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DIABETES: Will It Ever Be CURED?

While the end to diabetes is still in the distant future, strides in genetic research are showing promise.

FERTILE GROUND:
EDCs & Male Hormones

THE DEEPEST CUT:
Is the Whipple Procedure Still Relevant?

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Hormone Science to Health

Be Prepared: Developing the Next Generation of Endocrinologists



Richard J. Santen, MD

From my perspective, the younger members of the Endocrine Society represent the lifeblood of a vibrant Society, both now and in the future. The Society is highly committed to a comprehensive approach to enhance the career development of these individuals. Whether a student, fellow, or young endocrinologist starting a career in a full-time position, a wide range of programs and activities are specifically

designed to meet important needs. The Society's current career development programs have impacted young professionals at many levels. Beginning with a robust outreach program, the Society has been very successful at recruiting new trainee members, already increased to more than 3,100. A high priority goal of the Society is to provide a strong portfolio of programs aimed at creating a pipeline of young scientists working at the cutting edge of research and clinical practice.

The Society provides opportunities for exposure to endocrine science through research experiences and fellowships, networking opportunities, and skill training to those at the earliest stages in the endocrine career spectrum, including the undergraduate, early graduate, and medical student levels. At the next level, fellows who have demonstrated accomplishments in endocrine research receive intensive leadership and professional development support. Specifically, the Society conducts targeted workshops that focus on helping fellows better understand the business of research while providing hands-on grantsmanship training that will increase their success in transitioning into independent researchers.

An entire day is devoted to the specific needs of students and fellows on the day prior to the Annual Meeting during a program called the Early Career Forum. This is a workshop that highlights translational plenary lectures presented by internationally recognized investigators who are also outstanding communicators. Two tracks, one clinical and the other basic, provide interactive breakout sessions that focus on education and skills development. The day concludes with the Early Career Reception, an informal meeting place that welcomes all early attendees and recognizes **ENDO** abstract travel award winners.

During **ENDO**, several popular programs provide specific information and advice for trainees and early career attendees. For example, the Career Development Workshops offer relevant career advice to trainees and early career professionals on a wide range of topics. A record number of 11 workshops were held at **ICE/ENDO 2014** featuring the lab and practice

management workshops, the promotion and tenure workshop, and the evening grant-writing sessions: all very well received and attended. In addition, trainees are recognized for their early career accomplishments by having their posters identified for special consideration in the Presidential Poster Competition. A number of structured networking activities are designed to facilitate mentorship opportunities for early career members. Feedback each year from the attendees has fostered a spirit of continuous improvement.

All early career events are held in the Career Center, the hub of activity for young scientists wishing to attend the trainee oral competitions and other focused sessions, to connect with colleagues, or simply take a coffee break.

I would like to emphasize the many awards that are offered to students, fellows, and early career professionals. In 2015, the Society's early career awards will serve to recognize excellence in research, support participation in scientific education, and provide generous support for fellowships and research projects and career endeavors.

As you can see, there are many exciting opportunities within the Endocrine Society that promote the development of early career professionals while building a community where the next generation of endocrinologists will thrive. I'd like to congratulate the members of the Trainee and Career Development Core Committee and the Minority Affairs Committee for their outstanding efforts in creating programming that is supportive and nurturing for anyone focused on a career in endocrine science or medicine.

The Society is currently seeking to best understand the major challenges facing the next generation and considering ways to further enhance career development. You can rest assured that the Society will continue to be diligent in its efforts to develop outstanding early career programs and opportunities for trainees to learn, engage, and connect with professionals in the field.

Most importantly, your opinions and ideas are essential in helping us create quality programming, and I welcome you to submit any comments and suggestions to me at President@endocrine.org. **EN**

Richard J. Santen, MD
President, Endocrine Society

SEPTEMBER 2014

ENDOCRINE NEWS

THE LEADING MAGAZINE FOR ENDOCRINOLOGISTS

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

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

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Endocrine News is published 12 times a year by the Endocrine Society, 2055 L Street, NW, Suite 600, Washington, DC 20036
Phone 202-971-3636 • Fax 202-736-9708
www.endocrine.org

Print ISSN 2157-2089 Online ISSN 2157-2097
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This month's cover story, "Diabetes: Will It Ever Be Cured?" (p. 8), dives into the research being conducted in labs around the world. Strides have been made, most notably in genetic research, which could be the first step to finding an elusive cure. According to Society president Richard J. Santen, MD, "We are learning much more about the biology of diabetes, and it is beginning to pay major dividends," he tells author Terri D'Arrigo. "As time goes on, our increased understanding will play a key role in altering the course of the disease."



Mark A. Newman

Endocrine-disrupting chemicals (EDCs) remain a focus of the Endocrine Society. In April, we ran a cover story on their links to childhood illnesses. This month, Eric Seaborg writes about the possible links between EDCs and male hormones in "Fertility in the Modern Male: Still More Questions than Answers," (p. 12). While evidence suggests that EDCs do affect male reproduction, finding definitive links to specific conditions is still a daunting task. Still, most experts agree that avoiding these compounds is never the wrong course of action.

Aaolok Mehta writes about one of the only options available for patients diagnosed with pancreatic cancer: The Whipple Procedure. In "Knife's Edge" (p. 16), Mehta details the statistics for this procedure and treating this deadly cancer, but at this point there isn't much hope for complete survival. As Eugene P. Ceppa, an assistant professor of surgery at Indiana University School of Medicine in Indianapolis says, "Even the smallest, earliest detected lesions can have bad outcomes. The pancreas is a very fickle organ; it doesn't like to be operated on."

Finally, remember that **ENDO 2015** is taking place much earlier this year: March 5 – 8 in San Diego. Go to www.endocrine.org/endo-2015 to register today. **EN**

Mark A. Newman,
Managing Editor, Endocrine News

Why Endocrinology?

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

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

Dear Endocrine Society Management, Staff, Editors, Reviewers, & Authors,

My heartfelt thanks to all of you for the condolences you have conveyed to my family and me after Scott's death. There have been so many thoughtful messages. A very special thank you to the Society staff for their efforts in helping make the May 18th celebration of his life so special by sharing your comments and memories with everyone present.

Throughout Scott's nine-year battle with his disease, you consistently showed care and concern and we were extremely grateful. All the support — cards, flowers, phone calls, and tasty meals — meant so much to us. Scott loved his job and considered himself very fortunate to have worked with such generous coworkers. I wish you continued success with publishing the journals he took such pride in managing.

Regards, Molly Herman

By Derek Bagley

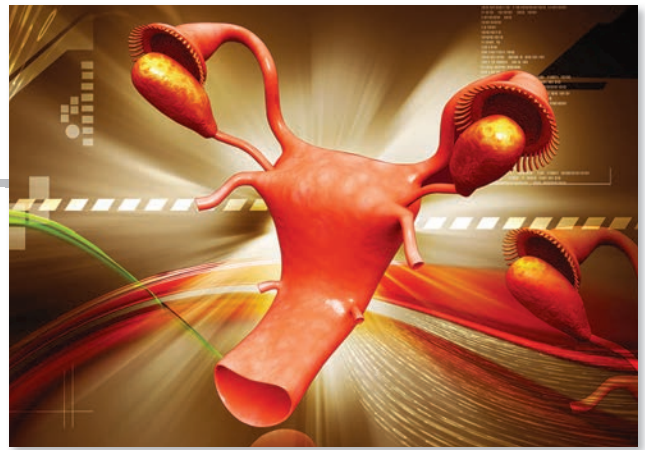
LOSS OF NTRK2/KISS1R SIGNALING in Oocytes Causes Premature Ovarian Failure

A recent mouse study may provide clues to early adult infertility, specifically premature ovarian failure (POF), a disorder that affects 1% of women of reproductive age.

Researchers led by Sergio R. Ojeda, DVM, of the Oregon National Primate Research Center/Oregon Health and Science University, and Manuel Tena-Sempere, MD, of the University of Cordoba, Spain, wrote in *Endocrinology* that identifying “the factors required for oocyte survival during the reproductive lifespan is an important endeavor because knowledge of the underlying pathways may provide significant new insights into the pathology of” the disorder.

Ojeda and his team looked at neurotrophins (NTs), which had been previously shown to provide developmental cues to non-neural cells, and contribute to the formation and development of follicles in the ovary. According to the scientists, oocyte-specific deletion of the *Ntrk2* gene that encodes the NTRK2 receptor (NTRK2) for neurotrophin-4/5 and brain-derived neurotrophic factor (BDNF) results in post-pubertal oocyte death, loss of follicular organization, and early adulthood infertility.

They studied NTRK2 receptors in mice before and at puberty and found that full-length receptors (NTRK2.FL) became expressed in oocytes at puberty because they are rapidly induced by the preovulatory gonadotropin surge.



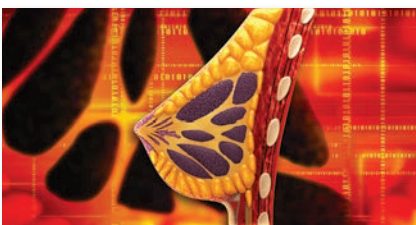
The authors observed that if there are no NTRK2.FL receptors, the gonadotropins are unable to activate the well-established oocyte PI3K/AKT-mediated survival pathway. They wrote, “A cell line expressing both [a truncated NTRK2 form] NTRK2.T1 and the kisspeptin receptor (KISS1R) responds to BDNF stimulation with activation of *Ntrk2* expression only if kisspeptin is present. This suggests that BDNF and kisspeptin that are produced by granulosa cells (GCs) of periovulatory follicles act in concert to mediate the effect of gonadotropins on *Ntrk2* expression in oocytes. In keeping with this finding, the oocytes of NTRK2-intact mice fail to respond to gonadotropins with increased *Ntrk2* expression in the absence of KISS1R.”

They concluded that the preovulatory gonadotropin surge promotes the survival of the oocyte by inducing the expression of NTRK2.FL receptors, setting in motion an AKT-mediated survival pathway. The authors wrote that their findings “also suggest that gonadotropins activate NTRK2.FL expression via a dual communication pathway involving BDNF and kisspeptin produced in GCs and their respective receptors NTRK2.T1 and KISS1R expressed in oocytes.”

APOBEC3B Linked to ER+ Breast Cancers

Elevated levels of the gene *APOBEC3B* is associated with poorer clinical outcomes in patients with estrogen receptor-positive (ER+) breast cancer, according to research recently published in *Hormones and Cancer*.

According to the study, *APOBEC3B* is a member of a larger family of polynucleotide cytosine deaminases with diverse physiological functions in innate and adaptive immunity, lipid metabolism, and heart development.



Researchers led by John W. Martens, PhD, of the Erasmus MC Cancer Institute in Rotterdam, Netherlands, wrote that there have been recent observations connecting DNA cytosine deaminase *APOBEC3B* to the genetic evolution of breast cancer, saying that the gene is a “major enzymatic source of somatic driver and passenger mutations in breast cancer.”

Martens and his team pointed out that *APOBEC3B* mRNA levels were related in 1,491 primary breast cancers to disease-free (DFS), metastasis-free (MFS), and overall survival (OS). They wanted to validate these results independently, so they used univariate Cox regression analysis to study patient outcome data in five additional cohorts comprising more than

3,500 breast cancer cases.

The scientists found that “increasing *APOBEC3B* expression as a continuous variable was associated with worse DFS, MFS, and OS (Hazard Ratio [HR]=1.20, 1.21, and 1.24, respectively; all $P<.001$). Also in untreated ER+, but not in ER-, lymph node-negative patients, high *APOBEC3B* levels were associated with a poor DFS (continuous variable: HR=1.29, $P=.001$; dichotomised at the median level, HR=1.66, $P=.0002$).” **These findings were confirmed in all five cohorts, suggesting that *APOBEC3B* is a “marker of pure prognosis, and poor outcomes for ER+ breast cancer.” The authors concluded that genetic aberrations induced by *APOBEC3B* contribute to breast cancer progression, writing that more aggressive treatments of ER+ tumors could target and eradicate *APOBEC3B*-high ER+ cells.**

African Americans Respond Better to **FIRST-LINE DIABETES DRUG**

African Americans taking the diabetes drug metformin saw greater improvements in their blood sugar control than white individuals who were prescribed the same medication, according to a new study published in the *Journal of Clinical Endocrinology & Metabolism*.

“Metformin is normally the first treatment physicians prescribe for type 2 diabetes, but the standard of care is based on clinical trials where the vast majority of participants were white,” says one of the study’s authors, L. Keoki Williams, MD, MPH, of Henry Ford Health System in Detroit, Mich. “We wanted to examine how the drug performed in an African American population. Our findings suggest that African Americans who have diabetes actually respond better to metformin than whites.”

