JANUARY 2014

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

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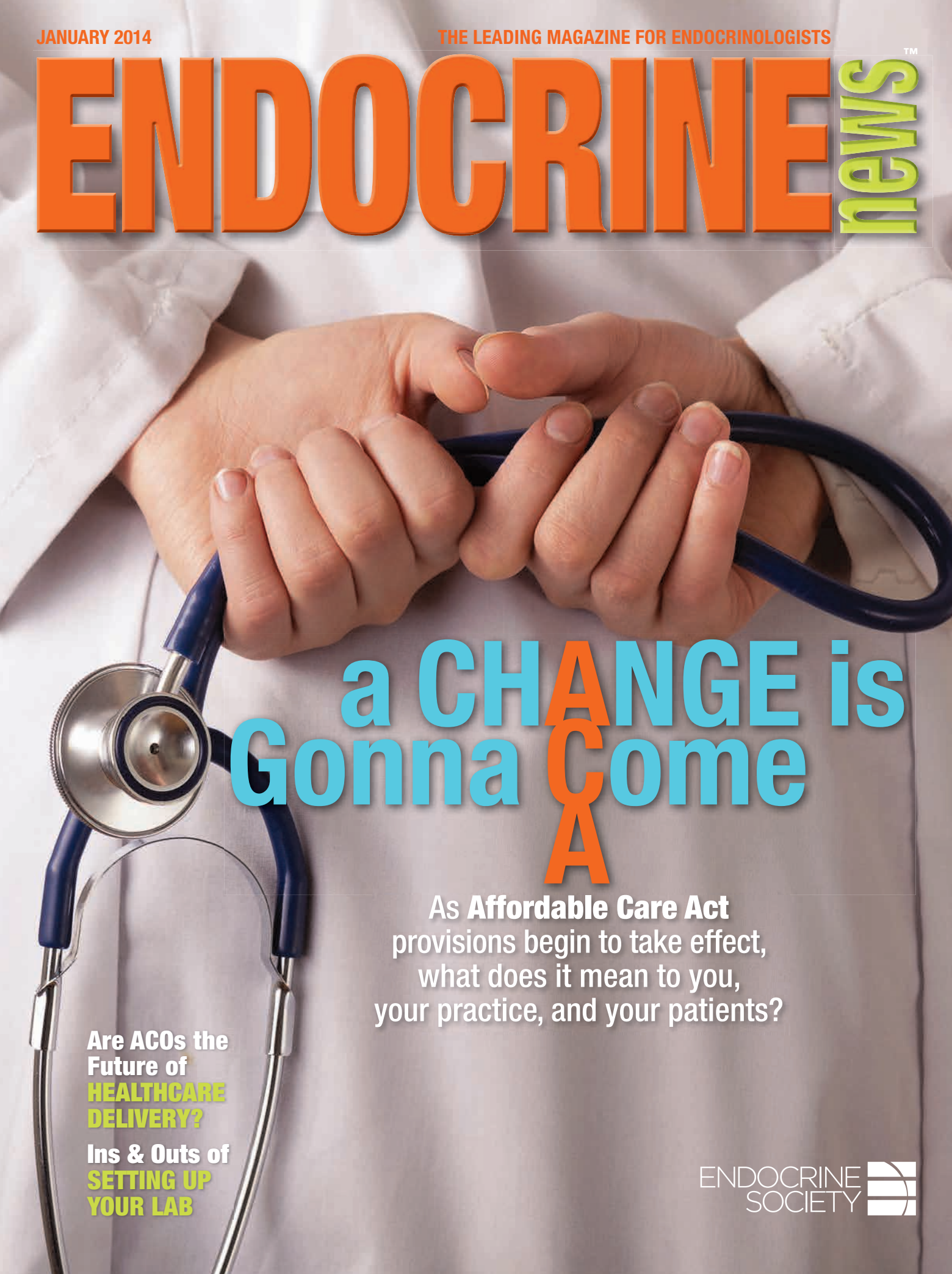

a CHANGE is Gonna Come

ACA

As **Affordable Care Act** provisions begin to take effect, what does it mean to you, your practice, and your patients?

Are ACOs the Future of HEALTHCARE DELIVERY?

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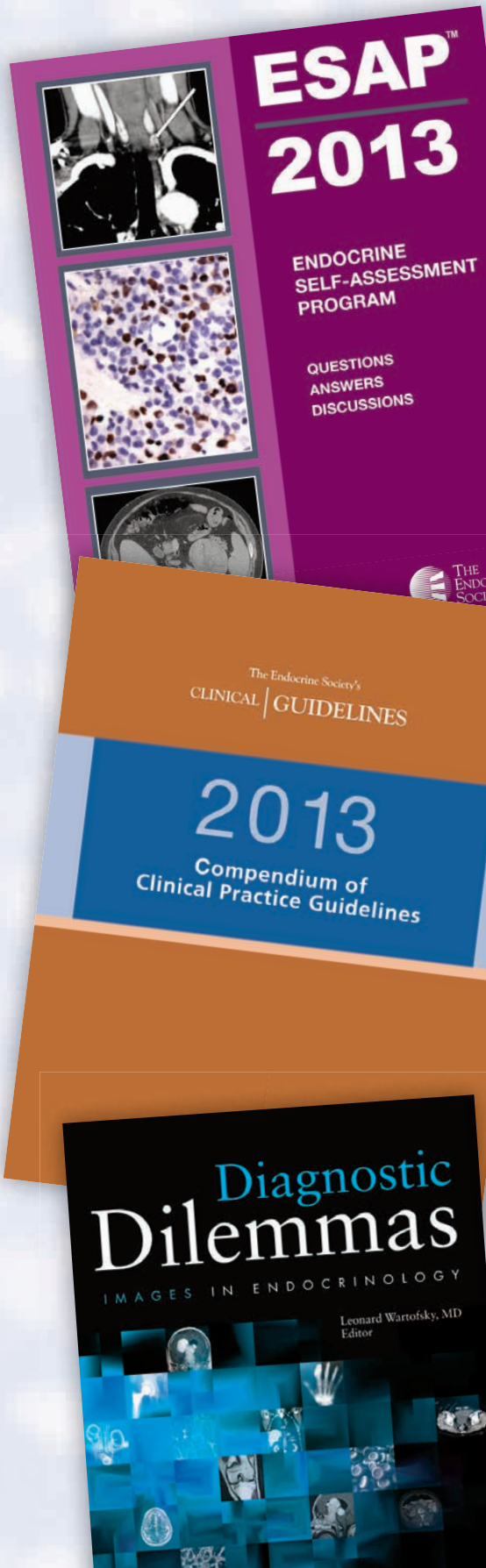

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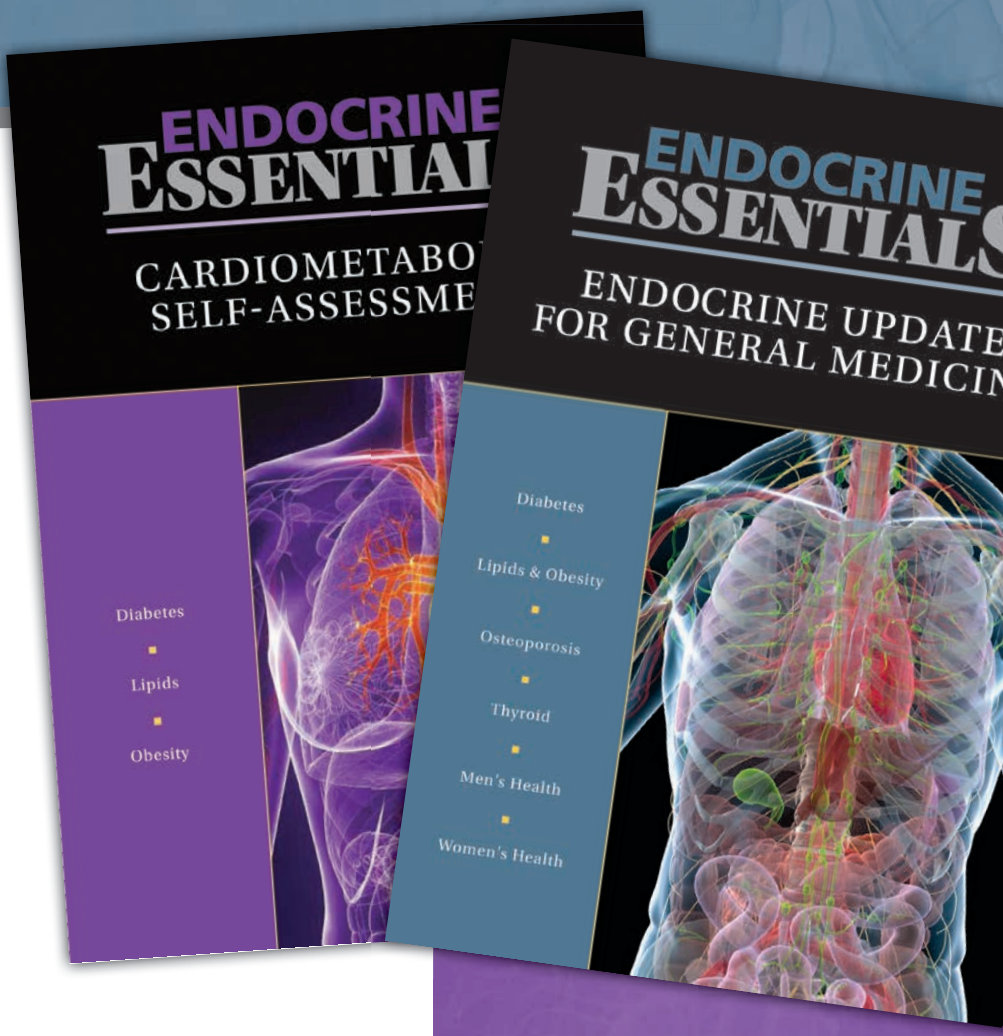

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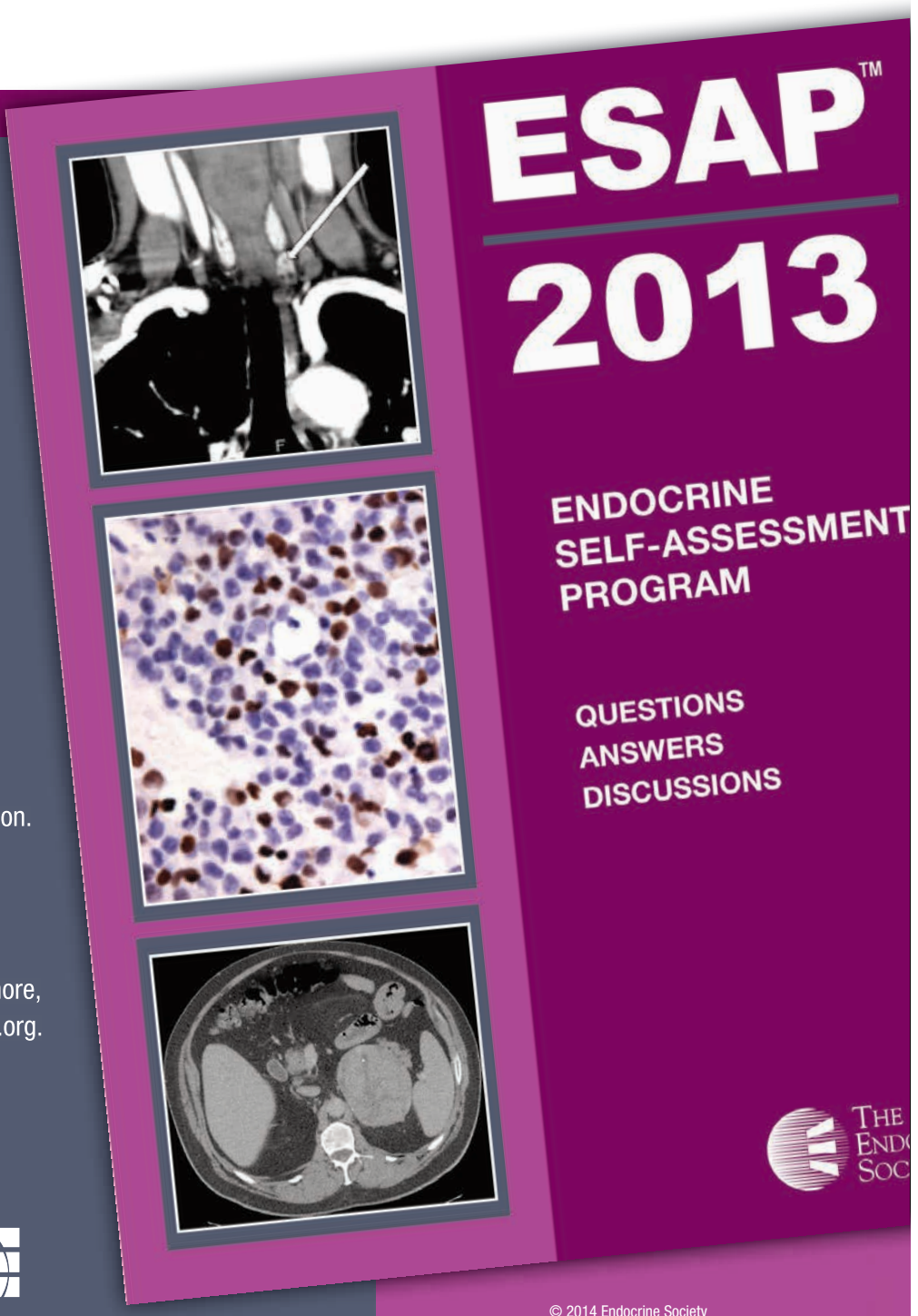

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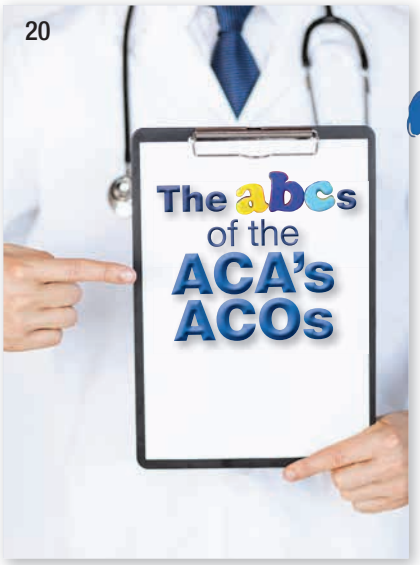

COVER Story

DEPARTMENTS

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ENDOCRINE SOCIETY
Hormone Science to Health

A New "Look" for the ENDOCRINE SOCIETY

As the Endocrine Society approaches its 100th anniversary, it does so with new branding that will take it into the next century as a global leader in hormone science, health, and disease.

ENDOCRINE SOCIETY

Hormone Science to Health

Teresa K. Woodruff, PhD

It is my great pleasure to share with you the Endocrine Society's new logo and tagline, launching this month after a comprehensive branding effort.

Our former logo, fondly known as the "bowling ball," meant many things to our members. Some saw a letter "e" in the mark, others a globe, and many felt that the three bars represented the tripartite nature of the membership. The logo served us well for the more than 25 years it represented the Society. But as we enter our next 100 years, it is important that our brand convey our position on the world stage, with a look that is welcoming, fresh, and contemporary.

In January 2013, Council began creating our new brand very deliberatively, appointing a task force composed of members from across our various constituencies who dedicated their time to engage in the creative process. Our task was simple: Tell the Endocrine Society's story in a meaningful way. Marry the intellectual goals of the Society with something tangible our members could embrace. Create a fresh springboard to the future.

We developed a set of design criteria and spent many hours debating various details of the logo — even down to the relative merits of serif versus sans serif fonts! We took our time, ensuring that we were creating a brand that would represent the Society as it enters the next century of growth. After nine months, we'd finally achieved our goal, creating the new logo and tag line found at the top of this column. My deepest thanks to the members of the task force who gave many hours to this process: Brad Anawalt, Carol Greenlee, Jennifer Larsen, Sethu Reddy, Paul Stewart, and Kristen Vella. The end results reflect your dedication to this task.

The new Endocrine Society logo is modern, forward-thinking, and multi-dimensional. It carries elements from the previous logo that members identified with — an evocative "e," the three bars of the tripartite membership — and a new element, a kinetic arc, representing momentum, marching forward, ever expanding our work, or it may embody the frontier of knowledge or even the edge of a globe, embracing the next generation of ideas from the entire world of endocrinology. In all these overt and subliminal ways, the Endocrine Society logo conveys professionalism, reflecting the Society, its members, and their work to the worlds of science, medicine, and to the public.

