Managing Your Diabetes ON A BUDGET
To improve the health of people living with diabetes

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EmPower, published by the American College of Endocrinology (ACE), the educational and scientific arm of the American Association of Clinical Endocrinologists (AACE), is dedicated to promoting the art and science of clinical endocrinology for the improvement of patient care and public health. Designed as an aid to patients, EmPower includes current information and opinions on subjects related to endocrine health. The information in this publication does not dictate an exclusive course of treatment or procedure to be followed and should not be construed as excluding other acceptable methods of practice. Variations taking into account the needs of the individual patient, resources, and limitations unique to the institution or type of practice may be appropriate.

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AACE is a professional medical organization with more than 6,000 members in the United States and more than 90 other countries. Founded in 1991, AACE is dedicated to the optimal care of patients with endocrine problems. AACE initiatives inform the public about endocrine disorders. AACE also conducts continuing education programs for clinical endocrinologists, physicians whose advanced, specialized training enables them to be experts in the care of endocrine diseases such as diabetes, thyroid disorders, growth hormone deficiency, osteoporosis, cholesterol disorders, hypertension and obesity.

ACE is a scientific and charitable medical organization dedicated to promoting the art and science of clinical endocrinology for the improvement of patient care and public health.
Dear Reader,

Welcome to the Spring 2014 EmPower issue! We hope you will find it very informative.

As this academic year approaches its end and we begin to plan for new trainees in Endocrinology to begin in hospitals and research labs in July, we recognize the gained expertise of those beginning a new phase in their professional careers – leaving training programs to begin their clinical careers. You may well see a new graduate in your neighborhood clinic, or working with endocrinologists you or your family members have been seeing at medical centers. Several of these trainees, from training programs across the U.S., have contributed to this EmPower issue.

You will learn about Cushing’s disease and disorder, you will learn about a problem of overproduction of another hormone, prolactin. Other areas reviewed include bone disorders, the challenge of managing diabetes with a limited budget, and more. All important topics! And let us know what you think about these pieces from these new endocrinologists.

We also highlight new, as well as lesser known, information about diabetes mellitus. The tools for management of diabetes continue to get better and better – more “user friendly.” Some of those tools are highlighted here. And medical literature continues to show the tremendous energy and effort among medical researchers, going into the understanding of diabetes and its associated conditions, how better to treat these, even how better to diagnose. And, as we approach the century landmark from the official discovery of insulin, we hope you enjoy a retrospective look at what led to this discovery.

So, as you begin to think of warm temperatures, sunny skies, flowers, take to heart the advice your medical team has given you regarding the simple steps that can help you keep your healthiest. Take a walk around the block, or bike to a local park with your children, your spouse, your partner. Walk through a farmer’s market... and bring home some fresh vegetables and fruits! Enjoy summer’s bounty!

Sincerely,

DONALD A. BERGMAN, MD, MACE
Executive Editor

DACE L. TRENCE, MD, FACE
Editor-in-Chief

DANIEL EINHORN, MD, FACP, FACE
President, American College of Endocrinology

Dr. Donald Bergman is in private practice in New York City and is board certified in internal medicine and endocrinology and metabolism. He is Clinical Professor of Medicine at Mount Sinai School of Medicine in New York City. Dr. Bergman is past president of AACE and ACE. In 2003, during his AACE presidency, Dr. Bergman founded EmPower, previously known as “Power of Prevention,” a program that encourages people to partner with their physicians in establishing healthy lifestyles and demonstrating the importance of primary and secondary prevention. He serves as Executive Editor of EmPower Magazine.

Dr. Dace Trence is Director of the Diabetes Care Center and Professor of Medicine at the University of Washington Medical Center in Seattle. She is also the University of Washington Endocrine Fellowship Program Director and Director of Endocrine Days, a medical education program for endocrinologists practicing in the Pacific Northwest. She is on the American College of Endocrinology Board of Trustees and chairs the CME Committee and is also chair of the AACE Publications Committee.

Dr. Daniel Einhorn is the 2013-2014 American College of Endocrinology (ACE) President. He is a clinical endocrinologist with Diabetes and Endocrine Associates, Medical Director of the Scripps Whittier Diabetes Institute, and a Clinical Professor of Medicine at the University of California San Diego.
Prior to starting my second year of training to be a specialist in diagnosing and treating diseases of metabolism, diabetes and nutrition, a “fellowship” that focuses on hormone disorders, I was honored to be the recipient of the Bender Fellowship at the University of Washington. This supported me as I focused on how to help low-income, uninsured persons struggling to maintain their health.

