamin D analogs — with rhPTH (1-84) indicated only when this management falls short — primarily due to the new drug's high expense and the need for daily injections, Shoback says.

## An Orphan Disease

The slow development of newer treatments is likely due to hypoparathyroidism's status as an orphan disease, with a U.S. prevalence estimated at 60,000 to 115,000 cases. About 75%



of these cases are a result of thyroid or other anterior neck surgery, according to a management guideline published in *The Journal of Clinical Endocrinology & Metabolism* in 2016.

“Although the conventional use of calcium and active vitamin D can control patients with hypoparathyroidism, they often require very high doses that raise concerns for unwanted complications of hypercalcemia, renal stones, renal calcinosis, impaired renal function, and ectopic calcifications,” the guideline notes. “Theoretically, PTH (1-84) is more attractive as a replacement hormone because the full-length peptide is exactly what is missing in this disease.”

“RhPTH (1-84) usually results in a 50% reduction in the calcium that people have to take and a similar reduction in activated vitamin D analog,” Shoback says. “When rhPTH (1-84) was approved, we had just short-term studies, maybe two or three years of data. Now we have five years of data in an open label study, done by clinical investigators with standard measurements taken at each point in time. The results

presented at [ENDO 2018] showed that the serum calcium values were maintained in the target range over time and the urinary calcium values — which tend to be too high in these patients — tended to come down over the course of the study. So that’s a distinct advantage of this medication over therapy with the usual calcium and activated vitamin D analog.”

## The RACE Trial

The results came from 49 patients enrolled at 12 centers around the U.S. and are part of the ongoing, open-label study of the safety, tolerability, and efficacy of rhPTH(1-84) known as the RACE trial (ClinicalTrials.gov identifier: NCT01297309). The abstract noted: “Oral calcium and calcitriol doses were reduced by 53.4% and 75.7%, respectively, while albumin-adjusted serum calcium levels were maintained within the target range.”

“In terms of safety, which was the primary focus of the study, the RACE data basically showed that the side effects were

“ In terms of safety, which was the primary focus of the study, the RACE data basically showed that the side effects were comparable in frequency to what was seen in the initial placebo-controlled trials. No new side effects emerged. The kind of side effects that people saw over time really related mainly to low blood calcium, which is a typical side effect of this disease.” ”

— DOLORES M. SHOBACK, MD, PROFESSOR OF MEDICINE; DIRECTOR, UCSF TRAINING PROGRAM IN DIABETES, ENDOCRINOLOGY AND METABOLISM, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

comparable in frequency to what was seen in the initial placebo-controlled trials. No new side effects emerged,” Shoback says. “The kind of side effects that people saw over time really related mainly to low blood calcium, which is a typical side effect of this disease.”

Such long-term results are important to have for a medication that patients will need to take for many years, perhaps the rest of their lives, Shoback says.

“In terms of efficacy, the study showed that serum calcium was maintained at the same level as in the initial six-month, placebo-controlled part of the trial. Patients remained able to keep taking a reduced amount of calcium and activated vitamin D supplements during those five years,” Shoback says.

## Renal and Quality of Life Studies

Hypoparathyroidism is associated with an increased incidence of renal complications, so a separate study released as an abstract at **ENDO 2018** compared estimated glomerular filtration rates (eGFR) over a three-year period between patients treated with rhPTH (1-84) and a historical control cohort identified from the MedMining database using similar enrollment criteria to the RACE study. The study included 119 patients, 43 treated with rhPTH (1-84) and 76 historical control patients not treated with the drug. The historical cohort of patients not treated with rhPTH (1-84) showed a greater decline in mean eGFR compared with patients treated with the replacement hormone.



## AT A GLANCE

- ▶ Hypoparathyroidism is very rare, which is probably the reason it was the last endocrine disorder to have a replacement hormone available.
- ▶ When standard treatment of oral calcium and vitamin D fails to provide adequate management, recombinant human PTH (1-84) has been shown to reduce the need for these supplements while maintaining serum calcium levels in the target range.
- ▶ New studies show that the benefits of rhPTH (1-84) continue over the long term with no increase in side effects.





“ We now have five years of data that say that urinary calcium levels come down steadily, and kidney function remains stable. I think that is helpful in convincing a patient to take this kind of a medication and for the insurance companies to consider helping to support that.”

— DOLORES M. SHOBACK, MD, PROFESSOR OF MEDICINE; DIRECTOR, UCSF TRAINING PROGRAM IN DIABETES, ENDOCRINOLOGY AND METABOLISM, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

The three abstracts presented at **ENDO 2018** on rhPTH (1-84) can be viewed online:

- ▶ “Five-Year Efficacy and Safety of Recombinant Human Parathyroid Hormone 1-84 (rhPTH[1-84]) for the Treatment of Adults with Chronic Hypoparathyroidism: Analysis from the Open-Label Race Study”  
<http://www.abstractsonline.com/pp8/#!/4482/presentation/7268>
- ▶ “Comparison of 3-Year Estimated Glomerular Filtration Rates Between Recombinant Human Parathyroid Hormone (1-84) (rhPTH[1-84])-Treated Patients With Chronic Hypoparathyroidism and a Historical Control Cohort”  
<http://www.abstractsonline.com/pp8/#!/4482/presentation/7293>
- ▶ “Symptom Burden and HRQoL Reported Among Patients With Chronic Hypoparathyroidism: Impact of Treatment With rhPTH (1-84) and With Standard Therapy”  
<http://www.abstractsonline.com/pp8/#!/4482/presentation/7291>

Hypoparathyroidism is also associated with symptoms that diminish a patient's health-related quality of life. A third abstract reported on a web-based survey that compared 90 adult patients currently treated with rhPTH (1-84) and 47 adults on standard treatment. Patients on rhPTH (1-84) reported an average of 9.1 symptoms compared with 20.2 symptoms for patients on standard therapy over a recall period of 12 months. More patients on standard therapy than rhPTH (1-84) patients reported significant disease-associated interference with their lives (49% to 27%) and impact on work responsibilities (31% to 15%). The study did not control for baseline characteristic differences among patients that could affect the treatment outcomes between the cohorts and depended on patient recall.

All three studies were funded by Shire plc, the manufacturer of rhPTH (1-84).

## Treatment Decisions

The guideline suggests that greater use of rhPTH (1-84) may be warranted: “The decision to recommend rhPTH (1-84) depends, in part, on the extent to which the physician and the patient feel that good control is achieved by conventional therapy. In our view, the definition of good control goes beyond the mere maintenance of a serum calcium concentration within normal limits and the avoidance of symptomatic hypocalcemia. Subjects who require very large amounts of calcium and active vitamin D to maintain their serum calcium and to avoid hypocalcemia are at risk for serious long-term complications of such therapy.”

