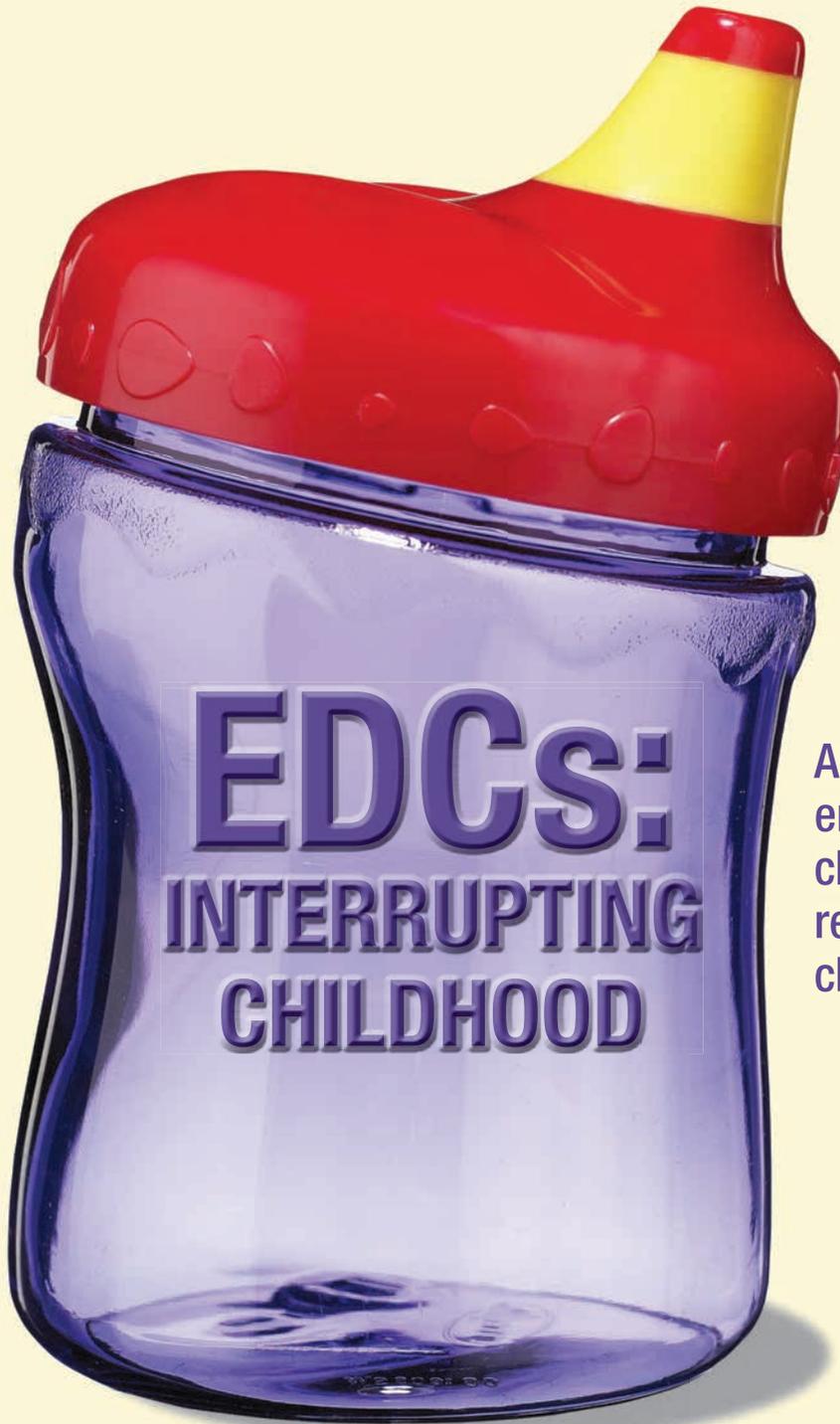


APRIL 2014

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

ENDOCRINE news™



**EDCs:
INTERRUPTING
CHILDHOOD**

A complex mix of endocrine-disrupting chemicals complicates research into childhood illnesses

**Boning Up:
OWNING OSTEOPOROSIS**

**Grudge Match:
INSULIN PENS VS. SYRINGES**

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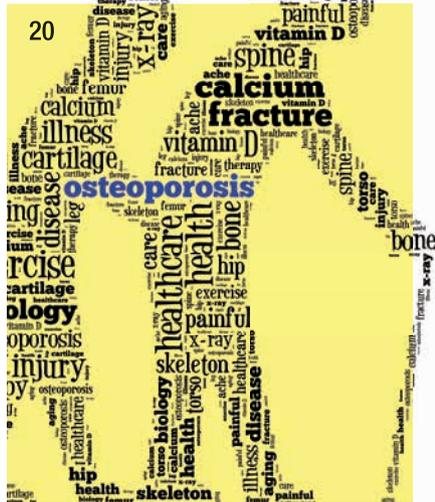


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14



20



24

COVER STORY

14 EDCs: Interrupting Childhood

By Aalok Mehta

A complex soup of hundreds of endocrine disruptors complicates research — and policy — on childhood illness.

20 Boning Up on Osteoporosis

By Eric Seaborg

Since most endocrine conditions have a direct correlation to bone formation, endocrinologists should take more ownership of this complex disorder.

24 Grudge Match: Pens vs. Syringes

By Terri D'Arrigo

Neither patients nor doctors — nor insurance companies — can decide on a preferred method to deliver insulin.

30 Competitive Advantage

By Derek Bagley

You'll face competition throughout your career, but overcoming it may be easier than you think.

32 Safe & Sound

By Melissa Mapes

While it may sound corny, "safety first" is a must in academic and clinical labs where the failure to follow proper procedures can have devastating consequences.

DEPARTMENTS

4 President's Viewpoint

Education abounds at ICE/ENDO2014

5 Editor's Page

April issue highlights

5 Letters to the Editor

Readers respond

8 Trends & Insights

News from the latest research

28 Research Roundup

Studies in the Society journals

34 Advocacy

Promoting research on the Hill

36 InTouch

Society news

44 Classifieds

Job opportunities

41 Hormone Health Network

Fact Sheet: What Does Estrogen Do?



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ICE/ENDO 2014: A Wealth of Learning Opportunities



Teresa K. Woodruff, PhD

ICE/ENDO 2014 is less than two months away, and I am looking forward to welcoming all of you to Chicago, my hometown, for a meeting that is destined to make history! Featuring the best in global endocrine research and practice, **ICE/ENDO 2014** will

provide attendees with countless opportunities to energize their basic and translational science and enhance their scholarly-based practice through top-notch science presentations, educational programs, and networking with colleagues from around the world.

The meeting will open with two plenary talks from Nobel Prize Winner Robert Lefkowitz, MD, and C. Ronald Kahn, MD, who will provide their expert perspectives on the history and future directions of research in the fields of G protein-coupled receptors and insulin signaling. A fantastic line-up of internationally renowned leaders in the fields of diabetes, metabolism, cancer, bone, and reproductive research, and hormone signaling will also present their work on our plenary stage at **ICE/ENDO**.

Researchers, make sure you attend the symposium “Navigating Biomedical Big Data” to learn how to access and analyze very large data sets and how to apply big data tools to your own research. We’ve also planned a new, unique opportunity for you to “Meet the NIH Program Directors” where you can learn about the



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missions of the National Institutes of Health and receive guidance on funding opportunities from representatives from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), and the National Heart, Lung and Blood Institute (NHLBI). In today's challenging funding environment, this program is a must-attend for all research scientists!

For clinicians eager to keep current with the rapidly evolving nature of clinical practice, there are plenty of opportunities to hear the latest updates from the experts

during meeting program favorites like Meet-The-Professor sessions, Year-In sessions, and Clinical Practice Guideline updates. The Master Clinician sessions will explore controversies surrounding the new lipid guidelines and the updated thyroid cancer guidelines. For clinicians who still have questions about ABIM requirements for Maintenance of Certification, don't miss “MOC Made Easy” and “Live Learning” sessions on how to navigate the process and earn certification points. An exciting new addition to this year's program is the symposium “Update in Endocrine and Metabolic Emergencies,” which will provide expert perspectives on the management of thyroid storm, hyponatremia, and inherited metabolic diseases.

Chicago is a fantastic location for our meeting, and I am sure that you will love discovering the world-class museums, dining, and entertainment the city has to offer. We are excited to host our endocrinology colleagues from the around the world at one of the largest annual meetings in the Society's history!

Please feel free to share your comments, questions, and ideas about **ICE/ENDO** and the Endocrine Society by writing to me via president@endocrine.org. **EN**

Teresa K. Woodruff, PhD
President,
Endocrine Society



APRIL 2014

ENDOCRINE NEWS

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

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

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

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This month's cover story approaches the topical subject of endocrine-disrupting chemicals (EDCs) from an entirely different perspective — their effects on children (p. 14). Writer Aalok Mehta has done an outstanding job in bringing this controversial, and even confusing, topic to light. One of the problems in discussing EDCs and children is the fact that nobody is completely sure exactly how many of these hormone-damaging substances are out there. For example, even though there are more than 80,000 chemicals registered with the EPA, one researcher says that only “scratches the surface” regarding the number of chemicals that could have endocrine-disrupting effects.

In “Boning Up on Osteoporosis” (p. 20), writer Eric Seaborg makes a compelling case for why endocrinologists should play a bigger role in this complex condition. According to Society member Nelson Watts, MD, director of Mercy Health Osteoporosis and Bone Health Services in Cincinnati, almost any endocrine disorder you can think of has some effects on bone, from Cushing's disease and diabetes to hyperparathyroidism and hypogonadism. “It's hard to think of an endocrine disease that doesn't in some way have some effect on calcium,” he says in the article.

In deciding whether a diabetes patient should use a pen or a syringe to administer insulin, many factors must be considered. Terri D'Arrigo weighs the pluses and minuses of both methods in “Grudge Match: Pens vs. Syringes” (p. 24). While many factors must be considered — from the types and amounts of insulin administered to the patient's dexterity and ability — cost needs to be considered, according to Linda Siminerio, RN, PhD, CDE, at the University of Pittsburgh Diabetes Institute. “Comparing pens to syringes is not as simple as saying one is better than the other,” she says. “Expense can be problematic for pens.”

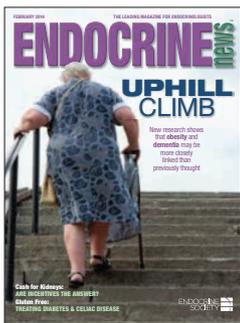
Associate editor Derek Bagley tackles the stress-inducing topic of how to deal with your professional rivals in the practice realm in “Competitive Advantage” (p. 30). Elliot Levy, MD, a clinical professor of medicine in the Division of Endocrinology at the University of Miami (Florida) School of Medicine says that the best way to deal with competition is to be the best physician you can be, adding that you should “just be better and smarter than they are.”

On a personal note, the Society is fully moved into its new offices in the heart of Washington, D.C. Not only is this location more comfortable and convenient, it's a home that the Endocrine Society membership can be proud of. I implore you to drop in the next time you're in the nation's capital. Until then, feel free to drop me a line at mnewman@endocrine.org. EN



Mark A. Newman

Mark A. Newman
Managing Editor, Endocrine News

**Dear Mr. Newman:**

The cover of the February 2014 *Endocrine News* made me think twice.

What I saw was an obese woman, possibly in her late 70s or even 80s (white and thinned hair); quite used to walking (had her system for carrying her purse across her chest and shopping bag with her cane); with good functional capacity (tackling a steep case of stairs and no leg edema) and no dementia (walking by herself and coming back from shopping). Obviously she had degenerative joint disease but she was not incapacitated.

A cynical thought occurred to me: I wondered if the picture was taken in Europe, otherwise she would have been driving. The point I want to make is that the woman in this picture is much better off than her contemporary who has coronary artery disease, peripheral vascular disease, congestive heart failure, and dementia, indicating some obese individuals can remain quite healthy and functional. The important question is “How can we identify and protect those who will not be able to climb those stairs when they get to her age?”

Sincerely yours,

Sidika E. Karakas, MD

Professor and Chief, Department of Internal Medicine
Division of Endocrinology, Diabetes and Metabolism
University of California, Davis

Editor's Response:

Dr. Karakas makes some very astute observations to be sure. While I don't know the history or the setting of the photograph we used on the cover of the February issue, the topic the cover illustrated — treating obesity and dementia — is going to be one that endocrinologists and other physicians will be dealing with for generations to come. *Endocrine News* will continue to feature articles on obesity and how it affects a variety of populations. Stay tuned ...

Mark A. Newman, Managing Editor, Endocrine News

Dear Mark:

I have been meaning to contact you to let you know that you are doing a great job with *Endocrine News*.

In my opinion, it has always been well done but now it is better. You are obviously willing to take on issues that need to be brought forward, such as many of the care delivery issues and patient-centered issues (patient aspects of care or disease).

Thanks for that.

Carol Greenlee, MD

Western Slope Endo, Grand Junction, Colo.

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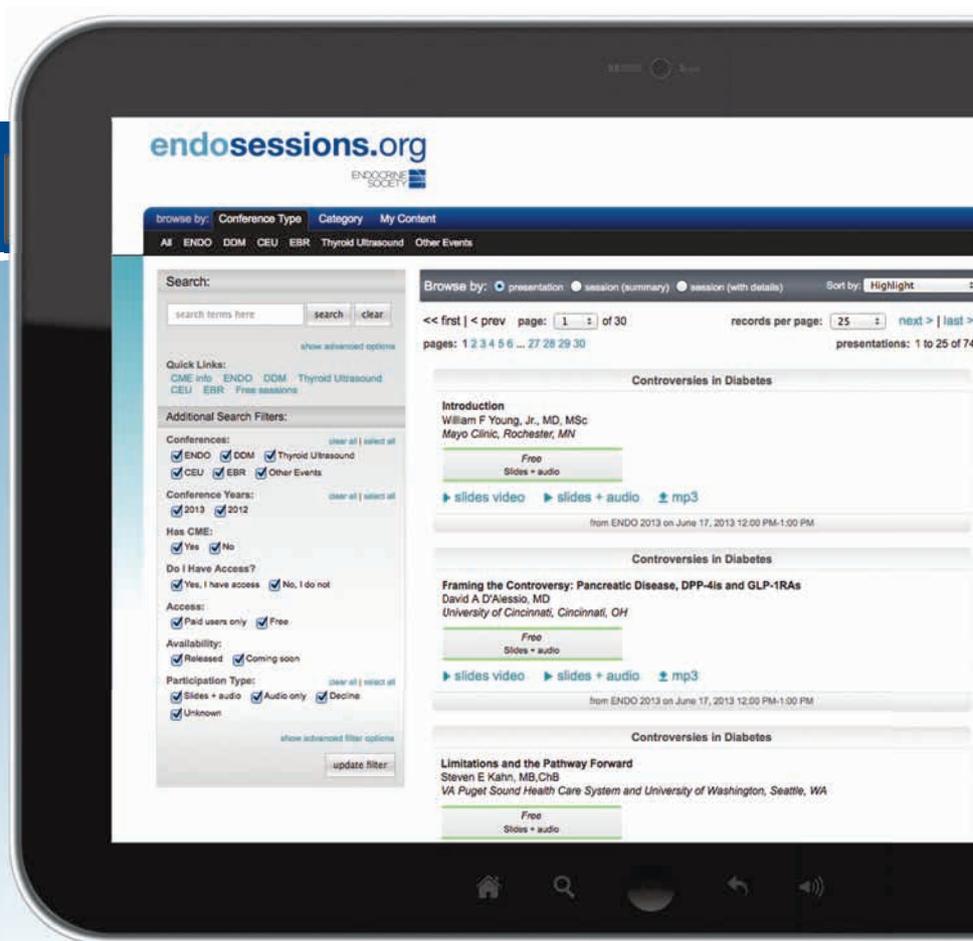
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By Derek Bagley

C-SECTION DELIVERY ASSOCIATED WITH OBESITY RISK

Infants delivered by Caesarean section (CS) may be at risk for obesity as adults, a study recently published in *PLOS One* suggests.