Diabetes, high blood pressure and high cholesterol can affect both quality and quantity of life, if not treated. These conditions do not discriminate – they can affect all age groups and all ethnic groups. Even on a limited income, there are many cost-effective ways to control these conditions, such as increasing physical activity and making better dietary choices and taking a look at the use of various herbs/spices, instead of salt to flavor food.

Managing Diabetes On A Budget

By Marisela Noorhasan, MD

Having diabetes mellitus (DM), specifically type 2 DM, means your body is not effectively using the insulin it is producing to metabolize your food, and
it is not producing as much as insulin as it should. Diabetes, if uncontrolled, can affect the heart, kidneys and eyes over time. Many people do not know they have diabetes and only become diagnosed when they have blurred vision and go to an eye specialist to check out their vision. Further questioning can reveal that additional symptoms such as frequent urination have been mistakenly linked to suspected problems such as an enlarged prostate, or “I am just getting older,” and the real diagnosis is then unfortunately delayed. Fatigue is another symptom of diabetes...and who is not fatigued from time to time? Even headaches and leg cramps can be signs of diabetes – so if you are experiencing these symptoms, get checked!

There are two types of diabetes, type 1 and type 2. Type 1 diabetes requires treatment with insulin because the pancreas cannot produce insulin, while type 2 diabetes can be treated in its early stages by taking pills. Very typically however, if you have type 2 diabetes, you will require insulin over time. This is due to the continued decrease of insulin production in your body, eventually requiring supplementation of insulin.

So how does one deal with diabetes on a low budget? Pills and insulin can be quite expensive! I spend a lot of time talking with the patients I see discussing the benefits of exercise, meal content choices and using spices. Exercise of just 30 minutes daily has been shown to maintain weight or even cause weight loss. And exercise can increase insulin sensitivity, meaning less insulin is needed to control your blood sugar. Exercise can be fun, and varying the exercise type can make exercise more interesting on a day-to-day basis. Start with simple stretches, jumping jacks, walks, jogging stationary in one spot, and/or lifting cans of soups as weights. Also, extra calories can be burned while doing housework chores: dance to music while you vacuum or wash dishes, or walk your dog rather than simply letting your dog out to the back yard. Lift your legs up and down—“march”—while talking on the phone. No need for fancy equipment or spandex outfits! Exercise does not have to mean going to a gym and paying monthly fees. TV exercise programs such as “Namaste Yoga” and “Kundalini Yoga” offer great yoga exercises. There are fun dance exercises available on CD that include “Bollywood Dance Workout,” “Dance & Be Fit” and “Shimm” that can be borrowed from your local library or followed on YouTube. Web-based free exercise programs can entertain while making exercises enjoyable. Try it!

Though supplements, in the forms of vitamins, herbs, minerals and spices, are not approved by the Food and Drug Administration (FDA), they are regulated under the Dietary Supplement Health and Education Act of 1994 (DSHEA) under a different set of regulations than those covering “conventional” foods and drug products. Thus, caution is necessary when taking supplements. But some herbs and even foods such as aloe, karalla, fenugreek, parsley, rosemary, eyebright and almond nuts may help to control blood sugars. Scientific data is clearly sparser than one would like to see in support of many claims of benefit. However, spices can make vegetables more interesting without adding salt, and who would eat cauliflower without some flavor enhancing? Limiting or avoiding foods such as rice and pasta, candies and sodas can lower blood sugars. And substituting artificial sweeteners for sugar can minimize post-meal blood sugar spikes.

There are cost-saving strategies even for medication required in the treatment of diabetes. Using generic rather than brand-name medications typically lowers your cost of prescription medications. Ordering a higher prescription dose of medication and cutting the medication to the prescribed dose can make the medication last twice as long. Metformin can be used with insulin to lower the insulin dose in insulin-resistant diabetes. Web resources can offer less costly supplies, such as meters and strips—but make sure these are reliable sources—speak with your doctor and/or diabetes educator as to whether these are reliable websites. Unfortunately, if it’s too good to be true, it could indeed be too good to be true. Many have paid for what turn out to be long-expired meter strips. Discuss with your health team how often your insulin syringe could be reused – data have been published showing reuse could be safe. Using insulin in vials rather than using prefilled insulin pens could be a big cost-saver, particularly if you are needing a lot of daily insulin. But those using small amounts of insulin might save money by switching to prefilled insulin pens!

