

JANUARY 2017

THE LEADING MAGAZINE FOR ● ENDOCRINOLOGISTS

Endocrine news

INTERNATIONAL

By the NUMBERS

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Meet the newest class of endocrinology pioneers.

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Hormone Science to Health

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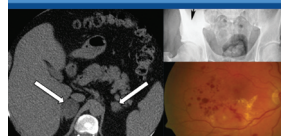
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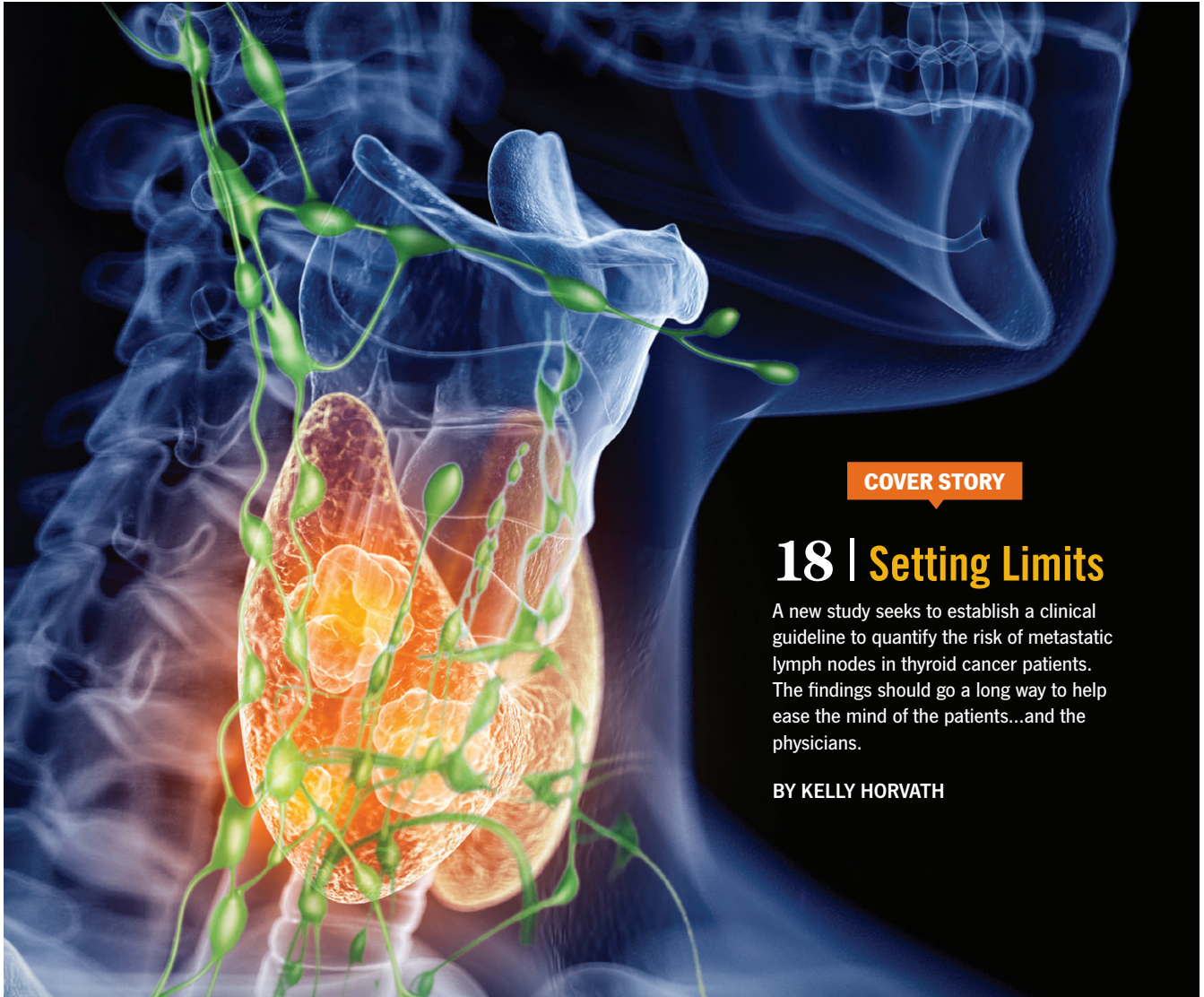
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COVER STORY

18 | Setting Limits

A new study seeks to establish a clinical guideline to quantify the risk of metastatic lymph nodes in thyroid cancer patients. The findings should go a long way to help ease the mind of the patients...and the physicians.

BY KELLY HORVATH

FEATURE

22 | 2017 Laureate Award Winners

For more than 70 years, the Endocrine Society has recognized the achievements of endocrinologists worldwide. Take a look at this year's distinguished recipients who join the list of prestigious practitioners and researchers.

FEATURE

30 | Sweet and Lowdown:

DO ARTIFICIAL SWEETENERS ACTUALLY CONTRIBUTE TO WEIGHT GAIN?

Controlled trials show non-nutritive sweeteners can sometimes help in weight loss, but observational and animal studies raise concerns about their risks.

BY ERIC SEABORG

TRI-POINT SERIES

35 | The Genetics and Epigenetics of Puberty

A wide-ranging look at puberty and the many mysteries that surround it, as well as the clinical management, new genetic tools, and how a variety of factors could influence the timing of this transition into adulthood.

BY ANA CLAUDIA LATRONICO, MD, PHD; RAVIKUMAR BALASUBRAMANIAN, MD, PHD, MRCP; WILLIAM F. CROWLEY JR., MD; SERGIO R. OJEDA, DVM; AND ALEJANDRO LOMNICZI, PHD




FROM THE **EDITOR**

Welcome to the Endocrine Society's Second Century

2016 WAS A GREAT YEAR FOR THE ENDOCRINE SOCIETY AS WE MARKED our 100-year anniversary with a year-long celebration we dubbed the “Year of Endocrinology.” You may have noticed that throughout 2016 *Endocrine News* adhered to each of the various months’ themes with at least two articles devoted to the month’s designation. Now that 2017 is here, we are going back to our normal policy of individual cover stories each month, but we will still adhere to a somewhat informal “editorial calendar” where the Endocrine Society’s activities will highlight a new topic each month, be it advocacy, education, the journals, or even the pages (web and printed) of *Endocrine News*.

As we embark on the new year, we are also debuting a few new types of articles for the magazine, mainly articles that will highlight various members and the work that you do. Helping us in that task is a brand new editorial advisory board. While not involved in the day-to-day operations of the magazine, this esteemed group of your colleagues will be aiding *Endocrine News* in making sure that we have content that will appeal to the vast array of our multi-faceted membership. To that end, I have made sure that we have physicians and scientists, veterans and early-career members, as well as representation from around the world (be sure to see who’s on the board on page ii).

The main reason for instituting this new group was not so much to act as “watch dogs” but to make the content more inclusive as well as to create more member-generated content. For example, we’ve been including the Tri-Point series for years. These pieces get members from each of our three constituencies — basic scientists, clinical scientists, and clinicians — to comment on a specific topic or treatment. In 2015 we instituted the “First Person” articles where members wrote about their endocrinology experiences from their specific points of view. In the past, we’ve featured Matthew Bouchonville, MD, who detailed his use of telemedicine in rural New Mexico, and Katy J. Brown, DO, who discussed her time in Ethiopia as part of the Society’s Ambassador Exchange Program. If you want to share your story, please let me know at mnewman@endocrine.org.

Going forward we want to put a variety of articles in *Endocrine News* that are written in the members’ voices, or even voices outside our membership rolls. One such column is called “Peer Review,” where we want to hear from professionals outside of the endocrinology field about their experiences in working with endocrinologists. We are also looking at featuring opposing viewpoints on a topic for a column called “Second Opinion.” This will allow people passionate about their views to be able to share them with our readers, not all of whom will agree with them. I think this would be an ideal way to maintain a healthy and vigorous dialogue among the diverse individuals that make up the exemplary membership of the Endocrine Society! 

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

JANUARY 2017

Endocrine news

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



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IN THIS ISSUE

JANUARY 2017



2 | FROM THE EDITOR

Endocrine News embarks on the Society's second century.

4 | PRESIDENT'S VIEWPOINT

Prioritizing support for the next generation of endocrinologists.

6 | IN TOUCH

Remembering past president P. Michael Conn; Allen Dalkin reflects on centennial celebration; Solutions needed for insulin prices

10 | ENDOCRINE

ITINERARY Scientific meetings of interest to endocrinologists from around the world.

12 | WHY ENDOCRINOLOGY?

Patients Are a Virtue, Part 2
BY DEENA ADIMOOLAM, MD

13 | DASHBOARD

Highlights from the world of endocrinology.

14 | TRENDS & INSIGHTS

Experts warn caution on new thyroid surgery technique; combination therapy may increase height potential in pubertal boys with ISS; women dissatisfied with long process to diagnose polycystic ovary syndrome

42 | PRACTICE RESOURCES: LAWYERING UP

When it's time to accept a new

position, you better have a lawyer who specializes in physician contracts on your side before you sign on the dotted line.

BY KURT ULLMAN

44 | LABORATORY NOTES: STORAGE WARS

Since laboratory space is at a premium, it's tempting to outsource specimen storage. *Endocrine News* weighs the pros and cons of moving specimen storage offsite or keeping it at arm's length.

BY MELISSA MAPES

46 | ADVOCACY

Obamacare repeal expected to come first in new Congress; NIH

funding in jeopardy; House & Senate pass 'Cures' Bill; Endocrine Society meets with NIH Office of Research on Women's Health

51 | HORMONE HEALTH NETWORK

Thyroid cancer: what you need to know

53 | CLASSIFIEDS

Career opportunities

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Hormone Science to Health



Prioritizing Support for the Next Generation of Endocrinologists

THIS MONTH I WOULD LIKE TO HIGHLIGHT THE Endocrine Society programs that focus on supporting trainees and early career members. The Society's current career development programs have centered on the career trajectories of young professionals across the career continuum, from undergraduate students to fellows in-training to junior faculty and early career professionals. Beginning with an active outreach program, the Society has recruited new trainee members and provided a diverse portfolio of programs aimed at creating a pipeline of young scientists working at the forefront of research and practice.

Training & Career Development

Endocrine Society programs provide students with opportunities for exposure to endocrine science through research experiences and fellowships, networking opportunities, and skills training. The Summer Research Fellowship (SRF) program gives undergraduate students, medical students, and first-year graduate students an opportunity to participate in a 10- to 12-week research program with a Society member. Students accepted into this program are offered education and career development through special programming at ENDO and a series of online interactive webinars. Previous participants reported that, in many cases, participation in the SRF has broadened their knowledge of endocrine science, specific lab techniques, and hypothesis development and strengthened their desire to pursue research careers in endocrine science and/or medicine.

ENDO, the Society's annual meeting, provides an effective forum for both students and fellows. The Early Career Forum, which takes place the day before ENDO, is a full-day workshop that provides a mix of translational plenary lectures presented by leaders in endocrinology and interactive break-out sessions

in separate clinical and basic science tracks. The Career Development Workshops offer relevant and beneficial career advice to trainees and early-career professionals in a wide range of topics. Specific workshops that will be held at ENDO 2017 will feature the lab and practice management workshops, the promotion and tenure workshop, and the evening mock study section. Trainees are recognized for their early career accomplishments by having their posters identified for special consideration in the Presidential Poster Competition. The meeting also offers several structured networking activities designed to create peer mentorship opportunities for early career members.

“

There are many exciting opportunities within the Endocrine Society that promote the development of early-career professionals while building a community in which the next generation of endocrinologists will thrive.

”

The Specific Aims Critiques activity is a new feature at ENDO 2017. This interactive experience will provide in-training and early career professionals with personalized feedback on the Specific Aims page of their NIH grant proposals. This one-on-one feedback provides a unique opportunity to have fresh eyes review and suggest improvements to K and F award submissions. In addition, sessions will also focus on the needs of international in-training members. The International Seminar Series at ENDO 2017 will include three workshops aimed to provide tips and tools to international trainees seeking fellowships, and eventually full-time positions, in the U.S. and abroad.


For those who cannot attend ENDO, the Endocrine Society recently launched the EndoCareers Online programming. This set of online education opportunities is designed around career development sessions offered by well-respected endocrine faculty. Fellows have access to a suite of career development resources, including 10-minute Power Talks on basic science and clinical career-related topics, full workshop recordings from the ENDO Career Development Workshops and the Early Career Forum, and live discussions in which fellows can ask questions of our faculty.

Leadership Development

At the next level, more senior fellows receive leadership and professional development support through targeted workshops that focus on helping fellows better understand the business of research while providing hands-on “grantsmanship” training that will increase their success in transitioning into independent research careers. One such program is the Future Leaders Advancing Research in Endocrinology (FLARE) program, now in its fifth year. This program provides trainees with a distinct set of leadership development and professional advancement opportunities including a leadership training workshop, a mentoring network to build relationships between trainees and dedicated mentors, and a Society-based internship program that includes participation on an Endocrine Society committee. These professional development activities are designed to enhance trainees’ confidence and identity as research professionals. This outstanding group of fellows has gone on to serve as speakers at Society early career programs, and several have received full-term appointments on committees and task forces of the Society.

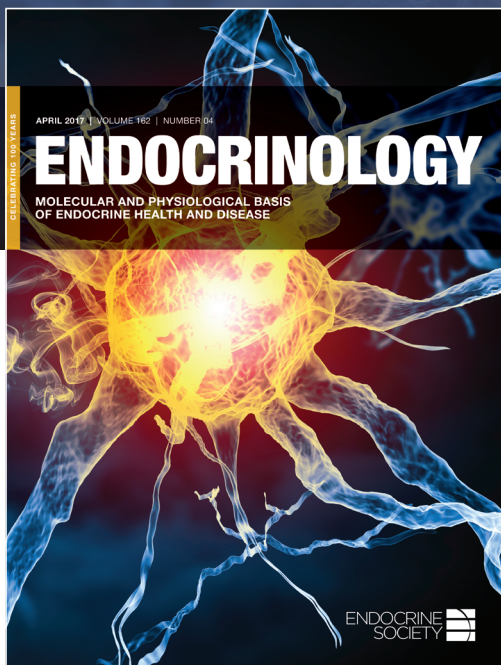
Awards & Recognition

In 2017, the Society’s early career awards will serve to recognize excellence in research, support participation in scientific education, and provide support for fellowships and research projects and career endeavors.

There are many exciting opportunities within the Endocrine Society that promote the development of early career professionals while building a community in which the next generation of endocrinologists will thrive. I’d like to congratulate the members of the Trainee and Career Development Core Committee and the Committee on Diversity and Inclusion for their outstanding efforts in creating programming that is supportive and nurturing for anyone focused on a career in endocrine science or medicine. If you have any questions or comments, feel free to contact me at president@endocrine.org. 

— Henry M. Kronenberg, MD, President, Endocrine Society

JANUARY 2017 MARKS THE DEBUT ISSUE OF THE MERGER OF *ENDOCRINOLOGY* AND *MOLECULAR ENDOCRINOLOGY*.



Editors-in-Chief: Andrea C. Gore, PhD and Stephen Hammes, MD, PhD

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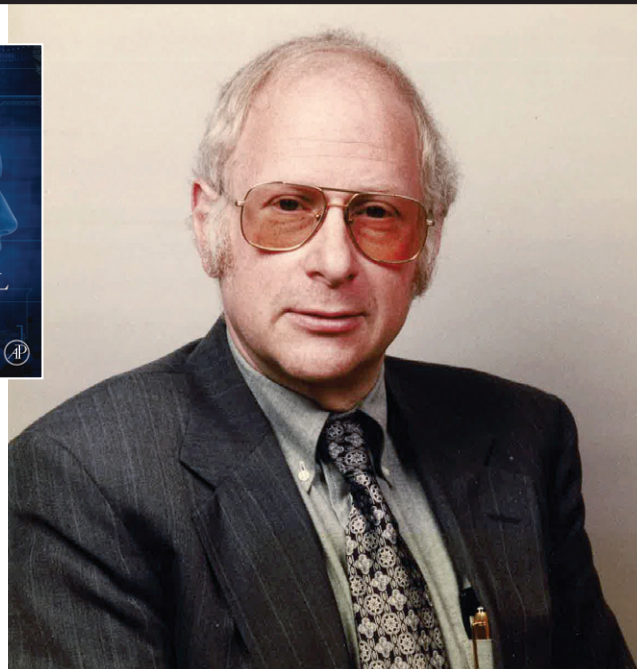
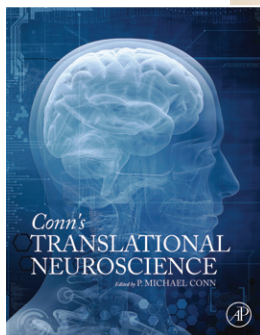
“Quality, authority, and leadership, as in all endeavors, lies in unity. With the merger of *Endocrinology* and *Molecular Endocrinology*, the Endocrine Society strives to publish the very best of endocrine science to the benefit of members, colleagues, and the global community.”

— Peter Fuller, AM, PhD, FRACP, Chair, Publications Core Committee, Endocrine Society, Head, Centre for Endocrinology and Metabolism, *Hudson Institute of Medical Research* and Head, Endocrinology Unit, *Monash Health, Australia*

Learn more at press.endocrine.org/endo

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Remembering Society Past President P. Michael Conn, PhD, MS

The Endocrine Society leadership is saddened to announce that valued friend and colleague P. Michael Conn, PhD, MS, died on November 26, 2016. Conn served as president of the Endocrine Society from June 1996 to June 1997.

Conn was a pioneer in discovering the signaling mechanisms used by the GnRH receptor and, in recent years, showed how the misfolding of mutant cell surface proteins, such as the GnRH receptor, could be corrected through the use of molecule chaperones in ways that revealed novel properties of the mutant proteins and could potentially be used to treat disease. His studies have implications for the treatment of reproductive disorders, diabetes, Alzheimer's disease, and cataracts.

During his presidential term, Conn founded the Hormone Foundation, the forerunner to the Hormone Health Network, the Society's public education arm. He also worked to raise public awareness of diabetes. The Society honored him with the Sidney H. Ingbar Distinguished Service Award, as well as the Ernst Oppenheimer Award and the Richard E. Weitzman Outstanding Early Career Investigator Award for his research achievements.