But the cost of the drug remains a stumbling block. “We now have five years of data that say that urinary calcium levels come down steadily and kidney function remains stable. I think that is helpful in convincing a patient to take this kind of a medication and for the insurance companies to consider helping to support that,” Shoback says. <sup>EN</sup>

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT VIRGINIA TWEEN CLAIRE ENGLER AND HER DO-IT-YOURSELF CGM IN THE JULY ISSUE.





**ENDO**2019

# SAVE THE DATE

**MARCH 23–26, 2019** **NEW ORLEANS, LA**  
ERNEST N. MORIAL CONVENTION CENTER

## KEY DATES

**ABSTRACT SUBMISSION OPENS: SEPTEMBER 5, 2018**

**EARLY REGISTRATION OPENS: OCTOBER 25, 2018**

[ENDOCRINE.ORG/ENDO](http://ENDOCRINE.ORG/ENDO)

© 2018 ENDOCRINE SOCIETY

ENDOCRINE  
SOCIETY 



# *Getting the ACT Together:*

The International Pediatric  
Adrenocortical Tumor Registry is a  
database for young patients afflicted with  
these rare tumors. The result has  
created more personalized and targeted  
care and has benefitted the patients'  
families and physicians.





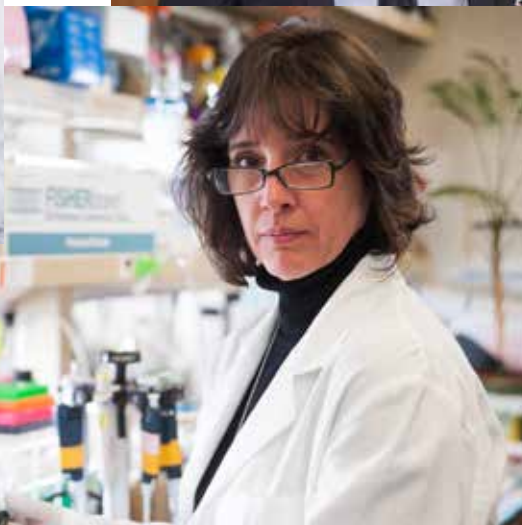
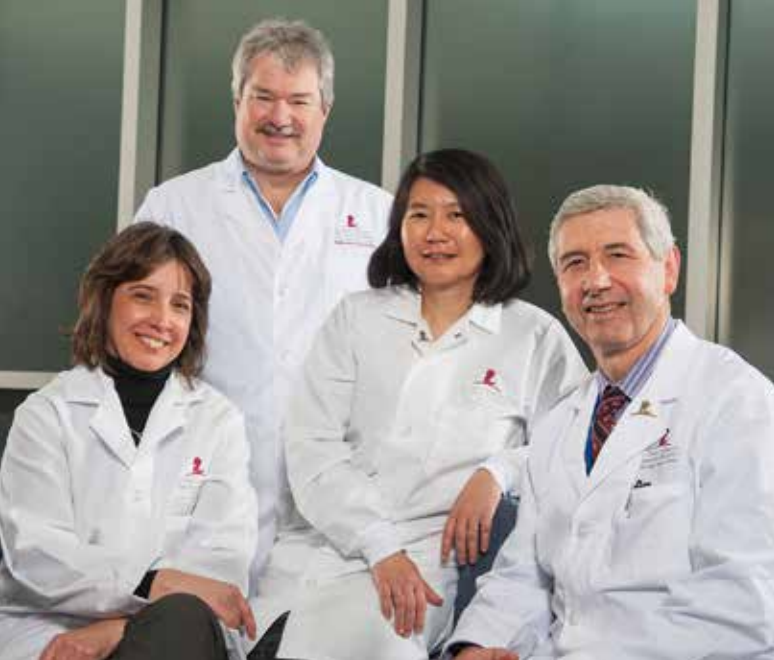
# TUMOR DATABASE IMPROVES PEDIATRIC CARE

BY DEREK BAGELY

**L**ast October, the *Journal of Clinical Oncology* published a paper that described the clinical features and outcomes in children with adrenocortical tumors (ACTs) without germline *TP53* mutations, by Emilia Modolo Pinto, PhD, of St. Jude's Children's Research Hospital in Memphis, Tenn., et al. Pediatric ACTs are cancers associated with germline mutations in the *TP53* tumor suppressor gene, but the authors of the paper point out that these tumors are also rarely associated with genetic constitutional disorders like Beckwith-Wiedemann syndrome (BWS), and that approximately half of children with ACTs don't actually have *TP53* germline mutations, and the tumorigenesis and tumor progression in these children are not well understood.

The results of that study show significant overlap of clinical features and prognostic factors in children with and without germline *TP53* mutations. There are differences between these two groups as well. The results allow Pinto and her team to be able to point to other factors that should be considered in children with ACTs, like constitutional abnormalities of the chromosome 11p15, and recommend the protein Ki-67 LI included in order to improve the risk classification of pediatric ACT.

This significant find was made possible by the International Pediatric Adrenocortical Tumor Registry (IPACTR) at St. Jude's Hospital. The registry was established 28 years ago with the goal of creating a database repository of the clinical and demographic features, treatment modalities, and outcomes of children and adolescents with ACTs, as well as perform molecular analysis of tumors and blood from those patients to clarify the mechanisms of adrenocortical



Clockwise from top: The team for molecular studies (l to r) Emilia M. Pinto, PhD, Gerald P. Zambetti, PhD, director, Academic Programs in Biomedical Sciences, Jinghui Zhang, PhD, chair, Computational Biology, Raul Ribeiro, MD, pediatric hematologist/oncologist; Carlos Rodriguez-Galindo, MD, chair, Department of Global Pediatric Medicine, St. Jude's, chair, Rare Tumors Committee, Children's Oncology Group (COG) and the primary investigator of COG for adrenocortical tumors with Pinto; Pinto in the lab.

**“ ... about 50% of children with ACTs carry a germline *TP53* mutation, irrespective of the tumor size and histology. Therefore, collaborations between endocrinologists and IPACTR investigators would facilitate discussions about the management of these tumors and provide information for parents and relatives.”**

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

tumorigenesis and provide consultation and recommendations for the management of ACTs in pediatric patients.

## Addressing a Knowledge Deficit

The motivation for creating the IPACTR came from the observation of a cluster of pediatric ACTs in southern Brazil, according to Raul Ribeiro, MD, a pediatric hematologist/oncologist at St. Jude's. ACTs represented two to three percent of pediatric cancer each year in the pediatric oncology unit of a hospital in Curitiba, Brazil. Some families saw two or more of their children develop ACTs.

