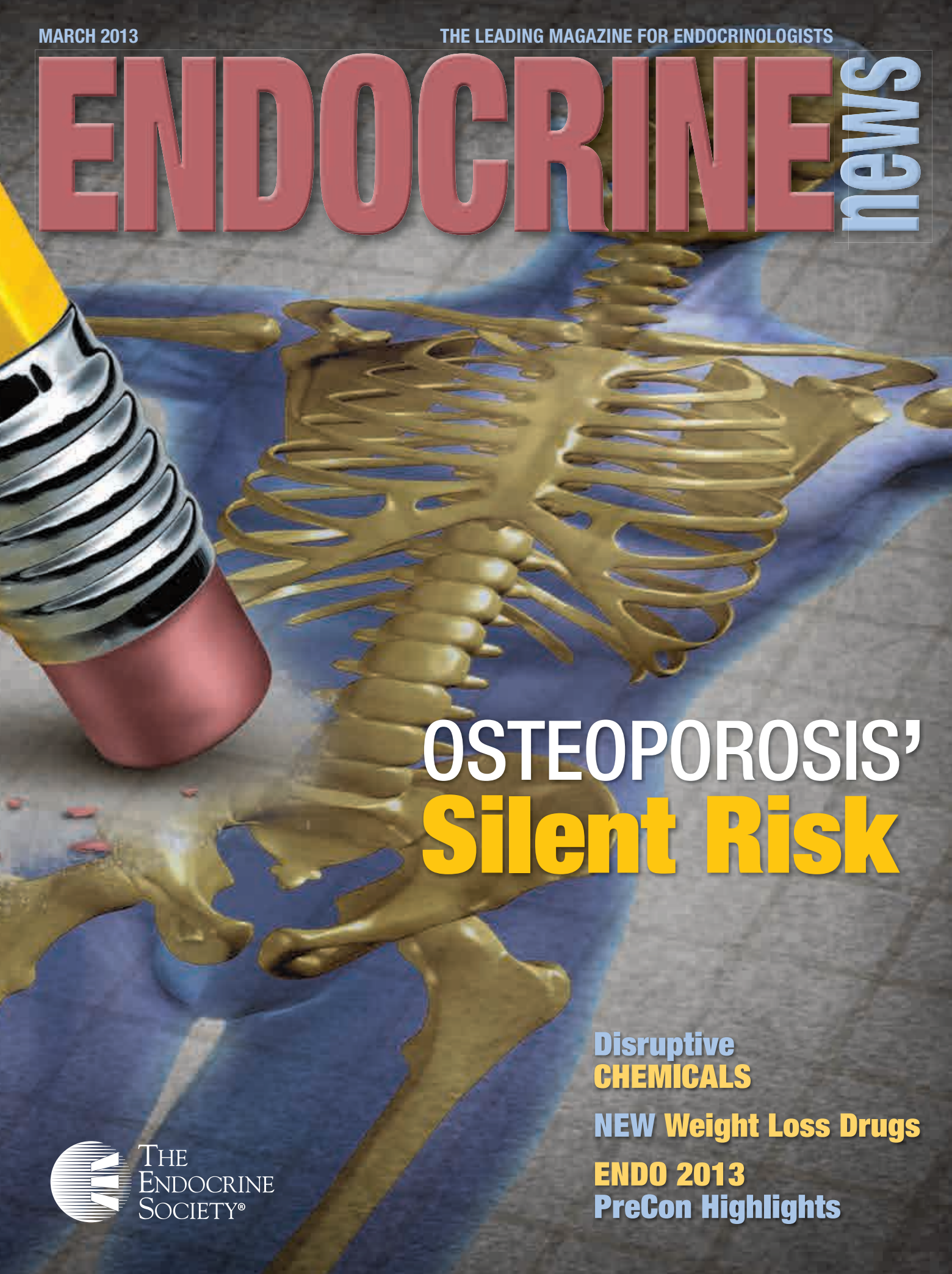
MARCH 2013

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

ENDOCRINE news



OSTEOPOROSIS' Silent Risk

Disruptive CHEMICALS

NEW Weight Loss Drugs

ENDO 2013 PreCon Highlights

The Endocrine Society®

SAVE $600 OR MORE

JOIN THE SOCIETY AND

SAVE $600 OR MORE

OFF THE NONMEMBER REGISTRATION FOR ENDO 2013.

- Discover the latest advances in endocrinology
- Present your research to a global audience
- Gain valuable practice management information
- Network with thousands of your colleagues

Join before you register to save $600 or more off the nonmember rate!

WWW.ENDO-SOCIETY.ORG/SAVE600

THE ENDOCRINE SOCIETY®

2014 Laureate Awards

CALL FOR NOMINATIONS

JANUARY – APRIL 12, 2013 (MIDNIGHT, EASTERN TIME)

- Fred Conrad Koch Award
- Robert H. Williams Distinguished Leadership Award
- Sidney H. Ingbar Distinguished Service Award
- Distinguished Educator Award
- Distinguished Physician Award
- Outstanding Clinical Practitioner Award
- International Excellence in Endocrinology Award
- Outstanding Achievement in Endocrine Science Award
- Edwin B. Astwood Award Lecture
- Gerald D. Aurbach Award Lecture
- Roy O. Greep Award Lecture
- Clinical Investigator Award Lecture
- Ernst Oppenheimer Award
- Richard E. Weitzman Memorial Award

Nominate Now – It's Easy!

NEW AWARD!

OUTSTANDING ACHIEVEMENT IN ENDOCRINE SCIENCE AWARD

Presented to a basic, clinical, or translational scientist for their outstanding recent research efforts (up to the past five-years) contributing to advances in the field of endocrinology.

Nominee must be a member of The Endocrine Society, domestic or international.

A simplified nomination form and useful resources make nominating easy. Learn more and begin nominating at www.endo-society.org/awards/LaureateAwards/Call-for-Nominations.cfm.

The Endocrine Society®

Awards will be presented at ENDO 2014: The 96th Annual Meeting & Expo in Chicago, Illnois | June 21–24, 2014.

COW 2013

7th Copenhagen Workshop on Endocrine Disrupters

Human environment, lifestyle and genes in endocrine disruption

Copenhagen, Denmark
May 28 - 31, 2013

MAIN TOPICS

- Effects of endocrine disrupters and lifestyle on reproduction
- Metabolic disease and environmental chemicals
- Human exposure
- The brain as a target for endocrine disruption
- Environment and epigenetic mechanisms
- Gene-environment interactions

www.reproduction.dk/cow2013

REGION H Rigshospitalet

GROWTH REPRODUCTION

GLOBAL EXCELLENCE IN HEALTH

VISIT ENDOEXPO

JUNE 15 – 17 | 10:30 AM – 4:00 PM DAILY | MOSCONE CENTER

ENDO*Expo* is the best place to have one-on-one conversations with exhibitors and receive insight that you just can't learn from a brochure or website.

ENJOY THE FUN AND INTERACTIVE ACTIVITIES THAT TAKE PLACE ON THE *EXPO* FLOOR.

- **ENDO Connect**
  Network with attendees and learn from technology experts. This is the perfect place to share data, discuss future collaborations, print CME certificates, and learn about new technology.
- **ENDO*Expo* Theater**
  The ENDO*Expo* Theater returns with exciting exhibitor presentations on products and services for endocrine physicians and scientists.
- **The Endocrine Society Booth**
  Get answers to your questions about the Society, including ENDO*Expo* activities, journals and publications, professional development opportunities, membership, and much more.
- **ENDO Store**
  A great place for convenient, one-stop shopping for the Society merchandise and clothing.
- **Posters**
  View scientific posters presented by your colleagues. You're guaranteed to find research of interest!

ENDOEXPO 2013

THE NEXT TIME YOU DISCUSS YOUR ENDO PLANS WITH FRIENDS AND COLLEAGUES, SUGGEST MEETING AT THE *EXPO*!

LEARN MORE AT WWW.ENDO-SOCIETY.ORG/ENDO2013

The Endocrine Society®

PATIENTS **EXPECT** HEALTH CARE PROVIDERS TO **KNOW** THE **BEST TREATMENT**

Optimize patient care with *The Endocrine Society's Clinical Practice Guidelines*. You can rely on the Society's evidence-based, high quality clinical practice guidelines to help improve both health care quality and health outcomes.

Recently published *Clinical Practice Guidelines* include:

Management of Hyperglycemia in Hospitalized Patients in Non-Critical Care Setting (January 2012)

Osteoporosis in Men (June 2012)

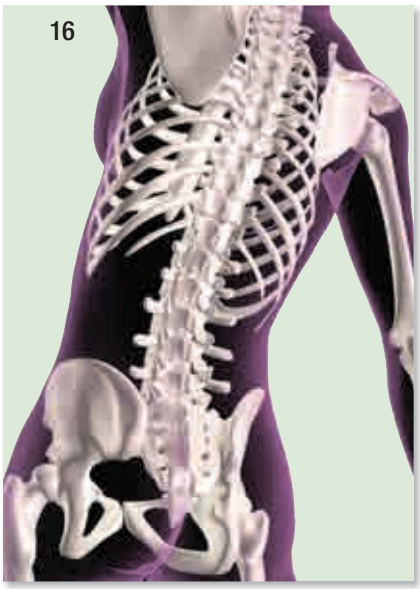
Management of Thyroid Dysfunction During Pregnancy and Postpartum (August 2012)

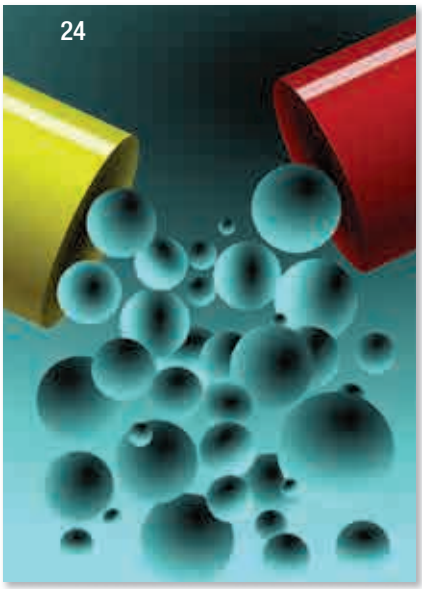
Evaluation and Treatment of Hypertriglyceridemia (September 2012)

PRICE PER TITLE: Nonmembers: $15 | Members: $10 | In-Training Members: $10

For more information or to view all *Clinical Practice Guidelines*, visit store.endo-society.org

THE ENDOCRINE SOCIETY®





COVER Story

DEPARTMENTS

THE ENDOCRINE SOCIETY®
www.endo-society.org

Scan this QR code with your smartphone or mobile device for **Endocrine News** Online.

Are You Enjoying the WEALTH OF BENEFITS Available to You?

William F. Young, Jr., MD, MSc

The Endocrine Society has some exciting enhancements to its publications program and important reminders of significant member benefits.

The Society's journals are some of our most important assets; they reflect growth and expansion and also reach a broad audience. The Society's publishing enterprise is constantly exploring and developing new ways to disseminate content that serves the membership and other audiences, including international ones. Our new digital strategy will further enhance the value of our publications for members, authors, and readers.

High-Tech Enhancements

To support the digital strategy, we've undertaken the following initiatives:

- **A full-text Endocrine Society journals App** for iPhone, iPad, and Android: More than 20,000 articles have been read since the app's launch last June. App usage is worldwide, with the highest activity in North America, South America, Europe, and Asia.
- **Mobile Web versions of the journals' websites,** launched last April: Members and subscribers can scan or review full-text content formatted to fit the screens of Apple, Android, and other devices. Any user can view article abstracts at no charge.
- **Subject microsites (m-sites) for the Society's journals**: M-sites are a class of journal websites created primarily to maximize discoverability of content and to drive traffic to the journal site. *JCEM's* Diabetes m-site will be the first of several sites to launch in the first quarter of 2013.
- **A Publication Hosting Platform:** Initiated in the third quarter of this year, the platform will not only offer competitive features and functionality (e.g., faster content searching) to members and subscribers, but will also enable the Society to realize new opportunities with digital scholarly content.
- **Endocrine Press:** Launching later this year, the Society's publishing imprint will serve as a platform for delivering authoritative and trusted knowledge to scientists, endocrinologists, primary care physicians, and allied health professionals. Content developed and published by Endocrine Press will be based on emerging needs of basic scientists and clinicians and will incorporate new online features and digital technologies.

Additional Membership Benefits

Most of us are aware of our access to world-renowned journals and registration discounts to ENDO. However, many other benefits are available to our members. Here are a few:

- **Advocacy:** The Society engages with the U.S. Congress and administration to advocate for matters important to endocrinologists, such as funding for research and physician reimbursement issues. We are well represented in the Federation of American Societies of Experimental Biology (FASEB) and in the American Medical Association's House of Delegates. Learn about these efforts at ***www.endo-society.or/advocacy.*** You can also contact Congress on pertinent issues at ***www.endo-society.org/congress.***
- **Journals:** Along with your access to the Society's peer-reviewed journals, members can view The Endocrine Legacy at ***www.endo-society.org/legacy.*** This comprehensive online archive includes all articles since each journal's inception (with the exception of articles published within one year of the most current issue). Members also save on page and color charges when they publish their work in our journals.
- **News & Literature:** Every week day you should receive the *Endocrine Daily Briefing*, a digest of the most important endocrinology-related news of the day. Each Friday the MedInfoNow email provides information on new books and journals in endocrinology.
- **Clinical Practice Guidelines:** Members can download free PDF copies of clinical practice guidelines at ***www.endo-society.org/guidelines,*** and print editions may be purchased at a discount. Members may also review and comment on guidelines before they are published.
- **Awards & Grants:** The Society provides more than 400 awards and grants per year, so be sure to visit ***www.endo-society.org/awards*** to learn more. Use EndoGrants Central, a database of funding opportunities, at ***www.endo-society.org/grants.***
- **EndoCareers:** Search the database or post an open position at ***www.endocareers.org.***
- **Mentor Exchange:** Access ***www.endo-society.org/mentor*** for advice from other members on a range of topics.
- **Affinity Partners:** From discounts with GEICO and Epocrates to a Society-themed credit card from Capital One, you have access to many useful products and services from select vendors. Learn more at ***www.endo-society.org/membership***

I hope you will make the most of your Society membership in 2013. If you have any comments or questions, please contact me at ***president@endo-society.org.***

William F. Young, Jr., MD,
President, The Endocrine Society

THE ENDOCRINE SOCIETY®

MARCH 2013

ENDOCRINE news

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

Endocrine News is a registered trademark owned by *The Endocrine Society*

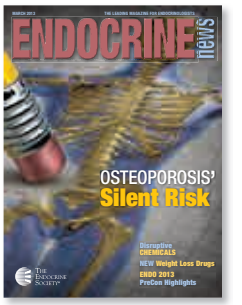
Endocrine News informs and engages the global endocrine community by delivering timely, accurate, and trusted content covering the practice, research, and profession of endocrinology.

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

Endocrine News® is published 12 times a year by The Endocrine Society, 8401 Connecticut Ave., Suite 900, Chevy Chase, MD 20815
Phone 301-941-0200 • Fax 301-941-0259
www.endo-society.org.

Print ISSN 2157-2089 Online ISSN 2157-2097

EDITOR'S PAGE



This issue takes a look at, among other topics, two very serious emerging health issues in endocrinology. Interestingly, prevention—as is the case with many health topics—is critical in both of these areas.

This issue's cover story looks at osteoporosis, a disease that affects 10 percent of women and two percent of men in the United States, but sadly, has remained well under the public radar. As Robert Recker, director of the Osteoporosis Research Center at Creighton University in Omaha, Nebraska, says: "The most important problem...is that the public, health professionals, and legislators do not recognize the extent of the problem. About 50 percent of all Caucasian women alive today will have a fracture due to osteoporosis before they die. Death rates from the fractures due to osteoporosis are greater than those from heart attacks, strokes, and breast cancer combined in women."

While pharmaceutical companies have made great headway in treating osteoporosis, the most important prevention and treatment of osteoporosis is likely to remain the same: diet and exercise. It's a common refrain for endocrinologists—whether treating osteoporosis, diabetes, or any other number of illnesses.

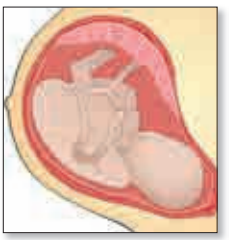
And, then there's an issue that all the diet and exercise can do little about—disruptive chemicals. Reading our article in this issue will give you pause—both for yourself and your patients. Bisphenol-A is just one of thousands of chemicals and compounds known as endocrine disruptors because of their potential to interfere with hormone action in animals and humans. These chemicals are used in everything from food cans and plastic water bottles to steering wheels and furniture. "Trying to avoid these chemicals is like trying to avoid breathing," R. Thomas Zoeller Ph.D., Professor of Biology at the University of Massachusetts at Amherst, tells *Endocrine News.* In this case, knowledge is power, especially for hormone-compromised patients.