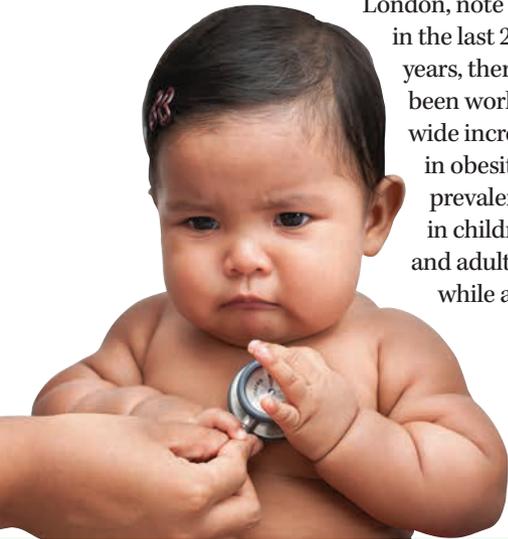
Researchers, led by Karthik Darmasseelane, of Imperial College of London, note that in the last 20 years, there have been world-wide increases in obesity prevalence in children and adults, while at the

same time, there has been a significant upward trend in CS births.

The scientists carried out a systematic review of 15 studies with a combined population of 142,702 subjects, “from ten countries, spanning four continents,” using a predefined search strategy, Pubmed, Google Scholar, and Web of Science. The studies reported adult anthropometry (BMI, height, weight, incidence of overweight/obesity) by mode of delivery. The review was conducted using an a priori protocol (registered on PROSPERO) following PRISMA guidelines for reporting systematic reviews and meta-analyses. “Results [were] illustrated using forest plots and funnel plots, and presented as mean differences or odds ratios (OR) and 95% confidence intervals,” the study says.

They then compared all CS to vagi-

nal delivery (VD) in “pooled-gender unadjusted analyses” and found that “mean BMI difference was $0.44 \text{ kg}\cdot\text{m}^{-2}$ (0.17, 0.72; $p = 0.002$), OR for incidence of overweight was 1.26 (1.16, 1.38; $p < 0.00001$) and OR for incidence of obesity was 1.22 (1.05, 1.42; $p = 0.01$).” “We found an average increase in BMI of almost $0.5 \text{ kg}\cdot\text{m}^{-2}$ in subjects delivered by CS compared to VD,” the authors wrote, “and an increased odds of overweight and obesity $>20\%$; these findings are consistent across sexes.” The researchers concluded that there is a strong association between CS and increased offspring BMI, being overweight and obese as adults. However, they pointed out that these findings were based on observational studies and “there is a need to determine whether this is causal, or reflective of confounding influences.”



VITAMIN D DEFICIENCY LINKED TO COMPROMISED IMMUNE FUNCTION

Vitamin D deficiency may be linked to compromised immune function in older individuals, according to a paper recently published in the *Journal of Clinical Endocrinology & Metabolism*.

Sean Strain, director of the Northern Ireland Centre for Food and Health at the University of Ulster, and the team investigated 957 Irish adults from the TUDA (Trinity Ulster Department of Agriculture) aging cohort study, aged 60 and older. The researchers measured serum 25-hydroxyvitamin D (25(OH)D), as well as the following biomarkers of inflammation; serum cytokines IL-6, TNF- α , IL-10, and C-reactive protein (CRP).

They found that participants who were vitamin D deficient were more likely to have high levels of these biomarkers, writing, “Concentrations of IL-6, CRP, and the ratios of IL-6 to IL-10 and CRP to IL-10 were significantly higher in individuals with deficient ($<25 \text{ nmol/L}$) serum 25(OH)D compared with

those with sufficient ($>75 \text{ nmol/L}$) status after adjustment for age, sex, and body mass index ($P < .05$). Vitamin D status was a significant predictor of the IL-6 to IL-10 cytokine ratio, and those participants defined as deficient were significantly more likely to have an IL-6 to IL-10 ratio $>2:1$ compared with those defined as sufficient.”

The authors noted that the inflammatory markers in question have been linked to cardiovascular disease, multiple sclerosis, Crohn’s disease, and rheumatoid arthritis, and wrote that the findings of this study could lead to potential health benefits for those conditions.

“The results indicate immune function may be compromised in older individuals with vitamin D deficiency,” according to lead author Eamon Laird, PhD, of Trinity College in Dublin. “Ensuring older individuals have optimal vitamin D levels may benefit immune function in this population, but this needs to be confirmed in randomized controlled trials.”



OVERWEIGHT CHILDREN EXPOSED TO PFCs AT HIGHER RISK FOR METABOLIC SYNDROME

Overweight eight- to 10-year-old children who had increased exposure to perfluorinated and polyfluorinated compounds (PFCs) — chemicals commonly found in stain and water repellants in carpet and furniture — show early signs of developing metabolic syndromes such as heart disease and diabetes, according to research recently published in the *Journal of Clinical Endocrinology & Metabolism*.

Clara Amalie G. Timmerman, MSC, of the University of Southern Denmark, and her team assessed PFC exposure and body mass index (BMI), skinfold thickness, waist circumference, leptin, adiponectin, insulin, glucose, and triglyceride concentrations in 499 eight- to 10-year-old children in 1997, using a subset of the European Youth Heart Study.

The researchers found no association between PFC exposures and adiposity or markers of glycemic control in normal-weight children. Among overweight children, however, they

found “an increase of 10 ng perfluorooctane sulfonic acid/mL plasma was associated with 16.2% (95% confidence interval [CI], 5.2%–28.3%) higher insulin concentration, 12.0% (95% CI, 2.4%–22.4%) higher β -cell activity, 17.6% (95% CI, 5.8%–30.8%) higher insulin resistance, and 8.6% (95% CI, 1.2%–16.5%) higher triglyceride concentrations, and an increase of 10 ng perfluorooctanoic acid/mL plasma was associated with 71.6% (95% CI, 2.4%–187.5%) higher insulin concentration, 67.5% (95% CI, 5.5%–166.0%) higher β -cell function, 73.9% (95% CI, 0.2%–202.0%) higher insulin resistance, and 76.2% (95% CI, 22.8%–153.0%) higher triglyceride concentrations.”

“Our results suggest that these chemicals, which linger in the environment for years, could represent an important public health hazard that merits further study,” says Timmerman. “Overweight children who were exposed to higher levels of PFCs tended to have higher

concentrations of insulin and triglycerides in their blood, and these metabolic changes could signal the beginnings of the metabolic syndrome.” However, the authors noted that while this is the first study to associate PFC exposure to metabolic syndromes in “a large cohort of prepubertal children,” there were some limitations to this study. They wrote, “Chance findings may explain some of our results, and due to the cross-sectional design, reverse causation cannot be excluded. The findings therefore need to be confirmed in longitudinal studies.”



EXPOSURE TO BISPHENOL A LINKED TO PROSTATE CANCER

It seems that people are exposed to bisphenol A (BPA) almost everywhere they go, and there's no shortage of research linking the endocrine disruptor to myriad conditions. Now, research in the journal *Endocrinology* has shown that exposure to BPA is associated with prostate cancer.

According to the article, prostate cancer is the second leading cause of cancer-related mortality in U.S. men. And while BPA itself is not a known carcinogen, the scientists note that in a study of 2,500 U.S. adults, 93% had detectable urine BPA, “indicating that humans are chronically exposed to this compound during routine daily activity.”

The study, led by Gail S. Prins, PhD, of the University of Illinois, utilized primary human prostate epithelial stem-like cells (PrEC) from the prostates of four disease-free donors aged 19-21. The PrECs were then combined with rat mesenchyme and

grown as renal grafts in nude mice in order to assess *in vivo* carcinogenicity. The mice formed normal human prostate epithelium at one month.

Of their methods, the authors wrote, “Developmental BPA exposure was achieved through oral administration of 100 μ g or 250 μ g BPA/kg BW to hosts for two weeks post-grafting, producing free-BPA levels of 0.39 and 1.35 ng/ml serum, respectively. Carcinogenesis was driven by testosterone plus E2 treatment for two to four months to model rising E2 levels in aging men.” They found that the incidence of malignancies (intraepithelial neoplasia and adenocarcinoma) increased from 13% in oil-fed controls to 33%-36% in grafts exposed *in vivo* to BPA. “Continuous developmental BPA exposure through *in vitro* (200 nM) plus *in vivo* (250 μ g/kg BW) treatments increased HG-PIN/cancer incidence to 45%

($P < 0.01$),” they wrote.

The researchers also did *in vitro* work directly on the human prostate stem and progenitor cells, and found that BPA directly activates rapid signaling pathways in the stem and early progenitor cells, paralleling the actions of estradiol and resulting in increased self-renewal of the stem cell population, i.e., increasing their numbers. Thus, direct actions were shown, in addition to increased rates of estrogen-induced carcinogenesis *in vivo*.

Prins and her team concluded that their findings demonstrate that “human prostate stem-progenitor cells are direct BPA targets and that developmental exposure to BPA at low doses increases hormone dependent cancer risk in the human prostate epithelium.” They go on to suggest that humans may be susceptible to prostate diseases after exposure to doses of BPA that are routinely found in humans.