“At the time, published information regarding the management of these tumors and counseling of the families was virtually nonexistent; the most popular pediatric oncology compendium included less than a page about ACT,” Ribeiro says. “Therefore, St. Jude and Brazilian investigators began collaborating to address the lack of knowledge about pediatric ACT in general and to understand the causes of the pediatric ACT cluster in Brazil. We reasoned that a registry for this rare tumor that was open to the entire international community would enable enough cases to be collected to address the lack of knowledge concerning this disease.”

Here's how it works: When physicians, healthcare providers, or parents ask St. Jude physicians about how to manage a child's ACT,



they are invited to participate in the IPACTR. The tumor is histopathologically reviewed and then genetic counseling is offered to the patient and relatives if patient is *TP53*-positive. All of this is free of charge.

“In summary, the registry offers the opportunity to collect clinical and demographic information, the family history of cancer, laboratory information, details of treatment practices, and outcome data for children and adolescents with adrenocortical tumors,” Pinto says. “Biological material, including tumor and blood samples from the patient and their relatives, allows us to perform collaborative investigations to understand the biology of the disease and ultimately improve the outcomes for these patients.”

There are about 400 patients from around the world currently enrolled in the IPACTR. Pinto says that parents will call and discuss doubts and new developments in the family. “Often, concerns regarding the long-term complications of chemotherapy or of early exposure to virilizing hormones are discussed,” she says.

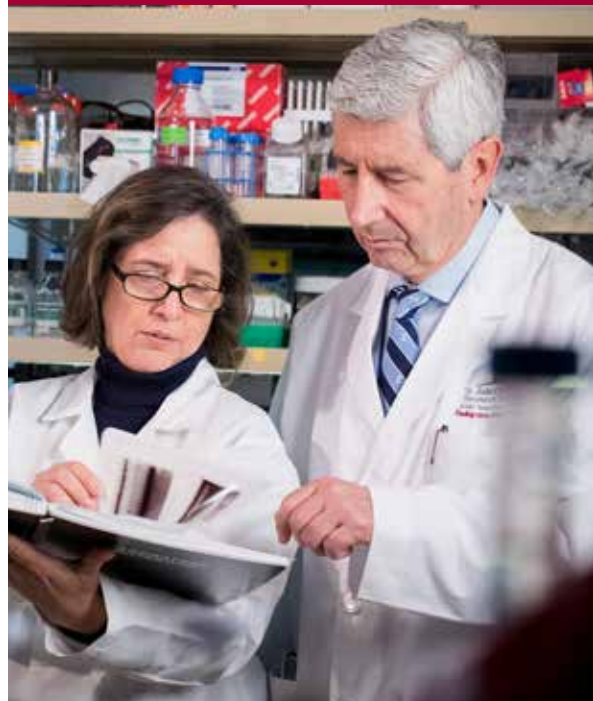
Pinto is part of a multidisciplinary team that analyzes and interprets the clinical, imaging, molecular, genetic, and histopathologic data to help in treatment decisions for each patient. She attends conferences around the world and has authored several papers in the field. When asked about a typical day working at the IPACTR, she exclaims that there’s no such thing. “Each day is different and is usually split between laboratory work, which includes routine molecular and genetic assays, as well as designing and performing specific DNA-based tests according to the genetic profile of the patient that will improve the accuracy of diagnosis, and time spent in research,” she says. “I’m involved in several projects to elucidate the molecular mechanisms operating in pediatric ACT cells.”

“The most exciting part of being involved in the IPACTR is the opportunity to do research and learn more about this rare disease and contribute to helping our little patients,” Pinto continues.

## Multidisciplinary Collaboration

And it’s because of that rarity that each case counts. Pinto says that even a small ACT with a “benign” histology that’s completely resected might hide a *TP53* mutation. Patients with ACTS are usually referred to an endocrinologist before an oncologist, in contrast to most other pediatric tumors, since small ACTs are often associated with endocrine manifestations and do not exhibit mass effect. A surgeon removes the tumor and diagnosis is established by histopathology. Pinto says pediatric oncologists are called in for large tumors or metastasis. “The problem with this approach is that about 50% of children with ACTs carry a germline *TP53* mutation, irrespective of the tumor size and histology,” she says. “Therefore, collaborations between endocrinologists and IPACTR investigators would facilitate discussions about the management of these tumors and provide information for parents and relatives.”

The IPACTR was instrumental in Pinto and her team demonstrating that there are at least two distinct pathways in pediatric adrenocortical tumorigenesis: *TP53*



Pinto and Ribeiro discussing molecular findings of their research.

## AT A GLANCE

- ▶ The International Pediatric Adrenocortical Tumor Registry (IPACTR) was created to better serve pediatric patients with these rare tumors, as well as their families and the physicians who treat them.
- ▶ About half the patients with adrenocortical tumors have germline *TP53* mutations, and the IPACTR was able to help researchers determine the pathway for tumor growth in the other half of patients.
- ▶ These findings – and the IPACTR itself – allow for more personalized and targeted approaches to treatment of children with adrenocortical tumors.

“

In some cases, there may be a somatic *TP53* mutation, resulting in faster tumor growth and increased potential for metastasis. **These biological insights are correlated with outcome information available in the IPACTR, resulting in more rational recommendations for children with newly diagnosed ACTs.**

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

Catherine Lam, PhD, and Pinto created the St. Jude Collaborative Rare Endocrine (CoRE) Tumor Referral Clinic that brings patients with adrenocortical tumors and their families to St. Jude for expert consultations.