This issue will give you plenty to think about. Enjoy.

Eleanore Tapscott
Senior Director of Publications

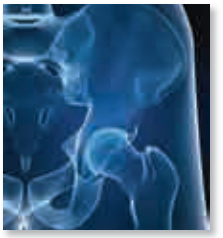
ENDOCRINE NEWS ONLINE EXCLUSIVES

The articles below are online only at ***www.endo-society.org/endo_news.***
See ***Endocrine News*** *Online* to read them and related links.



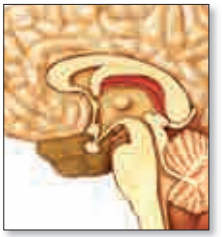
BPA Found in Fetal Livers

New data indicates BPA poses greater risk to fetuses, which cannot metabolize the compound as well as adults.



Bone Loss After Bariatric Surgery

Skeletal unloading and hyperparathyroidism play key roles in bone loss following bariatric surgery.



RNA-Binding Proteins and Puberty Start

Lin28b and its associated miRNA complex play a permissive role in the initiation of puberty.

Intermedin's Role in **FERTILITY**

Intermedin, a peptide expressed in many of the body's major organs, has been shown to have important benefits in establishing pregnancy. A new study seeks to discover how intermedin (IMD)—found in organs such as the gastrointestinal tract, lungs, placenta, uterus, and ovaries—is expressed during reproductive implantation.

Madhu Chauhan, PhD, led a team of investigators from the University of Texas at Galveston who examined human abortion tissues from 5–14 weeks pregnancies. The team reported finding the presence of IMD at day 5 after fertilization. IMD levels were significantly lower in the serum of pregnancies spontaneously aborted compared to electively aborted pregnancies.

In their article published in *The Journal of Clinical Endocrinology & Metabolism*, the authors say their study is the first to show a likely involvement of IMD in human embryo implantation and placental development via regulation of trophoblast invasion at the maternal-fetal interface. This suggests a physiological role for this novel peptide in establishment of human pregnancy, they added. The researchers also reported that treatment with IMD may have positive effects on the outcomes of assisted fertilization procedures and further improve the success rates of fresh embryo transfer.

—Glenda Fauntleroy

Gene Affects **FISH SEXUALITY**

A newly discovered gene could play a role in the ability of some fish to change their sex as adults. When researchers led by Kataaki Okubo, PhD, of the University of Tokyo screened for genes in the medaka, a member of the large teleost family, they discovered a new member of the heme-binding protein gene family that they named hepb3. Expressed in the meninges, the membrane enveloping the brain parenchyma, hepb3 is a transcriptional target of estrogens of ovarian origin. The expression of hepb3 appears to contribute to the development of sex differences in the teleost brain, the researchers write in *Endocrinology*.

—Eric Seaborg

GASTRIC BYPASS Device Aids in Diabetes Treatment

Obese patients with type 2 diabetes may have good results with a device used in gastric bypass surgeries, finds a study in *The Journal of Clinical Endocrinology & Metabolism*.

For one year, researchers evaluated 20 obese patients with diabetes who were implanted with a duodenal-jejunal bypass liner (DJBL). Participants all had a 10-year history of diabetes with hemoglobin A1c levels above 7.5 percent. At the end of study, patients lost an average of 6.5 kg and had significantly lower blood glucose levels.

The authors, led by Ricardo Cohen from the Center of Excellence of Metabolic and Bariatric Surgery in Brazil, concluded that the DJBL might represent an effective adjuvant to standard treatment of type 2 diabetes patients.

—Glenda Fauntleroy

Estrogen Mitigates Female Mid-Life **MEMORY LOSS**

Recently, scientists led by Jill M. Daniel, PhD, at Tulane University in New Orleans found that prior estradiol administration improved spatial memory in middle-aged rat dams and increased expression of the estrogen receptor a (ERa) in the hippocampus, but the impact duration was unknown. "Our data indicate that mid-life estrogen exposure can have positive impacts on memory and the hippocampus well beyond its period of exposure," Daniel says of the scientists' latest study.

In their paper, first published online in *Endocrinology*, the researchers report that ovariectomized dams treated with estradiol exhibited the expected enhancements in memory, as indicated by their better ability to navigate a maze 8 months postexposure, and hippocampal ERa expression compared to vehicle-treated controls. However, half of the hormone group was subsequently given the insulin-like growth factor-1 (IGF-1) receptor antagonist JB1, which disrupted the ERK/MAPK pathway necessary for activating IGF-1 and ERa receptors, with consequent decline in maze performance.

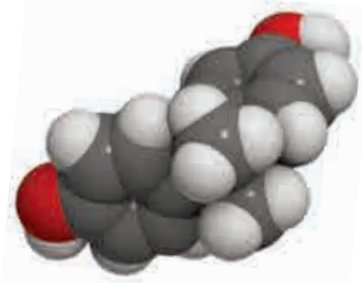
The researchers conclude that even short-term estrogen use during the "critical period" in recently menopausal women may confer long-term cognitive benefits. "Further, [our data] suggest that IGF-1, which can activate ERa via ligand-independent mechanisms, mediates the effects," adds Daniel.

—Kelly Horvath

BPA Found in **FETAL LIVERS**

A new study has found the ubiquitous chemical bisphenol A (BPA) in the liver tissue of fetuses, raising concerns that not only are fetuses exposed to this endocrine-disrupting chemical, but they lack the ability to metabolize and eliminate it as adults do.

BPA has been found in the urine of about 95 percent of the people who have been tested, but few studies have looked for it in tissues. Researchers led by Dana Dolinoy, PhD, of the University of Michigan School of Public Health in Ann Arbor,



examined the livers of 50 first- and second-trimester fetuses from a fetal tissue bank for a study that can be found online in *The Journal of Biochemical and Molecular Toxicology*.

The researchers detected no conjugated BPA in a pair of adult liver specimens used as controls, whereas more than 70 percent of the fetal liver samples contained it. The amount varied widely, with some fetuses showing high levels of exposure. The fetal livers contained free BPA at levels three times those of the conjugated form, a notable finding because free BPA normally represents only 10 to 30 percent of total BPA in adult urine samples. A potential explanation for the difference is that the fetal livers contained low levels of several enzymes responsible for metabolizing the chemical compared with adult livers.

Although BPA is hard to avoid given its widespread use in plastics and cans, its danger is sometimes downplayed because it is metabolized quickly. But this argument does not hold true in fetuses, according to Dolinoy.

The data indicates that BPA poses a greater risk to fetuses, which are unable to metabolize the compound as well as adults.

—Eric Seaborg

CORTISOL and **INTERFERON TAU** May Affect Pregnancy

The biological mechanics that occur in the uterus to support a fertilized egg during early pregnancy involve a complicated role of hormones, according to a new study.

Researchers investigated whether HSD11B1-derived cortisol has a biological role in endometrial function and embryo development during the early days of pregnancy in sheep.

In one of two separate experiments, for example, bred female sheep (ewes) were administered an inhibitor of HSD11B1 or recombinant ovine interferon tau at 10 to 14 days after being mated with fertile rams. The inhibition of HSD11B1 activity in the uterus was shown to prevent development of the embryo; however, interferon tau had a positive effect on embryo implantation in ewes that were administered prostaglandins.

"Our study provides novel insights into the biological roles of HSD11B1 and cortisol during early pregnancy," says study author Thomas Spencer, PhD, of the Department of Animal Sciences at Washington State University. In their article appearing in *Endocrinology*, the researchers conclude that interferon tau, prostaglandins, and cortisol together regulate endometrial functions crucial for the embryo development and implantation during early pregnancy in sheep.

—Glenda Fauntleroy

Teenage Girls Who Smoke Face Greater **OSTEOPOROSIS RISK**

Teenage girls who smoke accrue less bone during this critical growth period, which could raise their risk of osteoporosis later in life.

Researchers led by Lorah D. Dorn, Ph.D., of the Cincinnati Children's Hospital Medical Center, looked at that the effects of self-reported smoking, symptoms of depression and anxiety, and alcohol use on bone accrual in 262 healthy girls aged 11 to 19. The girls received three annual clinical exams where they were measured for total body bone mineral content and bone mineral density (BMD).

A higher rate of smoking was associated with lower bone accrual, with the greatest impact seen in the lumbar spine region and the hips, areas of particular concern in osteoporosis. Bone mass was essentially equal among participants at age 13, but the difference grew as the girls progressed through their teen years. By age 19, a heavy smoker had foregone the equivalent of a year of BMD gain compared with a nonsmoker.

Girls who reported depressive symptoms had lower lumbar spine BMD, but their total bone mineral content was not affected. The researchers called this effect worrisome because it occurred at sub-clinical levels of depression. Alcohol use had no effect on any bone outcomes.

Studies in adults have shown a link between smoking and decreased bone health, the researchers write in the *Journal of Adolescent Health,* but this is the first to draw the link in the critical adolescent period, when 50 percent of bone accural occurs.

—Eric Seaborg

Swap Sugary Soda for **COFFEE**

Substituting a cup of coffee for a sugar-sweetened soda could lower one's risk of diabetes, and caffeine doesn't appear to be the difference.

That conclusion comes from a study comparing the effects of caffeinated and caffeine-free forms of coffee, tea, sugar-sweetened beverages, and artificially sweetened beverages. A team led by Frank B. Hu, MD, MPH, PhD, of the Harvard School of Public Health, followed 75,000 women from the Nurses' Health Study and 39,000 men from the Health Professionals Follow-up Study to look for an association between self-reported beverage consumption and the development of type 2 diabetes.

After the researchers controlled for major lifestyle and dietary risk factors, they found a significantly greater risk of diabetes among subjects with a higher intake of sugar-sweetened beverages, with or without caffeine, in both groups. Coffee consumption, with or without caffeine, was associated with a lower diabetes risk in both groups. Despite some short-term metabolic studies that suggest caffeine increases blood glucose concentrations and decreases insulin sensitivity, the authors suggest in the *American Journal of Clinical Nutrition* that the association between sugary beverage consumption and diabetes is a result of sucrose and high--fructose corn syrup and not a joint effect of caffeine and sugar.

—Eric Seaborg

ROR Decrease Linked to **LIVER DISEASE**

Retinoid-related orphan receptors (RORs), intracellular transcription factors best known for their tissue development and circadian rhythm roles, are now the subject of a study suggesting a novel function. RORs negatively regulate SULT2A1 in rodents, but the mechanism remains unclear; moreover, their involvement with human SULT2A1 was unknown.

Wen Xie, MD, PhD, at the University of Pittsburgh School of Pharmacy, and his team used promoter reporter gene and electrophoretic mobility shift assays to demonstrate that RORs bind to ROR and constitutive androstane receptor (CAR) response elements found in the SULT2A1 gene promoter.

In their paper, to be published soon in *Molecular Endocrinology*, the researchers report a positive correlation between the expression of hydroxysteroid sulfotransferase (SULT2A1), an enzyme that detoxifies bile acids and deactivates androgens, and RORs in human livers, the converse of its negative regulation by RORs in rodents. The researchers conclude that SULT2A1 is a transcriptional target of ROR and CAR.

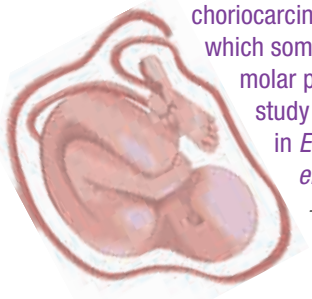
—Kelly Horvath

EDVs May Improve **PLACENTAL** Overgrowth Treatment

Ectopic and molar pregnancies, along with placental accrete are characterized by placental overgrowth. A new drug delivery system under investigation may provide more effective and less invasive treatments.

Researchers from the University of Melbourne reported the results of a proof of principle study testing the EnGeneIC delivery vehicle's (EDV) effectiveness in treating trophoblast growth on the placental surface. A proof of principle study occurs in the early stages of clinical drug development after a medication shows promising results in animals. Its purpose is to determine whether an investigation drug is active on a pathophysiological mechanism and works effectively.

In the current study, researchers discovered EDVs using a targeting antibody to pinpoint Epidermal Growth Factor Receptor on the placental surface provided a significantly greater uptake of the drug doxorubicin than the same system used without the targeted antibody or the drug used alone. Researchers are finalizing phase I studies where they note the drug is tolerated in humans. University of Melbourne Associate Professor Stephen Tong says it's conceivable researchers will soon be using the EDV system to deliver doxorubicin in drug trials to treat ectopic pregnancy, placenta accreta, and choriocarcinoma, the latter of which sometimes results from molar pregnancies. The study is to be published in *Endrocrinology [endo.endojournals.org].*



—Carol Bengle Gilbert

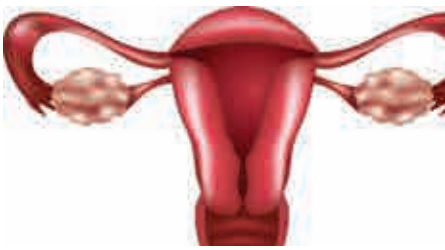
PCOS and the Brain

Polycystic ovarian syndrome (PCOS) affects more than 100 million women around the world and is a common cause of infertility and irregular menstrual cycles.

While the cause of PCOS is unknown, most women with the disorder show a significant increase in luteinizing hormone (LH) pulse frequency and decreased follicle stimulating hormone production, which is suggestive of increased gonadotropin-releasing hormone (GnRH) pulse frequency.

It is becoming increasingly clear that the syndrome may derive from altered regulation of reproduction by the brain," says study author Rebecca Campbell, PhD, of the University of Otago School of Medical Studies in New Zealand.

In their study published in *Endocrinology*, researchers aimed to determine the negative and positive feedback effects of estrogens on the



pituitary regulation of LH with the use of prenatal androgen (PNA)-treated mouse model of PCOS. Mice were administered estradiol and examined for hormonal changes and GnRH neuron activation. The study reported that PNA-treatment results in PCOS-like phenotype that included impaired estradiol negative feedback. Researchers "hope to be able to advance what little understanding we have about the neuroendocrine pathology of PCOS in order to shape novel therapeutic targets and preventative technology for the future treatment of PCOS," Campbell says.

—Glenda Fauntleroy

Adipokine Plays Role in Regulating **FOOD INTAKE**

The complex process of hormone signaling plays a key role in regulating food intake, and a new study points to a previously unsuspected role of plasminogen activator inhibitor 1 (PAI-1) in suppressing satiety signals from the upper gut.

PAI-1 is an adipokine that is present at higher levels in the plasma of obese individuals and in the stomachs of those infected with Helicobacter. It is known as the principal extracellular inhibitor of urokinase and tissue plasminogen activators, but its roles in gastric and metabolic functions have not been explored.

G.J. Dockray, PhD, and a team from the University of Liverpool in the U.K. used transgenic mice that overexpressed PAI-1 to look for the adipokine's effects on gut-brain signaling. In wild type mice, the signaling peptide cholecystokinin inhibited food intake, but the mice that overexpressed PAI-1 in gastric parietal cells were insensitive to its signals. Infecting mice with H. felis increased the gastric abundance of PAI-1 and reduced the satiating effects of cholecystokinin. PAI-1 also inhibited cholecystokinin activity in cultured vagal afferent neurons.

In an article awaiting publication in *Endocrinology*, the researchers say this evidence that PAI-1 suppresses food-intake signals suggests that the links between adipokines and the gastrointestinal tract are stronger than hitherto supposed.

—Eric Seaborg

FETAL GROWTH RESTRICTION Linked to High Glucocorticoid Exposure

While fetal growth restriction affects between 4 and 8 percent of all pregnancies and has been strongly associated with stillbirth and neonatal deaths, the condition's cause remains unknown.

In a new study published in *Endocrinology*, researchers examined whether increased exposure to glucocorticoids could play a role in fetal growth restriction by altering the fetus' chorionic plate arteries and contributing to the change in blood flow.

"Glucocorticoids have potent effects on the blood vessels in the placenta that deliver oxygen and nutrients to the baby," says author Rebecca Lee Jones, PhD, from the University of Manchester, United Kingdom. "These vessels constrict more following chronic exposure to glucocorticoids and this could contribute to the baby being growth restricted, due to reduced supply of nutrients to the baby."

The study's investigators examined placentas obtained soon after full-term vaginal and Caesarean deliveries and performed biopsies of the chorionic plates. They concluded that chronic exposure to elevated glucocorticoids did show increased vascular resistance.

Jones explained that women most at risk for chronic exposure to elevated glucocorticoids includes those who are stressed and will have raised levels of the stress hormone cortisol and women in threatened preterm labor who are given synthetic glucocorticoids to help to mature the premature baby's lungs.