The observational study used medical and pharmacy records from Henry Ford Health System to examine blood sugar control in 19,672 people with



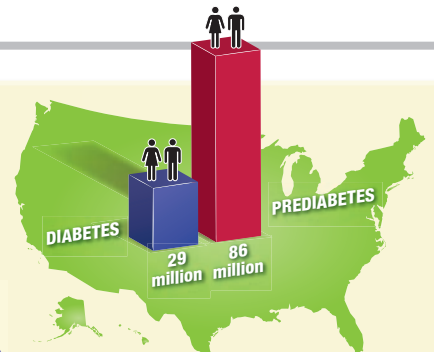
diabetes who were prescribed metformin between January 1, 1997, and June 2, 2013. Among the participants, 7,429 were African American and 8,783 were white. Using pharmacy records, the researchers estimated each individual’s exposure to metformin and other diabetes medications. Each study participant had at least two hemoglobin A1c (HbA1C) blood sugar measurements taken at least four months apart while they were on metformin.

Because the HbA1C test measures a person’s average blood sugar level

from the past three months, researchers ran an analysis to measure the change in participants’ blood sugar levels in relation to the amount of metformin taken. The study found the maximum dose of metformin was associated with an absolute decrease in HbA1C values of 0.9% among African Americans. In contrast, the same analysis found a 0.42% reduction in HbA1C numbers among whites.

“When one considers that the goal HbA1c level for individuals being treated for diabetes is less than 7% and that the average starting HbA1c level in our patients was around 7.5%, these differences in treatment response are clinically important,” Williams says. “Moreover, since African Americans are more likely to suffer from diabetic complications when compared with white individuals, it is heartening to observe that metformin is likely more effective at controlling blood glucose in the former group.”

Fast FACTS About Diabetes



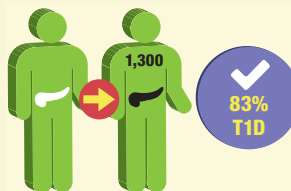
In the U.S., 29 million people have diabetes and 86 million people have prediabetes.

2012

\$245 billion

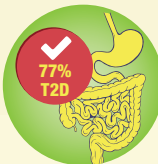
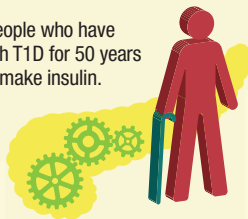
In 2012, diagnosed diabetes cost \$245 billion.

Each year, approximately 1,300 people with T1D have pancreas transplants. 83% of these have no symptoms of diabetes after a year.

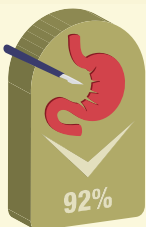
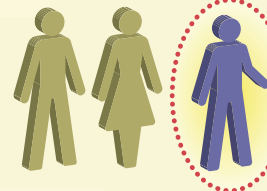


At least 1 out of 3 people will develop T2D in their lifetime.

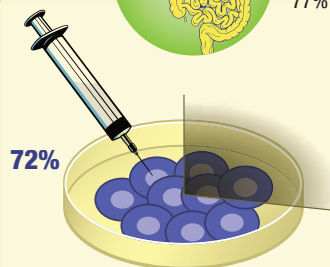
Some people who have lived with T1D for 50 years can still make insulin.



Bariatric surgery resolves almost 77% of T2D cases.



Bariatric surgery leads to a 92% reduction in mortality from T2D.

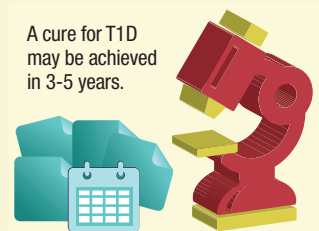


72% of Americans support stem cell research.



Around 80 people per day are diagnosed with T1D in the U.S.

A cure for T1D may be achieved in 3-5 years.



DIABETES: Will It Ever Be CURED?

While the end to diabetes is still in the distant future, strides in genetic research are showing promise.

By Terri D'Arrigo

AT-A-GLANCE

- Researchers at Columbia University in New York have learned to convert human gastrointestinal cells into insulin-producing cells by turning off the FOXO1 gene.
- The Columbia team has also learned that FOXO1 degrades in overstressed beta cells so they produce insulin. Then the beta cells revert back to a more basic, undifferentiated type of cell.
- A team at the Joslin Diabetes Center in Boston has identified immune cells in mice that had minimal effects on destroying beta cells in type 1 diabetes, and instead actually promoted their growth.
- At the University of North Carolina at Chapel Hill, researchers are investigating the use of viral vectors to transfer genes into the beta cells as a way of helping the beta cells avoid attack.

Immunology and beta cell function have long been two core areas of research in the hunt for a cure for diabetes. But in recent years, scientists have made discoveries that could lead to genetic therapies that allow the body's own cells to combat and even rid itself of the disease. Researchers are learning to turn gut cells into insulin-producing cells, replenish beta cells once thought decimated beyond hope, and use viral vectors to deliver genes into beta cells that may protect them from attack by the immune system.

And that's just for type 1.

For type 2 diabetes, researchers have found evidence that beta cells do not burn out and die as previously thought, but instead revert to more primitive cells or ones with altered function, leading some scientists to believe that if they can prevent this dedifferentiation or somehow push dedifferentiated cells to turn back into beta cells, they could prevent or cure type 2.

"Findings like these represent a shift in our thinking," says Richard J. Santen, MD, president of the Endocrine Society and professor of medicine, endocrinology, and metabolism at the University of Virginia School of Medicine in Charlottesville. "We are learning much more about the biology of diabetes, and it is beginning to pay major dividends. As time goes on, our increased understanding will play a key role in altering the course of the disease."

Replace and Regenerate

At Columbia University in New York, a team led by Domenico Accili, MD, professor of medicine, has made several discoveries about FOXO1, a protein that controls when genes are switched on or off.

In research published in the March 11, 2012, *Nature Genetics*, the team found that deactivating FOXO1 in progenitor cells in the small intestines of newborn mice resulted in the cells becoming insulin-producing cells. In follow-up research published in the June 30, 2014, *Nature Communications*, Accili's team conducted similar experiments in human intestinal cells derived from stem cells. Within seven days of FOXO1 deactivation, the cells began to produce insulin in response to glucose.

The gut was a logical place to look for cells that could be manipulated into becoming insulin-producing cells, says Accili. "There is enough kinship between insulin-producing cells in the pancreas and hormone-producing cells in the gut that this is not that big of a leap to make. It's not like we're asking a gut cell to become a neuron or muscle fiber."

Using gut cells may be particularly advantageous over using cells from other parts of the body, Accili adds. "In type 1, the main issue is destruction of insulin-producing cells by the immune system, but the gut has immune privilege. It is always exposed to foreign antigens in food, and it has a different immune response that may be more permissive and might give the cells a break."

The lifespan of gut cells may also give them an advantage, Accili says. "Cells in the gut turn over very fast, every seven to 10 days, so even if the cells are attacked, they might be able to withstand it long enough for newer cells to take over."

In separate research published in the September 14, 2012, *Cell*, Accili's team found evidence that FOXO1 plays a role in the release of insulin by beta cells. In a mouse study, the team saw that when a beta cell is stressed, such as when it is bathed in glucose, FOXO1 moves from the cell's cytoplasm into its nucleus, and the cell produces insulin. However, if the cell remains stressed for too long, FOXO1 degrades and the cell stops producing insulin. What's more, once the cell stops



"We are learning much more about the biology of diabetes, and it is beginning to pay major dividends. As time goes on, our increased understanding will play a key role in altering the course of the disease."

— Richard J. Santen, MD, president of the Endocrine Society and professor of medicine, endocrinology, and metabolism, University of Virginia School of Medicine, Charlottesville



“Even if we can’t get rid of the insulin resistance in type 2, we might be able to generate enough beta cells to overcome the insulin resistance and get rid of diabetes.”

— George L. King, MD, research director and chief scientific officer, Joslin Diabetes Center, Boston

producing insulin, it reverts back to a more basic, undifferentiated type of cell.

These findings challenge the prevailing thought about the development of type 2, which is that beta cells die from overwork caused by insulin resistance.

“In terms of type 2, FOXO1 is a marker of a process we are trying to prevent, dedifferentiation,” Accili says. “In the pancreas, we would look at protecting differentiation, or maybe finding a way to force redifferentiation.”

Researchers at Joslin Diabetes Center and Harvard Medical School in Boston have taken another approach: beta cell regeneration in the pancreas. Their work is inspired in part by the Joslin 50-Year Medalist Study, in which researchers found that the pancreases of 66% of participants were still producing small amounts of insulin even after 50 years of diabetes.

“That means there are residual beta cells, and there is something to work with,” says George L. King, MD, the center’s research director and chief scientific officer. “We are looking for ways of helping the body regenerate those cells. We believe that several growth factors and beta cell regeneration factors can play a part.”

One team, led by Douglas Melton, PhD, adjunct investigator at Joslin and co-director of the Harvard Stem Cell Institute, published a paper in the May 2013, *Cell* describing how betatrophin, a hormone primarily expressed in liver and fat, is associated with the growth of beta cells in mice.

Another team, led by Rohit N. Kulkarni, MD, PhD, principal investigator at Joslin and associate professor of medicine at Harvard Medical School, published a paper in the January 2014, *Diabetes* in which they identified immune cells in mice that had minimal effects on destroying beta cells in type 1 and instead actually promoted their growth.

King says that this research could be just as important for type 2 as type 1. “Even if we can’t get rid of the insulin resistance in type 2, we might be able to generate enough beta cells to overcome the insulin resistance and get rid of diabetes,” he says.

Protect and Defend

Altering or turning off the body’s attack on beta cells has been a major hurdle in the race for a cure for type 1. A team led by Thomas Serwold, PhD, investigator in Joslin’s Section on Immunobiology, is studying the role of the thymus in the autoimmunity that destroys beta cells. Normally other cells in the thymus train T cells not to attack the body’s own cells, and most of the T cells that fail the training are destroyed before they can leave the thymus. However, some of the faulty T cells do get out into the body, and those that target beta cells in the pancreas cause type 1 diabetes.

“Dr. Serwold is looking at how we might target how the thymus programs these cells,” says King. “The thymus is a master organ for immune tolerance, and redeveloping or reprogramming it could be an exciting approach to decreasing autoimmunity in type 1.”

At the University of North Carolina at Chapel Hill, Roland Tisch, PhD, professor of microbiology and immunology, and his team are investigating the use of viral vectors to transfer genes into the beta cells as a way of helping the beta cells avoid attack. The vectors come from the adeno-associated virus (AAV), a benign virus that infects humans but generally does not cause any harm. These AAV vectors are popular among cell biologists because of their track record for safety.

“The guts of the virus, the DNA, have been used over many years to transfer genes to different cell types and tissues in animals, but are now also being used in the clinic for genetic disorders such as hemophilia and various eye disorders,” Tisch says.

In Tisch’s lab, researchers are using these vectors to transfer genes that encode certain cytokines (proteins important to cell signaling). These cytokines have anti-inflammatory properties known to disrupt T cells should the T cells attack.

“The gist is that we are trying to indirectly tweak T cells, which will help protect the beta cells from destruction,” Tisch says. “Different cytokines can affect different T cells, so the catch is figuring out which ones are the most effective.”

Although widespread genetic therapies that could cure diabetes are still years away, such innovative research offers hope for the 382 million people across the globe with diabetes.

“It’s this kind of highly innovative, basic research that will inform how efforts go forward,” says Santen. “As our knowledge expands, we will be able to pursue ways not only of curing diabetes, but ultimately of preventing it.” **EN**

— D’Arrigo is a health and science writer based in Holbrook, N.Y., and a regular contributor to Endocrine News. She wrote about depression and diabetes in the August issue.



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FERTILITY and the Still More Questions than Answers

While some think that male reproduction is another endocrine function that could be adversely affected by endocrine-disrupting chemicals, not everybody is convinced. Does a solid link between male hormones and EDCs truly exist?

By Eric Seaborg

The effects of chemicals like phthalates and bisphenol A (BPA) continue to grab headlines, as do stories blaming them for potential declines in fertility. This attention may lead more patients to ask their physicians whether environmental exposures could be causing their fertility problems.

And the answer still seems to be that although studies continue to illustrate ways that endocrine-disrupting chemicals (EDCs) can perturb reproductive systems, definitive answers are elusive, and many skeptics question whether the disruptions are strong enough to cause measurable consequences.

One of the latest examples of this new evidence is a study associating phthalate levels in men with a longer time to pregnancy in their partners. The phthalate family of plasticizers has come under scrutiny because they are ubiquitous, used in products ranging from plastic bottles and cosmetics to meats, cheeses, and some medical devices. They are metabolized much more slowly than another chemical that has faced scrutiny lately, namely BPA.