The task force also helped create a tag line for the Society, which you'll see in the graphic at left: Hormone Science to Health. The tag line captures the unique, translational nature of our membership, explaining who we are and what we're trying to accomplish. It relays the essence of our mission in the simplest of terms.

You may have also noticed another change ... there is no longer a "The" in the official name of the Society. This may not seem like a big deal, but for years, the dreaded "The" has plagued the operations of the Society. It had to be capitalized (a violation of our beloved *Chicago Manual of Style*), led to some awkward sentence structures, and pushed us down to the "T" section of any alphabetized list of societies or companies at conferences. Clearly, we belong in the "E" section! We, therefore, bid farewell to the "The," making us all "Endocrine Society" members.

Our new brand will launch on our website and in our publications this month, and the rollout will continue through the **ICE/ENDO 2014** meeting in Chicago. Our journals and books will also carry the new mark starting in January, but under the imprint of the recently launched Endocrine Press, the publishing arm of the Society. The Endocrine Press logo is shown below:

ENDOCRINE PRESS

an imprint of the Endocrine Society

I'm excited to share the new Endocrine Society brand with you. I hope you find it an energizing yet scholarly interpretation of our multi-faceted Society. In the end, each of us is the Endocrine Society brand — I hope you will embrace this new identity as you continue to expand your work in the service of endocrine science and medicine. EN

Teresa K. Woodruff, PhD
President,
Endocrine Society

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JANUARY 2014
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The mission of the *Endocrine Society* is to advance excellence in endocrinology and promote its essential and integrative role in scientific discovery, medical practice, and human health.

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As each New Year is celebrated at the stroke of midnight on December 31st, hopes are high for what the coming year will bring. We are all well aware of the myriad changes that go into effect this month as the Affordable Care Act becomes a way of life for physicians, patients, insurance companies, and essentially every single American, so we felt that it was vital to include articles that speak specifically to the practice of endocrinology.

To that end, this issue contains two feature stories on ACA: one is essentially an overview on how it will affect endocrinologists ("A Change Is Gonna Come", p. 15), while the other gives us the ins and outs of a new healthcare delivery system, the Accountable Care Organization ("The ABCs of ACA's ACOs", p. 20). Both of these articles have been thoroughly researched by one of our ace writers, Eric Seaborg. However, as diligent as he is and as deep as he dug, changes were being made up until press time so some of the information contained may have changed since we went to press. But it's a great place to start.


Mark A. Newman

Aside from these articles on the implementation of the ACA, we have a nice roundup of smartphone apps that could prove beneficial to you and your patients. "An Appetite for Apps" on page 30 by Glenda Fauntleroy gives us a rundown on the various apps that could make your life just a little easier, since almost anything is more convenient when it's literally "at your fingertips."

This issue also sees a change in the Laboratory Notes series of articles. Longtime contributor Melissa Mapes has taken on the task of creating articles that deal solely with the "nuts and bolts" running of an in-house lab, and to start us off she has a short but comprehensive piece on the initial steps you need to take in setting up your lab in "Putting it Together" on page 32.

Along with the new healthcare law and a refocused Laboratory Notes, there's another big change going on here at the Endocrine Society, as we get a new CEO for the first time in a quarter of a century. *Endocrine News* is excited to welcome Barbara Byrd Keenan to the Endocrine Society as she takes the reins on January 6. We will have more from Barbara in the February Editor's Page, but feel free to welcome her at **bkeenan@endocrine.org**. And as always, if you have any questions or comments, feel free to contact me at **mnewman@endocrine.org**. EN

Mark A. Newman
Managing Editor, Endocrine News

Correction: In the November issue of *Endocrine News*, we mistakenly ran a photo of Sharon E. Oberfield, MD, instead of a photo of Ilene Fennoy, MD, to accompany the Tri-Point article on Type 2 Diabetes in Adolescents. Dr. Fennoy is pictured at left. *Endocrine News* regrets the error.

By Derek Bagley

VITAMIN D and MUSCLE STRENGTH in Adults

Vitamin D has been shown to offer no improvements in muscle strength for adults, according to a Norwegian study recently published in the *Journal of Clinical Endocrinology and Metabolism*.

The paper's lead author, Kirsten V. Knutsen, of the University of Oslo, wrote that while vitamin D has multiple biological effects, "some of which appear to impact muscular functioning," the effect of vitamin D on muscle strength in adults has not been established. The researchers also noted that vitamin D deficiency is "prevalent worldwide," and in Norway especially, common among immigrants from Africa, the Middle East, and Asian countries.

The scientists evaluated 251 healthy adult males and females aged 18 to 50 years with a "non-Western immigrant background" in a randomized, double-blind, placebo-controlled trial. Participants were given daily supplementation of 25µg (1000 IU) vitamin D_3, 10µg (400 IU) vitamin D_3, or placebo over the course of 16 weeks. They measured for primary outcomes of the differences in participants' jump heights between pre- and post-intervention. They also measured for secondary outcomes the differences in hand-grip strength and chair-rising tests, in which participants were instructed to rise from a sitting position and to sit down again five times without using the chair arms, as fast as possible.

The results showed that percentage in jump height did not differ between those receiving vitamin D supplementation and those receiving the placebo. There were no significant effects of the intervention of vitamin D3 on either the primary or secondary outcomes.

The authors concluded, "Daily supplementation with 25 or 10µg vitamin D_3 for 16 weeks did not improve muscle strength or power measured by the jump test, handgrip test, or chair-rising test in this population with low baseline vitamin D status."

BARIATRIC SURGERY Improves Sexual Functioning in Obese Women

Women who underwent bariatric surgery for obesity experienced an improvement in overall sexual functioning, a study published in the November 4 issue of *JAMA Surgery* shows.

Scientists, led by David B. Sarwer, PhD, of the Perelman School of Medicine at the University of Pennsylvania, Philadelphia, assessed a prospective cohort study of 106 women who had weight-loss surgery — 85 of whom underwent Roux-en-Y gastric bypass, and 21 of whom underwent laparoscopic adjustable gastric banding. One year after surgery, the women had lost a mean of 32.7% of initial body weight and 33.5% of initial body weight at postoperative year two.

Two years after surgery, the women reported "significant improvements in overall sexual functioning and specific domains of sexual functioning: arousal, lubrication, desires, and satisfaction" based on the Female Sexual Function Index — a 19-item questionnaire that assesses six domains of sexual functioning. The women also showed improvements in sex hormone levels when assessed by blood samples, as well as significant improvements "in most domains of quality of life."

The authors concluded that "these results suggest that improvements in sexual health may be added to the list of benefits associated with large weight losses seen with bariatric surgery. Future studies should investigate if these changes endure over longer periods of time, and they should investigate changes in sexual functioning in men who undergo bariatric surgery."

Primary Hyperparathyroidism GOES UNDIAGNOSED

People who have primary hyperparathyroidism (PHPT) often go undiagnosed, even though lab results indicating hypercalcemia could signal a problem and be an early warning sign of PHPT, according to a paper published in the December issue of the journal *Surgery*.

Allan Siperstein, MD, of the Cleveland Clinic's Endocrine Surgery Department, and his team noted that when PHPT is recognized, "a review of the medical record reveals elevated calcium and/or parathyroid hormone (PTH) values have been present for longer periods of time." Therefore, they set out to examine electronic medical records (EMR) and "gain insight into the incidence of undiagnosed and unrecognized PHPT."

The researchers examined the EMR of 2.7 million patients and found that 54,198 (2%) had hypercalcemia (>10.5 mg/dL). They then took a two-year sample of 7,269 hypercalcemic patients and discovered that only 33% had PTH levels checked. When stratified by calcium level, PTH was checked in 31% of those with calcium values between 10.6 and 11, and increased to 52% when calcium values were greater than 12. Overall, At least 43% of patients with elevated calcium were likely to have primary hyperparathyroidism with just over half of these confirmed by elevated PTH values and the remaining estimated to have PTH by chart review.

They concluded that unlike elevated blood sugars or cholesterol, typically prompting evaluation and treatment, elevated calcium values are often not evaluated. There is clearly opportunity for early recognition and treatment for patients with hyperparathyroidism.

MIDRANGE TESTOSTERONE LEVELS Better for Older Men

Optimal androgen levels — meaning they are neither low nor high — in older men are associated with lower mortality, according to a study recently published in the *Journal of Clinical Endocrinology and Metabolism*.

Researchers led by Bu Beng Yeap, MBBS, FRACP, PhD, of the University of Western Australia, have shown that older men who have high levels of testosterone (T) may be prone to just as many health concerns and even a higher mortality risk.

The body metabolizes T into dihydrotestosterone (DHT), and the authors noted that a previous study showed an association between low DHT levels and risk of ischemic heart disease (IHD). They also looked at estradiol levels (E_2), as "the association of DHT or E_2 levels with ill health in aging men is controversial."

The population-based cohort study analyzed the mortality rate in a group of 3,690 community-dwelling men between the ages of 70 to 89 in Perth, Western Australia. Participants' testosterone and DHT levels were measured between 2001 and 2004. Researchers analyzed the group's survival rate as of December 2010.

To accommodate "nonlinear associations," the men's hormone levels were analyzed as quartiles. Men in the second and third quartiles (midrange levels — 9.8 to 15.8 nmol/L) had lower all-cause mortality than their counterparts in the first and fourth quartiles. "Levels of T, calculated free T, and DHT corresponding to values within the third quartile were consistently associated with the lowest risk of dying of any cause."

"In conclusion," the authors wrote, "optimal circulating total T is a robust biomarker for survival in aging men. However, higher DHT levels are associated with reduced IHD mortality, consistent with a possible cardioprotective influence of androgen exposure," although they noted that further research is needed.

COUP-TFII Plays Role in Inflammation, Endometrial Diseases

Chicken ovalbumin upstream promoter-transcription factor II (COUP-TFII) plays a role in controlling the expression of inflammatory cytokines, a study recently published in *Molecular Endocrinology* has shown.

What's more, COUP-TFII — an orphan nuclear receptor involved in cell-fate specification, organogenesis, angiogenesis, and metabolism — regulates a subset of genes in endometrial stroma cell decidualization, such as those involved in cell adhesion, angiogenesis, and inflammation.

This discovery by a group of investigators led by Drs. F. DeMayo, S. Tsai, (Baylor College of Medicine) S. Young (University of North Carolina), B. Lessey (Greenville Health System), and J. Jeong (Michigan State University) may provide a key insight into COUP-TFII's role in embryo implantation and endometrial diseases such as endometriosis, a disease that affects about 6% – 10% of women and occurs in 40% – 50% of infertile women. The most common — and debilitating — symptom is chronic pelvic pain.

The scientists collected human endometrial samples of full-thickness endometrium from 23 regularly cycling women with no history of endometriosis between the ages of 18 and 50 who were undergoing a hysterectomy. These samples were collected at the time of surgery in order to examine COUP-TFII in the endometrium throughout the menstrual cycle. They then obtained biopsies from another 47 regularly cycling women aged 18 to 50 "to compare COUP-TFII expression patterns of euptopic endometrium between with and without endometriosis." Moreover, they collected biopsies during the secretory phase of the menstrual cycle from nine patients diagnosed with endometriosis to compare differential expression of COUP-TFII between eutopic and ectopic endometrium of same patient.

DeMayo and team then "interrogated" the COUP-TFII by using a "small interfering RNA-mediated loss of function approach" in primary endometrial stromal cells they collected and found that COUP-TFII had a "selective effect on gene expression." The researchers demonstrated that "COUP-TFII is spatially and temporally expressed in endometrial stroma cells during the menstrual cycle in women. Furthermore, COUP-TFII was found to be reduced in stroma cells of ectopic lesions in endometriosis patients. Cistromic and transcriptomic analyses demonstrated that COUP-TFII regulates processes critical for human endometrial stroma cell decidualization in vitro. Specifically, COUP-TFII is responsible for the down regulation of inflammatory genes during decidualization. This may contribute to the function of decidual stroma cells in pregnancy and the pathology observed in endometriosis."

GHRELIN SUPPRESION After RYGB Surgery

Obese patients with type 2 diabetes (T2D) who undergo Roux-en-Y gastric bypass (RYGB) surgery may develop a return to normal regulation of acylated ghrelin (AG), which leads to improved glucose control, according to a study recently published in the *International Journal of Obesity.*

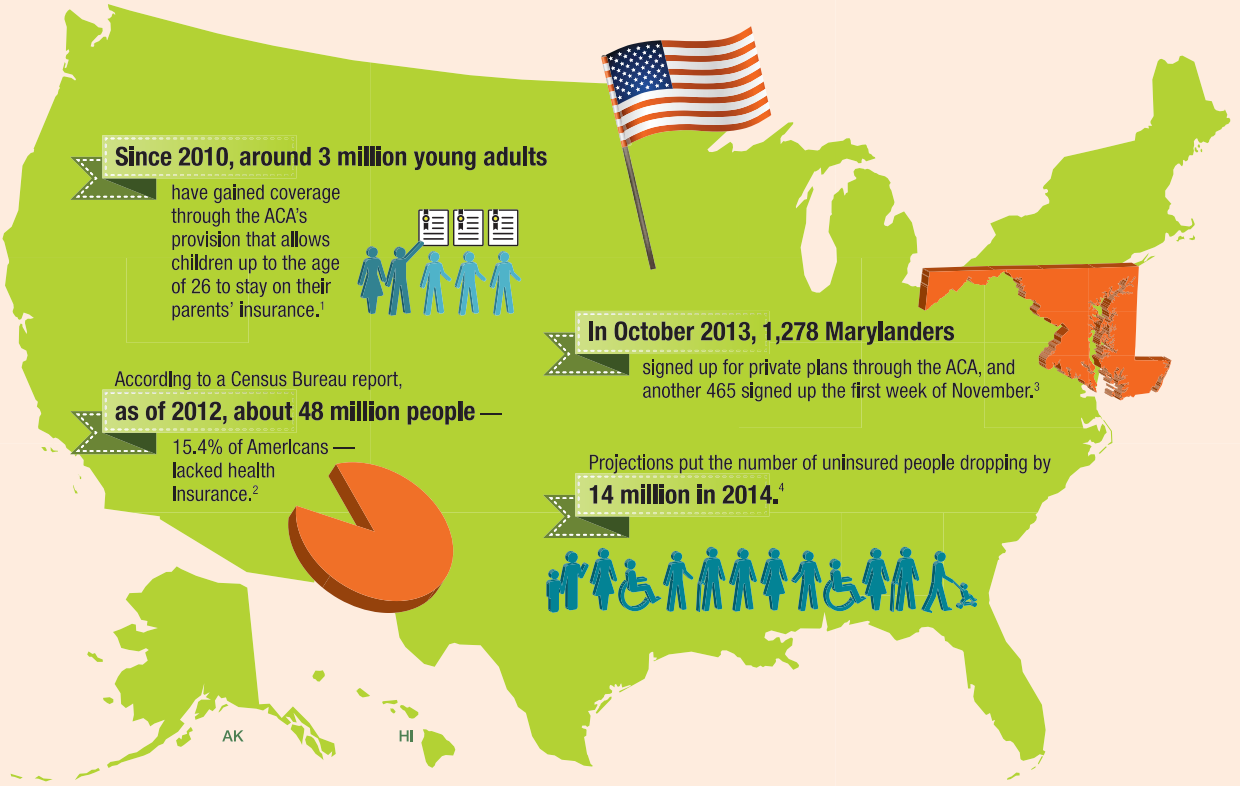
AG is a gluco-regulatory/appetite hormone, and Sangeeta R. Kashyap, MD, at the Cleveland Clinic, and her team wanted to investigate whether the hormone had any effect on glucose metabolism and body composition after RYGB. The authors wrote, "Acylated ghrelin appears to be more important in appetite regulation, as it has potent effects on hypothalamic food initiation centers and adipogenesis. In addition, total/acylated ghrelin reduces glucose-stimulated insulin secretion and attenuates glucose uptake. Thus, given the improvement in body fat and glycemic control following bariatric surgery, it seems reasonable to expect that bariatric surgery could suppress acylated ghrelin in obese individuals with type 2 diabetes." However, until now, there had been no data on the effects of bariatric surgeries on acylated ghrelin in people with type 2 diabetes.