He served as the editor of numerous professional journals and book series and was editor-in-chief of *Endocrinology* as well as *The Journal of Clinical Endocrinology & Metabolism*. His latest book, *Conn's Translational Neuroscience*, was published in October by Elsevier.

Conn won the J. J. Abel Award of the American Society for Pharmacology and Experimental Therapeutics; the Miguel Aleman Prize, Mexico's national science medal; and the Stevenson Award of Canada. He also received a MERIT Award from the National Institutes of Health.

"Dr. Conn will be sorely missed by his colleagues and peers in the endocrinology field," says Endocrine Society president, Henry M. Kronenberg. "His research revolutionized the way we view the fates of mutant proteins that can result in disease. His work opened new avenues to treat a variety of conditions."

Conn was the senior vice president for research, associate provost, Texas Tech Health Science Center in Lubbock, Texas. Prior to this position he was the director of the Office of Research Advocacy, senior scientist in Reproductive Sciences & Neuroscience, and professor of physiology and pharmacology, cell biology and development, and OB/GYN at Oregon Health & Science University in Portland, Ore.

In lieu of flowers, the Conn family has requested that memorial donations be made to scientific societies that Conn belonged to, including the Endocrine Society. Donations can be made to the Society at <http://endocrine.org/membership/donations-endo> or mailed to the Society at 2055 L Street NW Suite 600, Washington, DC 20036.

European Commission Proposal Leaves Public Exposed to Harmful EDCs



“ More than 1,300 studies have found connections between EDC exposure and serious health conditions such as infertility, diabetes, obesity, hormone-related cancers, and neurological disorders, according to the Society’s 2015 Scientific Statement.”

On December 19, the Endocrine Society expressed disappointment in the European Commission’s revised proposal on defining and identifying endocrine-disrupting chemicals (EDCs), citing unnecessarily narrow criteria for identifying EDCs that will make it nearly impossible for scientists to meet the unrealistically high burden of proof and protect the public from dangerous chemicals.

A new provision in the revised proposal also creates an extremely problematic exemption for EDCs that act by regulating the growth of harmful organisms via the endocrine system. This exemption would include pesticides that prevent certain insects from growing or reproducing, even though these chemicals also could have effects on non-target species.

More than 1,300 studies have found connections between EDC exposure and serious health conditions such as infertility, diabetes, obesity, hormone-related cancers, and neurological disorders, according to the Society’s 2015 Scientific Statement.

The European Union is the largest single economy with regulations specific to EDCs. Enforcement of these regulations requires the European Commission to propose criteria to identify EDCs. The latest proposal asks for an unrealistically high level of scientific evidence for endocrine disruptors, limiting the ability to identify and regulate EDCs.

To effectively identify EDCs, the Endocrine Society supports creating multiple categories based on the amount of evidence that exists to show how specific chemicals act as EDCs, similar to the classification scheme used for carcinogens. This would help prioritize chemicals for assessment and regulation and allow for incorporating new data as more studies are published. The latest proposal from the European Commission does not include categories for identifying EDCs.

Failure to effectively regulate EDCs comes with a high price tag. Recent studies have found that adverse health effects from EDC exposure cost the European Union more than €163 billion each year in healthcare expenses and lost productivity.

As the European Parliament and member countries consider whether to implement the European Commission’s criteria, the Society will continue to advocate for criteria that reflect the state of the science.

— SPECIAL COMMENTARY —

Centennial Sentiments

Alan Dalkin reflects on how his involvement in last year's centennial celebration heightened his passion for the Society's work and made him enthusiastic about its future.



“ It is abundantly clear to me that the Endocrine Society has been, and continues to serve as the glue to hold a vast and diverse and talented membership together with an overarching goal of developing better clinicians, scientists, and educators.”

Participating in our Society's Centennial Celebration has been a truly rewarding experience for me. Working with the talented authors of *Special Edition ESAP: Historical Perspectives for Today's Clinician* (past presidents among them) was a labor of love. We could highlight the medical and educational contributions made by members of the Endocrine Society that have had astounding impact on how we deliver care today.

On a personal level, during my hunt for information on our past presidents, I was struck by the greatness of the men and women who have led our Society. When developing each vignette, I felt that it was important to go beyond the historical information readily available and to share stories and personal experiences of each past president.

As an example, I located and cold-called the son of one past president, hoping to gain a new perspective for a better portrayal of this great man. Initially I was met with silence as I stumbled over my introduction and tried to convince him that I was not a reporter or someone prying into the family. But, after describing the celebratory project and what I already knew of his father's contributions to our field of endocrinology, we soon struck up a conversation full of personal family history and warmth and enthusiasm for the Endocrine Society. It was due to the Endocrine Society that he and I reopened a chapter in history and rekindled the fondness his father had for this organization. In a similar vein, and with the help of the Society's staff, we unearthed some incredible information from the written archives for a host of vignettes that highlighted how each president felt personally connected to the Society.

Through this project, it is abundantly clear to me that the Endocrine Society has been, and continues to serve as the glue to hold a vast and diverse and talented membership together with an overarching goal of developing better clinicians, scientists, and educators. The *Special Edition ESAP* is a historical project that highlights the incredible past which forms our foundation. As I look back on 100 years of accomplishments and contributions, I am confident that the next 100 years will hold more of the same for the Society.

Alan Dalkin, MD, chair, Special Edition ESAP: Historical Perspectives for Today's Clinician council member, physician-in-practice seat



FDA Expands Indication for Dexcom's G5 Mobile CGM

On December 20, the FDA issued an expanded indication for Dexcom's G5 Mobile Continuous Glucose Monitoring (CGM) System that will allow the device to replace fingerstick blood glucose testing for diabetes treatment decisions in people 2 years of age and older. Previously, the system was approved only to complement fingerstick testing, but the FDA has now approved it to replace the traditional fingerstick test confirmation.

Previously, glucose levels had to be calibrated at least two times per day using blood obtained from fingerstick tests, but the FDA's recent ruling now enables patients to make treatment decisions based solely on the real-time readings from their CGM device.

The Endocrine Society has strongly advocated for this change and is pleased with the FDA's decision. As previously reported, Society member Dr. Nicholas Argento testified in support of this change. The Society also launched a grassroots campaign that garnered scores of letters to the FDA from clinicians, and has worked with DiaTribe to ensure that the FDA heard from a range of voices. We will continue to advocate for Medicare coverage of CGM.



Endocrine Society Calls for Solutions Regarding Insulin Price Crisis

The Endocrine Society lauds Novo Nordisk's and Eli Lilly and Company's recent announcements that the manufacturers would provide access to more affordable insulin to patients who need this life-saving therapy. The Society is concerned that rising insulin prices are making it more and more challenging for people with diabetes who are dependent on insulin to get the treatments they need.

Novo Nordisk will limit price increases for its therapies, including insulin, while Lilly will offer discounted prices on insulin products purchased through a partnership with Express Scripts. The Society hopes that other entities in the insulin supply chain including manufacturers, pharmacy benefit managers, and insurers will also demonstrate similar restraint to address this important issue.

People with type 1 diabetes are unable to produce their own insulin and need insulin treatment to maintain their glucose control. People with the more common type 2 diabetes do not produce enough insulin and may need insulin treatment as well. Many people with diabetes depend on insulin, yet increasing prices creates a dangerous barrier to access this critical therapy.

The Society strongly advocates for people with diabetes who depend on insulin to treat their disease to have affordable access to this life-saving therapy. The Society will work with all stakeholders to determine both the cause of increasing prices as well as additional ways to ensure access to insulin.

The Society believes that with greater transparency across the insulin supply chain, stakeholders can work together to make drug pricing more predictable, reduce out-of-pocket costs, and help patients and providers have access to affordable, patient-centered therapies. ^{EN}



Orlando, Fla., April 1 – 4, 2017

The Endocrine Society holds its annual meeting within arm's reach of the "happiest place on Earth" in Orlando. With over 9,000 attendees, nearly 3,000 abstracts, and over 200 other sessions, it is the leading global meeting on endocrinology research and clinical care. The meeting also hosts other satellite and pre-conference events, such as our Early Career Forum and Hands-On Thyroid Workshops.
www.endocrine.org/endo-2017

53rd Annual Clinical Diabetes and Endocrinology

Aspen, Colo., January 21 – 24, 2017

This conference will address multifaceted approaches to management and treatment of type 1 and type 2 diabetes, including both existing and emerging therapeutics; osteoporosis management and treatment; testosterone therapy in men and women; diagnosis and treatment of pituitary disorders; drug therapy for Graves disease; subclinical thyroid disease; adrenal insufficiency management; case studies in obesity and dyslipidemia; and much more.
marlin@njhealth.org

Keystone Symposium on Obesity and Adipose Tissue Biology

Keystone, Colo., January 22 – 26, 2017

This meeting will bring together cell biologists, biochemists, geneticists, physiologists, drug developers, and clinical researchers, thereby facilitating knowledge exchange and interactions leading to elucidation of better treatments for obesity and diabetes.
info@keystonesymposia.org

2017 Gordon Research Conference on IGF & Insulin System in Physiology and Disease

Ventura, Calif., March 12 – 17, 2017

This meeting will present cutting-edge research on the roles of IGFs and insulin and their signaling pathways in normal physiology and in major diseases. The program will bring together investigators around the globe who are at the forefront of this exciting field to discuss key aspects of the IGF and insulin biology.
cduan@umich.edu

Endocrine Board Review 2017

Chicago, Ill., September 26 – 27

Unlike other board preparation meetings, the Endocrine Society's Board Review (EBR) courses offer a comprehensive mock-exam format with case-based ABIM-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.
www.endocrine.org/ebr

Sex and Gender Factors Affecting Metabolic Homeostasis, Diabetes, and Obesity

Tahoe City, Calif., March 19 – 23, 2017

The goal of this meeting is to fill a need in the scientific community by connecting interdisciplinary groups of scientists who normally would not have an opportunity to interact. This group includes investigators studying sex differences, the role of sex hormones, the systems biology of sex and the genetic contribution of sex chromosomes to metabolic homeostasis and diseases.
info@keystonesymposia.org

World Congress on Osteoporosis Osteoarthritis and Musculoskeletal Diseases Florence 2017

Florence, Italy, March 23 – 27

European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) and International Osteoporosis Foundation (IOF) sponsor the world's leading clinical conference on bone, joint, and muscle health created for healthcare professionals, researchers, and young scientists. Abstract submission deadline: January 13.
leisten@humacom.com

19th European Congress of Endocrinology

Lisbon, Portugal, May 20 – 23, 2017

The largest European gathering of endocrinologists and endocrine scientists from around the world converge at this annual meeting with the aim of shaping the future of endocrinology to improve science, knowledge, and health across Europe and beyond.
www.ece2017.org

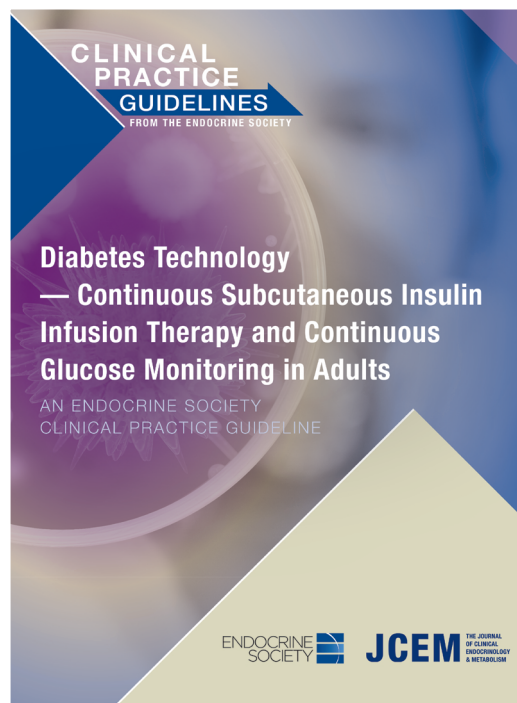
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WHY ENDOCRINOLOGY?

Patients Are a Virtue

BY DEENA ADIMOOLAM, MD, Assistant Professor, Division of Endocrinology, Diabetes and Bone Disease, Icahn School of Medicine at Mount Sinai, New York, N.Y.

Continued from part one of Adimoolam's "Why Endocrinology?" column in the December issue.

During my continuity clinics in residency I learned how to provide thorough and compassionate care from my mentor, Andre Sofair, MD, MPH. He cultivated me into becoming a more thoughtful physician, and understanding a patient for who they are, and to not be blinded by a diagnosis. Many of my clinic patients struggled with obesity and diabetes. I saw firsthand how complicated these diseases truly were, and I struggled through the good and the bad times with my patients. My colleagues used to refer their own difficult cases of diabetes and obesity to me as a resident because they knew I enjoyed these patients the most. I loved the challenge of taking care of difficult patients who struggled with non-compliance or who posed as a clinical dilemma. I found myself fascinated by the physiology of diabetes and obesity. Most importantly, nothing else brought me greater satisfaction and happiness than seeing my diabetic patient's A1c improve or my obese patients lose weight. Most often these patients did better because I spent the time educating them and answering their questions. I was intrigued with the power of lifestyle change and how it cured some of my diabetic patients. Outside of diabetes and obesity, I found myself drawn to other areas of endocrinology like pituitary and thyroid disease. I always chose endocrine cases to present at conferences and rounds because I found the physiology of hormones and feedback loops so interesting. By my second year of residency, I knew endocrinology was my calling.


During my fellowship training at Yale I was lucky to have compassionate mentors like Silvio Inzucchi, MD, who introduced me to the world of endocrinology, and so many interesting patients. He taught me how to think outside of the

box and improve on my physical examination skills to make a diagnosis. His zest for teaching inspired me to pursue a career as a clinician educator. While working with him and all the outstanding faculty members in the division of endocrinology at Yale, I realized that a career in endocrinology will never be boring. Every case was different, and every case can be learned from. I felt that more than a doctor every day, I was an educator. I was a teacher to not just my patients, but to other colleagues and students about endocrine diseases.

“
I am so thankful every day for the wonderful mentors in my life, and the gift of patient stories that we as physicians are so lucky to hear.

”

Endocrinology is now my outlet to continue my work as an educator and as an advocate to make a change in this world. The patients that I see every day fuel my interest in medical journalism – where I utilize their stories and circumstances to spread education and awareness to people throughout the world. I use media to share a message of prevention and recognition of many endocrine diseases, especially diabetes and obesity. As a member of the Endocrine Society, I have also had the opportunity to continue this work with Society members who share in my vision and passion. I work closely with the Endocrine Society's Hormone Health Network to spread awareness on various endocrine diseases through patient education tools and media.

As I begin my early career in endocrinology, my goal remains the same — to provide a better future for patients in the community and abroad, where medical complications and emergencies can be prevented with education, guidance, and compassionate care. I am so thankful every day for the wonderful mentors in my life, and the gift of patient stories that we as physicians are so lucky to hear. 

As the Endocrine Society embarks on its second century, *Endocrine News* will continue to tell the stories of how endocrinologists chose this remarkable field. If you would like to share your story with our readers around the world, contact Editor Mark A. Newman at mnewman@endocrine.org.

“ It is quite common to have the thyroid removed along with an incidental lymph node, . . . [but] is one random lymph node enough? Are two enough? Five? No one really knew. We embarked on this study to better inform physicians and patients about the adequacy of LN evaluations and what that may mean from a risk-benefit perspective for the patient.”

— JULIE A. SOSA, MD, MA, from Duke Clinical Research Institute and the Duke Cancer Institute in Durham, North Carolina, who was part of a team researchers who wanted to find a definitive answer as to how many lymph nodes are needed to determine if thyroid cancer has metastasized in “Setting Limits” on page 18.

FROM THE CENTURY OF
ENDOCRINOLOGY TIMELINE

1947:

*Nobel Prize in
Physiology or
Medicine awarded to
Carl F. Cori, Gerty T.
Cori, and Bernardo
A. Houssay*



In 1947, the Nobel Prize in Physiology or Medicine was divided, one half jointly to Carl Ferdinand Cori and Gerty Theresa Cori, née Radnitz “for their discovery of the course of the catalytic conversion of glycogen” and the other half to Bernardo Alberto Houssay (Society member) “for his discovery of the part played by the hormone of the anterior pituitary lobe in the metabolism of sugar.”

For more about the Century of Endocrinology, go to: www.ESCCentennial.org/timeline.

< 25%

Of products marketed to black women score low in potentially hazardous ingredients, including endocrine-disruptors.

— SOURCE: ENVIRONMENTAL WORKING GROUP.

11%

of medical school students who had suicidal thoughts, while 27% of medical school students suffered from depression.

— SOURCE: JAMA

14

The number of years that hot flashes can continue as a symptom of menopause, though the median length of time is 7.4 years.

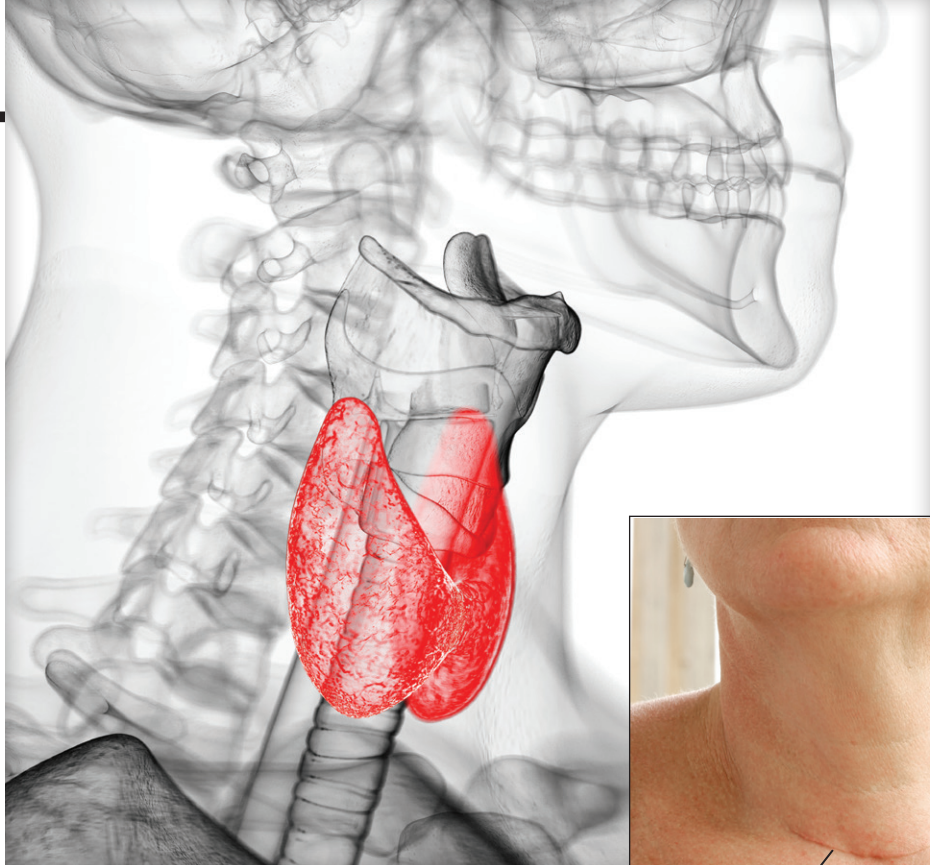
— SOURCE: JAMA INTERNAL MEDICINE



SHUTTERSTOCK.COM/CARTOONRESOURCE

BY DEREK BAGLEY

New Thyroid Surgery Technique Leaves No Visible Scar, but Experts Warn Caution



The new technique eliminates the traditional thyroid surgery scar as seen here.