Phthalates and Fecundity

In a prospective study published in *Fertility and Sterility*, researchers led by Germaine Buck Louis, PhD, of the National Institutes of Health, enrolled 501 couples

“There is a possibility that EDCs could affect male reproductive function, but the evidence is inconclusive. Until we can reassure patients that it does not appear to be the likely explanation, it is sensible to avoid prolonged exposure to potential toxins.”

— Brad Anawalt, MD,
professor of medicine,
University of Washington,
Seattle

in Michigan and Texas who were planning a pregnancy. The researchers tested the urine of both the male and female partners for 14 phthalate metabolites and BPA, then followed the couples' success at attaining pregnancy. They found that in males, high levels of three phthalates were associated with a longer time to pregnancy. The researchers described this effect as a 20% drop in fecundity, which refers to the probability of becoming pregnant in a single menstrual cycle. Buck Louis puts that effect in context by noting it “is pretty much what we see with cigarette smoking.”

But in females, high levels of two of the 14 phthalates were associated with shorter times to pregnancy, and there was no association of BPA levels in either males or females.

Sheela Sathyanarayana, MD, MPH, assistant professor of pediatrics at the University of Washington in Seattle, said that the study stands out from others because it involved both members of a couple, rather than just the female or male. And the couples were from the general population, rather than pre-selected for infertility problems.

A phthalates expert, Sathyanarayana says that the results make sense “because phthalates have a direct anti-androgenic effect on male testes. There have been several studies that show that phthalates lead to low testosterone and changes in sperm quality and



MODERN MALE

AT-A-GLANCE

- Whether male fertility as measured by semen quality is declining continues to be hotly debated.
- There is plenty of evidence that endocrine-disrupting chemicals (EDCs) can interfere with reproductive systems, but linking these effects to population trends or individual conditions remains a challenge.
- Most experts urge caution when it comes to EDCs and counsel avoiding exposure through awareness and healthy lifestyle choices.

function. The evidence for phthalates is actually quite good when you look at male fertility, that phthalates are true anti-androgens and can adversely affect male reproductive outcomes.”

Phthalates and Reduced Testosterone

However, a recent study in the *Journal of Clinical Endocrinology & Metabolism* does seem to show a link between EDCs and reduced testosterone levels in not just men, but women and children as well. In a cross-sectional study of the general U.S. population from 2011 to 2012, data from the U.S. National Health and Nutrition Examination Survey showed that multiple phthalates were associated with significantly reduced testosterone in both males and females regardless of age.

Since various animal and cellular studies have shown that some phthalates block the effects of testosterone,

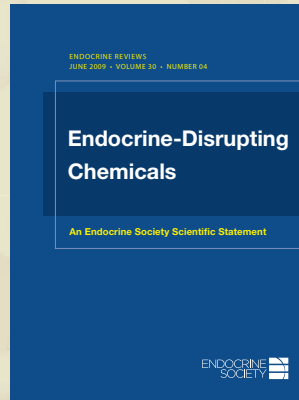
study authors John D. Meeker, MS, ScD, and Kelly K. Ferguson, PhD, of the Department of Environmental Health Sciences at the University of Michigan in Ann Arbor set out to prove if the same was true in humans. These compounds are commonly used in plastics and personal care products, items that everyone uses on a regular basis with few exceptions.

Not Everyone is Convinced

But it's these kinds of studies that will add to the conviction of those concerned about EDCs, but do little to change the minds of those who remain skeptical of any clear and present danger. Stephen Safe, PhD, a distinguished professor and director of the Center for Environmental and Genetic Medicine at Texas A&M University, says that many studies of the effects of EDCs tend to cherry-pick their results, and he wonders how much

OnPOINT from the Endocrine Society

The Endocrine Society's Scientific Statement on endocrine-disrupting chemicals, which contains a section on reproductive systems, can be found at www.endocrine.org/edc.



significance to assign to a survey of a large number of chemicals, most of which had no effect: “The study by Buck Louis and coworkers found a very small correlation with males and a 20% reduction in fecundity and nothing else.”

Safe says that such studies are important, but “let’s see if this is repeatable” before drawing any conclusions. He notes that the effects of the potent estrogenic endocrine disruptor diethylstilbestrol (DES) were evident in every human study, but the effects of phthalates and other EDCs being studied today give variable results.

Bald Eagles as Poster Children

That endocrine disruptors can have devastating effects on reproduction was demonstrated by the effects of the pesticide DDT on bald eagles. Bald eagles once seemed to be on a fast road to extinction, but have been repopulating the country since DDT was banned.

As top predators, they were repositories for the persistent DDT, but so far there is no DDT-like chemical in humans. And even as evidence mounts for EDC effects on endocrine systems, any signal would be difficult to spot amidst other changes over time that could adversely affect reproduction, such as more couples postponing child-bearing until later in life, the increase in obesity, and dietary changes.

Are Sperm Counts Dropping?

One of the primary measures proposed for male reproductive capacity has been sperm and semen quality, and a key paper on the topic was published in 1991 by a team lead by Niels Skakkebaek of the University of Copenhagen. That meta-analysis touched off years of debate over its thesis that sperm counts were dropping globally while testicular cancer, hypospadias, and cryptorchidism were increasing. The paper was criticized for many methodological flaws and eventually largely discredited, says Brad Anawalt, MD, a professor of medicine at the University of Washington in Seattle. And later studies on sperm counts and quality have had inconsistent results. “On the basis of the conflicting results of studies to date, it is difficult to make any firm conclusions about whether there is a global trend toward decreased average sperm counts in humans,”

Anawalt wrote in the *Asian Journal of Andrology*. In fact, one of the authors of that original Skakkebaek article, Richard Sharpe, PhD, of the University of Edinburgh in Scotland, has since all but repudiated his positions, becoming a skeptic of the evidence of strong effects of endocrine disruption.

Skakkebaek himself continues to be one of the leading proponents of the dangers of EDCs. His team recently published an in vitro study in *EMBO Reports* recounting that a variety of EDCs applied at concentrations present in bodily fluids interfered with sperm functions.

Endocrine Society Statement on EDCs

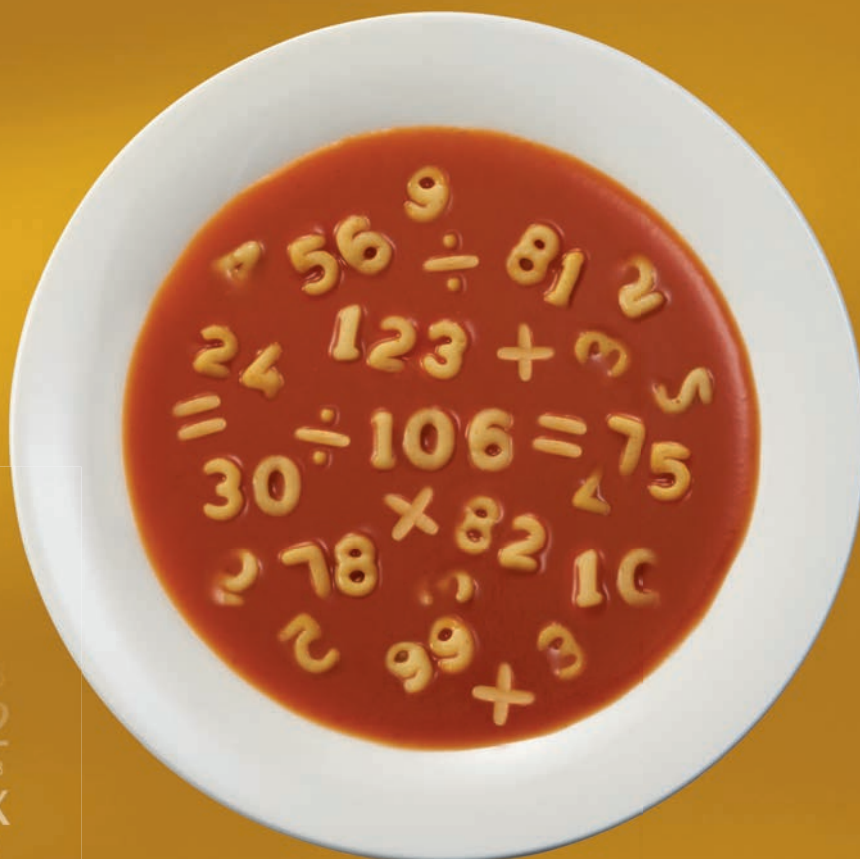
Endocrine Society leaders are concerned enough about the potential problems from EDCs that the Society published a scientific statement described as “an exhaustive summary of the scientific background that justifies concern for the effects of EDC exposures to humans and wildlife.” It stresses that “in the absence of direct information regarding cause and effect, the precautionary principle is critical to enhancing reproductive and endocrine health.”

Andrea Gore, PhD, one of the authors of the Endocrine Society scientific statement and editor of the journal *Endocrinology*, recommends an abundance of caution regarding exposure to EDCs, especially for both men and women planning a family. Many of the precautions sound a lot like the advice physicians generally give: Live a healthy lifestyle, and eat thoroughly washed fresh fruits and vegetables. Buy organic if you can afford it, especially for vegetables with large surface areas like lettuce and spinach. Avoid canned foods and foods stored in plastics, and don’t use plastic in the microwave.

And as for the patient who asks whether phthalates or other environmental exposures could be causing a fertility problem, Anawalt advises: “I think that the take-home message for clinicians needs to be that there is not enough evidence that that is the cause. There is a possibility that EDCs could affect male reproductive function, but the evidence is inconclusive. Until we can reassure patients that it does not appear to be the likely explanation, it is sensible to avoid prolonged exposure to potential toxins.” **EN**

— Seaborg is a freelance writer based in Charlottesville, Va. He wrote about endocrinologists’ influence in the June issue.

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KNIFE'S EDGE



For those diagnosed with pancreatic cancer early enough, difficult Whipple surgery remains the best option.

By Aalok Mehta

Few cancers are as deadly as pancreatic cancer. A silent killer, it often causes no symptoms during its early stages and is typically found only after it has already spread to nearby organs or into the bloodstream. More than half of patients will not survive a full year with the diagnosis; just 6% last five years or more, according to the American Cancer Society.

Even those who are diagnosed early, before the cancer has spread, however, have a difficult road ahead of them. Any chance at a cure requires surgery — and all of the available options are difficult, both in terms of the surgery itself and in terms of a long prognosis.

By far the most common option is the pancreatoduodenectomy (commonly called the Whipple procedure), in which surgeons remove the head of the pancreas, the gallbladder, and the bile duct, as well as portions of the stomach and small intestine. Roughly 2% to 3% of patients will die as a result of the surgery itself, never having a chance to leave the hospital due to infections, bleeding, or other acute complications.

A high rate of complications and the potential return of the cancer create additional problems. Roughly half of pancreatic cancer surgery patients will develop some sort of complication, and 10% to 20% manifest a severe

AT-A-GLANCE

- Surgery remains the only chance for a cure for pancreatic cancer, but less than a quarter of patients are diagnosed early enough to be eligible.
- The Whipple procedure carries high risk of death and complications, but is still superior to removing the entire pancreas.
- Surgeon experience and access to a multidisciplinary team can help minimize risk of complications, but researchers have otherwise remain largely stymied in improving treatments.

complication, most commonly a pancreatic fistula in which pancreatic secretions begin leaking. Overall, surgical patients have only a 20% to 25% chance of surviving five years.

“Even the smallest, earliest detected lesions can have bad outcomes,” says Eugene P. Ceppa, an assistant professor of surgery at Indiana University School of Medicine in Indianapolis. “The pancreas is a very fickle organ. It doesn’t like to be operated on.”

The difficult decisions facing pancreatic cancer patients highlight the disease’s persisting stubbornness. Unlike most other major cancers, including lung, colorectal, breast, and prostate cancer, pancreatic cancer death rates have slowly crept upward in the United States in the past decade.

No Good Surgical Alternatives

In addition to hiding deep within the body, where it can avoid most forms of imaging, pancreatic cancer also affects a vital organ. The pancreas produces several important hormones and digestive enzymes, including insulin.

These vital functions help explain the significant number of pancreatic cancer patients who aren’t initially eligible for surgery due to malnourishment. In addition to the cancer competing with healthy cells for nutrients, these patients typically suffer from a combination of appetite loss and an inability to properly digest fat, Ceppa says.

But the lack of good surgical alternatives to the Whipple underscores the overall importance of the pancreas even more. Although the exact surgery used is determined by the location of the pancreatic tumor and other factors, by preserving enough of the organ to maintain the production of insulin and digestive juices, Whipple patients face fewer metabolic complications than patients undergoing full removal of the pancreas, known as total pancreatectomy.

“We try to avoid them at all costs,” says Matthew Katz, an assistant professor of surgical oncology at the University of Texas MD

Anderson Cancer Center. “It leads to diabetes, malnutrition, and other complications. Patients just don’t do very well afterwards. It’s a harder operation chronically to manage.” He performs just one to two such surgeries each year, compared to 80 or more Whipple procedures.