The researchers evaluated 53 obese, "poorly controlled" patients with T2D in the Surgical Treatment and Medication Potentially Eradicate Diabetes Efficiently (STAMPEDE) trial, a prospective, randomized control study. The participants either received intensive medical therapy (IMT), a combination of IMT and RYGB surgery, or IMT and sleeve gastrectomy (SG), then "a mixed-meal tolerance test at baseline, 12, and 24 months (m), for evaluation of AG suppression (post-prandial minus fasting) and beta-cell function (oral disposition index; glucose-stimulated insulin secretion x Matsuda index)."

RYGB and SG produced "comparable" reduced body fat in the patients at one year and two years, but IMT had no effect. The scientists seemed to have expected the results of IMT, as they wrote that long-term compliance to IMT is often poor and usually leads to additional pharmacological treatment. Beta-cell function improved in the RYGB patients and was better at two years than patients who received IMT. At two years, the bariatric surgeries lowered post-prandial AG more than IMT, and AG suppression was better following RYGB at two years than IMT or SG. "At 24m," the researchers wrote, "AG suppression was associated with increased post-prandial GLP-1 (r=-0.32, P<0.02) and decreased android fat (r=0.38; P<0.006)."

Kashyap and her team concluded the "enhanced AG suppression persists for up to two years after RYGB," which results in reduced body fat and improved insulin secretion, and the findings may explain why patients who undergo RYGB surgery experience improved glucose control.

Fast FACTS About the Affordable Care Act



Since 2010, around 3 million young adults

have gained coverage through the ACA's provision that allows children up to the age of 26 to stay on their parents' insurance.[1]

In October 2013, 1,278 Marylanders

signed up for private plans through the ACA, and another 465 signed up the first week of November.[3]

According to a Census Bureau report,

as of 2012, about 48 million people —

15.4% of Americans — lacked health insurance.[2]

Projections put the number of uninsured people dropping by

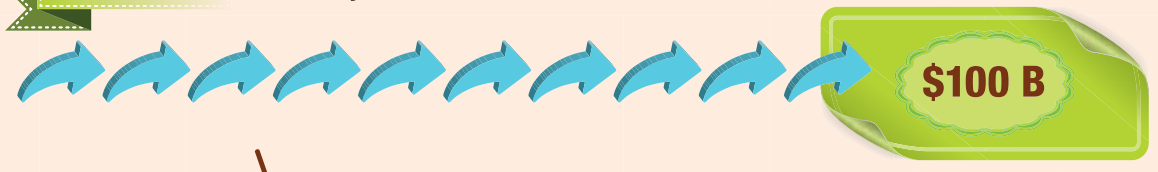
14 million in 2014.[4]

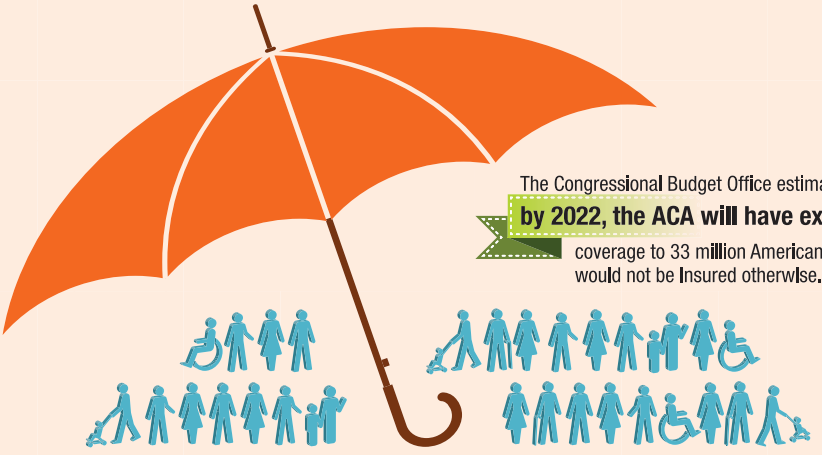
In 2016, 24 million people

will be exempted from the Individual Mandate provision of the ACA.[5]

The ACA will save more than

$100 billion over the next 10 years.[6]





The Congressional Budget Office estimates that

by 2022, the ACA will have extended

coverage to 33 million Americans who would not be insured otherwise.[7]

Represents 1,000,000 people

Sources:
1 whitehouse.gov
2 New York Times
3 Washington Post
4 Congressional Budget Office
5 Congressional Budget Office
6 Congressional Budget Office
7 Washington Post

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a CHANGE is Gonna Come

As **Affordable Care Act** provisions begin to take effect, what does it mean to you, your practice, and your patients?

By Eric Seaborg

January 1 was a key date in the rollout of the Affordable Care Act (ACA). New insurance policies sold on health exchange websites went into effect, as did a batch of new requirements for those policies. After the bitter controversy, sweeping predictions pro and con, and even a government shutdown in a failed attempt to stop it—what's next?

Massachusetts is a natural place to look for guidance because the ACA is largely based on that state's healthcare reform law that passed several years ago. The Massachusetts law contains many of the provisions in the ACA, such as a requirement that individuals carry health insurance or pay a penalty, requirements for policies, and fees and taxes.

And, based on the Massachusetts experience? One can expect incremental change, more patients with health insurance, and probably better outcomes associated with access to care. But, probably not revolutionary change. Polls in that state indicate that the reform is broadly popular among patients and physicians.

AT-A-GLANCE

- The ACA is based on a Massachusetts health-reform law that expanded the number of people with insurance coverage and enjoys broad support.
- An influx of new patients could challenge healthcare professionals to find innovative and efficient ways of providing care.
- Controversies over the law show no signs of abating, and the outcome of battles over issues like expanding Medicaid to cover more patients will affect its success.

Approval in Massachusetts

Provided that the problems with the ACA's rollout are adequately resolved and do not lead to major changes in the law, one can expect a substantial increase in the number of people with insurance coverage — in Massachusetts, some 98% of the population now has coverage.

This better coverage has led to improvements in overall care of many patients, in the experience of Enrico Cagliero, MD, an associate physician at Massachusetts General Hospital with an active practice in the diabetes center. Working in an academic center, Cagliero is accustomed to seeing indigent patients, but the number is down because "clearly the number of patients without insurance has decreased dramatically." For many of these patients, the coverage translates to better care. For example, many diabetic patients need eye procedures that were unobtainable when they could not pay, but now patients with even the most basic kinds of insurance have options. Cagliero says he has also seen improvements in diabetes control because medications are more available. Even the greater availability of simple items like blood sugar test strips has improved glucose control for some patients.

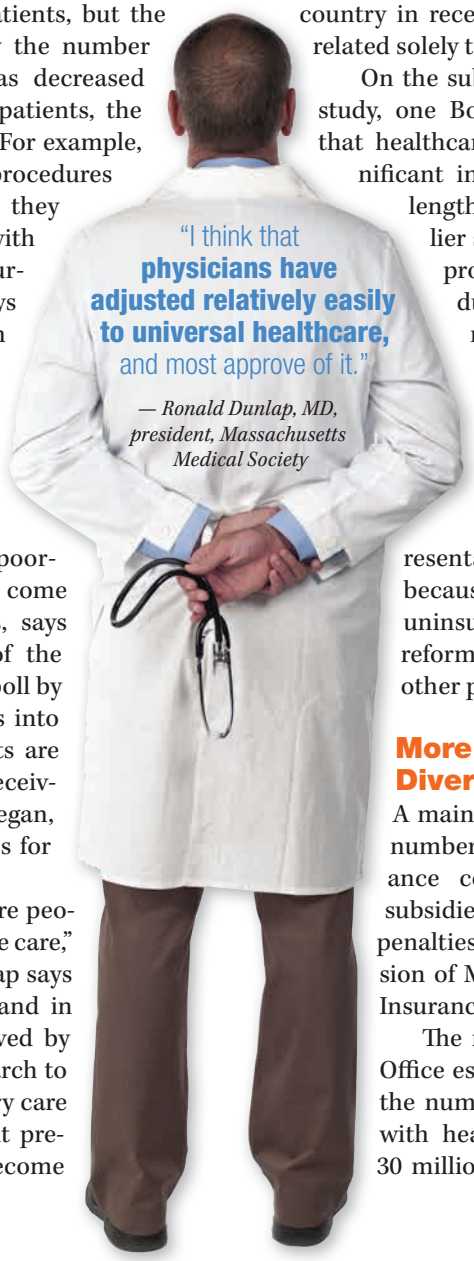
The improved care of these poorest patients has apparently not come at the expense of other patients, says Ronald Dunlap, MD, president of the Massachusetts Medical Society. A poll by the society found that seven years into the reform, Massachusetts patients are as satisfied with the care they are receiving as they were before reform began, despite reporting longer wait times for appointments with physicians.

"We have managed to take more people into the system and deliver more care," Dunlap told *Endocrine News*. Dunlap says that there are still gaps in care, and in areas that were already underserved by physicians prior to the law, the search to find and wait times to see a primary care physician may have worsened. But predictions that the system would become overloaded have not come true. "I think that physicians have adjusted relatively easily to universal healthcare, and most approve of it," he says.

A trend that Dunlap senses Massachusetts physicians find stressful, however, is toward consolidation of practices in the state, perhaps in response to a feeling of needing more infrastructure to deal with electronic records and quality assessment systems as part of new payment models such as accountable care organizations. Hospitals and other healthcare organizations have been buying physicians' practices all over the country in recent years, so whether this trend is related solely to healthcare reform is unclear.

On the subject of greater demand, in a 2013 study, one Boston University researcher found that healthcare reform did not result in a significant increase in hospitalizations, longer lengths of stay, or higher costs. An earlier study by another Boston University professor found that inpatient procedures increased among lower- and medium-income Hispanics and whites after the health reform law went into effect. Hispanic patients underwent 22% more elective surgeries, including knee and hip replacements.

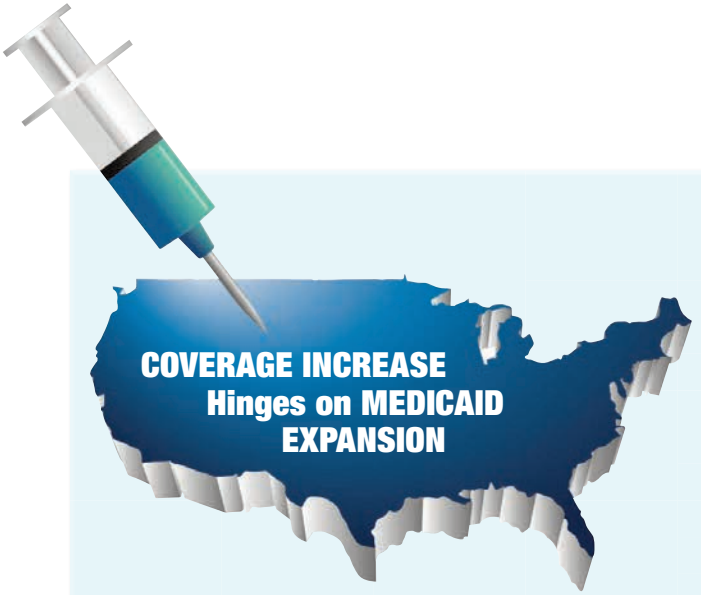
Massachusetts may not be representative of the rest of the country because it had a relatively low number of uninsured patients even before its health reform law. So, will its success translate to other parts of the country?



More Patients, Diverse Providers

A main goal of the ACA is to increase the number of Americans with health insurance coverage through incentives and subsidies for buying health insurance, penalties for not buying it, and an expansion of Medicaid and the Children's Health Insurance Program (CHIP).

The nonpartisan Congressional Budget Office estimates that the ACA will increase the number of people below Medicare age with health insurance coverage by 25 to 30 million people in the next decade. That



One of the key aims of the Affordable Care Act is to increase the number of people covered with some kind of health insurance, and making more people eligible for Medicaid was intended to be a key tool for doing so.

But last year's Supreme Court ruling made Medicaid expansion optional for states, and many states have balked. As of the end of October, some 26 states and the District of Columbia were moving ahead with expansion. The failure to expand would leave millions of people without coverage, particularly because many of the states declining to expand have some of the highest rates of uninsured residents. Their lack of insurance could, in turn, squeeze hospitals and other providers in those states because one of the compromises embedded in the law was that hospitals would accept lower payments with the expectation that they would be treating fewer uninsured patients.

Medicaid expansion was designed to be a good deal for the states. The federal government pays about 60% of the costs of the current Medicaid program. In the expanded version, people with family incomes up to 133% of the federal poverty line are eligible for Medicaid (that's about $29,000 for a family of four). The federal government will cover 100% of the cost for these newly eligible people in 2014 and 2015, then pay a share that declines to 90% from 2020 on.

Many Republican governors turned down the deal for both ideological and financial reasons. Medicaid spending is already a huge portion of state budgets, second only to education, so some opponents say that any expansion would come at the expense of funding for education, public safety, and other priorities.

But the opposition to expansion has weakened considerably over time. In Ohio, Gov. John Kasich sidestepped the legislature and pursued expansion through a decision by an otherwise obscure state board with power to adjust the state budget. Florida Gov. Rick Scott, a harsh critic of the ACA, decided his state should expand Medicare, although he could not convince the legislature to go along. Pennsylvania Gov. Tom Corbett has proposed a plan that would allow people newly eligible for Medicaid to use federal funds to buy private coverage on the health insurance exchange. (If Terry McAuliffe is elected governor of VA, he has promised to pursue Medicaid expansion, too.)

The South Dakota Medical Association has urged the state's governor to expand Medicaid, arguing that without coverage, uninsured people will continue to get expensive care at emergency rooms instead of more appropriate settings, and hospitals will shift the costs to the patients with private insurance.

"Hospitals ... gave up $155 billion in future Medicare payment reductions to gain 30 million new paying patients and consented to the reduction of disproportionate share payments intended to compensate them for their bad debts and charity care. A cancelled Medicaid expansion would place the safety net hospitals in those states at serious economic risk," Jeff Goldsmith, PhD, a professor of public health sciences at the University of Virginia, wrote on The Health Care Blog.

There is a precedent for states changing course on Medicaid. Many states did not participate when the program was introduced in 1965, but most implemented it within five years. The last state to do so was Arizona in 1982. This time around Republican Gov. Jan Brewer forged a bipartisan coalition to push expansion through the legislature.

growth represents an increase from today's 82% to 92% of the nonelderly population, but is down from estimates made before last year's Supreme Court decision that gave states the choice of opting out of the planned expansion of Medicaid. Only about half the states are expanding, but some may be reconsidering that decision (see sidebar above). The Obama administration's decision to put off for a year, until Jan. 1, 2015, the mandate for employers with more than 50 employees to provide coverage will slow the growth in coverage as well.

An influx of millions of new patients will pose a challenge to the healthcare system, says Atul Grover, MD, PhD, chief public policy officer of the Association of American Medical Colleges (AAMC), particularly to the teaching hospitals that his organization represents. The extent of Medicaid expansion is a key concern of the AAMC because these hospitals face cuts in Medicare and disproportionate share payments written into the ACA. They could accept the cuts when the provisions of the law were being worked out based on the assumption that more patients would have coverage to pay for the services they receive. "The hospital cuts in the ACA were hopefully to be balanced out by an expansion of insurance. If states fail to follow through on the Medicaid expansion, that could lead to further, severe losses for many of our safety-net teaching hospitals that are already barely breaking even," Grover says.

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— Atul Grover, MD, PhD, chief public policy officer, AAMC

The AAMC's other big concern is that it had been projecting looming shortages of physicians and other healthcare professionals even before the ACA passed. An influx of patients from the ACA could accelerate those shortages, although Grover notes that in Massachusetts patients have not experienced difficulty obtaining care: "In primary care in particular, they have figured out how

Individual and Employer MANDATES

One of the most controversial provisions of the Affordable Care Act is the so-called "individual mandate" that people must either be covered by health insurance or pay a penalty.

The penalty is $95 or 1% of income in 2014, $325 or 2% of income in 2015, and $695 or 2.5% of income in 2016 (but no more than the cost of an average basic plan). These penalties often work out to much less than the cost of insurance.

But the experience in Massachusetts — the ACA was largely modeled on that state's 2006 healthcare reform law — shows that low penalties do seem to be effective at getting people on the insurance rolls. Even with penalties of only 50% of the lowest-cost premium on the state's insurance exchange, that law has decreased the number of uninsured in the state from 10% to 2% of the population.

The Massachusetts law itself is viewed favorably — 74% of residents want it to continue versus 9% favoring repeal. But the mandate remains much less popular, with 51% supporting it, according to a 2011 poll by the Harvard School of Public Health and *The Boston Globe*.