A team of surgeons at Mount Sinai Beth Israel Hospital in New York City late last year performed the first endoscopic transoral thyroidectomy in New York, a procedure that's also one of the first of its kind in the nation. The results were published in *Surgical Endoscopy*.

The surgeons, led by William B. Inabnet III, MD, the Eugene W. Friedman, MD, professor of surgery and chair for the Department of Surgery at MSBI and chief of Endocrine Surgery Quality for the Mount Sinai Health System, removed the thyroid gland by making three small incisions inside the mouth underneath the lower lip. Inabnet inserted ports through the incisions, including an endoscope. Once a working space within the neck area was created, Inabnet preserved the critical structures and removed the thyroid gland through the largest of the incisions.

“Out of all of the approaches, this is the one type of thyroid operation where there is no sign that the patient underwent surgery,” says Inabnet. “This procedure is best equipped for smaller nodules and early-stage papillary thyroid cancer. I anticipate it will evolve for other applications going forward.”

However, while this technique may provide a cosmetic benefit to those patients who are worried about a visible scar, there is the concern with this alternative endoscopic approach (as with all endoscopic approaches) that it provides less than optimal

exposure and visibility, according to Leonard Wartofsky, MD, professor of medicine at Georgetown

University School of Medicine and editor-in-chief of *Endocrine Reviews*. “If it's my neck I would want the surgeon to readily identify and carefully preserve parathyroid glands and the recurrent laryngeal nerves and to be able to visualize extent of possible tumor to allow for its maximal removal and that of any involved lymph nodes,” he says. “Issues of ‘seeding’ of tumor along the endoscopic track have not been fully resolved as yet. Most of my patients have no problem in accepting a small incisional scar on the neck in exchange for assurances of optimal visualization for the procedure.”

R. Michael Tuttle, MD, of Memorial Sloan Kettering Cancer Center in New York, agrees, pointing out that the traditional method only leaves a small scar in most patients and has long been considered a safe and effective approach for all types of thyroid surgery. “As surgeons explore these alternative approaches for purely cosmetic purposes, it is very important that studies be done to document that these alternative approaches are as safe and effective as the traditional thyroid surgery techniques,” he says. “We need to be certain that we are not sacrificing oncological outcomes or accepting higher risks to the parathyroid glands or recurrent laryngeal nerves simply for cosmetic reasons.”

Combination GH and Aromatase Inhibitor Therapy Increases Height Potential in Pubertal Boys with ISS



Combining aromatase inhibitors (AIs) and growth hormone (GH) was shown to increase the height potential in pubertal boys with idiopathic short stature (ISS) when compared to treating ISS with either drug separately, according to a study recently published in *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Nelly Mauras, MD, of Nemours Children's Health System in Jacksonville, Fla. point out that short children's linear growth is hindered by estrogen's effect on epiphyseal fusion. "Increasing height potential in growth-retarded children during puberty is often complicated by the inexorable tempo of epiphyseal fusion caused by pubertal sex steroids, greatly limiting the time available for growth," the authors write.

They write that treatment for ISS with GH has shown positive results, but when administered during puberty there is very limited time to increase height as the growth plates fuse. The investigators set out to look at the safety and efficacy of treating with GH versus AIs (which block the conversion of androgens to estrogens), versus a combination of both. They analyzed the results of 76 pubertal boys around 14 years old, all with ISS (height SDS -2.3), randomized into three cohorts. These participants were treated daily with either AIs, GH, or AIs/GH for two to three years. The boys treated with just AIs for 24 months saw a height increase of 14 cm, those treated with GH for 24 months grew an extra 17.1 cm, and at the patients treated with both saw a height increase of almost 19 cm over 24 months. "Those treated through 36 months grew more," the authors write. These results contrast with the expected gain in height of a child with a height SDS of -2.0 of +10cm.

Findings: Based on these results, the researchers conclude that the combination AI/GH treatment improved linear growth in boys with ISS more than treatment with either AIs or GH alone. "Linear growth was improved further with more prolonged (36 months total) treatment in those with residual growth potential. Regardless of the length of treatment, near-final height gains were: AI, +18.2 (1.6) cm; GH, +20.6 (1.5) cm; and AI/GH, +22.5 (1.4) cm; resulting in the following near-adult height SDS: AI, -1.4 (0.1) cm; GH, -1.4 (0.2) cm; and AI/GH, -1.0 (0.1) cm," they write. The treatments had an excellent safety profile and no major impact on bone mineralization.

Women Dissatisfied with Long Process to Diagnose Polycystic Ovary Syndrome



A large international survey of women with polycystic ovary syndrome (PCOS) found nearly two in three were dissatisfied with the length of time they waited and the number of healthcare professionals they had to see before they received a diagnosis, according to a new study published *The Journal of Clinical Endocrinology & Metabolism*.

Researchers led by Melanie Gibson-Helm, PhD, of Monash Centre for Health Research and Implementation and the School of Public Health and Preventive Medicine at Monash University in Melbourne, Australia, point out that a previous Australian survey showed that PCOS diagnosis is often delayed, involves many healthcare professionals, and ultimately leaves women still asking questions about their condition. “This study aimed to investigate women’s diagnosis experiences, information provided, main concerns about PCOS and support needs in a large group of women with PCOS primarily in North America and Europe. The findings will inform an international initiative to improve diagnosis and education to better meet women’s needs and optimize early engagement with evidence-based management,” the authors write.

Nearly half of the 1,385 women surveyed internationally for this current study saw three or more healthcare providers before they were diagnosed. The diagnostic process took more than two years for a third of the survey respondents. A

total of 1,550 women responded to the survey, but 165 were excluded because they didn’t meet the eligibility criteria or they completed less than half of the questions. Respondents lived in 32 countries.

“Given the prevalence of PCOS, it is important for women and healthcare professionals to be more aware of the condition,” says one of the study’s authors, Helena Teede, FRACP, PhD, of Monash University. “Despite the misleading name, PCOS is not primarily an ovarian condition, but instead is a hormonal disturbance with diverse health effects that is largely inherited. The process of diagnosing PCOS needs to be improved, and the diverse set of metabolic, reproductive and psychological features need to be understood and addressed.”

In the cross-sectional study, women with PCOS who were at least 18 years old and had been diagnosed with the condition by a physician were asked to complete an online questionnaire. Researchers built on initial studies in Australia and worked with two large PCOS patient support groups — U.S.-based PCOS Challenge and U.K.-based Verity — to distribute the questionnaire to their website visitors, mailing lists, and social media followers with an international reach. “We were interested in women’s diagnosis experience and satisfaction with information and educational materials they received at the time of diagnosis,” Teede says.

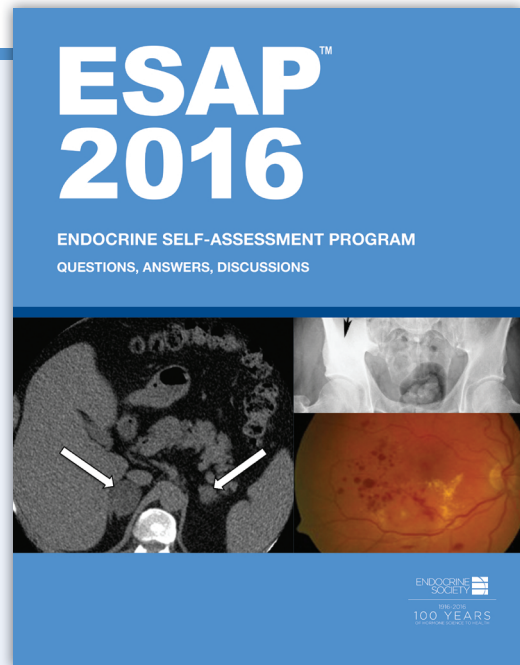
“Despite the misleading name, PCOS is not primarily an ovarian condition, but instead is a hormonal disturbance with diverse health effects that is largely inherited. The process of diagnosing PCOS needs to be improved, and the diverse set of metabolic, reproductive and psychological features need to be understood and addressed.”

Reports of months- or years-long waits for a diagnosis and visits to multiple healthcare professionals were common among the survey respondents. Women who waited more than six months for a diagnosis were more likely to report being dissatisfied with the process than those who were diagnosed in a shorter period.

Less than a quarter of the survey respondents were satisfied with the information they received about common treatments for PCOS, including lifestyle management and medications, when they were diagnosed with the condition. More than half reported that they didn't receive any information about long-term PCOS complications or emotional counseling or support.

Findings: “Our findings show women are dissatisfied with the diagnosis experience and that there are clear opportunities to improve awareness, diagnosis, and health outcomes for women with PCOS,” Teede says. “The survey results, along with a new international guideline and awareness ad education initiative, will be used to inform international efforts to improve PCOS education and care.” ^{EN}

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“ It is quite common to have the thyroid removed along with an incidental lymph node . . . [but] is one random lymph node enough? Are two enough? Five? No one really knew.”



Setting LIMITS

BY KELLY HORVATH

A new study seeks to establish a clinical guideline to quantify the risk of metastatic lymph nodes in thyroid cancer patients. The findings should go a long way to help ease the mind of the patients...and their physicians.

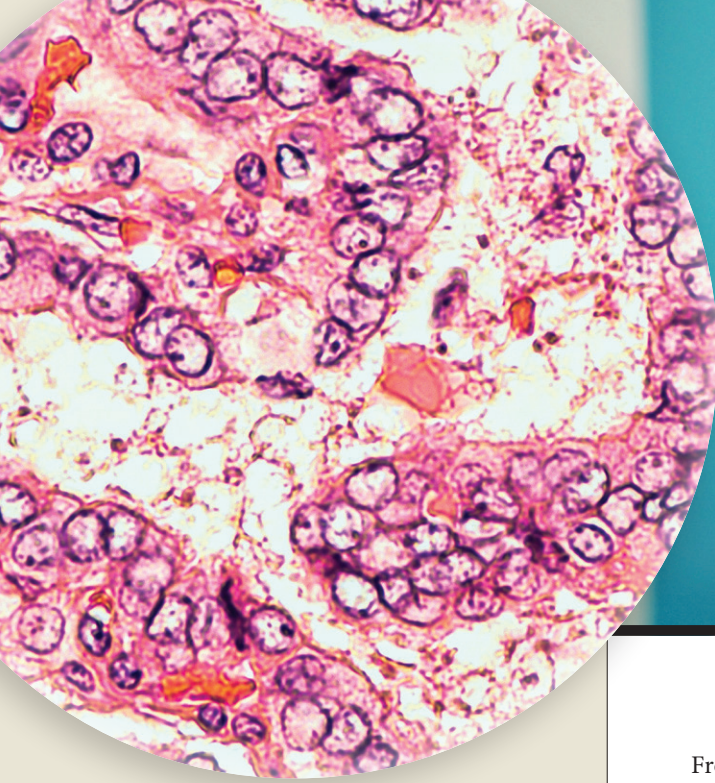
With thyroid cancer incidence on the rise, especially papillary thyroid cancer, surgical tumor resection is a critical component of the overall treatment plan, which might also include one or more of several adjuvant treatment options such as concomitant lymph node (LN) dissection.

The American Cancer Society notes that although an estimated 62,450 new cases of thyroid cancer will be diagnosed in the U.S. in 2016, fortunately, the death rate (about 1,980 deaths from thyroid cancer) has not increased alongside incidence. Nevertheless, five-year survival rates for stage IV papillary thyroid cancer remain at only about 51%, and lymphovascular invasion is a key risk factor for occult, recurrent, or persistent disease.

With standards yet to be established regarding the number of LNs a surgeon might remove to help determine the existence of occult disease — in addition to variations in clinical management — thyroid cancer patients may be undergoing unnecessary or even inappropriate treatments that could possibly carry risk for debilitating complications.

LYMPH NODE ASSESSMENT MODEL

In “How Many Lymph Nodes Are Enough? Assessing the Adequacy of Lymph Node Yield for Papillary Thyroid Cancer,” published in the *Journal of Clinical Oncology*, a team of researchers from the Duke Clinical Research Institute and the Duke Cancer Institute in Durham, N.C., including Julie A. Sosa, MD, MA, and Terry Hyslop, PhD, set out to provide as definitive an answer as currently possible to the question posed in the title of their pioneering study.



CHARACTERISTICS OF PAPILLARY THYROID CANCER

- ▶ Peak onset ages are 30 to 50 years old
- ▶ Occurs more often in females by a 3:1 ratio
- ▶ The prognosis directly related to tumor size. (<1.5 cm [1/2 inch] is a good prognosis.)
- ▶ Accounts for 85% of thyroid cancers due to radiation exposure
- ▶ In more than 50% of cases, it spreads to lymph nodes
- ▶ Distant spread (to lungs or bones) is uncommon
- ▶ The overall cure rate is very high (near 100% for small lesions in young patients)

Source: endocrineweb.com

From previous investigations, the team found that the median number of LNs removed is two, but this practice is largely arbitrary. Because occult disease is, by definition, not readily identifiable with existing imaging studies, determining whether it exists can currently be done only by pathologic examination. “It is quite common to have the thyroid removed along with an incidental lymph node,” explains Sosa, “. . . [but] is one random lymph node enough? Are two enough? Five? No one really knew. We embarked on this study to better inform physicians and patients about the adequacy of LN evaluations and what that may mean from a risk-benefit perspective for the patient.”

Retrospectively analyzing National Cancer Database data from 38,653 patients diagnosed from 1998 to 2012 with localized ≥ 1 -cm papillary thyroid cancers who underwent thyroidectomy with one or more LNs surgically examined, researchers used a mathematical model in a stepwise fashion to first estimate risk of false-negative LN dissection; second, prevalence of true-positive LNs; and, finally, risk of occult disease.

CLINICAL DECISION-MAKING: IT'S A TEAM EFFORT

Although the risks of central lymphadenectomy are not typically life threatening and absolute contraindications do not exist, complications can certainly negatively impact patient quality of life; therefore, careful reckoning of risks versus benefits is critical. These risks, explains Sosa, include increased risk of transient or permanent hypoparathyroidism and hypocalcemia, necessitating calcium and vitamin D supplementation by mouth, as frequently as every four to six hours, as well as dysfunction of the recurrent laryngeal nerve, resulting in the inability to speak (or even breathe, which could require a tracheostomy), and the external branch of the superior laryngeal nerve, resulting in a change in volume and pitch of voice and the inability to sing or speak loudly.

Thus, in a patient with a tumor not likely to have metastasized, knowing prior to surgery what that risk most likely is would prove an invaluable tool for

“ We embarked on this study to better inform physicians and patients about the adequacy of [lymph node] evaluations and what that may mean from a risk-benefit perspective for the patient.”

— JULIE A. SOSA, MD, MA, DUKE CLINICAL RESEARCH INSTITUTE, DUKE CANCER INSTITUTE, DUKE UNIVERSITY, DURHAM, N.C.

designing the ideal treatment plan. Says Sosa: “There is a quandary faced by the entire healthcare team — for the surgeon, whether to take the lymph nodes out; for the endocrinologist, whether to give radioactive iodine, in part based on the information obtained about lymph nodes during surgery; and for the patient, whether the information and treatment will result in better survival. We are trying to quantify the risk.”

Patient input is particularly important in this context. “If a patient is anxious about the risk of harboring occult metastases, evaluation of more lymph nodes can bring peace of mind,” Sosa explains. “However, if a patient is very risk averse, then surgery can be tailored accordingly.”

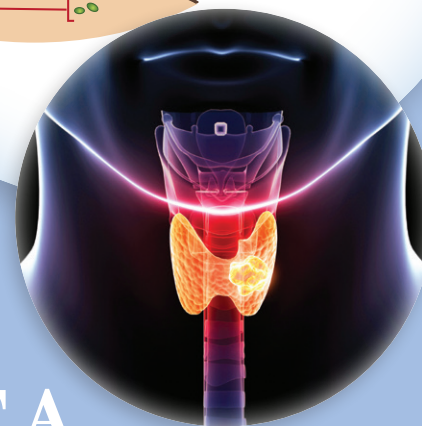
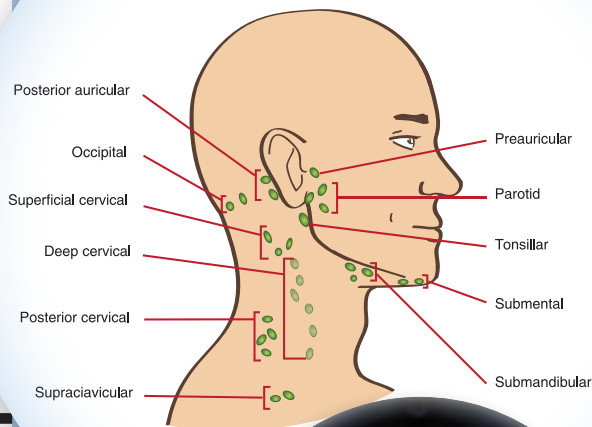
POTENTIAL CLINICAL GUIDELINES ON THE HORIZON

Quantify risk they did, concluding that in a patient with a 1–2-cm tumor (T1b disease) removing six LNs that test negative would suffice to provide 90% confidence that the cancer has not metastasized. The number of LNs needing to be removed rises to nine if the tumor is 2–4 cm (T2 disease) and to 18 if the tumor is >4 cm and/or is associated with minimal extrathyroidal extension (T3 disease).