Of particular concern from total pancreatectomies is a very brittle form of diabetes characterized by large, unpredictable, and dangerous swings in blood glucose levels. “Managing this is awful,” Ceppa says. “It really negatively affects the patient’s quality of life.”

Small Steps

Despite the challenges, physicians are exploring adjustments in treatment and technique to help improve outcomes for Whipple surgery patients, as well as ways to minimize the complications patients face afterwards.

As with many other surgeries, research has demonstrated that surgeon experience is a key factor. As surgeons gain experience with the Whipple, their patients tend to develop pancreatic fistulas at lower rates, for example. Katz says MD Anderson, as “a very experienced center,” sees fistula rates one-half to one-third the national average.

Alone, however, a surgeon is likely to have only a limited impact. Rather, for complex, multi-system operations such as the Whipple, ready access to multidisciplinary teams of highly trained physicians are likely to factor heavily on patient outcomes. “You need a multidisciplinary team to provide cancer care other than

surgery,” Katz says. “It’s not just technical performance that matters.” Without adjuvant therapy, perioperative care, nutritionists, and geriatricians, “you are not going to reap the full benefits of the operation.”

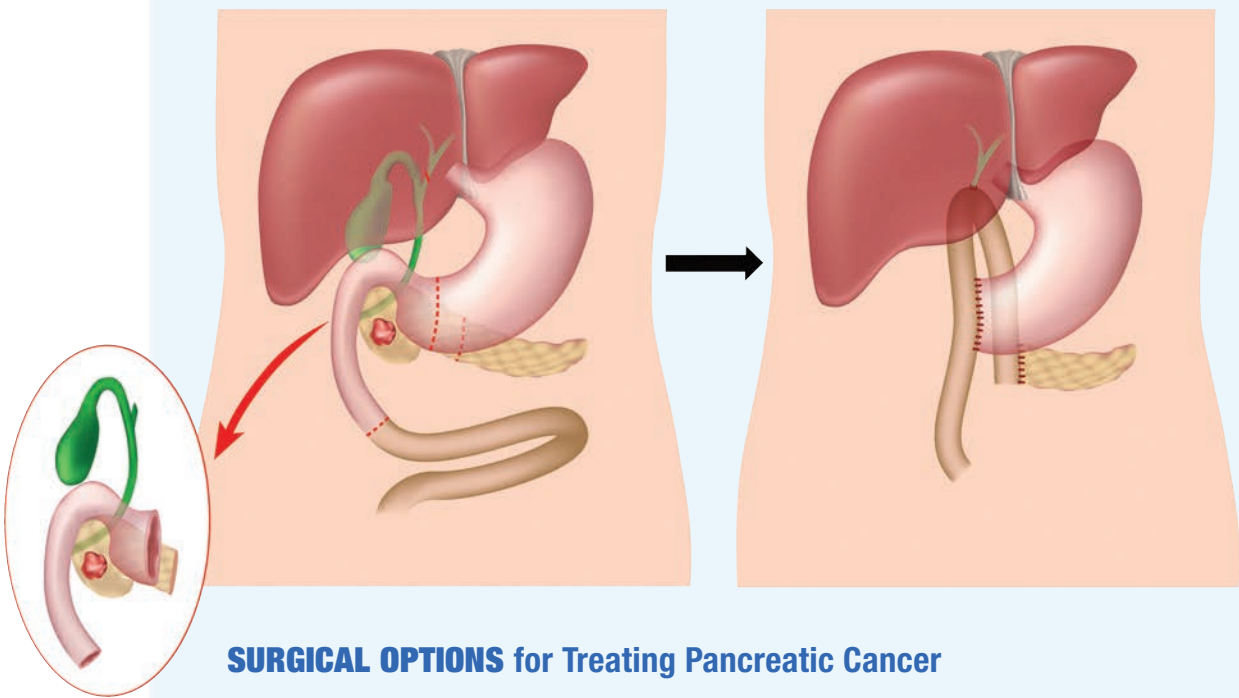
“The outcomes are better [with a multidisciplinary team],” Ceppa adds. “Timeliness is better; coordination is better; all of the critical captains are present in the conversation simultaneously. It’s definitely recommended. It would be like getting a travel agent to plan a vacation to a foreign country for you, that you are not familiar with or speak the language of, versus trying to plan it yourself.”



“Even the smallest, earliest detected lesions can have bad outcomes.

The pancreas is a very fickle organ. It doesn’t like to be operated on.”

— Eugene P. Ceppa,
assistant professor of surgery, Indiana University
School of Medicine, Indianapolis.



SURGICAL OPTIONS for Treating Pancreatic Cancer

Surgery is the only possibility for a long-term pancreatic cancer cure. However, only about 20% of patients are diagnosed early enough and are healthy enough for surgical treatment. Even then, the prognosis is grim; the five-year survival rate for surgery patients is still only 20%-25%.

Depending on the location of the tumor, the three major surgical options are the following:

- **Pancreatoduodenectomy (Whipple procedure):** removal of the head of the pancreas, gallbladder, bile duct, and portions of the stomach and small intestine; enough of the pancreas is kept to produce digestive juices and insulin.
- **Distal pancreatectomy:** removal of body and tail of pancreas, plus spleen.
- **Total pancreatectomy:** removal of entire pancreas, gallbladder, spleen, common bile duct, lymph nodes, and parts of the stomach and small intestine.

— American Cancer Society, *Cancer Facts & Figures 2013*

Many Options, One Outcome

Other developments include more aggressive use of pre-operative therapies to improve surgical outcomes. Pancreatic cancer surgeries are normally followed by adjuvant chemotherapy to kill lingering or new cancer cells, but more centers are now starting newly diagnosed pancreatic cancer patients on a round of chemotherapy prior to surgery. “We give a lot more therapy before surgery,” Katz says. “A lot more.”

However, there is “no census” on whether to use pre- or post-operative chemotherapy and the topic remains controversial, Ceppa says, with about 50% of doctors using each strategy. Success at shrinking tumors pre-operatively, moreover, can be caused by strong responses to the medications and less aggressive cancer strains. Research has found little difference in the strategies, with the exception that patients that present with tumors not amenable to surgery be reevaluated after chemotherapy in case their tumors shrink to more manageable sizes.

Equally ambiguous are the impacts of robot-assisted and laparoscopic techniques for Whipple surgery. Such techniques are being used more often, but remain a small

fraction of the overall number of pancreatic cancer surgeries performed in the United States. Studies have found similar outcomes between traditional and laparoscopic techniques, with some of the benefits of minimally invasive techniques counterbalanced by the longer operation time. The average open Whipple takes four to six hours, while a laparoscopic operation takes six to eight, Ceppa says. This might improve significantly in coming years, he says, as surgeons gain more expertise in applying minimally invasive surgical techniques to Whipple surgery.

Ultimately, though, researchers have made little improvement in pancreatic cancer treatments over the past decades, and the outcomes — even for those eligible for potentially curative surgery — remain grim. Because of its deep location in the body, a lack of early symptoms, and limited biomarkers to detect, pancreatic cancer remains difficult to diagnose during its initial stages. “Unfortunately,” Katz says, “in recent years there have been only a few major developments in treating pancreatic cancer.” **EN**

— Mehta is a freelance writer based in Cambridge, Mass. He wrote about EDCs and childhood illnesses in the April issue.

Congratulations to all finalists of the Oral Abstract Award in Reproductive Science (ICE/ENDO 2014 Annual Meeting)

Ansh Labs is a proud sponsor of the recent ICE/ENDO 2014 Annual Meeting. Our management team and scientific staff have been presenting, attending, and exhibiting at the International Congress of Endocrinology and Endocrine Society conferences for the past 3 decades. Ansh Labs is a young company, but our team has been working together for over 20 years. We are a science-driven organization and have always enjoyed ENDO for the quality of the research presented from talented scientists and physician researchers from around the world.

It has been our pleasure over the years to sponsor rising stars in endocrinology. As Ansh Labs, we continued this tradition with the sponsorship of The Oral Abstract Award in Reproductive Science, which honors the top ranked abstracts in reproductive endocrinology at ICE/ENDO 2014 and ENDO 2015. The 2014 Awardees were invited to present at a Special Oral Session in Reproductive Endocrinology.

We take this opportunity to recognize the finalists of the Oral Presentations in Reproductive Science award. A total of 323 abstracts were submitted under the reproductive endocrinology category. 239 (74%) of the submissions requested that they be considered for the award. Only six oral presentations were selected for the initial award. All oral presentations were ranked by a panel of expert judges at ENDO 2014, and the top two presentations were honored with an additional award for their achievement.

Kristen Tolson and Joseph Kurian, on behalf of Ansh Labs, please accept our warmest congratulations for receiving this honor from your fellow clinical and research professionals. Recognition of such achievements certainly reflects on your individual drive and commitment to excellence. We at Ansh Labs are proud to have sponsored this award and to have you feature your prestigious work.



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Oral Presentations in Reproductive Science Supported by Ansh Labs

***Joseph Kurian**, "The Methylcytosine Dioxygenase Ten-Eleven Translocase-2 (Tet2) Enables Elevated GnRH Gene Expression and the Typical Development and Maintenance of Reproductive Function."

Wisconsin National Primate Research Center
University of Wisconsin-Madison, Madison, WI

***Kristen Tolson**, "Kisspeptin Signaling Is a Novel Player in Obesity, Metabolism, and Glucose Homeostasis in Female Mice."

Reproductive Medicine
University of California, San Diego, La Jolla, CA

Alberto Ferlin, "Male Reproductive Function Is Genetically Determined By Polymorphisms in Fshb and FSHR Genes."

Department of Medicine
University of Padova, Padova, Italy

Channa Jayasena, "Comparing the Effects of Pituitary Versus Hypothalamic Stimulation of the Human Reproductive Axis Using Equimolar Intravenous Infusions of Kisspeptin-10, Kisspeptin-54 and Gonadotrophin Releasing Hormone (GnRH) in Healthy Men."

Investigative Medicine
Imperial College London, London, United Kingdom

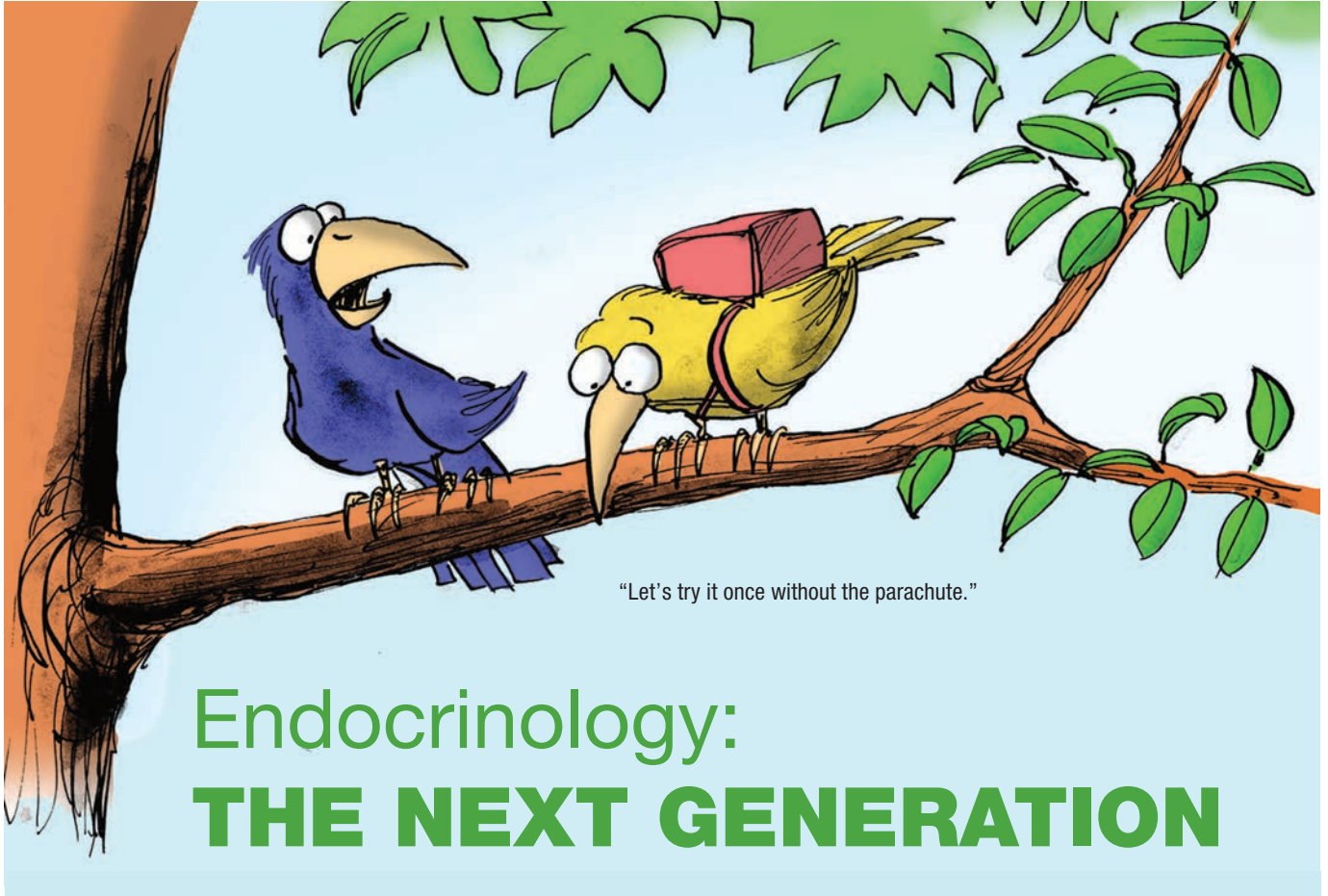
Kim Jonas, "Single Molecule Analysis of GPCR Transactivation Via PD-PALM Reveals Oligomeric Complexes That Regulate Signal Sensitivity."