—Glenda Fauntleroy

Gas6 Linked to **CHILDHOOD OBESITY**

In the context of alarming rises in worldwide childhood obesity and concomitant metabolic disorders, most notably type 2 diabetes mellitus, clues to obesity's pathogenesis are invaluable.

Fone-Ching Hsiao, MD, at the Taipei Medical University in Taiwan, led a team to follow the trail of one such clue. Growth arrest–specific 6 (Gas6), a vitamin K–dependent protein expressed widely in both immune and fat cells, has been shown to promote adipocyte survival in mice. Added to another clue that the presence of abundant immune cells within adipocytes corresponds with inflammation and insulin resistance, the researchers homed in on Gas6 as a potential mediator and determinant of adipocyte numbers, conducting a cross-sectional study of 832 Taiwanese adolescents, average age 13.3 years, grouped as lean, overweight, or obese.

In their paper, to be published soon in *The Journal of Clinical Endocrinology & Metabolism*, the researchers report that the overweight and obese groups had higher levels of circulating Gas6, which correlated positively with greater insulin resistance and circulating proinflammatory cytokine levels.

The researchers conclude for the first time that Gas6 plays a significant role in childhood obesity and its resulting disease-causing inflammation. Future studies should clarify this role and whether it is a causative one, they add.

—Kelly Horvath

Lower Fat Consumption Contributes to **WEIGHT LOSS**

When it comes to weight loss, all calories are not created equal. Lee Hooper, PhD, at the University of East Anglia, United Kingdom, and her team of scientists turn the "calories in, calories out" aphorism on its head in an attempt to once more determine the ideal proportion of dietary fat.

Commissioned by the World Health Organization Nutrition Guidance Expert Advisory Group, meta-analyses of 33 randomized controlled trials, in North America, Europe, and New Zealand involving 73,589 men, women, and children, consistently showed that without changing total energy intake but reducing the proportion of fat for at least 26 weeks resulted in average weight loss of 3.8 pounds, a .51 loss in BMI, and a reduction in waist circumference of .3 centimeters. In their paper, published in *British Medical Journal*, the researchers report that each one percent reduction in fat intake corresponds to 0.67 pounds lost; they also report lower total cholesterol and low-density lipoprotein levels, total/high-density lipoprotein ratio, and systolic and diastolic blood pressures.

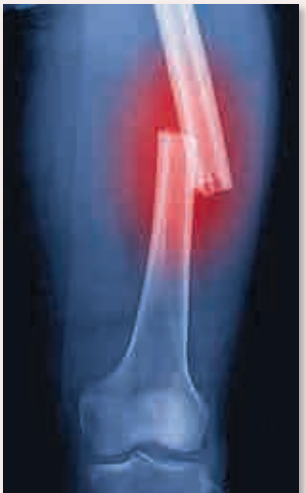
"The results prove for the first time that weight loss can happen without trying to lose weight simply by choosing foods lower in fat," says Hooper. Although the effect was the same regardless of type of fat, it makes sense to cut down primarily on saturated fat to also reap cardiovascular benefits along with weight loss, she adds.

—Kelly Horvath

Bisphosphonates Contribute to Atypical **FEMUR FRACTURE**

The debate continues: Does bisphosphonate use contribute to atypical, low-energy femoral fracture risk as studies have suggested, or are other risk factors more pertinent?

Nicola Napoli, MD, PhD, at the Università Campus Bio-Medico di Roma, Italy, and Washington University in St. Louis, led a team to find out. The team used Study of Osteoporotic Fractures data, which uniquely included prospective risk factor data prior to patients sustaining fractures. Using radiographic reports (rather than ICD codes), they identified 45 subtrochanteric/diaphyseal femur fractures out of a total of 1,722 hip and femur fractures among 9,704 women.



In their paper, to be published soon in *The Journal of Clinical Endocrinology & Metabolism*, the researchers report increasing age, positive diabetes mellitus status, and low hip bone mineral density as independent risk factors for atypical femoral fractures as well as a marginal risk increase among bisphosphonate users (9 of the 45 women who sustained atypical fractures), which corresponds with other study findings. However, because their study was limited to U.S. white women over age 65 years, results may differ among other groups. Incidentally, the researchers also found a positive correlation between femoral neck hip fractures and oral steroid use and a negative correlation between atypical femur fractures and oral estrogen use.

Although incidence of the atypical fractures compared to other hip fractures as well as overall bisphosphonate use (11.7%) was low, the researchers conclude that bisphosphonate use cannot be excluded as a risk factor. Future studies should clarify how bisphosphonate use interacts with preexisting risk factors to contribute to increased fracture incidence, they add.

—Kelly Horvath

PHPT More Symptomatic in China

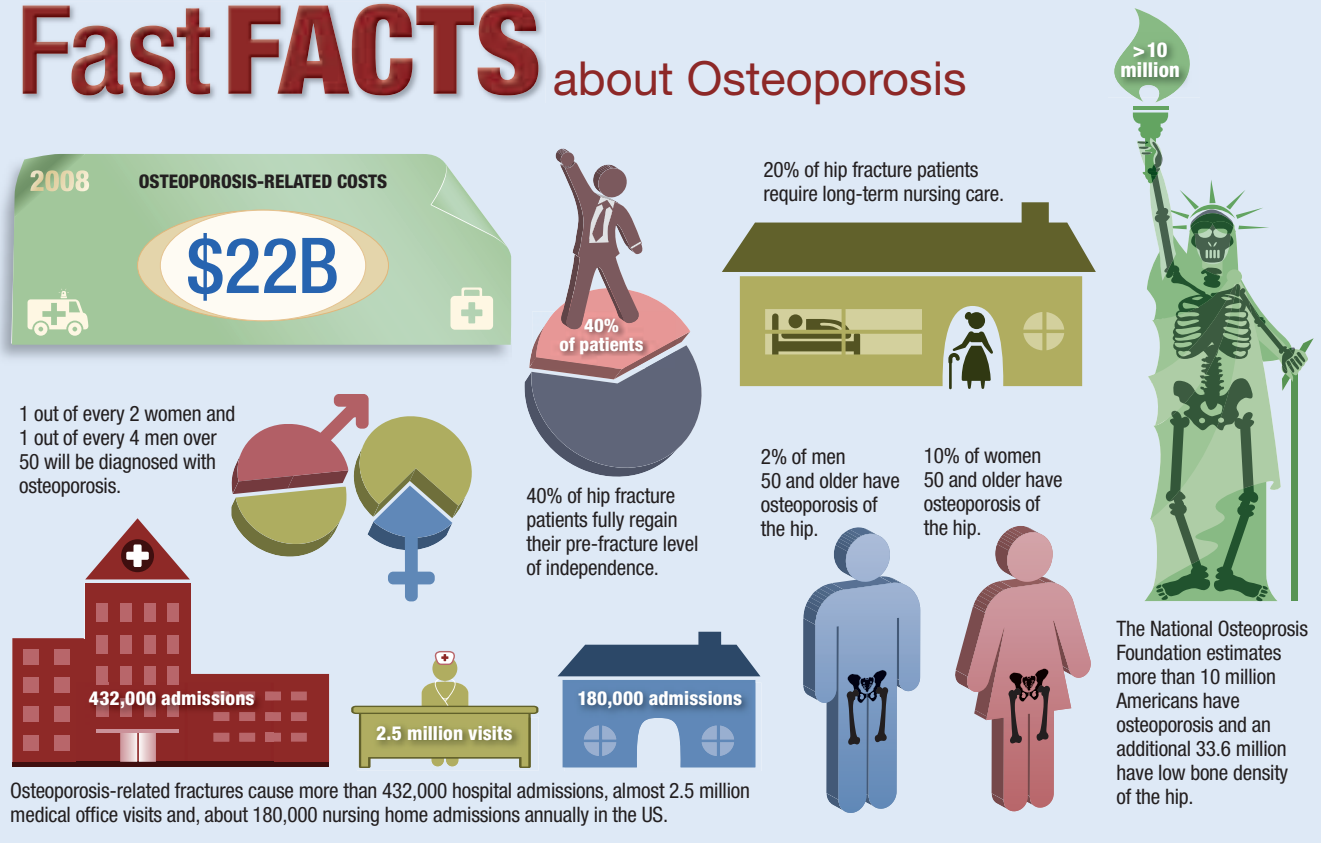
Primary hyperparathyroidism (PHPT), the third most common endocrinopathy in Western countries, is typically asymptomatic; however, in developing countries as recently as 1994, specifically China, it not only commonly presents acutely symptomatically but also with a different biochemical profile.

Jian-min Liu, PhD, at the Shanghai Jiao-tong University School of Medicine and the Shanghai Clinical Center for Endocrine and Metabolic Diseases, led a team of scientists to characterize any changes in the clinical picture of PHPT in Chinese patients visiting their clinic between 2000 and 2010 and determine what might contribute to symptom development.

In their paper, soon in *The Journal of Clinical Endocrinology & Metabolism*, the researchers report that both asymptomatic and total PHPT incidence increased and that serum calcium and parathyroid hormone (PTH) levels higher than 2.77 mmol/L and 316.3 pg/dl, respectively, cause clinical manifestations including polydipsia, polyuria, urolithiasis, bone pain, and fatigue. Parathyroid carcinoma has decreased from its peak of 5.96 percent of cases, which was the highest rate worldwide, and all of those patients were symptomatic with significantly higher PTH levels. Researchers conclude that PHPT in China is evolving clinically and biochemically, and they attribute the increase in diagnosis of asymptomatic PHPT to routine thyroid ultrasonography.

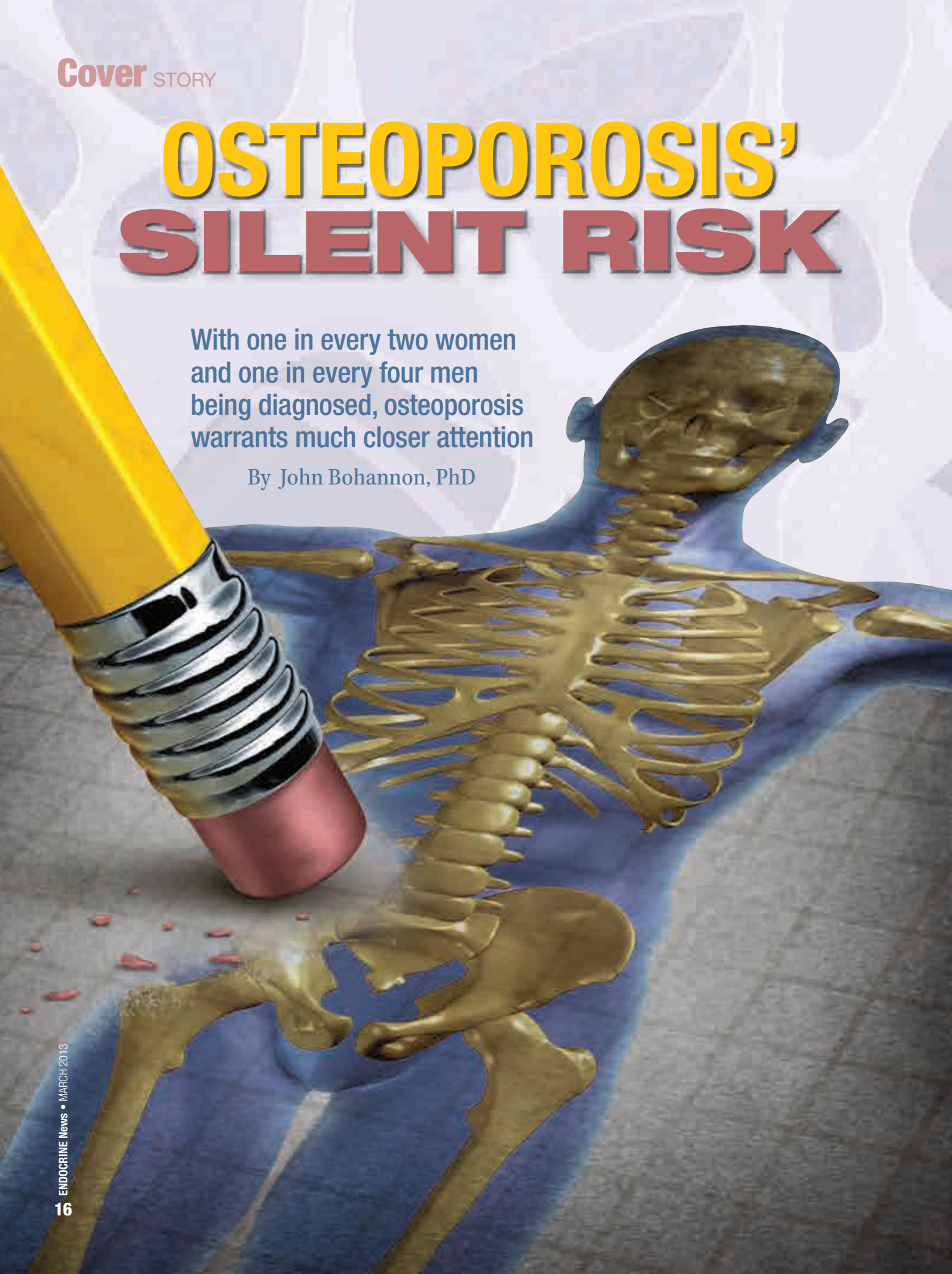
--Kelly Horvath

Fast FACTS about Osteoporosis



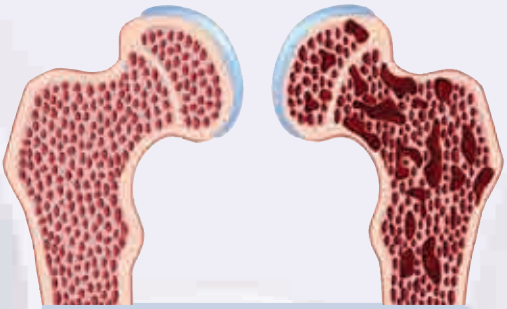
Sources: National Osteoporosis Foundation, CDC, and Osteoporosis International

OSTEOPOROSIS' SILENT RISK



With one in every two women and one in every four men being diagnosed, osteoporosis warrants much closer attention

By John Bohannon, PhD



CHANGES TO THE BONES
Osteoporosis changes the internal structure of bones, especially in the spongy matrix inside the ends of long bones, in the hips, and the spine. If left unchecked, large pores form in that matrix—hence the disease's name—making bone so fragile it can shatter with the slightest impact.

It took a while before Shelley Powers finally went to her doctor. She had experienced back pain before, but this felt different, and it had dragged on for months. She left that first visit none the wiser. X-rays showed nothing wrong. Her habits and environment hadn't changed in any way that would explain it. But after a few more doctor visits and discussions about her family history, a possible explanation emerged: osteoporosis.

It seemed outlandish to be diagnosed with a disease associated with old age. This was 7 years ago when Powers was 53. She has always been thin, active, and ruddy with health. Her doctor sent her to a specialist to get a DXA test (dual X-ray absorptiometry), which measures the mineral density of bone by subtracting out the X-ray absorption due to soft tissue. The lower the density, the more fragile the bone. Sure enough, her bone density was far below the typical value. "That confirmed it," says Powers. "And after that, I had to become very educated very quickly."

> "The most important problem...is that **the public, health professionals, and legislators do not recognize the extent of the problem."**
>
> *— Robert Recker, director of the Osteoporosis Research Center at Creighton University in Omaha, Nebraska*

The risks lying in her future were scary indeed. Osteoporosis changes the internal structure of bones, especially in the spongy matrix inside the ends of long bones, in the hips, and the spine. If left unchecked, large pores form in that matrix—hence the disease's name—making bone so fragile it can shatter with the slightest impact. The killer is a hip fracture. A quarter of osteoporosis patients who suffer a hip fracture die within 6 months due to complications.

The disease caught Powers by surprise, and she is not alone. "The most important problem... is that the public, health professionals, and legislators do not recognize the extent of the problem," says Robert Recker, director of the Osteoporosis Research Center at Creighton University in Omaha, Nebraska. "About 50 percent of all Caucasian women alive today will have a fracture due to osteoporosis before they die. Death rates from the fractures due to osteoporosis are greater than those from heart attacks, strokes, and breast cancer combined in women." And yet, until relatively recently, the disease was off the public health radar.