“We do not know the exact probability for each unique patient, but our conclusions are based on patterns within a very large set of data,” Hyslop says. “This information can help surgeons tailor their resections. The data might help the pathologist be more fastidious in finding lymph nodes in the specimens. Then endocrinologists and their patients can make decisions about the need for other treatment based on good pathologic evidence. Knowing how many lymph nodes would need to be assessed to truly be certain of the risk of occult disease can help them with dynamic staging, adjuvant treatment choice, and intensity of follow-up.” ^{EN}

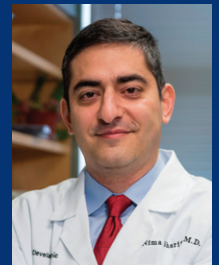
HORVATH IS A FREELANCE WRITER BASED IN BALTIMORE, MD. SHE WROTE ABOUT THE LINK BETWEEN ENDOCRINE-DISRUPTING CHEMICALS IN UTERO TO BREAST CANCER IN ADULTHOOD IN THE OCTOBER ISSUE.

Lymph nodes of the neck and head



AT A GLANCE

- ▶ In patients with papillary thyroid cancer, an average of about 50% will have nodal metastases at diagnosis.
- ▶ To rule out occult nodal disease with 90% confidence, six, nine, or 18 nodes would need to be removed and examined, depending on the stage of the tumor.
- ▶ In prophylactic removal of central neck nodes that may or may not contain cancerous tissue not visible in pre-surgical imaging, removal and testing of three, four, or eight lymph nodes is recommended, depending on tumor stage.



THE ENDOCRINE SOCIETY 2017 LAUREATE AWARD WINNERS

For more than 70 years, the Endocrine Society has recognized the achievements of endocrinologists worldwide. Valued at more than \$66,000, the Laureate Awards recognize endocrinologists for seminal research, meritorious service, leadership and mentorship, innovation, international contributions, education, translation of science to practice, and lifetime achievement.

The distinguished recipients on the following pages join a prestigious list of past award recipients, all of whom have advanced scientific breakthroughs, medical practice, and human health around the world. Award categories honor the achievements of endocrinologists at all stages of their careers, recognizing those at the pinnacle of the field as well as young endocrinologists who are making a mark.

The dedication, commitment, and achievements of current and past award recipients have earned each a place in Endocrine Society history as well as the history of the practice and science of endocrinology.



Outstanding Scholarly Physician Award

**Rebecca S. Bahn, MD,
FRCPI**

Rebecca S. Bahn, MD, professor of medicine at the Mayo Clinic College of Medicine is the winner of the Endocrine Society's Outstanding Scholarly Physician Award for 2017. This award recognizes outstanding contributions to the practice of clinical endocrinology in an academic setting. Dr. Bahn is internationally known in the thyroid and endocrine communities for her work on thyroid-related eye disease, which has spanned more than 30 years. Her research has elucidated important aspects of the pathogenesis of this disorder, and she has also been at the forefront in designing novel therapies for patients afflicted with this condition. She was one of the first investigators to establish an orbital fibroblast model system, and she and her group led the way in documenting TSH receptor expression on these target cells. She also described the critical pathogenic role of orbital cytokines and other factors in promoting adipocyte and fibroblast differentiation. These studies led to clinical trials of octreotide and more recently rituximab for the treatment of thyroid eye disease. She is the author of many highly cited review articles on thyroid eye disease, and she is a highly sought after national and international speaker.

In addition to her work on thyroid eye disease, Dr. Bahn has served as president of the American Thyroid Association and as chair of the ATA guidelines task force on the management of hyperthyroidism. She has been a mentor to more than 20 clinical and research fellows, and has been an ardent advocate for women in science. She is the recipient of the 2014 Woman of the Year award from the American Thyroid Association's Women in Thyroidology group. She has been the associate dean for Research Career Development at the Mayo Clinic, and has also been the principle investigator of an NIH Grant designed to promote research in women's health. Dr. Bahn epitomizes the concept of a clinician scholar, and is certainly a most deserving recipient of our Society's 2017 outstanding Scholarly Physician Award.

— DAVID S. COOPER, MD



Outstanding Public Service Award

Larry D. Bowers, PhD

Throughout his distinguished career, Larry D. Bowers, PhD, has made numerous outstanding contributions to the fight against abuse of performance-enhancing anabolic steroids and other hormones in sport.

Dr. Bowers served as the laboratory director for the then International Olympic Committee-accredited laboratory at Indiana University from 1992 to 2000. During this time, Dr. Bowers researched new methods of detection and contributed to the understanding of metabolism of hormones such as anabolic steroids and growth hormone derivatives. His work contributed to the implementation of intra-individual reference range monitoring for detecting testosterone abuse. Since joining the U.S. Anti-Doping Agency (USADA) in 2000, he has continued to advocate for scientific excellence by his leadership in the Partnership for Clean Competition research funding agency and his organization of the USADA Annual Symposium on Anti-Doping Science. The latter brings together experts from fields like endocrinology and anti-doping to focus on future scientific challenges for anti-doping.

Dr. Bowers has served on numerous scientific, professional, and sport federation committees and boards and has provided expertise to a various governmental agencies and Congress. He was the primary author of the initial World Anti-Doping Agency International Standard for Laboratories, which serves to harmonize anti-doping laboratory performance globally. Bowers has been involved in many of the advances in anti-doping since joining USADA, including the identification and characterization of the first designer steroid, tetrahydrogestrinone; cooperation with law enforcement in investigations like BALCO; non-analytical positives; and adjudication of complex scientific cases involving allogeneic blood transfusions and isotope ratio mass spectrometry to identify exogenous testosterone use.

In recent years, Dr. Bowers has worked to incorporate the principles of perceptual deterrence into USADA's policies to make testing and educational resources more effective. It is Dr. Bowers' demonstrated dedication to protect clean athletes and the value of sport that makes him a worthy Outstanding Public Service Laureate Award recipient.

— RICHARD V. CLARK, MD, PHD, FACP



Outstanding Clinical Practitioner Award

Daniel Einhorn, MD, FACP, FACE

Daniel Einhorn, MD, FACE, FACP, is a graduate of Yale University (Summa Cum Laude) and of Tufts Medical School (Alpha Omega Alpha). He did his post-graduate training in psychiatry and then medicine at the Beth Israel Hospital (BIH) and his endocrinology fellowship at the Thorndike Laboratories at BIH and was appointed instructor in medicine at Harvard. He is board certified in internal medicine and in endocrinology. He went to San Diego, Calif., to create a large inpatient diabetes center and since 2000 has served as medical director of the Scripps Whittier Diabetes Institute.

Dr. Einhorn served over 20 years on the national board of the American Association of Clinical Endocrinologists and has served as its president and as president of the American College of Endocrinology (ACE) of which he is an ongoing trustee and a founding trustee of the ACE Foundation. He proudly served on the Endocrine Society Clinical Affairs Committee and has frequently been a faculty member for ENDO annual meetings, including the Meet the Professor sessions.

Dr. Einhorn is president of Diabetes and Endocrine Associates, a private practice with his long-standing colleague, Raymond Fink, MD. He has made important contributions to the teaching program at the University of California, San Diego, where he is clinical professor of medicine. He is also advisor to six start-up biotech companies, is associate editor of the *Journal of Diabetes*, and is a trustee of the famed La Jolla Playhouse.

Over the years, Dr. Einhorn has become a clear clinical thought leader in endocrinology through leading consensus conferences, participating in guideline creation, innumerable CME lectures, and scientific advisory boards. Dr. Einhorn is beloved by his many devoted patients and the doctors in his community.

—ALAN J. GARBER, MD, PHD



Gerald D. Aurbach Award for Outstanding Translational Research

Eva L. Feldman, MD, PhD

Dr. Eva Feldman, MD, PhD, is an exceptional clinician-scientist who has devoted her career towards understanding diabetic neuropathy (DN), improving treatment options for her patients, and educating healthcare professionals on DN diagnosis and treatment.

With over 25 years of continuous NIH funding, her reputation is internationally recognized and she is an opinion leader in neurology. As a young neurologist, she developed a simple screening tool to diagnose DN, the Michigan Neuropathy Screening Instrument (MNSI). The initial paper describing this tool has been cited over 430 times, and the MNSI is now used worldwide and she oversees its use in multiple clinical trials (e.g. SEARCH, CACTI).

In the laboratory, her pioneering studies on neuropathy pathogenesis in metabolic diseases using cell-based models, novel mouse models, and human subjects has identified dyslipidemia during diabetes as a key driver of nervous system damage, leading to new clinical guidelines on patient care, and she serves as the principal investigator on grants aimed at completing comprehensive transcriptomic, proteomic, and metabolomic phenotyping of DN subjects to understand and drive the development of novel therapies.

Her work is reflected in over 350 manuscripts, 69 book chapters, and four books, and her numerous accolades include membership in the National Academy of Medicine and in 2016, Dr. Feldman received the National Physician of the Year for Clinical Excellence award from Castle Connolly in New York. She also directs the A. Alfred Taubman Medical Research Institute at the University of Michigan, is a past president of the American Neurological Association, and has mentored nine graduate students and over 100 research and clinical fellows throughout her career.

In summary, Dr. Feldman's exceptional clinical knowledge of DN, coupled with her passion for understanding its clinical course, identifying and treating affected patients, and educating colleagues on DN has transformed the DN landscape. She is an excellent example of the caliber of individual this award represents and is truly deserving of this award.

—DEREK LEROITH, MD, PHD



Outstanding Clinical Investigator Award

Joel Finkelstein, MD

Joel S. Finkelstein, professor of medicine at Massachusetts General Hospital and Harvard Medical School, is the recipient of the Endocrine Society's 2017 Clinical Investigator Award.

Dr. Finkelstein's work has generated new concepts in endocrine physiology while providing new information that has directly changed patient care. His early work describing osteoporosis in young men with GnRH deficiency led to the discovery that peak bone mass is compromised in men with histories of delayed puberty. With Dr. Matthew Smith, he demonstrated that antiresorptive agents can prevent GnRH agonist-induced bone loss in men with prostate cancer.

He supervised a group of medical residents at MGH who found that over half of medical inpatients were vitamin D deficient, a finding that raised awareness of the public health importance of vitamin D. He led the first randomized controlled trial demonstrating that daily teriparatide administration exerts an anabolic effect on bone in humans and later reported that bisphosphonates surprisingly attenuated teriparatide's anabolic effect.

As an investigator with the Study of Women's Health Across the Nation (SWAN) for nearly 25 years, he and his colleagues have characterized many of the physiologic and psychosocial changes that women experience across the menopause transition, including a comprehensive natural history of transmenopausal bone loss and the gradual decline in Anti-Müllerian Hormone levels that allows for accurate and precise predictions of the timing of the final menstrual period.

His group's recent work has established the levels of testosterone at which the key features of male hypogonadism begin to develop, thereby providing a physiologically based definition of male hypogonadism. Additionally, his group found many of the key features of male hypogonadism are due to estrogen deficiency rather than androgen deficiency. For this body of work, the Endocrine Society is pleased to present the 2017 Laureate Award for Clinical Investigation to Dr. Joel Finkelstein.

— ALVIN C. POWERS, MD



Sidney H. Ingbar Distinguished Service Award

Janet Hall, MD, MSc

Since her first service to the Endocrine Society as an abstract reviewer in 1990, Dr. Hall has served continuously on journal boards, Society committees, and/or in Society leadership positions. She has been a strong advocate of clinical and translational research both within and outside the Society; as chair of the Clinical Research Task Force, which resulted in restructuring the Research Affairs Committee to encompass Basic and Clinical Science Subcommittees; as the first Society vice president for clinical sciences and as the Society representative to the board of FASEB where she established and was the inaugural chair of the Clinical Research Subcommittee of FASEB's longstanding Public Advocacy Committee.

In addition, Dr. Hall has consistently advocated for close relationships across all of the Society's constituencies. Her nuanced understanding of the important issues for each constituency and her recognition of the thought leaders across the Society were particularly important on the AMSC, the Nominating and Laureate Awards Committees, on two separate Strategic Planning Committees, and as president of the Society.

Dr. Hall's service to the broader endocrine community is evidenced by her active participation in Women in Endocrinology, serving on and chairing the Nominating and Awards Committees and serving as president. Likewise, her service on review panels, advisory boards, and working groups has been extraordinary. In addition to two terms as a permanent member of an NIH study section, she has served more than 25 times as an ad hoc reviewer or site visit member and is a current member of the exam committee of the American Board of Internal Medicine.

With 25 years of exceptional service to the Endocrine Society and to the professional endocrinology community, Dr. Hall is an outstanding candidate for this award.

— NANCY WEIGEL, PHD, ON BEHALF OF WOMEN IN ENDOCRINOLOGY



Roy O. Greep Award for Outstanding Research

Klaus H. Kaestner, PhD

I am delighted to nominate Klaus H. Kaestner, PhD, for an Endocrine Society Roy O. Greep Award for Outstanding Research. Dr. Kaestner's work has combined innovative mouse genetics with state-of-the-art functional genomics to understand the molecular basis of the development and function of the liver and endocrine pancreas. He discovered the molecular basis of initiation of liver development (*Nature* 2005), and has made major contributions to our understanding the metabolic function of the liver. (*Cell Metabolism* 2005, 2009). He also has contributed groundbreaking studies of the epigenetic and chromatin landscape of the adult liver (*Nature Str Mol Biol* 2011) as well as embryonic stem cells (*Cell* 2012). In addition, Dr. Kaestner has combined genetic and genomic tools to explain the sexual dimorphism in liver cancer in mammals (*Cell* 2010).

Dr. Kaestner's work on the endocrine pancreas has been equally outstanding, elucidating unexpected roles and relationships between the earliest stages of development and the adult function of this vital organ in mouse models (*JCI* 2004; *Genes & Development* 2007, 2008). Most recently he has pioneered the epigenetics of human islets, leading to deeper understanding of islet cell plasticity (*JCI* 2013) and unprecedented insights into the pathology of beta cell dysfunction, including the discovery of microRNAs that are misregulated in beta-cells of type 2 diabetics (*Cell Metabolism* 2014) and aberrant DNA methylation that occurs with aging (*Cell Metabolism* 2015). Dr. Kaestner has also been a leader in multiple NIDDK-sponsored consortia, including the Beta Cell Biology Consortium, and the Human Islet Research Network (HIRN) consortium.

I have cited just a fraction of Dr. Kaestner's contributions, which in sum constitute a remarkable body of work that is notable not only for its quality, but for its innovation, thematic continuity, and importance to endocrinology. Dr. Kaestner's accomplishments make him highly deserving of an Endocrine Society Roy O. Greep Award Outstanding Research.

— MITCHELL A. LAZAR, MD, PHD



Outstanding Educator Award

Laurence Katznelson, MD

Professor Laurence Katznelson, MD, has had a very productive career as a clinical investigator in neuroendocrinology, making important contributions to our understanding of acromegaly, Cushing disease, and hypopituitarism. Moreover, he is clearly one of the elite endocrinology and internal medicine educators in the U.S.

As the director of the Endocrine Training Program at Stanford, he reconfigured the training curriculum, adding new fellow-based lectures and interdisciplinary conferences. Dr. Katznelson has won the Endocrine Division Teaching Award in an election by fellows and faculty, and he received the Excellence in Teaching Award from the School of Medicine.

He also served on the leadership council for APDEM. Larry has had a profound and lasting influence on endocrine training nationwide through his role as the director the Endocrine Society's Early Investigators Workshop for Trainees Program. Through this venue, Dr. Katznelson extended his educational outreach to literally hundreds of endocrine fellows around the world.

Dr. Katznelson is currently the Associate Dean for Graduate Medical Education (GME). In this role, he has succeeded in promoting training in quality improvement, spearheading wellness initiatives to prevent burnout and stress, and expanding recruitment and retention of under-represented minorities into the training programs and faculty. He is now a leader in GME on a national level.

Dr. Katznelson recently served as the chair of the task force for developing guidelines on the management of acromegaly for the Endocrine Society. He has served as chair for the Special Programs Committee, a committee tasked with expanding educational programs in endocrinology. He also served as AACE's task force chair for the 2011 update to the Acromegaly Guidelines, and he is also currently the chair of the Pituitary and Neuroendocrine Research Committee for AACE. In recognition of his work in education, he was awarded the H. Jack Baskin, MD, Endocrine Teaching Award at the AACE Congress Meeting in 2015.

— ANDREW HOFFMAN, MD



Fred Conrad Koch Lifetime Achievement Award

Walter L. Miller, MD

Walter L. Miller, MD, is distinguished professor emeritus of pediatrics in the Division of Endocrinology at UC San Francisco, where he served as chief of Endocrinology and director of the Pediatric Endocrinology Fellowship for almost two decades.

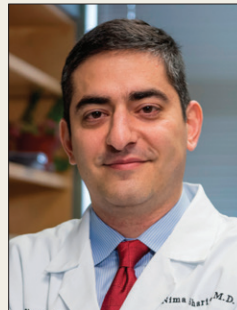
His career has been characterized by his courage to attack difficult scientific problems, his versatility to solve multiple disease-specific mysteries, and his dedication to mentoring. His laboratory cloned the human cDNAs for *CYP11A1*, *CYP17A1*, *FDX1*, *FDXR*, *TNX* overlapping *CYP21A2*, *CYP27B1*, and three *CP2* transcription factors. He determined the genetic basis for isolated 17,20-lyase deficiency, congenital lipoid adrenal hyperplasia, the contiguous gene syndrome of 21-hydroxylase deficiency with *TNX*-deficient Ehlers-Danlos syndrome, vitamin D 1 α -hydroxylase deficiency, and the P450-oxidoreductase deficiency spectrum including Antley-Bixler syndrome.

His work established many fundamental paradigms of the genetics, cell biology, biochemistry, and biophysics of human steroidogenesis and its disorders. He has mentored 107 research and clinical trainees, yielding 25 professors, 17 associate professors, 18 assistant professors, and 15 scientists in industry. His papers have been cited more than 21,000 times and he has been elected to the American Society for Clinical Investigation, the Association of American Physicians, and Fellowship in the American Association for the Advancement of Science.