As a balance against the stick of the mandate, there is a carrot to encourage people to buy insurance: federal tax credits are available to people with incomes up to 400% of the federal poverty line (about $88,000 for a family of four). Small businesses with fewer than 25 workers can receive tax credits for up to 50% of premium costs. Employers with 50 or more full-time employees that do not offer coverage or offer coverage deemed unaffordable will incur penalties. And employers with more than 200 employees must automatically enroll new full-time employees in coverage. The Obama administration delayed enforcement by a year (until Jan. 1, 2015) of the mandate that employers with more than 50 employees offer coverage.

These mandates are part of a big bargain among stakeholders such as insurers, providers, pharmaceutical companies, and the government: Each player could afford to give up something if enough people were covered with some form of insurance.

For example, insurance companies could afford to waive pre-existing conditions if they knew that a patient could not simply wait until a disorder appeared, then buy insurance. Similarly, hospitals could accept lower Medicaid reimbursement rates if they took less of a loss from treating uninsured patients who never paid.

to use other healthcare professionals, nurse practitioners and physician's assistants, to improve access."

Fear of the Marketplace

Many of these newly covered patients will be buying insurance on the exchanges that have experienced so much trouble in starting up, despite their aim of providing easier access for individuals and small employers. Businesses with fewer than 25 workers can receive tax credits up to 50% of premiums, and the exchanges could benefit physician practices.

"Most physicians are small businessmen who provide health insurance to their employees" and so may find the offerings and subsidies available at the exchanges helpful, according to Allan R. Glass, MD, an adviser to the Endocrine Society on policy, advocacy, and physician payment issues.

These online marketplaces are designed to allow individuals and small businesses to easily compare insurance policies. Although originally envisioned as being run by the states, most states declined to do so, and left the task to the federal government. The exchanges certify plans as containing standardized essential benefit packages to make it easier for buyers to know what they are being offered and provide information to help consumers understand the options. Because they will also streamline the process for enrolling in Medicaid and the Children's Health Insurance Program, they could lead to an increase in Medicaid rolls if consumers shopping for a policy learn of their eligibility for Medicaid.

The contents of the essential benefits packages are defined primarily by the states where they are offered based on the customary local policies already available, but they also have to meet standards for deductibles and out-of-pocket costs.

A state's choices can greatly affect the policies. For example, any plans sold in Maryland will include coverage of bariatric surgery, but just across the Potomac River in Virginia, bariatric surgery coverage will be an expensive add-on that could cost an extra $1,500 a month, according to an analysis by *Kaiser Health News*.

And although benefits like those will be determined by states, the ACA has been phasing in "patient protection" requirements over time, with the final ones kicking in on Jan. 1. The ACA eliminates annual and lifetime limits on coverage, restricts the conditions under which insurers can cancel coverage, requires plans to allow parents to include any children under 26 in their plans, eliminates pre-existing conditions exclusions, prohibits insurers from charging higher rates due to gender or health status, requires insurers to cover patients in clinical trials, and requires policies to cover preventive

services such as mammograms and colonoscopies without charging a deductible, co-pay, or co-insurance.

Unwelcomed Surprises

All of the provisions do not apply to "grandfathered" plans, which are most health insurance plans that were in force when the ACA became law in March 2010. These plans do not have to follow rules such as providing preventive care without patient cost-sharing. Some 36% of those enrolled in employer plans in 2013 were enrolled in such plans, down from 48% in 2012, reports the Kaiser Family Foundation. A plan loses this status if significant changes are made in it.

Many policies do not meet this grandfathering criteria, and that led to millions of consumers who buy their own coverage receiving cancellation letters from insurers. The cancellations were an unwelcome surprise, given President Obama's promise that people could keep their plans if they liked them. The cancellations occurred because the policies did not meet the ACA's greater coverage requirements, and Obama's change in policy to allow insurers to continue to offer them is a partial and difficult-to-implement fix.

These individual buyers who will need to seek new policies are the very ones most dependent on the exchanges that have been so troublesome, and that could mean trouble for the ACA.

"If the start-up problems and computer issues that the health exchanges have encountered turn out to be severe and prolonged, there could be a major impact on the size and composition of the risk pool. These factors are critical to the viability of the entire program," says Endocrine Society adviser Glass. If a higher proportion of sicker patients — those most motivated to have coverage — plod their way through the exchanges while healthy patients find the process too troublesome, insurers would need to raise premiums to compensate.

Opportunities Yield Concerns

In addition to the opportunity for buying insurance, Glass says that there are some things in the ACA that endocrinologists will generally like, along with some concerns. On the positive side, there are some demonstration grants for new ways of looking at medical liability, proposals for simplification of claims processing, and a provision for collecting additional statistics and reports and funding studies aimed at improving diabetes care. A provision that raised Medicare reimbursement for bone density testing expired after two years, and medical societies are trying to get the level restored.

The ACA also created a pair of potentially significant initiatives. The Patient-Centered Outcomes Research Institute is a nonprofit organization created to back difficult-to-fund comparative effectiveness research. The Center for Medicare and Medicaid Innovation is another new creation, within the Centers for Medicare and Medicaid Services, with a mission of finding new payment and delivery methods that improve care and health while lowering costs, including the effort exploring accountable care organizations (see related story, page 20).

Glass said a new entity is causing some people concern — the Individual Payment Advisory Board is a 15-member panel appointed by various political officials that is "set up as the court of last resort with regard to keeping Medicare expenditures in check ... . If Medicare expenditures are rising too fast, then this committee will be allowed to make recommendations to bring those expenditures in line." The board can cut payments to physicians and other providers, but can't change anything related to the beneficiaries or their costs. The board's proposals go into effect unless Congress stops them, and it is doubtful that the current Congress could agree on any response. Glass says that some observers fear that this panel could put the burden of cutting costs of Medicare on providers even further. But because Medicare's cost growth rate has slowed, the trigger provisions for this board to act have not been met in recent years. "It's a potential concern, but at this point it has not been in effect," Glass says.

Glass acknowledged that the ACA remains very controversial and full of unknowns, but says that providing greater access to health insurance is a laudable goal considering that, for many conditions that occupy endocrinologists such as diabetes, earlier intervention can improve outcomes. The ACA's success in that endeavor remains to be seen. EN

— Seaborg is a freelance writer in Charlottesville, Va., and a regular contributor to Endocrine News.

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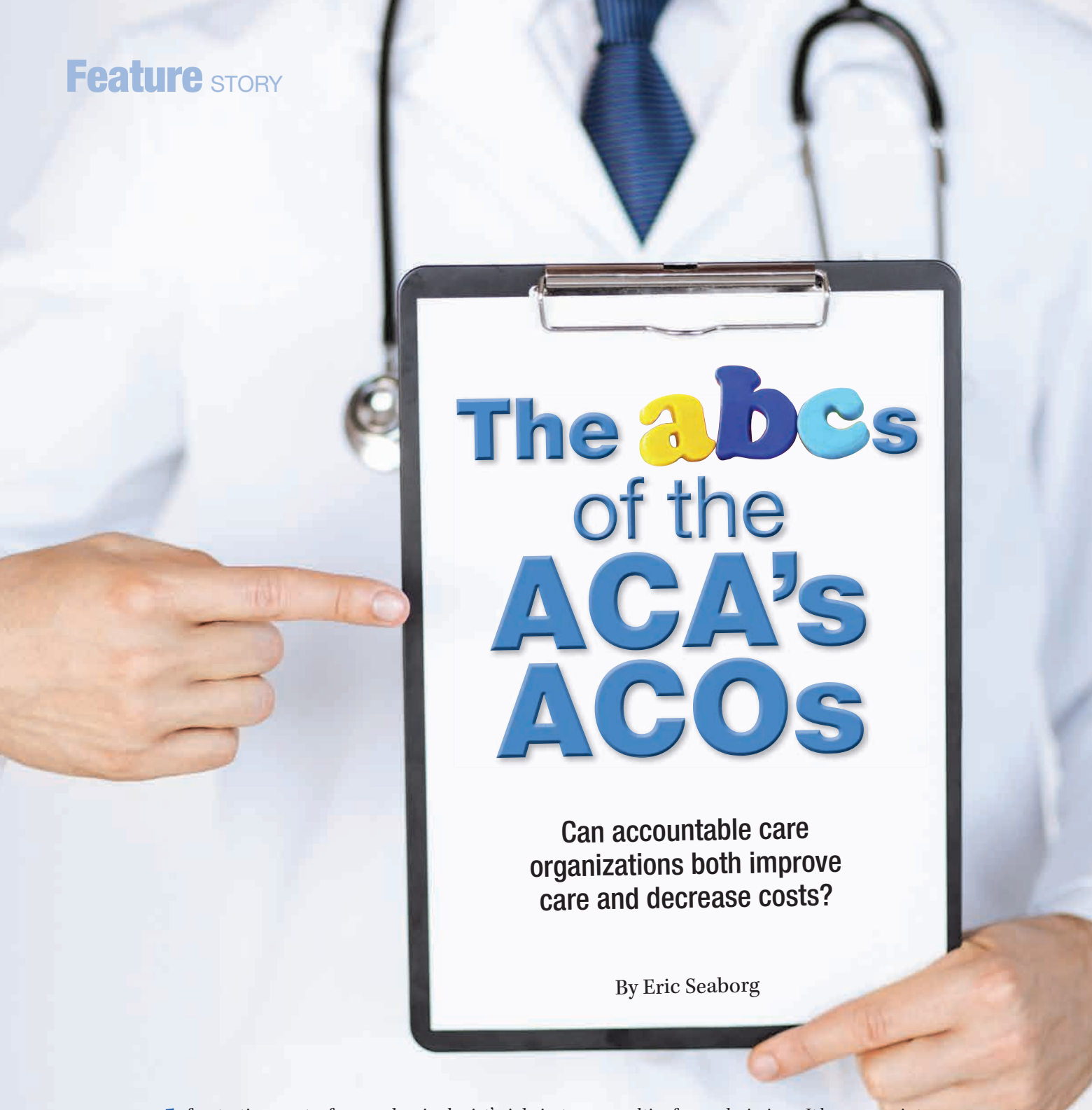

The abcs of the ACA's ACOs

Can accountable care organizations both improve care and decrease costs?

By Eric Seaborg

A frustrating part of an endocrinologist's job is to watch as the noncompliant diabetes patient deteriorates, with crises leading to frequent emergency room visits, leading to revolving-door hospital stays. By finding innovative interventions for working with 600 of its highest risk patients, New York's Mount Sinai Hospital has cut down significantly on those visits and hospital stays. Over a two-year period, the Preventable Admissions Care Team (PACT) reduced 30-day readmissions by 43% and emergency room visits by 51%.

The pilot initiative began in response to incentives in the Affordable Care Act that allow providers to earn bonuses for better outcomes, but threaten them with penalties for readmissions. It has grown into an accountable care organization (ACO) called Mount Sinai Care serving more than 22,000 Medicare beneficiaries.

"Our ACO has been in the Medicare Shared Savings Program for 16 months, and we are bending the cost curve," says Mark Callahan, MD, who heads Mount Sinai Care. "We are below our baseline for cost. We have also submitted our first set of quality metrics, and we achieved 100% on that, which we are very proud of."

In a case reported in *The Wall Street Journal*, this team approach improved the status of one diabetes patient so much that she went from 12 emergency room visits and five hospital stays in 2012 to a single

AT-A-GLANCE

- Both Medicare and private insurers are moving toward ACOs as a payment model.
- ACOs may accelerate changes in an endocrinologist's practice, including leading a team-based approach to complex conditions.
- ACOs are challenged to improve patient care while cutting costs and promise to be a big part of medicine's future.

hospitalization in 2013. That meant a drop in Medicare's costs from almost $44,000 in 2012 to less than $7,000 for the first eight months of 2013. As a participant in the Medicare Shared Savings Program, Mount Sinai stands to benefit from that decrease.

But beyond the monetary impact is the impact on patient care, and endocrinologists have an important role to play in this major new direction in medicine, according to Ronald Tamler, MD, PhD, head of Mount Sinai's diabetes center.

ACOs are one of the fastest growing parts of Medicare, with more than 4 million beneficiaries enrolled. That's a tremendous number considering that the program began just three years ago. Medicare pays an ACO a capitated rate determined by the expected costs of treating a certain population. If the ACO can meet quality criteria and keep the cost below an assigned benchmark, it keeps a portion of the savings. And Medicare is not the only payer betting on ACOs to play a significant role in holding down costs while improving care. Private insurance companies are moving into them, too.

"The majority of care that patients with diabetes receive does not come directly from an endocrinologist. It comes from a variety of team members, such as primary care doctors and physician extenders, other specialties, ophthalmology, nephrology, cardiology, and so on. **The role of an endocrinologist ... has been changing to become partners for creating best practices** for these patients that are consistent throughout the organization."

— Ronald Tamler, MD, PhD, clinical director, Mount Sinai Diabetes Center

The PACT

As part of its PACT pilot, Mount Sinai created its own predictive algorithm that analyzes electronic health records to automatically calculate the risk of readmission for every patient who gets admitted to the hospital. Those who are rated as being at high risk for readmission are targeted for special intervention.

The hospital invested heavily in the effort, hiring new social workers and care coordinators who begin their intervention while the patient is in the hospital, and follow up intensively after discharge. They do what they can to improve compliance, making home visits, making sure patients keep their appointments, solving transportation challenges, helping with benefits issues, and even getting involved with housing problems. "These are the things we have found that lead patients to fall through the cracks and have their illnesses not controlled and end up in the emergency room or in the hospital unnecessarily," Callahan tells *Endocrine News*. Social workers have been known to meet patients early in the morning and accompany them to ensure they get to crucial appointments like dialysis treatments. One hospitalization averted can cover the cost of several months of a social worker's salary, Callahan says. And based on the success of its program, Mount Sinai received a federal grant to fund some social workers.

A high-risk diabetes patient might be assigned a nurse practitioner as a primary care provider and a care coordinator, along with a team of caregivers that could include an endocrinologist, a diabetes educator, and an ophthalmologist as well as other specialists to address complications, such as a cardiologist. The team provides consistency in care and communicates freely to keep each other informed about a patient's status.

Tamler says that the ACO approach has expanded his role from that of the traditional endocrinologist toward being an "intellectual spearhead" to see that good diabetes treatment is delivered largely outside of the endocrinologist's office. But he says that this change in the role of endocrinologists is not limited to ACOs: "The majority of care that patients with diabetes receive does not come directly from an endocrinologist. It comes from a variety of team members, such as primary care doctors and physician extenders, other specialties, ophthalmology, nephrology, cardiology, and so on. The role of an endocrinologist ... has been changing to become partners for creating best practices for these patients that are consistent throughout the organization."

Tamler notes that diabetes patients in a related initiative, the Patient-Centered Medical Home, have clearly benefited from the approach, with a 1.4% reduction in hemoglobin A1C levels, a three-pound weight loss, and a 40% increase in ophthalmology screening rates. "In the traditional model of care, you wait for a patient to come in," he says. "In the ACO model of care, you want to ensure that whether a patient actively reaches out to you or not, that patient is receiving good care. So it puts

OnPOINT from the Endocrine Society

The Endocrine Society supports new healthcare delivery systems, such as ACOs, if they are developed to take into consideration the unique needs of endocrinologists and the patients they treat. Go to **www.endocrine.org/p4p** for the Society's position statement and more details.

much more of the emphasis on the outreach toward the patient."

Another difference in his practice is his involvement with computers and information technology: "We help devise systems that will facilitate population management [and] best practices."

The Affordable Care Act contains incentives for greater adoption of electronic medical records, and Callahan and Tamler agree that the ACO's achievements would not be possible without tapping the data in these records. The records not only allow providers to crunch the numbers to identify patients who are at risk, but can also be used to spot patterns and problems within an organization, such as where care is not being delivered appropriately.

Pioneer ACOs

While Mount Sinai appears to be making progress, first-year results have been mixed from a Medicare experiment called the Pioneer ACO program. The program featured 32 large organizations, considered some of the most experienced with capitation programs. Under the rules, providers not only shared savings but could face financial risks for not meeting goals.

All 32 Pioneer ACOs met the program's quality goals, exceeding industry benchmarks on 15 measures and outperforming managed-care plans on diabetes measures such as blood pressure and cholesterol control. Overall, they held down spending compared with fee-for-service programs, increasing 0.3% instead of 0.8%, and saving Medicare almost $90 million. But most savings came from a few providers. Although 18 of the Pioneer ACOs lowered their costs, only 13 did so enough to reach the level for shared savings. Fourteen actually had higher costs.