Institute of Reproductive & Developmental Biology
Imperial College of London, London, United Kingdom

Panneerdoss Subbarayalu, "Androgen-Responsive Mir-471 Expression in Sertoli Cells Is Essential for Phagocytosis of Apoptotic Germ Cells, Germ Cell Development and Complete Male Fertility."

Greehey Children's Cancer Research Institute,
University of Texas Health Science Center at San Antonio,
San Antonio, TX





Being a mentor helps a physician influence and guide the next generation of endocrinology physicians. Being a mentee helps smooth transitions throughout their career.

By Kurt Ullman

A mentor is a senior physician who acts as a guide or adviser to another person. Mentoring is becoming recognized as an important piece of the development of the mentor, the mentee, and the profession of endocrinology.

"If we as a Society want to continue to be vibrant and active, it is imperative that we not only recruit, but also retain, the young individuals who will be the next generation's leaders," says Richard J. Santen, MD, president of the Endocrine Society. "Particularly in endocrinology, it is important for senior members to help the younger ones through the various hurdles that are needed for success. As we try to enhance their careers, mentorship is really the key."

Characteristics of a Good Mentor

There are a number of behaviors that are characteristic of a good mentor. Santen thinks the most important is the motivation to expend some of their time and energy to help others be successful. The second is an altruistic quality and unselfishness.

"One of the most important things for a mentee to look for in a mentor is the ability to sit down and have open communication," says Michelle Y. Rivera-Vega, MD, clinical educator at Nemours Children's Hospital in Orlando, Fla. "As a new physician and researcher, I don't have everything figured out. Therefore, my mentor should be able to help me form my



"Sometimes it's good to get a different perspective."

goals and then help develop the timeline to meet them.”

Another important consideration is to make sure the expectations of both sides are in congruence. “As a young physician, mentorship is a valuable tool as you have someone guiding you; not to follow in their footsteps, but to gain what you want as a person,” says Rivera-Vega. “The mentee has to know that the mentor is there to point you in the right direction to meet your goals. But it is important to remember that they aren’t there to solve all of your problems.”

Multiple Mentors?

Many mentees may need more than one mentor. Both Santen and Rivera-Vega suggest a clinical mentor to help the younger doctor find key information, locate people to talk to about challenging cases, and assist in sorting out the tests and procedures they need to know about to provide good patient care.

“If someone is going into research, then a mentor can be useful in acclimating the younger physician to the needs of that situation,” says Santen, who is also a professor of medicine at the University of Virginia Health System in Charlottesville. “How to successfully compete for grant money and run their research studies are important. Another is to make sure they understand the requirements for promotion and tenure.”

The third is a life mentor.

“They don’t necessarily have to work in the same field as you do,” notes Rivera-Vega. “This person should be able to help you sort through all the issues in your personal life that can have an impact on your professional. How you deal with a kid’s illness and similar things.”

Changing Needs, Changing Mentors

A mentor is not necessarily a lifetime commitment for either of you. Indeed, as a physician grows and matures in their field, the role of the mentor needs to change with it.

The mentor may start out as a teacher, educating the mentee in basics such as grant applications and tenure requirements. Later, there are other concerns related to how the mentee’s career is progressing. At some time, the mentor is often called on to consult with the mentee, as they become mentors on their own.

“As a mentee progresses in his or her career, the mentor generally assumes a role as a colleague,” Santen says. “This is a gradual process and may take years. However, several successful, independent investigators still refer to their mentors as mentors even when they have achieved international prominence.”

In some cases, it may be necessary



“He’s really taking to the training.”

What Makes a GOOD MENTOR?

Emma Eggleston, MD, and colleagues wrote in the *Journal of Clinical Endocrinology and Metabolism* about the most popular traits for an ideal mentor, including:

- Ability to provide feedback and constructive criticism
- Ability to foster and support the mentee’s independence
- Communication skills
- Accessibility
- Ability to be a role model and lead by example.

to change mentors, even early on. Probably one of the main reasons is just an inability to mesh personally. Missing interpersonal chemistry is a big issue in the success of a mentor/mentee relationship.

“If the mentee finds that the mentor isn’t willing to give up their time, that is a key indicator that perhaps they should find somebody else,” Santen advises. “If you feel your mentor isn’t looking out for your best interests over their own, it is probably appropriate to move on.”

A successful mentoring relationship is one that helps both sides. The younger physician gets the guidance they need to begin and maintain a successful career. The older one has the satisfaction of seeing the mentee flourish and knowing that they are influencing the next generations of endocrinology. **EN**



“Tomorrow I’ll teach you how to land.”

— Ullman, RN, MHA, is an Indiana-based freelance writer with nearly 30 years of experience. He wrote about non-compete clauses in the July issue.



TOOLS OF ENGAGEMENT

From science fiction becoming a reality to cutting-edge software breakthroughs, exciting new developments in medical technology have the potential to transform your laboratory.

By Melissa Mapes

Healthcare and technology have always gone hand in hand. The great discoveries of the ages have all improved the physical well-being of mankind in some way — from the capturing of electricity to the introduction of the smartphone. None of today's hospitals and research facilities could operate at an optimum level without power, and many of them are incorporating iPhones and tablets into medical devices, patient diagnosis, and data analysis.

The rate of invention has multiplied as advances build upon each other and make new findings faster and easier than ever. Among the many technologies

sweeping through medicine, a few standouts have emerged as game changers, likely to revolutionize endocrinology and healthcare as a whole.

Nanorobotics

The 1966 film *Fantastic Voyage* portrayed a seemingly impossible technology when a microscopic submarine was injected into a man's bloodstream to find and remove a blood clot in his brain. While the shrink ray that resized the watercraft remains a piece of science fiction, the filmmakers nearly predicted the nanobots in use 48 years later.

“BEST IN KLAS” Clinical Decision Support Systems

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Logical Images VisualDx	Clinical Decision Support — Point of Care Clinical Reference	Category Leader Award
Wolters Kluwer Pharmacy OneSource Senti7	Clinical Decision Support — Surveillance	Category Leader Award

— (From the January 2014 KLAS report, based on votes by providers)

About five years ago, researchers at the Micro/Nanophysics Research Laboratory at Australia’s Monash University developed a nanorobot one-quarter of a millimeter in length with the ability to swim through the bloodstream. A number of new projects popped up since — paving the way for an imaginary miracle device to become a reality.

Scientists intend to make the tiny bots perform a number of tasks, such as scraping plaque off of artery walls or finding cancer cells and injecting them with drugs. But, until recently, one major problem has stood in the way: battery life.

The nanorobots in most laboratories can only hold a minuscule battery that loses power in minutes, making it nearly impossible for the bots to complete their programmed task. At the Cockrell School of Engineering at the University of Texas, researchers are putting the finishing touches on what appears to be the tiniest, quickest, and longest-lasting nanomotor yet. Their little robots can last up to 15 hours and fit inside a single cell. The microscopic motor was recently the subject of a paper published in *Nature Communications*.

If the Texan research team can push their nano device through to clinical trials, then physicians may soon have access to a futuristic tool for highly targeted drug deliveries to diseased cells. Patients would simply have to swallow a pill or receive an injection to put the minuscule bots to work, like the fictional scientist and his blood clot in a B-movie from almost 50 years ago.

3-Dimensional Bioprinting

Need a new organ? In a few years, you may be able to order one from the printer. Naturally, you will not be stopping by the local Kinkos, nor will you call up a tech geek friend who built his own 3D printer in his garage. Rather, a few biotechnology companies have been incorporating human tissue into multi-dimensional printing in hopes of placing artificial organs on the market in the not-too-distant future.

3D printers use computer models to build anything from toys to blood vessels out of the material they are loaded with, such as plastic or human cells. A professor of bioengineering at Rice University, Jordan Miller, PhD, took his 3D printer to Washington, D.C., in May 2014, to demonstrate the possibilities. Right now, Miller recreates human blood vessels using sugar, but has the technology

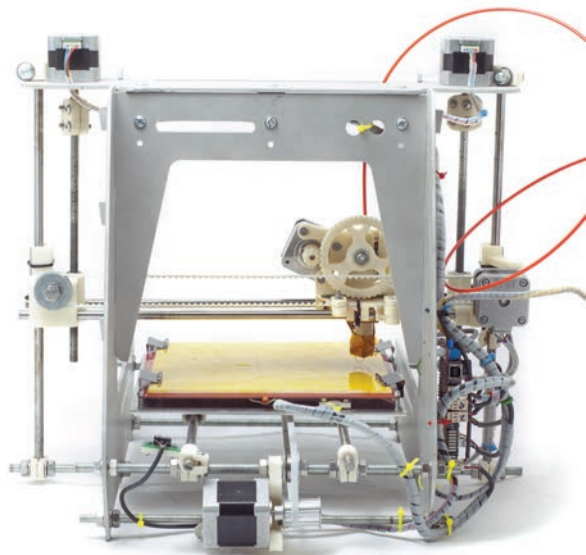
to build vessels and organs from cultured human cells.

It will be years before the methods for 3D-printing organs is perfected, but researchers like Miller are trying to help policy makers better understand their work in hopes of overcoming media sensationalism and preempting regulatory hurdles.

Other scientists, like Paul Frisch, PhD, of the Memorial Sloan-Kettering Cancer Center in New York, are using 3D printers to build replicas of patients’ hip, spine, and knee bones. This makes it easier to identify the location and size of abnormalities, like tumors. Potentially, hip replacements and the like could also be built in his lab.

Organovo, a biotech company in California, is working on a range of therapeutic uses of 3D-printing human tissue. Recently, the company’s primary focus has been liver tissue. Pharmaceutical companies are about to begin using their printed liver tissue for drug testing, which could lead to a better understanding prior to market release of how some medications affect the human liver.

3D printers have clearly come a long way from their introduction in the 1980s. With increasing practical applications for this technology popping up, funding for research will surely continue to increase, and custom-made organs and bones could reach hospitals within another couple decades.



A 3-D printer that can create everything from hip bones to blood vessels.

ENDOCRINE REVIEWS

CALL FOR NOMINATIONS AND APPLICATIONS FOR EDITOR-IN-CHIEF OF ENDOCRINE REVIEWS

The Endocrine Society seeks candidates for the position of Editor-In-Chief of *Endocrine Reviews* for a five-year term beginning January 1, 2015. *Endocrine Reviews* publishes bimonthly comprehensive, authoritative, and timely review articles balancing both experimental and clinical endocrinology themes, crystallizing the most significant clinical experience and current research in endocrinology and related areas such as cell biology, immunology, pharmacology, genetics, molecular biology, neuroscience, reproductive medicine, and pediatric endocrinology.

RESPONSIBILITIES

The Editor-In-Chief receives editorial and administrative support from Springer and the Endocrine Society's editorial office staff, as well as an honorarium. The Editor-In-Chief oversees the peer review process and content development, including the following:

- Selecting Editors and Advisory Board members
- Providing direction for the journal and its content by identifying emerging "hot" areas of importance and soliciting papers for submission
- Participating in meetings of the Publications Core Committee
- Participating in meetings with the Editors-in-Chief of the Society's other journals

NOMINATIONS

All members of the Endocrine Society are encouraged to suggest the names of potential candidates by contacting Nancy Rodnan, Senior Director of Publications for the Endocrine Society, at nrodnan@endocrine.org. Please submit your suggestions by September 12, 2014.