His honors include the Edwin B. Astwood and Clinical Investigator Awards from the Endocrine Society, the Clinical Endocrinology Trust Medal from the British Endocrine Societies, the Van Wyk Award from the Pediatric Endocrine Society, Distinguished Alumnus of Duke Medical School, and the Henning Andersen and International Awards from the European Society for Paediatric Endocrinology.

His passion not only to *make* the discoveries but to *communicate* this work to the endocrine community has made him the undisputed authority in molecular steroidogenesis for 30 years. His distinguished and highly productive career and lasting legacy unquestionably qualifies him to receive the Fred Conrad Koch Lifetime Achievement Award.

— RICHARD AUCHUS, MD, PHD



Richard E. Weitzman Outstanding Early Career Investigator Award

Nima Sharifi, MD

Nima Sharifi, MD, is the Kendrick Family Endowed Chair for Prostate Cancer Research at the Cleveland Clinic Foundation. He has quickly become a leader in castration-resistant prostate cancer (CRPC) research, using innovative strategies to boldly rewrite the pathways of androgen synthesis and to unravel the endocrinology of this deadly hormone-dependent cancer. His laboratory demonstrated that 3 β -hydroxysteroid dehydrogenase-1 (3 β HSD1) is a key enzyme for the conversion of adrenal-derived precursors to androgens in prostate cancer cells and that the pathway from dehydroepiandrosterone to dihydrotestosterone primarily proceeds via androstenedione and 5 α -androstenedione rather than testosterone. He then explained why some CRPC cells have high 3 β HSD activity, due to a common germline allele that blocks ubiquitination and markedly prolongs the protein half-life without altering activity. He also showed that human CRPC metastases select for this allele, which portends poor prognosis. Most recently, his laboratory demonstrated that abiraterone, a CYP17A1 inhibitor, undergoes metabolism to active metabolites and that the 3-keto- Δ 4-homolog is a potent inhibitor not only of CYP17A1 but also 3 β HSD, 5 α -reductase, and the androgen receptor.

His distinguishing features include his bold approach to challenge dogma, his talent for designing the difficult but critically important experiments to directly address questions, his fearlessness when incorporating foreign techniques and venturing outside his comfort zone to solve these problems, and his insistence on taking his work from the bedside to the bench and back to the bedside.

His work has been recognized with the 2014 American Association for Cancer Research Award for Outstanding Achievement in Cancer Research, an American Cancer Society Research Scholar Award, election to the American Society of Clinical Investigation, and three R01 grants. He is also a dedicated and skilled teacher, mentor, and clinical oncologist. He is a uniquely qualified physician-scientist and an ideal candidate for the Richard E. Weitzman Outstanding Early Career Investigator Award.

— RICHARD AUCHUS, MD, PHD (BEING PRESENTED BY GARY D. HAMMER, MD, PHD)



Outstanding Innovation Award

Matthias Tschöep, MD

It was with great pleasure that I nominated physician-scientist Matthias Tschöep, MD, for the 2017 Outstanding Innovation Award of the Endocrine Society.

Professor Tschöep, who currently serves as director of the Helmholtz Diabetes Center and Chair of Metabolic Diseases at the Technische Universität München, Germany, discovered several leading classes of novel drug candidates in the field of diabetes, obesity, and metabolic diseases. His innovative and reproducible basic science work has led to development of multiple distinct novel investigational therapeutic agents now being assessed in clinical trials.

As a postdoctoral fellow, Dr. Tschöep reported on the orexigenic, adipogenic, and metabolic effects of ghrelin (*Nature*, 2000, >3500 citations). This groundbreaking discovery added a fundamental pathway to the model of body weight and glucose control, and established a novel set of drug targets (*Nature Medicine*, 2009; *Science*, 2010). He also was the first to report that ghrelin levels are regulated by both food intake and body weight (*Diabetes*, 2001; *J Endocrinol Invest*, 2001). He went on to collaborate with the chemist Richard DiMarchi to co-discover a paradigm shifting series of gut hormone-derived unimolecular polyagonists that target several neuroendocrine receptors, reduce body weight and improve glucose tolerance with unprecedented efficacy (*Nature Chemical Biology*, 2009; *Science Translational Medicine*, 2013, *Nature Medicine*, 2015).

Dr. Tschöep's innovative breakthroughs also encompass novel strategies for tissue-specific delivery of small molecules using peptide shuttles thereby more efficiently targeting pathological processes while minimizing toxic effects (*Nature Medicine*, 2012; *Cell*, 2016). In addition to more than 300 peer-reviewed publications, and numerous scientific awards (including Outstanding Scientific Achievement Awards of The Obesity Society 2009 and the American Diabetes Society 2011), Dr. Tschöep is an excellent collaborative colleague.

— DANIEL J. DRUCKER, MD



Outstanding Mentor Award

Margaret E. Wierman, MD

Margaret E. Wierman is a professor in medicine, physiology and biophysics and OBGYN at the University of Colorado. Throughout her career as a physician scientist, Dr. Wierman has mentored postdoctoral fellows, graduate and medical students, residents, and fellows with an infectious enthusiasm. She ensures each has a strong scientific foundation and intellectual curiosity to allow them to become “detectives” in understanding a complex patient or making an experimental advance in the laboratory.

Her insatiable thirst for new knowledge that she can apply to the bench and ultimately the bedside encourages trainees with a strong dose of perseverance when things don't always go right the first time. She helps each mentee to understand “the rules of the game” and to develop the skill sets and expertise to accomplish his or her goals. Dr. Wierman also provides the networking opportunities to her trainees that serve them well as they become independent investigators.

In addition to a commitment to individual mentoring, Dr. Wierman has developed and/or championed new programs or approaches to mentoring. Locally she developed and chairs the Colorado Clinical Translational Scientific Institute KTR mock study section program to help junior faculty in obtaining their first R type grant. Nationally, she set up the Women in Endocrinology Mentoring program that was later adopted by the Endocrine Society.

In her roles as president of Women in Endocrinology, on many Endocrine Society committees, Council, and as recent vice president clinical scientist, Dr. Wierman has encouraged the development of new initiatives to encourage mentoring across our constituencies of basic and clinical scientists and clinicians to support both individual development and enrich the diversity of the endocrine community. Margaret E. Wierman is most deserving of the 2017 Outstanding Mentor Award.

— JENNIFER RICHER, PHD



International Excellence in Endocrinology Award

Chandrika Wijeyaratne, DM, MD

It is my great privilege to nominate a remarkable physician, Dr. Chandrika Wijeyaratne, for the Endocrine Society's International Excellence in Endocrinology Award. She is professor of reproductive medicine in the Department of Obstetrics and Gynecology, University of Colombo, and Honorary Consultant Physician and Endocrinologist at the De Soysa Hospital for Women in Sri Lanka.

In 1993, Dr. Wijeyaratne became the first endocrinologist appointed to an academic position in Sri Lanka. She went on to establish Reproductive Medicine and Maternal Health as centers of excellence within the country. Her research interests include polycystic ovarian syndrome (PCOS), insulin resistance in South Asians, and medical disorders of pregnancy. She established a large database of local research in reproductive health and led several critical studies showing the high prevalence of metabolic dysfunction and gestational diabetes among South Asian women.

Dr. Wijeyaratne served as president of the Sri Lankan Endocrine Society and is president-elect of the Sri-Lanka Medical Association (SLMA). In 2008, she organized the largest project ever undertaken by the SLMA, obtaining over \$1 million from the World Diabetes Foundation to address the identification, control, and prevention of diabetes and cardiovascular disease (CVD) throughout Sri Lanka.

She has also left her mark on medical and postgraduate education, developing an innovative medical school curriculum and encouraging a large number of trainees to enter the field. She continues to see adults with complex endocrinopathies and serves as a clinical consultant for all pregnant women with severe endocrine complications.

As her extensive CV attests, virtually every aspect of endocrine research, education, clinical practice, and public health in Sri Lanka has been deeply impacted by Dr. Wijeyaratne's leadership. I can think of no worthier recipient for the International Excellence in Endocrinology Award than Dr. Chandrika Wijeyaratne.

— CAROLYN BECKER, MD



Outstanding Leadership in Endocrinology Award

Teresa K. Woodruff, PhD

Dr. Teresa Woodruff has been a remarkable leader within the Endocrine Society, at her institution, nationally, and globally.


Among her accomplishments as Endocrine Society president were overseeing changes in brand identity for the Society, a new logo and tagline, the purchase of the new Endocrine Society headquarters, and the hiring of a new CEO. She expanded the advocacy agenda and initiated changes in the Laureate Awards, so they reflect the diverse activities of the members.

At Northwestern, she is the vice chair for research in the Department of Obstetrics and Gynecology and director of the Northwestern University Center for Reproductive Science. Dr. Woodruff is the founder and director of the Oncofertility Consortium, a global program that provides fertility options to young cancer patients. She coined the term "oncofertility" which is now a medical specialty.

Dr. Woodruff is the founder and director of the Women's Health Research Institute, an organization that provides advocacy on sex-inclusion policies at the local and national level and she is a member of the NIH Office of Research on Women's Health council. She created the Women's Health Summer Academy program, including the Oncofertility Saturday Academy, which attracts girls from Chicago to lab and career building programs.

Her accomplishments have been recognized by numerous awards. In 2013, she was ranked 112th in *Time Magazine's* Most Influential People in the World list and in 2011 was awarded the Presidential Award for Excellence in Science, Mathematics, and Engineering Mentoring, which was presented in the Oval Office. In summary, Dr. Woodruff's accomplishments have had extraordinary and wide-reaching impact on the Endocrine Society, on endocrine research, on women's health and science mentoring, and on developing new options for preserving fertility in cancer patients.

— KELLY E. MAYO, PHD

A close-up photograph showing a hand holding a red aluminum can, tilted to pour a dark, carbonated beverage into a clear glass. The glass is filled with ice cubes and the liquid is bubbling. The background is plain white.

**Controlled trials
show non-nutritive
sweeteners can sometimes
help in weight loss, but
observational and animal
studies raise concerns
about their risks.**

Sweet & LOWDOWN:

Do Artificial Sweeteners Actually Contribute to Weight Gain?

BY ERIC SEABORG



A patient asks: “Do you recommend the use of artificial sweeteners, as in diet sodas, for weight loss?”

Do you respond:

- a.** Randomized controlled trials consistently show that diet sodas are helpful for weight loss when included in a program of diet and exercise.
- b.** The U.S. Dietary Guidelines Advisory Committee says that there is insufficient evidence to recommend the use of low-calorie sweeteners as a strategy for long-term weight loss and weight maintenance.
- c.** Reducing your intake of sugary beverages is a good thing.
- d.** Some observational studies have associated the use of non-nutritive sweeteners with weight gain, and animal studies suggest that they may perturb metabolism.

If you’ve read enough stories with leads like this, you know that “all of the above” is the correct response. And the debate over the role of sweeteners is growing in importance as their use continues to grow and as they turn up in more and more products — often without consumers being aware of them.

Lose Weight in Clinical Trials

“There is an overwhelming amount of evidence that they can be useful as a tool for weight management, when people are actually cognitively engaged in trying to lose weight ... as part of a program or following a plan,” says John C. Peters, PhD, professor and chief of strategy and innovation at the University of Colorado Anschutz Health and Wellness Center, Aurora. Peters was the lead author of a study published in the February issue of *Obesity* in which 303 overweight or obese participants were randomly assigned to consume 24 ounces of either water or non-nutritive-sweetened beverages every day. They also participated in a weight loss intervention program. At 12 weeks, the non-nutritive sweetener participants had lost more weight — 6 kg vs. 4 kg for the water group. After a year, the sweetener group maintained a loss of 6.2 kg compared with 2.5 kg for the water group.

This weight-loss benefit is consistent with the findings of other trials, Peters says. The benefit is generally attributed to the beverages’ ability to satisfy a need for sweetness without adding calories.

“However, such studies may not reflect all of the ways that consumers actually use the sweeteners and cannot account for counterproductive behaviors that may be prompted by consumer beliefs or expectations about the product, for example, giving themselves permission to eat the hot fudge sundae because they had a diet soda,” Peters says. “Most people actually add these to their diet. They don’t substitute them for regular sugar beverages.”

Observations of Weight Gain and More

This kind of use could be one reason that some observational studies have tied diet sodas to weight gain rather than loss. For example, investigators at the University of Texas Health Science Center at San Antonio studied 3,700 participants aged 25 to 65 years old. Those who were normal weight or overweight at baseline and consumed more than three artificially sweetened beverages a day were twice as likely to become obese within the next eight years compared with those who consumed none. In another study of 470 participants aged 65 or older at baseline who were followed for an average of nine years, the increase in waist circumference among self-reported daily diet soda drinkers was almost four times that of nondrinkers: 3.2 inches vs. 0.8 inches.

Last year, a study from *JAMA Pediatrics* of 3,000 mother-infant pairs found that daily consumption of artificially sweetened beverages by a mother during pregnancy was associated with a statistically significant increase in the infant’s BMI, and a twofold increase in the infant’s risk of being overweight at one year of age.

Susan Swithers, PhD, professor of behavioral neuroscience at Purdue University, West Lafayette, Ind., says of the observational data: “The more of those studies that get published, the more evidence we have that people who have chosen to consume diet sodas really don’t end up with better health outcomes, and in many cases, their risks are elevated. Accumulating evidence suggests that frequent consumers of these sugar substitutes may be at risk of excessive weight gain, metabolic syndrome, type 2 diabetes, and cardiovascular disease.”

However, many disagree with Swithers’ interpretation. “The largest observational trials, such as the two nurses’ health studies and the health professional follow-up study all show diet beverage use is associated with small weight loss,” Peters says. Analyses of the literature have come to conflicting conclusions, with a 2015 review in the *International Journal of Obesity* concluding: “Overall, the balance of evidence indicates that use of [low-energy sweeteners] *in place of sugar*, in children and adults, leads to reduced [energy intake] and [body weight], and possibly also when compared with water.” (*emphasis added*)

A criticism of many observational studies is that they cannot rule out a “reverse causality” explanation: The association appears not because diet sodas are causing weight gain, but because people at risk for and on the road to obesity drink more diet sodas than the general population.

But Swithers says that the human indications are backed up by many studies in animals in which causation is clearer: “Under certain circumstances, animals given artificial sweeteners end up gaining excess weight, becoming fatter, or showing metabolic deficits, for example, in terms of their ability to regulate blood sugar levels.”

Gut Instinct

With the gut microbiome receiving increasing attention in recent years, studies of sweeteners’ effects have raised concerns in this area. In a 2014 *Nature* study, researchers added saccharin, sucralose, and aspartame to the drinking water of mice.



The 2012 joint scientific statement from the American Heart Association and the American Diabetes Association says, “There are insufficient data to determine whether the use of [nonnutritive sweeteners] to displace caloric sweeteners in beverages and foods reduces added sugars or carbohydrate intakes, or benefits appetite, energy balance, body weight, or cardiometabolic risk factors.”

After a week, the artificial sweetener group had developed glucose intolerance, whereas comparison groups that drank plain water or sugar water had not. When the researchers treated the mice with antibiotics designed to kill the gut bacteria, the glucose intolerance disappeared.

They next fed a group of mice saccharin until the mice developed glucose intolerance. When they transferred the gut bacteria from these mice into mice that had not been exposed to saccharin, the injected mice developed glucose intolerance. DNA sequencing of fecal material found a different mix of bacteria in saccharin-fed mice compared with those not fed saccharin. The researchers also analyzed the gut bacteria of almost 400 people, and found that regular users of artificial sweeteners had differences in their microflora that have been associated with type 2 diabetes.

Teasing out the effects of sweeteners is complicated by the fact that there are a half dozen of them, and each has its own metabolic pathway. For example, aspartame is metabolized quickly into its components. The most studied sweetener is saccharin, but it has been supplanted as market leader by sucralose, brand name Splenda. Sucralose is largely unmetabolized and excreted in its original form, which means that it is still behaving as a sweetener in the lower gastrointestinal tract and other parts of the body.

A recent *Journal of Toxicology and Environmental Health* study of artificial sweeteners in breast milk may increase the urgency of finding answers to some of these questions. Breast milk samples were collected from 20 lactating volunteers and tested for artificial sweeteners. Saccharin, sucralose, and acesulfame-potassium were present in 65% of the samples. No aspartame was found, probably because aspartame is metabolized rapidly. But perhaps the most striking finding was that acesulfame-potassium was found in the breast milk of four participants who reported they had not consumed any food or beverages that contain it.

AT A GLANCE

- ▶ Random controlled trials show a modest weight benefit for artificial sweeteners used as part of a weight-loss program, but it is doubtful that consumers generally use them that way.
- ▶ Artificial sweetener proponents say it must be better to replace sugar with a calorie-free alternative, but critics respond that it is naive to think that is the primary role sweeteners play — and observational and animal studies indicate they may come with health risks.
- ▶ Recommendations from organizations like the U.S. Dietary Guidelines Advisory Committee say there is insufficient evidence to recommend using sweeteners for goals like weight loss.



“ There is an overwhelming amount of evidence that [artificial sweeteners] can be useful as a tool for weight management, **when people are actually cognitively engaged in trying to lose weight ...** as part of a program or following a plan.”

— JOHN C. PETERS, PHD, PROFESSOR,
CHIEF OF STRATEGY AND INNOVATION,
UNIVERSITY OF COLORADO ANSCHUTZ
HEALTH AND WELLNESS CENTER, AURORA

Although the sweeteners were detected at trace levels, the sucralose concentrations were “at levels that infants can perceive as sweet,” according to study author Allison Sylvestry, PhD, assistant professor in the department of exercise and nutrition sciences at George Washington University’s Milken Institute School of Public Health. “So the big question is, what does that mean for the infants’ developing taste preferences, the colonization of their gut microbiomes, and their future risk of metabolic impairments? The rodent data shows that early life exposure to acesulfame-potassium, whether it is *in utero* or during lactation, leads to changes in taste preferences. And metabolic impairments have also been shown following early life exposure to aspartame in animal models.”

Guideline Recommendations

Given the complexities and unknowns, perhaps the most evidence-based answers to the patient’s question can come from recent guidelines. The 2012 joint scientific statement from the American Heart Association and the American Diabetes Association says, “There are insufficient data to determine whether the use of [nonnutritive sweeteners] to displace caloric sweeteners in beverages and foods reduces added sugars or carbohydrate intakes, or benefits appetite, energy balance, body weight, or cardiometabolic risk factors.”