Restless Bones

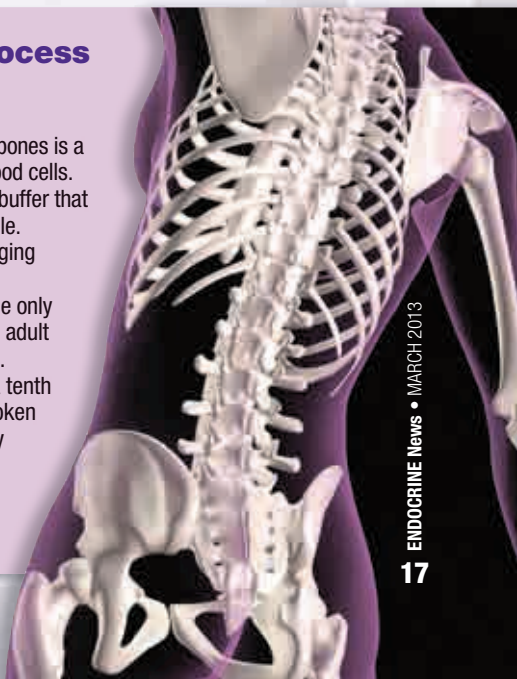
Bones are more complicated than they seem. The soft marrow inside of bones is a factory for making new blood cells. The hard mineral part is a buffer that keeps the pH of blood stable. And most surprisingly, bones are constantly changing themselves. The skeleton seems like the only permanent structure in the adult body, but that is an illusion. At any given time, about a tenth of bone tissue is being broken down and built back up by teams of cells, and all of this is finely tuned by the endocrine system.

Calcium is the big player in this story. Everything from muscle contraction to neuronal signaling requires calcium ions to function. The vast majority of one's calcium is locked up in hydroxyapatite, the crystals of calcium and phosphate that make bone hard. The remodeling cells are always poised on the surface of bones, waiting for molecular signals. When the concentration of calcium dissolved in the blood dips too low, cells called osteoclasts are triggered to break bone down to release minerals into the blood stream. Once blood calcium gets high enough, cells called osteoblasts are triggered. They grab calcium and phosphate from the bloodstream to rebuild bone.

In a healthy person, these negative feedback loops keep bone density and blood calcium levels steady. In osteoporosis, this homeostasis goes off kilter, causing bone to break down too quickly or rebuild too slowly.

Complicated Process INSIDE BONES

- The soft marrow inside of bones is a factory for making new blood cells.
- The hard mineral part is a buffer that keeps the pH of blood stable.
- Bones are constantly changing themselves.
- The skeleton seems like the only permanent structure in the adult body, but that is an illusion.
- At any given time, about a tenth of bone tissue is being broken down and built back up by teams of cells.
- It is all finely tuned by the endocrine system.



This is what makes a cure for the disease so elusive, says Recker. "Its cause is complex, involving both genetic and environmental factors." The ultimate problem, bone density, is controlled by a tangled endocrine circuit. The thyroid gland broadcasts a small polypeptide hormone called calcitonin that binds to osteoclast cells and slows down the rate of bone destruction. Balancing that signal, a gigantic polypeptide called parathyroid hormone (PTH) dials up the rate of bone breakdown. (To make matters more complex, the target of PTH is actually on the surface of the bone-building osteoblast cells, which then trigger their neighboring osteoclast cells with yet another signaling molecule.) Added to this are yet more layers of control, including the hormone estrogen, which decreases bone reabsorption and boosts bone formation. That is one reason why osteoporosis hits women around the same age as Powers. When estrogen levels plummet during menopause, a woman can start losing as much as 5 percent of her bone per year.

Treatment Approaches

Once Powers was diagnosed, there was no question that she would need medication immediately. "I just had so many risk factors," she says. She had a previous wrist fracture, she is petite—with thin bones to match—and has a family history of osteoporosis. "My father was diagnosed with it after he broke both hips and his spine." The question was, which meds would work for her?

The big guns in the osteoporosis pharmacy are the bisphosphonate drugs. The first to come on the market was Fosamax in the 1990s, and several others—Actonel, Boniva, Reclast—have followed. Bisphosphonates bind to bone and inhibit osteoclasts from breaking it down, but they can have nasty side effects. The drugs come as a pill that can cause ulcers in the esophagus. There is also a question about whether the drugs change bone structure for the worse over the long term, making unusual fractures of the thigh bone more likely. And some nasty litigation is underway, with patients claiming that the drugs have caused a deterioration of the jaw bone only seen in workers at match factories.

Rather than bisphosphonates, Powers' doctor started her on a relatively new drug called Forteo. It is actually a fragment of the PTH protein.

Which MEDS work

- **Fosamax, Actonel, Boniva, Reclast**
  Bisphosphonate drugs bind bone and inhibit osteoclasts from breaking down, but they can have nasty side effects.
- **Forteo**
  The new drug is actually a fragment of the PTH protein and can directly stimualte the formation of new bone, but NIH has warned that it should be a drug of last resort.
- **Zoledronic acid**
  A single dose of this type of bisphosphonate has been shown to dramatically decrease fracture risk—at least in rats.

AT-A-GLANCE:

- The big guns in the osteoporosis pharmacy are the bisphosphonate drugs.
- Forteo is the only osteoporosis med that can directly stimulate the formation of new bone.
- New treatments for osteoporosis are on the horizon.

There are some worrying indications from rat studies that it can increase risk for bone cancers. The NIH has warned that it should be considered a drug of last resort. But Forteo is also the only osteoporosis medication that can directly stimulate the formation of new bone. And new bone is what Powers needed. So in spite of the risks, she started the daily injections.

She's glad she did. "The pain was gone within a month," she says. "I may have had microfractures in my lower lumbar." The hormone could have reversed that crumbling. After 2 years of Forteo, she went on Fosamax.

New treatments for osteoporosis are on the horizon. A bisphosphonate that does not upset the gastrointestinal tract is being developed by Mission Pharmacal. And a study recently demonstrated that a single dose of a bisphosphonate called zoledronic acid can dramatically decrease fracture risk—at least in rats.

But the most important prevention and treatment of osteoporosis is likely to remain the same: diet and exercise. "I've been completely off meds for 2 years now," says Powers. She has a daily ritual of mineral water and yogurt for calcium and vitamin D, while Pilates and hiking in the California hills give her bones a healthy dose of stress.

In retrospect, Powers' back ache was the best thing that could have happened to her. "One out of every two women and one out of every four men over 50 will be diagnosed with osteoporosis," says Powers, and yet most will only find out after a severe fracture. She has become a board member of American Bone Health to help get the word out. "People need to get themselves screened. This disease is very preventable." EN

—Bohannon is a freelance writer in Boston and a regular contributor to Endocrine News.

ENO LINKS For additional links related to this feature, please visit Endocrine News Online at www.endo-society.org/endo_news.

The most important prevention and treatment of osteoporosis is likely to remain the same: **diet and exercise.**

THE V-Go® GIVES YOUR PATIENTS FREEDOM TO GO

For adults with Type 2 diabetes

The V-Go mimics the insulin pattern of the body by providing a continuous preset basal rate of insulin over 24 hours and on-demand bolus dosing at mealtimes.*[1]

Convenient and easy to use

The V-Go works with no electronics, batteries, infusion sets, or programming.

New co-pay assistance program

Patients pay no more than $25 (maximum benefit of $220) for each 30-day supply.

To learn more, speak to Valeritas Customer Care live 24/7 at 1-866-881-1209 or visit www.go-vgo.com/simple.

Important Risk Information: If regular adjustments or modifications to the basal rate of insulin are required in a 24-hour period, or if the amount of insulin used at meals requires adjustments of less than 2-Unit increments, use of the V-Go Disposable Insulin Delivery Device may result in hypoglycemia. The following conditions may occur during insulin therapy with the V-Go: hypoglycemia (low blood glucose) or hyperglycemia (high blood glucose). Other adverse reactions associated with V-Go use include skin irritation from the adhesive pad or infections at the infusion site. The V-Go should be removed before any magnetic resonance imaging (MRI) testing.

*If you follow the V-Go *Instructions for Patient Use.*

Reference: 1. Polonsky KS, et al. *N Engl J Med.* 1988;318:1231-1239.

valeritas

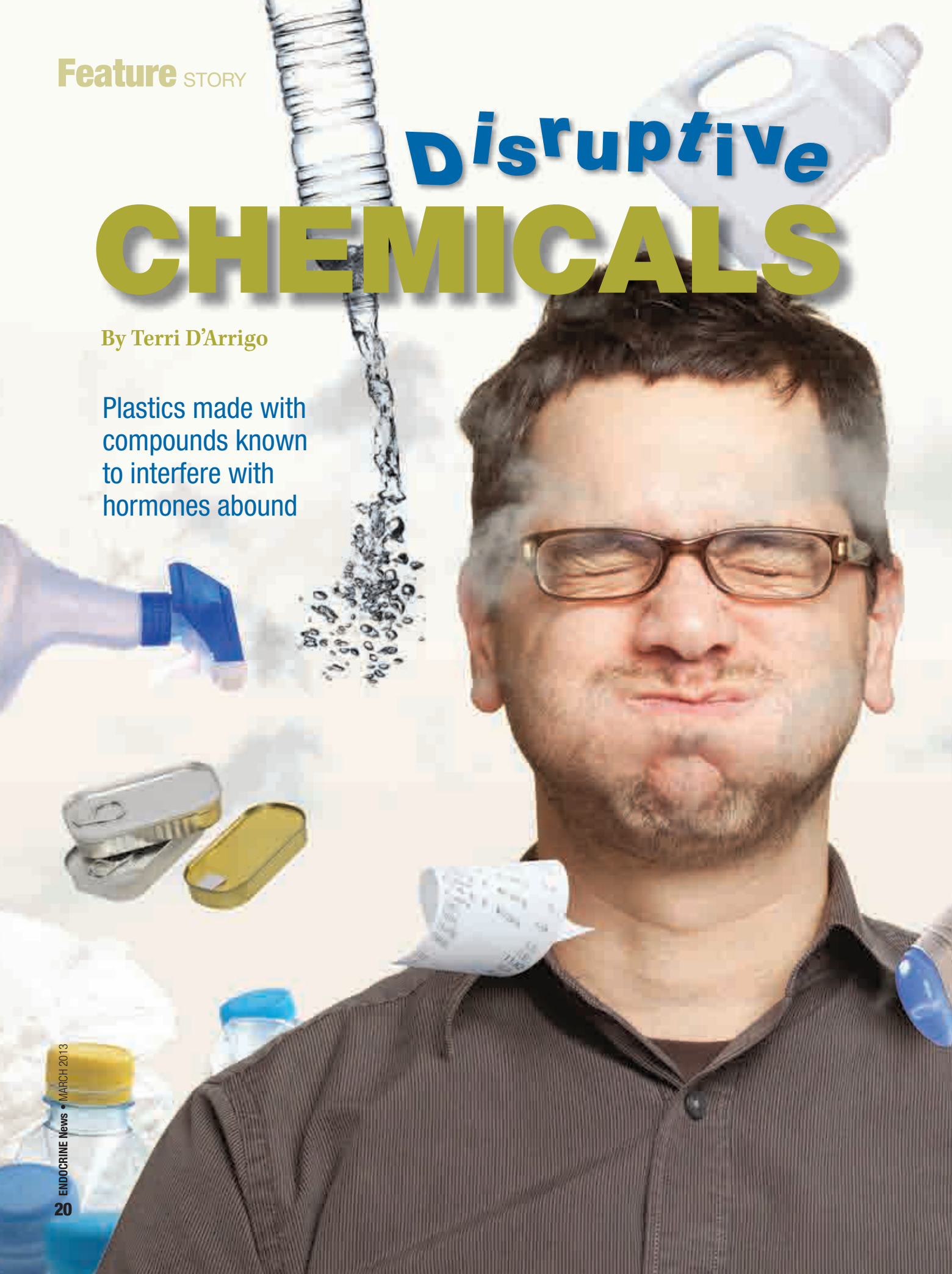
VGO® DISPOSABLE INSULIN DELIVERY
FREEDOM TO GO

ART-428 Rev: A 12/2012

Disruptive CHEMICALS

By Terri D'Arrigo

Plastics made with compounds known to interfere with hormones abound



AT-A-GLANCE:

- **Studies suggest an association between BPA and obesity, diabtes, heart disease, and more.**
- **Phthalates are anti-androgenic, working against male hormones.**
- **Studies suggest an association between prenatal and childhood exposure to PBDEs and poorer attention, decreased fine motor coordination, and lower IQ.**

In 2009, DelMonte canned green beans made headlines when *Consumer Reports* revealed they were among 18 other products found to contain the industrial chemical bisphenol-A (BPA) at levels known to be harmful to animals. A media brouhaha ensued, sparking renewed interest among consumers about what might be in their food that is not on the label.

Bisphenol-A is one of thousands of chemicals and compounds known as endocrine disruptors because of their potential to interfere with hormone action in animals and humans. These chemicals are used in everything from food cans and plastic water bottles to steering wheels and furniture. As the government sorts through the research to determine the fate of plastics containing endocrine disruptors, consumers are left to fend for themselves.

"Trying to avoid these chemicals is like trying to avoid breathing," says R. Thomas Zoeller, PhD, professor of biology at the University of Massachusetts at Amherst. "They're tough to pin down because manufacturers are not required to divulge what is in their plastics. Right now, industry is protected because they say that information is proprietary."

However, a familiarity with the most common endocrine disruptors and the products that often contain them can help consumers make better choices, he says.

Here's the lowdown:

BISPHENOL-A

Bisphenol-A mimics estrogen in the body. Animal studies suggest an association between BPA and obesity, diabetes, heart disease, immune dysfunction, and changes in reproductive organs. In 2008, the National Toxicology Program of the U.S. Department of Health and Human Services published a monograph expressing "some concern for effects on the brain, behavior, and prostate gland in fetuses, infants, and children at current human exposures to bisphenol-A."

Derived from petroleum, BPA is used in food packaging, plastic bottles, dental sealants, thermal paper used for cash register receipts, and other products. Approximately 6.4 billion pounds of BPA are produced throughout the world each year, and it's detectable in 90 percent of the population.

Buying products that are labeled BPA-free may help, but those products may contain bisphenol-S (BPS), an alternative that may be just as harmful, says Tracey Woodruff, PhD, MPH, professor and director of the Program on Reproductive Health and the Environment at the University of California–San Francisco.

"There hasn't been much testing for BPS, but what studies there are suggest that it, too, has endocrine-disturbing properties," Woodruff says. She adds that plastics manufacturers have thousands of alternatives from which to choose. "If they take out BPA, they'll just use the next thing on the shelf that may or may not have potential effects. No one is really sure what they're using in 'BPA-free' bottles."

Although it may seem hopeless to try to eliminate exposure to BPA, there are a few ways consumers can cut their exposure to it and other mem-

MAJOR OFFENDERS

- **BPA** is used in food packaging, plastic bottles, dental sealants, thermal paper used for cash register receipts, and other products.
- **Phthalates** are used in personal care products such as nail polish, deodorant, lotion, and shampoo; home décor such as flooring and shower curtains; insect repellant; hospital equipment such as tubing and IV bags; and car dashboards, steering wheels, and gearshifts.
- **Polybrominated diphenyl ethers (PBDEs)** are used as flame retardants in electronics, carpets, upholstery, and foam furniture.

bers of the bisphenol family, says Theo Colborn, PhD, president of the Endocrine Disruptor Exchange in Paonia, Colorado, and professor emeritus at the University of Florida–Gainesville. "Go back to buying foods in their raw state, and avoid buying products that are packaged. Shop the perimeter of the grocery store."

Frederick vom Saal, PhD, Curators' professor in the Division of Biological Sciences at the University of Missouri, notes that if consumers must use plastic containers, it is best to wash them by hand and to avoid using them in the microwave. "Heat breaks the bond that links BPA and polycarbonate, which frees the BPA to wreak havoc."

"Trying to avoid these chemicals is like trying to avoid breathing. They're tough to pin down because manufacturers are not required to divulge what is in their plastics. **Right now, industry is protected because they say that information is proprietary."**

— R. Thomas Zoeller, PhD, Professor of Biology University of Massachusetts at Amherst

PHTHALATES

Phthalates are nearly as common as BPA. They're used in personal care products such as nail polish, deodorant, lotion, and shampoo; home décor such as flooring and shower curtains; insect repellant; hospital equipment such as tubing and IV bags; and car dashboards, steering wheels, and gearshifts.

Phthalates are anti-androgenic, meaning they work against androgens, male hormones. A literature review published in the October 2008 issue of *Environmental Research* by Shanna Swan, PhD, of the University of Rochester's Department of Obstetrics and Gynecology, summarized the health outcomes associated with prenatal exposure to phthalates, such as asthma, eczema, and, in baby boys, partially descended testes. The review also noted low sperm count, DNA damage in sperm, decreased sperm motility, increased insulin resistance, and decreased levels of thyroid hormones in men.

Although it is nearly impossible to avoid exposure to phthalates from car interiors or hospital equipment, consumers would be wise to do their homework regarding personal care products, says Zoeller. "Anything you apply to your body is a drug delivery tool. Phthalates are fat soluble, and when you rub them on your skin, they will be absorbed."