(Continued on page 6)
MANAGING HIGH BLOOD PRESSURE

High blood pressure or hypertension hardens the arteries and causes the heart to work harder. Exercise, minimizing salt in your diet, losing weight and minimizing stress are important ways to prevent as well as treat high blood pressure. The same exercises used for treatment of diabetes can be used for hypertension. Foods such as tamarind drink, spinach, beans, sunflower seeds, bananas, spinach, squash, cantaloupe, garlic, celery, lemon, honey, ginger, cumin seeds and cayenne pepper may help to reduce blood pressure because they are rich in magnesium and potassium. Avoid salty food, put away your salt shaker, eat fewer preserved foods, frozen dinners and canned foods, as these are typically high in salt. Also, avoid overindulging in alcohol — it can increase blood pressure. For those requiring medication, splitting higher dose pills to get a smaller prescribed dose is another means for cost savings, but this should not be done with pills marked as “extended release” or “slow release.”

HELPING TO CONTROL CHOLESTEROL

Cholesterol is a fat produced by the liver and is also taken in by diet. Cholesterol is necessary for regulating body function. But too much cholesterol can cause health problems. It can narrow the space inside arteries for blood flow to the heart, the brain and the legs. If cholesterol is not controlled, it can lead to heart disease, strokes and leg amputation. A diet high in fatty food, smoking, excess alcohol intake and obesity are associated with an increase in bad cholesterol, LDL (low density lipoprotein). Herbs and foods which can reduce cholesterol are: dandelion root, pumpkin seed, oats, sunflower seeds, whole grain breads, broccoli, cabbage, carrots, oranges and salmon. Exercise also can reduce cholesterol.

As diabetes, high blood pressure and cholesterol are contributing factors for heart disease, stroke, and even death, it is important to check for these conditions to know if treatment is necessary. Being cost conscious does not mean having less to offer you! And thank you Bender Fellowship, for supporting me in this journey!
It is estimated that one third of the U.S. population will be diagnosed with diabetes mellitus by the mid part of this century...perhaps even sooner if the rising trend in newly diagnosed diabetes cases continues. The vast majority of these diabetes cases will be type 2, the diabetes that results from the body’s own insulin not working as it should (what is referred to as “insulin resistance”), plus progressively less insulin being produced by the body’s pancreas.

In the early stages of diabetes type 2, medication might not be necessary. Dietary changes, combined with increased physical activity, can be very effective in controlling blood sugar. Recommended dietary changes typically include an emphasis on decreasing sugary liquid and food intake and often also decreasing total calories to lose weight. Physical activity should be increased—which does not mean having to swim the ocean to China and back every night—but making an effort to routinely (daily) walk, garden, bike. The goal is to make muscles work, as this makes the body more sensitive to insulin...and more likely to make the insulin that is being made more efficient in its work in helping keep blood sugars within normal levels.

As time progresses, medication will usually be needed to bring the blood sugar level down to normal levels. There are a variety of pills that work in different ways to help the body regulate sugar levels. Although typically (Continued on page 8)
one pill is prescribed, with doses adjusted depending on how well it works to get the blood sugar to goal levels. However, there is now a major, long-term study that is trying to answer a very important question: would it be better to start on a combination of two drugs?

Funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), part of the National Institutes of Health (NIH), The GRADE (Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness) Study is looking at a combination of metformin and one of four other drugs. More information can be found at https://grade.bsc.gwu.edu. The results of this study, however, will not be known for some years. So, for now, the usual treatment approach is to add another pill if control of the blood sugar is not obtained at full dose of your first prescribed medication. This dual pill approach might even require a third pill. But at some point, even if pills have worked, they might not work as they did when first prescribed. Experts in the field know from a study done in the past, the UKPDS (United Kingdom Prospective Diabetes Study), that when used to control blood sugars to as normal a level as possible, pills failed for 50 percent of patients within three years and for 75 percent of patients within nine years. When this happens, there is a choice of injectable medicine: a GLP-1 (glucagon-like polypeptide-1) agonist or insulin.