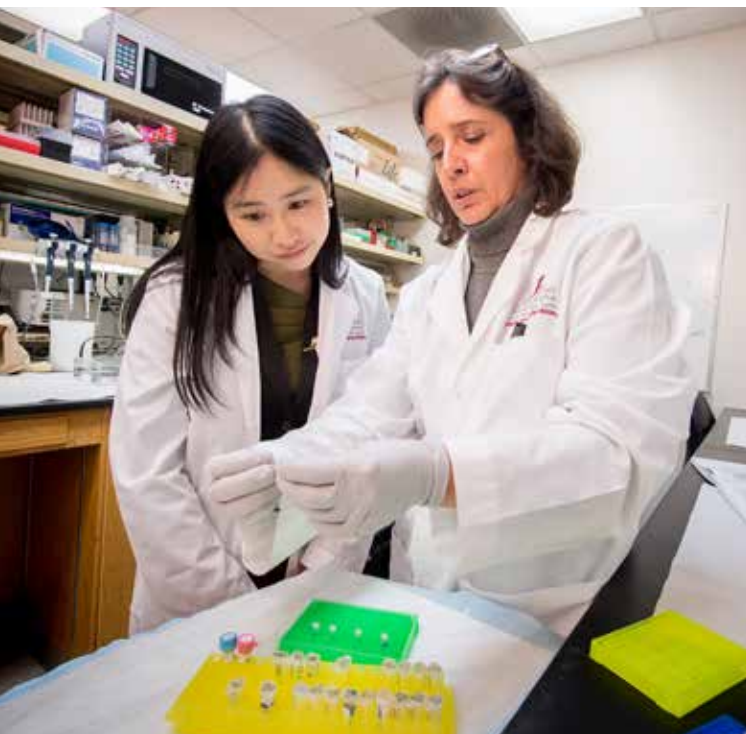


Photo: Courtesy of St. Jude's Hospital

mutations and chromosome 11 abnormalities. Patients with *TP53* mutations develop tumors that grow rapidly and accumulate many genomic changes. The tumorigenesis in patients with BWS or another chromosome 11 abnormalities includes overexpression of IGF-2 inducing the proliferation of embryonal adrenal cortex cells. The tumor develops through a mutation in beta-catenin.

“The accumulation of genomic changes in these cases is very slow; patients can have large tumors without distant metastasis, and these tumors can be managed with surgery alone,” Pinto says. “However, in some cases, there may be a somatic *TP53* mutation, resulting in faster tumor growth and increased potential for metastasis. These biological insights are correlated with outcome information available in the IPACTR, resulting in more rational recommendations for children with newly diagnosed ACTs.”

This finding means there could be more targeted approaches to treating ACTs in these pediatric patients since they have the opportunity to have their tumors analyzed in detail, as well as receive genetic counseling and surveillance for carriers. “Enrollment in the protocol would not cause extra work for the attending physician, because the informed consent is obtained by phone directly from parents. St. Jude is the [institutional review board] of reference,” Pinto says.

“We hope that our experience will stimulate colleagues to develop models to study other rare pediatric diseases,” she continues.” **EN**

BAGLEY IS THE SENIOR EDITOR OF *ENDOCRINE NEWS*. HE WROTE ABOUT PROVIDER BIAS IN RECOMMENDING WEIGHT LOSS SURGERY FOR YOUNGER PATIENTS IN THE JULY ISSUE.