Zoeller recommends visiting the Environmental Working Group's website (ewg.org), which contains a database of cosmetics and guides to various consumer products. He uses GoodGuide, a smartphone application that provides product ratings for health, environmental friendliness, and social responsibility when users scan in UPC symbols. Developed in part by Dara O'Rourke, PhD, associate professor in the Department of Environmental Science, Policy, and Management at the University of California–Berkeley, GoodGuide relies on research and other parameters to rank the products. Visitors to the website (goodguide.com) may search the product database as well.

Finally, vom Saal suggests avoiding plastics with recycling codes 3 and 7, which are more likely to contain BPA or phthalates.

POLYBROMINATED DIPHENYL ETHERS (PBDES)

Polybrominated diphenyl ethers (PBDEs) are used as flame retardants in electronics, carpets, upholstery, and foam furniture. As these products age and break down, PBDEs enter the environment via dust, where they are inhaled or ingested. A study published by researchers at the University of California–Berkeley in the November 15, 2012, issue of *Environmental Health Perspectives*, suggests an association between prenatal and childhood exposure to PBDEs and poorer attention, decreased fine motor coordination, and lower IQ in children.

"Flame retardants, namely PBDEs, are a hot topic because they are so widespread," says Woodruff. She likens their pervasiveness to that of polychlorinated biphenyls (PCBs), which were used in paints, plastics, rubber products, and industrial equipment until they were banned in the U.S. in 1979 for health and environmental reasons.

"There are indications that PBDEs, like PCBs, will hang around in the body for 20 years," Woodruff says.

OnPOINT from The Endocrine Society

In the September 2012 issue of *Endocrinology*, the Endocrine Society published a position statement asserting that the age when exposure occurs matters: Developing fetuses, infants, and children are especially vulnerable. The position statement summarizes the Society's suggestions for strengthening the EPA's Endocrine Disruptor Screening Program. View the abstract at *http://endo.endojournals.org/content/153/9/4097.abstract*.

"Now there is compelling evidence that they affect neurocognitive development. The effect on IQ is comparable to exposure to lead."

REGULATORY LIMBO

That endocrine disruptors are so common begs the question: What is the government doing about them?

The Environmental Protection Agency (EPA) launched the Endocrine Disruptor Screening Program in 1996, and the National Center for Toxicological Research at the Food and Drug Administration (FDA) maintains the Endocrine Disruptor Knowledge Base as a resource to help scientists develop computational predictive toxicology models as alternatives to animal testing, which is both expensive and time-consuming.

Yet despite the collective knowledge of researchers in both academia and government suggesting that many of these chemicals are more harmful than previously thought, the wheels of federal regulation turn slowly. For example, Canada banned BPA in baby bottles in 2007; the FDA did the same five years later, in July 2012—well after 11 states had already banned the substance in those proucts. This, after the agency declared in March 2012 that it found no convincing evidence to support the belief that BPA is a hazard to humans, and that it will continue to allow use of BPA in cans and other food packaging.

Some researchers feel they are waging an uphill battle. "We've been jousting with the FDA over their risk assessment process for years," says vom Saal, referring to scientists and endocrinologists across the field of endocrine disruptor research.

Vom Saal says that the FDA's methods assume that the effect of these chemicals depends on the dose, an approach that he says current research proves is outdated. Along with Zoeller, Colborn, and others, he co-authored a 78-page literature review published in the June 2012 issue of Endocrine Reviews that describes how low doses of endocrine disruptors may cause a disproportionate amount of harm compared to high doses.

"Over the past 60 years, [the field has] amassed enough knowledge that anyone who studies hormones knows that receptors are more sensitive to low doses, and that at high doses, you shut the cells' response system down," vom Saal says. "The FDA's approach is a century out of date, like using iron lung technology to treat polio."

In the September 2012 issue of *Endocrinology*, the Endocrine Society published a position statement asserting that the age when exposure occurs matters: Developing fetuses, infants, and children are especially vulnerable. The position statement, written by Zoeller, Woodruff, vom Saal, and others, summarizes the Society's suggestions for strengthening the EPA's Endocrine Disruptor Screening Program.

"What we were warned about before with endocrine disruptors pertained to much higher levels. Now we know that much lower levels can have bad effects," says Colburn. "We could go on collecting evidence for another 10 years, but when you get right down to it, the laws need to be changed." EN

—D'Arrigo is a health and science writer based in Holbrook, New York, and a regular contributor to Endocrine News.

Developing fetuses, infants, and children are especially vulnerable.

How to Reduce PBDE EXPOSURE

The Center for Environmental Research and Children's Health notes that consumers can reduce their exposure to PBDEs by repairing or replacing worn or torn furniture, mattresses, upholstery, or other foam products; using a damp mop or dust cloth to control household dust; and choosing baby products and furniture that contain polyester, down, wool, or cotton instead of foam.

TRACK PRODUCTS with an App

GoodGuide provides product ratings for health, environmental friendliness, and social responsibility when users scan in UPC symbols. GoodGuide relies on research and other parameters to rank the products. Visitors to the website (goodguide.com) may search the product database as well.

ENO LINKS For additional links related to this feature, please visit Endocrine News Online at www.endo-society.org/endo_news.

Help on the SCALE

First new weight-loss drugs in a decade offer new options but can't replace patient motivation in combating obesity

By Eric Seaborg

Two new weight-loss drugs that won Food and Drug Administration (FDA) approval for long-term use could provide important new weapons in the battle against obesity.

The drugs reflect a shift in the way physicians and regulators think of weight loss, from a cosmetic issue to the serious health threat of the obesity epidemic. The drugs could offer a middle ground for some patients between the invasiveness of bariatric surgery and the more modest successes of diet and exercise.

"There are a variety of responses to medications," says Daniel Bessesen, MD, chief of endocrinology at Denver Health Medical Center. "Some people don't lose much weight at all, but other people lose a lot of weight. So we are more and more thinking of weight-loss medicines as not having a fixed effect, but something that people could try and see if they have a really good benefit."

The new drugs could offer a turning point, says Donna Ryan, MD, professor emeritus at the Pennington Biomedical Research Center in Baton Rouge, Louisiana. "We are finally on the verge of understanding when to use the drugs, how to use the drugs, and how to develop safe and effective drugs," she says.

The two drugs are not radically new. Qsymia is a combination of two drugs already on the market—the appetite suppressant phentermine and an extended-release form of the anti-epileptic topiramate. Belviq, the brand name for lorcaserin hydrochloride, is a new formulation aimed at refining an old approach—suppressing appetite by activating serotonin receptors.

The drugs join orlistat as the only weight-loss drugs approved for long-term use. The FDA foresees patients who benefit from the new

drugs continuing on them indefinitely, as with statins or blood-pressure medications. Orlistat remains the only drug approved for weight loss in teenagers.

Just Part of the Recipe

The two approvals break a long drought with no new weight-loss drugs, and a period when more drugs left the market than joined it. In 1997, the drugs fenfluramine and dexfenfluramine were withdrawn because of evidence that they caused heart valve damage. Sibutramine left the market in 2010 amid concerns about an increased risk of heart attacks and strokes. The last addition to the market was in 1999, when the FDA approved orlistat, a lipase inhibitor designed to work by blocking fat absorption by the intestines.

Both Qsymia and lorcaserin are designed to be used in conjunction with a lifestyle intervention program emphasizing diet and exercise. For the drugs to work, the patient must be motivated, according to Ryan. "The drugs are intended to work through the biology of eating behavior, to reinforce your intention to eat less by promoting satiety and reducing hunger," she says.

And they are definitely not for cosmetic or casual weight loss. Both drugs are approved only for use in obese adults—those with a body mass index (BMI) of 30 or higher—or overweight adults with a BMI of at least 27 who have one or more weight-related condition such as hypertension, degenerative joint disease, type 2 diabetes, or dyslipidemia.

In clinical trials, after a year of treatment with the low-dose, starting formulation of Qsymia, patients lost an average of 6.7 percent of body weight more than with a placebo. With a higher daily dose, they lost 8.9 percent more body weight compared with a placebo. For lorcaserin, the average one-year weight loss was 3 percent to 3.7 percent greater than with a placebo, with 47 percent of patients meeting the FDA's minimum target of losing at least 5 percent of their body weight. Both drugs are also associated with favorable changes in other metabolic indicators such as blood pressure, high-density cholesterol, and waist circumference.

But the overall averages obscure how much some individuals benefit from the treatment. Qsymia was broadly effective—about 62 percent of patients on the lower dose and 69 percent on the higher dose lost more than 5 percent of their body weight. A sizable number of subjects experienced more than 10 percent weight loss, with some achieving 20 percent, which is approaching the range achieved through bariatric surgery, says Abraham Thomas, MD, MPH, head of the endocrinology, diabetes, bone, and mineral disorders division at Henry Ford Hospital in Detroit and chair of the FDA scientific advisory panel that recommended approval of both drugs.

FOR ADULTS ONLY

Qsymia and Belviq are definitely not for cosmetic or casual weight loss. Both drugs are approved only for use in obese adults—those with a BMI of 30 or higher—or overweight adults with a BMI of at least 27 who have one or more weight-related condition such as hypertension, degenerative joint disease, type 2 diabetes, or dyslipidemia.

A New Spin

Marketed by Vivus, Qsymia represents a fresh approach using established drugs. Phentermine has been in short-term use as an appetite suppressant since 1959. Topiramate is FDA-approved for use in epilepsy and migraine prevention, but has a history of off-label use for weight loss, although its mechanism of action is not known.

Qsymia incorporates the two in much lower doses than when each is used alone, in an attempt to synergize their results while reducing their side effects and allowing long-term use. The standard dose when phentermine is given as a single agent is 30 mg, compared with the recommended starting dose of 7.5 mg in Qsymia. The topiramate dose for migraine prophylaxis is up to 200 mg, compared with 42 mg in the starting dose of Qsymia. A higher dose formulation of Qsymia is also available with 15 mg of phentermine and 92 mg of topiramate.

Manufactured by Arena Pharmaceuticals, Belviq's mechanism of action—activating serotonin receptors to suppress appetite and make a patient feel full after eating a smaller amount of food—is reminiscent of fenfluramine, but lorcaserin is designed to work in a much more targeted fashion.

"Fenfluramine was a dirty drug. It hit all the serotonin receptors. This drug was developed to be very specific," Ryan says. Fenfluramine is believed to

LONG-TERM USE

Qsymia, Belviq, and **orlistat** are the only weight-loss drugs approved for long-term use. The FDA foresees patients who benefit from the new drugs continuing on them indefinitely, as with statins or blood-pressure medications. Orlistat remains the only drug approved for weight loss in teenagers.

AT-A-GLANCE:

- **The two drugs, Qsymia and Belviq, are not radically new.**
- **Both drugs are associated with favorable changes in blood pressure and cholesterol.**
- **Given the record of weight-loss medications, both drugs will face a high level of scrutiny.**

cause problems by attaching to the serotonin 2B receptors in heart valves. Lorcaserin is designed to be more selective, aimed at serotonin 2C receptors in the brain. It does not appear to activate the 2B receptors at the approved dose of 10 mg per day.

To allay concerns that it might activate this receptor, the manufacturer assessed the heart valve function through echocardiography of 8,000 patients during the clinical trials. Although there was some increase in valve abnormalities in the lorcaserin group, it was not statistically significant, and the FDA urges caution in using it in patients with congestive heart failure.

The FDA is requiring manufacturers of both Qsymia and Belviq to conduct several postmarketing studies, including long-term cardiovascular outcomes trials to assess effects on major events such as heart attack and stroke.

Trial and Error

Both Ryan and Bessesen noted that although lorcaserin did not lead to as much weight loss as Qsymia, the difference could be that lorcaserin is a single-agent drug, compared with the double-acting Qsymia. In the future, lorcaserin's effectiveness could possibly be improved by combining it with another agent, such as phentermine. But they discouraged clinicians from experimenting with such uses pending the publication of clinical data to support it.

"What we have learned in diseases like high blood pressure is that single medicines often don't do the job. If somebody is on a vasodilator for blood pressure then they will often hold on to salt and water, so they need to be on a second medicine, a diuretic to help with that," says Bessesen, who was part of the FDA panel that recommended approval of lorcaserin.

The three experts all made the comparison with blood pressure medications in terms of testing their effectiveness in a patient and continuing them if they work. The FDA recommends that if a patient does not lose 3 percent of body weight after 12 weeks on Qsymia, the drug should be discontinued or given at the higher dose to see if it can meet a target of a 5 percent loss in another 12 weeks. The FDA recommends discontinuing lorcaserin if it does not deliver a 5 percent loss after 12 weeks.

If it succeeds, the drug should be continued. "The modern view of obesity is that it is a chronic metabolic disorder, much like high blood pressure or high cholesterol," Bessesen says. "If you use a medicine for your blood pressure, it only works as long as you take it, because it doesn't fundamentally change your body. And I think that is how we see weight-loss medicines now."

Given the record of weight-loss medications, both drugs will face a high level of scrutiny. The FDA is requiring both manufacturers to conduct several postmarketing studies, including long-term cardiovascular outcomes trials to assess effects on major events such as heart attack and stroke. The European Medicines Agency rejected Qsymia for marketing in the European Union, although observers have ascribed this to internal politics and a wait-and-see attitude rather than genuine problems that the FDA missed. The agency has not yet ruled on lorcaserin.

Among its contraindications and side effects, Qsymia should not be used by patients with glaucoma or hyperthyroidism. It can increase heart rate, so is not recommended for patients with recent heart disease or stroke. Lorcaserin's side effects include serotonin syndrome, particularly if it is taken with another serotoninergic drug. It may cause disturbances in attention and memory. Neither Qsymia nor lorcaserin should be used during pregnancy.

Only time will tell how effective the new drugs will be under real-world conditions or how physicians will incorporate them into their practices. But as obesity rates continue to rise, they may offer a possible additional option, along with a new challenge for integrating them into treatment. EN

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

CONTRAINDICATIONS AND SIDE EFFECTS

QSYMIA

- Should not be used by patients with glaucoma or hyperthyroidism.
- Can increase heart rate, so is not recommended for patients with recent heart disease or stroke.
- Should not be used during pregnancy.

BELVIQ

- Side effects include serotonin syndrome, particularly if it is taken with another serotoninergic drug.
- May cause disturbances in attention and memory.
- Should not be used during pregnancy.

ENO LINKS For additional links related to this feature, please visit Endocrine News Online at www.endo-society.org/endo_news.

MYSTERIOUS HYPERLIPIDEMIA: A Case Study From ESAP

A 51-year-old man has had combined hyperlipidemia for years without cardiovascular complications. He has been treated with a variety of lipid-lowering agents, but is not taking any medication now. His mother also has a mixed dyslipidemia, with elevations of both triglycerides and LDL cholesterol, and had a stroke at age 71 years. His maternal uncle has combined hyperlipidemia and had a myocardial infarction at age 56 years. The patient's general health has been excellent, but he does not follow a diet nor does he exercise. He has not smoked cigarettes for the past 12 years.

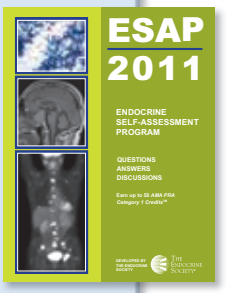
On physical examination, blood pressure is 138/84 mm Hg. He weighs 180 pounds and is 69 inches tall (BMI = 26.6 kg/m2). There are no xanthelasmas, xanthomas, or carotid bruits. You detect no hepatosplenomegaly. Peripheral pulses are full and equal without bruits.

Recent laboratory studies from his primary care physician's office include the following:

Analyte, mg/dL	Initial	8 Weeks of Gemfibrozil	16 Weeks of Gemfibrozil
Total cholesterol	224	247	242
Triglycerides	395	140	123
HDL cholesterol	35	45	42
LDL cholesterol	109	174	175

QUESTION

The Endocrine Self-Assessment Program (ESAP) is a self-study program aimed at physicians seeking certification or recertification in endocrinology, program directors interested in a testing and training instrument, and individuals simply wanting a self-assessment and a broad review of endocrinology. ESAP 2011 is available in both print and online formats. It consists of 160 multiple-choice questions in all areas of endocrinology, diabetes, and metabolism. There is extensive discussion of each correct answer, a comprehensive syllabus, and references. ESAP is updated annually with new questions and new syllabus materials. Learn more at *www.endocrineselfassessment.org.*



Which one of the following best explains the increase in the serum LDL-cholesterol concentration that has occurred over the past 4 months?