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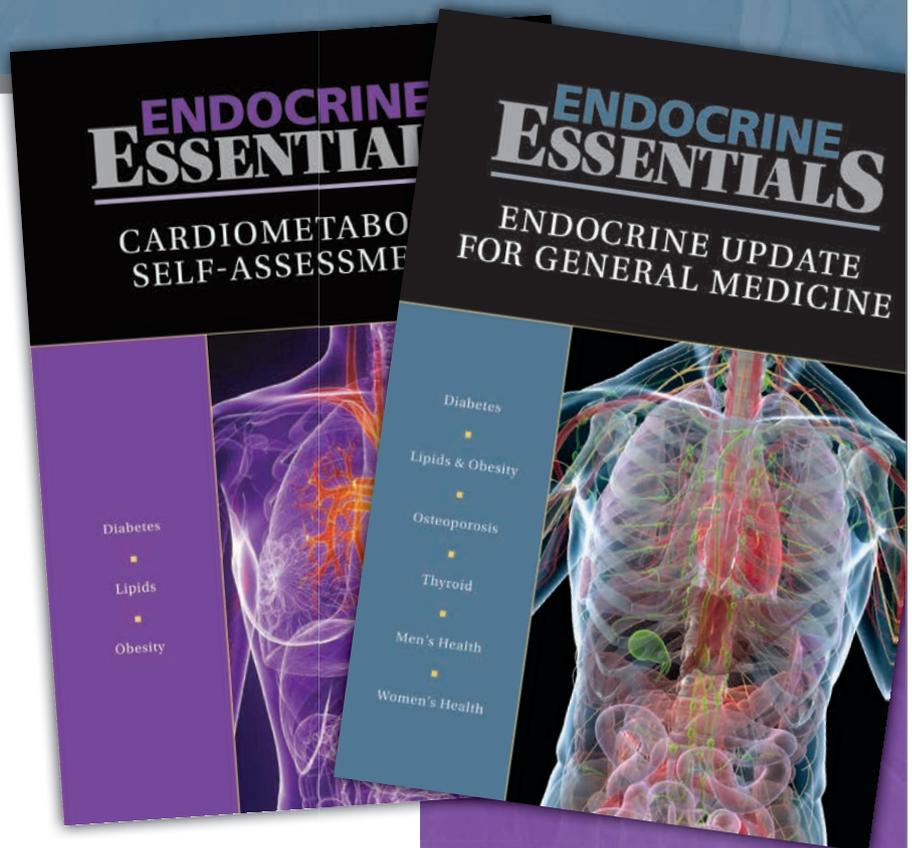
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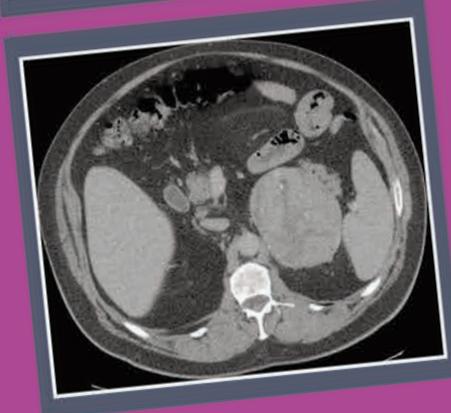
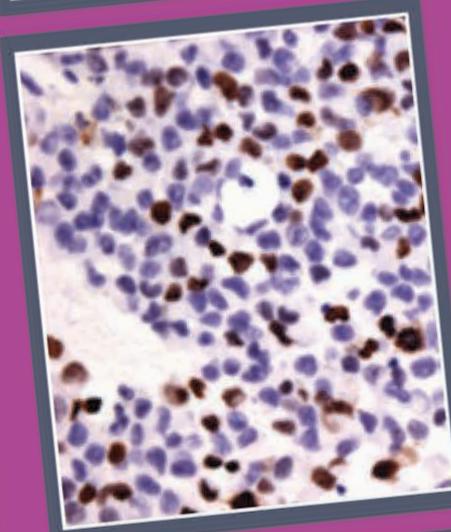
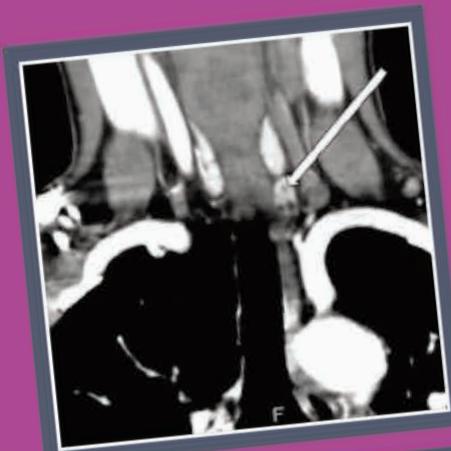
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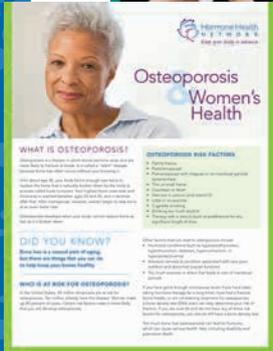
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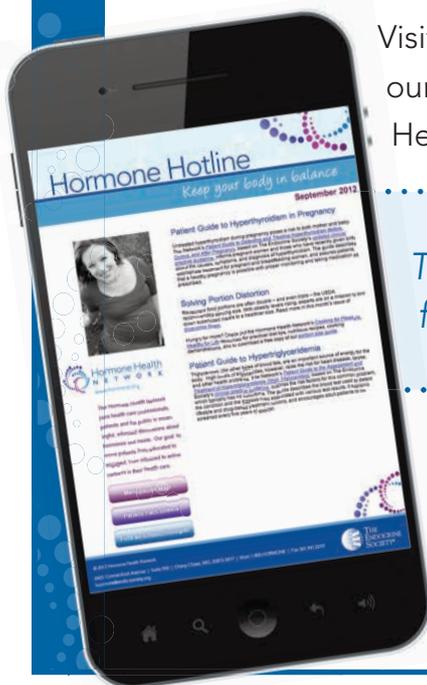
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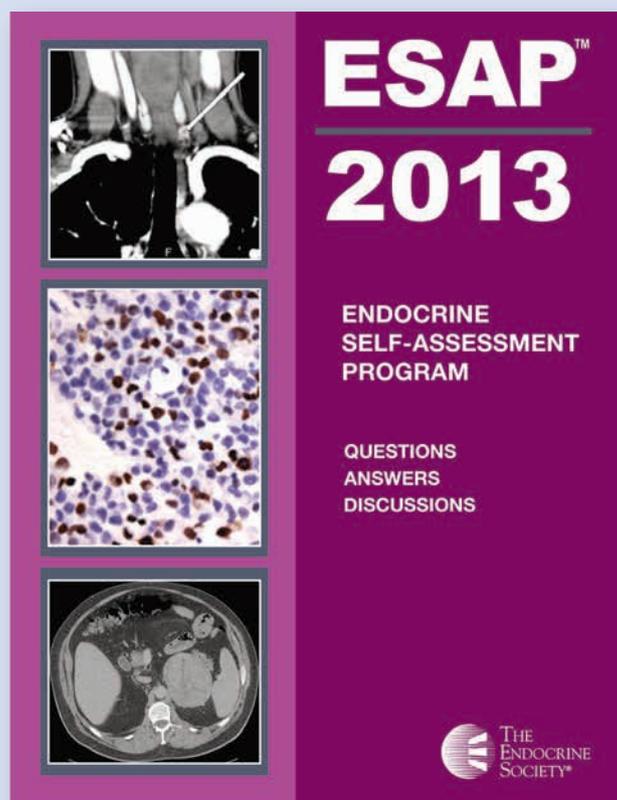
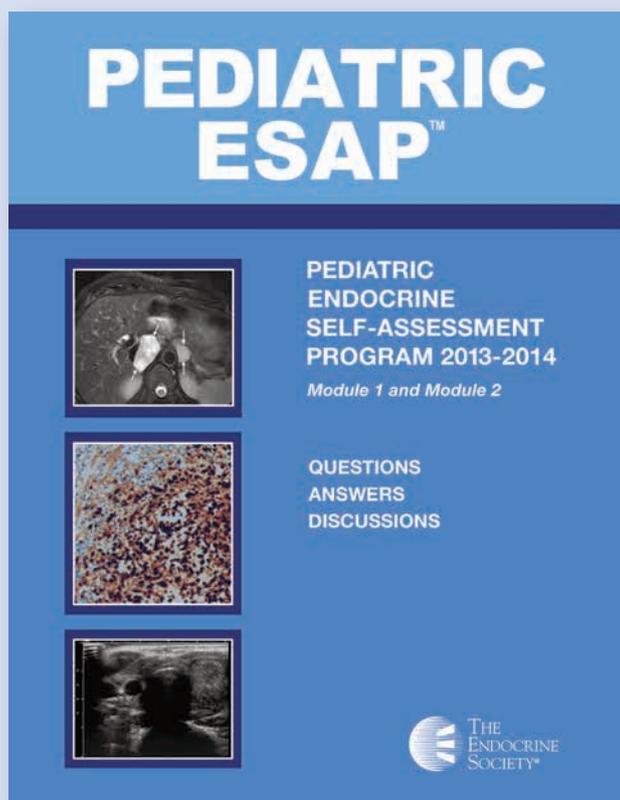
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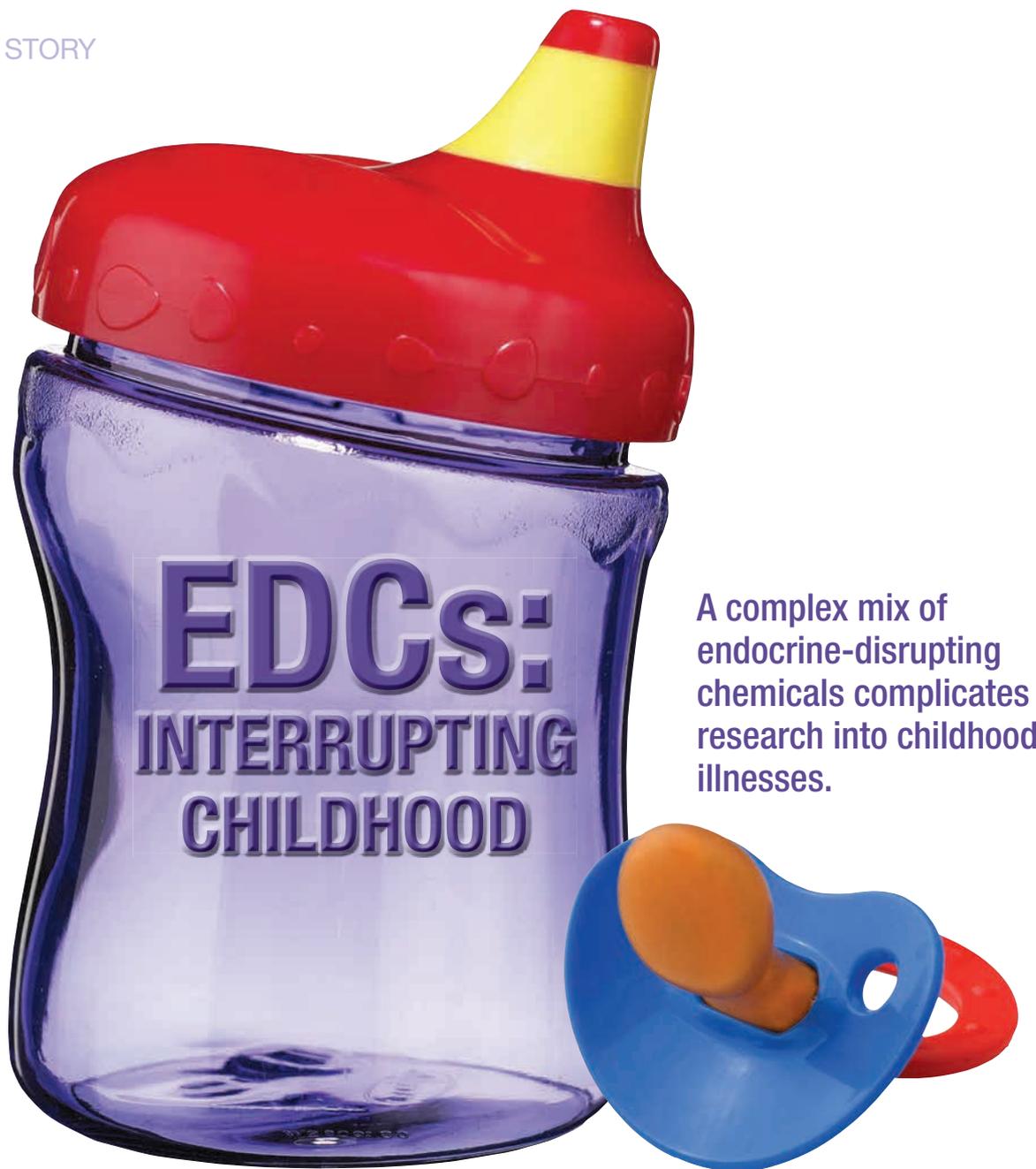
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A complex mix of endocrine-disrupting chemicals complicates research into childhood illnesses.

By Aalok Mehta

If the campaign against endocrine-disrupting chemicals (EDCs) has a public-enemy No. 1, that role probably falls to bisphenol-A (BPA). For more than a decade, the ubiquitous petroleum derivative — used in food packaging, can liners, plastics, and many other consumer products — has swirled at the center of pro-health movements, conflicting scientific studies, and heated political debates. Although evidence continues to accumulate that BPA can be harmful to human health, to this day uncertainties linger about how much and whether the amount that seeps into food reaches the threshold of harm. Expert panels have expressed some concern about BPA's neurological and behavioral effects on infants and children, but to help settle the outstanding questions, the National Institute of Environmental

Health Sciences and other groups are pouring more than \$30 million into new scientific studies.

But focusing on BPA — or phthalates and certain pesticides, other commonly mentioned EDCs — may be missing the forest for the trees. The story emerging from the last decade of research paints a much more complicated picture, in which hundreds of different endocrine disruptors may combine minute effects over long periods of time to harm infants and children. Think less poison, more death from a thousand cuts.

The resulting impacts are complex and subtle. They may even make it impossible to prove that any particular endocrine disruptor is causing cardiovascular disease, type 2 diabetes, obesity, thyroid disorders, earlier puberty in girls, male reproductive disorders, or a host

AT-A-GLANCE

- Instead of a handful of particularly dangerous chemicals, hundreds of endocrine-disrupting chemicals (EDCs) may combine tiny effects to harm human health.
- Little safety data exists for the vast majority of chemicals used in the U.S., including hundreds of potential endocrine disruptors.
- Linking specific endocrine-disrupting chemicals to childhood illnesses is extremely challenging and may not be possible.
- Based on current evidence, most experts recommend taking a precautionary approach to EDC policy, including more bans and restrictions.



“Things are not going to get better until we start requiring the groups that make chemicals to start testing for safety.”

— Andrea Gore, professor, pharmacology and toxicology, University of Texas, Austin

of other hormone diseases that scientists suspect are linked to EDCs.

“We humans each have something like a hundred chemicals on board [in measurable quantities] at any one time,” says R. Thomas Zoeller, a professor of biology at the University of Massachusetts, Amherst. “How do we prove that ‘one’ is ‘the one’?”

An Impossible Task?

This complex mixture poses enormous difficulties for researchers examining how EDCs — which the Endocrine Society defines broadly as chemicals that can interfere with hormone action — might affect fetal and infant health. Low-level exposures can take years before causing any noticeable symptoms, and different EDCs can boost or block each other’s effects.

“The key question is: How do low-level, normal exposures to a fetus or infant cause changes in the endocrine system that play out later in life?” says Andrea C. Gore, a professor of pharmacology and toxicology at University of Texas, Austin. “We can’t make that connection in humans — the time lag is so great, and so much happens in the body during that time.” Researchers face other challenges as well, Gore adds; in many cases, scientists have not yet discovered the normal role of certain hormones, making it even more difficult to track the impact when things go wrong.

Ongoing health trends — particularly the obesity epidemic — create another challenge. EDCs accumulate in body fat, muddying the question of what is causing what. “If you ask me which is the bigger health threat — the food overconsumption or the extremely low levels of EDC in that food — then I would vote unreservedly for the food,” says Richard Sharpe, a professor and male reproductive health researcher at the University of Edinburgh. “We have unequivocal evidence that this causes obesity,

so why would you go for the much more speculative option?” The well-established trend toward earlier puberty in girls is similarly complicated, since obesity and stress contribute to precocious puberty but also tend to increase exposure to EDCs.

When it comes to specific links, “probably some of the better data comes from phthalates and male reproductive development and health,” says John Meeker, an associate professor of environmental health sciences at the University of Michigan in Ann Arbor. Researchers have found that phthalates have anti-androgenic effects — meaning they block the effects of male steroids — in multiple species, including humans. Like much EDC research, however, the human studies looked at data from a single date instead of tracking people over time, which is needed to provide stronger evidence that a chemical causes a disease, Meeker says.

The Bigger Picture

The overall case linking fetal and infant disorders to endocrine disruptors, however, is strong and getting stronger, scientists say. “I’m very confident, and that

OnPOINT from the Endocrine Society

The Endocrine Society has a Scientific Statement that addresses endocrine-disrupting chemicals available for download at: www.endocrine.org/edc. Additionally, the Hormone Health Network also has a scientific statement on EDCs available at: www.hormone.org/ssedc.



How Many EDCs ARE THERE?

There is little dispute that EDCs have permeated the environment. They can be detected in significant quantities in animals, food products, soils, and the human body. And they are numerous: According to the Endocrine Disruption Exchange, scientists have published peer-reviewed papers involving 906

potential endocrine-disrupting chemicals.

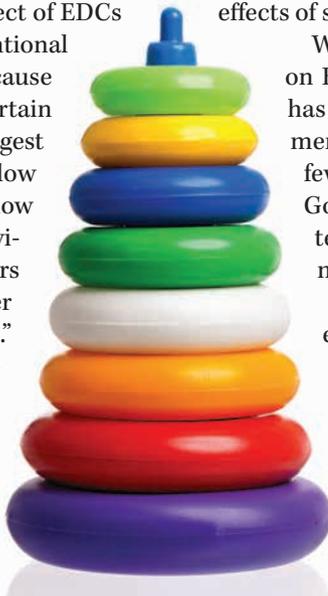
Because of a lack of basic data, however, no one understands the true extent of the issue. “The amount of data we have is amazingly low compared to what you think we would know,” says Amir Miodovnik, a developmental pediatrician at Boston Children’s Hospital.

For instance, in the U.S., chemical manufacturers have registered more than 80,000 chemicals with the Environmental Protection Agency, including 3,000 “high production volume” chemicals that are imported or produced at more than a million pounds annually. However, 43% of these high-volume chemicals have no testing data on basic toxicity, and only 7% have a full set of basic test data, according to a recent EPA survey. “I would say that we’ve only scratched the surface when it comes to identifying chemicals with endocrine-disrupting properties,” Miodovnik adds. — A.M.

confidence comes with a lot of information,” Gore says. She was one of the co-authors of a 2009 Endocrine Society statement finding that, based on existing evidence, EDCs have demonstrated impacts on reproductive development, cancer rates, metabolism, and other systems. The statement also emphasized that infants and children are particularly vulnerable to EDCs and called for additional research.

According to Gore, at certain critical periods, fetuses possess such small levels of hormones — in some cases none at all — that even small exposures can unbalance the delicate process of development. “This is known as the fetal basis for adult disease,” she adds, “and the concept has woven itself through endocrine research.”

This theory is reflected perhaps most intensely by a body of research suggesting that the effect of EDCs might not depend on their dose. Conventional medical theory holds that a chemical will cause negative effects only once it exceeds a certain level. Some recent findings, however, suggest that EDCs might cause harm at extremely low doses, or might cause opposite effects at low doses and high doses. “There is some evidence that the effect of endocrine disruptors may not be linear or monotonic,” Meeker says. “But it’s not accepted by everyone.” That might be understating the disagreement. A recent International Programme on Chemical Safety report assessing the state of EDC research found that “the issue of dose-response relationships is perhaps the most controversial issue regarding EDCs.”



Regardless, however, researchers warn that while low-level exposures might not seem to affect any given individual, they can still have broad implications. “These effects need to be appreciated in a larger context,” says Amir Miodovnik, developmental pediatrician at Boston Children’s Hospital. “Even a small drop in the average IQ of the population could dramatically increase the proportion of people who would be categorized as intellectually disabled.”

A Time for Action

For some researchers, the science remains too uncertain to recommend governmental action. “Any ban should be evidence-driven, not opinion-driven or speculation-driven,” Sharpe says. “For exposures in pregnancy, I would opt for a lower level of proof for precautionary reasons, but I would still want much more convincing evidence than currently available.”