# ENDO2018

## SESSION RECORDINGS

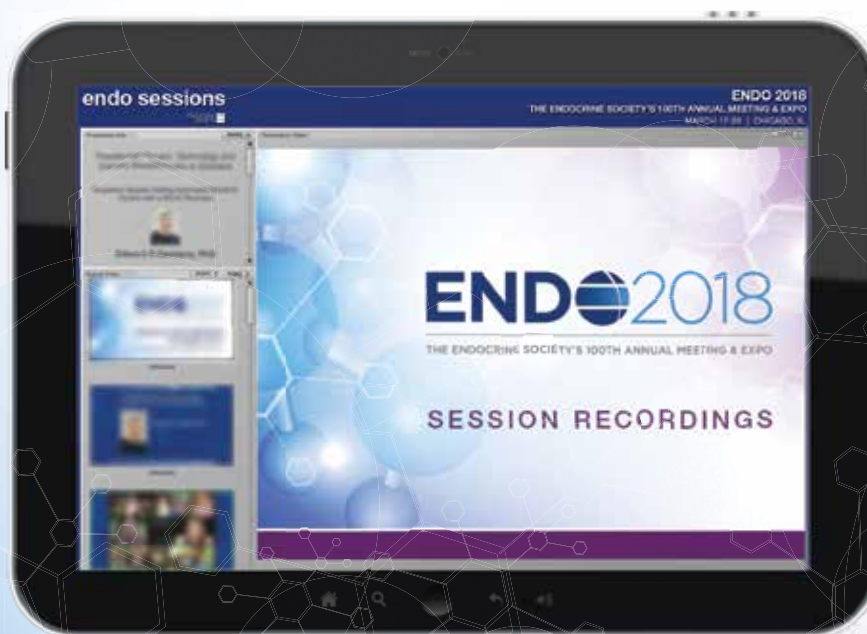
**ACCESS THE MEETING ONLINE ANY TIME WITH  
175 PRESENTATIONS FROM ENDO 2018**

ELIGIBLE FOR UP TO 150 AMA PRA CATEGORY 1 CREDITS™

AUDIO SYNCHRONIZED WITH SLIDES

EASILY DOWNLOADABLE MP3 FILES

INCLUDES PARTICIPATING CLINICAL AND TRANSLATIONAL SESSIONS

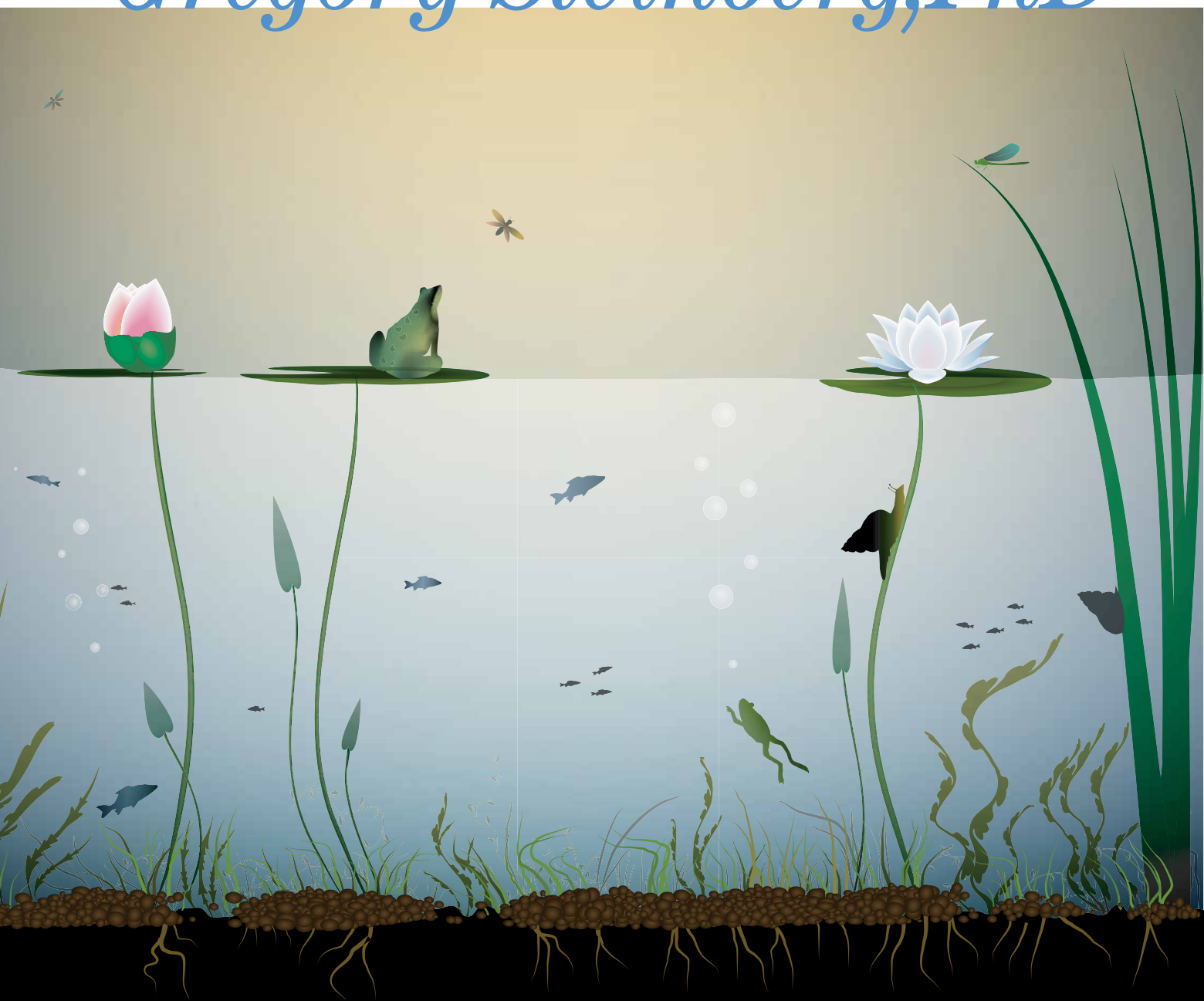


**GET YOUR SESSION RECORDINGS TODAY**

Nonmember: \$375 | Member: \$250 | Early Career/In-Training Member: \$200

[endosessions.org](http://endosessions.org)

# Q&A: *Gregory Steinberg, PhD*







**G**regory Steinberg, PhD, is a tenured professor in the Division of Endocrinology & Metabolism at McMaster University in Ontario, Canada, and co-director of the school's Metabolism and Childhood Obesity Research Program. In January, he was selected as one of the Endocrine Society's 14 leaders in the endocrinology field as winners of its prestigious 2018 Laureate Awards.

Steinberg was presented with the Richard E. Weitzman Outstanding Early Career Investigator Award, which recognizes an exceptionally promising young clinical or basic investigator. His work has established new paradigms by which energy sensing, endocrine factors, and commonly used medications regulate metabolism. *Endocrine News* caught up with Steinberg to learn more about what started him on the path to the research that has garnered him such praise.

**EN:** What did the honor of being presented the Early Career Investigator Award mean for you?

**Endocrine News talks to 2018 Laureate: Richard E. Weitzman Outstanding Early Career Investigator Award, Gregory Steinberg, PhD, at McMaster University in Ontario about how he first set out to be a scientist as a child and why a diverse lab is the most effective lab.**

**BY GLENDA FAUNTLEROY SHAW**

**Gregory Steinberg:** The honor is really impressive because there are so many great endocrine researchers who are Early Career Investigators, so it was a huge surprise for me to win this award. There are so many incredible scientists who've won this award before me, so it certainly a real honor to be listed among them.

**EN:** At what point in your educational span, or your life, did you know science research was your career path?

**“Finding people with diverse experiences who are smarter than me and are just as excited about the science as I am has been really important for developing my great team.”**

**GS:** I actually knew at quite a young age I wanted to become a scientist. Like many other scientists, it started with a huge curiosity for nature and exploration. In grade 4, I participated in my first science fair at my school and I chose to do it on pond life. I still remember vividly my mother taking me out to the local pond and helping me catch frogs, tadpoles, and other creatures. A few days later, standing in front of my aquarium, microscope, and poster and explaining to the judges what it was all about, I still remember thinking ‘Wow, this is so much fun!’ From that point, on the annual science fair was one of major highlights of my year and I knew I wanted to become a scientist.

**EN:** What is the ultimate research goal of your laboratory?

**GS:** We want to understand how the body adapts to changes in nutrient availability as we think that understanding this will help us develop new ways to treat diabetes, obesity, cardiovascular disease, and certain cancers.

**EN:** With a team that includes undergraduates, graduates, and post docs, how do you find the combination of researchers at different educational stages work together to answer your research questions?

**GS:** I think that finding people with diverse experiences who are smarter than me and are just as excited about the science as I am has been really important for developing my great team.

**EN:** What's one thing you would tell other future young investigators on how to excel? Can you share something you learned from a mentor that you always keep in mind?

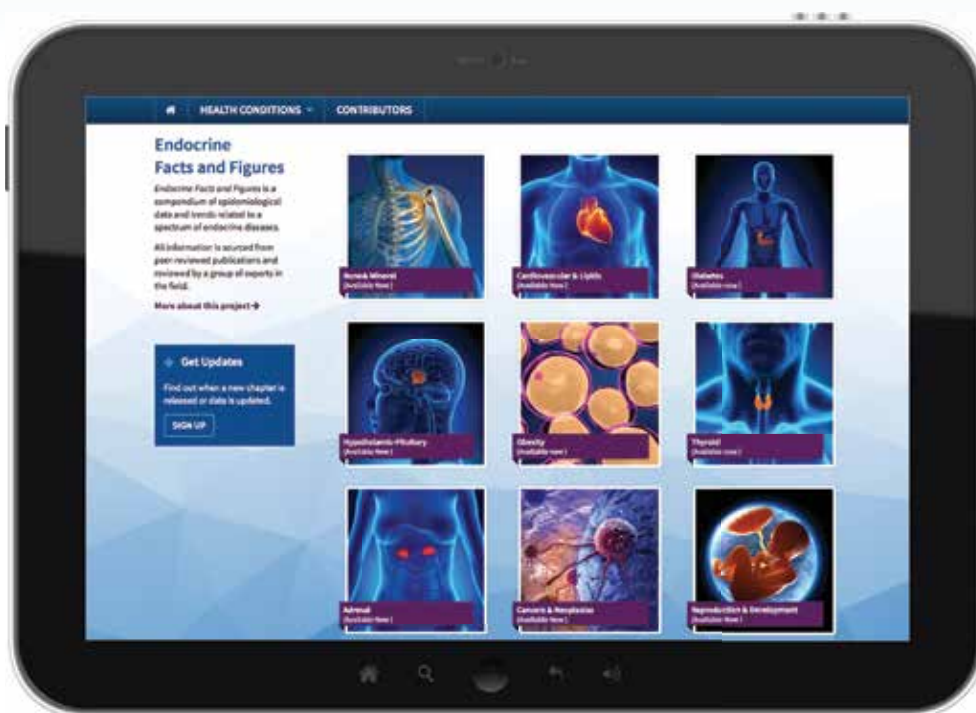
**GS:** I've been fortunate to have many great mentors across diverse areas and I think this diversity is very important for helping young investigators excel. For example, during my undergraduate and graduate training, mentors such as Lawrence Spriet and David Dyck at the University of Guelph provided me with a detailed understanding of integrative physiology and metabolism. This was then complemented by my postdoctoral mentor Bruce Kemp in Australia where I learned about protein biochemistry. Since starting my faculty position at McMaster University, I've been fortunate to be mentored by clinician scientists such as Hertzell Gerstein who have helped me develop my science further by making sure the questions we're asking in the lab are clinically relevant. Each of these mentors taught me to think about metabolism in a very different way. And I think this kind of diverse training allows a researcher to approach a problem in a unique way so that he or she is able to identify and tackle the most important questions using a variety of different approaches. <sup>EN</sup>