**THIS IS NOT A TIME TO PANIC!**

Although a discussion about the need to start insulin can come as an unwelcome surprise, it does not mean that there has been a failure on your part to manage your diabetes. Remember that earlier in this article it was mentioned that part of the problem of type 2 diabetes is the progressive inability of the pancreas to make insulin. So, for many people with type 2 diabetes, there will come a need to start the use of insulin. And great progress has been made in the tools that are made for insulin use.

First, syringes have become shorter and thinner and are now 6 millimeters (about ¼ inch) in length and 31 gauge thickness (for comparison, as a measure of thinness, a safety pin is typically 17-18 gauge, and the larger the gauge, the thinner the needle). Many lancets used for doing fingerstick blood sugar checks are in the 28-30 gauge range, so they are thicker than insulin syringes!

Second, insulin can also be given through pen devices. These are either pens that are disposable after the contained insulin is used up or beyond recommended duration of use, or pens that are metal and designed to hold cartridges containing insulin—the cartridge being the disposable part—once the contained insulin has been used or has gone beyond the recommended
duration of use. Needle tips that are put on the pen for insulin injection are available even in shorter sizes: 4 millimeters (about 1/6 inch), 5 millimeters (about 1/5 inch) and 8 millimeters (1/3 inch). Proper technique should be reviewed with your diabetes team, but studies show that learning how to use a pen is much easier than learning how to use an insulin syringe.

Some pens even come with a memory feature that records what your last injected insulin amount was and when it was given. But pens can be more expensive than insulin given through syringes, and health insurance coverage varies. Some insurance policies do not cover pens, some only under very specific conditions. Yet it makes sense to do some investigation into your costs for pens versus insulin bottles and syringes.

Insulin bottles should be discarded at 30 days from opening due to concerns over changes in insulin efficacy (potency), which could mean a lot of insulin having to be discarded if the doses you are using are small. As one pen contains 300 units of insulin, and typically there are 5 pens to a box, it might be more economical to use a pen if your daily insulin dose need is a small one. Your one box of pens might last you longer with less insulin having to be tossed. This is something that you should definitely review with your diabetes team!

Third, insulin can be given through reservoirs, commonly known as pumps. The American Association of Clinical Endocrinologists (AACE) has just updated a review of the status of insulin pumps in the U.S., under the guidance of diabetes specialist Dr. George Grunberger in collaboration with other experts in diabetes care. Insulin pumps are not new tools in diabetes. They have been used for more than 35 years. But the technology has improved dramatically over the years, and use also has increased dramatically. In the U.S. in 2005, an estimated 20 to 30 percent of individuals with type 1 diabetes (the diabetes that results from lack of insulin being produced by the pancreas) and less than one percent in those individuals with type 2 diabetes on insulin therapy, were using insulin pumps. The U.S. Food and Drug Administration (FDA) estimated that 375,000 pumps were in use in the U.S. in 2007, up from approximately 130,000 in 2002. And the numbers are increasing!

Several different pumps are available on the market. Some have insulin in a contained pod, put on the skin, that is controlled by a separate device, much like a PDA. Other pumps have the capacity to be linked to a continuous blood sugar sensor that can shut the pump down for a period of time if a pre-determined low blood sugar level is sensed. Some pumps have the capacity to receive glucose (blood sugar) data from your glucose meter, allowing the use of computer-based programs located in the pump that can help decide how much of an insulin dose might be required for a meal, or to bring down a high blood sugar to more normal levels. But pumps require much skill in preparation to ensure optimal operation. Education in how best to use the pump to help you with your diabetes is a critical part of preparing for pump use. And pumps are very expensive.

A possible alternative is the recently available “patch pump”—a disposable reservoir of insulin designed to work for 24 hours and then disposed of. It delivers one of three different constant rates of insulin over 24 hours and also allows a variable amount of insulin to be given before meals. This is a less-costly alternative to typical insulin pumps, but is limited in the amount of daily total insulin that can be delivered in this manner.

