

# ENDOCRINE news™

## JUST RIGHT: HOW MUCH **VITAMIN D** IS ENOUGH?



Some experts say that higher intakes of vitamin D could lead to big health benefits, while others question the evidence for this claim. Fortunately, clinical trials could provide answers to this controversial question soon.

**LOOKING TOO HARD:**  
Behind the Thyroid Cancer Epidemic

**GOOD SPORTS:**  
Treating Diabetes in Athletes



HMG-CoA  
reductase is part  
of the LDL-C  
metabolism story<sup>1</sup>

But PCSK9  
also plays an  
important role in  
LDL-C regulation<sup>2</sup>

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## New pathway discoveries are uniting the cholesterol conversation.

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By inhibiting HMG-CoA reductase and reducing cholesterol biosynthesis, statins help lower LDL-C.<sup>1</sup> PCSK9, another important protein involved in cholesterol metabolism, promotes degradation of the LDL receptor, thereby increasing LDL-C levels.<sup>2</sup> **In discussions of cholesterol metabolism, the roles of HMG-CoA reductase and PCSK9 should go hand in hand.**

Join the conversation at [DiscoverPCSK9.com](http://DiscoverPCSK9.com).

**HMG-CoA** = 3-hydroxy-3-methylglutaryl coenzyme A; **PCSK9** = proprotein convertase subtilisin/kexin type 9; **LDL-C** = low-density lipoprotein cholesterol.

**References:** **1.** Toth PP. *Drugs*. 2010;70:1363-1379. **2.** Zhang D, Lagace TA, Garuti R, et al. *J Biol Chem*. 2007;282:18602-18612.

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*Hormone Science to Health*

## Hormone Assay Methodology: The Lifeblood of Endocrinology



Richard J. Santen, MD

This letter reflects on an area that is making significant strides and concurrently generating controversy, *hormone assay methodology*. We are in an exciting time of new and improved methods, which provide a means to enhance our research and clinical practice. This is not the first time we have experienced such a period, and we know that periods of transition often create controversy while at the same

time serve to highlight critical issues. These transitions present us with a unique opportunity to advance the field by embracing the process of change.

Accurate hormone measurements are the lifeblood of our specialty and are critical to physicians in practice as well as basic and clinical scientists. More than five decades ago, radioimmunoassays (RIAs) were introduced, initially for insulin and then for all peptide and steroid hormones. Because of their superior sensitivity, specificity, and precision, RIAs gradually replaced bioassays over a prolonged period of transition. We are now entering the era of mass spectrometry for measurements of steroid and protein hormones. This evolving methodology enhances even further the specificity, precision, and sensitivity of hormone measurements. We are again entering a transition period where issues of practical implementation arise. The costs, both for instrumentation and per sample, and issues of standardization have created controversy.

Several years ago the Endocrine Society recognized the need to guide this transition process and undertook a number of initiatives. An overarching principle is that normal ranges for hormones must be comparable and not dependent upon the assay used. Guidelines for treatment of hormonal disorders rely on valid hormone assays that yield similar normal ranges among comparable groups. We have learned from measurements of testosterone and estradiol that some widely used assays do not yield the same result on the same sample. The solution to this problem requires the ability to trace an assay to a chemically pure standard or, when no pure standard is available, to an agreed upon reference material.

An initial step involved a 2008 Centers for Disease Control and Prevention (CDC) workshop with Endocrine Society participation, which outlined key principles regarding hormone assays. This motivated the ES to hold a consensus conference in 2010 and to

spearhead the establishment of a coalition of organizations dedicated to standardizing testosterone assays. Called **PATH** (**P**artnership for the **A**ccurate **T**esting of **H**ormones), this organization provides education and outreach to physicians and policy makers, and lends technical support to the CDC testosterone standardization project, which is available for all laboratories. Through the efforts of PATH and other stakeholders, significant progress has been made in standardizing testosterone measurements. The Society and PATH are now planning to introduce standardization to improve the quality of measurements for other hormones as well.

In the spring of 2013, the Society published a position statement on estradiol testing (*J Clin Endocrinol Metab*, April 2013, 98(4):1376–1387), calling for universally recognized standards and improved methods. In March of this year, we sponsored a workshop on improving estradiol measurements, along with cosponsors PATH, the American Association for Clinical Chemistry, and Penn State Hershey College of Medicine. The workshop identified challenges associated with current estradiol measurement methods, and attendees discussed the advantages and disadvantages of different methods in specific contexts.

As we look to the future, tests with improved sensitivity, specificity, and precision at reasonable cost will be increasingly used but likely at a gradual pace. In the meantime, standardization should be our proximate goal for acceptance of assays regardless of methodology. As with the history of RIAs replacing bioassays, I anticipate that new methodologies will gradually replace RIAs. At this time, mass spectrometry offers the most promise, but we will always remain open to the new and innovative. We all recognize there is still a long way to go before we realize the full diagnostic and clinical potential of these tests. I am confident that we will remain diligent and that ultimately, we will arrive at a time when we gain more knowledge and improve treatment through superior-quality hormone assays. Feel free to contact me at [president@endocrine.org](mailto:president@endocrine.org) if you have any questions or comments. **EN**

Richard J. Santen, MD  
President, Endocrine Society

NOVEMBER 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.

President: **Richard J. Santen, MD**  
rjs5y@virginia.edu

President-Elect: **Lisa H. Fish, MD**  
lisafishmd@gmail.com

Past President: **Teresa K. Woodruff, PhD**  
tkw@northwestern.edu

Secretary-Treasurer: **Kenneth H. Hupart, MD**  
hupart@numc.edu

Executive Director & CEO: **Barabara Byrd Keenan**  
bbkeenan@endocrine.org

Senior Director of Publications: **Nancy Rodnan**  
nrodnan@endocrine.org

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

Production Manager/Art Director: **Cynthia Richardson**  
crichardson@endocrine.org

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

Prepress & Printing: **Cenveo Publishing Services**  
www.cadmus.com

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**E**ric Seaborg takes on the controversial topic of vitamin D, specifically, the proper dosage, in “Just Right: How Much Vitamin D is Enough?” (p. 11). There is no doubt that vitamin D “does a body good,” as the old milk commercials used to say. But what is up for debate is how much is enough and how much is simply too much? Studies and experts have disagreed with one another for years. According to JoAnn Manson, MD, DrPH, a professor at Harvard Medical School who served on a recent Institute of Medicine (IOM) task force on reference intakes for vitamin D, “The message that is going out to the public is that the higher the intake of vitamin D the better, and I think even many clinicians are confused and question this assumption.” Hopefully, a host of research studies will answer these lingering questions once and for all, but it’s not likely.

Here’s an interesting statistic: in the last four decades, the number of thyroid cancer cases have tripled while the mortality rate has pretty much stayed the same. Kelly Horvath writes about this phenomenon in “Diagnosis Overkill” on page 14, where she talks to Michael Tuttle, MD, at Memorial Sloan Kettering in New York, who believes that some clinicians are looking for this cancer somewhat overzealously. “If you look hard enough, you can find thyroid cancer, but if you are finding something that is not life-threatening and is not likely to hurt somebody, then you have to question — what is the benefit?” he says.

Treating diabetes patients who are also serious athletes is the topic of “Physical Therapy” by associate editor Derek Bagley (p. 18). Research has shown that exercise greatly affects glycemic control in patients with type 1 diabetes, so a personalized care plan is of the utmost importance for these patients. According to Raymond J. Davey, PhD, of the Telethon Institute for Child Health Research, in Perth, Australia, there’s no doubt that an active lifestyle is important for people with T1D, “therefore, I’d suggest that the best approach is to find an exercise type or program that provides the greatest enjoyment to increase the likelihood of adhering to regular exercise.”

I started my journalism career when I was a freshman at the University of Alabama writing about making the transition from a small town marching band into to a big-time college band. It was published in *Marching Bands & Corps* magazine. I suppose I’m continuing that theme 31 years later with a similar article on how kids with chronic conditions such as diabetes are making the transition from childhood into adulthood with the help of online toolkits (“Growing Pains,” p. 22). Back in college, I remember a fellow trumpet player who wore an insulin pump. While at band practice one day, a drum major had to run across the street to get him a candy bar when his numbers bottomed out. Luckily, college freshmen entering school three decades later have their pick of online tools to help them find support, manage their diabetes, and find suitable healthcare providers rather than having to rely on the kindness of a classmate. But, the kindness of others is still a big part of these new toolkits as well. **EN**



Mark A. Newman

Mark A. Newman,  
Editor, Endocrine News

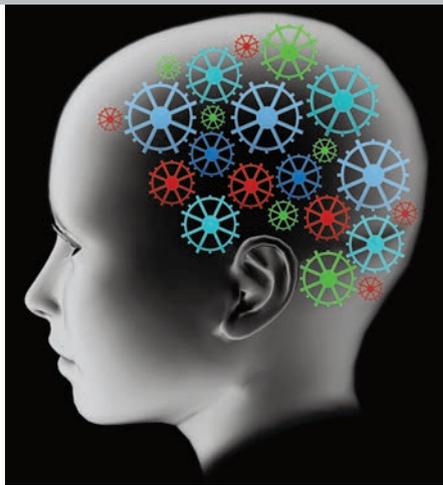
By Derek Bagley

## BPA'S IMPACTS on Brain and Behavior

Bisphenol A (BPA), the oft-criticized chemical found in many plastic consumer items, has been linked to brain and behavior alterations, including increased hyperactivity and stress, according to a recent rodent study, with the results published in *Endocrinology*.

Researchers led by Heather B. Patisaul, PhD, of North Carolina State University in Raleigh, pointed out that there have already been links between prenatal BPA exposure and altered affective behaviors in children based on epidemiological data, “but the mechanisms are unclear.” In order to determine these mechanisms, the scientists studied prairie voles, “a novel animal model for neuroendocrine toxicology,” since the prairie vole is more “prosocial than lab rats or mice.” “It’s compelling to see them in a species that shares many social characteristics with humans,” Patisaul says.

Patisaul and her team exposed male and female prairie vole pups orally to 5 ug/kg bw/day, 50 ug/kg bw/day, or 50 mg/kg bw/day BPA or vehicle over postnatal days (PNDs) 8-14. The subjects were then tested as juveniles in “open field and novel social tests and for partner preference as adults.” Afterward, their brains were collected and assessed



for immunoreactive (-ir) tyrosine hydroxylase (TH; a dopamine marker) neurons in the principal nucleus of the bed nucleus of the stria terminalis (pBNST) and TH-ir, OT-ir, and AVP-ir neurons in the paraventricular nucleus (PVN) of the hypothalamus.

The authors wrote, “Female open field activity indicated hyperactivity at the lowest dose and anxiety at the highest dose. Effects on social interactions were also observed, and partner preference formation was inhibited at all dose levels. BPA masculinized pBNST TH-ir neuron

numbers in females. Additionally, 50 mg/kg bw BPA exposed females had more AVP-ir neurons in the anterior PVN and fewer OT-ir neurons in the posterior PVN.” Even at the lowest doses of BPA, the chemical eliminated sex differences in the PVN TH-ir neuron numbers, and sex reversed it at the highest dose. However, “minimal behavioral effects were observed in BPA-exposed males.”

The authors concluded that exposure to BPA altered the social behavior of the prairie voles, as well as the associated limbic system, especially in the females. The behavioral changes were accompanied by altered OT- and AVP-ir cell numbers in subregions of the PVN, and TH-ir cell numbers in the pBNST. They wrote, “These data support the hypothesis that BPA alters affective behaviors, potentially via disruption of OT/AVP pathways.”

## VITAMIN D Shows Promise in ICU Patients



Researchers in Austria have determined that vitamin D may have effects on critically ill patients, according to a study recently published in the *Journal of the American Medical Association*.

The scientists, led by Karin Amrein, MD, MSc, of the Medical University of Graz, noted that vitamin D status has historically been linked to increased mortality and morbidity in patients who are critically ill but while that association is clear, a causal association has never been proven.

Amrein and colleagues conducted the VITdAL-ICU trial, a randomized double-blind, placebo-controlled, single-center trial from May 2010 through September 2012 at five ICUs that included a medical and surgical population of 475 critically ill adult white patients with vitamin D deficiency ( $\leq 20$  ng/mL) who received either vitamin D<sub>3</sub> (n = 237) or a placebo (n = 238). Vitamin D<sub>3</sub> or a placebo was given orally or via nasogastric tube once at a dose of 540,000 IU followed by monthly maintenance doses of 90,000 IU for five months.