GLENDIA FAUNTLEROY SHAW IS A FREELANCE HEALTH EDITOR/WRITER BASED IN CARMEL, IN. SHE IS A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS*.

# ENDOCRINE FACTS AND FIGURES

*Endocrine Facts and Figures* is a compendium of epidemiological data and trends related to a spectrum of endocrine diseases.

All information is sourced from peer-reviewed publications and reviewed by a group of experts in the field.



## TOPICS CURRENTLY AVAILABLE INCLUDE:

BONE & MINERAL • CARDIOVASCULAR & LIPIDS • DIABETES • HYPOTHALAMIC-PITUITARY  
OBESITY • THYROID • ADRENAL • CANCERS & NEOPLASIAS • REPRODUCTION & DEVELOPMENT

Visit [endocrinefacts.org](http://endocrinefacts.org) to view the reports, watch interviews with experts, and sign up to receive future content alerts when new information is published.

## Endocrine Experts Build Influence at Policy Meetings in the EU

**B**uilding on our previous international efforts to identify and regulate endocrine-disrupting chemicals (EDCs), Society members continue to develop relationships with international regulatory agencies and advance our impact in multi-stakeholder approaches to chemicals management.”

Our participation in these meetings reflects the continued success of the Advisory Group in positioning Endocrine Society members to advise policy makers at multiple levels.

### Joint Research Centre Seeks Input on Integrative Approaches to Science

On June 19-20, and at the invitation of the European Commission’s Joint Research Centre (JRC), Heather Patisaul, PhD, attended a meeting titled Bridging Across Methods in bioSciences (BEAMS). The meeting was established to begin a conversation among key stakeholders with expertise in advancing basic, applied, and translational bioscience research, and identifying ways to reduce barriers to effective integration of scientific knowledge. Meeting organizers focused on addressing the following questions:

1. How will knowledge sharing help to bridge across different scientific methods?
2. What means of knowledge sharing can accomplish this?
3. How can effective forms of knowledge sharing be supported?

Participants at the meeting were highly motivated and engaged in the discussions on a variety of issues, including integrated approaches to testing and assessment (IATA) for harmful chemicals like EDCs. During the discussions, Patisaul described the important role that the Endocrine Society plays in bringing together diverse viewpoints, through workshops and meetings



Heather Patisaul

like ENDO, to address complicated problems in the endocrine field. The European Commission will use insights gained from discussions at the BEAMS meeting and future multi-stakeholder events as they explore opportunities to address major interdisciplinary issues through collaborative research activities.

Patisaul notes, “Participants at the BEAMS meeting appreciated that the Endocrine Society has experience bringing diverse stakeholders, including researchers, nurses, clinicians, and others together to address major public health issues.”

### Endocrine Perspective Included in OECD Meetings

On June 25-29, Laura Vandenberg, PhD, attended a series of meetings organized by the Organization for Economic Cooperation and Development (OECD), including meetings of the Working Party on Hazard Assessment (WPHA) and the extended Advisory Group on Molecular Screening and Toxicogenomics (EAGMST). In recent years, the Society has been highly engaged in the development of OECD guidance documents and resources. The WPHA and EAGMST meetings presented an opportunity to describe the details and scientific rationale for our recommendations related to these and other OECD projects. Vandenberg was also able to highlight our priorities for the testing and assessment of chemicals for endocrine effects during discussions with representatives from various national and EU regulatory agencies.





Laura Vandenberg

During the meeting, Vandenberg clarified the Society's support for systematic review as a tool for chemical reviews and how features of systematic review help agencies deliver transparent, reproducible, and unbiased decisions. Reflecting on the value of participating at this meeting, Vandenberg

commented that, "It is critically important to build relationships with groups like OECD to ensure that chemical testing and assessment approaches can evaluate effects on the endocrine system."

Participants at the meetings also discussed how scientific review processes can help OECD develop more reliable sources of mechanistic information for regulatory agencies, and how to identify truly adverse events that demand action from a clinical perspective. Our unique input was valued by participants, and we were encouraged to stay involved in future OECD meetings and projects. For instance, OECD encouraged us to participate in a forthcoming workshop on systematic literature review that will take place in October.

## Endocrine Society Weighs in on New EDC Strategy

As reported previously in *Endocrine News*, on May 24 Barbara Demeneix, PhD, DSc, BSc, participated in a briefing hosted by Pavel Poc, Member of the European Parliament. The meeting drew interest from the European Parliament and European Commission, including from the office of the Secretariat General,



Barbara Demeneix

reflecting the high priority that the Commission places on this issue. In response to continued pressure from the Endocrine Society and public interest from civil society organizations, in June the Commission released a draft roadmap outlining plans for a new community strategy on EDCs.

On July 12, Demeneix met with Julien Mousnier, Head of Unit, Citizens and Security from the Secretariat General, to discuss the Endocrine Society's perspective and what should be included in the revised strategy on EDCs. Demeneix explained why the scientific consensus on EDCs supports the need for improved protection from EDC-associated harms, and how the strategy could take advantage of the latest endocrine science to address public health concerns. She also described regulatory gaps and areas where consumers lack the ability to act on the information they receive due to inconsistent approaches to EDCs in different sectors of the economy.

The Endocrine Society submitted detailed comments on the roadmap during the public consultation, outlining the need for a broad approach to EDCs that covers cosmetics and other consumer products. We also described research areas that should be supported to build confidence in decision-making, though we stressed that for many chemicals we have enough knowledge to take action right now.