The bottom line: if you hear insulin mentioned, don’t despair. You DO have options! ☯
What do you call kids who don’t let type 1 diabetes stand between them and their dreams?
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It takes a special type of kid to handle the rigors of high school, manage the daily demands of type 1 diabetes, and grow into great young adults. That’s why at Lilly, we’re proud to support the Diabetes Scholars Foundation, offering scholarships to help them pay for college.

To learn more about these scholarships, visit diabetesscholars.org/Lilly. And take this page to discuss with your healthcare provider. For more information about all the helpful programs Lilly offers families with type 1 diabetes, visit lillydiabetes.com.
How to Help Your Loved One Cope with Diabetes

BY THE NATIONAL DIABETES EDUCATION PROGRAM

Diabetes is a hard disease to manage alone. But here’s the good news: people are able to manage diabetes better if they have strong support from their family and friends.

If someone you love has diabetes, there are steps you can take now to help your loved one manage his or her condition. The first thing to do is learn all you can about this disease, which affects nearly 26 million Americans and could lead to serious health problems such as heart disease, stroke, blindness and nerve damage.

After you’ve learned about diabetes, be sure to ask your loved one how you can help him or her handle it.

Above all, keep in mind that you’re there to help the person you love live a full and active life while managing diabetes. Here are some suggestions. Just remember that every action HELPS:

Help your loved one write a list of questions to ask his or her health care team.

Eat well. Support your loved one by making meals that include fruits, vegetables and whole grains.

Listen. Being a good listener is often the most important thing you can do to help.

Practice good care by asking your loved one if he or she would like reminders about scheduling doctor appointments, checking blood sugar levels and taking medicine.

Suggest activities you can do together, such as walking, dancing or gardening.

For more resources from the National Diabetes Education Program to help your loved one live well with diabetes, visit www.YourDiabetesInfo.org/HealthSense, or download or order copies of Help a Loved One Cope with Diabetes.

The U.S. Department of Health and Human Services’ National Diabetes Education Program is jointly sponsored by the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) with the support of more than 200 partner organizations.
Obesity has become one of the most serious health problems Americans face today. About one in three adults is obese, and another one of the three is overweight. About one in seven of America’s young people are obese and at increased risk of becoming obese adults. Obesity has been shown to increase the risk of developing many other medical problems including heart disease, stroke, some kinds of cancer and diabetes. As we try to face this problem, a number of questions come to mind.

**WHAT MAKES US WANT TO EAT?**

Normally, the brain responds to many signals from within the body and from the external environment to help it to know when it is time to eat and when eating should stop. We are all familiar with things in our environment that seem to increase our appetites, such as the smells of food nearby, food advertisements, parties with friends, group meals and even emotional triggers, like stress, which can change our drive to eat.

Through recent scientific research, we are also learning more about hormone signals within the body that affect our appetites and how many calories we burn. Our bodies produce hormones that send signals to our brains telling it about our food needs. Insulin is one of these hormones. Others include leptin, ghrelin and glucagon-like peptide-1 (known as GLP-1). These hormones help to tell the brain how much energy is available from recent meals and how much energy is in long-term storage as fat.
HOW ARE THESE HORMONES AND THE BRAIN INVOLVED IN OBESITY?

One area of the brain is thought to be among the most important in putting together all the bodily and environmental signals about eating. This area is called the hypothalamus [hi-po-thal-a-mus]. Hormones from the body go to the brain and especially to the hypothalamus to help control hunger and fullness. Each hormone has its own functions. Leptin is produced by fat cells. When energy stores in fat get low, less leptin goes through the blood to the brain, causing the hypothalamus to increase hunger and slow metabolism. Insulin, which comes from the pancreas, tells the brain whether glucose (sugar) is available to be used as energy. Two other important hormones that help to regulate appetite come from the gut. Ghrelin [grel-in] comes mostly from the stomach and acts in the brain to increase hunger. GLP-1 is released from the intestine when food is present and acts in the brain to make us feel full. At any time, the brain is working hard to combine all of these (and many other) signals to help determine how hungry you feel and how much energy your body will burn. Not only do these four hormones affect your sense of appetite, but they also alter the pleasure or sense of reward you experience from food.

WHAT CHANGES OCCUR IN APPETITE-REGULATING HORMONES DURING OBESITY?