The primary outcome was the length of stay at the hospital, while length of ICU stay, the percentage of patients with 25-hydroxyvitamin D levels higher than 30 ng/mL at day seven, hospital mortality, and six-month mortality

were also measured. Neither the primary outcome nor the secondary outcomes were statistically significantly different for either group. In the predefined subgroup of patients with severe vitamin D deficiency ( $\leq 12$  ng/mL;  $n=200$  or 42% of the total population), hospital mortality was significantly lower with 28.6% for vitamin D<sub>3</sub> compared with 46.1% in the placebo group.

“Although the primary endpoint, length of hospital stay, was negative,” Amrein says, “this is the first study that shows a significant hospital survival benefit in severely vitamin D deficient ICU patients (absolute difference 17.5%, number needed to treat six). As evident in the Kaplan Meier curves, a numerical difference became apparent at two weeks after study inclusion. This may be highly relevant also to other, less severely ill patients, but the high event rate in this patient population possibly enabled us to generate the hypothesis that vitamin D<sub>3</sub> indeed is crucial for survival in severe acute illness. If future studies confirm the benefit of vitamin D treatment for hospital

survival in ICU patients, this would be spectacular as vitamin D has few side effects and is inexpensive. Currently, however, only small doses (up to 200 IU daily) of vitamin D are given in the ICU. There are also not too many interventions that have ever reduced hospital mortality in critically ill patients. Until we have further data, it may be worthwhile testing for vitamin D deficiency in severely ill patients and consider giving the currently by the Endocrine Society recommended doses of 1500 to 2000 IU of cholecalciferol per day to this vulnerable patient group. If future studies confirm the benefit of vitamin D treatment for hospital survival in ICU patients, this would be spectacular as vitamin D has few side effects and is inexpensive. Currently, however, only small doses (up to 200 IU daily) of vitamin D are given in the ICU. It may be worthwhile testing for vitamin D deficiency in severely ill patients and consider giving the currently by the Endocrine Society recommended doses of 1500 to 2000 IU of cholecalciferol per day to this vulnerable patient group.”

## Metabolic Determinants of T2D Non-Remission Status after Bariatric Surgery

Research recently published in *Diabetes, Obesity and Metabolism* may provide insights into why some patients achieve diabetes remission after bariatric surgery while others don't.

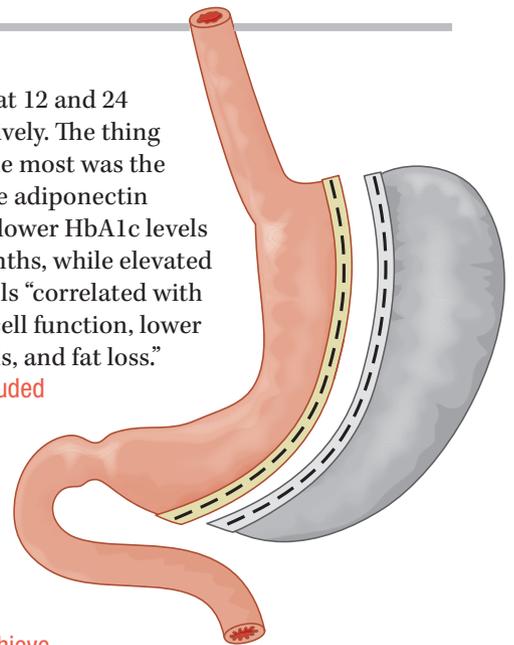
Sangeeta R. Kashyap, MD, of the Cleveland Clinic, and her team noticed that while bariatric surgery “can produce complete and persistent type 2 diabetes remission,” around 30% – 70% of patients do not achieve remission, “despite marked weight loss.”

The team analyzed in total 40 adults [mean body mass index  $36 \pm 3$  kg/m<sup>2</sup>, age  $48 \pm 9$  years, glycated haemoglobin (HbA1c)  $9.7 \pm 2\%$ ] undergoing bariatric surgery [Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG)] enrolled in the Surgical Treatment and Medication Potentially Eradicate Diabetes Efficiently (STAMPEDE) trial. They defined T2D remission as “HbA1c  $<6.5\%$  and fasting glucose  $<126$  mg/dl (i.e.  $<7$  mmol/l) without anti-diabetic medication.” They then studied a number of factors in the participants: “Indices of insulin secretion and sensitivity were calculated from plasma glucose, insulin and C-peptide values during a 120-min mixed-meal tolerance test. Body fat, incretins (glucagon-like polypeptide-1, gastric inhibitory peptide, ghrelin) and adipokines [adiponectin, leptin, tumour necrosis factor- $\alpha$ , high-sensitivity C-reactive protein (hs-CRP)] were also assessed.”

Kashyap and colleagues looked at the 37 patients who had complete follow-up data after 24 months and found that bariatric surgery induced T2D remission rates

at 40% and 27% at 12 and 24 months, respectively. The thing that stuck out the most was the fact that baseline adiponectin levels predicted lower HbA1c levels at 12 and 24 months, while elevated adiponectin levels “correlated with enhanced beta-cell function, lower triglyceride levels, and fat loss.”

The authors concluded that smaller rises in adiponectin, which mediates insulin action and adipose mass, may be why some patients do not achieve T2D remission up to two years after bariatric surgery. They wrote, “Elevated adiponectin was linked to improved glycaemic control and paralleled by higher pancreatic beta-cell function and multi-organ insulin sensitivity, irrespective of gut hormone responses. Together with reductions in hs-CRP, our adiponectin data extend previous clinical work and show that bariatric surgery effectively promotes diabetes remission by lowering adiposopathy.” However, they note that future work must be done to determine whether targeting adiposopathy by decreasing body fat and/or increasing adiponectin after bariatric surgery leads to better diabetes remission rates in obese adults, as adipose tissue appears intimately involved in the cross-talk between skeletal muscle, liver, and pancreatic glucose homeostasis.



**Dear Mr. Newman:**

I am writing you concerning the cover story on "Gathering Storm," which used to be a very serious and fatal complication of hyperthyroidism.

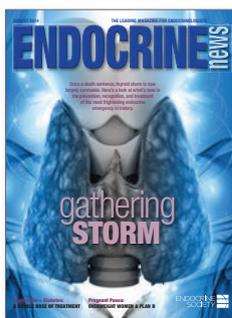
In 1970, I published an article in *JAMA* on a new treatment of this emergency by plasmapheresis (*JAMA* 214: 1275-1279, 1970).

The plasmapheresis procedure is a life-saving technique, available in all hospitals accredited with good outcomes when traditional treatment fails (anti-thyroid drugs, B. blockers and steroids).

Plasmapheresis drastically reduces the total hormone (TH) protein found in the circulation with a prolonged half-life unaffected significantly by traditional treatment.

Patients with thyroid storm are very sick patients with a high TH load, significantly higher than the average hyperthyroid resulting in total systemic decompensation of the patient (*South. Med. J* 65: 372-374, 1972).

Early detection of thyroid storm and prompt recognition of traditional therapy failure should result in



performance of plasmapheresis as a last resort to save the patient's life.

The technique has been credited with saving many lives over the past 44 years; evidenced by the abundant communications received over the years and should be emphasized as a viable solution to an otherwise fatal outcome.

Sincerely yours,

Fuad S. Ashkar, MD, FACE

Chief of Staff, Kendall Regional Medical Center

Clinical Professor Voluntary Faculty

University of Miami, Miller Medical School

### Why Endocrinology?

Of all the practices you could've chosen, what made you choose endocrinology? *Endocrine News* wants to know your thought process for choosing this practice for a future article.

Whether you're a basic scientist, practicing clinician, clinical scientist, just beginning your career, or wrapping it up, *Endocrine News* wants to know why endocrinology appealed to you as a practice or field of study.

## Fast FACTS About Vitamin D



More than 40 million U.S. adults have or are at risk of developing osteoporosis.

The recommended daily allowance (RDA) of vitamin D for those between ages one and 70 is 600 international units (IU) per day.

**600 IU per day**

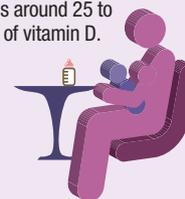


As many as half of older adults in the U.S. with hip fractures have vitamin D levels less than 30 nmol/L.

**Less than 30 nmol/L vitamin D**

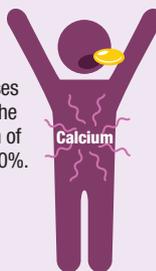


Human milk only provides around 25 to 78 IU/L of vitamin D.



Vitamin D increases the efficiency of the body's absorption of calcium 30% – 40%.

**Calcium**



**800 IU per day**



For those 71 and older, the RDA of vitamin D is 800 IU per day.

The vitamin D toxicity threshold is 10,000 to 40,000 IU per day.

**40,000 IU**

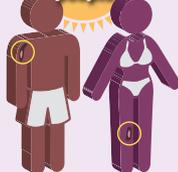
**10,000 IU**



The use of calcium and vitamin D supplements by postmenopausal women was associated with a 17% increase in the risk of kidney stones over 7 years.



**2 million people**



Vitamin D comes mainly from sun exposure, but more than 2 million people in the U.S. are diagnosed with skin cancer each year.

# JUST RIGHT: HOW MUCH VITAMIN D IS ENOUGH?



Some experts say that higher intakes of vitamin D could lead to big health benefits, while others question the evidence for this claim. Fortunately, clinical trials could provide answers to this controversial question soon.

**By Eric Seaborg**

**T**here is little debate over the role of vitamin D and calcium in bone health, but the question of whether much higher intakes of vitamin D could have a host of nonskeletal benefits remains hotly debated. New studies linking vitamin D deficiency to nonskeletal problems are popping up with great frequency, but correlation is not causation, and most meta-analyses have not found evidence to bolster claims of wide-ranging benefits.

“We are at a crossroads in terms of vitamin D research,” says JoAnn Manson, MD, DrPH, a professor at Harvard Medical School who served on a recent Institute of Medicine (IOM) task force on reference intakes for vitamin D. “We have numerous observational studies suggesting associations between low vitamin D levels and increased risk of myriad diseases, but we don’t yet know whether there is a cause and effect relationship. We do know that vitamin D deficiency is a health problem ... associated with bone disorders. The real issue is whether you have greater health benefits from exceeding, rather than meeting, the recommended dietary allowance for vitamin D. We don’t yet know that giving vitamin D supplementation will lower the risk of cardiovascular disease, cancer, diabetes, cognitive decline, depression, and a host of other diseases.

The message that is going out to the public is that the higher the intake of vitamin D the better, and I think even many clinicians are confused and question this assumption,” Manson says.



**“The message that is going out to the public is that the higher the intake of vitamin D the better, and I think even many clinicians are confused and question this assumption.”**

— JoAnn Manson, MD, DrPH, professor of medicine, Harvard Medical School/ professor of epidemiology, Brigham & Women's Hospital, Boston

## AT-A-GLANCE

- The question of whether higher intakes of vitamin D can provide benefits beyond bone health continues to be controversial, but clinical trials should provide more definitive information soon.
- As a hedge in case some potential benefits do pan out, many endocrinologists see no harm in shooting for 25-hydroxyvitamin D levels from 30 to 50 ng/ml.
- The Institute of Medicine recommends daily intakes of 600 IU for people aged 1 to 70 and 800 IU for those older, but an Endocrine Society guideline suggests even higher intakes could be beneficial.

Will vitamin D fulfill the promise that many predict or turn out to be the next vitamin E? Large randomized trials testing the effects of moderate to high doses are under way that could provide answers soon.

## Associations Piling Up

Journals seem to be filled with studies like the recent one in *Neurology* that linked low vitamin D levels with an increased risk of dementia and Alzheimer's disease, an article that received a good deal of attention in the lay press.

Recent articles in the *Journal of Clinical Endocrinology & Metabolism* include: A study in Ireland linked low vitamin D with poor physical function in severely obese patients. Another Irish study found that markers of inflammation were higher in vitamin D-deficient older patients. A meta-analysis tied a 10 nmol/L (4 ng/ml) increase in vitamin D levels to a 4% increase in survival among cancer patients. A meta-analysis of observational studies linked low vitamin D with schizophrenia.

Of course, these studies cannot differentiate whether low vitamin D levels cause the disorders or the disorders themselves contribute to the low vitamin D levels, or some combination of the two. In addition, people with low vitamin D levels because of poor general nutrition are more likely to be ill, and conditions such as obesity and a lack of outdoor physical activity can also contribute to low levels, Manson says.

## Dueling Guidelines

Another element complicating the interpretation of these studies is that they use different definitions of deficiency and sufficiency. “There is no consensus definition of vitamin D deficiency,” the U.S. Preventive Services Task Force noted in a recent draft statement on vitamin D screening.