## Appropriations Update: NIH Receives Funding Increase from Congressional Committees, Final Outlook Uncertain

Continued pressure on lawmakers has made a funding boost for the National Institutes of Health (NIH) in fiscal year (FY) 2019 a priority for Congress, but there remains a great deal of work to do before any funding increase becomes law. At the time this article was written, the House and Senate have taken only some of the necessary steps to advance the Labor – Health & Human Services (LHHS) Appropriations Bill that funds the NIH.

In the Senate, the LHHS bill was approved by the full Appropriations Committee on June 28. The Senate included a robust \$2 billion increase for the NIH, consistent with the Endocrine Society's requested increase for the NIH. Meanwhile, the House version of the LHHS bill that contained a \$1.25 billion increase for the NIH was approved by the LHHS Subcommittee on June 15 but has yet to proceed to the full Committee for a vote. During a full Committee markup on July 11 appropriators had the chance to introduce amendments to the bill. The increase for the NIH remained unchanged as legislators spent their time on amendments related to the reunifications of children separated from their parents at the U.S.-Mexico border.

The proposed increases for the NIH only happen with the active advocacy of Endocrine Society members and other researchers across the U.S. In addition to successful advocacy in support of increased funding, we also secured the inclusion of specific language in the report accompanying the appropriations bills in the House and Senate. These reports give Congress the ability to give direction to federal agencies and call attention to important issues facing the research community. Our recommended

report language encouraged the NIH to explore increasing the modular budget cap for grant applications, to reduce administrative burdens on research. We also requested the inclusion of language that would direct the NIH to report on trans-NIH research conducted on polycystic ovary syndrome (PCOS) and comorbidities. The NIH is also asked to develop a trans-NIH research action plan to address gaps in PCOS research and comorbidities.

Despite progress made on the bills, Congress is still far from finished. In both the House and the Senate, at the time this article was written, there were no plans to bring either bill to the floor for a vote by the full chamber. It is likely that debate on the LHHS bills and other funding issues will continue through September, resulting in the need for another Continuing Resolution to fund the government at the beginning of FY 2019.

### Take Action

We will continue to work with the Congress to improve the outlook for research funding, but we need your help. Join our advocacy campaign at [www.endocrine.org/takeaction](http://www.endocrine.org/takeaction) to tell your member of Congress to support \$39.3 billion for the NIH in FY 19. Taking action is quick and easy and it will have an impact!

## Endocrine Society Advocates for Women's Health

**T**he upcoming Supreme Court nomination hearings and confirmation will highlight judicial opinions on women's healthcare. In addition, but perhaps not in the headlines, there are several efforts by the Trump Administration that would impact access to care for women's health services. The Endocrine Society has prioritized its advocacy efforts on women's health issues and we are working on a number of proposed regulatory changes, and legislation that affect women's access to preventive and reproductive care.

Infertility affects one in eight couples, often because of chronic conditions, diseases of the endocrine system, structural problems within the reproductive system, or treatment for other diseases such as cancer. Unfortunately, many insurance plans do not offer coverage for infertility treatments, cryopreservation, or adoption, leaving those affected to pay the high costs of treatments and/or adoption out-of-pocket. The Access to Infertility Treatment and Care Act (S.2960/H.R.5965), legislation introduced by Senator Cory Booker (D-NJ) and Congresswoman Rosa DeLauro (D-CT) builds upon existing laws and ensures that all Americans who need and want infertility treatment services have access to them. We are proud to endorse this legislation and are advocating on Capitol Hill for its passage.

Another endocrine condition that greatly impacts the health of women, Polycystic Ovary Syndrome (PCOS), is challenging to diagnose and is associated with comorbid conditions such as diabetes and heart disease. We have partnered with PCOS Challenge, one of the leading nonprofit patient support groups for women and adolescents with PCOS, to raise awareness on Capitol Hill and to urge the National Institutes of Health to increase its focus on research addressing comorbid conditions as most of the funded research focuses on the reproductive effects of the condition.

Finally, the administration has proposed regulations that could limit women's access to care. One proposed change would make it



easier for healthcare providers to refuse to treat a patient because the service violates their religious or moral convictions. Another proposal places restrictions on Title X grant recipients that will make many current grantees and other clinics ineligible, thereby making it more difficult for low-income women and adolescents to access reproductive healthcare services. We have weighed in with our concerns that the proposed changes will impact women's ability to control their reproductive health and access services from a provider of their choice.

Ensuring that all Americans have equal access to affordable, adequate healthcare is a top priority of the Society, and we will continue to work with women's health champions in Congress, our partners in the advocacy community, and our members to protect this right. <sup>EN</sup>



# TEST YOUR KNOWLEDGE WITH **PEDIATRIC ESAP™** **2017-2018**

Solve 100 New Cases In  
One Module, Now Delivering:

- Interactive online modules and printed reference book
- Peer-review comparisons for each question
- Detailed overall performance report
- Lab values in conventional and SI Units
- 40 ABP MOC Part 2 points and 40.0 AMA PRA Category 1 Credits™

Dedicated to the needs of your pediatric endocrinology practice.

Order online at  
[endocrine.org/store](http://endocrine.org/store)

## PEDIATRIC ESAP™ 2017-2018

PEDIATRIC ENDOCRINE SELF-ASSESSMENT PROGRAM  
QUESTIONS, ANSWERS, DISCUSSIONS



ENDOCRINE  
SOCIETY

ENDOCRINE  
SOCIETY



VISIT OUR NEW **JOB BOARD**  
TO FIND YOUR NEXT JOB.



SET UP AN [ENDOCAREERS.ORG](http://EndoCareers.org)  
ACCOUNT FOR ACCESS TO THE BEST  
JOBS AND CAREER TOOLS.

Visit [endocareers.org](http://endocareers.org), your source  
for scientific and clinical endocrinology  
job opportunities.



© 2017 ENDOCRINE SOCIETY

# UPSTATE

## MEDICAL UNIVERSITY

**Upstate Medical University, Department of Medicine:**  
Applications are invited for faculty positions in the Division of Endocrinology, Diabetes and Metabolism at SUNY Upstate Medical University in Syracuse, New York. Positions will be focused primarily on patient care and teaching at our faculty group practice site (Joslin Diabetes Center, University Endocrinologists and Osteoporosis Center). We also seek endocrinologists whose primary focus is clinical and translational research in diabetes. Academic rank and competitive salary dependent on qualifications. Excellent benefits. The beautiful Central New York Fingerlakes region offers excellent schools, affordable housing, numerous recreational and social activities and gorgeous seasonal weather. MD/MBBS/DO, BC/BE in Endocrinology and New York State license or eligible.