In obesity, the amount of fat in the body increases. As body fat increases, leptin levels also increase. However, instead of high levels of leptin leading to fullness and decreased appetite, it appears that obese people become resistant to leptin’s effects. In other words, leptin works less and less effectively as body fat increases. This resistance to the effects of leptin may help explain why many obese people have normal or even increased appetite despite having large amounts of stored calories in their bodies in the form of fat.

In contrast to leptin, GLP-1 levels tend to be lower in obese subjects. Because GLP-1 is an important signal of fullness, lower levels of this hormone in obese people may also contribute to continued hunger despite excess body fat. The reasons why obese people become resistant to leptin and have changes in GLP-1 levels are not understood but are active areas that scientists are researching.

ARE THERE VISIBLE CHANGES IN THE BRAIN DURING OBESITY?

Yes, scientists have shown that when an animal eats a very high-fat diet and becomes obese, the hypothalamus becomes inflamed. Specialized cells that are known to come to the aid of injured or damaged tissues are found in this inflammation. In addition, when an animal has been on a high-fat diet and has been obese for a long time, some of the cells in the hypothalamus that are involved in telling the brain when the animal is full are lost. Studies suggest that this kind of inflammation in the hypothalamus is also happening in obese people.

There is active research to try to determine what causes these changes, if these changes are reversible when weight is lost, if they can be prevented, and if treatments of these changes in the brain might help control obesity in the future.

WHAT IS AVAILABLE NOW TO TREAT THESE CHANGES IN HORMONE LEVELS AND BRAIN FUNCTION IN OBESE PEOPLE?

New drugs are being developed to take advantage of our new understanding of the role of hormones in obesity. These include drugs that simulate the gut hormone GLP-1 (like exenatide [ex-EN-a-tide] and liraglutide [LIR-a-GLU-tide]) that are now being used for the treatment of type 2 diabetes mellitus. Currently, there are no treatments available to reverse leptin resistance or prevent the changes in the hypothalamus, but these are areas of ongoing research.

WHAT CAN I DO ABOUT OBESITY TODAY?

While scientists and doctors continue to work to better understand what causes obesity and to develop new treatments, there are many things individuals can do now. If you are concerned about your body weight, discuss it with your doctor and get help to develop a nutrition/diet plan that is right for you. Your doctor also can help you understand what kinds of exercise would be safe for you to start. Many people set goals to lose large amounts of weight, but studies show that losing only five to 10 percent of your body weight (10-20 pounds for someone who weighs 200 pounds) helps to lower blood pressure, lower cholesterol and improve blood sugars. By sticking to a nutrition and exercise plan that is customized to your needs, you can improve your overall health and reduce your risk of obesity and obesity-related diseases.

Dr. Kathryn Berkseth is a Senior Fellow in the Division of Endocrinology, Metabolism and Nutrition at the University of Washington in Seattle. She is a graduate of Carleton College and the University of Minnesota Medical School and completed residency in internal medicine at Mayo Clinic in Rochester, MN. She is board certified in Internal Medicine and Endocrinology and is interested in all aspects of clinical endocrinology, particularly the management of obesity and obesity-related diseases. Her research focuses on the relationship between hormones, obesity and the brain.
A TALE FOR THE AGES: How the Mystery of Diabetes Was Unraveled

BY MARY GREEN

Although it seems to have gained notoriety only recently as increasing numbers of people across the globe have fallen prey to the disease, countless brilliant minds have played a part in the fascinating history of diabetes mellitus. Scientists and physicians have been chronicling this devastating medical condition for more than 3,000 years, from the origins of its discovery to the dramatic breakthroughs in its treatment.

The earliest known mention of diabetes appeared in 1552 B.C. in a 3rd Dynasty Egyptian papyrus authored by Hesy-Ra, one of the world’s first documented physicians, who wrote about an illness resulting in frequent urination...which we now know is one of the key symptoms of the condition. And in the first century A.D., ancient Greek physician Aretaeus vividly described the destructive nature of an illness which he named “diabetes,” derived from the Greek word “siphon” (meaning flowing through), and rendered the earliest account of diabetic patients’ intense thirst and “melting down of flesh and limbs into urine.” Diabetes indeed appears to have been a death sentence in the

In the 1800s, physicians began to realize the role of diet in diabetes and began formulating special diets for their patients.