Two recent influential guidelines illustrate this point. In 2011, IOM guidelines on reference intakes for vitamin D used a blood level of 20 ng/ml of 25-hydroxyvitamin D as the benchmark for deficiency because that level meets the needs for good bone health for at least 97.5% of the population. That guideline addressed needs on a population and public health level but not treatment of specific medical conditions. That same year, the Endocrine Society guideline on the treatment and prevention of vitamin D deficiency agreed with this 20 ng/ml level. But the guideline classified levels from 21 to 29 ng/ml as “insufficient” and recommended that people aim for a level of 30 ng/mL or higher.

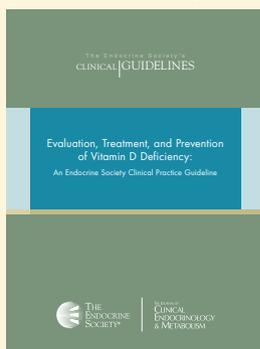
## Increased RDAs

The 2011 IOM guideline greatly increased the recommended dietary allowances (RDA) for all age groups: For people from 1 to 50 years old, the RDA increased from 200 to 600 international units (IU) a day; for people 50 to 70 years old, from 400 to 600 IU; and for those over 70, from 600 to 800 IU. The Endocrine Society guideline agreed that people need “at least” these intakes to maximize bone health and muscle function, but that raising the blood level above 30 ng/mL could require substantially more, on the order of 1,500–2,000 IU per day. The carefully worded guideline says, “It is unknown whether 1,000 IU/day is enough to provide all the potential nonskeletal health benefits associated with vitamin D.”

Those nonskeletal benefits are the subject of lively debate, but there is a logical underpinning for the belief that vitamin D could have far-reaching effects, according to Michael F. Holick, MD, PhD, director of the General Clinical Research Unit and Bone Health Care

## OnPOINT from the Endocrine Society

The Endocrine Society clinical practice guideline, *Evaluation, Treatment, and Prevention of Vitamin D Deficiency*, is available at [www.endocrine.org/vitaminD](http://www.endocrine.org/vitaminD). In 2012, the Society published a Scientific Statement called “The Non Skeletal Effects of Vitamin D” available at [www.endocrine.org/nonskeletal](http://www.endocrine.org/nonskeletal).



Clinic at Boston University Medical Center. Holick chaired the expert panel that wrote the Endocrine Society guideline. “We know that basically every cell in your body has a vitamin D receptor. The vitamin D receptor has been found in the brain, skeletal muscle, colon, breast, prostate, and the list goes on. Cells that have a vitamin D receptor respond to 1,25-dihydroxyvitamin D. It regulates their growth and hormone production. It has a lot of different functions,” Holick tells *Endocrine News*.

Although many meta-analyses have failed to find significant nonskeletal effects, Holick believes these analyses have weaknesses because they are dominated by older studies in which vitamin D intakes were too low.

“Most studies have never used 1,000 and 2,000 IUs per day of vitamin D, and we think that that is the dose that most children and adults need, respectively, to satisfy their vitamin D requirements. A study in Finland showed that when children received 2,000 IUs of vitamin D a day during their first year of life, it reduced the risk for developing type 1 diabetes by 88% later in life. There is a lot of information out there to suggest that improvement in your vitamin D status will improve your overall health and welfare,” Holick says.

Stephen Fortmann, MD, a senior researcher at the Kaiser Permanente Center for Health Research, says that a strong rationale for purported benefits may not translate into actual benefits. For example, postmenopausal estrogen offered promise because it improved lipid levels as well as vascular function, but those effects “did not add up to preventing heart disease.” Fortmann was lead author of a study done at the behest of the U.S. Preventive Services Task Force and published in the *Annals of Internal Medicine* that surveyed a host of studies on vitamin and mineral supplements. The study concluded that there is “insufficient data to draw conclusions” about supplements having any effect in “preventing heart disease, cancer, or death.”

### Clinical Trials to the Rescue

This dearth of evidence is likely to change soon for vitamin D because large, randomized clinical trials are already in the pipeline. Manson is a principal investigator of the largest one. The VITamin D and Omega-3 Trial (VITAL) is testing the effects of taking 2,000 IU in supplements per day versus placebo in almost 26,000 adults over age 50. The primary focus is on prevention of cancer and cardiovascular disease, but data will be collected on a host of other disorders, including diabetes, hypertension, cognitive decline, depression, respiratory disorders, and autoimmune diseases. It’s an ongoing five-year trial, with preliminary results expected in about three years.

Another multi-year trial based at Tufts University will test whether daily supplements of 4,000 IUs will prevent or delay the onset of type 2 diabetes in people with prediabetes. Both trials are sponsored by the National Institutes of Health.

### For Patients who Can’t Wait

While awaiting that data, clinicians still need an answer for patients tempted to take large doses of vitamin D. Three endocrinologists interviewed for an *Endocrine News* article on osteoporosis in the April issue all aimed for levels of at least 30 ng/ml — with an eye toward maximizing bone health in at-risk patients.

Holick believes that maintaining a level of 40 to 60 ng/ml is desirable in the general population and a level up to 100 ng/ml is “perfectly safe.”

Others urge caution about going above 50 ng/ml. “The data are not clear cut, but some evidence of toxicity has been associated with levels above 50 ng/ml, including hypercalcemia and kidney stones,” says Clifford Rosen, MD, director of clinical and translational research at the Maine Medical Center Research Institute, who worked on the IOM guideline.

But even a level of 50 ng/ml leaves a lot of leeway above the IOM’s deficiency level of 20 ng/ml and the Endocrine Society’s sufficiency level of 30 ng/ml. And it leaves a lot of leeway for taking supplements — the IOM guideline found that intakes as high as 4,000 IU/day should be safe for adults, although long-term risks of such high intakes are unknown. **EN**

— Seaborg is a freelance writer based in Charlottesville, Va. He wrote about male reproduction and EDCs in the September issue.



“A study in Finland showed that when children received 2,000 IUs of vitamin D a day during their first year of life, it reduced the risk for developing type 1 diabetes by 88% later in life.

**There is a lot of information out there to suggest that improvement in your vitamin D status will improve your overall health and welfare.”**

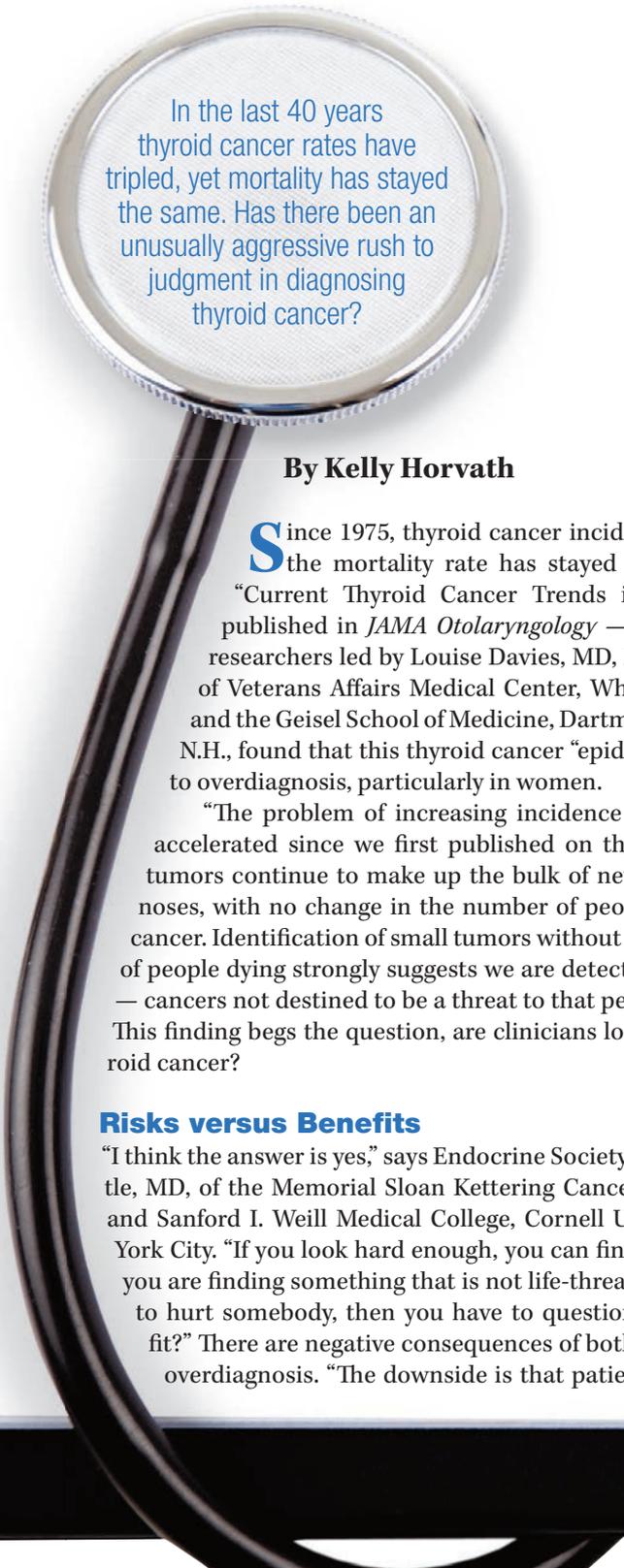
— Michael F. Holick, MD, PhD, director of the general clinical research unit and bone healthcare center, Boston University Medical Center

### BE CAREFUL with that Lab Test

Even the question of how to measure vitamin D is unsettled. “A number of tests measure 25-hydroxyvitamin D, but it is not clear which is the best test or what the results mean,” the U.S. Preventive Services Task Force said in a recent draft statement on screening for vitamin D deficiency. “The accuracy of these tests is difficult to determine due to the lack of studies using an internationally recognized reference standard and the lack of a consensus on the cutpoint values used to define vitamin D deficiency.” The task force has scheduled a meeting in early December to work toward a consensus on testing.

Manson says that clinical labs are exacerbating the issue by recommending blood levels as high as 70 to 90 ng/ml, well above what the IOM considered a tolerable upper intake level. These labs’ misguided reference ranges “may be misleading clinicians into striving for much higher blood levels than are needed for optimal health,” she says.

# Diagnosis Overkill



In the last 40 years thyroid cancer rates have tripled, yet mortality has stayed the same. Has there been an unusually aggressive rush to judgment in diagnosing thyroid cancer?

By Kelly Horvath

Since 1975, thyroid cancer incidence has tripled, while the mortality rate has stayed virtually the same. In “Current Thyroid Cancer Trends in the United States,” published in *JAMA Otolaryngology — Head & Neck Surgery*, researchers led by Louise Davies, MD, MS, of the Department of Veterans Affairs Medical Center, White River Junction, Vt., and the Geisel School of Medicine, Dartmouth College, Hanover, N.H., found that this thyroid cancer “epidemic,” was attributable to overdiagnosis, particularly in women.

“The problem of increasing incidence of thyroid cancer has accelerated since we first published on the topic in 2006. Small tumors continue to make up the bulk of new thyroid cancer diagnoses, with no change in the number of people dying from thyroid cancer. Identification of small tumors without changes in the number of people dying strongly suggests we are detecting subclinical disease — cancers not destined to be a threat to that person’s life,” says Davies. This finding begs the question, are clinicians looking too hard for thyroid cancer?

## Risks versus Benefits

“I think the answer is yes,” says Endocrine Society expert R. Michael Tuttle, MD, of the Memorial Sloan Kettering Cancer Center and the Joan and Sanford I. Weill Medical College, Cornell University, both in New York City. “If you look hard enough, you can find thyroid cancer, but if you are finding something that is not life-threatening and is not likely to hurt somebody, then you have to question — what is the benefit?” There are negative consequences of both overtreatment and of overdiagnosis. “The downside is that patients may end up with a

## AT-A-GLANCE

- Both overtreatment and overdiagnosis of thyroid cancer can cause negative outcomes for patients, consequences that could be avoided by a shared decision-making approach between patient and clinician.
- Enlarged thyroid cancers have the same 99% survival rate as do tiny, millimeter-sized thyroid cancer nodules.
- Even with thyroid cancers that have begun to grow, a delayed surgical approach is just as effective as an up-front, immediate surgical approach.

surgery they don't need, and another downside is that they are now labeled as cancer patients," Tuttle adds.

Surgery — typically total thyroidectomy — carries a 1% – 2% chance of damaging the patient's voice and a 1% – 2% chance of causing permanent hypoparathyroidism and requiring lifelong medication. "One or two percent seems very low unless it happens to be you, in which case it's 100%," Tuttle says. That trade-off seems particularly high for a disease that probably will not ever harm the patient. Notably, before detection methods improved in the 1990s, autopsy commonly uncovered thyroid nodules in patients that died of other causes and were never aware of the neck tumors.