A Idiosyncratic response to gemfibrozil
B Common response to gemfibrozil
C Recent dietary indiscretion
D Progressive onset of hypothyroidism
E Development of hepatic steatosis

answer on page 30

MASTER CLINICIAN SESSIONS AT ENDO 2013: CALL FOR CASES

Do you have a particularly perplexing adrenal nodules, osteoporosis, or type 2 diabetes mellitus case? Interested in hearing expert analysis of your case? Submit your case for consideration for **ENDO 2013** by leading experts in these fields. Cases will be selected for presentation during the Master Clinician sessions based on their teaching value. To submit your cases, visit ***www.endo-society.org/endo2013/program-and-events.cfm.***

Master Clinican Sessions **CALENDAR**

TYPE 2 DIABETES MELLITUS
Saturday, June 15, 9:30-10:30 a.m.
Moderator: Om P. Ganda, MD, Harvard Medical School
Experts: David A. D'Alessio, MD, University of Cincinnati, and Helena W. Rodbard, MD, FACP, MACE, Endo Metabolic Associates

ADRENAL NODULES
Monday, June 17, 4-5 p.m.
Moderator: Richard J. Auchus, MD, PhD, University of Michigan
Experts: Massimo Terzolo, MD, University of Turin (Italy), and Baha M. Arafah, MD, Case Western Reserve University

OSTEOPOROSIS
Tuesday, June 18, 1:30-2:30 p.m.
Moderator: Robert A. Adler, MD, Virginia Commonwealth University School of Medicine
Experts: Richard Eastell, MBChB, MD, University of Sheffield (UK), and Michael R. McClung, MD, FACP, Oregon Osteoporosis Center

EndoCareers®


Dr. Aditi Bhargava

MENTOR SPOTLIGHT

Students, fellows, and early career professionals all have the opportunity to engage with the endocrine community via the Endocrine Society. Dr. Aditi Bhargava, Associate Professor in the Department of Surgery at the University of California San Francisco (UCSF) Center for the Neurobiology of Digestive Diseases, recently shared her perspective on engaging young people through mentoring and committee service. Bhargava, a dedicated mentor to students participating in the Society's early career programs, currently serves as a member of the Research Affairs Core Committee and previously served on the Minority Affairs Committee (MAC).

Q *How did you get started in The Endocrine Society and what advice do you have for young people wanting to get involved?* I got started by signing up to serve on the MAC at one of the Endocrine Society annual conferences. Instead of simply writing in my name, I specified why I was particularly interested in being part of the MAC. The rest is history. I would strongly recommend that students and fellows interested in committee service talk with other members who serve on the committees and with the Society staff. Both can provide invaluable suggestions that can help you decide which committee might be the best fit for you.

Q *What is your area of specialty and what initiated your interest in this area?* I specialize in the area of molecular neuroendocrinology. Molecular biology has always fascinated me, but understanding molecular mechanisms in the perspective of physiology is what makes molecular biology relevant. The work I started as a postdoctoral fellow in the laboratory of Drs. David Pearce and Mary Dallman at UCSF, that dealt with understanding the molecular actions of mineralocorticoid and glucocorticoid receptors in sodium homeostasis in the kidney and neuronal function in the brain, really caught my attention. It was fascinating to me as a molecular biologist, that acute activation of the stress hormones/axis could have protective effect in the short-term, but can be pretty detrimental to the cell's physiology in the long-term, if activated chronically.

Q *What have been some of the most rewarding and challenging moments of your career?* Research is my passion, so every time an experiment works, and we prove our hypothesis, those moments are always rewarding. The most rewarding was receiving the Quest Diagnostic Award for my presentation at the Endocrine Society and the Young Investigator Award from the American Physiological Society. The most challenging moment was establishing myself as an independent investigator and finding adequate funding for research. Unfortunately, as an early-mid-career investigator, this challenge still remains.

Q *What would you recommend to a student in search of a good mentor?* Talk to other mentees. Make sure that the mentor has the time for you and is willing to help. Sometimes, you may want to have more than one mentor—one for your career and the other for personal advancement.

Q *What specific Society programs would you recommend for young endocrinologists?* Get involved with the Trainee and Career Development Core Committee and participate in trainee and early career programs, both during the annual meeting and throughout the year. The Early Investigator Workshop in the fall is a great program for early career investigators. EN

CONGRATULATIONS FLARE WINNERS

The Endocrine Society would like to congratulate the winners of the FLARE Internship and FLARE Mentoring Network Travel Awards. These awards recognize the early achievements of young endocrine students and fellows and provide resources to help them expand their leadership skills through a year of service on Society governance committees or personalized mentoring. To see a list of these future endocrine leaders, and to learn more about the program, please visit ***www.endo-society.org/FLARE.***

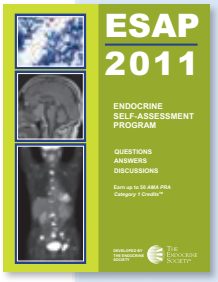
SAWIN LIBRARY MAKES BOOKS AVAILABLE FOR LOAN

Did you know that the Clark T. Sawin Memorial Library houses over 4,500 books, and many of them are available for loan to Society members free of charge? Search the library's online catalogue by visiting ***www.endo-society.org/about/sawin*** and request one of our thousands of books by contacting the Endocrine Society's librarian at ***librarian@endo-society.org***.

IN MEMORIAM

The Endocrine Society is saddened by the passing of members **Dr. John E. Jones** of Midlothian, Virginia, and **Dr. Erlio Gurpide** of Chester, Connecticut.

MYSTERIOUS HYPERLIPIDEMIA: A Case Study From ESAP



ANSWER

The Endocrine Self-Assessment Program (ESAP) is a self-study program aimed at physicians seeking certification or recertification in endocrinology, program directors interested in a testing and training instrument, and individuals simply wanting a self-assessment and a broad review of endocrinology. ESAP 2011 is available in both print and online formats. It consists of 160 multiple-choice questions in all areas of endocrinology, diabetes, and metabolism. There is extensive discussion of each correct answer, a comprehensive syllabus, and references. ESAP is updated annually with new questions and new syllabus materials. Learn more at *www.endocrineselfassessment.org.*

question on page 27

The answer is:
B. Common response to gemfibrozil

Analyte, mg/dL	Initial	8 Weeks of Gemfibrozil	16 Weeks of Gemfibrozil
Total cholesterol	224	247	242
Triglycerides	395	140	123
HDL cholesterol	35	45	42
LDL cholesterol	109	174	175

This patient has familial combined hyperlipidemia. In affected patients, fibrate therapy either increases or has no effect on the serum LDL-cholesterol level. Fibrates increase traffic through the lipolytic cascade with increased removal of triglyceride from VLDL. Since LDL particles are derived from VLDL that have been rid of most triglyceride, fibrate treatment in patients with hypertriglyceridemia often causes a rise in LDL cholesterol (Answer B); this is not an idiosyncratic response (Answer A). In contrast, fibrates modestly reduce the LDL-cholesterol concentration (by approximately 5%-15%) in patients with lesser elevations of triglyceride. The mechanism(s) for this has not been defined.

The increase in the serum LDL-cholesterol concentration caused by a fibrate can be a problem in patients with familial combined hyperlipidemia because they have an increased risk of coronary heart disease. Although this effect can be transient in some, many need the addition of a second medication to optimize their lipid profile. In contrast to fibrates, treatment of hypertriglyceridemic patients with nicotinic acid rarely increases serum LDL-cholesterol values. For this reason, niacin is a good choice for persons with familial combined hyperlipidemia.

The use of a statin in combination with gemfibrozil will correct the undesirably high serum LDL-cholesterol value that resulted from the gemfibrozil, as well as complement the changes in triglyceride and HDL-cholesterol levels produced by gemfibrozil. Despite the additive risks of myopathy in patients treated with gemfibrozil and a statin, the combination is generally safe and effective, especially when the statin is taken at lower dosages. Adverse events occur in approximately 3% of patients who take gemfibrozil, so the combination should be reserved for patients with, or who are at high risk for, coronary heart disease.

The likelihood that the patient developed intercurrent hypothyroidism (Answer D) over 16 weeks is remote. The patient has no obvious risk for hepatic steatosis (Answer E), and this condition is not typically related to an increase in LDL cholesterol. Dietary indiscretion (Answer C), with increased caloric and fat intake, would more typically affect triglycerides and account for no more than a 5% to 10% increase in LDL cholesterol.

Additional Resources:

For more information, see the following UpToDate topic review(s) in the ESAP program:
http://www.uptodate.com/contents/primary-disorders-of-ldl-cholesterol-metabolism?source=search_result&selectedTitle=1~150 EN

Society and AMA Work to IMPROVE DIABETES PREVENTION

The National Diabetes Prevention Program (NDPP) will soon ensure more people at risk for diabetes have access to programs to improve their health. A relationship between The Endocrine Society and the American Medical Association's (AMA) House of Delegates (HOD) allows the Society to advocate for policies that will benefit endocrinologists and their patients. Last November, AMA HOD unanimously adopted a resolution introduced by the Society calling for an expansion of NDPP.

The NDPP, a primary prevention program based on National Institutes of Health-sponsored research, can reduce a participant's chances of developing type 2 diabetes by 58 percent (average) through lifestyle and behavioral changes. Primarily provided through YMCAs across the country and covered by some major health insurers, NDPP was authorized through a provision in the Affordable Care Act, which required the U.S. Centers for Disease Control and Prevention (CDC) to establish rules and standards for participating organizations.

The resolution requires the AMA to:

- Support physician-prescribed evidence-based diabetes prevention programs;
- Support the expansion of the NDPP to more CDC-certified sites across the country; and
- Push for the program to become a Medicare benefit and be covered by all private insurers.

The Society's AMA HOD delegates—Susan Sherman, MD; Robert Vigersky, MD; Amanda Bell, MD; Daniel Spratt, MD, and Vineeth Mohan, MD—worked with delegates of the American Association of Clinical Endocrinologists (AACE) and American College of Preventive Medicine (ACPM), who co-sponsored the resolution, to ensure passage.

The Society will continue to work

The NDPP, a primary prevention program based on National Institutes of Health-sponsored research, **can reduce a participant's chances of developing type 2 diabetes by 58 percent (average) through lifestyle and behavioral changes.**

with its numerous partners, including the AMA, on this effort to ensure that those at risk for developing diabetes have access to the program.

Additional Resolutions

The Society also co-sponsored resolutions introduced by the ACPM and the American College of Physicians (ACP), both of which were adopted by the HOD. The ACPM's resolution called on the AMA to oppose the use of the Prevention and Public Health Fund for deficit reduction funding and to support its use solely for programs that advance prevention and public health initiatives. This fund, which is an important source of funding for programs such as the NDPP, has been targeted as a source of dollars to reduce the deficit.

The Society also co-sponsored the ACP's resolution focused on sequestration. The new policy calls on the AMA to work with Congress to develop a fiscally responsible alternative to prevent the automatic cuts that would endanger critical health programs.

Stronger Voice

Maintaining a seat in the AMA allows the Society to influence policy that will impact endocrinologists. Participation in the HOD has allowed the Society to gain support for policies related to bioidentical hormones, endocrine disrupting chemicals, generic drug bioequivalence, and access to diabetes testing supplies, to name a few.

This seat also allows the Society to have a voice at the AMA Resource Relative Value Scale Update Committee (RUC) and CPT Editorial Panel, which make recommendations to the Centers for Medicare and Medicaid Services related to payments for specific services.

In order to maintain its seat and continue working with the AMA to support important policy initiatives, the Society must have at least 1,000 members in the AMA before April 2013. All Society members who are eligible to join the AMA are encouraged to do so to ensure that endocrinologists' concerns continue to be heard at the national level. Visit ***www.ama-assn.org*** to learn about membership in AMA. EN

JOIN AND BE HEARD

Maintaining a seat in the AMA allows the Endocrine Society to influence policy that affects endocrinologists. This seat also allows the Society to have a voice at the AMA Resource Relative Scale Update Committee and CPT Editorial Panel, which make recommendations to CMS. To maintain its seat, the Society must have 1,000 members in the AMA before April 2013. To learn more and join the AMA, *visit* ***www.ama-assn.org.***

Secrets of EXOTIC LAB ANIMALS

By Melissa Mapes

Strange animals have long piqued the interest of scientists. About 2,000 years ago, Aristotle and Pliny the Elder wondered at the unusual sex characteristics of the spotted hyena. They noted the seemingly hermaphrodite genitalia of the females in addition to their larger size and general dominance over males. The reasons behind this "masculinization" of the female spotted hyena has perplexed scientists ever since. The creatures, which once roamed Europe, live in matriarchal clans in Sub-Saharan Africa and are the only mammals in existence in which the females lack an external vaginal opening. Instead, they urinate, copulate, and give birth through a pseudo-penis. No other species of hyena, of which there are four total in existence, has this bizarre genital apparatus.

SPOTTTED HYENA Scientific Interest

- Uncovering secrets of sexual development.
- Targeting specific areas of the thyroid for iodine therapy in hyperthyroidism.
- In fertility treatments, delivering drugs that stimulate the production of eggs for in vitro fertilization.

Interested in solving the long-standing mystery of the "masculinization" of female spotted hyenas and uncovering other secrets of sexual development, Dr. Steve Glickman of the Field Station of the University of California, Berkeley, and colleagues brought the spotted hyena to their 29-acre lab. The Field Station operates under the philosophy that animals are best studied in an area that closely resembles their natural environment. Space is a rare and expensive luxury in laboratories, making the Field Station an unusual and valuable commodity for researchers working with exotic animals like the hyena.

Hyenas and Sex Hormones

Glickman called upon Dr. Geoffrey Hammond of the Child and Family Research Institute in Vancouver, British Columbia, to investigate how exposure to sex steroids may be responsible for the spotted hyena's urogenital and social characteristics. Hammond suggested taking samples from all the hyena species to see how genetically similar they are. The team then compared sex-hormone binding globulin (SHBG) gene sequences, structures, and steroid-binding properties among the four types of hyena. They found that the spotted hyena has a very unique dilution of nine nucleotides that are responsible for coding proteins in a signal secretion polypeptide. The spotted hyena lacked three residues that were present in all other hyena species, thus producing abnormally low SHBG at five to 10 times less than the other species and causing the amounts of free androgen and free estrogen to be much elevated. The researchers concluded that this abnormality likely influences the masculinization of the female spotted hyena.

Spotted Hyenas live in matriarchal clans in Sub-Saharan Africa and are **the only mammals in existence in which the females lack an external vaginal opening.** Instead, they urinate, copulate, and give birth through a pseudo-penis.

Hammond had never worked with hyenas prior to the experiment, but came away believing that the Field Station and Glickman's work have much to contribute to the world of science, especially sexual development. "The hyena project is in some jeopardy due to the funding scenario, but is really important at this particular point in time," he explains.

The 10,000 genomes project is sequencing the spotted hyena, and likely the oddwolf genome, which will open many doors for further research. Hammond anticipates the results of the sequencing to be available within a year.

"When we performed our genetic analysis, it was very clear to us that the identity at the genetic level between these four species of hyenas that look and behave very differently is almost the same as between us and chimpanzees. And yet it's the only one that has this very strange phenotype. When we have these genome sequences available to us, we will be able to pinpoint the genetic differences between them."

Tree Shrews and Sleep Research

The unique characteristics of exotic species offer some advantages for endocrinology research that regular lab rats and mice cannot replicate. In addition to the sex hormone scenario presented by the spotted hyena, tree shrews have proven to be an ideal candidate for neurobiology studies and other topics. These rodents are actually close relatives of primates and have the largest brain-to-body mass ratio of all mammals. They operate as a suitable, and much smaller, replacement for chimpanzees and other primates in a laboratory environment.

Tree shrews are actually close relatives of primates and **have the largest brain-to-body mass ratio of all mammals.**

TREE SHREW Scientific Interest

- Sleep-related issues in tree shrews may offer insight into the same sleep factors for humans.
- Increasing number of studies are looking at the genetic similarities to humans.
- Tree shrews' ability to function with high levels of blood alcohol may introduce a better way to treat alcohol poisoning in humans.

Dr. Eberhard Fuchs of the German Primate Center's Clinical Neurobiology Laboratory and Professor at the Medical School of the University of Göttingen first came in contact with tree shrews while studying biology and sociology at the University of Munich.

"It was the time when the stress paradigm of tree shrews was being developed by Achim Raab," he explains. "They were looking for mammals that demonstrated strong territorial behavior." From these initial studies, researchers found that the tree shrew worked quite well for sociological and neurobiological studies. Now, Fuchs is publishing articles on the results of sleep disruption and other sleep-related issues in tree shrews, which may offer insight into the same sleep factors for humans.

One key to the tree shrew's importance, according to Fuchs, is its exclusively day-active nature. He describes the creature as "an excellent model for sleep research." Many of his past studies have also focused on stress and depression because tree shrews can demonstrate symptoms very similar to that of a depressed person. By administering various antidepressants, he found that the animals respond quite well to certain medications. Other rodents are usually unsuitable for such research.