APPLICATIONS

Applicants for the position should submit the following material:

- Description of qualifications
- Statement outlining how the candidate plans to oversee the journal, including goals for content, target readership, acceptance criteria, and editorial policy
- Proposed Associate Editors, areas of expertise, and process for editorial decision-making
- Discussion of the present status of the journal, opportunities for growth and enhancement, and plans to achieve goals
- Curriculum vitae

Applications are due by **September 30, 2014**, and should be e-mailed to Nancy Rodnan (nrodnan@endocrine.org). Please call 202-971-3669 to ensure that your submission has been received. Selected candidates will be contacted by the search committee chair and asked to provide more details. The Publications Core Committee will interview finalists in person at its October 2014 meeting and choose a candidate to recommend to the Endocrine Society Council.

PUBLICATIONS CORE COMMITTEE

The search process is being undertaken by the Publications Core Committee and is overseen by its chair, Margaret Shupnik, PhD.



An example of a hand-held device with access to a clinical decision support system.

Decision-Support Software

With a shortage of primary care providers and specialists alike, physician-extenders like nurses and physician's assistants have become more important than ever to the practice of medicine. To help practitioners make efficient, accurate diagnosis and find the proper course of treatment, doctors have teamed up with software programmers to build decision support systems.

These programs incorporate into electronic health records (EHRs) to track and analyze patient information. They sprung up alongside the federal requirements for "meaningful use," which necessitate a data-driven approach to healthcare.

KLAS, the primary independent evaluator of EHRs, describes the five elements of a clinical decision support system (CDS) as: "order sets, multi-parameter alerting, nursing care plans, reference content, and drug information databases." Essentially, they provide a vast index of knowledge that helps keep patients safe and make practitioners' jobs significantly easier.

Archimedes IndiGO, for example, is a CDS that combines clinical information with an individual patient's physiology and medical history to create a tailored treatment plan. IndiGO makes recommendations based on both health factors and insurance coverage to find drugs and other treatment options covered under the patient's plan.

Many decision support software options are competing for market share, and the best among them each offer unique characteristics and methods for revolutionizing the medical practice. Like EHRs, time will determine the systems that become industry standards. According to KLAS, "these CDS tools are only just beginning to scratch the surface of their potential."

The same can be said for all three technology sets. Nanorobotics, 3D printing, and decision support software are rapidly advancing, but still in their adolescence. Only a single aspect of their future is ensured: We will be hearing a lot about them in the years to come. **EN**

— *Mapes is a Washington D.C.-based freelance writer and a regular contributor to Endocrine News.*

Senate LHHS Bill and Report Incorporates Endocrine Society Priorities

By Joseph M. Laakso, PhD

The federal appropriations process directs spending for a number of agencies and programs that support Endocrine Society researchers and enable practicing endocrinologists to treat patients more effectively. The Senate and House Appropriations Subcommittees on Labor, Health and Human Services and Related Agencies (LHHS) are responsible for funding, among other things, the National Institutes of Health (NIH) and also the National Diabetes Prevention Program (NDPP). Many Endocrine Society researchers rely on grants from the NIH to support work towards improving our understanding of human biology and discovering cures for endocrine diseases. The NDPP is a public-private partnership working to “establish local evidence-based lifestyle change programs for people at high risk for type 2 diabetes.” Endocrinologists who treat patients with diabetes have been encouraged by the success of the NDPP and are eager to see the program continue to expand.

Because of the critical importance of the NIH and the NDPP to Endocrine Society members and to public health generally, the Endocrine Society considers federal funding of the NIH and NDPP to be key advocacy priorities. On July 24, the Senate Appropriations Committee released the text and report language for the fiscal year (FY) 2015 LHHS bill. The Senate bill provides significant increases in funding for both the NIH and the NDPP. The Senate proposes to fund the NIH at approximately \$30.5 billion, an increase of over \$600 million. The NDPP would also receive \$15 million, an increase of \$5 million. The strong support expressed for these initiatives in the Senate LHHS bill reflects the combined efforts of the Endocrine Society staff, members, and advocacy coalition partners. Society members helped drive these successes by participating in advocacy campaigns to show grassroots support for the NIH. Also, clinicians advocated for increased

NDPP funding during the Societys Clinician Hill Day.

Additionally, the Endocrine Society has been working to raise awareness of the importance of considering sex differences as a critical biological variable in preclinical research, where appropriate. To encourage federal agencies to pay more attention to this issue, the Senate LHHS Appropriations report includes language supporting the NIH in efforts to study sex and gender differences in research. Specifically, the Committee commended the NIH “on the recent policy announced to begin assessing sex and gender as important biological variables in pre-clinical trials. Results that are more applicable to one gender may lead to recommendations or conclusions that should, but do not, differentiate between men and women.” The Committee also requested an update in 2016 on progress by the NIH towards implementing the policies.

While the Senate bill and report are important actions taken by the Congress, there is still more work and negotiation that must take place before a final appropriations bill is enacted. At the time this article was written, the likely near-term outcome is that Congress will attempt to pass a Continuing Resolution (CR) to fund the government from the beginning of FY 2015 through mid-November, to give legislators additional time to craft a final appropriations package. As the Congress works towards a final appropriations package for FY 2015, the Society will build on its successes and continue to put pressure on legislators to support Endocrine Society member priorities, such as the NDPP and steady, sustainable increases for the NIH. Additionally, the Society will continue to engage with the NIH and other stakeholders as policies to address sex differences are developed. **EN**

— Laakso is the associate director, Science Policy, at the Endocrine Society. He can be reached at jlaakso@endocrine.org.



IN MEMORIAM: E. Chester “Chip” Ridgway, MD



The Endocrine Society, its members, and the worlds of endocrinology research and education are mourning the loss of *Endocrine Reviews* editor-in-chief, E. Chester “Chip” Ridgway, MD, who lost his battle with pancreatic cancer on July 30. He was 72.

A Society past president (2003 – 2004), Ridgway was the senior associate dean for academic affairs at the University of Colorado Health Sciences Center in Aurora. Prior to being named editor-in-chief of *Endocrine Reviews* in 2010, he was one of that journal’s associate editors for five years, and was on the editorial board of the *Journal of Clinical Endocrinology & Metabolism* from 1984 to 1987. His work outside the pages of the Society’s journals was just as voluminous: He served on the Society’s Nominating Committee (1993 – 1995) and served one-year term as chairman; he was on the Council (1996 – 1999); the Awards Committee (2006); and chaired the Government Relations Committee from 2004 to 2008. He was also awarded the Society’s Women in Endocrinology Mentor Award in 2005 and the Robert H. Williams Distinguished Leadership Award in 2009.

“We were all saddened to hear about the recent passing of Chip Ridgway, one of the most stellar members of the Endocrine Society. We have lost a wonderful colleague,” says Society president Richard J. Santen, MD. “From the patients he treated and the young physicians and research assistants he mentored, to his groundbreaking thyroid research, Chip’s impact on the field of endocrinology and medicine is immeasurable. He will be greatly missed.”

Aside from his leadership role with the Society, Ridgway also served a term as president of the American Thyroid Association in 1996 and is the co-author of the book, *Your Thyroid: A Home Reference*. He was an expert in the study of the thyroid stimulating hormone and its regulation of the thyroid and had authored or co-authored more than 200 journal articles.

However, despite his role as one of the world’s leading

thyroid researchers, Ridgway took great pride in the number of endocrine fellows he guided on their paths. By his own estimate, Ridgway trained more than 100 clinical endocrine fellows and more than 30 endocrine fellows in research throughout his career. These trainees are currently division heads, section heads, or members of academic endocrine departments, in addition to chairs of medicine and deans of medical schools.

“Chip was a wonderful mentor to so many endocrine trainees who began their careers in Colorado and within his division (the Division of Endocrinology, University of Colorado),” says Carol Lange, PhD, professor of medicine and pharmacology, Division of Hematology, Oncology, and Transplantation, University of Minnesota Masonic Cancer Center in Minneapolis. “He always provided advice that was in one’s best interest and for the greater good. Sometimes this is really what one needed to hear, and not necessarily what one wanted to hear. His wisdom and his wit will be missed.”

Ridgway received his undergraduate degree from Dartmouth College in 1964 and his MD degree from the University of Colorado School of Medicine in 1968. Following his residency and fellowship at Harvard Medical School, he joined the faculty at Harvard University and the Massachusetts General Hospital where he was head of the Thyroid Unit. In 1985 he was recruited back to the University of Colorado School of Medicine as the head of the Division of Endocrinology, Metabolism, and Diabetes, a position he held until 2007. In 1995, Ridgway was appointed senior associate dean for Academic Affairs within the School of Medicine. In 2006, he was appointed executive vice chair for the Department of Medicine and served as interim chair for the Department of Medicine during 2010. In November 2011, Ridgway was awarded the designation of Distinguished Professor at the University of Colorado.

“It has been a tremendous privilege and gift to have known Chip Ridgway over these past 25 years as a mentor, as a colleague, and most importantly as a friend,” says Bryan R. Haugen, MD, professor of medicine and pathology, and head of the Division of Endocrinology, Metabolism, and Diabetes at the University of Colorado in Denver. “I am who I am because of Chip in so many ways. Not just as an endocrinologist, scientist, clinician, and administrator, but also as a husband, father, son, and friend. He taught me so much in that thoughtful and gently guiding way so many of us know. There are few people in this world who have so profoundly touched so many people, and Chip Ridgway is one of the rare ones. He will be deeply missed by so many.” **EN**

— Mark A. Newman

ENDO 2015

Where Insight, Innovation, and Your Work Converge

At **ENDO** you can customize your experience by selecting from a host of sessions on a variety of topics in endocrinology. It's also a great opportunity to present your original research to an international gathering of your peers.

Do it all at the first major endocrinology meeting of the year: **ENDO 2015**, coming March 5 through 8 to the San Diego Convention Center in San Diego, Calif.

Present Your Work, Advance Your Career

There are countless benefits to presenting your abstract at **ENDO 2015**, including: sharing your research and receiving valuable feedback from an international audience and connecting with potential mentors and training opportunities. Journalists see **ENDO** as a premier source of breaking research and exciting clinical trials in the field of endocrinology. More than 75 reporters covered **ICE/ENDO 2014**, increasing the public's understanding of hot topics in endocrinology.

**Get your abstracts in early this year:
The deadline is November 11, 2014.**

TAKE THE FAST TRACK TO PUBLICATION

The ENDO 2015 Clinical Trials Express Program lets you feature your work and puts you on the fast track to publication.

When your clinical trial is accepted for abstract presentation at **ENDO 2015**, you may submit it for expedited review as a manuscript in *The Journal of Clinical Endocrinology & Metabolism*. That can lead to online publication within four weeks of acceptance.

Plenty to Discover at Plenary Sessions

Endocrinology experts from around the globe will converge to deliver their cutting-edge research and state-of-the-art clinical care during this year's 16 plenary lectures. Exciting advances in the fields of obesity, diabetes, cancer, reproductive disorders, and signaling will be featured.

The Presidential Plenary on Thursday will provide new understandings of personalized menopause management. James Ingle, MD, of the Mayo Clinic will examine the roles of genetics in therapy responses, and public advocate and professor JoAnn Manson, MD, DrPH, will outline the biomarker data that informs today's menopause management decisions.

New Offerings Stimulate Professional Improvement

ENDO 2015 will feature three new Clinical Practice Guideline sessions designed to improve individual practices and the profession at large. The sessions will focus on the latest guidance on adrenal insufficiency, menopause, and Cushing's syndrome treatment.

Two Master Clinician sessions also promise to educate and enlighten, as clinicians and experts will evaluate challenging cases involving the diagnosis and management of pituitary tumors and neuroendocrine tumors.

Innovative Sessions, Unprecedented Access

This year's lineup of new Meet the Professor sessions connect you to authorities on topics ranging from testosterone therapy to Paget's disease to pediatric lipid disorders.

Next-generation sequencing tools and chronic kidney disease controversies are just two of more than 70 intriguing symposia spanning the spectrum of endocrinology and health. Check out the full scientific program to make the most of every minute, visit endo2015.org.

Get with the Programs — Starting Now

Registration for **ENDO 2015** is now open! Visit endo2015.org to secure your spot at the earliest and best **ENDO** yet. **EN**

ENDOCRINE AND METABOLIC MEDICAL EMERGENCIES Reunite a Student and Teacher at ICE/ENDO 2014

Not only were connections created amid the hustle and bustle of the record-breaking **ICE/ENDO 2014** in Chicago in June, but old acquaintances were renewed.

One such renewal took place at the Endocrine Society's booth in the middle of the exhibit hall at McCormick Place when Ming Li, MD, PhD, a fellow in endocrinology in the fellowship program of Diabetes and Endocrinology at the University of Minnesota ran across Glenn Matfin, MD, a consultant physician in the UK's National Health Service and editor of *Endocrine and Metabolic Medical Emergencies*, the first book published by the Society's own imprint, Endocrine Press.

Matfin had served as a preceptor in the fellows' continuity clinic in the Division of Endocrinology, Diabetes, and Metabolism at the University of Minnesota where he saw endocrinology patients with Li, who says Matfin was "great with case-based teaching."