As for being labeled as cancer patients, Tuttle says they begin to behave and to think differently, which can precipitate a different set of negative consequences. "My patients tell me that before they got their thyroid cancer diagnosis they described their lives as 'before college or after college' or 'before I got married or after I got married.' When they get that diagnosis, their story changes to 'before thyroid cancer and after thyroid cancer.' It's a pivotal point in their lives," he explains.

Patients begin to define themselves in terms of having cancer, which becomes an emotional burden. Even when they are told not to worry because the cancer is small and probably will not progress, all they hear is, "I have cancer." Some spend the rest of their lives wondering if they will fall into that 1% – 2% that dies of thyroid cancer or experiences recurrence. "This drive to find every little small thyroid cancer and get it treated is certainly part and parcel of our medical community, and I'm not certain that's a good thing," Tuttle laments. "When you're trying to find thyroid cancer, you have to balance not only the benefit but also these unexpected consequences."

## To Treat or Not To Treat ... and, If So, When?

The question then becomes, what would happen if papillary microcarcinoma (PMC), tumors 1 cm or less,

went untreated? "Probably nothing," says Tuttle. Because the overall survival rate is 99%, size is not a factor here, according to research. "The hard part is that the vast majority of them never do anything, but there are a small number of them that grow and metastasize. It's that small number that grow and metastasize that has everybody worried," Tuttle says. Nevertheless, detecting and treating a 1-mm tumor does not improve on the survival rate of detecting and treating a 4-cm tumor.

In the face of these data, the decision to pursue more aggressive therapies for thyroid cancer should be made after due consideration and probably a period of watchful waiting. "By and large, if we find a small thyroid nodule, we should resist the urge to stick the needle into it," Tuttle says. He recommends telling the patient it might or might not be thyroid cancer and an ultrasound will be repeated in a year. The vast majority will not have changed or grown, and the observation phase continues. If it has begun to grow, or if it has metastasized to a lymph node, "that marks one that was going to behave a little more aggressively, and you appropriately treat it at that time," Tuttle says. "The key point is that this is not melanoma; this is not pancreatic cancer — you've got time here."

The efficacy of this so-called "salvage therapy" — that is, waiting until something changes to treat — for thyroid cancer was demonstrated recently in "An observational trial for papillary thyroid microcarcinoma in Japanese patients," published in *World Journal of Surgery*. Researchers led by Yasuhiro Ito, MD, PhD, of the Kuma Hospital in Kobe, Japan, studied PMC in 1,395 patients and found that

**“If you look hard enough, you can find thyroid cancer,** but if you are finding something that is not life-threatening and is not likely to hurt somebody, then you have to question — what is the benefit?”

— R. Michael Tuttle, MD,  
Memorial Sloan Kettering Cancer Center/  
Joan and Sanford I. Weill Medical College,  
Cornell University, New York City

those tumors that did grow or metastasize in the cohort of 309 observation patients who did not undergo immediate surgery were treated very well with surgery at a delayed date after follow-up of five or 10 years.

### **Risk-Adapted Therapy**

Knowing that thyroid cancer is still very treatable even if it has progressed is enough for many patients to be comfortable with the wait-and-see approach; however, some patients prefer immediate biopsy. “It’s important to have the discussion up front,” Tuttle says. “I’m not saying it’s wrong to stick a needle into something small, but the patient needs to understand all of the ramifications, whereas some doctors just assume that the earlier they treat, the better. The patient needs to understand that treatment is not just a pure benefit.” Davies agrees. “Women have been affected by the problem more than men, and should be advised of both the potential harms, as well as benefits, of working up and aggressively treating incidentally detected small, asymptomatic thyroid findings,” she says.

The decision-making process between surgery and observation should be shared, but with PMC, the choice is most often between two right answers. As the expert, the clinician should guide the process, but ultimately support the patient in either approach, as long as the patient truly understands the risks and benefits of both.

However, as the idea spreads that thyroid cancer might be generally overtreated, endocrinologists are beginning to see patients with serious clinical risks rejecting surgery or who look for miracle cures in herbs and other unconventional treatments. “Thus far nobody’s been successful, and they eventually come back for surgery,” Tuttle says. “We’re not saying that thyroid cancer never needs to be treated; go stick your head in the sand. We’re saying that low-risk thyroid cancers that are a large proportion of what

we’re dealing with shouldn’t be overtreated yet not to ignore real thyroid cancer and the aggressive stuff that needs to be treated in an appropriate and aggressive fashion.”

This “risk-adapted therapy” allows the clinician to slow down and be cautious with low-risk patients, but to get high-risk patients appropriately diagnosed and treated.

Another aspect of thyroid cancer that demands a more balanced view is with access to care. While most PMC patients are being overdiagnosed, some populations with inadequate access are being undertreated, such as African American men, as reported in the March issue of *Endocrine News*, probably due to presentation at a more advanced stage. “Everybody wants to deal with thyroid cancer as one big group, and it’s not,” Tuttle says. “The general concept here is not to convey the idea that thyroid cancer is not cancer. There are people who die of thyroid cancer, and there are patients who need to be diagnosed sooner than they are.”

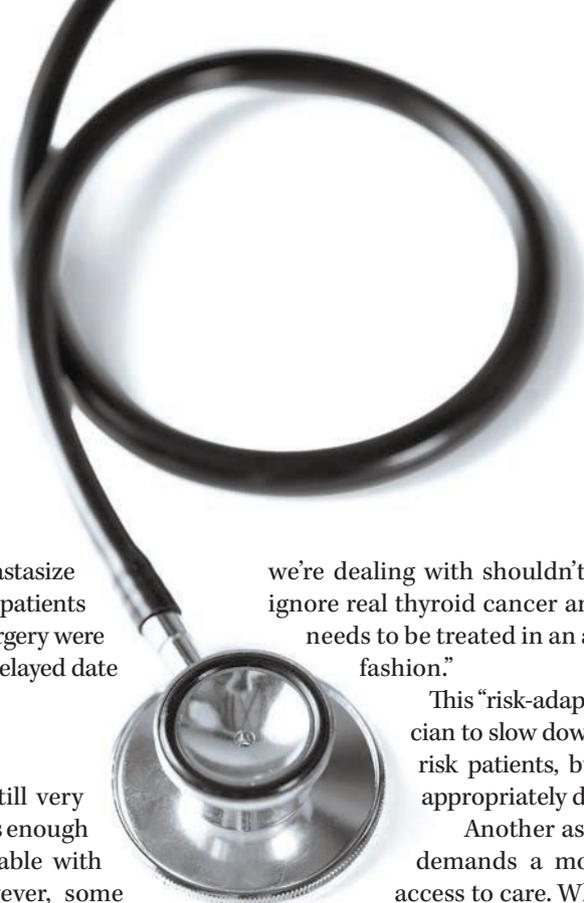
Experts agree, however, that much of the problem of overdiagnosis of thyroid cancer can be mitigated with frank patient conversations and perhaps a higher threshold to biopsy, particularly for women. Although the clinician cannot know which microtumors might become problematic, active surveillance probably will not hurt the patient’s prognosis. Moreover, less aggressive, though still experimental, therapies may be in the offing, such as very targeted laser treatment. Partial thyroidectomy or a minimalist surgical approach is sometimes another possibility. As has been demonstrated with other cancers such as breast and prostate, shared decision making in which the patient understands that he or she faces risks alongside any potential benefits, can go a long way toward reducing unnecessarily aggressive treatment. **EN**

“Small tumors continue to make up the bulk of new thyroid cancer diagnoses, with no change in the number of people dying from thyroid cancer.

**Identification of small tumors without changes in the number of people dying strongly suggests we are detecting subclinical disease — cancers not destined to be a threat to that person’s life.”**

— Louise Davies, MD, MS,  
Department of Veterans Affairs  
Medical Center, White River Junction,  
Vt./Geisel School of Medicine,  
Dartmouth College, Hanover, N.H.

— Horvath is a freelance writer based in Baltimore, Md. She wrote about delayed puberty in the October issue.





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# Physical Therapy

When a patient with diabetes is also an athlete, there are myriad concerns, preparations, and precautions for patient and doctor alike.

By Derek Bagley

Emily Westfall does her “long runs” on the weekends, 10 to 12 miles to train for a half marathon. She likes to run these miles mid-morning, so the temperature is just right, not too cold, not too hot. She wakes up at 8:00 to hit the pavement by 10:00.

But in those two hours pre-run, Westfall has to prepare for the two-hour run ahead. Westfall has type 1 diabetes (T1D), which means there’s a lot to do before, during, and after the run. “If it’s a 10-mile run,” she says, “I’d assume I’d do that in an hour and a half to two hours, so I’ll probably do a two-hour [basal] reduction at eight o’clock, two hours before my run.”

Westfall reduces her basal to 70% between 8:00 and 10:00, then resumes the basal to normal right before she starts running. She keeps her pump on during the run and carries a Camelbak hydration pack stocked with glucose tabs, granola bars, and “running goo.” She brings her test kit and some type of liquid, usually straight water or some kind of carbohydrate/electrolyte mixture.

During the run, Westfall tests her blood sugar. “I trained myself to test while running,” she says. If she needs to treat, she’ll “pull over” and do what needs to be done. “I try to pretend like it’s a race,” Westfall says, “so I try not to stop to test or do any other treatment stuff. What I would do in a race is try to jog it through. I don’t know if that’s necessarily ‘kosher,’ but that’s how I do it.”

After the run, Westfall does another temporary basal

reduction for an hour, but she also has to bolus. “I normally spike right after coming back from a run,” she says. “I’ll do a small one-and-a-half unit bolus, and I’ll test my blood sugar more often over the next three or four hours.”

Westfall has an intimate knowledge of the complicated dance of exercise and diabetes beyond her own personal experience. She’s a research assistant at the Barbara Davis Center for Childhood Diabetes at the University of Colorado, Aurora, so she’s able to see the spectrum. “There are people who make it a bigger deal, there are people who make a big enough deal to be safe, and then there are people who don’t even think about it,” she says. “We have kids in the clinic who say, ‘Well, I’m on the track team,’ and they have the same thought that I had: I have diabetes and if I go low, I’ll drink juice. But you have to balance out that high aspect too, because if your blood sugar is high, you’re not going to be able to exercise at the optimal level.”

## Physical Education

Research has also shown that it can be tricky to manage diabetes with exercise. That’s not to say diabetic patients shouldn’t exercise; far from it. Exercise increases insulin sensitivity and lowers blood sugar levels, which are obvious benefits to these patients, but things get dicey when blood glucose levels drop too much during or after exercise, as the body increases its utilization of glucose for fuel.

Paul Wadwa, MD, also of the Barbara Davis Center for Childhood Diabetes at the University of Colorado, said

during his presentation at ENDO 2013 in San Francisco that the challenges are mostly in T1D patients, “when it comes to exercise and insulin adjustments.” Diabetic patients, especially those with T1D, must then know how their physical activities affect them and make real-time adjustments with their medications and food intake, as exercise increases the risk of hypoglycemia. A number of studies have also taken other factors into consideration, shedding new light on ways for controlling diabetes symptoms while staying fit.

“Challenges exist for patients with diabetes who are at risk for hypoglycemia when they exercise,” Wadwa says. “I am most concerned about patients on insulin. This includes all patients with T1D and a much smaller percentage of T2D patients. Patients on oral medications with the risk for hypoglycemia (such as those taking sulfonylureas) would also be at risk, but the adjustment in oral medication around exercise should be less challenging than the adjustments in insulin doses.”

Thomas P. J. Solomon, PhD, of the University of Copenhagen, Denmark, and his team wanted to understand the so-called “intersubject variability” in glycemic control following exercise as a way of individualizing treatment for diabetic athletes and published their findings in the *Journal of Clinical Endocrinology & Metabolism (JCEM)*. In this study, the researchers found that around 90% of subjects had an increase in insulin sensitivity following exercise but only around two-thirds of subjects had a reduction in blood glucose levels, as measured by either HbA1c, fasting glucose, or the two-hour glucose during an oral glucose tolerance test (OGTT). They did not find a relationship between the training-induced change in insulin sensitivity and the training-induced change in glucose levels.

However, the scientists did find that the training-induced change in the insulin secretory response to oral glucose ingestion (a marker of beta-cell function) was reflected by the training-induced change in glucose levels.

Solomon and his team concluded that intersubject variability in restoring glycemic control following physical activity is explained by changes in insulin secretion. “Thus,” they wrote, “baseline and training-induced changes in beta-cell function may be a key determinant of training-induced improvements in glycemic control.”