**Please reply to: Dr. Ruth Weinstock, SUNY Upstate Medical University, Department of Medicine, Room 353 CWB, 750 East Adams Street, Syracuse, NY 13210.**

*SUNY Upstate Medical University is an AA/EEO/ADA employer committed to excellence through diversity. Applications from women and minorities strongly encouraged.*



## RECRUIT THE BEST CANDIDATES WITH ENDOCAREERS

Find the right endocrinologist for your job opening by advertising with EndoCareers®. With print, online, and package opportunities, you can trust your message will reach your target audience with EndoCareers®.

[endocareers.org](http://endocareers.org)

To speak with a representative for print advertising opportunities, contact Dan Simone at [dsimone@pmny.com](mailto:dsimone@pmny.com) or 212.904.0360. For questions about our job board, please contact the Endocrine Society at [endocareers@endocrine.org](mailto:endocareers@endocrine.org) or 202.971.3636.



© 2017 ENDOCRINE SOCIETY





Hormone Health  
NETWORK®  
FROM THE ENDOCRINE SOCIETY

Rx

**DIAGNOSIS:**

**Patient Resource Deficiency**

**TREATMENT:**

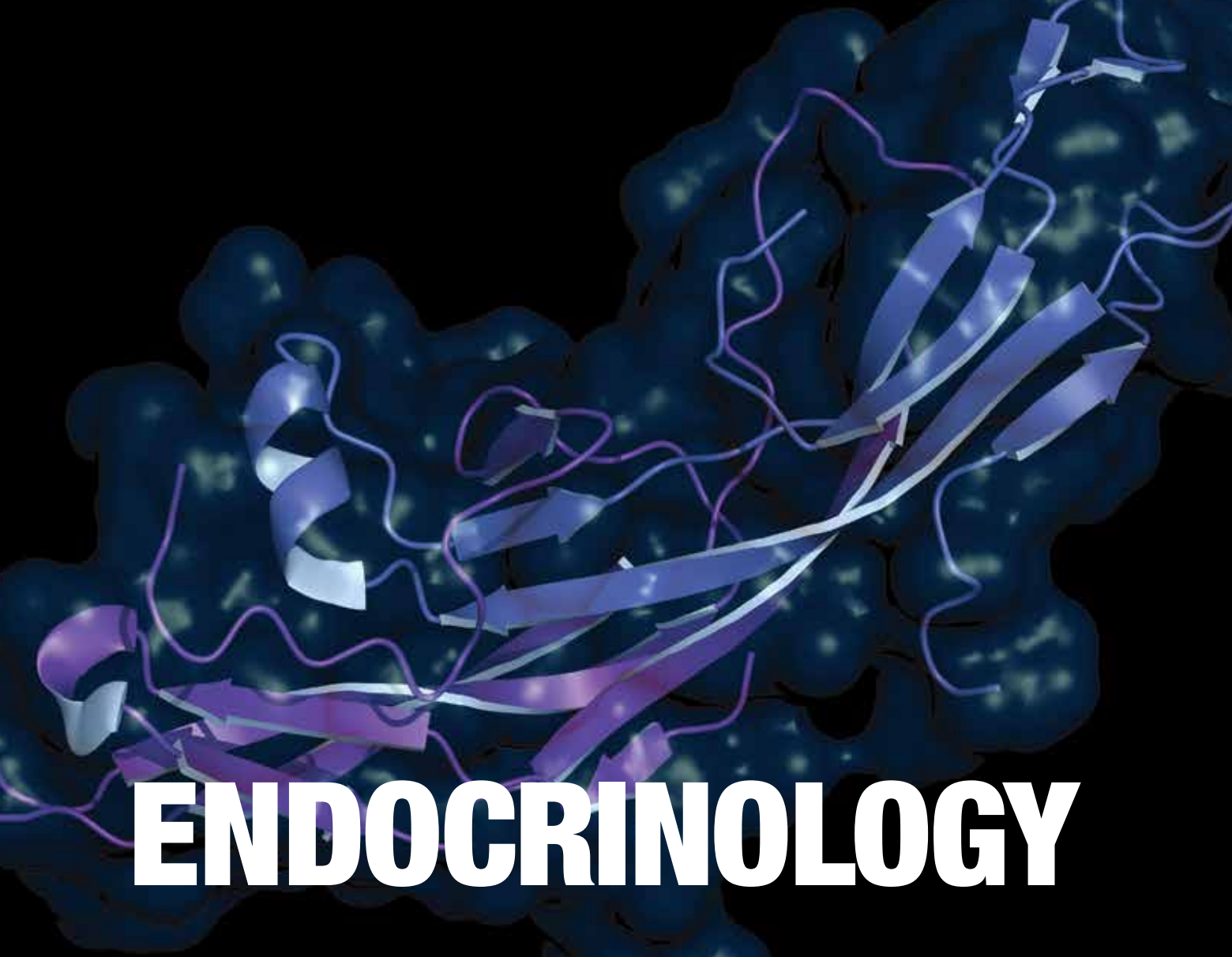
**Visit [hormone.org](http://hormone.org)**

Hormone.org is your number one patient resource portal. Backed by Endocrine Society experts, we are committed to supporting positive conversations that encourage patients to become active partners in their healthcare.

Signature \_\_\_\_\_







# ENDOCRINOLOGY

**NEW IN 2018! SOCIETY MEMBERS  
WHO PUBLISH IN *ENDOCRINOLOGY* GET  
THEIR FIRST EIGHT PAGES FREE!**

**VIEW DETAILS, AND ADDITIONAL BENEFITS  
AT [ACADEMIC.OUP.COM/ENDO](http://ACADEMIC.OUP.COM/ENDO)**



# EBR CEU

ENDOCRINE BOARD REVIEW  
CLINICAL ENDOCRINOLOGY UPDATE

## 2018

## REGISTER NOW

NEW THIS YEAR! CEU EXPANDS TO TWO CITIES—MIAMI AND ANAHEIM—MAKING IT MORE CONVENIENT FOR YOUR SCHEDULE. EBR WILL OCCUR IN MIAMI ONLY.

### EBR/CEU

MIAMI, FL

ENDOCRINE BOARD REVIEW

SEPTEMBER 4-5, 2018

CLINICAL ENDOCRINOLOGY UPDATE

SEPTEMBER 6-8, 2018

### CEU

ANAHEIM, CA

OCTOBER 19-21, 2018

[ENDOCRINE.ORG/CEU](http://ENDOCRINE.ORG/CEU)

ENDOCRINE  
SOCIETY 