As Matfin's former student, Li says he was really proud seeing his mentor's work on the shelf. "It is a great accomplishment on his part to not only have authored several outstanding chapters himself," he says, "but also to have convened some of the greatest minds in endocrinology from all over the world to pass on their collective wisdom in this comprehensive volume."

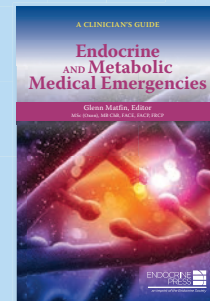
Li doesn't just have accolades for Matfin; he also praises *Endocrine and Metabolic Medical Emergencies* from a fellow's perspective, saying that as a comprehensive review of endocrinology emergencies, it not only provides many useful and practical algorithms and tips in clinical management of endocrinology emergencies, but also thoroughly discusses the pathophysiological bases of these conditions.

Specifically, Li says, the discussions for many of the topics are broad in scope and not limited to pure endocrinology, but also include other aspects

Glenn Matfin, MD, editor of *Endocrine and Metabolic Medical Emergencies* — the first book from the Society's Endocrine Press — signs a copy for his former student, Ming Li, MD, PhD, an endocrinology fellow at the University of Minnesota in Minneapolis at **ICE/ENDO 2014** in Chicago.

— Photo by David Tulchinsky

You can purchase your copy of *Endocrine and Metabolic Medical Emergencies* by going to www.endocrine.org/emme. Fellows can get this bestseller as an ebook for as low as \$30!



of clinical medicine that are potentially affected by the particular condition discussed. "As we get used to the fact that endocrinology has more or less become a mostly outpatient practice, this volume gave us a timely reminder that we are physicians first, then endocrinologists," he says. "And the patients should be treated as a diseased human being instead of an endocrine condition that was described in some text book." **EN** — Mark A. Newman

ICE/ENDO 2014 Research Generates Headlines

Research presented at **ICE/ENDO 2014**, the joint meeting of the Endocrine Society and the International Society of Endocrinology, was featured in the pages of prominent media outlets across the country and around the world.

To date, more than 1,700 separate articles and reports have covered **ICE/ENDO 2014**. The meeting was highlighted in a number of top-tier outlets, including *The Chicago Tribune*, *Scientific American*, *Nature*, *The Philadelphia Inquirer*, and *The New York Daily News*.

The Society hosted five news

conferences on site featuring some of the most compelling and newsworthy findings presented at the meeting. More than 60 reporters participated in press conferences (both on site and via webcast) and registered to attend the meeting.

One of the hottest stories was a Reuters Health article about a new way to measure salivary cortisol levels using a smartphone and disposable test strip. The story was picked up by a variety of media outlets, including *The Chicago Tribune* and *The New York Daily News*. An abstract from the National Institutes of Health's

National Institute of Diabetes and Digestive and Kidney Diseases examining how cold temperatures may activate brown fat also generated significant media coverage from outlets such as WebMD and *The Daily Mail*.

Other outlets that reported on **ICE/ENDO 2014** include: Huffington Post, *Shape* magazine, *Prevention*, *Parents* magazine, and *U.S. News & World Report*.

The news conferences, which were moderated by members of the Society's Advocacy and Public Outreach Core Committee, can be viewed in their entirety online at www.endowebcasting.com.

Endocrine Society Urges ABIM to Suspend New MOC Requirements

When the Internal Medicine Summit hosted by the American Board of Internal Medicine (ABIM) took place in Washington, D.C., in July, the Endocrine Society joined with 25 organizations representing nearly all internal medicine subspecialties in voicing concerns regarding ABIM's Maintenance of Certification (MOC) program.

While the Society supports the MOC system's goals of continuous learning and improvement, its members have significant concerns with the unintended consequences of the new changes to the program.

The more stringent demands of MOC will likely diminish clinicians' available time for patients and negatively impact the quality of care. Furthermore, clinicians engaging in other professional roles, like research, may be pushed out of clinical practice entirely, placing a burden on the endocrine workforce at a time of

increasing patient need.

The Society and other attending subspecialty organizations were unanimous in their concerns about MOC regarding the unreasonable financial burden on physicians, the limited utility of the secure exam, and the desire for a broader scope of professional activities to be recognized within the MOC system.

In light of these and other concerns, the Society is urging ABIM to conduct a formal analysis of all possible unintended consequences of the new MOC requirements, with input from all professional societies and other stakeholders. During this process, the Society asks that the ABIM suspend its new MOC requirements.

The Society sent a letter to ABIM on June 5th highlighting its concerns and recommendations regarding the MOC program. The letter can be found at <https://www.endocrine.org/abim>.

Coming Soon! Laureate Awards Call for Nominations

Beginning October 1, the Laureate Awards Committee will accept nominations for the 2016 award cycle. Visit the awards Web page to learn more!

Event CALENDAR

SEPTEMBER 2 – 6, 2014, SAN FRANCISCO, CALIF. Endocrine Board Review and Clinical Endocrinology Update • [Endocrine.org/SF](http://www.endocrine.org/SF)

SEPTEMBER 12, 2014, WASHINGTON, D.C. ACA Implementation: Impact on the Patient with Diabetes • <http://www.endocrine.org/meetings/policy-summit>

SEPTEMBER 14 – 17, WASHINGTON, D.C. 10th International Meeting of Pediatric Endocrinology www.pedsendo.org

SEPTEMBER 15 – 19, 2014, VIENNA, AUSTRIA 50th European Association for the Study of Diabetes Annual Meeting • www.easd.org

Recipients Announced for the Society's 2014 EARLY CAREER AWARDS

The Endocrine Society is pleased to recognize young endocrinologists for their exceptional accomplishments in endocrinology. Visit the Society's Awards & Grants pages to view this year's recipients. Check out the variety of awards the Society has to offer and get a head start preparing yourself for the 2015 awards season. For more information, go to www.endocrine.org/awards.

Endocrine Reviews Tops the “Endocrinology and Metabolism” Journals List

In Thomson Reuters' recently released annual *Journal Citation Report* (JCR) for 2013, *Endocrine Reviews* ranked first in Impact Factor among the 123 journals in the “Endocrinology & Metabolism” category.

A highly regarded metric used to measure a journal's success, the 2013 Impact Factor is calculated by taking the number of citations made in 2013 to articles published in 2011 and 2012, and then dividing that number by the total number of articles published in 2011 and 2012.

Endocrine Reviews retained its ranking as the top journal in the field of Endocrinology & Metabolism, with an Impact Factor of 19.358 for 2013. The total number of citations received is another measure of success for journals tracked by the *Journal Citation Report*. The Society's *Journal of Clinical Endocrinology & Metabolism* ranked first in the number of citations received in 2013.

“We are thrilled that *Endocrine Reviews* has once more earned the highest Impact Factor in the category of Endocrinology & Metabolism,” says Margaret Shupnik, PhD, the Society's Publications Core Committee Chair. “This great achievement would not be possible without the excellent work of our authors, reviewers, and editors.”

Endocrine Reviews publishes bimonthly comprehensive, authoritative, and timely review articles balancing both experimental and clinical endocrinology themes. **EN**



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



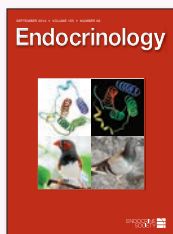
Synthetic Glucocorticoid Reduces Human Placental System A Transport in Women Treated with Antenatal Therapy

• Melanie C. Audette, John R. G. Challis, Rebecca L. Jones, Colin P. Sibley, and Stephen G. Matthews • *We conclude that women who are at risk of preterm labor and receive sGC but deliver at term have significantly*

reduced placental system A amino acid transporter activity. Altered placental transporter function could impact on fetal growth and may contribute to developmental programming reported in both animal and clinical studies.

Racial Differences in Peripheral Insulin Sensitivity and Mitochondrial Capacity in the Absence of Obesity

• James P. DeLany, John J. Dubé, Robert A. Standley, Giovanna Distefano, Bret H. Goodpaster, Maja Stefanovic-Racic, Paul M. Coen, and Frederico G.S. Toledo • *When compared to CW, AAW have similar hepatic insulin sensitivity, but a muscle phenotype characterized by both lower insulin sensitivity and lower mitochondrial oxidative capacity. These observations occur in the absence of obesity and are not explained by physical activity. The only factor associated with lower insulin sensitivity in AAW was mitochondrial oxidative capacity. Because exercise training improves both mitochondrial capacity and insulin sensitivity, we suggest that it may be of particular benefit as a strategy for diabetes prevention in AAW.*



Glucagon-Like Peptide (GCGL) Is a Novel Potential Thyrotropin (TSH)-releasing Factor (TRF) in Chickens: I Evidence for Its Potent and Specific Action on Stimulating TSH mRNA Expression and Secretion in the Pituitary

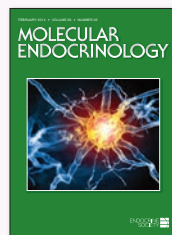
• Guian Huang, Chen He, Fengyan Meng, Juan Li, Jiannan Zhang, and Yajun Wang • *The potent*

and specific action of GCGL on pituitary TSH expression and secretion, together with the partial accordance shown among the temporal expression profiles of GCGL in the hypothalamus and GCGLR and TSH β in the pituitary, provides the first collective evidence that hypothalamic GCGL is most likely to be a novel TSH-releasing factor (TRF) functioning in chickens. The discovery of this novel potential TRF (GCGL) in a non-mammalian vertebrate species, i.e. chickens, would facilitate our comprehensive understanding of the hypothalamic control of pituitary-thyroid axis across vertebrates.

Polybrominated Diphenyl Ether (DE-71) Interferes with Thyroid Hormone Action Independent of Effects on Circulating Levels of Thyroid Hormone

• Ruby Bansal, Daniel Tighe, Amin Denai, Dorothea F. K. Rawn, Dean W.

Gaertner, Doug L. Arnold, Mary E. Gilbert, and R. Thomas Zoeller • *Tissue PBDEs were in the μ g/g lipid range, only slightly higher than observed in human fetal tissues. Thus, PBDE exposure reduces serum T4, but does not produce effects on tissues typical of low TH produced by PTU, demonstrating that the effects of chemical exposure on serum T4 levels may not always be a faithful proxy measure of chemical effects on the ability of thyroid hormone to regulate development and adult physiology.*



Crosstalk between Nuclear MET and SOX9/ β -Catenin Correlates with Castration Resistant Prostate Cancer

• Yingqiu Xie, Wenfu Lu, Shenji Liu, Qing Yang, Brett S. Carver, Estelle Li, Yuzhuo Wang, Ladan Fazli, Martin Gleave, and Zhenbang Chen • *Our findings reveal for the first time an essential role of nMET association with*

SOX9/ β -Catenin in CRPC in vitro and in vivo, highlighting nuclear receptor tyrosine kinases (RTKs) activate cell reprogramming to drive recurrence and targeting nMET would be a new avenue to treat recurrent cancers

Hey U(PS): Metabolic and Proteolytic Homeostasis Linked via AMPK and the Ubiquitin Proteasome System

• Sarah M. Ronnebaum, Cam Patterson, and Jonathan C. Schisler • *This review serves to identify the current understanding of the interplay between AMPK and the UPS and to promote further exploration of the relationship between these regulators of energy utilization and amino acid availability within the cell.*



Inhibin at 90: From Discovery to Clinical Application, a Historical Review

• Yogeshwar Mankanji, Jie Zhu, Rama Mishra, Chris Holmquist, Winifred P.S. Wong, Neena B. Schwartz, Kelly E. Mayo, and Teresa K. Woodruff • *In this review, we provide a comprehensive summary of our current understanding of the*

biological role of inhibin, its relationship with activin, its signaling mechanisms, and its potential value as a diagnostic marker for reproductive function and pregnancy-associated conditions.

Current Approaches and Recent Developments in the Management of Head and Neck Paragangliomas

• David Taieb, Alexandre Kaliski, Carsten C. Boedeker, Victoria Martucci, Tito Fojo, John R. Adler, Jr., and Karel Pacak • *This review will also particularly emphasize current and emerging knowledge in genetics, imaging, and therapeutic options, as well as the health-related quality of life for patients with HNPGLs.*

YOUR THYROID

WHAT YOU NEED TO KNOW



Hormone Health
NETWORK®
Keep your body in balance

The thyroid makes hormones that travel through your bloodstream and regulate how your body breaks down food and uses it for energy. It is part of the endocrine system, which includes the pituitary gland, hypothalamus, thymus, pineal gland, testes, ovaries, adrenal glands, parathyroid and pancreas.

Visit hormone.org for more information.