And the 2015 scientific report of the U.S. Dietary Guidelines Advisory Committee says: “There is insufficient evidence to recommend the use of low-calorie sweeteners as a strategy for long-term weight loss and weight maintenance. Since the long-term effects of low-calorie sweeteners are still uncertain, those sweeteners should not be recommended for use as a primary replacement/substitute for added sugars in foods and beverages.” ^{EN}

SEABORG IS A FREELANCE WRITER BASED IN CHARLOTTESVILLE, VA. HE WROTE ABOUT THE ENDOCRINE SOCIETY’S NEW CLINICAL PRACTICE GUIDELINE ON TREATING PRIMARY ALDOSTERONISM IN THE SEPTEMBER ISSUE.



The Genetics and Epigenetics of Puberty

BY ANA CLAUDIA LATRONICO, MD, PHD;
RAVIKUMAR BALASUBRAMANIAN, MD,
PHD, MRCP; WILLIAM F. CROWLEY JR., MD;
SERGIO R. OJEDA, DVM; AND ALEJANDRO
LOMNICZI, PHD

A wide-ranging look at puberty and the many mysteries that surround it, as well as the clinical management, new genetic tools, and how a variety of factors could influence the timing of this transition into adulthood.



In 2005, the editors of *Science*, celebrating the journal's 125th anniversary, posed 125 unanswered questions that it predicted would fuel active research in the following century. High on the list of mysteries was “what triggers puberty?” Indeed, this question has perplexed clinicians, scientists, and parents for centuries.

Though we still lack a clear answer, technological and theoretical advances over the past 10 years have gotten us closer than we have ever been to a solution. Next generation sequencing approaches have uncovered genes never before implicated in the neuroendocrine control of puberty. At the same time, our understanding of gene regulation beyond the DNA sequence, so

called epigenetics, has revealed insights into molecular switches in the brain that both silence and activate activity of gonadotropin-releasing hormone (GnRH) and associated neurons.

In this Tri-Point, a pediatric endocrinologist discusses the discovery of novel genetic causes of both delayed and precocious puberty. Next, two clinician-scientists describe how new genetic tools have uncovered a suite of genes regulating the development and function of GnRH neurons. Finally, two basic scientists describe new advances in our understanding of epigenetic regulation of GnRH secretion, shedding light on how genetic polymorphisms, nutrition, and environmental exposures may affect the timing of puberty.

A Clinical Practitioner's Perspective

— ANA CLAUDIA LATRONICO, MD, PHD

Pubertal timing is influenced by complex interactions among genetic, nutritional, environmental, and socioeconomic factors. The timing and onset of puberty varies widely in the general population. Early or delayed timing of puberty in girls or boys is associated with increased risks for several adverse outcomes across a range of oncogenic, cardiometabolic, gynecological or obstetric, gastrointestinal, musculoskeletal, and neurocognitive conditions. Frequently, my patients with distinct pubertal disorders have questioned me as to why do they have this problem. Fortunately, understanding of the molecular genetics of human pubertal disorders, such as congenital hypogonadotropic hypogonadism and central precocious puberty, has advanced tremendously in the past 20 years, and I have been able to give them some of the answers.

Congenital Hypogonadotropic Hypogonadism

Congenital Hypogonadotropic Hypogonadism (CHH) also known as isolated GnRH deficiency, (IGD) is genetically heterogeneous, with both sporadic and familial cases. Several modes of inheritance were identified in this condition, including X chromosome-linked recessive, autosomal recessive, and dominant. To date, more than 25 different genes have been implicated in CHH; in patients with CHH, genetic testing is useful for diagnosis, prognosis, and genetic counseling. Inheritance pattern and presence of additional phenotypic features such as anosmia, cleft lip or palate, dental agenesis, ear anomalies, congenital hearing impairment, renal agenesis, bimanual synkinesis, skeletal anomalies, or early onset of morbid obesity might guide genetic testing.

Combining CHH with specific associated phenotypes can increase the probability of finding causal mutations by targeted gene sequencing. However, oligogenic forms (mutations in several genes, <6) have been identified in CHH. Genetic counseling can be difficult and the transmission risk may be variable when CHH patients carry several mutations in different genes. More recently, we have used pooled targeted sequencing of known genes using next-generation DNA sequencing technology for better and complete genetic diagnosis of CHH. Notably, reversibility of CHH can occur in both male and female cases (approximately 10% - 15%). This phenomenon highlights the importance of environmental (epigenetic) factors such as sex steroid treatment on the reproductive axis in

modifying the phenotype. Interestingly, rare loss-of-function mutations in *IGSF10*, a gene that codifies a factor involved in embryonic migration of immature GnRH neurons, were recently identified in several unrelated families with self-limited delayed puberty using exome and candidate gene sequencing, indicating the role of genetic factors in a wide spectrum of conditions characterized by delayed puberty, from self-limited delayed puberty to functional or permanent hypogonadotropic hypogonadism.

Central Precocious Puberty

I have always been surprised by the high prevalence of idiopathic Central Precocious Puberty (CPP) cases, especially in girls. The evidence of familial CPP (up to 20%) as well as my previous work in genetic causes of peripheral precocious puberty, such as testotoxicosis, stimulated my research group to investigate the potential role of genetic factors in these families. Recently, using whole-exome sequencing, we identified a gene, *MKRN3*, in the premature reactivation of GnRH secretion leading to CPP in nonsyndromic children. After this discovery, a growing list of loss-of-function mutations of *MKRN3* was described in patients with CPP from both sexes and different ethnic backgrounds. Indeed, these mutations now represent a frequent cause of familial CPP (around 40% of the studied cases). *MKRN3*, an imprinted gene located on the long arm of chromosome 15 (Prader Willi critical region), encodes makorin ring finger protein 3, which is the first factor with an inhibitory effect on GnRH secretion. *MKRN3* protein is derived exclusively from RNA transcribed from the paternally inherited copy of the gene due to maternal imprinting. Segregation analysis of the families with CPP due to *MKRN3* defects clearly demonstrated an autosomal dominant inheritance with complete penetrance. Because of the imprinting pattern (maternally silenced) of *MKRN3*, the CPP phenotype can be inherited from an asymptomatic father who carries a *MKRN3* defect.

Our studies showed that the familial nature of CPP is likely under-recognized due to the difficulty of obtaining a precise family history from the father's side and the likelihood for under diagnosis of early testicular enlargement. Interestingly, the identification of the *MKRN3* loss-of-function mutations as a cause of CPP has impacted current clinical investigation of this common pediatric condition. For instance, routine screening by brain MRI is not useful in patients with a clear family history, such as two siblings with CPP. In these



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HIGHLIGHTS

Congenital hypogonadotropic hypogonadism is genetically heterogeneous (>25 different genes) with several modes of inheritance.

Loss-of-function mutations of *MKRN3* gene represent a frequent cause of familial central precocious puberty (40% of the studied cases).

Genetic testing is useful for diagnosis, prognosis, and genetic counseling in human pubertal disorders.

“ I have always been surprised by the high prevalence of idiopathic Central Precocious Puberty (CPP) cases, especially in girls.”



familial cases, genetic studies should precede brain MRIs, which might be postponed (in non-mutant cases) or even avoided in those patients with identified loss-of-function *MKRN3* mutations. In addition, the financial costs to perform the genetic analysis of *MKRN3*, an intronless gene, are significantly lower than a brain MRI scan in children, who usually need anesthesia support.

Finally, next generation sequencing analysis, including pooled target sequencing, whole-exome, or whole-genome sequencing, will improve the molecular genetics diagnosis

of human pubertal disorders, promoting earlier diagnosis and personalized approaches to genetic counseling. The clinical use of next generation sequencing is expected to increase rapidly in the coming years with decreasing costs, increasing availability, and high diagnostic yield. New genetic findings affecting regulatory genomic regions, microRNAs, or methylation sites (epigenetic phenomena), leading consequently to abnormal gene expression, are also expected to be discovered as causes of human pubertal disorders in the near future.

Clinical-Scientists' Perspective

— RAVIKUMAR BALASUBRAMANIAN, MD, PHD, MRCP, AND WILLIAM F. CROWLEY JR., MD

GnRH Neurons: The Master Regulator of Human Puberty

Developmentally, a series of dynamic and complex genetic networks oversee the ontogeny of the GnRH neurons and their ability to coordinate the hypothalamic secretion of GnRH that eventually triggers puberty and sustains the reproductive axis throughout adulthood. Despite growing understanding of the genes controlling the physiology of GnRH's secretion and action, the full constituency of the genetic and epigenetic networks that are responsible for the pubertal transition remains incomplete. Given the evolutionary importance of reproduction in speciation, these pathways must have had to continually adapt and evolve to overcome the myriad of powerful adverse environmental challenges that each organism must have faced.

The need for such tightly regulated controls argues strongly for the presence of a highly conserved, multi-

tiered network of neurodevelopmental and neuroendocrine genes controlling GnRH. In keeping with this notion, the study of humans with Isolated GnRH deficiency [IGD] (also referred to in the literature as congenital hypogonadotropic hypogonadism), representing a “human knock out” model for GnRH deficiency, has been prismatic in unraveling the fascinating ontogeny of GnRH neurons. Combined with the study of animal models of hypogonadotropic hypogonadism in which interventions can be induced, research over the last three decades has enabled an explosion in the discovery of novel genes governing puberty.

Genes and Pathways that Govern Puberty in Humans

The initial insights into the genetic control of puberty came from the study of humans with Kallmann's Syndrome (KS). KS patients display complex syndromic phenotypes and were subsequently found to harbor deletions and



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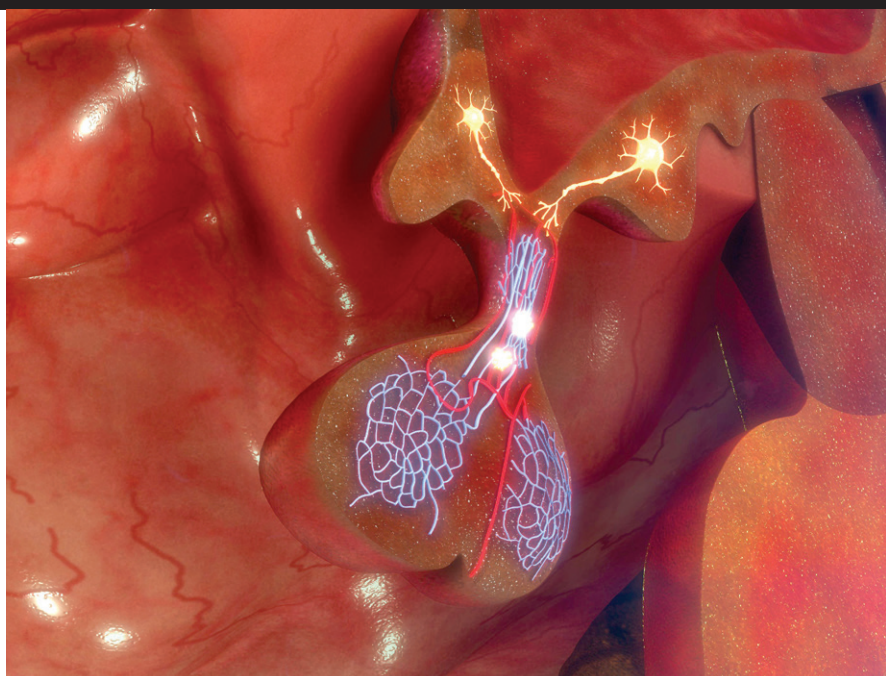
HIGHLIGHTS

Genetic studies in humans with IGD have provided unprecedented insights into the genes and pathways that govern GnRH neurogenesis, migration, secretion, and function.

The advent of next-generation sequencing will hasten the genetic discovery process and likely unravel novel insights into the genetic and epigenetic control of puberty.

These discoveries will provide opportunities to translate these findings to help diagnosis and therapy of both rare and common reproductive conditions.

“**Developmentally, a series of dynamic and complex genetic networks oversee the ontogeny of the GnRH neurons and their ability to coordinate the hypothalamic secretion of GnRH that eventually triggers puberty and sustains the reproductive axis throughout adulthood.**”



mutations in the *KALI* gene (now called *ANOS1*). A series of fascinating clinical investigative studies in these patients subsequently confirmed what had previously been demonstrated in fetal mice by Donald Pfaff and his colleagues at Rockefeller University: GnRH neurons had embryonic origins from outside the central nervous system, emanating from the olfactory placode! Following these initial seminal observations, >25 genes have been shown to cause IGD, each of which either disrupts embryonic migration of GnRH neurons (neurodevelopmental genes, causing the anosmic form of IGD or KS) or affects GnRH secretion/action (neuroendocrine genes, causing the normosmic form of IGD [nIGD]) or play a role in both migration as well as function (overlap genes, causing either KS or nIGD or in some cases both phenotypes in a single family).

To uncover the above genes, clinical investigators have used several complementary approaches:

- (i) homozygosity mapping in endogamous pedigrees (*KISS1*, *KISS1R*, *TAC3*, *TACR3*);
- (ii) mapping genes in genomic alterations/contiguous gene syndrome/copy number changes (*FGFR1*, *WDR11*, *SEMA3A*);
- (iii) bioinformatic pathway approaches (*IL17RD*, *FGF17*, *DUSP6*, *FLRT3*, *SPRY4*);
- (iv) candidate gene approaches (*GNRH1*, *GNRHR*, *FGF8*, *PROK2*, *PROKR2*, *NSMF*);
- (v) study of syndromic IGD phenotypes (*CHD7*, *SOX10*, *HS6ST1*, *LEP*, *LEPR*, *PCSK1*, *NROB1*, *RNF216*, *OTUD4*, *TUBB3*, *POLR3A*, *POLR3B*, *PNPLA6*, *DMXL2*); and
- (vi) more recently exome sequencing +/- homozygosity mapping (*FEZF1*, *CCDC141*, *SEMA3E*).

Translation of Genetic Findings from IGD: Bench to Bedside

These discoveries have not only shed remarkable new light on the origins and functions of GnRH neurons that could not have been obtained in other ways, but, perhaps more importantly, they have initiated novel 'therapeutic cascades' that ultimately may lead to new diagnostic and therapeutic opportunities. In particular, two novel hypothalamic neuropeptide signaling systems (kisspeptin and neurokinin B), now known to lie upstream of GnRH and govern its secretion, are at the forefront. Promising investigations to determine kisspeptin's potential diagnostic/therapeutic role in several reproductive disorders are currently underway with several pharmaceutical firms beginning to develop kisspeptin analogues. Likewise, identification of novel neurodevelopment genes encoding the neural crest pathway (*SOX10*, *CHD7*) have begun to improve our fundamental understanding of the embryonic origins of GnRH neurons in ways that were not possible prior to the The Human Genome Project. Collectively, these studies now suggest a contribution from the neural crest cells in addition to the known contribution from the placodal cells.

Genetic Crossroads: Next-Generation Sequencing, Genome-Wide Association Studies, and the Role of Epigenetics in Puberty

In addition to the known Mendelian inheritance of IGD, a previously unappreciated genetic feature of IGD has also emerged. A systematic search of eight IGD genes in nearly 400 IGD cases showed that ~3% of these cases unexpectedly harbored mutations in more than two known IGD genes, thus establishing the presence of 'modifying genes' or oligogenicity as a novel characteristic of IGD's genetic architecture. Fascinatingly, as opposed to most Mendelian mutations that are unique or 'private,' some mutations that occur in IGD patients are recurrent, occurring in IGD individuals from different geographical regions and varied ancestry. More detailed studies

of the origin of these recurrent mutations have revealed that some represent ancient founder alleles. For example, one recurrent *PROKR2* mutation (L173R) represents a 9,000-year-old loss of function mutation in this reproductive controlling gene! These founder alleles argue for the possibility of variants contributing to some as-yet-unknown survival benefit and consequently able to undergo positive selection across populations and time. In some cases, KS and normosmic IGD occur within a single family sharing a similar genetic milieu. In other rare instances, monozygotic twins had been known to be discordant for IGD, suggesting that additional genetic, epigenetic, or environmental factors may also influence the expression of the IGD phenotype. The role of epigenetics is also suggested from the fact that some IGD patients with known mutations may recover spontaneously later in life, signaling a reversal of GnRH deficiency.

Despite this remarkable progress, it is clear that several novel genes remain to be discovered and the collaboration between clinicians seeing these patients and clinical investigators investigating their genetics will remain crucial in the future. The growing genetic, clinical, and molecular complexity of IGD clearly warrants an integrated investigatory approach that combines the deep phenotyping of IGD patients, the use of emerging next generation sequencing (NGS) to aid novel gene discovery,

and the use of bioinformatics to expand the biology of these evolving genes and their related signaling pathways. With reducing sequencing costs and increasing access to whole exome and whole genome technologies, further novel genes, potential regulatory and non-coding variants, and epigenetic modifications that cause IGD are likely to be discovered.

However, these approaches will also lead to a surge in data and the need for prioritization and functional validation, which are two key challenges to avoid false positive associations. Finally, several of the Mendelian genes that govern puberty are also being detected via genome-wide association studies (GWAS) of common reproductive complex traits in large populations. The results of these studies suggest that the genetic control of reproduction represents a continuum ranging from common variants with low effect size that underlie many common reproductive conditions (such as hypothalamic amenorrhea) to rare variants with high effect size that result in extreme phenotypes such as KS. The precise biological basis of the onset of human puberty has been cited as one of the critical unanswered scientific questions in the 21st century. The prismatic human model of IGD and concurrent advances in genomic technologies now provide an unprecedented opportunity to unravel the black box of puberty.

Basic Researchers' Perspective

— SERGIO R. OJEDA, DVM, AND ALEJANDRO LOMNICZI, PHD

By identifying genes required for puberty, genetic approaches have led to magnificent breakthroughs in understanding the pubertal process in humans. Genome-wide association studies have, however, hinted at a much greater complexity by demonstrating the existence of more than 100 polymorphisms associated with the timing of puberty in human females. And yet, all of these modifications in DNA sequence together explain less than 5% of pubertal disorders, including idiopathic precocious puberty and delayed puberty. The inescapable conclusion is that information other than that provided by DNA sequence must play an important role not only in the etiology of pubertal disorders, but also in defining normal variability in the timing of puberty. At the risk of oversimplification, we submit that epigenetics provides the most robust means of integrating cues and coordinating gene networks involved in the neuroendocrine control of puberty.