Given these results, nine ACOs dropped out of the Pioneer program, with seven of them moving to the less-stringent Medicare Shared Savings Program, where participants do not face the risk of losses. Two dropped out entirely. A spokesperson for one of these, Presbyterian Health Care of Albuquerque, N.M., told media outlets that because his organization works in a low-cost area already, cutting costs as a Medicare ACO did not seem practical.

Private ACOs

Private insurers already have agreements with more than 200 ACOs. In 2009, seven healthcare providers entered into an ACO-like "Alternative Quality Contract" (AQC) with Blue Cross Blue Shield of Massachusetts. The agreement is based on a global budget and quality benchmarks approach, in which providers face financial risks for excessive spending and are rewarded for performance on 64 quality measures.

In a study published last year in *Health Affairs*, Harvard Medical School researchers compared results for patients in practices covered by the AQC with those of a control group from providers not participating in the contract. They found that quality of care improved at a lower cost in areas such as chronic care management, adult preventive care, and pediatric care within organizations participating in the AQC compared to control organizations. "Groups in the AQC spent 3.3% less than fee-for-service groups in the second year" of the program, the study said. "Savings were largely achieved through shifting referrals to less expensive providers and settings rather than reductions in utilization."

Of course, ACOs have their critics, such as Jeff Goldsmith, PhD, president of the consulting group Health Futures. Goldsmith finds the Pioneer ACO results comparable to those at the start of the Physician Group Practice demonstration program Medicare began in 2005. That program also provided bonuses for meeting spending reduction and quality improvements goals, until it was abandoned as unworkable in 2010.

Another question mark for ACOs is their ability to cut or control costs year after year: How much can be squeezed out once efficiencies have been implemented? Saving money by working with the most expensive, highest risk patients is like picking the low-hanging fruit — where do you go next?

Mount Sinai dove in to ACOs to stay ahead of the market, and Callahan says that in the next few years the financial models may change greatly: "But I think it will still involve having physicians and hospitals being at risk for quality and at risk for utilization. Just about every major insurance company has talked with us about some kind of an ACO model for their patients." EN

— Seaborg is a freelance writer in Charlottesville, Va., and a regular contributor to Endocrine News.

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WEAPONS OF MASS DESTRUCTION: Neuroendocrine Control of Body Weight

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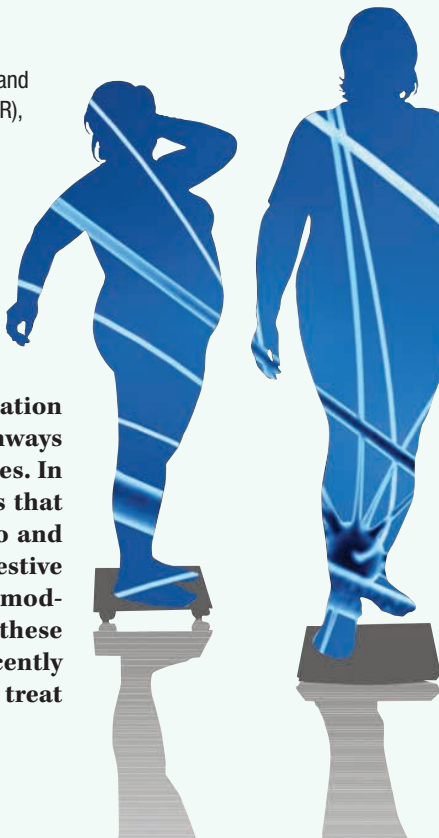


The prevalence of obesity and associated metabolic disorders such as type 2 diabetes is increasing in developed countries. The mechanisms controlling appetite and body weight are complex, making treatment a significant clinical challenge. Nonetheless, the recent explosion of new information concerning the roles of neural circuits and neuroendocrine signaling pathways to control body weight regulation holds promise for new and better therapies. In this TriPoint, a basic scientist discusses research in cell and animal models that are defining novel processes by which peripheral signals are transmitted to and interpreted by the central nervous system to modulate appetite and ingestive behaviors. A clinical researcher describes how the information from these models is being translated into humans and provides additional evidence for these pathways gained from research in humans. Finally, a clinician discusses recently approved agents as well as those in the pipeline and how they will be used to treat obesity in patients.

BASIC RESEARCHER PERSPECTIVE

HIGHLIGHTS

- Key metabolic signals such as leptin and neurotransmitters such as **serotonin directly target key neurons in the brain** to regulate food intake and energy balance.
- **Key circuits in the hypothalamus regulate peripheral metabolism** independent of changes in body weight.
- Novel genetic approaches and mouse models have greatly aided the **understanding of how neurons in the hypothalamus regulate food** intake and body weight.

The past two decades have been a wild ride for investigators in the fields of neuroendocrine control of food intake, body weight, and glucose homeostasis. The discovery of leptin and the elucidation of the role of the central melanocortin system in regulating energy balance were catalysts that propelled the fields forward. These and other discoveries were key as the rates of obesity and diabetes are still a major challenge for patients and clinicians around the globe. Leptin is a key hormone secreted by adipocytes that is required for the regulation of energy balance, glucose homeostasis, and nearly every neuroendocrine axis.

The melanocortin system is made up of neurons whose cell bodies reside in the arcuate nucleus of the hypothalamus. The central melanocortin system is comprised of pro-opiomelanocortin (POMC) neurons and agouti related protein (AgRP) neurons. POMC neurons produce α-melanocyte-stimulating hormone (α-MSH), an endogenous agonist of melanocortin 4 receptors (MC4Rs). α-MSH and other MC4-R agonists regulate food intake, body weight, and glucose homeostasis. Conversely, AgRP neurons secrete AgRP, the endogenous MC4R antagonist.

Complex Brain Circuits

One of the most important lessons we have learned concerns the remarkable division of labor among these brain pathways. Not surprisingly, the neural circuits

controlling energy balance are exceptionally complex, with a segregation of duties between neurons that control energy expenditure and food intake. Moreover, sets of neurons in the hypothalamus respond to metabolic cues and regulate glucose homeostasis (including hepatic glucose production) in a manner that is dissociable from changes in food intake and body weight.

These concepts have been highlighted by genetic loss and restoration (rescue) studies. For example, we now know that leptin acts in distinct populations of neurons to regulate energy expenditure, food intake, and glucose homeostasis. Contrary to early predictions, direct leptin action on POMC neurons regulates hepatic insulin sensitivity and glucose production but does not significantly regulate food intake and body weight. Instead, leptin acts on other neurons including those in the lateral hypothalamus and brainstem to regulate food intake.

Another example of this complexity of these regulatory pathways is in the heterogeneity in seemingly similar classes of neurons. Electrophysiological studies indicate that the responses of POMC neurons are remarkably segregated. In particular, metabolic signals (e.g., leptin, insulin, serotonin, etc.) act acutely on nonoverlapping populations of POMC neurons to change their membrane potential and firing rates. Thus, after more than 15 years, the old adage "the more we know the less we know" seems ever more appropriate and much remains to be done if we are to develop more rationale strategies to combat the growing epidemic of obesity and diabetes.

Another key concept is the remarkable plasticity of the circuits controlling energy balance, especially during development. For example, developmental ablation of key orexigenic (i.e., appetite stimulating) neurons (AgRP/NPY) in mice produces very mild effects on food intake and body weight. In marked contrast, ablation of the very same neurons in adult mice produces frank anorexia and eventually starvation. Complex developmental patterns of gene expression may underlie or enable this flexibility. For example, some neurons that express POMC during development do not express POMC in adult neurons. These and other observations need to be considered when assessing the results of studies using genetic modified mice. They also suggest that events during development may irreversibly alter the neural circuitry underlying energy balance and related processes.

New Technologies Allow Selective Targeting

An appreciation of the complexity of the system demanded the field raise its game to the next level. Fortunately, new tools exist that allow acute manipulation of neuronal activity. These techniques have allowed investigators to directly test the role of identified neurons in regulating particular functions. The use of optogenetics and designer channels (and drugs targeting them) have led the way. Briefly, these approaches allow researchers to express light or chemical-sensitive channels into identified groups of neurons.

These engineered channels enable scientists to acutely activate or inhibit the activity (i.e., firing rates) of these neurons in a reversible fashion. For example, activation of AgRP neurons by light or designer drugs has clearly established their roles in regulating feeding. Currently, these types of approaches are being applied to several CNS circuits to help identify the role of distinct classes of neurons in regulating energy balance. Going forward it will be important to develop additional genetic tools that allow manipulation of key genes in chemically identified neurons in adult animals, thereby circumventing the issues of developmental complexity, plasticity, and compensation.

Summary

These basic science discoveries paved the way to the approval of the first anti-obesity drugs in years. Hopefully, these advances will give physicians new tools in their arsenal to treat patients struggling with obesity, diabetes, and related conditions. Currently, bariatric surgery represents a treatment option commonly chosen by doctors and patients. It is noteworthy that the field is now investigating the molecular and physiological basis for the effectiveness of the different bariatric surgeries in causing sustained weight loss and the associated improvement in glucose homeostasis. Hopefully, mechanistic insights drawn from these investigations will enable the pharmaceutical and biotech industries to develop targeted therapies that circumvent the need for invasive surgeries to induce sustained weight loss and diabetes remission. EN

HIGHLIGHTS

- Obesity and cachexia result from **disrupted homeostatic signaling** among the brain, gut, and adipose tissue.
- Human studies rely on **surrogate measures of neuronal activity** to study the central control of body weight.
- Integrative models of afferent peripheral signaling with **brain centers involved in weight regulation** have become increasingly more complex.

Body Weight Regulation Enters the Scientific Mainstream

Much has changed in the past 20 years with regard to how we approach research into the physiology of weight regulation. Prior to this, obesity was viewed primarily as a behavioral disorder and clinical trials were dominated by innumerable approaches to lower calorie intake using personal and group motivational behavior techniques. The obesity research landscape shifted dramatically with the discovery of mutations in the leptin gene in obese mice in 1994, catapulting to the forefront the concept of physiological regulation of a body weight "set point." The first reports of leptin-deficient humans soon followed. In an important test of the relevance of leptin signaling and proof of concept for the existence of a body weight set point in humans, leptin replacement in children with this deficit completely reversed their severe, early-onset obesity.

Since then, using improved techniques to discover and study novel neurotransmitters and neuroelectrical modulators in animal models, the basic research literature began to build the neural architecture whereby the brain governs body weight. In one of the more remarkable realizations that emerged from these animal studies, disruptions in the homeostasis of this system result in both unwanted weight gain and weight loss. Obesity and cachexia, therefore, represent opposite ends of the disease spectrum involving the same weight regulation systems.

Challenges of Translational Human Research

Following Willie Sutton's lead, when it comes to understanding the control of body weight, the "money," so to speak, is in the brain. Not unexpectedly, determining which of the findings in animals are relevant to humans has been challenging.

At the cellular level, neuronal modulation leading to appetite regulation may take place by transynaptic delivery of neurotransmitters (e.g., dopamine, serotonin) or neuroendocrine factors (e.g., α-melanocyte stimulating hormone), by propagation of a depolarization potential from one neuron to another, or both. Several advances in brain imaging have allowed for indirect measures of brain activity in humans. For example, functional magnetic resonance imaging (fMRI), arterial spin labeling (ASL), and positron emission tomography (PET) measure physiological markers of neuronal activity (e.g., increased blood flow to, and glucose uptake by, active neurons and supporting cells) or neurotransmitter binding (e.g., dopamine) to receptors. However, these techniques remain surrogates of actual neuronal activity, and the spatial and temporal resolutions currently available do not provide the granularity to determine functional communication within or between nuclei of the hypothalamus and brainstem.

In addition, the list of peripheral hormonal and other modulators of body weight is expanding rapidly, making it important to integrate these new findings with existing physiological constructs. For example, studying the brain response to drinking a glucose beverage would seem a straightforward proposition. However, alterations in brain activity measured during the simple act of ingesting glucose involve far more than responses to rising blood glucose levels. As soon as the drink is started, taste receptors in the mouth and then stretch receptors in the esophagus and stomach immediately send signals to the brain. Shortly thereafter, secretion of several gut hormones (e.g., insulin, cholecystokinin, glucagon-like peptide 1) and inhibition of others (e.g., ghrelin) that have central brain receptors occur in anticipation of or in response to the rise in glucose.

Metabolism of glucose by bacteria in the gut microbiome, as well as in the liver (e.g., lactate), results in generation of additional centrally acting metabolic substrates. Finally, a generally poor understanding of the blood-brain-barrier transport and pharmacologic properties of many hormones and substrates often makes guesswork of whether measured changes in brain activity correspond with binding of a hormone or nutrient with its receptor or are the result of neural signaling downstream from the original activation site. Therefore, the simple act of swallowing and digesting glucose elicits a cascade of neurological and hormonal signals that converge, temporally overlap, and make interpretation of subsequent brain responses difficult. In other words, it's complicated.

Summary

We are still just beginning to understand the fundamentals of the physiology underlying neuroendocrine control of body weight regulation and the pathophysiology that results in expression of obesity and cachexia in humans. Like most chronic diseases, the reality is that

the complexity of this system defies our original hope for a simple model that lends itself easily to experimentation and points to an obvious and efficacious treatment. As we move forward with these studies, though, one of the largest areas of research growth has been in revisiting behavioral models of food intake using the brain imaging techniques mentioned above. Game theory, impulsivity control, and "reward" centers are all being explored as regulators of increased food intake in obese patients. Since the vastly expanded cortex in humans, compared to animals, provides complexity of thought as well as behavior, this leaves a large, uncharted territory to study. EN

CLINICAL PRACTITIONER PERSPECTIVE

HIGHLIGHTS

- Human body weight is regulated by a **complex machinery formed by multiple peripheral signals** produced by the gastrointestinal tract, pancreas, and adipose tissue, which are integrated by the central nervous system with other central signals, including the dopaminergic, adrenergic, serotonergic, opioid, and endocannabinoid regulatory pathways.
- **The clinical use of weight loss drugs to fight obesity** has been a major challenge due to low efficacy, unacceptable adverse events, and/or toxicity.
- The next generation of anti-obesity drugs targeting the **neuroendocrine control of weight** will likely focus on monotherapy with more selective, effective, and safer compounds, or combined therapies with lower doses of different agents acting on distinct regulatory mechanisms of energy homeostasis.

Several signals produced by the adipose tissue and gastrointestinal tract (GIT) are involved in the regulation of energy homeostasis and body weight. The central nervous system (CNS) is responsible for integrating these peripheral signals with other information that arises from the external and internal milieus, including the dopaminergic, adrenergic, serotonergic, opioid, and endocannabinoid (EC) regulatory pathways. All these input signals trigger several compensatory responses to maintain a balance between energy intake and expenditure. The malfunctioning of one or more components of this complex machinery might result in energy imbalance and significant changes in body weight. The outstanding scientific advances in our understanding of this machinery have opened new opportunities for the development of novel pharmacologic strategies for the treatment of obesity.

Weight Loss Drugs: A History of Failures and Withdrawals

The landmark discovery of leptin in 1994 unleashed a wave of expectations regarding its potential to solve the obesity pandemic. Unfortunately, leptin therapy has proved to be effective only for the few patients who have congenital leptin deficiency. The vast majority of obese individuals are leptin-resistant and refractory to therapy. Similarly, drugs targeting different hormone systems within the GIT have not yet met their promise as anti-obesity agents. In the past decade, the clinical use of synthetic compounds acting as pharmacological blockers of the EC receptor CB1 (CB1R) attracted special attention for the treatment of human obesity and its co-morbidities. Nevertheless, the initial enthusiasm was replaced by disappointment with the withdrawal of Rimonabant from the market due to reports of serious psychiatric adverse events. In the same direction, old and not so old compounds that modulate dopamine, norepinephrine, and serotonin availability in the CNS, such as amphetamine derivatives and selective serotonin reuptake inhibitors, have been either banned or approved only for short-term use because of their toxicity and/or cardiovascular safety. As a consequence, the lipase inhibitor Orlistat is currently the only anti-obesity drug approved for long-term therapy in most countries around the world.