Although tree shrews take up more space than mice and are therefore more expensive, Fuchs says that the institute's directors have been very supportive of his projects. The close genetic relationship to primates and comparatively small size make tree shrews a perfect compromise for such experiments. "They share very many similarities to primates, and an increasing number of studies are looking at the genetic similarities between humans and tree shrews. They have very well developed brains, and so for psychopathology studies in particular, they are ideal animals instead of mice or rats." Other areas of study for tree shrews have included myopia and hepatitis.

Fuchs is currently seeking other locations in Europe that are interested in exploring research with these animals, but the appeal of the tree shrew has already extended its reach to Canada. Dr. Marc-André Lachance, a microbiologist from the University of Western Ontario, examined the Malaysian pen-tailed tree shrew's special ability to metabolize massive amounts of alcohol. The animals live exclusively on fermented nectar that contains up to 3.8 percent alcohol.

Tree shrews with several times the legal limit of blood alcohol levels appear to have no signs of intoxication. Dr. Lachance hopes that this mystery, once solved, may introduce a better way to treat alcohol poisoning in humans.

While exotic animals are unlikely to become standard practice, innovative scientists may find great success by choosing a creature specially suited to their topic area. Working with a bone-crushing carnivore like the spotted hyena may present unique challenges but also unique benefits that can be found in no other animal. The obstacles of space and funding are ever present, but not insurmountable, as experts like Glickman and Fuchs have demonstrated. Additionally, Hammond is optimistic that the mapping of genomes will help unlock the secrets of animals like the spotted hyena. "We might even be able to explain a phenomenon that has been around since Aristotle described it in Ancient Greece," he says. EN

While exotic animals are unlikely to become standard practice, **innovative scientists may find great success by choosing a creature specially suited to their topic area.**

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

ENO LINKS For additional links related to this feature, please visit Endocrine News Online at www.endo-society.org/endo_news.

FACT SHEET

Hormone Health NETWORK
Keep your body in balance

Radioactive Iodine Treatment for Hyperthyroidism

WHAT IS HYPERTHYROIDISM?

The thyroid gland, located at the front of your neck, makes hormones that control your metabolism—the way your body uses energy. Hyperthyroidism, also called overactive thyroid, occurs when your thyroid gland makes too much thyroid hormone. Too much thyroid hormone speeds up many of the body's functions. If untreated, an overactive thyroid can lead to other health concerns, such as heart problems.

The main cause of hyperthyroidism is Graves' disease, in which the immune system attacks the thyroid. Less often, hyperthyroidism occurs when the thyroid has one or more nodules (lumps) that make too much thyroid hormone.

DID YOU KNOW?

Radioactive iodine is a generally safe treatment that can cure hyperthyroidism (overactive thyroid gland).

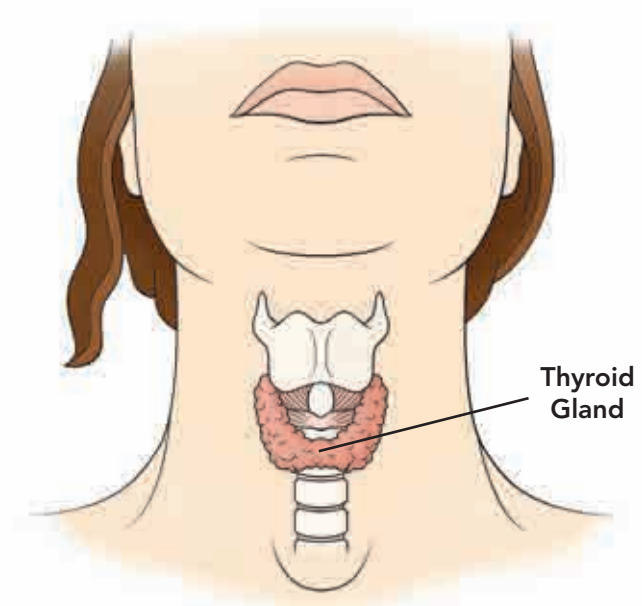
WHAT IS THE TREATMENT OF HYPERTHYROIDISM?

The goal of treatment is to lower the amount of thyroid hormones. Treatment options include

- **Radioactive iodine (RAI).** Also called radioiodine, RAI is a common and long-used treatment for hyperthyroidism.
- **Surgery.** This removes the thyroid gland (called thyroidectomy).
- **Antithyroid drugs.** These medicines are given for months or even years. Sometimes people take them to prepare for RAI or surgery.

HOW DOES RADIOACTIVE IODINE TREATMENT WORK?

Iodine is important for making thyroid hormones. Just as the thyroid naturally collects iodine from the foods we eat, it does the same with RAI. Because RAI has a small amount of radiation, it destroys thyroid cells. Afterward, the gland no longer makes as much thyroid hormone. RAI rarely affects other parts of the body.



RAI, also called iodine 131 (I-131), is given as a single-dose capsule or liquid. Most often, you will not need a hospital stay. It can take 6 to 18 weeks or more to get the full effects of RAI treatment. During this time, you may need antithyroid drugs.

WHO SHOULD NOT USE RAI?

For safety reasons, these people should not get RAI treatment:

- Pregnant and breastfeeding women or those planning to become pregnant in the next six months
- People who cannot follow radiation safety precautions
- Young children who haven't tried other treatment options first
- Some people with active Graves' ophthalmopathy (thyroid eye disease)

CAN I HAVE RAI TREATMENT IF I AM ALLERGIC TO SHELLFISH?

It is a myth that people who are allergic to shellfish will have an allergic reaction to a small dose of iodine. Even among people who are allergic to the radiocontrast dye in some imaging tests, most are not allergic to RAI.

HOW SHOULD I PREPARE FOR RAI?

If you are taking antithyroid drugs, stop them five to seven days before treatment. Do not stop taking beta blockers (drugs such as atenolol) if your doctor has prescribed them.

Avoid drugs and foods that are high in iodine for as long as your doctor instructs. Foods high in iodine include iodized salt, seaweed and other seafood, and dairy products. Multivitamins often contain iodine, so check the labels.

Some radiation stays in your body for a few days after RAI treatment. Your health care provider will give you a list of precautions to take after treatment to minimize others' exposure to the radiation.

Follow these safety measures after RAI treatment:

- Sleep in a separate bed (more than six feet away) from other adults for three or more days after treatment. Sleep apart from children and pregnant women for two weeks or longer.
- In daytime, keep more than six feet away from children and pregnant women for at least one day.
- Avoid prolonged time in public places or transportation (planes, trains, buses) for at least three days. Do *not* stay in a hotel or motel right after treatment.

WHAT ARE THE SIDE EFFECTS OF RAI?

RAI is generally safe. Sometimes neck pain can result. Yet, this does not last long, and pain medicine can help relieve the discomfort.

Most people will have hypothyroidism (underactive thyroid) after treatment. This shortage of thyroid hormones may be temporary but often is lifelong. It is easily treated, though, with synthetic (manmade) thyroid hormone.

The risk of thyroid cancer does not seem to increase in patients who receive RAI.

IS RAI TREATMENT A CURE?

In most patients, the first RAI treatment cures hyperthyroidism. Some, however, will need a second RAI treatment.

Questions to ask your doctor

- **What are the pros and cons of RAI compared with other treatments?**
- **How long should I stay on a low-iodine diet before RAI treatment?**
- **What side effects will I have?**
- **When may I return to work after RAI treatment?**
- **After treatment, how long should I avoid close contact with my family members and pets?**

RESOURCES

- Find-an-Endocrinologist: *www.hormone.org* or call *1-800-HORMONE (1-800-467-6663)*
- Hormone Foundation information about hyperthyroidism: *www.hormone.org* (search for hyperthyroidism)
- National Endocrine and Metabolic Diseases Information Service (National Institutes of Health): *www.endocrine.niddk.nih.gov*
- American Thyroid Association: *www.thyroid.org/patients*

EDITORS

Bryan Haugen, MD
James V. Hennessey, MD
Leonard Wartofsky, MD

April 2012

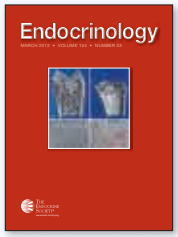
The following studies will be published in Endocrine Society journals. Before print, they are edited and posted online, in each journal's Early Release section. You can access the journals via ***www.endo-society.org.***

Theca cell–derived BMP4 and BMP7 down-regulate Cx43 expression and decrease GJIC activity in human granulosa cells. This biological effect is most likely mediated by a Smad-dependent pathway. Chang, Hsun-Ming; Cheng, Jung-Chien; Leung, Peter C.K. *Theca-Derived BMP4 and BMP7 Down-Regulate Connexin43 Expression and Decrease Gap Junction Intercellular Communication Activity in Immortalized Human Granulosa Cells.*

Osteocalcin level might be an independent indicator of cardiovascular risk and global health in elderly Caucasian men. Confavreux, Cyrille B.; Szulc, Pawel; Casey, Romain; Boutroy, Stéphanie; Varennes, Annie; Vilayphiou, Nicolas; Goudable, Joelle; Chapurlat, Roland D. *Higher Serum Osteocalcin Is Associated With Lower Abdominal Aortic Calcification Progression and Longer 10-Year Survival in Elderly Men of the MINOS Cohort.*

Women with PCOS have higher global adiposity and increased amounts of visceral adipose tissue compared with control women, especially in the ip and mesenteric depots. Borruel, Susana; Fernández-Durán, Elena; Alpañés, Macarena; Martí, David; Álvarez-Blasco, Francisco; Luque-Ramírez, Manuel; Escobar-Morreale, Héctor F. *Global Adiposity and Thickness of Intraperitoneal and Mesenteric Adipose Tissue Depots Are Increased in Women With Polycystic Ovary Syndrome (PCOS).*

KLLN might be used as a potential prognostic marker for risk management and as a novel therapy target for advanced prostate carcinomas. Wang, Yu; Radhakrishnan, Deepa; He, Xin; Peehl, Donna M.; Eng, Charis. *Transcription Factor KLLN Inhibits Tumor Growth by AR Suppression, Induces Apoptosis by TP53/TP73 Stimulation in Prostate Carcinomas, and Correlates With Cellular Differentiation.*



Mig6 may be a novel target for preventing glucocorticoid-induced impairments in functional ß-cell mass. Holloway, Kimberly R.; Barbieri, Andreia; Malyarchuk, Svitlana; Saxena, Madhurima; Nedeljkovic-Kurepa, Ana; Mehl, Mathieu Cameron; Wang, Allison; Gu, Xin; Pruitt, Kevin. *SIRT1 Positively Regulates Breast Cancer Associated Human Aromatase (CYP19A1) Expression.*

GR dimers play important role in anti-inflammatory actions of GCs/GR. Vandevyver, Sofie; Dejager, Lien; Tuckermann, Jan; Libert, Claude. *New Insights Into the Anti-inflammatory Mechanisms of Glucocorticoids: An Emerging Role for Glucocorticoid-Receptor-Mediated Transactivation.*

Dual inhibitors of PI3K and mTOR may enhance alkylating agent-mediated cytotoxicity and provide a novel regimen in the treatment of invasive PAs. Dai, Congxin; Zhang, Bo; Liu, Xiaohai; Ma, Sihai; Yang, Yakun; Yao, Yong; Feng, Ming; Bao, Xinjie; Li, Guilin; Wang, Janxin; Guo, Kai; Ma, Wenbin; Xing, Bing; Lian, Wei; Xiao, Jianqi; Cai, Feng; Zhang, Hongbin; Wang, Renzhi. *Inhibition of PI3K/AKT/mTOR Pathway Enhances Temozolomide-Induced Cytotoxicity in Pituitary Adenoma Cell Lines in Vitro and Xenografted Pituitary Adenoma in Female Nude Mice.*

Hypothalamic and/or mesocorticolimbic dopaminergic circuits are targets for hormonal activation of social reward. Bell, Margaret R.; Sisk, Cheryl L. *Dopamine Mediates Testosterone-Induced Social Reward in Male Syrian Hamsters.*

New critical components of the CRHR1 signaling machinery, which selectively controls the early and late phases of ERK1/2 activation, are identified, providing new potential therapeutic targets for stress-related disorders. Bonfiglio, Juan J.; Inda, Carolina; Senin, Sergio; Maccarrone, Giuseppina; Refojo, Damián; Giacomini, Damiana; Turck, Christoph W.; Holsboer, Florian; Arzt, Eduardo; Silberstein, Susana. *B-Raf and CRHR1 Internalization Mediate Biphasic ERK1/2 Activation by CRH in Hippocampal HT22 Cells.*

SIRT1 is significantly up-regulated in invasive ductal carcinoma relative to normal tissue adjacent to tumor, further suggesting a role of SIRT1 in breast cancer. Holloway, Kimberly R.; Barbieri, Andreia; Malyarchuk, Svitlana; Saxena, Madhurima; Nedeljkovic-Kurepa, Ana; Mehl, Mathieu Cameron; Wang, Allison; Gu, Xin; Pruitt, Kevin. *SIRT1 Positively Regulates Breast Cancer Associated Human Aromatase (CYP19A1) Expression.*

Beckers, Albert; Aaltonen, Lauri A.; Daly, Adrian F.; Karhu, Auli. *Familial Isolated Pituitary Adenomas (FIPA) and the Pituitary Adenoma Predisposition due to Mutations in the Aryl Hydrocarbon Receptor Interacting Protein (AIP) Gene.*

Moeller, Hanne B.; Rittig, Soren; Fenton, Robert A. *Nephrogenic Diabetes Insipidus: Essential Insights into the Molecular Background and Potential Therapies for Treatment.*

What a Difference a Day Makes:

ENDO 2013 Preconference Events

Some of the best events at **ENDO 2013** happen before the conference begins. By arriving in San Francisco one day early, attendees can benefit from targeted, one-of-a-kind programming—like spending time on the frontlines of diabetes care, polishing ultrasound thyroid examination techniques, or picking up tips and contacts from career development experts.

EndoCareers® Early Career Programs

Friday, June 14, 8:00 AM - 7:30 PM

Crucial skills, powerful contacts, fresh outlook—at **ENDO 2013's** Early Career Programs, fellows, students, junior faculty, and mid-career professionals will have several opportunities to take another step toward the top.

The ***Early Career Forum (8:00 AM - 6:00 PM)*** offers students and fellows in-depth perspectives from experts on career and skills development. Participants will explore options for pursuing careers in academia, industry, private practice, and alternative paths. They'll also practice competencies like CV development, grant writing, teaching, mentoring, publishing papers, and leading seminars. Lunch features a meal plus valuable networking with mentors and advice on maintaining work-life balance.

At the ***Promotion & Tenure Workshop (1:00 - 7:00 PM),*** junior faculty and early to mid-career professionals will gain insight into the way forward with a lunch session focused on the importance of involvement with The Endocrine Society's Committees. After that, they'll break out into two unique sessions detailing the relevant skills clinicians and basic scientists need to get a promotion or earn tenure.

All are invited to network with faculty mentors, catch up with colleagues, and build on the day's sessions at the ***Early Career Reception (6:00 - 7:30 PM).***

Diabetes Diagnosis and Management

Friday, June 14, 9:00 AM - 5:30 PM

DDM offers clinicians the chance to interact with expert faculty for a full-day workshop focused on advanced practice challenges, case discussions, emerging therapies, and more.

Participants will earn CME credits interacting with renowned diabetes clinicians and researchers as they share case studies, novel approaches, and up-to-date information on pharmaceutical and lifestyle diabetes treatments. Attendees can test their new knowledge during break-outs and symposia throughout the day.

Hands-on Thyroid Ultrasound Workshops

Advanced: Friday, June 14, 8:00 AM - 1:30 PM

Introductory: Friday, June 14, 1:30 - 6:30 PM

Seating is limited for clinicians interested in our uniquely hands-on introductory and advanced thyroid workshops. Register now to learn and practice ultrasound techniques under the guidance of expert faculty—and earn CME credits in the process.

Introductory participants will perform fine needle aspiration (FNA) and practice ultrasound techniques on simulated nodules. Advanced participants will perform FNA and use ultrasound techniques to examine cervical lymph nodes and parathyroid adenomas in patients with thyroid cancer and hyperparathyroidism. Each program begins with four didactic lectures.

Make sure you're in attendance for the only workshops with this much hands-on interaction. EN

EVENT REGISTRATION

Register now for a preconference event to get the most from your **ENDO 2013** experience. You'll be surprised the difference a day can make! Go to *www.endo-society.org/endo2013* for more information.

Photo credit: *Kropic 1/Shutterstock.com*

CLINICAL ENDOCRINOLOGY UPDATE 2013

SEPTEMBER 26–28, 2013
NEW ORLEANS, LOUISIANA
HYATT REGENCY NEW ORLEANS

REGISTER TODAY

FOR THE MOST TRUSTED CLINICAL UPDATE MEETING!