In 1889, physicians Oskar Minkowski and Joseph von Mering discovered that the removal of the pancreas from a dog caused diabetes to develop.
ancient era: Aretaeus did attempt to treat it, but could not provide a good prognosis. He commented that "life (with diabetes) is short, disgusting and painful."

In the Middle Ages, diabetes was known as the “pissing evil.” And until the 11th century, diabetes was commonly diagnosed by “water tasters,” who tasted the urine of people thought to have diabetes to see if the excretion was sweet like honey. Thus, the Latin word “mellitus,” meaning honey, was added to the term diabetes.

EARLY TREATMENT OF DIABETES
As physicians learned more about diabetes, they began to understand how it could be managed. One of the first diabetes treatments involved prescribed exercise, often horseback riding, which was thought to relieve excessive urination.

And one of the earlier connections between diabetes and diet was identified in 1870 while Paris was under siege by Germany during the Franco-Prussian war. French physician Apolonaire Bouchardat noted that glucose disappeared from the urine in some of his diabetes patients as a result of war-related food rationing. Bouchardat’s advice to his patients was “mangez le moins possible,” meaning “eat the least possible.” Consequently, a number of fad diabetes diets were introduced to treat diabetes, among them the “oat cure,” in which the majority of the diet was made up of oatmeal; the milk diet; the rice cure; and “potato therapy.” Italian diabetes specialist Catoni even went so far to isolate his patients under lock and key in order to get them to follow their special, low-carbohydrate diets.

Despite these discoveries, diabetes continued to inevitably lead to premature death.

DISCOVERING INSULIN
The first big breakthrough that ultimately led to the use of insulin in treating diabetes occurred in 1889. German physiologist Oskar Minkowski and physician Joseph von Mering, researchers at the University of Strasbourg in France, were the first to remove the pancreas of a dog to determine the effect on digestion. The animal developed signs of diabetes and died soon thereafter, providing the first clue that the pancreas plays a key role in regulating the concentration of glucose.

Once the connection between the pancreas and diabetes was established, researchers’ efforts were focused on treating diabetes with pancreas extracts. Eventually researchers developed experimental pancreatic extracts that allowed diabetic dogs to properly digest food. In 1921, a young Canadian physician named Frederick

(Continued on page 16)
Banting theorized that pancreatic digestive juices could be harmful to the pancreas secretion produced by the islets of Langerhans. He wanted to ligate (bind with a bandage or ligature) the pancreatic ducts in order to stop the flow of nourishment to the pancreas, causing the pancreas to degenerate and lose its ability to secrete the digestive juices. The cells thought to produce an antidiabetic secretion could then be extracted from the pancreas without being harmed.

For the next year, Banting, medical assistant Charles Best and biochemist Bertram Collip tested his hypothesis and refined their approach in the laboratory, ultimately developing and purifying a pancreatic extract until the “insulin” treatment—named by Banting’s research sponsor Professor John Macleod—was refined and ready for human testing. They gave it to a young boy dying of diabetes, and within 24 hours the boy’s blood sugar had dropped to within normal limits.

The following year, Banting and Macleod were awarded the Nobel Prize in Physiology or Medicine and, shortly thereafter, medical firm Eli Lilly began large-scale production of the extract and was producing enough insulin for patients throughout the North American continent within the year. Banting is honored for his extraordinary contribution by World Diabetes Day, which is held on his birthday, November 14.

Additional advancements in the diagnosis and treatment of diabetes mellitus followed the discovery of insulin. In the 1940s the link was made between diabetes and long-term complications with kidney and eye disease. In 1944, the standard insulin syringe was developed, ensuring diabetes management was more uniform. In 1953, tablets for testing urine glucose became widely available, and urine test strips appeared on the market the next few years. Sulfonylureas, oral drugs that help lower blood glucose levels, were introduced in 1955, which helped sufferers of type 2 diabetes control their blood sugar levels by stimulating the pancreas to develop more insulin. And in 1959, two major types of diabetes were recognized: type 1 (insulin-dependent) and type 2 (non-insulin-dependent) diabetes. In 1964, the first strips for testing blood glucose were used. The first blood glucose meter, costing approximately $500 and intended for use in doctors’ offices, was introduced in 1970, as was the insulin pump. The hemoglobin A1c test was devised in 1979 in order to create a more precise blood sugar measurement.