For most others, however, the evidence doesn’t need to be definitive to support taking proactive action on EDCs. Rather, they recommend adopting a philosophical maxim known as the precautionary principle. Often cited in debates about climate change, this principle involves erring on the side of caution when environmental damage or human health is at stake. In the medical realm, this would translate to bans or restrictions on many EDCs unless their manufacturers are able to prove

“If you ask me which is the bigger health threat — **the food overconsumption or the extremely low levels of EDC in that food — then I would vote unreservedly for the food.**”

— Richard Sharpe, professor and male reproductive health researcher, University of Edinburgh

the compounds are not harmful. The Endocrine Society statement also recommends taking a precautionary approach “until such time as conclusive scientific evidence exists to either prove or disprove harmful effects of substances.”

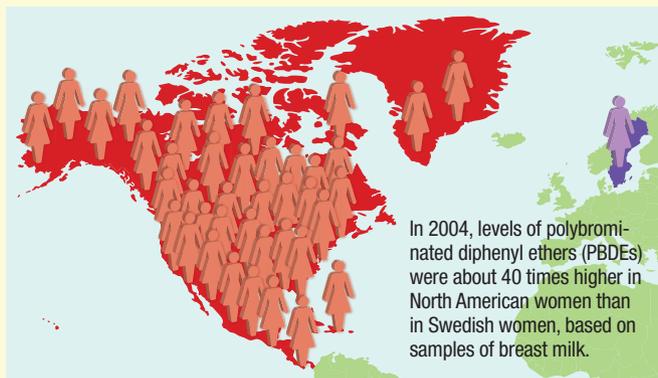
With the exception of a few modest bans on BPA in infant bottles and cups, this vision has yet to come to pass, however. The government is “beyond slow in taking action. Very few chemicals have actually been banned,” Gore says. “Things are not going to get better until we start requiring the groups that make chemicals to start testing for safety.”

Others echo the call for increased government action. “We may not be able to say proof,” Zoeller adds, “but how much information is enough to regulate when our children — and grandchildren — are involved?” **EN**

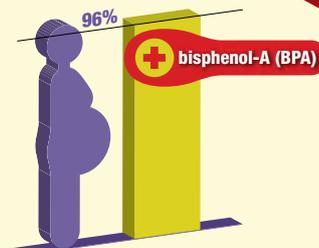
— Mehta is a freelance writer based in Cambridge, Mass. He wrote about the market for kidneys in the February issue.

Fast FACTS About EDCs

A 2000 report documented 2,300 pesticide exposures in American schools from 1993 to 1996.



In 2004, levels of polybrominated diphenyl ethers (PBDEs) were about 40 times higher in North American women than in Swedish women, based on samples of breast milk.

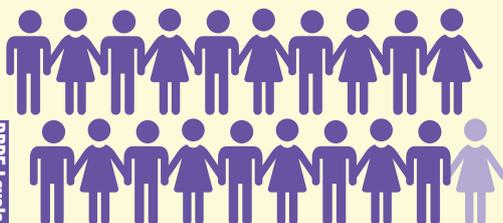


A 2011 study showed that 96% of the pregnant women surveyed tested positive for bisphenol-A (BPA).



As of October 2013, there are nearly 1,000 endocrine-disrupting chemicals on The Endocrine Disruption Exchange's (TEDX) list.

A 2008 study showed that 19 out of 20 children tested had PBDE levels an average of 3.2 times higher than their mothers.



Most of the 2,000 chemicals that come on the market each year don't go through even simple tests to determine toxicity.



Lead can lessen a child's I.Q. by 3 to 5 points.

Sources: The Endocrine Disruption Exchange, Natural Resources Defense Council, *Environmental Health Perspectives* – University of California San Francisco, *Environmental Science & Technology* – Indiana University, Environmental Working Group, General Accounting Office; California State University, *The New York Times* – Mount Sinai Medical Center

DRUM ROLL ANNOUNCING THE 2014 ELECTION RESULTS

The Endocrine Society's Nominating Committee is pleased to announce the results of the 2014 Election that concluded on December 23, 2013. Congratulations to the following Society leaders who will assume their new positions at the Society's Annual Business Meeting on June 24, 2014 during ICE/ENDO 2014 in Chicago.

President-Elect (Physician-in-Practice)
Lisa H. Fish, MD

Vice President (Basic Scientist)
Carol A. Lange, PhD

Council (Clinical Scientist seat)
R. Michael Tuttle, MD

Council (At Large Seats)
Bradley Anawalt, MD
Genevieve Neal-Perry, MD, PhD



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AT-A-GLANCE

- For those at risk of osteoporosis, bone experts recommend adequate calcium and vitamin D intake, including supplements as needed.
- Patients on long-term treatment with the most commonly used osteoporosis drugs, bisphosphonates, may benefit from a drug holiday after several years.
- Because most endocrine conditions affect calcium metabolism and bone formation, endocrinologists could play a bigger role with osteoporosis.

Just as a heart attack is a serious failure of the cardiovascular system, a fragility fracture signals a failure of the skeletal system. Just as no clinician would fail to assess and treat the underlying risk factors in a patient with a myocardial infarction, any bone fracture in an older patient calls for an evaluation for osteoporosis and possible treatment, says Suzanne Jan de Beur, MD, associate professor of medicine at Johns Hopkins University School of Medicine and director of endocrinology, diabetes, and metabolism at the Johns Hopkins Bayview Medical Center, in Baltimore.

The disturbing clinical outcomes of hip fractures in patients over 50 highlight the dangers involved — a 25% one-year mortality rate, with 50% of patients never returning to their previous levels of function.

And the common impression that this is a women's disease can lead to missed diagnoses, considering that a fifth of the cases are men. "Of the two million fractures each year due to osteoporosis, about 600,000 are in men," says Nelson Watts, MD, director of Mercy Health Osteoporosis and Bone Health Services in Cincinnati and lead author of an Endocrine Society guideline on osteoporosis in men. Men are diagnosed on the order of 10 years later in life than women, which can make a broken hip that much more problematic. And the number of cases in both sexes can be expected to increase as the population ages.

Given that most of the conditions endocrinologists deal with have implications for calcium metabolism and hence bone, they should be more involved in bone management and not leave them to other specialties, Watts urges.

Developments and Controversies

Diagnosis and treatment continue to improve and evolve, along with recent developments and controversies, including disagreements about calcium and vitamin D supplements, recommendations for a drug holiday



“Almost any endocrine disorder you can think of has some effects on bone,

including Cushing's disease, diabetes, overtreatment with glucocorticoids for Addison's disease or other adrenal insufficiency, hyperparathyroidism, hypopituitarism that leads to deficiencies in gonadal steroids, and hypogonadism.

It's hard to think of an endocrine disease that doesn't in some way have some effect on calcium.”

— Nelson Watts, MD, director, Mercy Health Osteoporosis and Bone Health Services, Cincinnati

from osteoporosis treatment, improved results from combining current drugs, and promising medications on the horizon.

Diagnosis is more accurate than ever with the advent of the World Health Organization's sophisticated online Fracture Risk Assessment Tool (FRAX) for calculating a patient's risk by taking into account many factors in addition to a T-score from a DXA bone scan. Because two-thirds of vertebral fractures are asymptomatic, recent guidelines from the National Osteo-

porosis Foundation also point out the utility of examining spine x-rays for occult fractures for a better picture of a patient's fracture risk, according to Jan de Beur.

Supplemental Questions

Although some studies and many mainstream media reports have raised issues about the value of calcium supplements and their potential association with cardiovascular events, bone experts do not question their role in treating osteoporosis. Watts notes that calcium is the raw material for building bone, so it is hard to believe one could maintain good bone without it. Although there is no clear evidence that calcium supplements benefit the general population, studies show that the combination of calcium and vitamin D reduces

OnPOINT from the Endocrine Society

The Endocrine Society has a Clinical Practice Guideline that deals with male osteoporosis: *Osteoporosis in Men: A Clinical Practice Guideline*: www.endocrine.org/osteoporosis. Additionally, the Hormone Health Network has a variety of fact sheets and patient guides addressing osteoporosis: www.hormone.org/bone. The Endocrine Society is developing a guideline on the Pharmacological Management of Osteoporosis in Post-Menopausal Women, which is expected to be released in 2015.



On the HORIZON

The mainstays of osteoporosis treatment have been the bisphosphonates, which primarily rely on inhibition of bone resorption. A pair of drugs in clinical trials offer fresh approaches.

- **Odanacatib** inhibits cathepsin K, an important enzyme in the bone resorption process. In contrast to the bisphosphonates, odanacatib inhibits resorption without interfering with bone formation. The results from a Phase 3 study are expected early this year.
- **Romosozumab** is an antibody to sclerostin, which inhibits the development of bone-forming cells. Recently published results from a Phase 2 multicenter clinical trial found that romosozumab produces encouraging gains in bone density in a short time.

fractures in people with osteoporosis. Pauline Camacho, MD, director of the Loyola University Osteoporosis and Metabolic Bone Disease Center in Maywood, Ill., recommends a daily calcium intake of 1,200 mg from all sources to help prevent bone loss, which is the level recommended by the Institute of Medicine (IOM) for women over 50.

Watts and Jan de Beur concur with this recommendation, and all three experts noted the importance of taking a dietary history. Although they questioned the studies showing increased cardiovascular risk from calcium supplements, they agreed that the wisest course is to aim for a daily total calcium intake of about 1,200 mg but not to exceed it to avoid potential pitfalls of high intake, such as kidney stones. Jan de Beur recommends dietary adjustments to increase patients' calcium intake, preferring dietary calcium to supplements because it is accompanied by other nutrients. "There are no studies that demonstrate that dietary calcium is associated with coronary events, and some studies show there is a protective effect," Jan de Beur says. Supplements should make up for any dietary shortfalls.

The Vitamin D Conundrum

The question of how much vitamin D is enough has been the subject of dueling guidelines in recent years. The IOM recommended a vitamin D blood level of 20 ng/ml, but shortly thereafter the Endocrine Society published a guideline recommending a level of 30 ng/ml to not simply avoid deficiency but to ensure sufficiency.

Jan de Beur and Watts say that the IOM guideline was population based, and regardless of its role in the general

population, vitamin D is an important nutrient for people concerned about osteoporosis. "In the bone field, we have clung to the idea that you'd like to have a level of at least 30 ng/ml," Watts says. Jan de Beur aims for a level of 32 ng/ml, whereas Camacho shoots for levels in the 40s or 50s. Camacho says that vitamin D has a very wide therapeutic range, with literature reports of toxicity usually associated with levels in the 150 ng/ml range. She leaves herself a cushion because of the variability of laboratory assays. Because dietary vitamin D is elusive, there is no controversy about turning to supplements.

Drug Holiday

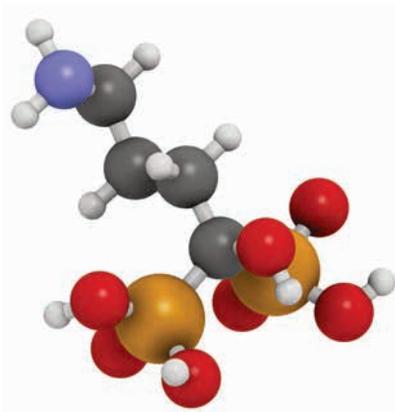
Another current concern relates to how long to maintain continuous treatment with the most commonly used drugs, bisphosphonates. Bones are constantly being remodeled through the formation of new and the resorption of old tissue. Bisphosphonates' benefits are based on slowing bone resorption, but they slow creation at the same time. After several years of treatment, the benefits diminish, and, although the problems remain rare, there is an increase in osteonecrosis of the jaw and atypical fractures of the femur (mid-femur fractures not involving a fall).

"One of the unique things about bisphosphonates is that they accumulate in bone, and so even after we stop giving them, there is a reservoir from which the drug continues to be released, and can provide a lingering benefit," Watts says. And although clinicians lack hard data for making their choices, left with the challenge of balancing risks of osteoporosis versus risks of treatment, guidelines are endorsing the concept of a drug holiday.

Jan de Beur says it is unlikely long-term studies will settle the issue, so "we are going to have to rely on expert opinion" and clinicians' practices vary. She reassesses her patients on oral bisphosphonates after five years. If their bone density is stable and they have an acceptable T-score, she gives them a drug holiday until there is a reason to restart it, such as a drop in bone density, a fracture, or an increase in bone resorption markers. Some physicians simply use a set time period off. Jan de Beur keeps patients with severe osteoporosis on bisphosphonates for 10 years, but avoids exceeding that time. Camacho treats patients with a low or moderate risk of fracture for five years, and then gives them a holiday. She treats patients who are elderly or severely affected for 10

RESOURCES for Osteoporosis Management:

- Screening for Osteoporosis in Men: A Clinical Practice Guideline from the American College of Physicians: <http://annals.org/article.aspx?articleid=740825>
- 2013 Clinician's Guide to Prevention and Treatment of Osteoporosis (National Osteoporosis Foundation): <http://nof.org/hcp/clinicians-guide>
- World Health Organization fracture risk assessment tool (FRAX): <http://www.shef.ac.uk/FRAX/tool.aspx>



“One of the unique things about bisphosphonates is that they accumulate in bone, and so even after we stop giving them, **there is a reservoir from which the drug continues to be released, and can provide a lingering benefit.**”

— Nelson Watts, MD, director of Mercy Health Osteoporosis and Bone Health Services, Cincinnati

years, then gives them a very brief holiday.

Watts says the approach can vary by the specific drug being used, with high-risk patients benefiting from 10 years of treatment with oral alendronate but six years being adequate with zoledronic acid. “Our approach is to monitor bone density, and in the lower risk patient, continue the holiday until the bone density shows a significant drop. In the higher risk patients, we restart treatment after two years off, regardless of how well things are going, and

restart after a year off if bone density drops,” he says.

For treatment of those higher risk patients with severe osteoporosis, recent studies are finding better results by combining treatments. Denosumab is another “antiresorptive,” but it works in a somewhat different fashion from the bisphosphonates. A RANK ligand inhibitor, it interferes with a primary source of the signal for bone removal. Teriparatide is a parathyroid hormone fragment, and is the only drug approved in the U.S. aimed at bone formation. Recent studies show that in combination, the two have additive effects.

Added Role for Endocrinologists

Fractures are often considered the province of orthopedics and bone scans of rheumatology, but narrow interpretations can overlook the myriad conditions that can lead to weakened bones. “Almost any endocrine disorder you can think of has some effects on bone, including Cushing’s disease, diabetes, overtreatment with glucocorticoids for Addison’s disease or other adrenal insufficiency, hyperparathyroidism, hypopituitarism that leads to deficiencies in gonadal steroids, and hypogonadism. It’s hard to think of an endocrine disease that doesn’t in some way have some effect on calcium,” Watts says. So diagnosis should include a comprehensive evaluation for causes of secondary osteoporosis — which is another reason endocrinologists should take greater interest in and ownership of the condition. **EN**

— Seaborg is a freelance writer based in Charlottesville, Va. He wrote about the Affordable Care Act in the January issue.

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ENDOCRINE SOCIETY



GRUDGE MATCH: Pens vs. Syringes

Taking insulin is a cornerstone of care for millions who have diabetes, and the most common method of insulin delivery in the U.S. is injection via needle and syringe. Roughly 20% of insulin users wear an insulin pump, 15% use insulin pens, and less than 1% use jet injectors.

Insulin pumps can be expensive, with the average price hovering around \$6,500, not including the disposable supplies that have to be replenished regularly, such as infusion sets, cartridges, and batteries. Although jet injectors may seem like a dream come true for patients who fear needles, they have been known to cause bruising and more pain than injections.