Epigenetic Control of Gene Regulatory Networks

The concept that epigenetics play a major role in the neuroendocrine process controlling the timing of puberty has been established in the last few years. Work from other fields provides unquestionable support for the idea that entire gene networks are subject to epigenetic regulation, and that this regulation is furnished by a myriad of molecules. These include enzymes that modify the methylation status of DNA, and others that post-translationally modify histones in regulatory genomic regions. More recently, the category of epigenetic regulators has been expanded to include a vast array of microRNAs, long noncoding RNAs, and methyl adenosine-modified messenger RNAs. It is also now clear that complex biological processes are controlled by a diversity of genes that operate within the constraints of a hierarchy.



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HIGHLIGHTS

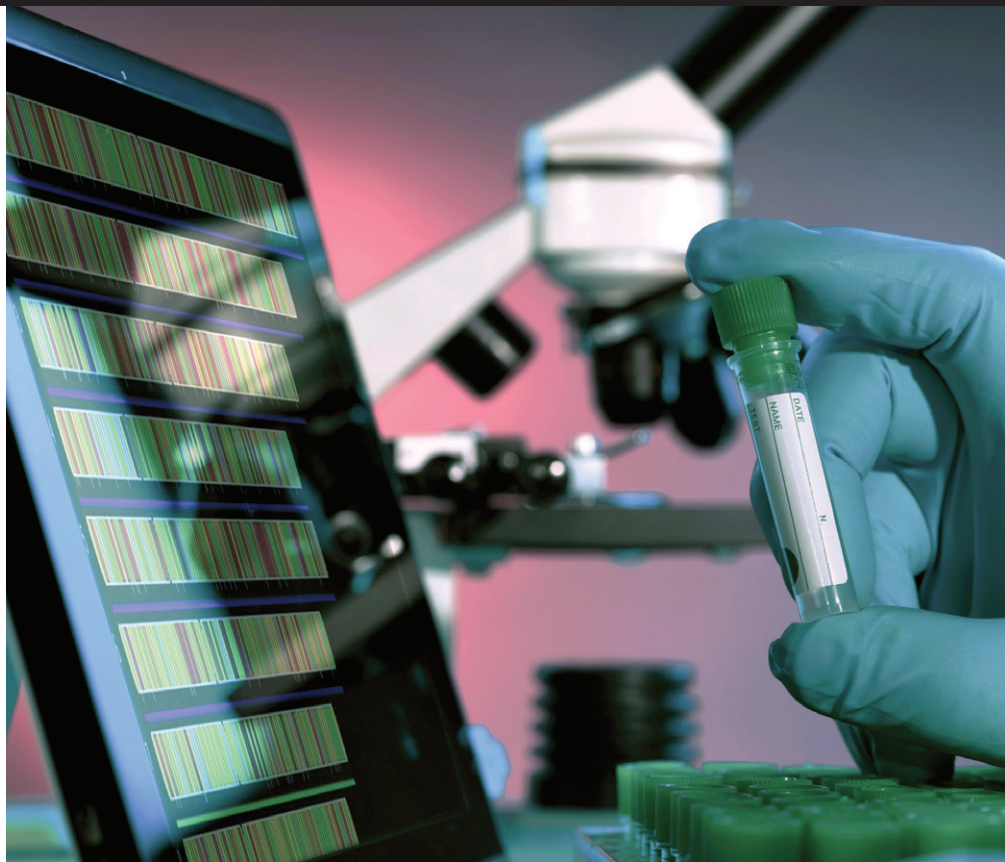
The timing of puberty is controlled by epigenetic mechanisms affecting the activity of hypothalamic neurons required for puberty to occur.

The epigenetic control of puberty depends on a balance between transcriptional repression and activation of gene expression.

The repressive control of puberty is provided by the Polycomb group of transcriptional silencers that restrains gene expression directly, and by zinc finger proteins that reduce gene expression by antagonizing the effect of the Trithorax group of transcriptional activators.

The transcriptional activation of puberty is provided by the Trithorax group of transcriptional activators, which counterbalances the repressive effect of the Polycomb group.

“The inescapable conclusion is that information other than that provided by DNA sequence must play an important role not only in the etiology of pubertal disorders, but also in defining normal variability in the timing of puberty.”



Epigenetic Changes Associated to Puberty


During normal peripubertal development, an increase in GnRH secretion is accompanied by reduced DNA methylation of the GnRH promoter. Another epigenetic change that appears to occur as puberty progresses is the deposition of “activating” histone marks at the promoter of the *Kiss1* gene in kisspeptin neurons involved in mediating the positive feedback of estrogen on gonadotropin secretion.

Epigenetic Control of the Timing of Puberty

The epigenetic control of the timing of puberty involves lifting of a repressive tone exerted by the Polycomb group (PcG) of transcriptional silencers on the *Kiss1* gene expressed in neurons of the hypothalamic arcuate nucleus (ARC), known as KNDy neurons because they produce the peptides kisspeptin, neurokinin B, and dynorphin. KNDy neurons are directly involved in the control of pulsatile GnRH release, which increases in a diurnal fashion with the advent of puberty. We also observed that these changes in PcG-mediated repression are complemented by post-translational histone modifications catalyzed by, or associated with, the Trithorax group (TrxG) of transcriptional activators. The presence of both systems of epigenetic regulation in KNDy neurons suggests that a switch from epigenetic repression to activation within these neurons underlies the developmental process by which pulsatile GnRH release is first kept in check before puberty, and then increases by late juvenile development to bring about the pubertal process.

An additional layer of repressive control appears to prevent the precocious activation of the GnRH pulse generator that could result from premature loss of PcG-mediated repression or an untimely surge of TrxG-dependent transcriptional activation. This repressive effect is exerted by members of a large family of more than 800 transcriptional repressors known as zinc finger proteins (ZNFs) because they contain multiple zinc finger motifs. Studying one of these proteins, GATAD1, suggested that ZNFs may keep puberty in check by promoting the erasure of TrxG-dependent histone marks associated with gene activation. GATAD1 exerts this effect on the promoter of downstream genes required for puberty to occur (such as *KISS1* and *TAC3*). Because this inhibitory influence decreases at puberty, it seems reasonable to conclude that once ZNF-dependent interference is lifted and PcG-mediated repression is lost, transcriptional activation can proceed unimpeded, setting in motion the pubertal process.

Perspective

Though exciting, these studies represent only the initial steps in the quest to unravel the role of epigenetics in the regulation of puberty. We envision that in the near future, new studies will identify epigenetic pathways linking alterations in nutritional availability, circadian cues, and man-made environmental toxins (including endocrine disruptors) with the timing, progression, and completion of the pubertal process. Furthermore, we predict that in a not-too-distant future, alterations in epigenetic regulation will be uncovered as an underlying cause of the intractable disorders of idiopathic precocious puberty and constitutionally delayed puberty. 

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Lawyering Up

When it's time to accept a new position, consider having a lawyer who specializes in physician contracts on your side before you sign on the dotted line.

BY KURT ULLMAN



Unless you are planning on spending your entire career in solo practice, you will have to negotiate an employment agreement. The wording of your contract may well determine your employment satisfaction.

“An employment contract is a big commitment and you want to make sure everything is right before you go into it,” says Dennis Hursh, a healthcare attorney at Hursh & Hursh, PC in Middletown, Pa. “Keeping both you and your potential employer satisfied with the relationship is mutually beneficial in the long term.”

Some physicians may think that having an attorney review your contract indicates mistrust in your colleagues. However, having someone look over the agreement and making sure you understand your rights and responsibilities, as well as those of your employer, can make the difference between a good experience or one that isn't so fulfilling.

Reflecting Things Important to You

“Most places initially give you a rather one-sided contract and that is as it should be since their attorney is supposed to reflect the things their client is concerned about,” says Hursh, who is author of *The Final Hurdle: A Physician's Guide to Negotiating a Fair Employment Agreement*. “But it is also understood that there are things important to you that you want to be reflected in the contract. My job is to make sure your objectives are covered to the greatest extent possible.”

Clarifying Language

A seasoned physician contract attorney can help the physician clarify language that may seem self-evident on the surface. One example Hursh pointed to was the definition of “work week.” The contract says 40 hours and that seems easy enough to understand. However, is that 40 office hours or 40 patient contact hours? If the latter, do you have to physically be in front of the patient or does that include hospital rounds?

Another area of concern frequently seen in employment contracts has to do with the physician voluntarily leaving the practice. Many contracts say that both sides have to give 60 days notice before the contract is terminated. On the surface that may seem fair, but that is often an unrealistically short amount of time for you to get hired at the next place.

“Many physicians underestimate the time it takes to find a new job,” Hursh says. “While you might be able to get an offer fairly quickly, actually getting credentialed and in a position to begin work can take much longer. If you agree to something less than 180 days, you may be looking at a time with no income.”

Non-compete clauses in the contract are likely to make the job search harder if not properly worded. Are you stopped from practicing within a certain radius of the office you worked in or the entire metropolitan area? How long is the clause in place?



“ An employment contract is a big commitment and you want to make sure everything is right before you go into it. Keeping both you and your potential employer satisfied with the relationship is mutually beneficial in the long term.”



Picking Your Attorney

When picking out the attorney you want to represent you, Hursh suggests finding one that has experience in reviewing physician employment contracts. There are many subtleties such as call requirements that a generalist attorney may not know about.

He points to one example where the new person was to do all hospital call. To compensate the physician, the money from all laboratory services ordered at the hospital would be income for the doctor.

“It seemed a simple enough way to acknowledge the extra work,” Hursh explains. “The problem is that a regulator would look at that arrangement as paying for referrals which is fraud. It wasn’t nefarious, just an honest mistake that someone not well acquainted with healthcare law would have missed.”

Finding a healthcare-savvy member of the bar can be a challenge; there is no professional association or interest group of physician contract attorneys. Hursh suggests searching on the Internet for “physician contract reviewers” as a first cut.

After getting a list of possible attorneys, first look for those with membership in the American Health Lawyers Association. After that, review the websites of those you are interested in hiring. You want to know their background and experience in the specific task of physician employment contracting.

“Generally you want to know how many contracts a person has reviewed,” Hursh says. “Look for a focus on the subject. Some may do certificates of need, handle Medicare and Medicaid law and, oh by the way, an occasional physician contract. That person may be better than the person who specializes in torts or wills, but still not see some of the subtle considerations in the agreement.”

Don’t be concerned if many of these attorney practices are not the biggest ones around. Many of the larger health-related groups of lawyers will not take on physician clients because of concerns about conflict of interest with hospital clients.

“Attorneys do these kinds of contracts on a daily basis while the doctor may only change contracts two or three times their entire career,” Hursh says. “If nothing else, the physician now knows what is expected of them going forward.” ^{EN}

ULLMAN, RN, MHA, IS AN INDIANA-BASED FREELANCE WRITER WITH NEARLY 30 YEARS OF EXPERIENCE. HE WROTE ABOUT CARE COORDINATION SOFTWARE IN THE JUNE 2016 ISSUE.

Storage Wars

Since laboratory space is at a premium, it's tempting to outsource specimen storage. *Endocrine News* weighs the pros and cons of moving specimen storage offsite or keeping it at arm's length.

BY MELISSA MAPES



Changing healthcare policies have led to new realities at medical labs. Reimbursements and test volume are down, making efficiency and smart budget management more essential than ever. Some laboratories are turning to outside storage facilities to reduce the costs associated with keeping specimens in-house. But what are the tradeoffs?

According to a recent report by Wendy M. Banker, MPA, titled “Could Specimen Storage Outsourcing Help Labs Compete in Today’s Cost Conscious Environment?,” a strong argument exists for using external storage facilities. Space is among a lab’s most valuable commodities — fewer specimen blocks means more room for equipment and experiments. However, lab professionals fear losing the accessibility that in-house storage offers.

This fear, and other preconceptions about the risks of offsite storage, has perpetuated hesitation on the part of laboratory managers and directors. But processes and technology for storing specimens have improved, and renting outside space is looking more and more appealing from an economic perspective.

There is no “one size fits all” solution, so laboratory professionals must weigh storage options based on the particular circumstances of their facility. The following factors are a summary of the variables to consider when deciding where to house slides and specimen blocks.

Access

“Lab storage practices vary greatly across organizations, however in-house is the dominant approach used today,” Banker explains in the report. She describes the storage practices of most organizations as “fragmented” — meaning spread throughout a number of spaces around the facility. Specimens tend to be organized by age so that the newest samples are the closest and oldest are tucked further away.

By keeping storage onsite, researchers enjoy the convenience and quick turnaround of pulling specimens. A staff member can be sent to track down the item and it can be returned to the requestor in as little as minutes. But this assumes a meticulously organized and maintained storage system with adequate staffing to keep things running smoothly. It is not unusual for specimens to end up misplaced when lab workers lack training or rely on a flawed organizational system.

Some lab managers and directors also question whether or not tracking down specimens is the best use of staff time. Every hour a staff member spends searching for a lost specimen is an hour that they are not contributing towards tests and other daily operations. Allocation of valuable resources is a key consideration in the decision to store onsite or offsite. Human resources are precious, as is space, and the opportunity cost of devoting these to storage grows with the size and age of the lab.

For smaller and newer labs with fewer specimens, offsite storage

may not be necessary. Larger labs and those with older blocks taking up room, however, may want to seriously consider their options.

Quality Control

Lab managers and directors cite the safety and security of specimens as two additional reasons to keep storage within their facility. This gives them more control over the environment that blocks and slides are kept within, while moving offsite requires a leap of faith that an outside company will properly protect and care for their specimens.

“In many climates, specimen storage requires rigorous controls, such as temperature and humidity monitoring, and even pest prevention,” the report states. Participants in the study almost unanimously claim to use temperature control like air conditioning, but fewer enforce controls around humidity and fire prevention.

As volume increases, it becomes more expensive and challenging to adhere to best practices for lab storage. With the fragmented reality that most labs face, specimens end up in multiple rooms with varying suitability for storage. Thus, the perception that onsite storage guarantees better care is often untrue.


Labs can solve the problem of quality control by consolidating into one space and consistently regulating that single environment. Reputable offsite storage companies work to maintain ideal standards for storage and can solve this problem when consolidation in-house is not an option. Either way, there is no 100% guarantee against disaster should a terrible accident or weather-related catastrophe occur. But fragmentation appears to be the riskiest scenario when speaking of day-to-day degradation.

Economics

Nailing down the economics of internal versus external storage proved tricky for Banker. “Participants state the costs to store specimens are low importance and for many this is because costs are absorbed at the corporate level,” she writes. Her research found that lab managers and directors perceived outside storage as pricier, but “there was no viable comparison as none were able to cite the actual cost of managing specimens in-house, including the real estate and resource line items on their budget.”

Without access to such information, Banker could not draw conclusions as to the economic tradeoffs of outsourcing lab storage. She notes, however, that organizations are actively seeking cost-saving measures given the drop in reimbursements — strategic use of space is certainly a part of that conversation.

Overall, the report found that a hybrid solution could suit the needs of most labs. The entirety of specimens rarely needs to be kept on site, but newer and more valuable specimens may make sense to keep in-house. According to the study, “on average, only about 10% of all slides and blocks are recalled at some point and most requests come within the first three years of slide/block storage.”

To balance considerations of cost and accessibility, lab managers and directors might consider outsourcing blocks and slides more than three years old. The right decision depends on specific lab circumstances, but this provides an easy rule of thumb to use as a reference. 

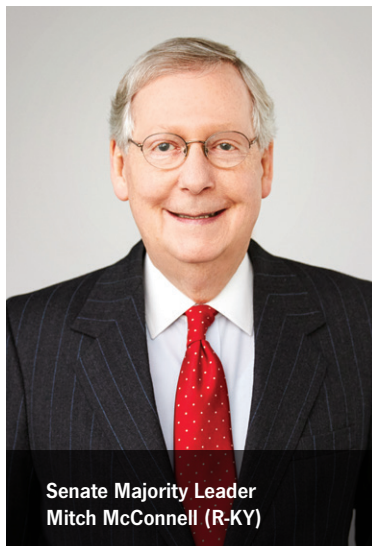


THE LEGAL IMPLICATIONS OF SPECIMEN STORAGE

No matter where a lab stores its blocks and slides, legal liability comes into play when specimen damage occurs. Banker's report states that, “Although seen as highly important, labs report they are not performing well at reducing the risk of litigation due to inadequately preserved specimens.” Flooding and pest control are two often-noted issues. To reduce the risk of litigation, “labs should document storage-specific policies and develop procedures that include regular audits of storage space and workflow processes.” This takes time and resources to enact.

Outsourcing specimen storage does not necessarily mean that all liability is shifted to the storage company — this depends on contract specifics and local laws. However, vendors that specialize in lab storage often dedicate significant resources to keeping best practices in place and protecting their facilities against natural disasters, which lifts some of the burden off of individual laboratories.

MAPES IS A WASHINGTON, D.C.-BASED FREELANCE WRITER AND A REGULAR CONTRIBUTOR TO *ENDOCRINE NEWS*. SHE WROTE ABOUT THE TOP SCIENTIFIC DISCOVERIES OF 2016 IN THE DECEMBER ISSUE.



Senate Majority Leader
Mitch McConnell (R-KY)



Obamacare Repeal Expected to Come First in New Congress

Senate Majority Leader Mitch McConnell (R-KY) has announced that a resolution to allow for the replacement of the healthcare law would be the first item of business for the Senate in the next Congress, starting Jan. 3. It is expected that to dismantle the law, Congress will use a budget process, known as reconciliation, that only requires a majority vote and no filibusters. It is important to note, however, that even with majorities in Congress and a Republican president, repeal and replacement of Obamacare will be difficult. Replacing the healthcare law — and making sure voters don't lose their coverage — is harder than it sounded on the campaign trail.

Obamacare dramatically overhauled the entire healthcare industry. It transformed not only the insurance industry, but also the way hospitals, physicians, and pharmaceutical companies are paid by the government. It affected the Medicare program and expanded Medicaid, allowing states to cover millions more Americans.