Novel Medications, New Hopes, Old Fears

In 2012, after an interval of 13 years, the FDA approved two new drugs to battle obesity. The first one was lorcaserin (Belviq, Arena Pharmaceuticals), a selective serotonin 5HT2c receptor agonist that regulates appetite and reduces food intake, with no effect on energy expenditure. In clinical trials, lorcaserin promoted a significant, but still modest, weight loss compared to placebo, with a mean body weight change of 4.5% to 5.8% after one year. Its mechanism of action is similar to that of fenfluramine, which was withdrawn from the market due to heart valve damage. In rats, lorcaserin increased the incidence of mammary and brain tumors, but current evidence shows a large margin of safety in humans. Nevertheless, an old

fear is back, as Arena recently notified the Committee for Medicinal Products for Human Use (CHMP) of its withdrawal of its application for marketing authorization for Belviq in Europe due to the lack of time to address all of the CHMP's safety concerns.

The second approved drug is a combination of the long-established anorectic agent phentermine with the antiepileptic drug topiramate in an extended-release formulation (PHEN+TOP ER; Qsymia, Vivus). In clinical trials, the mean percentage change of body weight at one year with PHEN+TOP ER was 7.8% to 10.9%, values significantly greater than in the placebo groups. Again, an old fear has surfaced, as PHEN+TOP ER therapy is associated with elevations in resting heart rate (similarly to sibutramine), which may increase the risk for fatal arrhythmias. Another concern includes topiramate-related teratogenicity, and for this reason, the FDA's approval required a risk evaluation and mitigation strategy (REMS).

Summary: Old Targets, New Concepts

The next round of the fight against obesity will likely rely on old targets. We will continue to bear witness of the endless search for more selective, effective, and safe compounds acting on specific neurotransmitters and receptors within the CNS. Despite the problems with the first CB1R antagonists, there is a hope that peripherally restricted CB1R antagonists might avoid the known undesirable side effects of the central blockers.

Pharmacological interventions on GIT-brain signaling pathways are now a reality for the treatment of type 2 diabetes and might prove valuable for weight loss in obesity. For instance, the GLP-1 analogues exenatide and liraglutide can result in weight loss and are promising alternatives, alone or in combination with compounds targeting other GIT and metabolic receptors, for future use in non-diabetic obese population.

The novel concept of combining lower doses of two drugs that act simultaneously in different regulatory mechanisms within the brain has attracted considerable attention. Besides Qsymia, ongoing trials in this area include the association of bupropion with the opioid antagonist naltrexone in a sustained release (Contrave) or with the anti-epileptic zonisamide (Empatic). And, there are more to come, based on the premise that the combined therapies might result in higher efficacy with fewer side effects. Only time will tell if this is true. Meanwhile, I would not be surprised if a new anti-obesity agent is discovered by serendipity among the various preparations in the pipeline primarily aimed for the treatment of diabetes, hypertension, depression, and other diseases. **EN**

— This article was reviewed by Daniel J. Bernard, PhD, and Margaret E. Wierman, MD, of the Endocrine Society's *Research Affairs Core Committee.*

For a complete list of refernces, go to: **endocrinepress.org**

An Appetite for APPS

Physicians now have myriad options at their fingertips to get information.

By Glenda Fauntleroy

The days of physicians reviewing the latest research news or checking drug interactions from their office desktop computers are slowly becoming a thing of the past. Tablet and smartphone use is at an all-time high as 51% of physicians use a mobile healthcare-related application (app) on their smartphones every day, and 30% use apps on their tablets, according to a recent report from American EHR Partners.

But physicians are not alone in wanting medical information on the go. Consumers are also using apps to manage their own health and wellness. Industry experts estimate that by 2017, half of the 3.4 billion smartphone or tablet users worldwide will use mobile health apps, reports Forbes.

Here's a look at some apps that promise to make the lives of physicians and endocrinology patients much easier:

REFERENCE

EPOCRATES. The top-ranked app among physicians, according to the American EHR survey. Lets physicians review drug prescribing and safety information for thousands of brand, generic, and over-the-counter drugs and perform dozens of calculations such as body mass index, LDL cholesterol estimation, and glomerular filtration rate. There are also pill identification displays. Free or a subscription upgrade for Epocrates Essential for $159/year. Available for iPhone/iPad and Android.

MEDSCAPE. Medscape has become the go-to reference app, boasting 3 million users who make up one of two physicians and three of four medical students in the U.S. Includes drug reference tools, evidence-based disease and condition reference, the latest medical news by specialty, and accredited continuing education courses. Free. Available for iPhone/iPad, Android, and Kindle Fire.

EPONYMS. Popular with students, this app contains a short description of more than 1,700 medical eponyms — medical phrases or pathologies that are named after key people. $1.99. Available for iPhone/iPad and Android.

PATIENT EDUCATION

VISIBLE BODY HUMAN ANATOMY ATLAS. Top-selling human anatomy learning and teaching app on the market. Includes male and female models, each with more than 3,800 anatomical structures. All the structures in both models are rendered in true 3D. View any combination of anatomy, rotate freely, and adjust the zoom area. $29.99 or free preview version. Available for iPhone/iPad.

DRAWMD. Displays anatomical pictures that physicians can draw on top of and layer as needed to explain hard-to-understand anatomy, conditions, and procedures to patients. Enhances patient-doctor communication. drawMD offers several apps for different specialties, such as urology, ob/gyn, pediatrics, and cardiology to name a few. Physicians can also upload their own images for demonstration. Free. Available for iPhone/iPad.

NETWORKING

DOXIMITY. Another of the top five apps in American EHR survey, this networking tool offers physicians the chance to connect with more than 200,000 other physicians in the network. Includes HIPAA-compliant faxing, emailing, and text messaging. Physicians can also create a profile to highlight their CV. Free. Available for iPhone/iPad.

DICTATION

DRAGON DICTATION. A voice-recognition app that allows users to speak and instantly see their texts, email messages, or Tweets. Boasts a speed up to five times faster than typing on a keyboard. Free. Available for iPhone/iPad.

FOR PATIENTS

DIABETES IN CHECK. Helps patients manage their condition with digital coaching by a certified diabetes educator, blood glucose tracking, medication tracking, hundreds of diabetes-friendly recipes with photos, and a carb tracker database of more than 80,000 foods. Free. iPhone/iPad.

MYFITNESSPAL. A popular weight loss calorie counter, diet and exercise journal. Users can add their personal stats, (such as, height, age, sex, weight, target weight) and the app will work out how many calories can be consumed each day to hit the weight goal in the specified timeframe. Users record what they eat each day and input their activity. Free. Available on iPhone/iPad and Android.

— Fauntleroy is a freelance writer in Carmel, Ind., and a regular contributor to Endocrine News.

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

Risk of Developing Diabetes and Cardiovascular Disease in Metabolically Unhealthy Normal-Weight and Metabolically Healthy Obese Individuals • KoKo Aung, Carlos Lorenzo, Marco A. Hinojosa, and Steven M. Haffner • *The risk of developing DM and CVD is increased in MUH-NW and MHO individuals. Screening for obesity and other metabolic abnormalities should be routinely performed in clinical practice to institute appropriate preventive measures.*

Insulin-Like Peptide 3 (INSL3) in Men With Congenital Hypogonadotropic Hypogonadism/Kallmann Syndrome and Effects of Different Modalities of Hormonal Treatment: A Single-Center Study of 281 Patients • Séverine Trabado, Luigi Maione, Hélène Bry-Gauillard, Hélène Affres, Sylvie Salenave, Julie Sarfati, Claire Bouvattier, Brigitte Delemer, Philippe Chanson, Yves Le Bouc, Sylvie Brailly-Tabard, and Jacques Young • *INSL3 is as sensitive a marker as T for the evaluation of altered Leydig cell function in CHH/KS patients. INSL3 levels correlate with LH levels in CHH/KS men showing, together with the rise in INSL3 levels during hCG therapy, that INSL3 secretion seems not constitutively secreted during adulthood but is dependence on pituitary LH.*

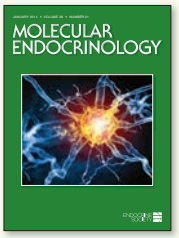
Muscle Anatomy and Dynamic Muscle Function in Osteogenesis Imperfecta Type I • Louis-Nicolas Veilleux, Martin Lemay, Annie Pouliot-Laforte, Moira S. Cheung, Francis H. Glorieux, and Frank Rauch • *Children and adolescents with OI type I have, on average, a significant force deficit in the lower limb as measured by dynamic force tests. Nonetheless, these data also show that OI type I is compatible with normal muscle performance in some individuals.*

TGF-{beta}1 Regulation of Multidrug Resistance P-glycoprotein in the Developing Male Blood-Brain Barrier • Stephanie Baello, Majid Iqbal, Enrrico Bloise, William Gibb, and Stephen G. Matthews • *TGF-β1 regulates P-gp at the fetal and neonatal BBB, and both ALK5 and ALK1 pathways are implicated in the regulation of P-gp function. Aberrations in TGF-β1 levels at the developing BBB may lead to substantial changes in fetal brain exposure to P-gp substrates, triggering consequences for brain development.*

Synergistic Activation of Steroidogenic Acute Regulatory Protein Expression and Steroid Biosynthesis by Retinoids: Involvement of cAMP/PKA Signaling • Pulak R. Manna, Andrzej T. Slominski, Steven R. King, Cloyce L. Stetson, and Douglas M. Stocco • *These findings delineate the molecular events by which retinoids influence cAMP/PKA signaling and provide additional and novel insight into the regulation of StAR expression and steroidogenesis in mouse Leydig cells.*

Steroidogenic Factor 1 Promotes Aggressive Growth of Castration Resistant Prostate Cancer Cells by Stimulating Steroid Synthesis and Cell Proliferation • Samantha R. Lewis, Curtis J. Hedman, Toni Ziegler, William A. Ricke, and Joan S. Jorgensen • *SF1 stimulates steroid accumulation and stabilizes centrosome homeostasis to mediate aggressive prostate cancer cell growth within a castrate environment. These findings present a new molecular mechanism and therapeutic target for deadly CRPC.*

The Intestinal Epithelial Insulin-Like Growth Factor-1 Receptor Links Glucagon-Like Peptide-2 Action to Gut Barrier Function • Charlotte X. Dong, Wen Zhao, Chloe Solomon, Katherine J. Rowland, Cameron Ackerley, Sylvie Robine, Martin Holzenberger, Tanja Gonska, and Patricia L. Brubaker • *The effects of GLP-2 on intestinal barrier function are dependent on the IE-IGF-1R and involve modulation of key components of the tight junctional complex.*



Cell-Specific Actions of a Human LHX3 Gene Enhancer During Pituitary and Spinal Cord Development • Soyoung Park, Rachel D. Mullen, and Simon J. Rhodes • *The human LHX3 enhancer-driven Cre reporter transgenic mice also provide a valuable tool for further developmental studies of cell determination and differentiation in the pituitary and nervous system.*

Hepatic-Specific Accessibility of Igf1 Gene Enhancers Is Independent of Growth Hormone Signaling • Mahalakshmi Santhanam and Dennis J. Chia • *Robust GH-stimulated hepatic Igf1 gene transcription utilizes tissue-specific mechanisms of epigenetic regulation that are established independent of GH signaling.*

M-Protein Is Down-Regulated in Cardiac Hypertrophy Driven by Thyroid Hormone in Rats • Andrei Rozanski, Ana Paula C. Takano, Patricia N. Kato, Antonio G. Soares, Camilo Lellis-Santos, Juliane Cruz Campos, Julio Cesar Batista Ferreira, Maria Luiza M. Barreto-Chaves, and Anselmo S. Moriscot • *The M-protein expression is strongly and rapidly repressed by T3 in cardiomyocytes, which represents an important aspect for the basis of T3-dependent sarcomeric deleterious effects in the heart.*

Putting It TOGETHER

What you need to know when setting up your in-house laboratory.

By Melissa Mapes

Physicians and researchers rarely encounter the opportunity to design a new state-of-the-art laboratory from the ground up. The more likely scenario is assignment to a decades-old lab in need of updates and reorganization. Either way, the same universal principles for effective lab set-up can be applied to any workplace to ensure maximum safety, productivity, and quality control.

April Barts, MT, executive director of Clinical Laboratory Consulting, led an endocrinology lab for 10 years before becoming a nation-wide consultant. She recommends checking state regulations as the crucial first step for anyone working on a lab. "Depending on your state, you may have specific regulations that a lot of physicians are not aware of," she explains. "We call those 'regulatory states,' which have their own criteria outside of the federal."

Rules & Regulations

National regulations originate from the Centers for Medicaid & Medicare Services (CMS), which oversee all lab testing performed on humans in the U.S. through the Clinical Laboratory Improvement Amendments (CLIA). These lengthy federal rules require a lot of paperwork and technical knowledge, as do the additional state requirements, which can all be found on the CLIA website.

"You definitely need to educate yourself," Barts says. "And make sure that whoever oversees these regulations has lab experience." In her consulting work, Barts has encountered numerous scenarios where an office administrator without proper credentials was placed in charge of CLIA and state compliance. Because the administrator did not understand the technical language, the lab failed to meet regulations and was forced to bring in an outside expert for help.

As a result of such costly foibles, Barts emphasizes the importance of hiring a qualified lab director. She also says to ensure that the qualifications of all staff members are well documented. "The guidelines are set very clearly on the CLIA website as to what they require for a laboratory director and staff for training," she says.

Documentation, in general, is a crucial part of creating and managing a lab successfully. All relevant activities laid out in CLIA and state regulations should be recorded and organized. Devising a filing system is step three, but Barts also recommends obtaining accreditation from a CLIA-approved entity, like the Commission on Office Laboratory Accreditation (COLA) or the College of American Pathologists (CAP). Accreditation brings peace of mind to physicians and staff about the quality and compliance of their lab, and helps to avoid government penalties for any regulatory oversights. "COLA has a wonderful manual that gives everything you need step-by-step for a start-up lab," Barts says.

Check List for SETTING UP YOUR LAB

- Check state and federal regulations
- Hire a qualified lab director
- Devise a filing system and consider the help of an independent accreditor
- Make a prioritized list of equipment and search for deals on orders
- Create a safe floor plan that focuses on the necessary work stations
- Continue documentation and monthly quality assurance tests

Bit by Bit

Once staffing, regulations, and paperwork are in place, the physical arrangement of the lab can begin. *Science* magazine claims in its article series, "The Art of Laboratory Feng Shui," that a prioritized list of equipment and other resources is necessary. Base this list on the tests and experiments that will be conducted in the lab. Most practices and hospitals negotiate discounts or start-up specials from retailers to buy these items in bulk. Work with the department's purchasing staff to find out which stores carry the relevant inventory and then place initial orders.

A floor plan should be developed around the same time. Think about the workflow of each test and the stations that the lab will need, while also considering safety. Improper

Regulation and Accreditation

- Clinical Laboratory Improvement Amendments (CLIA) **cms.gov/clia**
- Commission on Office Laboratory Accreditation (COLA) **cola.org**
- College of American Pathologists (CAP) **cap.org**

placement of chemicals or tools can result in disastrous consequences, such as explosions. Although it is common sense to keep acids and bases separate, it would not be the first time that a lab technician without proper training made the mistake of placing the two near each other. If the gases from ammonia and nitric acid intermingle, they will form an explosive dust akin to the ammonium nitrate concoction used in the Oklahoma City bombing in 1995.

Rob Bossio, PhD, scientist at Cabot Microelectronics and former Organic and General Chemistry lecturer at University of Michigan Dearborn, told *Science* that he has seen water-sensitive materials like alkali metals stored under and around sinks in labs. He recommends storing these materials in cool, dry places or desiccators with a tight seal to prevent contamination. "Science is only going to get more expensive, there's no need to waste money on buying materials and reagents again because of negligent care," he says.

Generally, lab equipment costs around $10,000 per year, but researchers can save on set-up by buying basic tools, like timers, from a grocery store rather than a bio supply house. If working at a university, other departments may be willing to share tools, which can also save a lot of cash.

Tests and experiments may begin after collecting and arranging all laboratory resources, but there is still much work to be done. Barts says that monthly quality assurance tests and continued documentation of activities and training are essential. With any luck, the qualified lab director hired during step two will be able to take the reins on such projects and allow physicians to focus on their work.

After all, the most important resource for any lab is, of course, the staff. The money saved from borrowing lab equipment and negotiating discounts should be invested in the recruitment of dedicated, well-trained employees who will ensure the laboratory runs safely, efficiently, and within regulations for many years to come. EN

— Mapes is a freelance writer in Washington, D.C., and a regular contributor to Endocrine News.