The big question is why insulin pens are not more popular in the U.S., whereas in Europe and Japan, they comprise from 66% to 75% of insulin prescriptions. It's not for lack of patient appreciation: In the November 2011 issue of the *Journal of Diabetes Science and Technology*, a review of 43 studies that compared patient-reported outcomes for insulin pen devices found that

patients preferred pens over vial and syringe for myriad reasons, including ease of use, less pain, and greater perceived social acceptance.

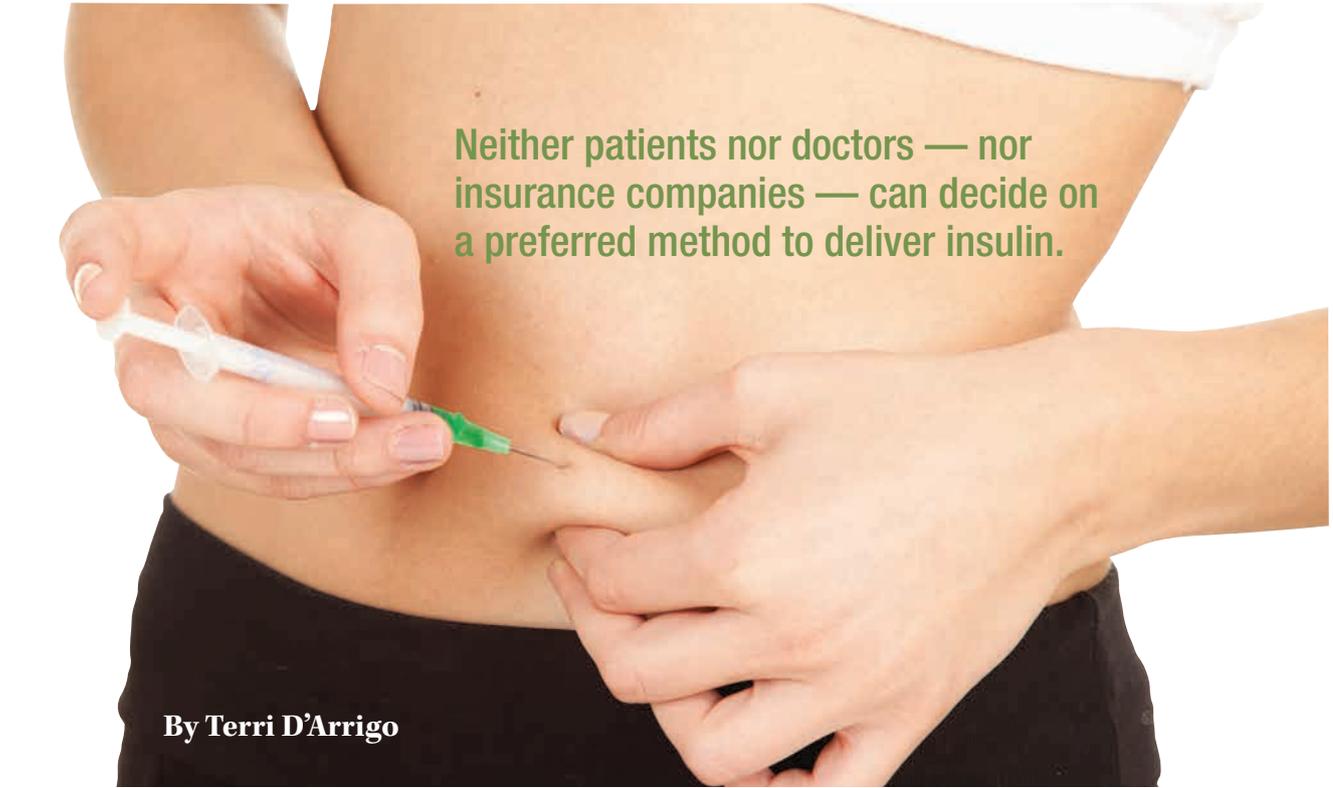
Indeed, patients are generally receptive to pen use — if their physicians bring it up. A study published in the March 2008 issue of *Diabetes Care* found that physician encouragement had a tremendous impact on pen use: Patients whose physicians discussed insulin pens were 100 times more likely to use an insulin pen than those whose physicians did not discuss pen use or who discouraged pen use.

One reason pens have not caught on here may be payer reimbursement, says Maria J. Redondo, MD, PhD, MPH, assistant professor of pediatrics at Baylor College of Medicine in Houston and co-author of the 43-study review. “Pens are more expensive than vial and syringe, and different insurance companies cover different pens depending on the formulary.”

Inconsistent insurance coverage seems counterintuitive to Carl V. Asche, PhD, research professor of

AT-A-GLANCE

- Not all insurance companies or payers cover all insulin pens. All providers — physicians, nurse practitioners, and pharmacists — should be aware of the costs to the patient, regardless of which method of insulin delivery is most appropriate.
- Pens may be easier for some patients or caregivers with impaired vision or dexterity, but those with arthritis may have a tougher time pushing a pen's plunger down.
- Physicians should remember to prescribe the needles as well as the pen.
- Syringes may be more appropriate for people who take large doses of insulin or who take more than one kind of insulin at a given time. It is not possible to mix insulins in a pen.



Neither patients nor doctors — nor insurance companies — can decide on a preferred method to deliver insulin.

By Terri D'Arrigo

medicine and director of the Center for Outcomes Research at the University of Illinois College of Medicine at Peoria. Asche co-authored a review appearing in a supplement to the June 2010 issue of *Diabetes Technology and Therapeutics* that found an association between insulin pen use and greater patient adherence to insulin regimens and decreased use of healthcare resources and their associated costs compared to the use of vial and syringe.

“Managed care has not embraced pens here, but without factoring cost offsets for things like improved outcomes and lower overall healthcare costs [among insulin pen users], it’s not clear to me how insurers come to that decision,” says Asche.

Whether the Affordable Care Act will affect reimbursement for pens remains to be seen. In the meantime, physicians can work with their patients to determine whether pens might be more suitable than vial and syringe by keeping several key considerations in mind.

Dosing Factors

One advantage insulin pens offer is that they require fewer steps than vial and syringe. Although some pens require users to pop a cartridge in, most pens are disposable and come pre-filled with insulin. Users need only to check the cartridge to ensure there are no bubbles, prime the needle if there are, then dial up their dose and inject.

“Using a vial and syringe requires more steps and a larger skill set. The more steps there are, the more opportunities there are for mistakes,” says Linda Siminerio, RN, PhD, CDE, professor of medicine and executive director at the University of Pittsburgh Diabetes Institute.

Depending on the patient’s insulin needs and which pen or syringe is being used, the size of the dose can be a determining factor.

“Many of the 100-unit syringes are marked in two-unit increments. That won’t work for patients who take an odd number of units,” says Zachary Weber, PharmD, BCPS, BCACP, CDE, clinical assistant professor of pharmacy practice at the Purdue College of Pharmacy in Indianapolis. “Generally, I counsel pharmacy students to be wary about making odd-number unit recommendations, but

it depends on how much insulin the person needs overall. If someone takes 60 to 80 units per day, a one-unit difference may not matter. But if the person takes less than 20 units per day, it will make a difference.”

In such cases, pens that offer single-unit dosing may offer an advantage. In fact, several studies indicate that insulin pens are more accurate than syringes for doses of less than five units.

However, the vial and syringe method has one key advantage over pens, says Siminerio. “If you have to take two different types of insulin, you can’t mix them

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it’s not clear to me how insurers come to that decision.”

— Carl V. Asche, PhD, research professor of medicine and director, Center for Outcomes Research, University of Illinois College of Medicine, Peoria



together in a pen. This will mean separate shots, which can be an issue for kids or anyone who wants to minimize their number of injections.”

Vision and Dexterity

Because pens are larger than syringes, require fewer steps in preparing injections, and produce a click that users can hear and feel as they dial a dose, they may be a better option for patients with impaired vision or dexterity, says Weber. But he noted one prominent exception: patients or caregivers who have arthritis.

“The plunger is larger in a pen than with a syringe, and pen needles tend to be a smaller gauge than needles used with syringes. That creates more resistance when pushing the plunger down, which can be a challenge for patients who have arthritis or joint problems in their hands, particularly in their thumbs,” Weber says.

He added that pens require a slightly longer injection time. “Pens require users to keep the needle under the skin for a few more seconds than syringes because of the difference in needle gauge. It takes longer for the liquid to be expelled with a pen,” Weber says. “Usually we tell pen users to count one-Mississippi-two-Mississippi up to five Mississippis for pens, versus three Mississippis for syringe.”

Two seconds may not seem like a big deal, but if pen users have tremors or lack hand strength, they may withdraw the needle too soon, insulin may leak out, and the patient’s blood glucose may remain high. If it happens enough, the patient may write the pen off as ineffective.

“This is the kind of thing clinicians don’t think about until they see a few thousand people with diabetes,” says Weber. “But it’s the details like this that can be why someone’s diabetes is not well-controlled.”

Addressing Misconceptions

Patients and physicians alike may have misconceptions or false assumptions about insulin pens.

“Some patients worry that the technology will make them harder to use,” says Redondo. “In the United States, the more technology-friendly patients tend to opt for insulin pumps, while those with less comfort with technology may prefer to stay with vial and syringe.”

Other patients may assume too much of insulin pens, says Weber. “I’ve seen patients who think that using a pen negates the need to check their blood glucose. They will do anything they can to minimize the burden of pricking their fingers and checking their blood glucose, but there is no evidence that using a pen makes a difference.”

Physicians may have misconceptions about pen needles, as well, particularly with respect to their patients with type 2 diabetes, says Siminerio. “There’s

an assumption that obese patients need longer needles, but the fact is that longer needles will go intramuscular instead of subcutaneous, so shorter needles are reported to be safer,” she says.

Siminerio adds that there is often confusion when it comes to prescribing needles. “Everyone expects someone else to prescribe the needle size. Physicians think the pharmacist will do it, pharmacists think the physician will do it, and the patient shows up at the pharmacy and ends up with whatever is available. Physicians need to remember to prescribe the needle size and think small.”

Redondo points out that the sheer number of insulin pens on the market can make it difficult for physicians to keep track of them all. “There can be a lack of familiarity with specific pens and what they can do. If physicians had that familiarity, they would be more likely to prescribe pens.”

One way to address this challenge is to consult with diabetes educators, Redondo says. “They tend to know all the newest pens and their features.”

Physicians who prescribe insulin pens should steer their patients toward diabetes educators from the start, says Siminerio. “Patients in several focus groups across demographics — African American, Latino, Caucasian — have all said that it would be better to have an in-person demonstration of how to use a pen before they go to the pharmacy. That’s where you can rely on educators.”

Money Talks

In the end, insurance coverage may be the deciding factor when choosing between pens and vial and syringe, says Redondo. “A physician may want to prescribe a pen, but maybe the patient’s insurance plan covers some pens, but not all of them, or not pens that would be most suitable for that particular patient. That will be more paperwork for the patient and physician with obtaining prior authorization.”

When it comes to expense, forewarned is forearmed, says Siminerio.

“Endocrinologists, primary care physicians, nurse practitioners, pharmacists — everyone needs information on cost. Too often, patients get a prescription for insulin therapy and when they get to the pharmacy that’s when they find out how much it costs,” Siminerio says. “Comparing pens to syringes is not as simple as saying one is better than the other. Expense can be problematic for pens.” **EN**

— *D’Arrigo is a health and science writer based in Holbrook, N.Y., and a regular contributor to Endocrine News. She wrote about treating diabetes accompanied by celiac disease in the February issue.*

“Using a vial and syringe requires more steps and a larger skill set.

The more steps there are, the more opportunities there are for mistakes.”

— *Linda Siminerio, RN, PhD, CDE,
professor of medicine and executive director,
University of Pittsburgh Diabetes Institute*



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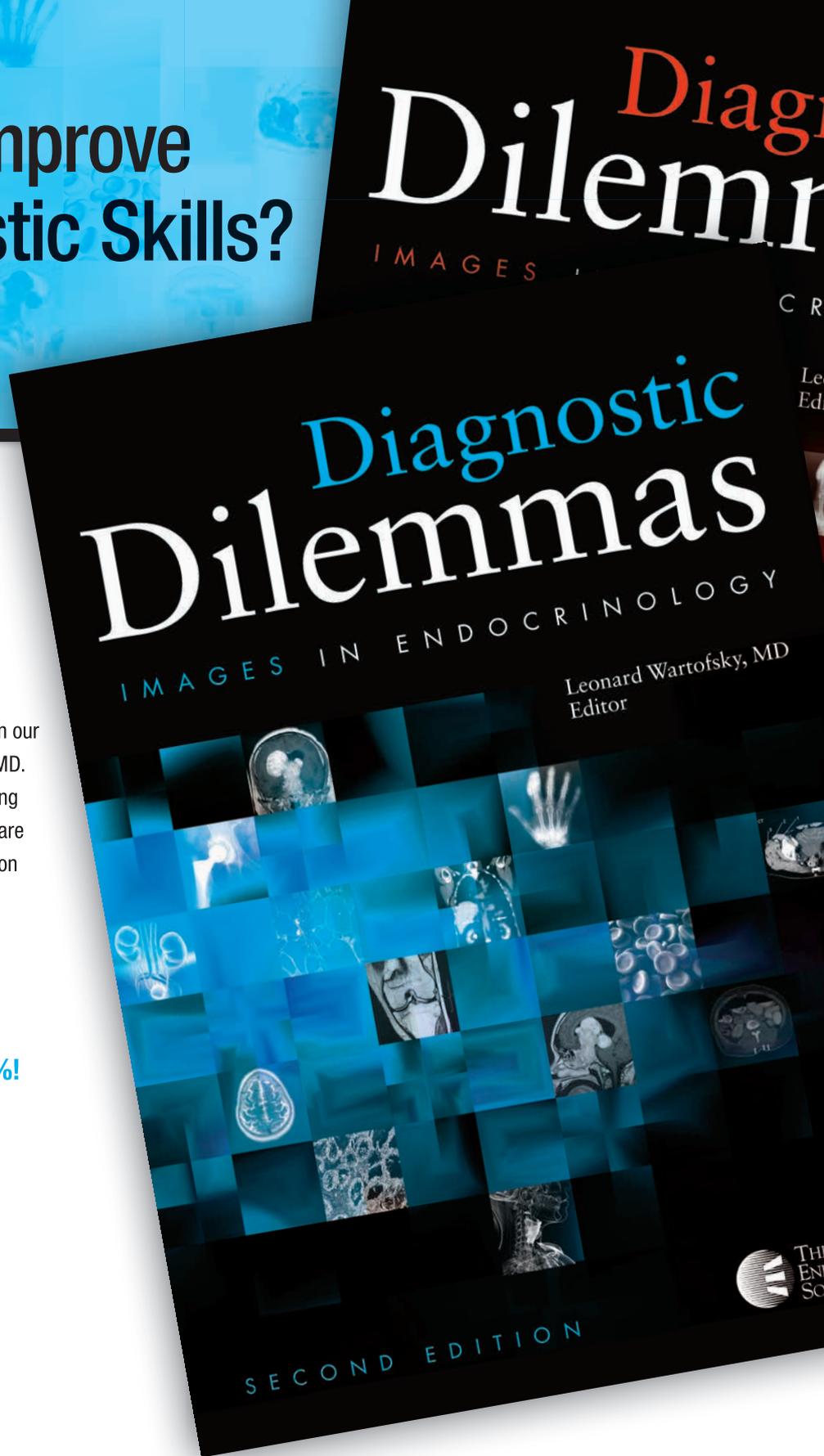
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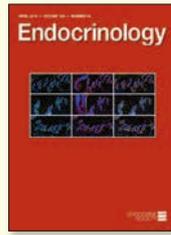
The following studies, among others, will be published in Endocrine Society journals. Before print, they are edited and posted online in each journal's Early Release section. You can access the journals at www.endocrine.org.