Solomon also notes that future work should conduct a large-scale randomized controlled trial using more sophisticated

## AT-A-GLANCE

- Patients with diabetes, especially type 1 diabetes, face a number of challenges while exercising because they are at risk for hypoglycemia.
- Research points to a number of factors that affect glycemic control in T1D patients while they’re exercising.
- Athletic, diabetic people should find personalized plans, usually through trial and error, for glycemic control.

techniques for measuring beta-cell function. “Furthermore,” he adds, “it would be prudent to stratify participants based on pre-intervention beta-cell function. In this way, solid conclusions regarding the potential role of pancreatic beta-cell function in the adaptations to exercise training could be made.”

So those are things patients can’t necessarily control, but there are factors that they can do something about. Time of day and intensity of exercise can play a role in how well glucose levels are maintained.

Researchers in Australia found that the risk of “exercise-mediated hypoglycemia” increases during exercise and for several hours after moderate-intensity physical activity and published their findings in *JCEM*.

Raymond J. Davey, PhD, of the Telethon Kids Institute, Perth, Australia, and his colleagues had already reported a biphasic increase in glucose requirements to maintain euglycemia after late-afternoon exercise, “suggesting a unique pattern of delayed risk for nocturnal hypoglycemia.” So they set out to determine whether the same pattern of glucose requirements occurred if patients exercised earlier in the day.

The researchers measured the amount of glucose infused to maintain stable blood glucose levels as a surrogate for hypoglycemia risk. They showed that that glucose requirements are increased during and for 11 hours post-exercise in adolescents with T1D, suggesting an increased risk of hypoglycemia over this period.

“We suggest that this increase in glucose requirements is due primarily to an increase in peripheral glucose uptake,” Davey says. “Previously, we showed a different pattern of glucose requirements when exercise was performed in the late afternoon rather than at 12:00 pm. This suggests that the time of day when exercise is performed is an important determinant of hypoglycemia risk in adolescents with T1D.”

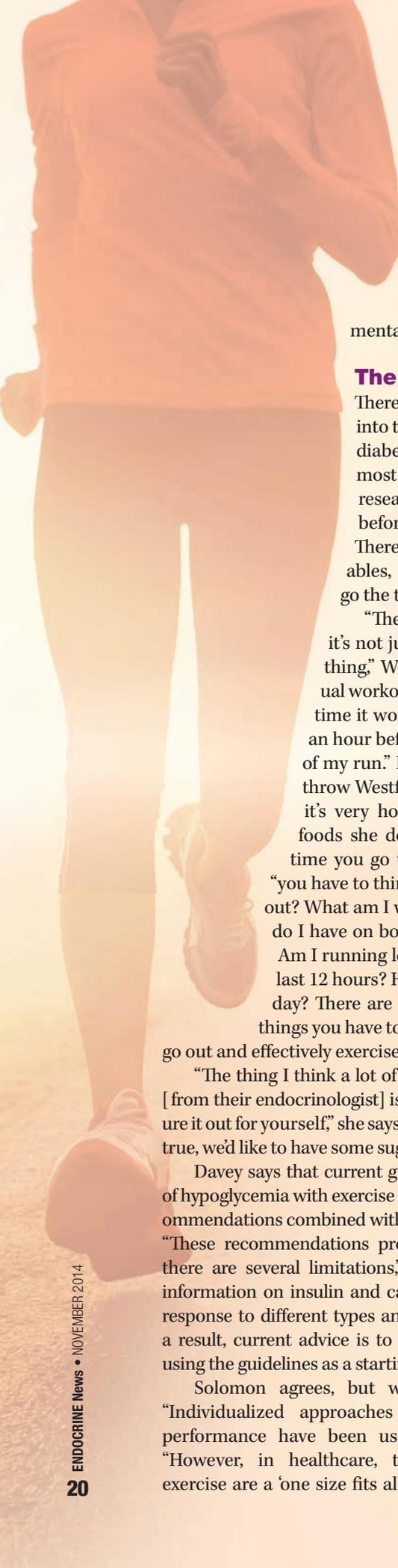
But again, Davey warns against generalizing. “It is important to mention that we assessed the risk of hypoglycemia following moderate-intensity



**“Challenges exist for patients with diabetes who are at risk for hypoglycemia when they exercise. I am most concerned about patients on insulin. This includes all patients with T1D and a much smaller percentage of T2D patients.**

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— Paul Wadwa, MD,  
Barbara Davis Center for  
Childhood Diabetes, University of  
Colorado, Aurora



exercise under the conditions described,” he says. “There are many studies that show that this risk is affected by numerous other factors including the intensity and duration of exercise, circulating insulin levels, and the availability of both supplemental and stored carbohydrates.”

### The Starting Line

There’s a lot of planning that goes into tailoring an exercise plan for diabetic, athletic patients, and most experts agree that more research needs to be conducted before settling on a perfect plan. There are just too many variables, so athletes usually have to go the trial-and-error route.

“The interesting thing is that it’s not just an individually personal thing,” Westfall says. “It’s an individual workout basis. I can say 90% of the time it works to reduce my basal rate an hour before my run, for the amount of my run.” But there are variables that throw Westfall’s planning off, like when it’s very hot out or when she’s eaten foods she doesn’t normally eat. “Every time you go to do a workout,” she says, “you have to think: ‘What’s the temperature out? What am I wearing? How much insulin do I have on board? What’s my basal rate? Am I running low? Have I had a low in the last 12 hours? Have I been running high all day? There are probably 17 to 20 different things you have to think about before you can go out and effectively exercise or train.”

“The thing I think a lot of patients don’t want to hear [from their endocrinologist] is ‘You’re going to have to figure it out for yourself,’” she says. “And while that’s ultimately true, we’d like to have some suggestions, a starting point.”

Davey says that current guidelines for the prevention of hypoglycemia with exercise in T1D offer generalized recommendations combined with a trial-and-error approach. “These recommendations provide a starting point, but there are several limitations,” he says, “such as limited information on insulin and carbohydrate adjustments in response to different types and intensities of exercise. As a result, current advice is to develop personalized plans using the guidelines as a starting point.”

Solomon agrees, but with a couple of caveats. “Individualized approaches for maximizing athletic performance have been used for decades,” he says. “However, in healthcare, the recommendations for exercise are a ‘one size fits all’ approach. Given the data

from our own group and that from studies such as the HERITAGE trial, showing the large variability in the health outcomes following training, an individualized approach for using exercise as medicine seems very sensible. However, there is no current evidence that can allow us to predict what type of exercise plan will lead to the biggest health gain for a specific individual.”

Solomon recommends the American Diabetes Association’s “excellent” baseline plan for adults with diabetes: more than 150 minutes per week of moderate-intensity aerobic exercise (50%-70% of maximum heart rate) combined with resistance training on at least two days a week with no more than two consecutive days without exercise.

Wadwa advises patients to over-prepare by keeping glucose and snacks on hand at all times during physical activity, and logging everything — blood sugar, food intake, what time of day the patient exercises. He also suggests that the patient train with someone who could help if he or she “runs into trouble.”

Westfall has found that the over-preparing approach works best for her. “What really helps me have successful training sessions and races is making sure I check off all that stuff on that list and have a plan,” she says. “I’d say it’s 60% preparation and 40% execution to make sure you balanced your ‘good’ blood sugars during your exercise.”

### Making Strides

Research in this particular field is ongoing, a kind of marathon itself, and the future looks bright. Solomon points to drug therapies as an interesting development. “What is particularly exciting right now are the advances being made with regards to the potential interaction between exercise and drugs commonly used to treat diabetes (e.g., metformin, rosiglitazone, statins), and the epigenetic adaptations to exercise (DNA methylation, microRNA expression).”

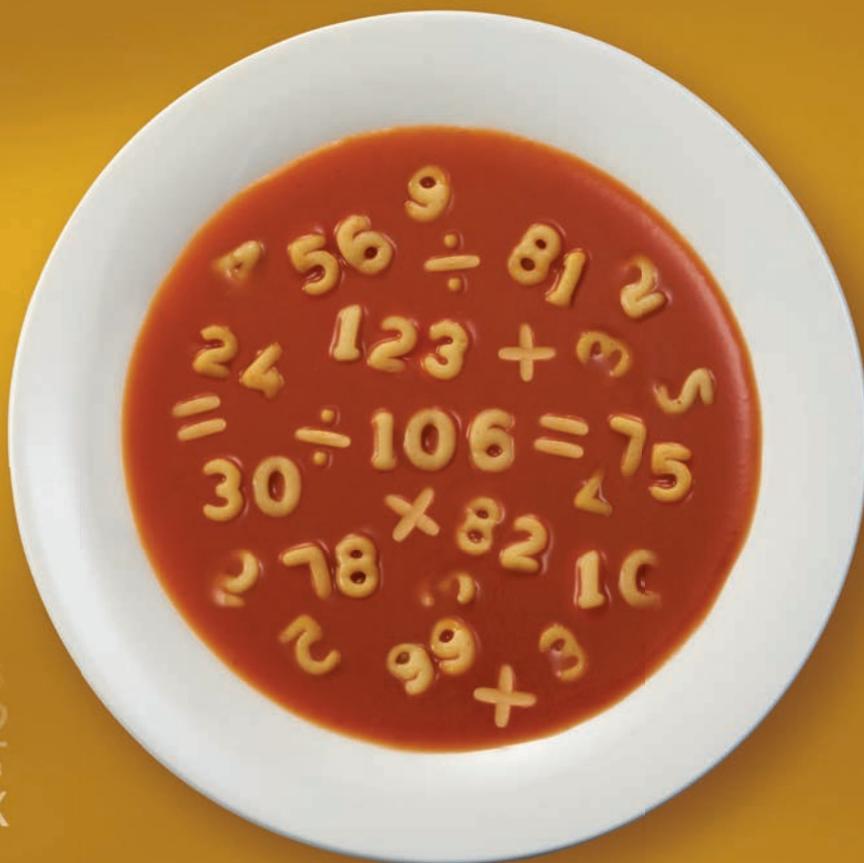
For now, the experts say that finding an activity that the patient enjoys is the first step toward maintaining an exercise schedule. “The health benefits of a physically active lifestyle are well established and particularly important for people with T1D,” Davey says. “Therefore, I’d suggest that the best approach is to find an exercise type or program that provides the greatest enjoyment to increase the likelihood of adhering to regular exercise.”

“I advise our pediatric patients to find exercise that they enjoy,” Wadwa says. “If they are miserable when they go to the gym, they are not going to want to go.”

Solomon agrees, commenting on obese patients who may lack motivation to engage in physical activity, which can often be a challenge. “Based on anecdotal observations from our own research experiences, enjoyment is key,” he says. “So to an obese individual with T2D who wanted to start exercising, I would suggest finding an environment in which they feel comfortable, an exercise mode which they find fun, and a social group with whom to interact and exercise with.” **EN**

— Bagley is the associate editor of Endocrine News. He wrote about online review sites in the October issue.

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## Growing Pains

The journey from childhood to adulthood can be wrought with challenges, especially for young people managing chronic health conditions. Now, online toolkits can help ease the stress and uncertainty of these life-changing transitions.

By Mark A. Newman

**F**or Amanda Rossi, a freshman biology major at Fordham University, diabetes is nothing new — she was diagnosed with type 1 when she was just two and a half years old. What was new, however, was venturing out on her own when she finally left her parents’ house in Woodbridge, Conn., to start college in New York City.

“Being away from my parents is hard. I miss having them here to give me a pat on the back, but I especially miss them checking up on my diabetes management,”

Rossi explains. “I no longer have the luxury of having someone to check my blood sugar in the middle of the night. If I go to bed with active insulin, I’m responsible for making sure I don’t go low.” Rossi adds that when she lived at home she would explain her concern about going low in the middle of the night to her mother who could check on her at 3 a.m. “Of course, I can set my own alarm and check myself,” she says, “but what if I don’t get up?”

She explains that there have been nights in the past



where her insulin levels have been too low to get up and get something to treat herself with. “And when that situation arises, I yell for my mom and dad, and they come running, apple juice in hand,” Rossi says. “I have learned that I have to take care of myself and make sure I have low supplies next to my bed at all times.”

Rossi is not alone. According to an article in a 2003 issue of *Diabetes Care*, each fall 2.3 million freshmen enroll in U.S. colleges and universities, with an estimated 7,700 of whom are living with type 1 diabetes. However, making this transition to adult care is not something that takes place the day after a child turns 18; it is an ongoing process that should feasibly begin with the pediatric healthcare provider around age 12, according to an article published in June 2011 in *Pediatrics*, but there are exceptions for children with chronic conditions. “Children and youth with special healthcare needs and their families may benefit from discussions regarding adult transitioning that begin earlier than 12 years of age,” the article states, adding that “some children with chronic medical conditions (e.g., asthma or diabetes) may be introduced to developmentally appropriate self-care at ages younger than 12.”