A complete repeal of the law would send the industry into chaos. It would end coverage for more than 22 million people, according to a Congressional Budget Office estimate — leaving many without access to healthcare benefits at all. Further, a complete repeal of the law would upend the insurance markets that rely on the law to encourage people to enroll in plans and it would cripple the hospitals, doctors, and even drug companies who rely on the income from those newly insured patients.

Repeal is still a winning political rallying cry. Despite the advances the health law has made, including reducing the uninsured rate to the lowest point in recorded history, the law remains

deeply unpopular. An average 45% of Americans viewed the law unfavorably over the course of 2016, compared to 41% who favored it, a Kaiser Family Foundation tracking poll shows.

Obamacare — and especially the public marketplaces it set up to sell insurance to Americans who otherwise had few options to buy it — has struggled, particularly over the last six months. It was plagued by bad headlines about insurance companies, including giants like UnitedHealth Group and Aetna abandoning most of the markets they were participating in, citing financial losses. As much as one-third of the country could only choose insurance plans from a single company during this fall's sign-up period.

Premiums for people buying insurance on the marketplaces also skyrocketed this autumn, thanks in part to Republican efforts to hamstring the Obama administration's efforts to implement and fund the legislation. In states like Tennessee and Arizona, monthly costs increased by more than 60% or even doubled. In Oklahoma, for example, 27-year-olds who paid \$250 per month for a mid-range insurance plan would now pay more than \$400 each month when coverage renews in January. A family of four in North Carolina might pay \$1,500 per month, up from \$900 per month.

Republicans jumped on those headlines, decrying the law for its impact on everyday Americans and the astronomical prices they are paying for their health insurance and their medical care. Now, however, if Republicans can repeal and replace the law as they intend to do, they may inherit the blame for rising premiums, sky-high deductibles, dwindling marketplace competition, and steadily climbing medical costs.

The reconciliation process appears to be the path forward for repeal. Reconciliation bills cannot be filibustered, so they need just 51 votes to pass the Senate, and a 50-50 tie could be broken by the new Republican vice president, Mike Pence.

But the process does not let Republicans repeal the entire text of the law. Only provisions that affect spending and taxes are allowed to be included in a reconciliation bill. Consequently, the law's controversial mandate that most Americans buy health insurance, as well as its unpopular penalty for foregoing it, could go. Its requirement that insurance companies sell policies to anyone, regardless of their health history or pre-existing conditions, could not. The expansion of the Medicaid program could be killed through reconciliation. Many other requirements for insurers, such as preventing them from rescinding sick patients' benefits or banning them from imposing annual or lifetime caps on coverage, could not.

In addition, there are parts of the law that Trump could begin to unravel on his first day in office. He could almost immediately direct the Internal Revenue Service to stop fining individuals who don't have health insurance coverage as the law's individual mandate requires. He could also stop paying some of the subsidies insurers get for covering especially low-income Americans, those with income up to 250% of the poverty line. The requirement that all insurance companies cover birth control for women could also be struck down administratively.

Currently, Republicans are working on various legislative "replacements" for Obamacare, but the new president and Republican leaders in Congress have also made it clear that they want whatever replaces Obamacare to minimize disruption to consumers as well as the health industry. It is likely, therefore, that the repeal package will provide a two- to three-year transition period. Still, that might not be enough time to find agreement on and implement changes. It took years of hearings to develop and pass the healthcare law the first time around, and another three years to get the exchanges up and running in each state.

The Endocrine Society has long advocated on behalf of the millions of Americans living with chronic, serious, and life-threatening endocrine diseases who need access to affordable health insurance and quality health care. We have supported policies that expand access to coverage, such as those that prevent preexisting condition exclusions and allow young people to remain on their parents' plans until age 26. We will continue to keep our members apprised of developments regarding the repeal and replacement of Obamacare.



NIH Funding in Jeopardy as Congress Failed to Pass Final Spending Bill

The Congress adjourned for 2016 without passing a final funding bill. Instead, the National Institutes of Health (NIH) and other federal agencies will be funded through a continuing resolution (CR) at FY 2016 levels until April 28, 2017. This temporary funding measure seriously hurts the NIH by limiting its budget and grant opportunities. It is critical that every member of Congress hear from his/her constituents in the research community about the importance of biomedical research and the need to provide NIH with at least \$34 billion in 2017.

TAKE ACTION: We encourage all Society members to join our online advocacy campaign urging the new Congress to pass a final spending bill with at least \$34 billion for NIH. Simply visit endocrine.org/advocacy. Our campaign provides a letter and will direct the letter to your Representative and Senators. You may also personalize the letter, if you choose to. Taking action will only take a moment of your time, but it will have real impact.

House and Senate Pass ‘Cures’ Bill



After three years of debate and consideration, the U.S. House of Representatives and Senate passed the biggest health reform bill since the Affordable Care Act. The legislation known as the 21st Century Cures Act is a controversial, bipartisan effort designed to spur medical innovation, improve the mental health system, and help the states deal with opioid abuse.

The legislation includes \$6.3 billion over a decade deposited in three dedicated accounts that would channel money to states responding to the growing opioid crisis, the NIH, and the Food and Drug Administration (FDA).

Like any piece of large legislation, there are some provisions in the bill viewed favorably and some that are worrisome. Supporters have touted the legislation as a means to get medical cures to patients faster; opponents argue that the bill's research spending is offset by cutting public health spending elsewhere and that the bill could seriously damage the regulatory authority of the FDA and compromise patient safety.

Research Funding

At a time when research funding is in jeopardy, the Cures Act would increase money for the NIH by about \$4.8 billion over 10 years. The bill also includes \$1 billion over two years to help state governments with opioid painkiller abuse prevention and treatment programs and it would expand Medicaid to children with severe mental illnesses. These are all things viewed positively by the public and most policy makers.

However, the NIH funds are not actually guaranteed as originally discussed, but rather they only materialize if federal appropriators approve them each year. In addition, nearly half of the funds for the legislation come from cutting \$3.5 billion from other public health efforts like immunizations and tobacco prevention. Further, the funding in the bill is strictly designated

to four initiatives at NIH: Precision Medicine; the Cancer Moonshot; regenerative medicine; and the BRAIN initiative, rather than across all Institutes and/or areas of study.

FDA Approval Process

A majority of the bill is devoted to the FDA and its approval process. Currently, before a new drug can come on the market, the drugmaker needs to present high-quality evidence in the form of randomized clinical trials to the agency. The bill, however, will allow drugmakers to submit “real-world evidence” as proof their drugs work. Critics of the measure contend that this would undermine the rigor of the FDA review process and result in drugs that are unsafe or ineffective. The bill would also allow drug companies to submit “summary-level reviews for new indication approvals instead of raw data, which the FDA currently requires. This would limit the ability of FDA reviewers to analyze the data and force them to rely on industry information.

While there were a small number of legislators who opposed some provisions, the bill passed by a landslide in the House of Representatives and Senate. Vice president Joseph R. Biden presided over the Senate's final procedural vote on the bill, tearing up as senators spoke in favor of the Cancer Moonshot initiative, which he has overseen since its launch following the death of his son to cancer. NIH director Francis Collins has spoken favorably about the bill. Some original opponents voted in favor believing this might be the best package of biomedical research measures they could before the new Congress and Trump administration. President Obama signed the bill into law and praised it during his weekly radio address. “There's a bill in Congress that could help unlock cures for Alzheimer's, end cancer as we know it, and help people seeking treatment for opioid addiction finally get the help they need,” Obama said. “It's an opportunity to save lives, and an opportunity we just can't miss.”

Summary of Provisions in Cures Act:

PRO	CON
\$4.8 billion over 10 years to NIH.	The increased funds only go to four projects, the Precision Medicine Initiative, the BRAIN Initiative, cancer research, and regenerative medicine using adult stem cells.
Provides \$500 million to the FDA over 10 years to implement new provisions.	Significant cuts to the Public Health and Prevention Fund is a major part of the budget offset.
Reauthorizes the NIH for FY 18-20	Specifies five-year terms for institute Directors – allows for reappointment without limit.
Creates a “Next Generation of Researchers Initiative” in the Office of the Director to coordinate, develop, modify, and prioritize policies and programs to improve opportunities for new researchers.	Directors of institutes must review and make final decisions on funding awards.
Requires the secretary of HHS and NIH director to take action to reduce administrative burden for researchers, for example by evaluating financial reporting requirements and laboratory animal regulations and policies.	The HHS Secretary must submit a report to Congress on efforts to prevent and eliminate duplicative biomedical research that is “not necessary for scientific purposes.”
Exempts voluntary information collected during NIH research from paperwork reduction initiatives	Congress still needs to vote every year to make the funds above available as part of the appropriations process.
Allows expanded use of other transactions authority by institutes with the approval of the NIH director and encourages the conduct and support of high-risk, high-reward research to address major challenges.	New review pathway for some drugs has the potential to miss important safety concerns with a particular medicine
Requires the NIH director to improve research related to minority populations.	Reduces the payment update that was included in the bipartisan Medicare and CHIP Reauthorization Act (MACRA) of 2015. Specifically, the update of 0.5 percent for fiscal year 2018, is changed to an update of 0.4588.
Requires the NIH director to update guidelines for the inclusion of women in clinical research to reflect the most current science.	
Requires that a working group be formed to develop recommendations towards a formal policy to enhance rigor and reproducibility of NIH-funded research. The working group shall consider analysis of sex as a biological variable.	
Establishes a Task Force on Research Specific to Pregnant and Lactating Women to provide guidance and advice with the goal of addressing gaps in knowledge and research regarding safe and effective therapies for pregnant and lactating women.	
Encourages NIMHD to include in its strategic plan ways to increase representation of underrepresented populations in clinical trials.	
Improves the ability of NIH and FDA scientists to attend scientific conferences.	
Speeds access to new drug therapies with a new review pathway	
Expedites interoperability among EHRs by developing or supporting a voluntary model framework and common agreement for the secure exchange of health information	
Exempts certain transfers of value from reporting requirements that health care providers have noted have a chilling effect on their engagement in CME (iejournal reprints) (I believe this provision was stripped out with the manager’s amendment)	
Sets payment amounts for Part B drugs infused through durable medical equipment, prosthetics, orthotics, and supplies (DMEPOS) items using the methodology used for most physician-administered drugs: Average Sales Price (ASP) plus 6%. Applying the ASP+6% methodology to DMEPOS infused drugs would result in payment amounts that reflect actual transaction prices. This change is based on findings from the HHS OIG which found that the current payment methodology –based on manufacturer sticker prices that were in effect in 2003 – currently over pays some drugs while underpaying for others	

Endocrine Society Meets with NIH Office of Research on Women's Health to Discuss Research Gaps & Policy Priorities



On Thursday, December 1, Janine Austin Clayton, MD, director of the NIH Office of Research on Women's Health (ORWH) and associate director of Women's Health Research at the NIH visited the Endocrine Society for a meeting with Endocrine Society member and associate director of the Center for Women's Health Research at the University of Colorado Anschutz Medical Campus, Jane Reusch, MD; and the director of the Center for Women's Health Research at the University of Colorado Anschutz Medical Campus, Judy Regensteiner, PhD.

During the meeting, participants discussed research gaps and opportunities identified during the National Conference on Women's Health Research, "Sex Differences Across the Lifespan: A Focus on Metabolism" (recently highlighted in the July *Endocrine News*). The group also discussed the new NIH policy on the "Consideration of Sex as a Biological Variable in NIH-funded Research." The meeting highlighted the many synergies between the policy priorities and research interests of ORWH and the Endocrine Society.

Several specific opportunities were identified during the meeting, including working together on developing educational resources about how to appropriately consider sex as a biological variable and promoting existing resources such as the online developed by ORWH.


NIH Office of Research on Women's Health Online Courses on Sex/Gender Differences

The NIH Office of Research on Women's Health has developed a series of online courses to provide a foundation for sex and gender accountability in medical research and treatment. After completing the courses, researchers, clinicians, and students in the health professions will be able to integrate knowledge of sex and gender differences and similarities into their research and practice.

- **The Basic Science and the Biological Basis for Sex- and Gender-Related Differences**
- **Sex and Gender Differences in Health and Behavior**
- **The Influence of Sex and Gender on Disease Expression and Treatment**

These CME/CNE/CPE courses are open to the public and offered at no cost. For more information, visit orwh.od.nih.gov/research/cme/

Participants in the Endocrine Society meeting with the NIH Office of Research on Women's Health (ORWH) included Joseph M. Laakso, PhD, associate director, science policy, Endocrine Society; Mila Becker, JD, chief policy officer, Endocrine Society; Jennifer Plank-Bazinet, PhD, research program officer, ORWH; Barbara Byrd Keenan, FASAE, CAE, CEO, Endocrine Society; Jane Reusch, MD, associate director, Center for Women's Health Research, professor of medicine, University of Colorado; Janine Austin Clayton, MD, director, ORWH and associate director for Women's Health Research, NIH; and Juliana M. Blome, PhD, MPH, associate director for science policy, planning, and analysis, ORWH.

The Endocrine Society regularly seeks opportunities to raise the profile of endocrine research at the NIH and discuss shared priorities with the leadership of NIH Institutes and Offices. We look forward to implementing the opportunities discussed during the meeting with ORWH and working together to advance women's health. For more information on specific projects or opportunities, please reach out to Joe Laakso, associate director of science policy at jlaakso@endocrine.org. 

THYROID CANCER

WHAT YOU NEED TO KNOW

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

Visit hormone.org for more information.



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



THYROID NODULES

— CELLS IN THE THYROID THAT FORM A TUMOR

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



THYROID CANCER DOESN'T ALWAYS HAVE SYMPTOMS

See your doctor if you notice:

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



CANCER DIAGNOSIS

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

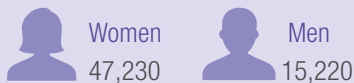
TYPES OF THYROID CANCERS

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

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

(IN BOTH MEN AND WOMEN)

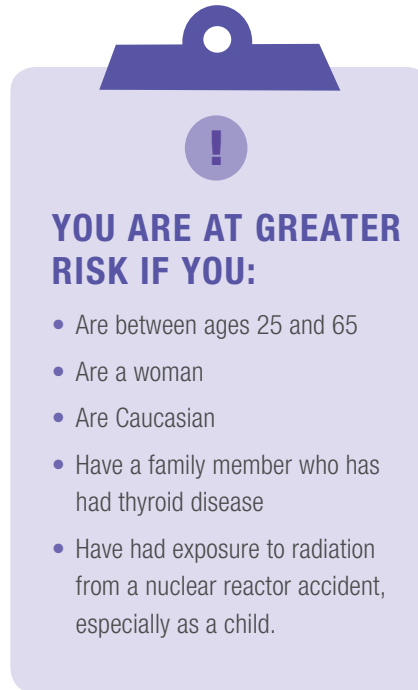
New cases per year: 62,450



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

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

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



YOU ARE AT GREATER RISK IF YOU:

- Are between ages 25 and 65
- Are a woman
- Are Caucasian
- Have a family member who has had thyroid disease
- Have had exposure to radiation from a nuclear reactor accident, especially as a child.

TREATMENT

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

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



Patients have questions. We have answers.

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



Hormone Health
NETWORK®
FROM THE ENDOCRINE SOCIETY

Change lives. Start with your own.

Aspirus is a nationally recognized, physician-driven health system based in Wausau which is located in the center of Wisconsin. The care we give to others is the reason Aspirus is thriving and unifying in spite of national health care changes.

There's a simple reason you chose a career in Endocrine Medicine. We invite you to practice it here:

- Join our Endocrinologist and three Nurse Practitioners who practice 100% outpatient consultative endocrinology
- Collaborate with a dedicated and experienced support team, including Certified Diabetic Educators
- Flexible scheduling
- Large referral area that includes 20 counties, willingness to do outreach is preferred
- Potential teaching opportunities available through the Aspirus Wausau Family Medicine Residency program and the Medical College of Wisconsin both onsite
- Above average compensation package that includes income guarantee and production bonuses
- Other incentives: potential for residency stipend, loan repayment of up to \$200,000 and sign-on bonus options
- J1 and H1-B visa possibilities
- We pride ourselves on excellence: Aspirus Wausau Hospital recently received recognition as one of the 100 Best Hospitals in America for 2016
- EPIC EMR used throughout the system

Endocrinology Opportunities Wisconsin \$75,000 Sign On Bonus



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Contact Jodi Wierzba at Jodi.Wierzba@aspirus.org or 800.792.8728

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The Joslin Diabetes Center, affiliated with Harvard Medical School and located in Boston, is the preeminent diabetes center in the world; a one-of-a-kind institution on the front lines of the diabetes epidemic. Joslin has revolutionized the diagnosis, treatment, and prevention of diabetes and its complications worldwide. Joslin is seeking a Clinical Endocrinologist to join its group of physicians, participating in clinical care and teaching. Must be BC in Internal Medicine and BC/BE in Endocrinology. Exposure to the greatest minds in diabetes, collaborative team approach, unique clinical care model all with ideal work/life balance. Opportunity for academic appointment at HMS.

For additional information and to apply, interested candidates are invited to visit: www.joslin.org

Joslin is an EOE M/F/Vet/Disabled

Endocrinologist

Prestigious multispecialty practice in a desirable NJ university town is seeking a BC/BE Endocrinologist to join a busy Endocrinology department.

Excellent opportunity leading to partnership.

Fax CV to Joan Hagadorn at:
(609) 430-9481
E-mail to: jhagadorn@msn.com



Endocrinology Physician - Assistant/Associate Professor of Medicine

Marshall University Joan C. Edwards School of Medicine in Huntington, WV, seeks Endocrinology Physician (Assistant/Associate Professor of Medicine) to provide evaluation and care as a faculty attending physician for outpatients in ambulatory practice and for inpatients as assigned on a rotational basis. Duties will include teaching students and residents in an inpatient or ambulatory setting, participating and presenting in medical rounds, participating in assigned committees at the University and related hospitals and performing endocrinology research.

Candidate must have a medical degree or foreign equivalent, must have completed a residency in Internal Medicine and a fellowship in Endocrinology, Diabetes and Metabolism or equivalent endocrinology fellowship program. Must have a clear and unrestricted West Virginia medical license at time of employment.

Send letter of application and current CV in PDF file format to:
smccallister@marshall.edu
Background Check Required.



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LATE-BREAKING ABSTRACT SUBMISSION PERIOD

JANUARY 19 – FEBRUARY 17

HOUSING DEADLINE

MARCH 7

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