Prevalence of Pituitary Dysfunction Following Severe Traumatic Brain Injury in Children and Adolescents: A Large Prospective Study • Claire

Personnier, Hélène Crosnier, Philippe Meyer, Mathilde Chevig-nard, Isabelle Flechtner, Nathalie Boddaert, Sylvain Breton, Caroline Mignot, Yamina Dassa, Jean-Claude Souberbielle, Marie Piketty, Kathleen Laborde, Jean-Philippe Jais, Magali Viaud, Stephanie Puget, Christian Sainte-Rose, and Michel Polak • *At one year post-severe TBI, pituitary dysfunction was found in 8% of our study sample. We recommend systematic hormonal assessment in children and adolescents 12 months after severe TBI and prolonged clinical endocrine follow-up.*

Development and Characterization of a Differentiated Thyroid Cancer Cell Line Resistant to VEGFR-Targeted Kinase Inhibitors • Crescent R. Isham, Brian C. Netzel, Ayoko R. Bossou, Dragana Milosevic, Kendall W. Cradic, Stefan K. Grebe, and Keith C. Bible • *Selection of thyroid cancer cells with clinically utilized therapeutics can lead to acquired drug resistance and altered in vivo xenograft behavior that can recapitulate analogous drug resistance observed in patients. This approach has potential to lead to insights into acquired treatment-related drug resistance in thyroid cancers that can be subjected to subsequent validation in serially collected patient samples — and that has potential to yield preemptive and responsive approaches to dealing with this important clinical problem.*



The 5¹-Deiodinases Are Not Essential for the Fasting-Induced Decrease in Circulating Thyroid Hormone Levels in Male Mice: Possible Roles for

the Type 3 Deiodinase and Tissue Sequestration of Hormone • Valerie Anne Galton, Arturo Hernandez, and Donald L. St. Germain • *This study shows that the systemic changes in TH economy as a result of acute food deprivation are not dependent on the D1 or D2, but are mediated in part by sequestration of T4 and T3 in tissues and their enhanced metabolism by the D3.*

Hyperplasia and Cellularity Changes in IGF-1-Overexpressing Skeletal Muscle of Crucian Carp • Dongliang Li, Qiyong Lou, Gang Zhai, Xuyan Peng, Xiaoxia Cheng, Xiangyan Dai, Zijian Zhuo, Guohui Shang, Xia Jin, Xiaowen Chen, Dong Han, Jiangyan He, and Zhan Yin • *The results indicate that the sustained overexpression of IGF-1 in crucian carp skeletal muscle promotes myofiber hyperplasia and cellularity changes, which elicit alterations in the body energy metabolism and skeletal muscle growth.*

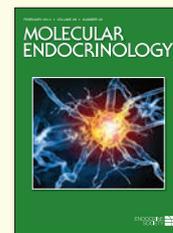
Circulating Glucagon-Like Peptide-1 (GLP-1) Inhibits Eating in Male Rats by Acting in the Hindbrain and Without Inducing Avoidance • Mukesh Punjabi, Myrtha Arnold, Elisabeth Rüttimeann, Mariana Graber, Nori Geary, Gustavo Pacheco-López, and Wolfgang Langhans • *The results implicate hindbrain GLP-1R and the AP in the eating-inhibitory effect of circulating GLP-1, but question the physiological relevance of the eating-inhibitory effect of intravenously infused GLP-1 under our conditions.*



Treatment with Thyroid Hormone • Bernadette Biondi and Leonard Wartofsky • *In this review, we critically discuss the thyroid hormone formulations that are*

available and approaches to correct replacement therapy with thyroid hormone in primary and central hypothyroidism in different periods of life and in patients with comorbidities.

Growth Hormone, Insulin-Like Growth Factor-1, and the Kidney: Pathophysiological and Clinical Implications • Peter Kamenický, Gherardo Mazzotti, Marc Lombès, Andrea Giustina, and Philippe Chanson • *We analyzed how GH and IGF-1 regulate renal development, glomerular functions, and tubular handling of sodium, calcium, phosphate, and glucose.*



Thioredoxin-Interacting Protein Stimulates its Own Expression via a Positive Feedback Loop • Junqin Chen, Gu Jing, Guanlan Xu, and Anath Shalev • *The results*

demonstrate for the first time that TXNIP modulates ChREBP activity and thereby uncover a previously unappreciated link between TXNIP signaling and cell metabolism.

FGFR4 Polymorphic Variants Modulate Phenotypic Features of Cushing Disease • Tae Nakano-Tateno, Toru Tateno, Maw Maw Hlaing, Lei Zheng, Katsuhiko Yoshimoto, Shozo Yamada, Sylvia L. Asa, and Shereen Ezzat • *FGFR4 transmembrane polymorphic variants can modulate cellular growth and sensitivity to glucocorticoid hormone negative feedback through distinct STAT3 modifications of relevance to the human forms of Cushing disease.*



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COMPETITIVE ADVANTAGE

By Derek Bagley

Competition is ingrained in the entire process of medicine, from bench to bedside, from the time someone decides to go to medical school, on through the interview trail, finding a position or starting a practice, and so it goes.

According to Kathryn Horwitz, PhD, of the University of Colorado School of Medicine, if you want to be a good scientist, “you have to have a fire in your belly,” as she said in an interview as part of the Endocrine Society’s Oral History collection in the Clark Sawin Library, in which she discussed the “competitive side of science.” She added that “you really have to want it badly. You want to do some good... But what you really want is to beat out all of those other bastards who are working in the same area that you’re in and do it better than they are!”

Practicing medicine indeed has noble pursuits, but ultimately, it’s a business, and like any other business, one of the main goals is to not only stay afloat and earn a living, but to “beat out” everyone else.

Fear, Greed, and Jealousy

Elliot Levy, MD, a clinical professor of medicine in the Division of Endocrinology at the University of Miami (Florida) School of Medicine led a workshop called “Setting Up and Negotiating Your Clinical Practice” at last year’s ENDO Early Careers Forum. He points out that knowing just how “different things are now” — from office overhead costs to the impact of the Affordable Care Act — is the first step in dealing with competition. For instance, determining exactly how much it costs to treat

You’ll face competition throughout your career, but overcoming it may be easier than you think.

each patient “will allow you to make an intelligent, level-headed choice about participating in an insurance plan,” and will keep you from making a business decision out of “fear, greed, or jealousy.”

Other things to consider: Knowing where your patients are coming from, what percentage of your patient population has Medicare insurance, and whether patients have PPO or HMO plans; where your referrals are coming from, whether they’re from other doctors, advertisements in local media, or other patients; and the concepts of only seeing patients for cash, accepting no insurance, and concierge medicine.

Armed with that knowledge, it’s easier to handle whatever competition may arise. Patients will still leave one doctor for another, but myriad factors contribute to that, whether it’s an insurance issue, about which little can be done, or the patient simply didn’t like the way he or she was treated during the visit, about which plenty can be done.



A Tangled World Wide Web

A research letter published online in February in the *Journal of the American Medical Association* acknowledged the trend of rating doctors online, stating, "Patients are increasingly turning to online physician ratings, just as they have sought ratings for other products and services." Lead author David A. Hanauer, MD, of the University of Michigan, and his team found that 59% of U.S. adults viewed physician rating sites as "somewhat important" or "very important" when choosing a doctor, based on the results of a nationwide survey in 2012.

The authors wrote that while there were limitations to their Internet-based survey — a 60% response rate and the possibility that most of the respondents were web-savvy and younger than most healthcare consumers — rating sites "may be useful to the public but the implications should be considered because the stakes are higher."

Take a look at any website that rates doctors and you'll see what criteria patients look for, such as how long the doctor spends with each patient, whether the doctor listens to his or her patients, timeliness, cleanliness, professionalism, and so on.

Using online reviews as a barometer of just how well your patients like you isn't an exact science, and usually the people who take the time to leave responses are only the ones who feel passionate enough either way to do so. Still, it's a good start. "All of these factors mean a tremendous amount to a patient," Levy says, "but often are never addressed or even considered by a doctor."

Satisfaction Guaranteed

But handling competition isn't just about keeping the patients happy; referring physicians need to be able to feel like they can count on you when they send a patient your way. Be flexible and accepting of patient's own schedules, even making time to see them over lunch or toward closing time. "Putting off a referral for six to eight weeks is a sure way of never receiving another referral from that doctor again," Levy says.

The best thing you can do to deal with competition is be the best doctor you can be, which means treating your patients and fellow doctors with the utmost care and dignity. "Once a patient sees you, that person should walk away very satisfied with your care, and will tell all their family and friends, and then tell their referring doctor what a good experience they had in your office," Levy says.

At the end of the day, don't worry about your competition, he adds, echoing Horwitz's comments from her oral history, "just be better and smarter than they are." **EN**

— Bagley is the associate editor of *Endocrine News*.
He wrote about health disparities and patient cultures in the March issue.

Announcing Endocrine Press!

In keeping with the mission to advance excellence in endocrinology, the Endocrine Society is pleased to announce the launch of Endocrine Press. This newly revamped publishing program will offer a wide scope of content, from peer-reviewed journals to scholarly books and other material, in both print and digital formats.

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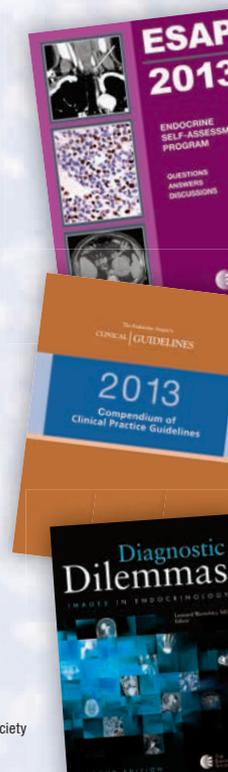
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SAFE & Sound

While it may sound corny, “safety first” is a must in academic and clinical labs where the failure to follow proper procedures can have devastating consequences

By **Melissa Mapes**

No lab director wants to receive a complaint from an inspector. But James Gibson, PhD, director of the Office of Environment, Health and Safety (EH&S) at UCLA, remembers one instance when a grievance brought a smile to his face.

A policy had recently been implemented in UCLA labs that clearly defined the rules for wearing personal protective equipment (PPE). When inspectors arrived for an annual review, they removed their PPE from a previous lab examination to avoid cross-contamination. Laboratory personnel refused entry because they were not wearing the proper gear — unaware of whom the visitors were. The inspectors complained to Gibson, but he felt pleased instead of disappointed because his colleagues had demonstrated an unflinching dedication to safety regulations.

Top-to-Bottom Safety

Gibson believes that consistent compliance comes from

strong leadership. He and his team aim to nurture an environment devoted to workplace safety in each and every lab. “Good safety culture almost always comes from the top. If the lab manager or supervisor leads by example and shows that they value workplace safety, then their employees tend to mirror that attitude,” he explains.

The rules of lab safety are extensive and often laborious. Lab managers must memorize long lists of state and federal regulations, such as no food, no drink, no entry without PPE, constant paperwork, and specific cleaning methods. Ideally, these rules become second nature through practice and reinforcement, but employees will not take regulations seriously if their supervisor does not.

To demonstrate commitment, Gibson emphasizes that workplace safety must be carried out year-round. “All too often, many laboratory researchers view lab safety as an administrative burden or something to be concerned with just before and during an annual inspection,” he says. The rules may seem draconian, but they

exist for a reason. Researchers and supervisors are responsible for the safety of everyone in the lab, and a small slip-up could result in dire consequences.

Immediate Dangers

The worst possible repercussion, according to Gibson, is a workplace injury. His office makes harm prevention its top priority. "In the vast majority of instances, non-complaint findings are quickly corrected," he says. "However, activities found to be IDLH [immediately dangerous to life or health] are immediately halted until the hazard is corrected."

Major accidents are unusual, but the dangerous chemicals and machinery used routinely in labs must never be taken for granted. Academic researchers often stay late and work alone, meaning they are unsupervised and frequently tired — a recipe for mishaps.

Experiments are at times put before safety in university labs. American Chemical Society surveys show that 70.5% of faculty and 52.1% of graduate students in the U.S. often or occasionally work alone in laboratories, which is banned in industry labs. Universities are thus more likely to encounter severe and occasionally catastrophic mishaps.

In one tragic example, Michele Dufault, a 22-year-old undergraduate student at Yale, stayed late to work on a chemistry project in the lab's machine shop in 2011. Her hair got caught in a lathe, and she was choked to death. Because she was likely alone, no one was able to come to her aid in time. Dufault had completed all required lab safety training and had used the machine many times previously. It was later discovered that the lathe was missing safeguards and not up to national safety standards.

A couple of years before Dufault's death, a young UCLA graduate student, Sheharbano Sangji, met a horrifying death when she accidentally exposed a pyrophoric substance to air. She was tiring tert-Butyllithium (tBuLi) — which combusts on contact with air — under a fume hood. The plastic syringe containing the tBuLi popped out of the barrel and the chemical ignited. The surprise caused her to knock over an open flask of hexane, which was also under the hood, though not part of the experiment.

The resulting fire consumed Sangji — who was not wearing a lab coat and may not have been wearing protective goggles. A fellow researcher tried to put out the

Deadly MISTAKES

- No protective eyewear or lab coat
- Uncovered chemicals
- Improperly maintained machinery
- Mishandling of combustible substances
- Unclean workspace
- Working alone or without supervision

flames by wrapping her in a lab coat and dousing her with water, but it was too late. She died 18 days later from the injuries.

Both accidents caused major stir in the world of academic labs. After Sangji's death, UCLA launched the UC Center for Laboratory Safety — the first center in the U.S. devoted entirely to improving the practice of lab safety through scientific research — and continues an unwavering dedication to safe practices. Yale responded by increasing safety training and limiting work hours in labs for undergraduates.

Despite the lessons offered by these tragedies, Gibson and other safety officers still face the ongoing challenge of negative attitudes toward regulations. He has formulated methods that help overcome this obstacle and keep lab safety on track.

Cultivating Compliance

"First, it's critical that we identify the hazards in the laboratory and train the researchers on how to work safely to mitigate any risk that might be present," Gibson says. The training and safety activities must be continuous and not a one-time introduction for new lab workers. His office provides daily guidance and oversight for UCLA laboratories.

"Another challenge is that researchers sometimes make incorrect assumptions about others' level of safety knowledge," Gibson continues. Researchers need to keep an eye out for one another and speak up if they see a colleague making a safety violation. It can be easy to get absorbed in one's own work, but, if a student leaves out an open container of a potentially dangerous chemical, classmates need to take notice and step in rather than assume the person knows what they are doing.

Finally, Gibson recommends close supervision. Everyone behaves a little better when they know they are being watched. "It's really the proverbial 'management by walking around.' It really works," he claims.

Now, even lab inspectors are called out for violations at UCLA. "It all comes down to developing and maintaining a culture of safety where trained and informed laboratory researchers automatically do the safe thing — sort of like putting on your seat-belt when you get into your car. You do it without even thinking." **EN**

— Mapes is a Washington, D.C.-based freelance writer. She wrote about obesity and dementia in the February issue.