Ready or not, for many young adults living with a

chronic condition, cutting the apron strings can be somewhat daunting. Aside from the usual issues of moving, starting college, or a new job, going through these already stressful life events are magnified when you’re dealing with an ailment that requires constant management.

### Easing the Transition Online

Now those young adults can simply go online for a number of tools that can make the transition from parental supervision to overseeing their own care go much more smoothly. The Transitions of Care initiative ([www.endocrinetransitions.org](http://www.endocrinetransitions.org)), spearheaded by the Endocrine Society, was created to help young adults who have hormone conditions navigate the shift from a pediatric to an adult healthcare team and offers resources for young adults, their parents, and healthcare providers.

“The transition to emerging adulthood, no matter who you are or where you are, is difficult; you don’t want to do kiddie things, but you’re not prepared to be an adult,” says Alan D. Rogol, MD, PhD, a professor emeritus at the University of Virginia in Charlottesville, and a member of the Endocrine Society’s Transitions of Care Task Force. “Add a chronic illness on top of that

### ONLINE SUPPORT Communities & Tools

- College Diabetes Network:  
[www.collegediabetesnetwork.org](http://www.collegediabetesnetwork.org)
- Transitions of Care initiative:  
[www.endocrinetransitions.org](http://www.endocrinetransitions.org)
- Got Transition:  
<http://www.gottransition.org/>
- Diabetes Hands Foundation:  
<http://diabeteshandsfoundation.org/>



## Participants in the **TRANSITIONS OF CARE**

Participants in the initiative include the Endocrine Society, the Pediatric Endocrine Society, the American Diabetes Association, the American Association of Diabetes Educators, JDRF, the International Society for Pediatric and Adolescent Diabetes, the Hormone Health Network, the American Academy of Pediatrics and the American College of Physicians. The program is supported by educational grants from Lilly USA, LLC, Medtronic Diabetes, and Novo Nordisk Inc.

and you have even more responsibilities, especially if your parents monitored your glucose and you were just the passenger. All of a sudden you have to take care of yourself, and you have to figure out how to find a doctor, get a prescription filled, deal with insurance. These are things the average teen doesn't have to deal with. It's an added burden."

The Transitions of Care website includes assessments to help young adults and their healthcare providers assess how ready patients are to independently manage their care and to identify patients' biggest worries. Toolkits with specific guidance for people with type 1 diabetes and growth hormone deficiency are currently available on the site. The type 1 diabetes toolkit incorporates links to fact sheets on various challenges facing young adults with the condition, such as managing diabetes safely in the workplace and in a college setting.

The site also features referral forms for pediatric and adult healthcare providers to share information about a patient's medical history. While the actual transfer may be marked by the patient's first visit to the adult care team, significant communication must take place between the pediatric and adult care providers to ensure a smooth transition. The Transitions of Care initiative provides the resources pediatric practices need to prepare young adults for the move to a new provider. The toolkits also include information to help adult healthcare providers plan for the first appointment and ensure they have detailed information about the new patient.

### **College Bound**

Another tool — the College Diabetes Network (CDN) — is designed specifically for college students with type 1 diabetes and provides a portal for peer support and help with access to better healthcare. Christina Roth, the CEO and founder of CDN, created it after she felt overwhelmed by the demands of

both college and dealing with her own diabetes. "It was tough to stay on top of classes, work, and all of my other commitments while worrying about my diabetes," she says. "I just wanted to talk to someone else who understood. I decided to hold a meeting for other students with diabetes who, like me, were feeling overwhelmed."

At that first meeting Roth found other students who had a lot of concerns about making the leap from home to campus while managing their diabetes. "What really surprised me was that I was getting emails from students with diabetes all over the country who were interested in starting, running, and sustaining their own groups, and who had experienced the same barriers that I had in finding members," she explains. "That's when it became clear to me that peer support is so vital to living with this disease, especially in environments like a college campus. And the College Diabetes Network was born."

CDN's newly launched website is filled with information for college students — especially freshmen away from home for the first time like Rossi — that lets them connect with other students going through the struggle of balancing college, adulthood, and diabetes. "We've created a timeline of actions for students with diabetes to take when preparing to move from home to campus," Roth says. "It includes action items such as making a plan for their diabetes supplies, preparing

a sick day kit, and creating communication plans with their family and healthcare teams." Roth adds that at the very least, a CDN chapter provides students with someone close by to call in a pinch, when they're running out of insulin when the pharmacy is closed, have a broken pump, etc.

Due to her involvement in the College Diabetes Network, Rossi's transition at Fordham has been much simpler because she's had a group of people to depend on when she became frustrated with her diabetes management. "It feels so good to know that there are people here to sympathize with the (literal) highs and lows that I am going through," she says. "People without diabetes can offer support and kind words, but they don't quite know what it feels like to have low blood sugar when the elevator is broken and you live on the fourth floor of your dorm, or how irritating it is to not know if the Jell-O in the café is sugar free or not." **EN**



**"People without diabetes can offer support and kind words, but they don't quite know what it feels like to have low blood sugar when the elevator is broken and you live on the fourth floor of your dorm."**

— Amanda Rossi, a freshman at Fordham University with type 1 diabetes (right) with her friend Nik O'Brien, who has learned how to check Amanda's blood sugar, change a pump site, and even insert and calibrate a glucose monitoring system.

— Newman is the editor of Endocrine News.

# Fiscal FITNESS

How to create your lab's budget in four simple, painless steps.

By **Melissa Mapes**

A wise man once said, "Never base your budget requests on realistic assumptions, as this could lead to a decrease in your funding." That man was Scott Adams, the author of the famous comic strip *Dilbert*. As he aptly points out, budgeting is a complicated process that can be influenced by institutional politics in addition to an evaluation of anticipated expenses and available funds. Not many people like to juggle the Excel spreadsheets, meetings, and paperwork that go into a budget, but it can be done — and done well — by following a few simple steps.

## Step One: Executive Bargaining

A laboratory manager's performance evaluation largely relies upon his or her ability to create and follow an efficient budget. This involves tracking expenditures, employing staff, keeping an inventory of lab supplies, and, perhaps most importantly, convincing the higher-ups to provide funding for these operations. Naturally, the authorities in charge of financing vary based on whether one works as a practitioner, academic, or industry researcher. A smart

first move requires identification of the appropriate leadership and in-depth budget discussions.

*Lab Manager* magazine conducted a survey of laboratory managers to discover how they maneuvered through this budgetary process. Dennis Busiere of the Monroe County Environmental Lab in Rochester, N.Y., replied that, "Prior to creating the budget, I meet with the senior management and highlight possible constraint issues and funding requirements."

By fostering a positive relationship with executives, a lab manager or researcher is more likely to obtain ample funding. Meetings should be scheduled well before fiscal deadlines to provide room for negotiating and presentations, if necessary. Like Busiere mentioned, there may be eligibility hoops to jump through and financial constraints to consider. Designing a budget prior to discussions with the approving authorities or reviewing grant guidelines will likely result in an extensive rewrite and a lot of wasted time.

Business discussions can also provide valuable

## BUDGET Expense Categories

- **Personnel** – each person, their title, and the compensation they will receive
- **Fringe Benefits** – overtime, workman's compensation, health benefits, etc.
- **Travel** – expenses for attending training or other project-related activities
- **Equipment** – machinery and other permanent property necessary for the lab
- **Supplies** – chemicals and other disposable items
- **Construction** – repairs and any other physical alterations to the lab or equipment
- **Consultants/Contracts** – lab consultants or temporary outside assistance
- **Other** – rent, utilities, and other regular bills

insight from the finance team. Their interpretation of the previous year's expenditures may be able to offer areas with saving opportunities, while upper management will have the chance to explain their expectations and goals for the coming year. Some negotiating may be required to gain support for one's projects, but engaging leadership in early discussions should improve the likelihood of reaching an agreement.

### Step Two: Experimental Research

Once the total sum of available funding has been confirmed, researchers and lab managers must select the experiments that can be feasibly completed within the budget. A list of desired projects and necessary equipment should be compiled. The list can then be categorized by primary, secondary, and tertiary items — with primary items including the absolute necessities and the tertiary items working as a “wish list.” Secondary items are those strongly desired but not absolutely critical to operations.

This can be a good time to consult with colleagues who have conducted similar projects to see the amount they wound up spending in the lab. Their experiences can act as a baseline to build and learn from.

An important point of comparison is personnel. How should funds be divided between technicians, postdocs, and other staff? A dollar amount needs to be assigned to each individual that encompasses all payment and expenses related to employing that person. Looking at the budget sheets for other research projects will help ensure that each member of the team is paid the “going rate” for his or her position.

The projected expenses for staff must also include “fringe benefits” like healthcare. According to *Science* magazine, this amount can range anywhere from 17% to 30% of total employee costs. Each institution varies, so it is important to confirm with the appropriate authorities before performing calculations.

Another major cost category is equipment. Ask vendors for price quotes on the list of machinery and

materials needed for the year's proposed experiments. Keep in mind that finding funding for equipment later in the year or project may prove challenging, especially if cash has already been allocated elsewhere. Again, learning from the successes and mistakes of others' budgets can help anticipate the expenses that might arise.

Costs like utilities, waste disposal, and maintenance should be relatively predictable. However, keeping a close watch on these bills — like all others — is necessary to avoid any unwanted surprises.

### Step Three: Monitor Monthly

Even the most elegant budget does little good if it is not properly executed. After adding up projections for costs and making sure that their total fits within lab funding, one needs to closely follow spending month-by-month to make sure that operations are running according to plan.

Anyone who works in the laboratory needs to be kept in the loop as to the progress of finances. By teaching researchers and employees to be judicious in their use of lab materials, costs can be minimized — potentially saving enough funds for the secondary and “wish list” items from step two.

*Science* magazine recommends a simple method called “calendarizations” for monthly tracking. The annual budget for basic needs like reagents and salaries is divided by 12. These numbers are a marker for measuring progress. Each individual can be assigned an annual supply budget that, once “calendarized,” determines whether he or she is using his or her fair share of resources in a given month.

If costs are consistently higher than anticipated, one might have to find additional funding mid-year. Where the money comes from depends, of course, on the type of lab or research, but financing tends to be universally more difficult to obtain after the start of the fiscal year. However, it is far better to submit a request or apply for a grant that is justified by monthly data than to run out of cash without any hard numbers to demonstrate additional needs.

### Step Four: Analysis

At the end of a project or year, the final crucial step of any budget is analysis. Crunching numbers can yield great insight into the strengths and weaknesses of one's initial budget plan. This process can be highly educational and will likely inform projections for the next budget.

A researcher that proves deft at managing funds appeals greatly to potential grant-givers and corporate or university leadership. Thus, effective budget design can be highly beneficial to any scientist's career. Bigger, better projects with a larger bottom line are more likely to find their way to the labs of a good money manager. Science always comes first, but studies require funding, and funds will not last without a budget. **EN**

— *Mapes is a Washington, D.C.-based freelance writer and a frequent contributor to Endocrine News. She wrote about the “Plan B” pill and overweight women in the August issue.*

## Lame Duck Congress Considers NIH Funding

Congress is scheduled to return to Washington for a “Lame Duck” session to complete work on items that were left unfinished before the mid-term elections.

Key among these will be Fiscal Year 2015 funding. Although the fiscal year began October 1, Congress was unable to agree to passage of 2015 funding bills before the election. Instead, it passed a temporary stop-gap funding measure known as a continuing resolution (CR) to keep federal agencies funded until December 11. The CR extends spending at the current rate of operations. Consistent with the NIH’s practice during previous CRs, non-competing research grant awards will be issued at up to 90% of the previously committed level and upward adjustments to awarded levels will be considered after FY 2015 appropriations are enacted.

In November, Congress must either pass a regular funding bill or pass another CR to avoid a government shutdown after December 12. While it appears that Congress does not want to cause a shutdown, it is unclear if it will follow regular business and pass a spending bill or rely on another CR.

The Endocrine Society will urge Congress to pass an omnibus spending package that includes funding for the NIH through a Labor, Health and Human Services (LHHS) appropriations bill before the end of the year. We strongly encourage Society members interested in NIH research to join our efforts by visiting our online advocacy center at [www.endocrine.org/advocacy](http://www.endocrine.org/advocacy) and sending a message to their representative and senators.

## Society Applauds USPSTF Type 2 Diabetes Screening Recommendations

On October 6, the U.S. Preventive Services Task Force (USPSTF) issued a draft recommendation statement and

evidence review on screening for abnormal glucose levels and type 2 diabetes mellitus. The task force recommended screening for abnormal glucose and type 2 diabetes in all adults over the age of 45. The Endocrine Society participated in the review of the recommendations and supports the recommendation statement.