Hormone Health NETWORK®

Polycystic Ovary Syndrome (PCOS)

A PATIENT'S GUIDE

Polycystic ovary syndrome (PCOS) is a common hormonal disorder among girls and women during their reproductive years. Normally, women make small amounts of "male" hormones (called androgens), such as testosterone, but women with PCOS produce slightly higher amounts. This hormone imbalance causes an assortment of health problems, such as irregular menstrual periods, too much hair on the body and face (hirsutism), and a very large number of follicles (small fluid-filled sacs where eggs develop) on the ovaries. These many follicles look like cysts, which is where the term "polycystic" comes from.

This guide for patients comes from The Endocrine Society's 2013 practice guidelines for physicians about the detection and treatment of PCOS.

Who gets PCOS?

Women and girls who are obese are more likely to have PCOS. It also seems to run in families.

Most often, PCOS symptoms first occur around the start of menstruation, but some women do not get symptoms until their early or mid-20s. Symptoms like excess facial hair and male-pattern baldness can continue even after a woman goes through menopause.

What causes PCOS?

The cause of PCOS remains unknown. There may be more than one cause.

The main problem in this condition is a hormone imbalance. There also is a link between PCOS, obesity, and resistance to insulin, the hormone that carries sugar from the blood into our cells. Many women with PCOS have too much insulin in their bodies because the insulin does not work as well as it should.

What are the signs and symptoms of PCOS?

- Menstrual problems:
  - Fewer menstrual cycles (less than 9 periods per year)
  - Lack of periods (amenorrhea)
  - Unpredictable heavy menstrual bleeding
- Infertility (trouble getting pregnant) due to not ovulating
- Excess or unwanted hair growth on your face and body
- Thinning hair on your scalp
- Weight gain or obesity, often around your waist
- Skin problems:
  - Acne on your chest, back, and face
  - Skin tags—small flaps of excess skin—on your neck and armpits
  - Dark, thick patches of skin on your neck, armpits, or groin, or under your breasts
- Depression or anxiety
- Poor sleep

Not all women with PCOS have all these problems. Each person may have a different mix of these features. Also, other conditions may cause some of these health concerns. For these reasons, PCOS can be hard to diagnose.

Which conditions mimic PCOS?

Before doctors diagnose PCOS, they must first rule out or exclude other conditions with similar symptoms. This is why they call PCOS "a diagnosis of exclusion."

SOME CONDITIONS THAT MIMIC POLYCYSTIC OVARY SYNDROME (PCOS)

Condition	What it is	Features similar to PCOS
Thyroid disease	Overactive or underactive thyroid gland	Irregular menstrual cycle
Prolactin excess	The body makes too much of the hormone prolactin	• Male-type hair growth in women • Irregular periods or lack of periods
Cushing syndrome	The body makes excess cortisol hormone	• Weight gain • Depression • Too much hair in women • Abnormal menstrual periods
Congenital adrenal hyperplasia	Inherited disorder that causes the body to make too little cortisol and too much male hormone	• Acne that is severe and early (before the teen years) • Infertility or decreased fertility • Facial hair in women and teen girls • Infrequent or absent menstrual periods

How does a doctor diagnose PCOS?

Experts suggest that a diagnosis of PCOS requires the following:

- **Women.** Have at least two of these features:
  - Excess male hormones
  - Problems with ovulation
  - Many pearl-sized follicles on one or both ovaries
- **Teen girls.** Have both of these features:
  - Excess male hormones
  - Infrequent or absent menstrual periods, mainly lasting more than two years after the start of menstruation
- No other cause of the symptoms

Your doctor will take your medical history, asking about your health and menstrual cycle. A physical exam should include measuring your height, weight, and waistline, and looking for skin and hair problems.

No single test detects PCOS. Sometimes a blood test is needed to measure your hormone levels. To check for a large number of follicles, your doctor may order an ultrasound (usually done through the vagina), which uses sound waves to take pictures of the ovaries. Most teens will not need an ultrasound because it is common to have many follicles at that age.

What tests do you need after diagnosis?

Women with PCOS may need tests to screen for health problems that occur more often in PCOS. These conditions can be serious and include

- **Diabetes, high blood glucose (sugar) levels.** After diagnosis of PCOS, you should have an oral glucose tolerance test. This fasting blood test checks for diabetes and prediabetes (high blood sugar levels that are not yet diabetes). Your doctor may want you to take this test every three to five years, but you may need to repeat it sooner if you gain a lot of weight or have symptoms of diabetes, such as frequent thirst or urination.
- **Heart and blood vessel (cardiovascular) disease.** Because women with PCOS are at increased risk for high blood pressure, you should have your blood pressure checked at each doctor's visit. After finding out you have PCOS, you may have a fasting blood test to check for high cholesterol and high levels of other blood fats (lipids), such as triglycerides. Lipids also can be too high in women with PCOS.
- **Endometrial (uterine) cancer.** Abnormal uterine bleeding is a possible sign of endometrial cancer, so tell your doctor if you have unexpected spotting between periods or bleeding after menopause. An ultrasound can find abnormalities such increased thickness of the uterine lining, which may lead to a biopsy to rule out precancer and cancer. But the guidelines do not recommend routine ultrasound screening for women with PCOS who do not have symptoms.
- **Sleep apnea.** Obstructive sleep apnea is when you stop breathing for short times while asleep. Symptoms include loud snoring, daytime sleepiness, and sometimes waking up gasping or short of breath. If you have any of these problems, your doctor may want you to do an overnight sleep study. It is important to treat sleep apnea because it raises the risk for diabetes, stroke, and heart disease.
- **Pregnancy complications.** Women with PCOS are more prone to gestational (pregnancy) diabetes, pregnancy-induced high blood pressure, and birth of a premature baby. Women who are overweight are more likely to have these complications. Talk to your doctor about what tests you need before you try to become pregnant and during pregnancy.

What is the treatment for PCOS?

Some medications can relieve symptoms of PCOS, and others rebalance your hormones.

The first treatment for most women and teens with PCOS is birth control pills or a contraceptive skin patch or vaginal ring. These medications contain female hormones that help protect the uterus and prevent unpredictable bleeding. They also lower androgen levels, reducing excess hair growth and improving acne. Birth control pills also prevent your uterine lining from thickening, thus lowering the risk of uterine cancer.

Ask your doctor if this treatment option is right for you. Some women should not take the pill due to specific risk factors.

Other treatment options for PCOS symptoms and complications are

- **Lifestyle changes.** If you are overweight, you should lose weight by exercise and eating a healthy, low-calorie diet. Weight loss lowers your risk for diabetes and heart disease. Losing weight also improves menstrual function and may help some women ovulate naturally.
- **Metformin.** This medicine helps lower blood sugar levels It is a suitable treatment for women with PCOS who have prediabetes or diabetes and who cannot lose weight through lifestyle changes. Metformin also seems to help menstrual cycles become more regular. It may be an option for women who cannot or do not want to take the pill. (Metformin does not prevent pregnancy.)
- **Fertility drugs.** Clomiphene citrate is most often the first treatment for women who do not ovulate and want to get pregnant. You take this drug by mouth for five days to stimulate ovulation. Another treatment to induce ovulation is letrozole.

More treatments are available to reduce unwanted hair growth, acne, and (to a lesser degree) scalp hair loss. Find more information about these treatments in the Hormone Health Network's fact sheet on PCOS.

There is no cure for PCOS. But with proper treatment and lifestyle changes, you can improve most of your symptoms and reduce your chance of developing health problems related to PCOS.

EDITORS

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Note to health care professionals: This patient guide is based on, and is intended to be used in conjunction with, The Endocrine Society's clinical practice guidelines (available at www.endo-society.org/guidelines/index.cfm).

The US EPA Office of Research and Development (ORD)
is seeking an internationally recognized science leader for the position of Endocrinologist in the National Center for Computational Toxicology (NCCT) in Durham (Research Triangle Park), North Carolina. ORD is filling this position using EPA's Title 42 Authority, which offers up to 5-year renewable term appointments at highly competitive, market-based salaries. The salary may be up to $250,000 per year, dependent upon qualifications, experience and other factors (e.g., current salary). The position is part of a larger EPA effort to use state-of-the-science approaches and technologies in its mission of protecting human health and the environment. Details are available at USAJobs.gov, announcement RTP-ORD-42-2014-0002

UNIVERSITY OF MICHIGAN INTERDISCIPLINARY FACULTY INITIATIVE IN REPRODUCTIVE SCIENCES

The Reproductive Sciences Program (RSP) at the University of Michigan seeks exceptional scholars for tenure-track positions in research areas that include: gonadal biology; stem cells and development; reproductive genetics and epigenetics; reproductive medicine; maternal-fetal interactions and medicine; bioengineering in reproduction; and reproductive physiology and endocrinology. Positions are available at the Assistant, Associate or Full Professor levels in the Medical School Departments of Cell and Developmental Biology, Obstetrics & Gynecology, Pediatrics, Molecular and Integrative Physiology, Urology, and in the School of Engineering Department of Biomedical Engineering. Candidates should have M.D., and/or Ph.D., degrees with relevant postdoctoral or fellowship training, a strong track record of published work in reproductive sciences (non-cancer) or stem cell biology related reproduction, and exceptional potential for conducting **Interdisciplinary Translational and Fundamental Research in the Reproductive Sciences**. Applications should include a curriculum vitae, a 1-2 page summary of research plans, and 3 letters of support. Applications will be reviewed as received until the positions are filled. Send applications to:

Gary Smith and Sue Moenter
c/o Kelly Studer
RSP Interdisciplinary Faculty Cluster Hire Search Committee,
6428 Medical Science I,
1301 East Catherine St,
Ann Arbor, Michigan, 48109-0617
Email: kstuder@med.umich.edu
website: http://www.med.umich.edu/obgyn/research/rsp/index.htm

U-M EEO/AA Statement: The University of Michigan is an equal opportunity/ affirmative action employer.

Endocrinologist Opportunities

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

- **Endocrinology at Geisinger Wyoming Valley Medical Center (GWV), Wilkes-Barre, Pa.**
- **The Endocrinology team at Geisinger-Patton Forrest, State College, Pa.**

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 4 hospitals, 43 community practice sites and more than 900 Geisinger primary and specialty care physicians.

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

GEISINGER
HEALTH SYSTEM

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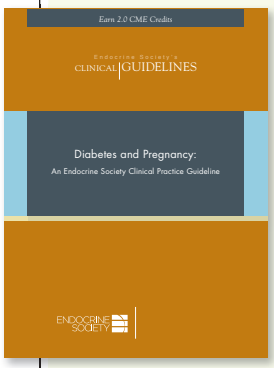
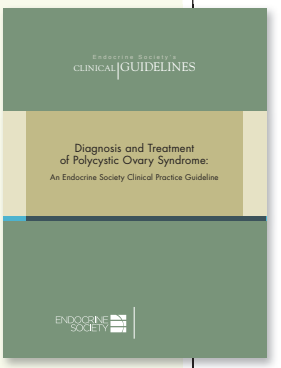


Two New Endocrine Society **Clinical Practice Guidelines** Now Available



This issue of *Endocrine News* contains complimentary copies of the Society's newest clinical practice guidelines (CPG): *Diabetes and Pregnancy* and *Diagnosis and Treatment of Polycystic Ovary Syndrome*. The Society established the CPG program to provide endocrinologists and clinicians with evidence-based recommendations in the diagnosis and treatment of endocrine-related conditions. Each CPG is created by a task force of experts in the field. Learn more about the Endocrine Society Clinical Practice Guidelines at www.endocrine.org/cpg, or email questions to: **govt-prof@endocrine.org**. EN

ONE ACCOUNT, ONE SOURCE, ONE DESTINATION FOR **THE LATEST SCHOLARLY CONTENT**

In addition to offering our books in digital format, Endocrine Press is now hosted on a new online platform to bring you access to the same high-quality content in a more user-friendly and robust format. You will be able to read, purchase, download, and save content across all Society journals and books while also linking to the Society's Clinical Practice Guidelines, Scientific Statements, and Patient Education Materials. Visit **endocrinepress.org** to experience the new platform. EN

Event **CALENDAR**

JANUARY 26–29, 2014
ASPEN, COLO.
Clinical Diabetes & Endocrinology in 2014
https://www.nationaljewish.org/Calendar/2014/50th-Annual-Clinical-Diabetes-and-Endocrinology-in-2014

FEBRUARY 1–2, 2014
HYDERABAD, INDIA
The International Clinical Update program in Endocrinology (ICUE)
http://icuendo.org/india/

MARCH 13–16, 2014,
PANAMA CITY, PANAMA
3rd Latin America Congress on Controversies to Consensus in Diabetes, Obesity and Hypertension (CODHy)
http://www.codhy.com/la/2014/

Call for Endocrine Healthcare Delivery & Education **ABSTRACTS!**

Among all of the science at **ICE/ENDO 2014**, the Endocrine Society also provides an opportunity to share the latest in **"Endocrine Healthcare Delivery & Education."** Are you engaged in educational research and delivery? Then we want you! **ICE/ENDO 2014** offers an unparalleled opportunity to highlight your work as an educator; submit your work today at **https://www.endocrine.org/endo-2014/attendees/abstracts-and-awards**.

Abstracts are being accepted through Jan. 29, 2014; 1:00 p.m. U.S. EST. EN

How is Your Training Program Doing?

Register Your Fellows for ESAP™-ITE 2014!

ESAP-ITE, the only in-training exam for endocrinology fellows, is the perfect online tool to measure your fellows' progress and knowledge of diabetes, endocrinology, and metabolism.

New for 2014: ESAP-ITE provides measurements in SI units, making the exam far more accessible to fellowship programs around the world.

Key Dates:

- **January 15, 2014:** Registration is open
- **April 1, 12:00 a.m. EDT through April 30, 2014, 11:59 p.m. EDT:** Proctoring available via your own program's computer facilities
- **Mid-May 2014:** Reporting of results

Give your fellows the vehicle to assess their knowledge in endocrinology and register them for **ESAP-ITE** at **http://endoselfassessment.org/ite.aspx** today!

If you have questions, please feel free to contact Society Services at 301-941-0210 or **societyservices@endocrine.org**. EN

Get Recognized: ENDOCRINE SOCIETY EARLY CAREER AWARDS

Navigating careers in science and medicine can be quite challenging for undergraduate, medical, and graduate students, postdoctoral fellows, medical fellows, junior faculty, and early career investigators. The Endocrine Society places high priority on helping early career members reach their career goals by offering a large number of abstract awards, travel grants, and research fellowships recognizing the early achievements of future endocrinologists.

For those considering submitting an abstract for **ICE/ENDO 2014**, the joint meeting of the 16th Annual International Congress of Endocrinology and the Endocrine Society's 96th Annual Meeting & Expo, or attending our Early Career Forum in June, there are abstract and travel award opportunities for you. The abstract awards offer both a chance to present your research at a national meeting and also recognition for your outstanding work. The Early Career Forum travel awards provide funding support to attendees of this exclusive workshop.

If you are an undergraduate student, medical student, or first-year graduate student, then the Summer Research Fellowship program is for you. This program provides a stipend to participate in an endocrine research project with a mentor from the Endocrine Society and to attend ICE/ENDO 2014, where you can attend symposia and plenary lectures on basic, clinical, and translational research topics in endocrinology, network with peers, and meet members of the Society. This program gives awardees the opportunity to become familiar with a career in endocrine research and the exposure to all the programs offered at the Society.

The Society offers a number of additional awards that may be of interest. Here's a quick summary of the Society awards currently available for early career professionals.

ENDO Awards and Travel Grants

- New! ISE Travel Grants: The International Society for Endocrinology awards up to 100 fellowship support grants to bring young endocrinologists from around the world to ICE meetings. Provided to endocrinologists 35 years old or younger who are first authors on a submitted abstract.
- New! Oral Abstract Award in Reproductive Science: provided to fellows and early career investigators who have submitted abstracts related to reproductive endocrinology. Supported by Mr. Gopal Savjani.
- New! Frontiers in Reproduction Abstract Award: provided to fellow and early career investigator participants of the Frontiers in Reproduction (FIR) program. Supported by Burroughs Welcome Fund.
- New! Helmsley Charitable Trust Award in Type 1 Diabetes: provided to fellows and early career investigators who have submitted abstracts related to type 1 diabetes. Supported by The Leona M. And Harry B. Helmsley Charitable Trust.
- The Endocrine Society Outstanding Abstract Awards: provided to authors of the best abstracts submitted for ENDO.
- Eugenia Rosemberg Abstract Award: provided to junior faculty/early career professionals within three years of completing a training program. Open to any abstract submitted in the basic science categories.
- Mara E. Lieberman Memorial Awards: provided to the top-scoring abstracts submitted by women. Award winners will be graduate students, post-doctoral fellows, or junior faculty.