For More INFORMATION

- UC Center for Laboratory Safety; <http://cls.ucla.edu/>
- Recent lab accidents in the news; <http://cls.ucla.edu/press/2014>



Senator Introduces Legislation to Provide Mandatory Funding for Biomedical Research

Congressional Appropriations Committees currently are working to determine fiscal year 2015 funding levels for federal agencies. As part of this process, the Endocrine Society has a great opportunity to encourage representatives and senators to support our recommended funding level for the National Institutes of Health (NIH) of \$32 billion.

All members of Congress may submit funding requests on behalf of specific programs, including the NIH. The requests from members of Congress are a very important factor the Appropriations Committees take into consideration when making funding decisions. The Endocrine Society has developed an advocacy campaign to encourage members of Congress to support our request.

Take Action: Please visit the Society’s online advocacy center (www.endocrine.org/advocacy-and-outreach/take-action) to email your senators and representatives today, asking them to submit appropriations requests in support of \$32 billion for NIH. Sending an email to your elected officials only takes a few moments but makes a big difference at such a critical time.

Senators Want to Establish Regenerative Medicine Research Strategy



Sen. Barbara Boxer (D-CA)

Senators Barbara Boxer (D-CA) and Mark S. Kirk (R-IL) introduced legislation to develop a national strategy to promote regenerative medicine research, including identifying priorities and funding sources.

The measure attempts to build on a Department of Health and Human Services (HHS) report that recommends leveraging advances in stem cell research to develop cures for diabetes, heart disease, renal failure, and spinal cord injuries, among other afflictions.

About \$4 billion of private sector spending on regenerative medicine has only yielded a handful of first-generation skin and cartilage substitutes, according to the HHS report. It notes government resources and coordination are necessary to create complex tissues and organs to replace those that are damaged or failing. Federal investment in the field from 1988 to 2001 is estimated to have totaled about \$250 million.



Sen. Mark S. Kirk (R-IL)

A comprehensive strategy would, among other things, speed development of a regulatory system at the FDA to evaluate the safety and efficacy of new products, according to the report.

The bill would direct the Government Accountability Office to identify all ongoing federal efforts and require HHS to create a coordinating council to develop a strategy.

“This bill will help make the promise of these medical breakthroughs a reality for this generation and generations to come”

— Senator Barbara Boxer (D-CA)

House and Senate Pass Pediatric Research Bill

Both the U.S. House of Representatives and the U.S. Senate have passed legislation that would authorize spending for NIH pediatric research grants by redirecting funds for national party conventions.

The bill (HR 2019 — Gabriella Miller Kids First Research Act) now goes to President Barack Obama for his signature. It would authorize \$126 million over 10 years for NIH pediatric research by redirecting federal funds from the Presidential Election Campaign Fund, which pays for both the Republican and Democratic nominating conventions.

House Majority Leader Eric Cantor, R-Va., campaigned vigorously for the measure as part of an effort to rebrand Republicans. Some House Democrats, however, opposed the bill, claiming that it distracted from deeper, Republican-supported sequester cuts to NIH funding, which amounted to \$1.55 billion last year.

Instead of the \$126 million funding the party conventions, it would be directed to the Common Fund at the NIH, supporting research into



Eric Cantor, House Majority Leader (R-VA)



Durbin Introduces Legislation to Provide Mandatory Funding for Biomedical Research

Senator Dick Durbin (D-IL) introduced legislation last week to create a trust fund to support a mandatory federal funding stream for biomedical research. The Endocrine Society endorsed the bill, called the American Cures Act (www.endocrine.org/americancures).

The bill would create a trust fund to provide additional resources for the NIH, Centers for Disease Control and Prevention, Department of Defense Health Program, and Veterans Medical & Prosthetics Research Program. The bill would increase funding annually for each agency and program at a rate of 5%.

The bill's introduction also shows how influential the Society's grassroots advocacy efforts can be. When Society President Teresa K. Woodruff, PhD, visited Sen. Durbin's office last fall, they discussed the importance of biomedical research funding and the crucial role it plays in the health and well-being of all Americans. During the conversation, Durbin noted the funding should be mandatory, not discretionary.

"We appreciate Sen. Durbin's continued leadership in championing for biomedical research," Woodruff said. Sen. Durbin has been selected to receive the Society's Distinguished Legislator Award for his work in this arena.



Sen. Dick Durbin (D-IL) and Endocrine Society president Teresa K. Woodruff, PhD, at the senator's office last fall. They had been discussing a federal trust fund for biomedical research, which plays an important role in the health of all Americans. Durbin will receive the Society's Distinguished Legislator Award for his continued support of biomedical research.

childhood cancer, as well as other pediatric diseases and developmental disorders. Although the bill would authorize spending on pediatric research, the money still must be appropriated through an appropriations measure.

The measure is named after Gabriella Miller, a 10-year-old Leesburg, Va., girl who died of cancer in October. She had advocated for increased funding for research of childhood cancers in multiple videos that went viral before her death.

The Endocrine Society has long held a position recognizing the enormous potential of stem cell research and the need for funding (www.endocrine.org/stemcell).

NHLBI Seeks Input on Strategies to Enhance Early-Stage Faculty Diversity

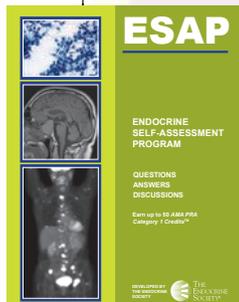
On March 11, the National Heart, Lung, and Blood Institute (NHLBI) issued a Request for Information (RFI) soliciting input on "strategies to strengthen the research

and training environment to enhance early-stage faculty diversity at diversity-focused institutions (DFIs)." The NIH is committed to enhancing the diversity of the biomedical workforce and recognizes that a diverse workforce is critical to advancing biomedical research. The RFI is focused on research topics of specific interest to NHLBI; however, any strategies and training programs implemented by NHLBI could be of interest to the broader research community.

The Endocrine Society provides input to the NIH to assist in the development of workforce diversity initiatives. Also, the Society advocates for ethnic and cultural diversity in the field of endocrinology through the activities of the Minority Affairs Committee.

Take Action: If you have interest or expertise in career development for underrepresented minorities in biomedical science, please respond to the RFI by April 28 at MailboxDiversityRFI@nih.gov. **EN**

A PERPLEXING THYROID NODULE: A Case Study from ESAP™



QUESTION

The Endocrine Self-Assessment Program (ESAP)

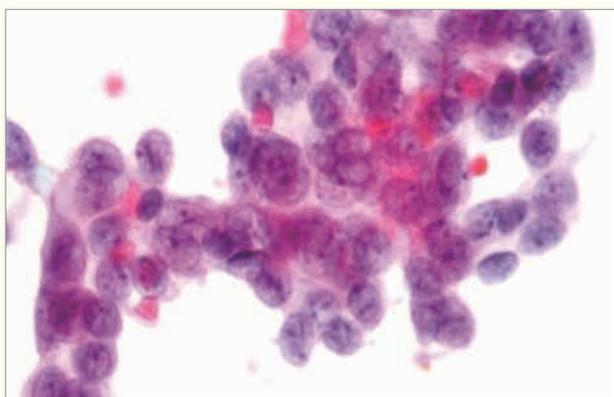
is a self-study program aimed at physicians seeking certification or recertification in endocrinology; program directors interested in a testing and training instrument; and individuals simply wanting a self-assessment and a broad review of endocrinology. ESAP is available in both print and online formats. It consists of 160 multiple-choice questions in all areas of endocrinology, diabetes, and metabolism. There is extensive discussion of each correct answer, a comprehensive syllabus, and references. ESAP is updated annually with new questions and new syllabus materials. Learn more at www.endoassessment.org.

A 45-year-old woman is referred for evaluation of a left thyroid nodule. She has been treated for five years by her primary care physician for documented Hashimoto disease and hypothyroidism, treated with levothyroxine, 112 mcg daily. Her thyroid gland has been normal in size but firm. During the last year, her physician noted an increase in size of the left thyroid lobe, now estimated to be 3 cm in diameter, and recently palpated a 2-cm nodule. The patient has not noted this change in size and has no symptoms of compression of neck structures (e.g., dysphagia, dysphonia). The patient smokes cigarettes, but otherwise has no notable medical history.

On physical examination, she appears healthy with normal vital signs. BMI is 26.2 kg/m². She appears to be

clinically euthyroid. Her right thyroid lobe is palpable and firm. The left lobe contains a 2- to 3-cm firm nodule with a smooth surface that moves well with swallowing. There are no abnormal lymph nodes palpable in the neck. The serum TSH concentration is 1.4 mIU/L.

You perform a fine-needle aspiration biopsy of the nodule with ultrasound guidance to verify needle placement. You then review the slides with the cytologist (see image below).



Which one of the following best describes the cytologic findings in this patient?

- A. Hashimoto disease
- B. Benign nodular goiter
- C. Suggestive of thyroid lymphoma
- D. Suggestive of papillary carcinoma
- E. Medullary thyroid carcinoma

answer on page 38

FLARE

FUTURE LEADERS ADVANCING RESEARCH IN ENDOCRINOLOGY

Congratulations to the FLARE Award Winners!

Congratulations to the winners of the Society's Future Leaders Advancing Research in Endocrinology (FLARE) Internship and Mentoring Network Travel Awards! FLARE Mentoring Network Travel Award winners receive free airfare and lodging to gain individualized, in-person mentoring from Society members. FLARE interns expand their leadership skills through a year of service on a Society governance committee. To view a list of the accomplished FLARE winners and learn more about the program, please visit <http://www.endocrine.org/FLARE>. **EN**



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The world's largest gathering of endocrinologists promises to deliver a plenary slate for the ages. At **ICE/ENDO 2014**, you'll hear from internationally renowned experts in the most rapidly evolving areas of endocrinology — including signaling, metabolism, cancer, diabetes, pediatric endocrinology, genomics, and the application of big data.

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Saturday's sessions begin with 2012 Nobel Laureate Robert J. Lefkowitz, MD, presenting his groundbreaking work on the historical understanding of G-protein coupled receptors — the largest, most versatile, and most ubiquitous family of cellular receptors. He will discuss how recent paradigm shifts in our understanding of their function may lead to novel classes of therapeutic agents.

C. Ronald Kahn, MD, of the Joslin Diabetes Center, will assess the incredible progress made over the past decade in defining molecular mechanisms of insulin action from the classical tyrosine kinase cascade to new aspects such as unique unoccupied insulin

receptor signaling, receptor and membrane molecule modifying interactions, and signaling feedback pathways in insulin resistance.

A Winning Array of Award Lectures

Five award lectures highlight the depth and variety of plenary sessions at **ICE/ENDO 2014**:

- The Edwin B. Astwood Award Lecture will feature **Domenico Accili, MD's** examination of the mechanisms of β cell failure and potential treatments for type 2 diabetes.
- **David M. Altshuler, MD, PhD**, will probe human genetic variation and type 2 diabetes inheritance during the Roy O. Greep Award Lecture.
- **James A. Fagin, MD**, will provide a comprehensive analysis of the most promising targets for thyroid cancer treatment in his Clinical Investigator Award Lecture.
- **Maria I. New, MD**, will illuminate recent advances in the prenatal diagnosis of congenital adrenal hyperplasia during the Endocrine Regulation Prize Lecture.

- **Peter J. Tontonoz, MD, PhD**, will enlighten attendees on the integration of metabolic and inflammatory signaling through liver X receptors during the Gerald D. Aurbach Award Lecture.

Other Noteworthy Sessions

Make plans to attend any of the following plenary sessions at **ICE/ENDO 2014**:

- **Teresa L. Wood, PhD**: Insulin and IGF Receptor Signaling in Stem Cell Homeostasis
- **Stuart H. Ralston, MD, FRCP**: Genetic Determinants of Bone Disease
- **Rosemary O'Connor, PhD**: IGF and Cancer Signaling
- **Susan E. Ozanne, PhD**: Early Environmental Influences on Type 2 Diabetes Risk
- **Michael A. Cowley, PhD**: Leptin: The Link between Obesity and Heart Disease?
- **Andrea C. Gore, PhD**: Endocrine Disruptors and the Neuroendocrine Control of Reproduction and Behavior
- **Dolores M. Shoback, MD**: Metabolic Bone Disease, the Calcium Sensing Receptor, and Parathyroid Hormone
- **Hertzel C. Gerstein, MD, MSc, FRCP**: Outcomes Trials in Diabetes

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question on page 36

The answer is: D

Hashimoto disease and hypothyroidism in this patient had been stable for some years until her physician palpated an enlarging left thyroid nodule. This development is worrisome because patients with Hashimoto disease have an increased incidence of differentiated thyroid cancer and thyroid lymphoma; the latter almost never occurs in the absence of Hashimoto disease.

The most efficient evaluation of thyroid nodules uses fine-needle aspiration biopsy, which is a rapid, safe, and relatively inexpensive diagnostic procedure. Currently, fine-needle aspiration biopsy is the most accurate diagnostic tool for thyroid nodules and has excellent correlation with surgical pathologic findings in many studies. For diagnosis of thyroid cancer, fine-needle aspiration biopsy has a sensitivity of 85%, a specificity of 80%, and a very low percentage of false-positive and false-negative results (i.e., about 2% to 5%, depending on the performing institution and whether ultrasound guidance is used). The apparent discordance between the sensitivity and specificity for cancer and the very low false-positive and false-negative

rates is because of classification of follicular neoplasm. Most patients are referred for surgery treatment because cytologic examination alone cannot distinguish between adenoma and differentiated follicular carcinoma, but only 20% actually have carcinoma.

Because thyroid nodules are so common, and because the cytologic distinction between benign and malignant nodules may not always be clear-cut, endocrinologists caring for patients must be familiar with the basics of interpreting thyroid cytology, so that they can interact intelligently with the cytologist.

Obtaining sufficient thyroid material is required for successful and accurate interpretation of thyroid specimens. Fifteen to 20% of aspirates are inadequate for interpretation. Fine-needle aspiration biopsy should be repeated in those cases and is adequate on the second aspirate about half the time. In samples that can be interpreted, cytologists look for the relationship between cellular material and colloid. The more colloid present in relation to cells, the more likely it is that the lesion is benign. The absence of colloid in cellular samples suggests a thyroid neoplasm. For most thyroid disorders, interpretation of cellular architecture is focused on the thyroid follicular cell. In benign disorders, follicular cells are a little larger than red blood cells, uniform in shape, have dark chromatin, and are not crowded or overlapping on the smears. Follicular tumors may have normal-appearing follicular cells, but contain little colloid.

Although no classic papillary fronds with vascular cores are present, the aspirate in this patient is suggestive of papillary carcinoma (Answer D). Follicular cells on the slides are more than five times larger than adjacent red blood cells. Their nuclei have delicate, vesiculated chromatin. Some of the follicular cells have nuclear grooves and others have nuclear inclusions. Almost no colloid is present. All of these findings are seen in pathologic material from papillary carcinoma.