Prior to the draft recommendation statement, the USPSTF recommended screening for type 2 diabetes only in asymptomatic adults with high systolic blood pressure. The draft statement takes into account recent scientific evidence that shows measuring blood glucose in adults at increased risk for diabetes and treating those who have impaired fasting glucose or impaired glucose tolerance with intensive lifestyle interventions has a moderate benefit in decreasing the risk for progression to diabetes.

## Webinar to Highlight New Glycemic Control Technology

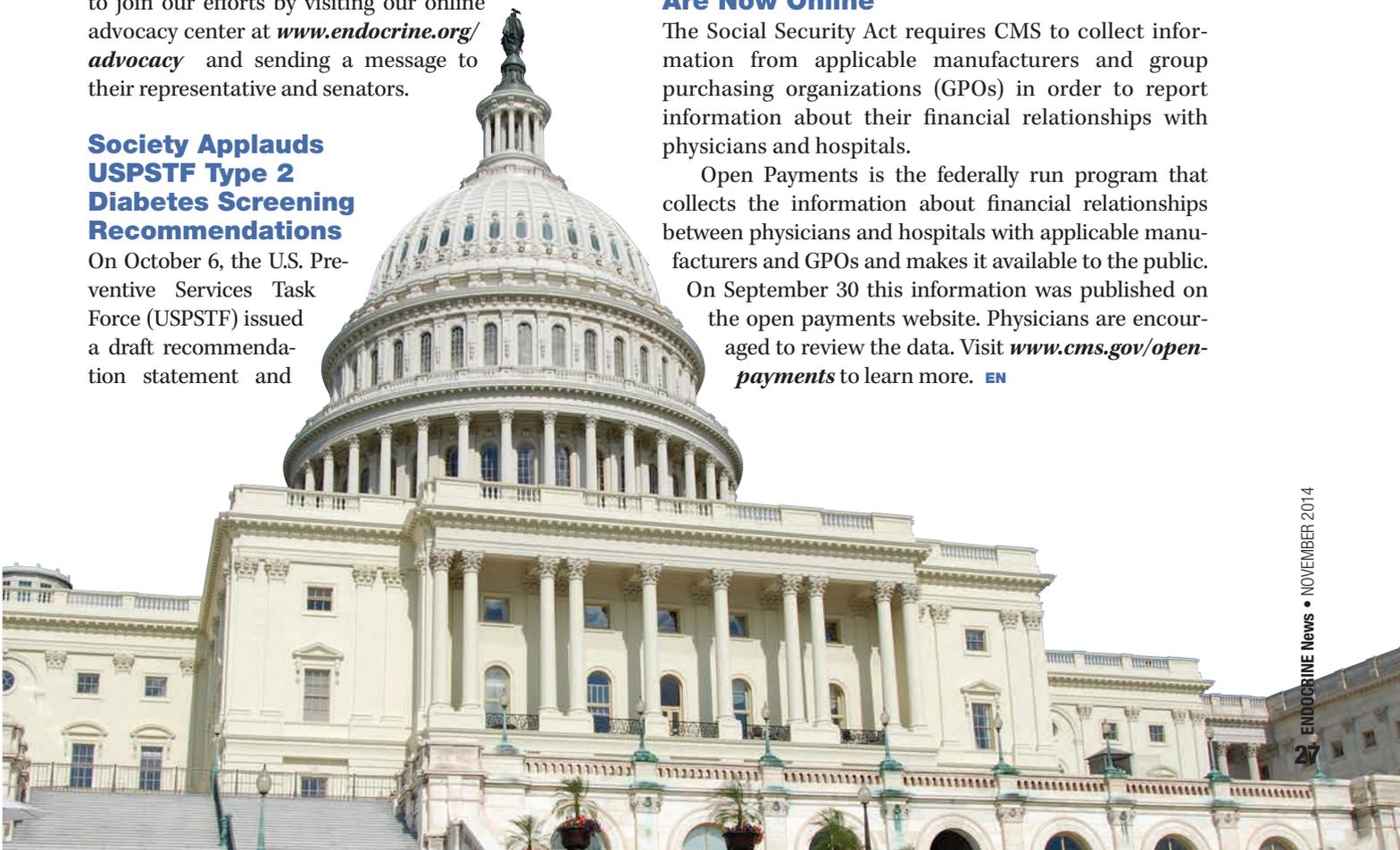
Healthy People 2020 will host a Spotlight on Health webinar highlighting “Emerging Technology to Improve Glycemic Control among Persons with Diabetes” Thursday, November 13, 2014, from Noon to 1:30 pm ET. The webinar will include information about the Endocrine Society’s Accurate Insulin Decisions program. For more information about the webinar, visit [www.healthypeople.gov](http://www.healthypeople.gov).

## Physician Financial Relationships Are Now Online

The Social Security Act requires CMS to collect information from applicable manufacturers and group purchasing organizations (GPOs) in order to report information about their financial relationships with physicians and hospitals.

Open Payments is the federally run program that collects the information about financial relationships between physicians and hospitals with applicable manufacturers and GPOs and makes it available to the public.

On September 30 this information was published on the open payments website. Physicians are encouraged to review the data. Visit [www.cms.gov/open-payments](http://www.cms.gov/open-payments) to learn more. **EN**

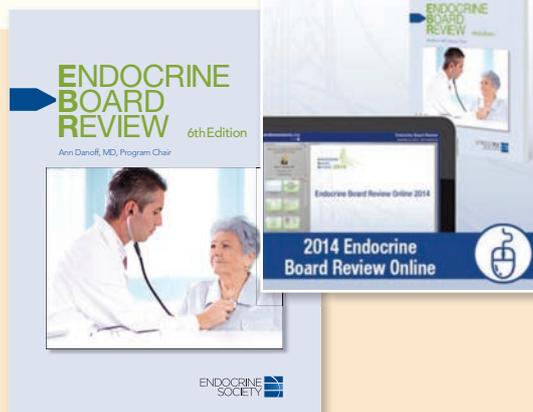


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For more information, visit [endocrine.org/ebproducts](http://endocrine.org/ebproducts).

\**Endocrine Board Review*, 6th Edition may also be purchased separately.



## Clinical Practice Guideline Update: Androgens in Women

The Endocrine Society has updated its Clinical Practice Guideline (CPG), advising against the use of testosterone therapy in women.

The CPG, published recently in the *Journal of Clinical Endocrinology and Metabolism*, is an update to the Society's 2006 recommendations, since new research has addressed concerns over testosterone and dehydroepiandrosterone (DHEA) therapies being used in women. There have also been advances in testosterone testing and measurement techniques in the past eight years.

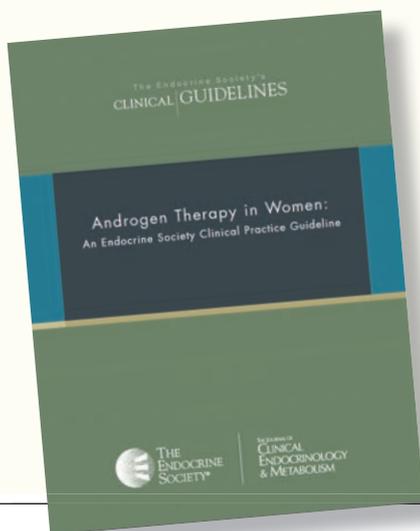
"Although limited research suggests testosterone therapy in menopausal women may be linked to improved sexual function, there are too many unanswered questions to justify prescribing testosterone therapy to otherwise healthy women," says Margaret E. Wierman, MD, of the University of Colorado in Aurora, and the Society's vice president of Clinical Science and chair of the task force that authored the guideline. "When we reviewed past studies, we found many women who had low testosterone levels measured by older or new techniques did not exhibit any signs or symptoms of

concern. As a result, physicians cannot make a diagnosis of androgen deficiency in women."

The updated CPG includes:

- Recommendations against making a diagnosis of androgen deficiency syndrome in healthy women because there is a lack of a well-defined syndrome and data correlating androgen levels with specific signs or symptoms are unavailable.
- Recommendations against the general use of T for the following indications: infertility; sexual dysfunction other than hypoactive sexual desire disorder; cognitive, cardiovascular, metabolic, or bone health; or general well-being.
- Recommendations against the routine use of dehydroepiandrosterone due to limited data concerning its effectiveness and safety in normal women or those with adrenal insufficiency.
- Recommendations against the routine prescription of T or dehydroepiandrosterone for the treatment of women with low androgen levels due to hypopituitarism, adrenal insufficiency, surgical menopause, pharmacological glucocorticoid administration, or other conditions associated with low androgen levels because there are limited data supporting improvement in signs and symptoms with therapy and no long-term studies of risk.
- Outlines for future research, since ongoing improvement in androgen assays will allow a redefinition of normal ranges across the lifespan. This may help to clarify the impact of varying concentrations of plasma androgens on the biology, physiology, and psychology in women and lead to indications for therapeutic interventions.

"Currently, there isn't enough evidence that any benefits outweigh the risks to most women," Wierman says. "More research is needed to determine the long-term safety of testosterone therapy in postmenopausal women." **EN**



## Remembering **William H. Daughaday, MD, (1918 – 2013)**



On May 3, 2013, former Endocrine Society president William H. Daughaday passed away at age 95. Sam Dagogo-Jack, MD, A.C. Mullins Professor in Translational Research, director, Division of Endocrinology, Diabetes & Metabolism, director, General Clinical Research Center, The University of Tennessee Health Science Center, Memphis, Tenn., calls Daughaday a “towering figure in endocrinology... and a pioneer neuroendocrinologist whose work led to the discovery of the somatomedins (Insulin-like

Growth Factors) that mediate the skeletal growth effects of Growth Hormone...and opened up the field of binding proteins (cortisol binding protein, IGF binding proteins) in endocrine physiology.”

Daughaday was one of Dagogo-Jack’s attending physicians and professors when he began his endocrinology fellowship training at Washington University in St. Louis, Mo., in 1990. “He quickly became a trusted mentor and was instrumental in my decision to commit to a career in academic endocrinology,” he says. “I sought his advice often and benefitted greatly from his deep understanding of life and academia. As a fellow and later junior faculty,

Dr. Daughaday painstakingly read my draft manuscripts and research grants, and used his vast experience and insight to make extremely valuable suggestions for improvement.”

Dagogo-Jack credits that degree of informal but hands-on, time-consuming “uber mentorship” with providing him quintessential training during his early development as an endocrinology faculty member at Washington University. “I am immensely grateful to have been influenced by such a gifted scientist and mentor,” he says.

Dagogo-Jack reached out to *Endocrine News* to share his poetic tribute to his late mentor, who had such a remarkable influence on his life.

Dr. Daughaday painstakingly read my draft manuscripts and research grants, and used his vast experience and insight to make extremely valuable suggestions for improvement.”

### Voice of the Oak

*Nary an empty seat, nary a sound  
Save the soft monotone that holds spell-bound,  
Shorn of crescendo and low in timbre,  
Yet luring no reverie or slumber.*

*Ears and eyes ajar, pupils dilating  
From dim light and surging adrenaline;  
Not fight or flee, acrophobia perhaps:  
The looming climb on the tree of science.*

*Clinical wisdom, endocrine vignettes,  
Delivered in still vocal packages;  
Wrapped within intertwined clues and secrets,  
Decoding rife and mysterious ailments.*

*Shy doyen of the scientific realm;  
Friend to adepts and novices the same;  
Sacrificing neither bench nor bedside,  
The pearls from the quiet sage resound.*

*Unmasker of mediators of man’s growth  
And of the proteins that carry them forth,  
Whence Nature’s laws of stature are laid bare,  
As the long and short are served with éclat.*

*Such simplicity, clarity, humor;  
Such perspicacity, insight, candor  
Forever inform and enrich each day  
In remembrance of the voice of Daughaday.*

— Daughaday’s obituary can be found at: <http://news.wustl.edu/news/Pages/25414.aspx>.

## Event CALENDAR

**DECEMBER 5 – 7, 2014,  
VIENNA, AUSTRIA**  
2nd World Congress of Clinical Lipidology  
[www.clinical-lipidology.com](http://www.clinical-lipidology.com)

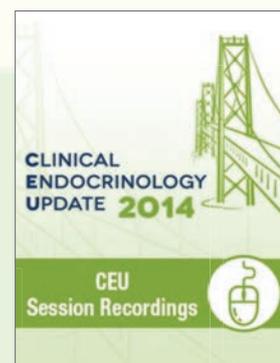
**DECEMBER 9, 2014,  
BERKELEY, CALIF.**  
Cell Symposium: Stem Cell Energetics  
[www.cell.com/press](http://www.cell.com/press)

**JANUARY 27 – FEBRUARY 1, 2015,  
BRECKINRIDGE, COLO.**  
Keystone Symposia on Systems  
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[www.keystonesymposia.org](http://www.keystonesymposia.org)

## Stay on Top of the Leading Developments with the **2014 CEU Session Recordings**

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Join Janet Woodcock, MD, director of the Center for Drug Evaluation and Research at the FDA, for a glimpse into how the FDA evaluates diabetes drugs for safety and efficacy.