Research Fellowship Awards

- The Endocrine Summer Research Fellowships: provided to undergraduate students enrolled in third year of schooling or beyond at the time of applying or first-year medical or graduate students.
- Acromegaly Clinical Research Fellowship Award: provided to clinical endocrine fellows conducting research in acromegaly. Supported by Pfizer, Inc.

Conference Travel Grants and Other Society Awards

- Early Investigators Award: provided to early career investigators within 10 years of their terminal degree granting date in recognition of outstanding achievements in endocrine research.
- Early Investigators Workshop: provided to 50 post-doctoral and clinical fellows for participation in a unique two-day workshop focused on research training and career development.
- Future Leaders Advancing Research in Endocrinology (FLARE) Awards: provided to graduate students and post-doctoral fellows from groups underrepresented in the biomedical sciences for participation in leadership and professional development programming.
- International Endocrine Scholars Program: provided to international scholars for participation in research training in labs of Endocrine Society members.
- Medical Student Achievement Awards: These awards are presented to outstanding MD or DO students who exhibit a strong interest in endocrinology.
- Minority Access Program (MAP) Summer Research and Career Development: provided to undergraduates from groups underrepresented in the biomedical sciences for participation in summer research internships and career development opportunities at ENDO.

Every early career member is encouraged to look at the travel awards and fellowship opportunities available through the Endocrine Society. The spectrum of possibilities is as diverse as our membership. EN

— Kristen Vella, PhD, co-chair, Trainee and Career Development Core Committee

Key Dates

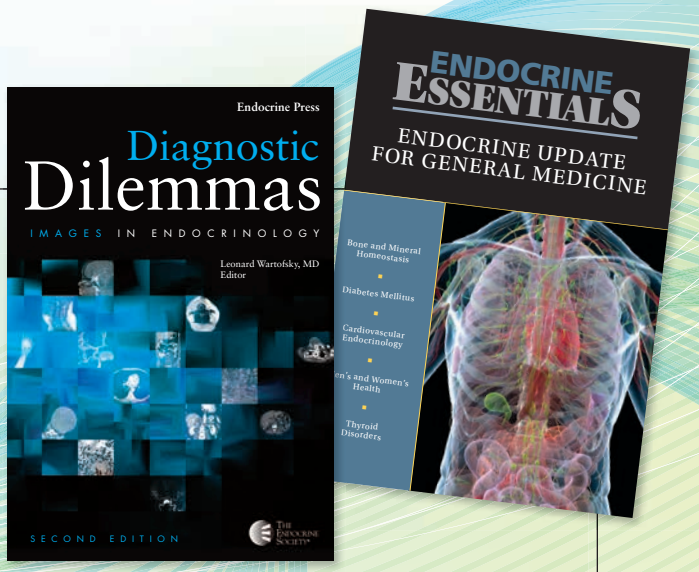
Application Deadline for all Awards:
January 29, 2014

Early Career Forum Travel Awards Notification Date:
February 28, 2014

Abstract and Travel Grant Award Notification Date:
March 28, 2014

Research Fellowship Award Notification Date:
Rolling notification

ENDOCRINE PRESS BUZZ, New Developments



Endocrine Press — the Endocrine Society's comprehensive books publishing program — continues to expand and improve, offering clinicians and researchers access to the leading, authoritative content on endocrine related issues.

Experts in the field are seeing the importance of what Endocrine Press is doing in its mission to enhance the Society's impact and influence. "It's exciting to see that people are taking notice of the forward-thinking of our books program," says Maxine Aldred, director of book development at the Endocrine Society.

The *Endocrine Essentials Series* captures and compiles new and current information on the diagnosis, treatment, and management of endocrine disorders. It covers a wide range of topics, providing invaluable reading for physicians at all levels. The second edition of *Endocrine Essentials — Endocrine Update for General Medicine* was "highly recommended" by Pediatric Endocrinology Reviews. The publication called the text "concise" and lauded each chapter's "useful references."

Diagnostic Dilemmas: Images in Endocrinology, 2nd Edition, the new and improved edition of one of the Endocrine Society's most popular titles, received a three-star review on Doody's Book Reviews from expert reviewer Meltem Zeytinoglu, MD, MBA of the University of Chicago Medical Center.

Zeytinoglu wrote that the second edition of *Diagnostic Dilemmas* "is an interactive and educational book of case vignettes well supported by up-to-date literature" and "an interesting, interactive series of challenging diagnostic cases for endocrinologists. She felt that the thyroid was "particularly well covered," although she would have liked to see more general endocrinology cases.

The second volume of *Diagnostic Dilemmas* from the Endocrine Society includes published cases from the "Images in Endocrinology" series of the *Journal of Clinical Endocrinology & Metabolism.* It has been updated and reformatted to challenge and test the reader's knowledge and ability to reach a diagnosis — in some instances of rare disorders or of unusual presentations of common endocrine disorders. *Diagnostic Dilemmas* was updated and reformatted so each case can be read as a standalone chapter, so the chapters can be read at any time and in any sequence. This book will never go out of date; readers will be able to come back to the cases or "diagnostic dilemmas" again and again to retest their diagnostic approach and the lessons learned.

And now the *Endocrine Essentials Series* and *Diagnostic Dilemmas* — along with the Endocrine Society's other books and journals — can be found online, available to read on a computer screen or downloaded to a mobile device, thanks to Endocrine Press' migration to Atypon, and its flagship ePublishing program Literatum.

"With Atypon, it will be a full-blown product where you can buy a chapter, download a book to a tablet, whatever you want to do," says Aldred. Investigators and clinicians will now have easier access than ever for books and journals already in the Endocrine Press catalogue, as well as new books coming in 2014.

Endocrine Press' upcoming title, *Endocrine and Metabolic Medical Emergencies*, edited by Glenn Matfin, MD, will be released for **ICE/ENDO 2014**. The volume will cover the science and clinical aspects of acute medical care, which is a major focus for many healthcare providers. Endocrine and metabolic emergencies constitute a large proportion of these patients, and many patients are experiencing major safety issues due to the lack of knowledgeable, up-to-date practical guidance.

The buzz surrounding Endocrine Press has helped the Endocrine Society broaden its book program by publishing a growing number of peer-reviewed books and other publications in a variety of formats, both print and digital. The experts agree that Endocrine Press is an excellent resource for the most up-to-date content from well-established and respected authors. To access the online content, visit **endocrinepress.org**. EN

Congress Reaches Budget Deal; SHELTERS RESEARCH FROM SEQUESTER IN 2014

Just before it recessed for Christmas, the Congress passed a bipartisan budget agreement that will eliminate a government shutdown in January and replace a major portion of the impending sequester cuts that have struck fear into many government-funded researchers.

The deal calls for the U.S. government to increase federal discretionary spending to about a trillion dollars in fiscal year 2014. The 2014 discretionary number is essentially half-way between a lower total adopted by the Republican-controlled House earlier this year and a higher number supported by the Democratic-led Senate. It is also $45 billion higher than what would have gone into effect in January 2014 as required by the 2011 law that created the sequestration mechanism.

The higher spending is intended, in large part, to ease the pain promised by the sequester. In 2013, the sequester required many agencies, including major research funders such as the National Institutes of Health (NIH), to cut their budgets by about 5%.

In 2014, the cuts were supposed to total between $90 billion and $100 billion, roughly split between defense and non-defense programs. Many research advocates — including NIH Director Francis Collins and the Endocrine Society — argued for ending those cuts because of the devastating impact to research.

The agreement eliminates about $65 billion in across-the-board domestic and defense cuts over the next two years. The extra money would be spread evenly between Pentagon and domestic spending, nearly erasing the impact of sequestration on the military while domestic programs, including health research funding, could fare particularly well because other funding moves — such as keeping in place cuts to the Medicaid healthcare program — would give Congress greater flexibility in spending.

Overall, the agreement appears set to remove about one-half of the sequester cuts planned for 2014, and one-quarter of those scheduled for 2015. Further relief could come from new revenue sources established by the plan, such as a new fee on airline tickets. Still, for the time being, planned sequester cuts remain in place in 2016 through 2020. And the deal will still require cutting some spending – and those details still need to be worked out. The agreement does not establish exactly how much each agency can spend, only the overall totals for broad categories of spending.

Next Steps

The House and Senate Appropriations Committees are expected to work into January on a spending bill to fund federal agencies through September 30, 2014. The first step will be approval of new spending allocations for the 12 appropriations subcommittees that will determine how the brokered spending level will be allocated among the various agencies and programs.

Endocrine Society Actions

- The Endocrine Society actively advocated throughout the summer and fall for a budget agreement that would repeal sequestration and protect biomedical research from further budget cuts. Activities included: online grassroots advocacy campaigns, Hill Days in Washington, letters to the editor, and multiple letters and visits to members of Congress and the White House.
- The Society hand delivered letters to Congress calling for quick passage of the budget agreement and urging the Appropriations Committees to provide the highest level of spending for the NIH as possible.
- The Society currently has an online grassroots campaign for all U.S. members to contact their senators and representatives to make one final push for the highest possible spending levels for the NIH. Please visit: **www.endocrine.org/advocacy-and-outreach/contact-congress**.

The budget agreement increases the amount of money available for domestic discretionary programs so there is a chance that NIH could receive an increase over its FY 2013 post-sequestration level. We need to make our voices heard as the appropriators finalize decisions about FY 2014 spending! EN

ENDOCRINE SOCIETY
Hormone Science to Health

The Endocrine Society thanks all of its members who participated in advocacy activities to fight sequester and protect federal funding of biomedical research.

Your efforts helped influence this outcome!

Congress Averts 25% Medicare Physician Payment Cut Through March 31; Continues to Work on Permanent "Doc Fix"

The Bipartisan Budget Act of 2013 (BBA) included a provision to prevent the 25% Medicare physician payment cut scheduled to begin January 1, 2014. The BBA provides for a 0.5% update from January 1 to March 31, 2014 and extends the floor for the Geographic Cost of Practice (GPCI) until April 1, 2014. This short-term relief will provide needed time for Congress to finalize a more permanent reform to physician payment under Medicare. To pay for these and several other Medicare changes, the BBA extended the 2% cut in Medicare payments due to the sequester for an additional year (2023) and made changes to Medicaid Disproportionate Share Hospital (DSH) allotments and Long-Term Care Hospital payments.

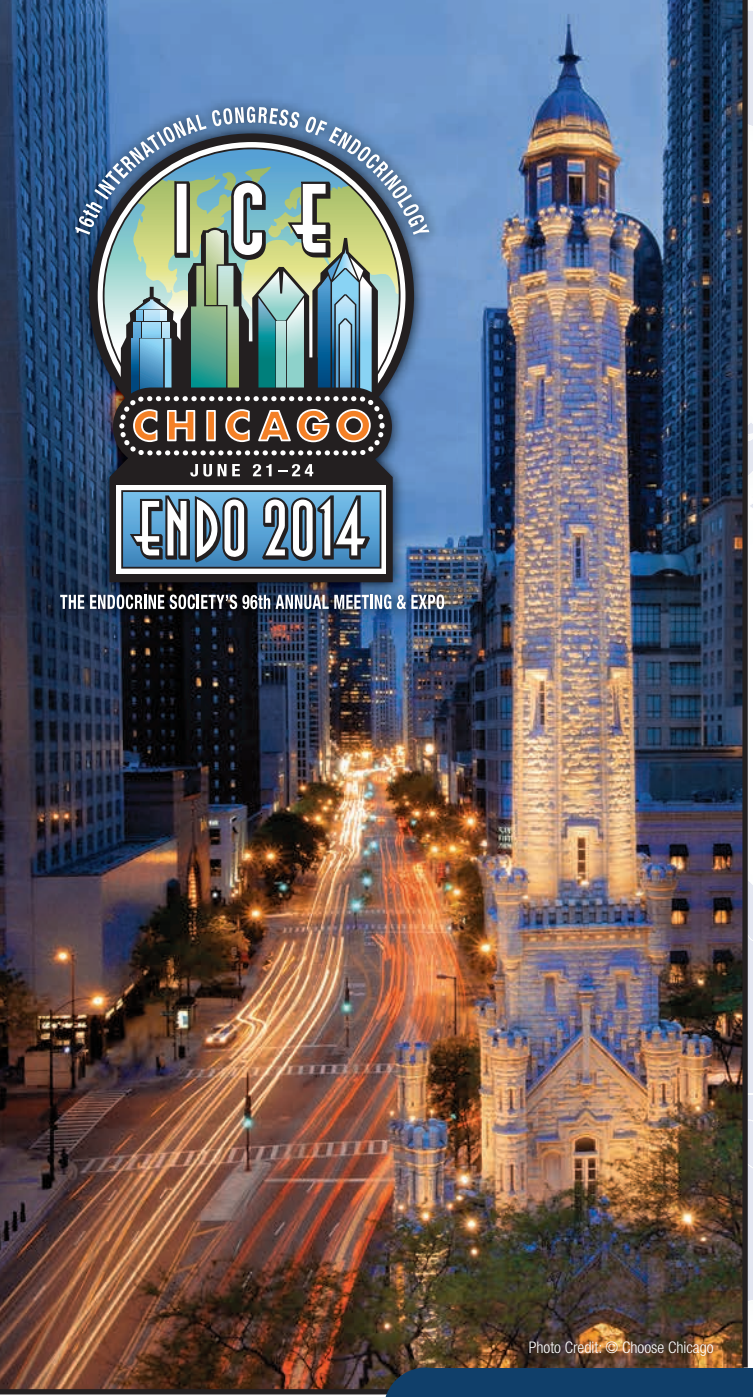
Additionally, in December, two congressional committees advanced legislation that would eliminate the annual routine for physician payment adjustments. The House Ways and Means Committee and the Senate Finance Committee passed similar bills to repeal the Sustainable Growth Rate (SGR) formula that drives annual reductions in Medicare payment for physician services. The main difference between the proposals is that the Ways and Means Committee bill provides a 0.5% update in physician fees for three years followed by a freeze in fees for seven years. The bill passed by the Senate Finance Committee would freeze fees from 2014 to 2023. Starting in 2017, the bills establish a Value-Based Performance Incentive Program (VBP), which consolidates and makes changes to the existing Medicare quality programs.

Next Steps

The Committee proposals now will need to be consolidated with a proposal passed by the House Energy & Commerce Committee and Congress must identify fiscal offsets to pay for adjustments to provider payments. With the short-term physician fee fix that was included in the budget bill, Congress will have the first quarter of 2014 to complete action on the SGR repeal bills or pass another short-term extension of the current payment rate.

Endocrine Society Activity

The Society met with staff from the Senate Finance and House Ways & Means Committees to advocate on behalf of endocrinology throughout the development of these new payment proposals and submitted comments outlining concerns with the discussion draft. These comments reiterated the Society's position on the repeal and replacement of the SGR and also focused on the measurement of quality and resource use through the proposed Value-Based Performance Payment Program and refinements to the proposed alternative payment models. The Society's comment letter, along with its position statement, can be accessed at **https://www.endocrine.org/advocacy-and-outreach.**



SHARE YOUR KNOWLEDGE AND EXPERIENCE

Submit your best science for oral, poster, and poster preview presentation during ICE/ENDO 2014 — the premier venue to share research, exchange ideas, and network with more than 10,000 endocrine researchers and practitioners.

RECEIVE SUPPORT FOR YOUR RESEARCH

The Endocrine Society provides students, fellows, and early career professionals abstract based awards.

APPLY FOR THE FOLLOWING AWARDS TODAY:

- The Endocrine Society's Outstanding Abstract Awards
- Eugenia Rosemberg Abstract Awards
- Mara E. Lieberman Travel Grants
- ***NEW!*** Oral Abstract Award in Reproductive Science (Supported by Mr. Gopal Savjani)
- ***NEW!*** Helmsley Charitable Trust Abstract Awards in Type 1 Diabetes

ALL ARE WELCOME TO SUBMIT

ABSTRACT SUBMISSION DEADLINE:
JANUARY 29, 2014, 1 PM ET

LEARN MORE AT WWW.ICE-ENDO2014.ORG

ise international society of endocrinology

ENDOCRINE SOCIETY