ABOUT YOUR THYROID

The thyroid secretes hormones that help regulate:

brain development and function

eyes

heart

skin and hair

weight/metabolism

intestine function

The thyroid is governed by the pituitary (called the "master gland"), a pea-sized organ located at the base of the brain.

The thyroid is a butterfly shaped gland at the front of the neck.



HOW IT WORKS

1

Pituitary gland checks amount of thyroid hormone in blood

2

Pituitary tells thyroid to make more or less hormone so there's always a balanced amount

3



Thyroid uses iodine (mainly from seafood and dairy products) to make thyroid hormone; iodine is absorbed through intestine into bloodstream, then makes its way to thyroid

4

Thyroid disorders occur when something goes wrong with the process, and too much or too little thyroid hormone is produced

THYROID DISORDERS:

occur when thyroid releases too many (overactive) or too few (underactive) hormones. These disorders frequently run in families, and are more common in women.

 HYPERTHYROIDISM = OVERACTIVE	<ul style="list-style-type: none"> • Increased bowel movements • Increased sweating • Weight loss 	<ul style="list-style-type: none"> • Irritability • Fatigue • Vision problems 	<ul style="list-style-type: none"> • Irregular menstruation (light) • Anxiety/nervousness
<p>..... NORMAL THYROID FUNCTION</p>			
 HYPOTHYROIDISM = UNDERACTIVE	<ul style="list-style-type: none"> • Constipation • Intolerance to cold 	<ul style="list-style-type: none"> • Weight gain • Dry skin, dry hair 	<ul style="list-style-type: none"> • Irregular menstruation (heavy) • Fatigue

IF YOU HAVE A THYROID DISORDER:

- ✓ Take your prescribed medication as directed
- ✓ Be aware of drug interactions



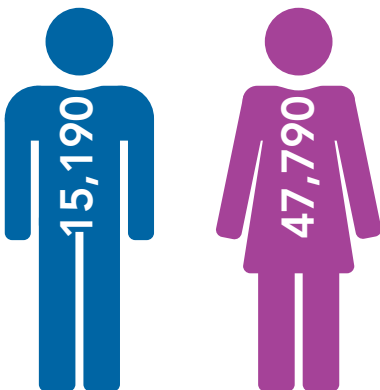
- ✓ Have your healthcare provider check for nodules



- ✓ Eat a balanced diet
- ✓ Get enough sleep and exercise



Estimated new cases of thyroid cancer in 2014:



NODULES

- Lump or swelling in thyroid gland
- No effect on thyroid function, usually no effect on thyroid hormone
- More than 90% are not harmful or dangerous, but some can be cancerous
- Nodules can be detected by a "neck check" by your healthcare provider

THYROID CANCER

- Most common endocrine cancer
- Occurs in all ages, children through seniors
- No symptoms in early stage
- About two out of every three people diagnosed are between ages 20 and 55

Patients have questions. We have answers.

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

Additional editing by Alan Farwell, MD, Boston Medical Center

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

PRESBYTERIAN HEALTHCARE SERVICES, Albuquerque, NM:

Presbyterian Healthcare Services is seeking BE/BC Endocrinology trained physicians to join Presbyterian Medical Group and our well established Endocrinology providers. Our medical group employs more than 600 primary care and specialty providers and is the fastest growing employed physician group in New Mexico. Presbyterian Healthcare Services is a locally owned, not-for-profit organization based in Albuquerque. Our integrated healthcare system includes eight hospitals in seven New Mexico cities, a medical group, multispecialty clinics and a health plan (over 400,000 members). We have been proudly providing care to New Mexicans for 105 years. In addition to a guaranteed base salary we also offer a sign on bonus, incentive bonus, malpractice, relocation, house hunting trip, health, dental, vision, 403(b) w/contribution from PHS 457(b), short & long term disability, CME allowance, etc. Albuquerque thrives as New Mexico's largest metropolitan center with a population of 700,000. Albuquerque has been listed as one of the best places to live in the United States by Newsweek, U.S. News & World Report, Money and Entrepreneur Magazines! Albuquerque is considered a destination city for most types of outdoor activities with 310 days of sunshine. Albuquerque is recognized as one of the most culturally diverse cities in the country. Its ethnic diversity is carried into its architecture, art, music, dance and cuisine. A truly diverse and multicultural city, Albuquerque offers you and your family a great variety of activities and entertainment including national theater productions, sporting events, golf courses ranked among the best in the country, the largest hot air balloon festival in the US, American Indian Cultural activities and much more. For more information, e-mail [Kelly Herrera at kherrera@phs.org](mailto:Kelly.Herrera@phs.org) or call 1-505-923-5662. H1B Opportunity. Visit our website at www.phs.org EOE

University of Michigan Endocrine Oncology Fellowship

Program General Information: The Endocrine Oncology Program (EOP) of the Comprehensive Cancer Center of the University of Michigan is accepting applications for a one-year advanced training fellowship in endocrine oncology. This program is one of the only multidisciplinary endocrine oncology programs in the nation that provides comprehensive evaluation and treatment of patients with endocrine neoplasias. Our team includes endocrine surgeons, endocrinologists, oncologists, nuclear medicine specialists, pathologists, interventional radiologists, radiation oncologists, genetic counselors and others who are leaders in their fields. Cases are reviewed weekly by our Multidisciplinary Endocrine Oncology Tumor Board. We offer the latest treatment options, including access to both standard and investigational therapies. The clinic's comprehensive approach encompasses the needs of the patient and the family. The EOP is actively involved in researching the causes and treatment of adrenal and other endocrine cancers. This program, established in 2005, brings experts in related fields together to provide coordinated, exceptional patient care. The Endocrine Oncology Fellowship Program will consist of a 12 month training period. In this clinical training program, physicians will acquire the skills and knowledge base for evaluating and treating patients with these complex

endocrine tumors. The curriculum will include outpatient management of patients with complicated endocrine neoplasias and hormonal disorders, including patients enrolled into Phase I-III clinical trials. Rotations in endocrinology, medical oncology, surgery, pathology, nuclear medicine and radiology. Upon completion of the program, an individual would be proficient in clinical care of these patients, primarily in the outpatient setting. While the primary focus of this Fellowship is clinical emersion, individuals will have protected time devoted towards an academic initiative, either a bench or clinical research project, during their training period. Academic opportunities will include routine conferences (e.g. multidisciplinary treatment-planning conferences, research conferences, grand rounds) and the education of medical students, residents, or fellows. Trainees will be encouraged to present clinical or research experiences at local, national or international meetings. Other opportunities will include focus on research, grant writing, and/or clinical trial design will be determined in association with the Endocrine Oncology leadership team and would depend on an applicant's prior exposure and training. Eligibility: Candidates must have completed a residency program in Internal Medicine and a fellowship training program in Medical Oncology or Diabetes, Endocrinology & Diabetes) and be board certified or board eligible in either specialty. There are no restrictions to the length of time from completion of fellowship training to subsequent application for the Endocrine Oncology Fellowship Program. Most of the clinical experience will take place in the outpatient setting. During the first two-six months, the fellow will function as a fellow with attending oversight. During the remainder of the fellowship, the fellow will function as an attending. Fellows will participate in the Endocrine Oncology clinic Tuesday AM and PM Sessions every week. In addition, 4 additional half-day clinics/week will be chosen from the list below (Each clinical experience requires a minimum of 3-4 month participation). Selection Process: 1. Completion of a U.S. accredited fellowship in Diabetes, Endocrinology and Metabolism or Medical Oncology in good standing. 2. Must have an active license from the Michigan Medical Board or be eligible to obtain a license or training permit from the Michigan Medical Board and, in the case of a foreign medical graduate, must be eligible for an appropriate Visa. 3. Completion of an application form. 4. Personal Statement (including goals and reason for pursuing an Endocrine Oncology Fellowship). 5. Curriculum Vitae. 6. Letters of recommendation (2) plus one from the fellowship program director. 7. Medical School transcripts. 8. USMLE scores. After a review of the required elements, a personal interview with faculty members will be arranged with outstanding candidates. All qualified applicants will receive consideration without regard to race, color, religion, sex, national origin, age, handicap, sexual orientation or veteran status. Interested applicants should contact Lisa K. Byrd (lisakb@umich.edu; 734-615-2421). Gary D. Hammer, M.D., Ph.D., Director – Endocrine Oncology Program, University of Michigan Comprehensive Cancer Center, ghammer@umich.edu. University of Michigan School of Medicine is accredited by the Accreditation Council for Graduate Medical Education (ACGME).

Endocrinologist Opportunities

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

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

About the Position at GMC

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

About the Position at GWV

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

About the Position at Geisinger-Patton Forrest

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

Geisinger Health System serves nearly 3 million people in Northeastern and Central Pennsylvania and has been nationally recognized for innovative practices and quality care. A mature electronic health record connects a comprehensive network of 5 hospitals, 43 community practice sites and more than 1000 Geisinger primary and specialty care physicians.

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

GEISINGER HEALTH SYSTEM

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Geisinger is a drug-screening employer; EOE/M/F/D/V

Pediatric Endocrinology

Penn State Hershey Children's Hospital

The Penn State Hershey Children's Hospital at the Penn State Milton Hershey Medical Center and the Penn State Hershey College of Medicine seek a Pediatric Endocrinologist at a rank of Assistant or Associate Professor. This will be the sixth physician to join our expanding Division of Pediatric Endocrinology.

Active in endocrine and diabetes service, the Division is interested in pioneering research and clinical trials and was awarded Best Children's Hospital by *US News & World Report* in 2012-2013. The Division's faculty is supported by a team of five nurses, two nutritionists, one social worker, one pediatric psychologist, and two administrative assistants.

The Department of Pediatrics has a strong interest and achievements in both laboratory and clinical research and maintains an active Office of Clinical Research. On-site access to an NIH-funded GCRC and a multidisciplinary Penn State Institute for Diabetes and Obesity offer additional opportunities for collaboration.

Individuals with excellent clinical and teaching skills, capable of providing the highest level of patient care and education, are invited to apply online at www.pennstatehersheycareers.com/jobs/77824

The Penn State Milton S. Hershey Medical Center is committed to affirmative action, equal opportunity, and the diversity of its workforce. Equal Opportunity Employer – Minorities/Women/Protected Veterans/Disabled.

PENNSSTATE HERSCHEY
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Medical Center



Coastal Connecticut

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

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

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

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

Email CV to Sally Williams, Manager of Physician Recruitment, at swilliams@lmhosp.org.

ENDOCRINE ESSENTIALS *Live*

The Endocrine Society is bringing top-quality clinical updates to your area with **Endocrine Essentials Live**. This regional series features two programs designed for both professional endocrinologists and primary care physicians treating endocrine-related diseases.

JOIN EXPERT FACULTY AT A PROGRAM CONVENIENT TO YOU.

SATURDAY, SEPTEMBER 20, 2014
► Atlanta, GA

SATURDAY, SEPTEMBER 27, 2014
► St. Louis, MO

SATURDAY, OCTOBER 25, 2014
► Charlotte, NC

SATURDAY, NOVEMBER 15, 2014
► Seattle, WA
► Manhattan Beach, CA

REGISTER TODAY!

ENDOCRINE ESSENTIALS PRO for endocrinologists will provide a clinical endocrinology update on acromegaly, hypogonadism, and bone disorders.

This activity is eligible for 5 AMA PRA Category 1 Credits™

This activity is supported by educational grants from Amgen, Lilly USA, LLC, Novo Nordisk Inc., and NPS Pharmaceuticals, Inc. as of August 1, 2014.

ENDOCRINE ESSENTIALS FOR PRIMARY CARE is a practical update on obesity, diabetes, and androgen deficiency for internists, general practitioners, diabetes educators, and other primary care providers.

This activity is eligible for 5.5 AMA PRA Category 1 Credits™

This activity is supported by educational grants from Lilly USA, LLC, Ethicon Endo-Surgery, Inc, Merck & Co., Inc., and Novo Nordisk Inc. as of August 1, 2014.

LEARN MORE AND REGISTER AT ENDOCRINE.ORG/EEL

ENDOCRINE SOCIETY

REGISTER TODAY FOR THE BEST RATES

ENDO 2015

THE ENDOCRINE SOCIETY'S 97TH ANNUAL MEETING & EXPO



MARCH 5-8, 2015 (THURSDAY-SUNDAY)
SAN DIEGO, CALIFORNIA

SAN DIEGO CONVENTION CENTER

BEGINNING IN 2015, ENDO, THE LARGEST GATHERING OF
ENDOCRINE PRACTITIONERS AND RESEARCHERS, WILL TAKE PLACE IN THE SPRING.

KEY ENDO 2015 DATES

REGISTRATION OPENS

JUNE 23, 2014

ABSTRACT SUBMISSION

SEPTEMBER 17 – NOVEMBER 12, 2014

LATE-BREAKING ABSTRACT SUBMISSION

DECEMBER 29, 2014 – JANUARY 12, 2015

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