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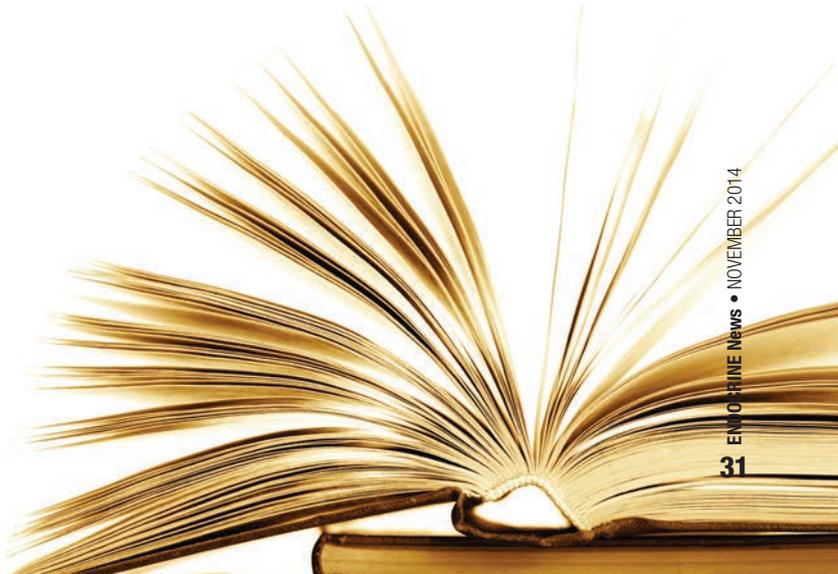
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THANK YOU!!

# Cancer Cachexia as a metabolic syndrome

Cancer cachexia, better referred to as cancer anorexia-cachexia syndrome (CACS), is a multifactorial syndrome that negatively impacts the functional performance, quality of life and prognosis of cancer patients.<sup>1-5</sup> Cancer cachexia is defined by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment.<sup>1</sup>



**60%-80%**  
of patients with  
advanced cancer are  
at risk of developing  
cancer cachexia<sup>6</sup>

The pathophysiology of cancer cachexia is characterized by a negative protein and energy balance driven by a variable combination of reduced food intake and abnormal metabolism.<sup>2</sup> In particular, cancer cachexia is often associated with an elevated basal metabolic rate, despite a decrease in physical activity and total energy expenditure. Muscle atrophy results from a decrease in protein synthesis, and increase in protein degradation, or a combination of both.<sup>7</sup>

**A recent consensus definition of cachexia rightly emphasizes that it is a metabolic syndrome, as it affects glucose, lipid, protein, and energy metabolism<sup>8,9</sup>**

Want to learn more about Cancer Cachexia?

**[www.cancercachexia.com](http://www.cancercachexia.com)**

A new place where state-of-the-art knowledge on Cancer Cachexia is gathered and shared.



1. Fearon K et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol* 2011;12:489-95. 2. Fearon K et al. Understanding the mechanisms and treatment options in cancer cachexia. *Nat Rev Clin Oncol* 2013;10:90-9. 3. Benner A et al. Definition and classification of cancer cachexia: an international consensus. *Lancet Oncol* 2013;10:90-9. 4. Bannani-Baiti N et al. What is cancer anorexia-cachexia syndrome? A historical perspective. *J R Coll Physicians Edinb* 2009;39:257-62. 5. Vaughan VC et al. Cancer cachexia: impact, mechanisms and emerging treatments. *J Cachexia Sarcopenia Muscle* 2013;4:95-109. 6. von Haehling S, Anker SD. Cachexia as a major underestimated and unmet medical need: facts and numbers. *J Cachexia Sarcopenia Muscle* 2010;1:1-5. 7. Del Fabbro E, Inui A, Strasser F. Cancer cachexia. Pocket books for cancer supportive care. Springer Healthcare 2012. 8. Chevalier S, Farsijani S. Cancer cachexia and diabetes: similarities in metabolic alterations and possible treatment. *Appl Physiol Nutr Metab*. 2014 Jun;39(6):643-53. 9. Evans WJ et al. 2008. Cachexia: a new definition. *Clin. Nutr.* 27(6): 793-99.

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**Coastal Connecticut**

L+M Medical Group (L+MMG), a multispecialty employed group that is affiliated with L+M Healthcare, is seeking an Endocrinologist for its Joslin Diabetes Center with sites in New London and Stonington, Connecticut, serving patients in eastern and shoreline CT, southern and western RI and Fisher's Island, NY. L+MMG is rapidly growing with currently ninety physicians and sixty-five non-physician providers with projections to reach one hundred physicians within the year.

The Joslin Diabetes Center is affiliated with the Harvard Medical School in Boston and it provides a comprehensive diabetes management program and endocrine services. Its mission is to provide state-of-the-art diabetes and endocrine medical care within a team setting. The team includes the following specialists: Diabetologist, Endocrinologist, Nurse Practitioner, Diabetes Nurse Educator, Registered Dietician and other Lawrence + Memorial specialists.

- Monday through Friday, 40 hours/week
- Call: 1 weekend in 4
- Collaborate with a dedicated and experienced support team
- Complete benefits package with relocation assistance
- Great opportunity for professional growth

There are a variety of housing options including year round waterfront homes, excellent schools, a safe family-oriented community and four seasons that provide an abundance of recreational activities.

Email CV to Sally Williams, Manager of Physician Recruitment, at [swilliams@lmhosp.org](mailto:swilliams@lmhosp.org).

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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 1000 Geisinger primary and specialty care physicians.

**For more information, please visit [Geisinger.org/careers](http://Geisinger.org/careers) or contact: John W. Kennedy, MD, Endocrinology Department Director c/o Kathy Kardisco, Department of Professional Staffing, at 800.845.7112 or [kkardisco@geisinger.edu](mailto:kkardisco@geisinger.edu).**

# GEISINGER HEALTH SYSTEM

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Nomination form, descriptions, and resources available at [endocrine.org/laureate](http://endocrine.org/laureate)

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Awards will be presented at ENDO 2016: The 98th Annual Meeting & Expo in Boston, MA, April 1 – 4, 2016.

# THE FIVE W'S OF EDCs



Hormone Health  
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## WHAT are EDCs?



**Endocrine disrupting chemicals**, or EDCs, are substances in the environment (air, soil, or water supply), food and beverages, and manufactured products that can interfere with the normal functioning of our body's endocrine system. Many of their effects on humans are still unknown and require more research.

(The endocrine system controls the way your body develops and functions. It produces hormones that travel to all parts of your body to maintain your tissues and organs, and to participate in overall health.)

Visit [hormone.org](http://hormone.org) for more information.

## WHY should I be concerned about EDCs?

EDCs are found in everyday household products. As of October 2013, there are nearly 1,000 chemicals on The Endocrine Disruption Exchange (TEDX) list: [endocrinedisruption.org](http://endocrinedisruption.org).

These chemicals are found in:

- Contaminated soil, water and air
- Food contaminated through chemicals in the food chain
- Food packaging: lining of cans, plastic
- Workplace: industrial chemicals, pesticides, fungicides
- Common household items: plastics, household chemicals, toys, flame-retardant fabrics, cosmetics, medications, antibacterial soaps

### Plastics

Bisphenol A (BPA), phthalates



### Industrial solvents/lubricants

Polychlorinated biphenyls (PCBs), dioxins



### Pesticides

Dichlorodiphenyltrichloroethane (DDT), methoxychlor, chlorpyrifos



### Fungicides

Vinoclozolin



### Herbicides

Atrazine



### Antibacterials

Triclosan



### Personal care products

Phthalates



### Textiles, clothing

Perfluorochemicals (PFCs)



### Children's products

Lead, phthalates, cadmium



Advocate for more research and improved federal regulations by contacting members of Congress:

[endocrine.org/advocacy-and-outreach/take-action/contact-congress](http://endocrine.org/advocacy-and-outreach/take-action/contact-congress)

# WHERE

do EDCs  
impact  
my body?

More research is  
needed, but we  
know EDCs affect:

## Response to stress

- Neurological and behavioral changes
- Reduced ability to handle stress

## Metabolism

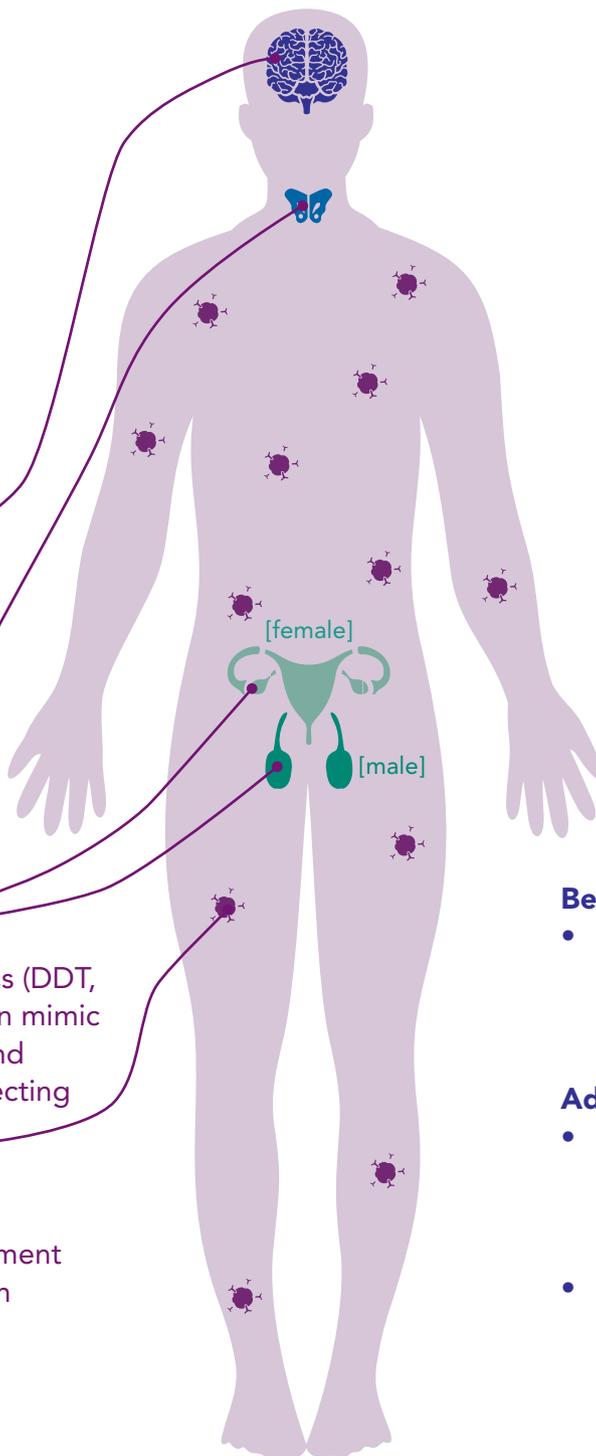
- Industrial chemicals can interfere with thyroid function

## Reproduction

- Virtually all classes of EDCs (DDT, BPA, phthalates, PCBs) can mimic or block effects of male and female sex hormones, affecting reproductive health

## Growth and development

- Neural development
- Disrupted sexual development
- Weakened immune system



# WHEN

do the  
effects  
take shape?

Endocrine, reproductive and/or neurological problems occur more frequently in humans with higher amounts of EDCs in their bodies. Health impact of low-level EDC exposure is still being researched.

## Before birth

- Interferes with fetal growth and development while the body's organs and tissues are still developing

## Adolescence, adulthood

- Affects sexual development, decreases fertility, causes diseases of male and female reproductive systems
- Increased risk of diabetes, obesity, and certain types of cancer

# WHO

regulates EDCs?

The federal government

- The Toxic Substances Control Act passed in 1976
- In 1996, Congress passed the Food Quality Protection Act and the Safe Drinking Water Act Amendments
- Current chemical screening programs are inadequate for finding endocrine disruptor effects
- Researchers are still working to define the relationship between the dose (low/high) of EDCs and how the body responds to it

### You have questions. We have answers.

The Hormone Health Network is your trusted source for endocrine patient education. Our free, online resources are available at [hormone.org](http://hormone.org).

Additional editing by Andrea Gore, PhD, University of Texas at Austin

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