Attend the 65th Annual Clinical Endocrinology Update (CEU) to receive the most important information about recent advances in the science and practice of endocrinology. Expert faculty will deliver updates on evaluation, diagnosis and management in an interactive and case-based atmosphere. Whether you are looking for a refresher or preparing for certification, this is the meeting you don't want to miss.

Attending CEU gives you:

- Three days of extensive quality learning on core endocrine topics
- A collaborative atmosphere featuring panel discussions and Meet-the-Professor case-based sessions
- Valuable study resources

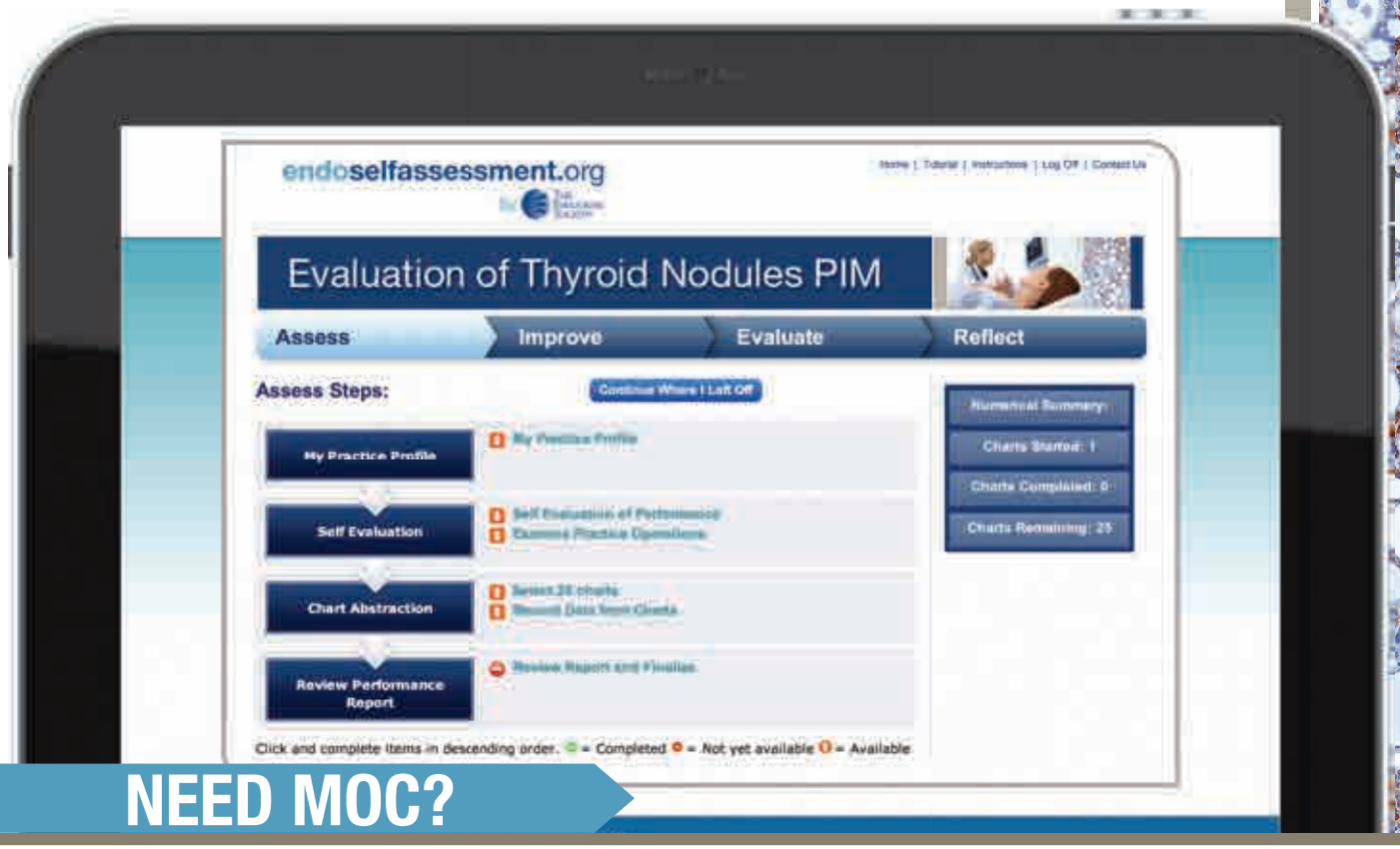
Learn more at www.endo-society.org/CEU!

Register By August 22

for discounted rates or call Society Services at 1.888.363.6762 (toll free in the US) or 1.301.941.0210.

The Endocrine Society®

www.endo-society.org



NEED MOC?

THE EVALUATION OF THYROID NODULES
Practice Improvement Module (PIM)

FROM THE ENDOCRINE SOCIETY

The first endocrine-specific Practice Improvement Module (PIM) is a Web-based, self-evaluation tool designed to assist you in evaluating your care of patients with thyroid nodules. Using data from your practice, including patient charts, our PIM allows you to:

1) Evaluate your performance in evaluating thyroid nodules;
2) Compare your performance to ATA and AACE/AME/ETA clinical guidelines through personalized reports;
3) Create and implement an individualized improvement plan; and
4) Reassess the impact of that improvement plan on your practice.

Complete the PIM, either individually or as a part of a practice team, and earn 20 points toward the Self-Evaluation of Practice Performance (Part 4) requirement of Maintenance of Certification (MOC) and claim up to *20 AMA PRA Category 1 Credits*™.

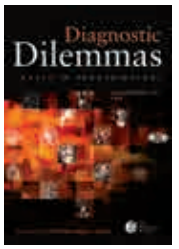
Evaluation of Thyroid Nodules PIM Task Force
Erik Alexander, MD | Carol Greenlee, MD, FACP, FACE | Susan Mandel, MD, MPH

For more information, visit endoselfassessment.org.

THE ENDOCRINE SOCIETY®

VISIT THE ENDO STORE ONLINE!

PUBLICATIONS & RESOURCES



Visit the Endocrine Society's online store and you'll notice something different. It's now easier to find and purchase the valuable self-assessment products, reference materials, and study guides you need in your work or practice. You'll also find some fun gifts and Society logo merchandise there.

VISIT WWW.ENDO-SOCIETY.ORG/STORE
AND PLACE YOUR ORDER TODAY.

THE ENDOCRINE SOCIETY®

www.endo-society.org

NOW AVAILABLE!

Are you up to date in endocrinology?

Purchase the new *Endocrine Self-Assessment Program* (*ESAP™ 2012*) to evaluate your competency in all aspects of endocrinology, diabetes, and metabolism.

ESAP™ 2012

The Endocrine Society's Premier Self-Assessment Resource

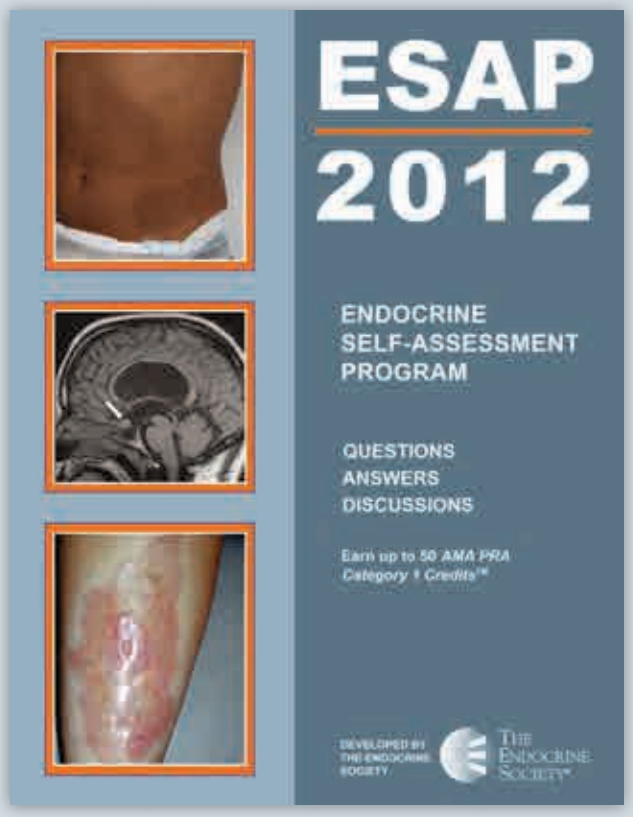
Based on the ABIM blueprint for certification, ***ESAP 2012*** is the perfect tool for physicians seeking certification or recertification, and clinicians simply wanting a self-assessment and a broad review of endocrinology.

ESAP 2012 provides 160 online interactive case-based questions and printed book. Each question features extensive discussion of correct and incorrect answers. Written by leaders in the field, ***ESAP 2012*** is designed to ensure you have the latest information from the experts.

Earn up to 50.0 *AMA PRA Category 1 Credits*™

To register or purchase ***ESAP 2012***, visit:
www.endocrineselfassessment.org,
to order by phone call
1.888.363.6762 or 301.941.0210
Monday — Friday, 8:30 AM – 5:00 PM ET.

Nonmembers Price: $350
Member Price: $250
In-Training Members Price: $199



THE ENDOCRINE SOCIETY®

CLASSIFIEDS

If you are interested in submitting classified advertising to *Endocrine News,*
please contact Christine Whorton at ***endocareers@endo-society.org*** or 800-361-3906.

Washington Endocrinologist:
Group Health Permanente, the Pacific Northwest's top-rated multi-specialty group, is currently seeking a BC/BE Endocrinologist to join our Group Practice. Group Health is dedicated to providing comprehensive, innovative, and patient-centered care to our patients. We lead the nation in EMR integration. We are looking for an additional provider to join our Endocrinologists in a stimulating setting. This provider will help to expand our Endocrinology services in the Seattle area with circuit-riding to Tacoma. The practice is exclusively outpatient consulting Endocrinology without hospital responsibilities. We offer generous benefits, competitive salaries, and the ability to become a shareholder in our Group Practice. For additional information regarding this position or to submit your CV, please visit our website at *www.grouphealthphysicians.org.*

Florida Endocrinologist:
Naples/Bonita Springs, Florida Endocrinologist Physician Needed: Striving multi-specialty clinic seeking full-time Endocrinologist. Outpatient only, no calls, competitive salary/benefits, starting bonus, partnership track, private practice. Fax: 239-594-5637; email: *choykml@hotmail.com.*

Endocrinologist – Five Member Practice – Major Midwest River City:
The Christ Hospital Health Network in Cincinnati, Ohio, seeks an endocrinologist to join a successful diabetes and endocrinology practice currently ranked as one of the nation's top 50 programs (*U.S. News & World Report's* Best Hospitals rankings 2012-2013). Join the employed physician division of this 550-bed, acute care Magnet® Status hospital that is the area's Most Preferred Hospital (17 consecutive years) and named a 50 Top Cardiovascular Hospital (Truven Health Analytics). Highlights of the practice include excellent compensation/benefits; 1:6 call schedule; CNP support for inpatient/outpatient care; research and resident teaching opportunity. Linda Minter, Physician Recruitment, *Linda.minter@TheChristHospital.com.*

ENDOCRINOLOGIST

Ochsner Health System

OCHSNER HEALTH SYSTEM in New Orleans is searching for a **BC/BE ENDOCRINOLOGIST to join our staff at Ochsner Baptist Medical Center**. Candidates with experience or directly from training are welcomed to apply. Areas of interest should include general endocrine disorders, diabetes, and endocrine disorders as related to pregnancy. This position is mainly outpatient based, but will serve a large Ob/Gyn group with significant inpatient consultation. Salary is competitive and commensurate with experience and training.

Ochsner Baptist Medical Center, with a deep-rooted history in Uptown New Orleans, is a fully accredited, full-service hospital staffed by more than 390 physicians. We have all private rooms, an ICU, 13 operating rooms, and a state-of-the art imaging center. We are proud to be distinguished by our excellence in specialty care and high patient satisfaction scores. Our newly renovated 24-hour full-service emergency department is staffed by a team of board-certified ER physicians.

The Ochsner Health System comprises 8 hospitals and more than 38 clinics across southeast Louisiana with over 1.5 million clinic patient visits annually. Ochsner is a major provider of graduate medical education with 23 ACGME-accredited residency and fellowship programs, including our Endocrinology Fellowship Program. Please visit our Web site at *www.ochsner.org*.

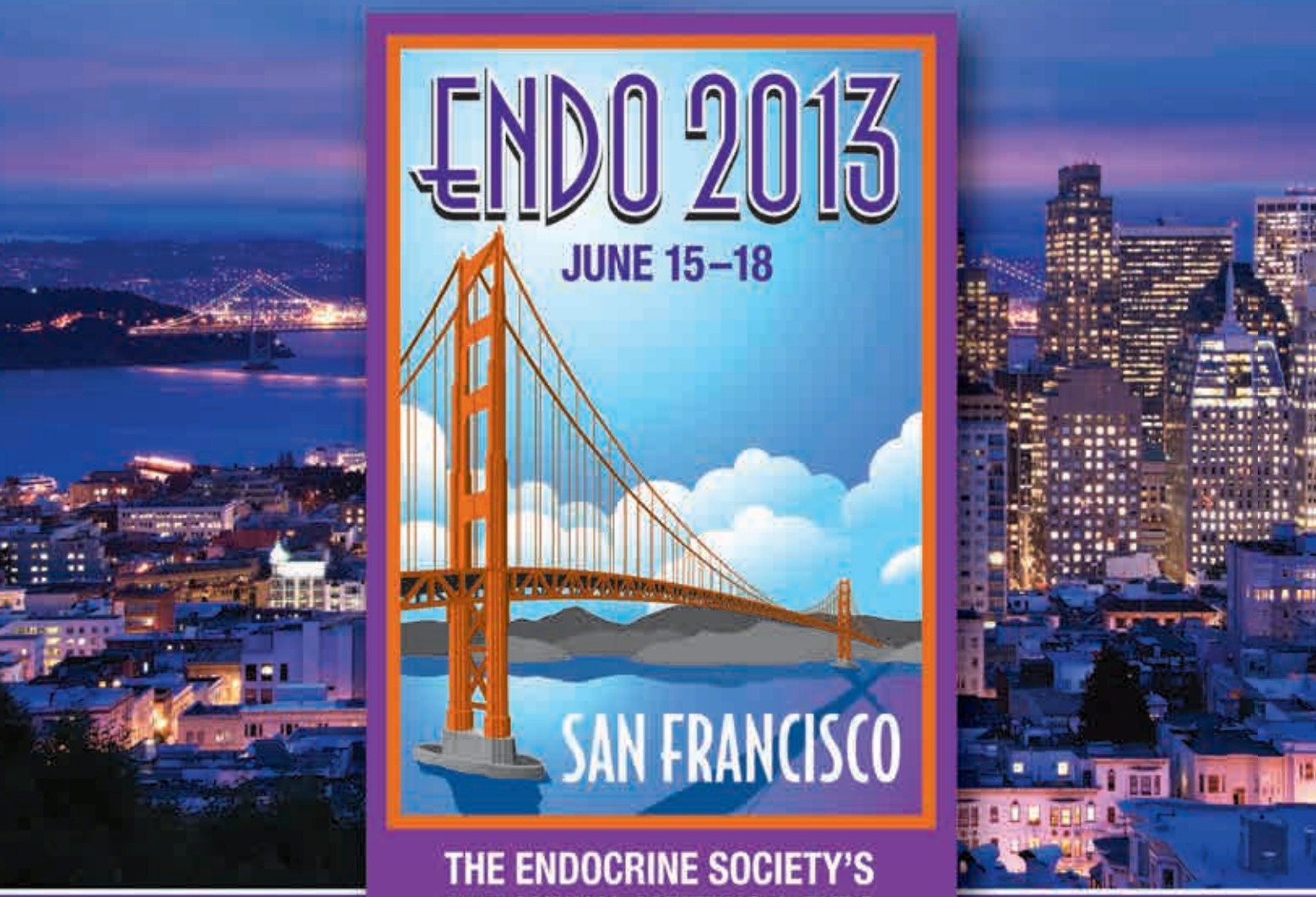
New Orleans is a cosmopolitan, historic city with a pleasant climate, unique architecture, multiple medical schools and academic centers, professional sports teams, world-class dining and cultural interests, and world-renowned live entertainment and music.

Please email CV to: *profrecruiting@ochsner.org*, Ref. # ABENDO1 or call 800-488-2240 for more information. EOE.

Sorry, no J-1 visa opportunities available.

REGISTER NOW FOR ENDO 2013

CELEBRATE 95 YEARS OF THE ANNUAL MEETING & EXPO



Register at www.endo-society.org/endo2013

THE ENDOCRINE SOCIETY®