The aspirates do not have lymphocytes, which excludes a cytologic diagnosis of Hashimoto disease (Answer A) or thyroid lymphoma (Answer C). The absence of colloid excludes a benign nodular goiter (Answer B). Medullary thyroid carcinoma (Answer E) may be suspected on fine-needle aspiration. However, distinctive nuclear features of medullary carcinoma cells (inconspicuous nucleoli, dusty neuroendocrine chromatin, multinucleation) and cytoplasmic borders that are poorly defined are missing from the present cellular material. In fact, the nucleoli and chromatin are prominent in this cytologic smear. More importantly, one would want calcitonin immunostaining, with or without amyloid stain, before entertaining this diagnosis. **EN**

NANCY RODNAN to Lead the Society's Publications Department

Nancy Rodnan has joined the Society as the senior director of publications. She will oversee all aspects of the Society's publishing enterprise, which includes five scholarly journals (*Journal of Clinical Endocrinology & Metabolism*, *Endocrinology*, *Molecular Endocrinology*, *Endocrine Reviews* and *Hormones and Cancer*), *Endocrine News*, and Endocrine Press, the Society's publishing imprint that issues print and electronic books as well as journals for a broad audience of healthcare professionals and patients.



"The Endocrine Society's journals rank among the most authoritative peer-reviewed biomedical research journals in the world," says executive director and CEO, Barbara Byrd Keenan. "Nancy's innovation, valuable experience, and proven record of accomplishment will help ensure the Society's publishing program continues to excel well into the future."

Prior to her employment at the Society, Rodnan led the publications department at the American Society for Biochemistry and Molecular Biology (ASBMB), managing the *Journal of Biological Chemistry*, *Molecular and Cellular Proteomics*, the *Journal of Lipid Research*, and other ASBMB publications for more than 10 years. Previously, Nancy had leadership positions in publications with the Federation of American Societies for Experimental Biology and the American Chemical Society.

"I feel fortunate to become part of an organization that is so well run and has such an excellent reputation in scientific publishing," Rodnan says. "I am looking forward to working with the talented staff in the Publications Department and exploring new opportunities in publishing that align with the overall strategic goals of the Society." **EN**

New from the Hormone Health Network DIABETES AND PREGNANCY AND PCOS PATIENT GUIDES

Visit www.hormone.org and download the Network's latest patient guides on diabetes and pregnancy and polycystic ovary syndrome (PCOS) and help your patients learn more about these conditions.

Diabetes and Pregnancy: A Patient's Guide, offers assurance to women with diabetes that, with proper care and planning, they can have both a healthy pregnancy and a healthy baby. The guide was created in collaboration with **DiabetesSisters**, a peer support group that offers education and support services to help women with diabetes live healthier, fuller lives.

The development of this patient guide was supported by an educational grant from Novo Nordisk Inc.

Polycystic Ovary Syndrome: A Patient's Guide, describes the risk factors for and symptoms of this common hormonal disorder among girls and women of reproductive age. The guide describes considerations when making a diagnosis, as well as tests needed to screen for health problems that occur more often in PCOS. While there is no cure for PCOS, the guide reassures women that treatment for symptoms and related disorders, along with a healthy lifestyle, can improve a woman's quality of life.

Event CALENDAR

APRIL 10 – 12, ORLANDO, FLA.

American College of Physicians
Internal Medicine 2014

<http://im2014.acponline.org/>

APRIL 26 – 30, SAN DIEGO, CALIF.

Experimental Biology 2014

<http://experimentalbiology.org/2014/Home.aspx>

MAY 3 – 6, VANCOUVER, BC, CANADA

Pediatric Academic Societies and Asian Society
for Pediatric Research

<http://www.pas-meeting.org/>

MAY 3 – 7, WROCLAW, POLAND

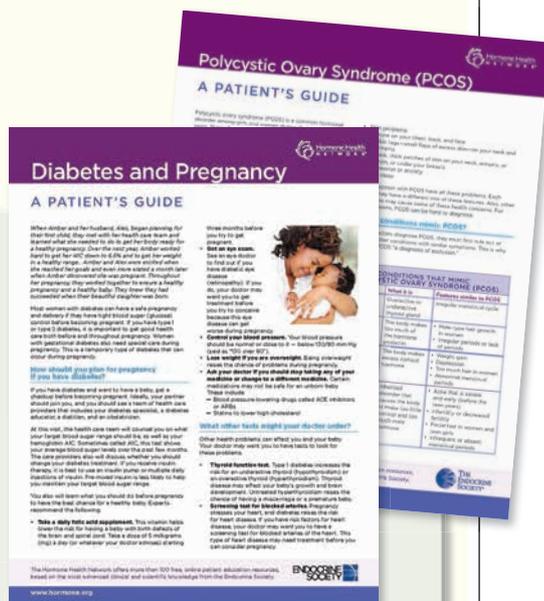
ECE 2014 European Congress of Endocrinology

<http://www.ece2014.org/>

MAY 14 – 18, LAS VEGAS

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PCSK9=proprotein convertase subtilisin/kexin type 9

References: 1. Lambert G, Spouke B, Choque B, Kastelein JJ, Hovingh GK. The PCSK9 decade. *J Lipid Res.* 2012;53:2515-2524. 2. Kwon HJ, Lagace TA, McNutt MC, Horton JD, Deisenhofer J. Molecular basis for LDL receptor recognition by PCSK9. *Proc Natl Acad Sci USA.* 2008;105:1820-1825. 3. Cohen JC, Boerwinkle E, Mosley TH Jr, Hobbs HH. Sequence variations in PCSK9, low LDL, and protection against coronary heart disease. *N Engl J Med.* 2006;354:1264-1272.

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What does

estrogen do?



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Keep your body in balance

Estrogen is one of two main sex hormones that women have. The other one is **progesterone**. Estrogen is responsible for female physical features and reproduction. Men have estrogen, too, but in smaller amounts.

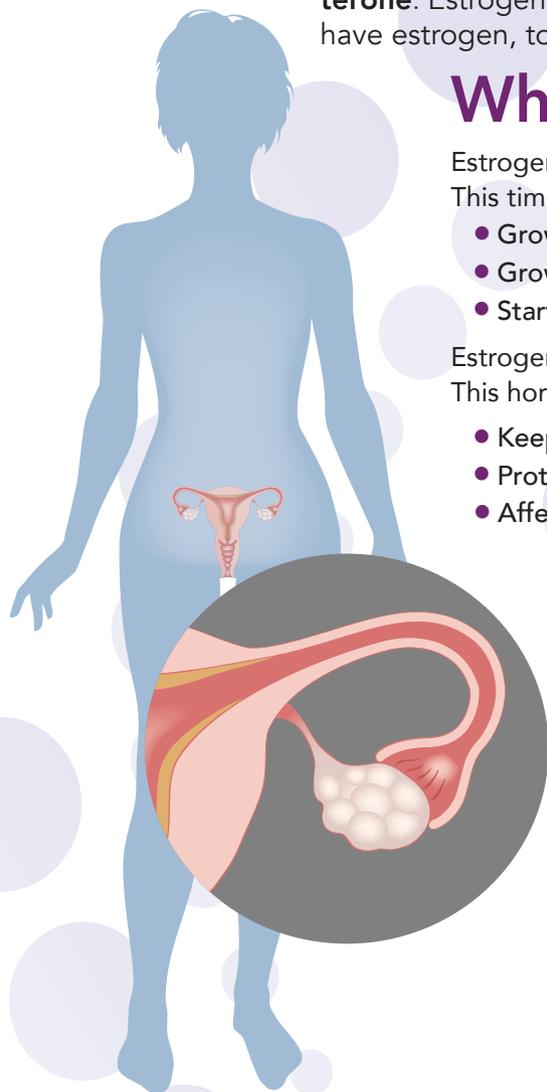
Why is estrogen important?

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

- Growth of the breasts
- Growth of pubic and underarm hair
- Start of menstrual cycles

Estrogen helps control the menstrual cycle and is important for childbearing. This hormone has other functions:

- Keeps cholesterol in control
- Protects bone health for both women and men
- Affects your brain (including mood), bones, heart, skin, and other tissues



How does estrogen work?

The ovaries, which produce a woman's eggs, are the main source of estrogen from your body. Your adrenal glands, located at the top of each kidney, make small amounts of this hormone. So does fat tissue. Estrogen moves through your blood and acts everywhere in your body.

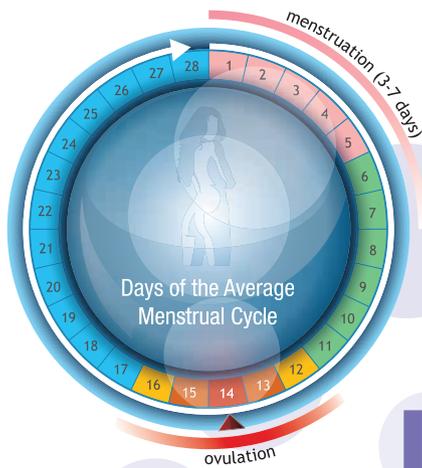
Your body makes three main types of estrogen:

What can go wrong with estrogen levels?

For many reasons, your body can make too little or too much estrogen. Or, you can take in too much estrogen, such as through birth control pills or estrogen replacement therapy.

You might want to keep track of your symptoms (changes you feel) by writing them down each day. Bring this symptom journal to your doctor.





Estrogen and your menstrual cycle

Your estrogen levels change throughout the month. They are highest in the middle of your menstrual cycle and lowest during your period. Estrogen levels drop at menopause.

How do you know what your estrogen level is?
 You will need to give a blood or urine sample to test your estrogen. Ask your doctor what your test results mean.

Low

Women. The most common reason for low estrogen in women is menopause or surgical removal of the ovaries.

Symptoms of low estrogen include:

- Menstrual periods that are less frequent or that stop
- Hot flashes (suddenly feeling very warm) and/or night sweats
- Trouble sleeping
- Dryness and thinning of the vagina
- Low sexual desire
- Mood swings
- Dry skin

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

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

High

Women. Excess estrogen can lead to these problems, among others:

- Weight gain, mainly in your waist, hips, and thighs
- Menstrual problems, such as light or heavy bleeding
- Worsening of premenstrual syndrome
- Fibrocystic breasts (non-cancerous breast lumps)
- Fibroids (noncancerous tumors) in the uterus
- Fatigue
- Loss of sex drive
- Feeling depressed or anxious

Men. High estrogen in men can cause:

- Enlarged breasts (gynecomastia)
- Poor erections
- Infertility

Words to know

endocrinologist (EN-doh-krih-NOLL-uh-jist): a doctor who treats people who have hormone problems, such as low estrogen.

hormone (HOR-mohn): a chemical made in a gland in one part of the body. The hormone travels through the blood to another part of the body, where it helps other cells do their job.

sex hormone: a hormone that affects and is made by the reproductive (sex) organs. It is responsible for secondary sex traits, such as breasts in women.

Where to learn more

Hormone Health Network estrogen information:

- Women's health: hormone.org/diseases-and-conditions/womens-health
- Gynecomastia (male breast enlargement): hormone.org/questions-and-answers/2011/gynecomastia

National Institutes of Health information:

- Estradiol test: nlm.nih.gov/medlineplus/ency/article/003711.htm

To find an endocrinologist near you:

hormone.org or call 1.800.HORMONE (1.800.467.6663)

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Endocrinologist Opportunities

Geisinger Health System (GHS) is seeking Endocrinologists for three locations:

- **Geisinger Medical Center (GMC), Danville, Pa.**
- **Geisinger Wyoming Valley Medical Center (GWV), Wilkes-Barre, Pa.**
- **Geisinger-Patton Forrest, State College, Pa.**

About the Position at GMC

- Join a team of 4 Endocrinologists, 1 Nurse Practitioners and 2 Certified Diabetes Educators in 100% Subspecialty Endocrinology Clinical Practice.
- Work collaboratively with Geisinger's community practice network to enhance diabetes care, as well as to work with multiple subspecialties to enhance inpatient care.
- Opportunities for clinical practice include serving as investigator on diabetes clinical trials, US-guided Thyroid Fine Needle Aspiration Biopsies and Continuous Glucose Sensors interpretation
- Engage in clinical mentoring and educational programs for medical students on the GMC campus, as well as internal medicine residents on rotation at GMC

About the Position at GWV

- Join a team of 3 Endocrinologists, 2 Nurse Practitioners and 3 Certified Diabetes Educators, and is positioned for additional growth
- Work collaboratively with Geisinger's community practice network to enhance diabetes care, as well as to work with multiple subspecialties to enhance inpatient care
- Opportunities for clinical practice include serving as investigator on diabetes clinical trials, US-guided Thyroid Fine Needle Aspiration Biopsies, Continuous Glucose Sensors and Bone Density interpretation
- Engage in clinical mentoring and educational programs for medical students and family medicine residents on the GWV campus, as well as internal medicine residents on rotation at GWV

About the Position at Geisinger-Patton Forrest

- Join a growing endocrinology department in a thriving, multi-specialty group practice, located in a progressive university town
- Provide 100% endocrinology subspecialty outpatient care and inpatient consultations
- Provide consultative care at Mt. Nittany Medical Center, State College, Pa., and Lewistown Hospital, Lewistown, Pa.

Geisinger Health System serves nearly 3 million people in Northeastern and Central Pennsylvania and has been nationally recognized for innovative practices and quality care. A mature electronic health record connects a comprehensive network of 5 hospitals, 43 community practice sites and more than 900 Geisinger primary and specialty care physicians.

Discover for yourself why Geisinger has been nationally recognized as a visionary model of integrated healthcare. For more information, please visit Join-Geisinger.org or contact: John W. Kennedy, MD, Endocrinology Department Director, Geisinger Health System c/o Kathy Kardisco, Department of Professional Staffing, at 1-800-845-7112 or kkardisco@geisinger.edu.

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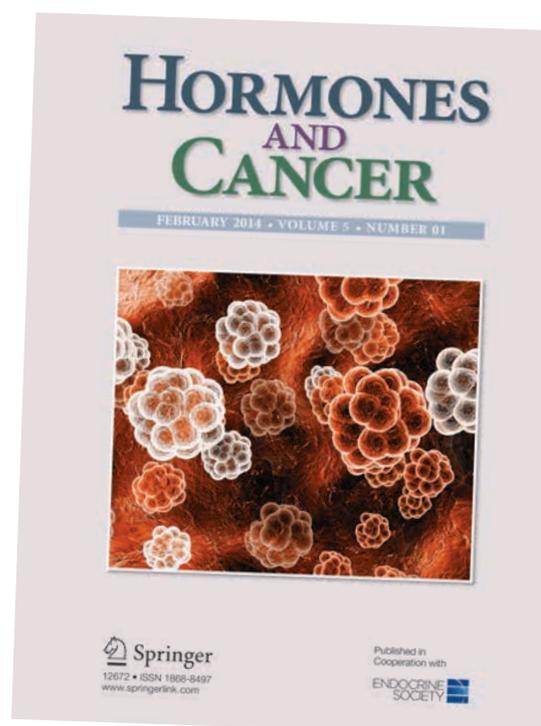
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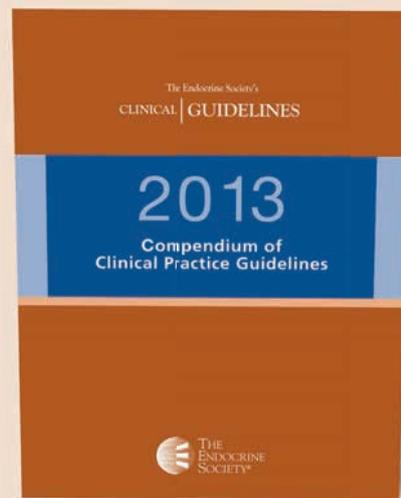
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