WHERE WE ARE TODAY

There’s no question that insulin is one of the most significant medical (and humanitarian) discoveries in history, but the path to a cure has remained elusive. And there are still many variables to diabetes that the medical community doesn’t fully understand.

Yet, although diabetes is still associated with a reduced life expectancy, the outlook for patients with the disease has improved dramatically. People with diabetes have a number of tools at their disposal to reduce their risk of health complications and can usually lead active and productive lives for many years after an initial diagnosis has been made.

As the 100th anniversary of the discovery of insulin approaches, diabetes researchers continue to work in earnest to find the answers to why we develop diabetes, with the goal to end diabetes forever.
A Diabetes Patient Recalls the Early Years of Treatment

BY MARY GREEN

In the early years of the 20th century, while European researchers were working diligently to unravel the mystery of diabetes, Elliott P. Joslin, M.D., an American pioneer in the treatment of the disease, was concurrently performing experimental work on how people with diabetes burn food as fuel, observing the effects of fasting and different amounts and combinations of carbohydrates, proteins and fats on diabetes. In 1918, Dr. Joslin published the first comprehensive guide for patients, which become a national bestseller—A Diabetic Manual for Doctors and Patients—and, in 1922, he oversaw the administration of the first trial of insulin in New England.

Meanwhile, the Boston-based diabetes clinic Dr. Joslin founded in 1898 grew in size and stature over the years and today is the world’s largest diabetes research center, diabetes clinic, and provider of diabetes education.

One of the early beneficiaries of the Joslin Clinic’s care was Gerald Tays.

Diagnosed with the condition in 1953 at age 12, after losing more than two dozen pounds in a single month, Tays’ illness shook his family to its core. He was a fit and active young boy, there was no history of diabetes amongst family members, and only a few months prior his older brother had died suddenly from a previously diagnosed aneurysm that had gone untreated. With the family’s unthinkable loss still fresh in everyone’s mind, Gerald’s aunt sprang into action and suggested that Gerald be taken to Joslin Clinic for treatment, where he was assigned to the care of Dr. Priscilla White.

His memories of the legendary Dr. Joslin, and the equally accomplished Dr. White, whose pioneering pregnancy studies showed the importance of strict blood glucose control and early delivery for fetal survival, are as fresh as the day he was diagnosed. “Although at the time I wasn’t seen by Dr. Joslin as a patient, he was very present in the clinic, very focused, very stern and very forceful,” Tays recollects. And while Tays found Dr. White’s gentle bedside manner more suitable to his adolescent-driven independent streak, the treatment he underwent was another matter entirely.

“We were just a step beyond the stone age,” Tays says. “There were no disposable items, no plastic items and it was difficult to travel.” In fact, Tays says the only syringes available to inject his life-saving insulin were glass syringes that had to be sterilized in alcohol after every use, and the large needles of the syringes had to be sharpened on stone. “To this day, I have a glass cigarette holder and also a metal tray from my aunt that we used for soaking my syringes,” he notes. “And, I had to go to the hospital the first thing every Saturday morning to get my blood glucose tested.”

Still, although his sports coaches treated him more gingerly following his diagnosis (as did his family members), his diabetes treatment regimen was successful and Tays continued to lead an active lifestyle, ultimately becoming a public park ranger, an occupation he held for decades until his retirement to Edmonds, Washington, a small town 20 miles outside of Seattle on the shores of Puget Sound.

Today, at 73, he marvels at the advancements in diabetes care over the decades that have made self-care easier, from early urine test strips for sugar to new sensors such as the continuous glucose monitoring system (“that testing equipment is the best”).

Over the years, Tays has managed to avoid many of the complications long-term diabetes patients experience and considers himself fortunate. “When I look back over my life as a diabetic, there have been very few peaks and valleys,” he says. “But my life has been based on one word: moderation. The one thing I would say to younger diabetes patients is, simply, be reasonable.”
SECONDARY OSTEOPOROSIS: Are You at Risk?

BY CORY WILCZYNSKI, MD

Osteoporosis [os’tē-ō-pō-rō’sis] is a common condition, affecting nearly 8 million women and 2 million men in the United States. The condition is one in which the bones become fragile and is due to an inherited, poor quality of bone structure combined with the effects of estrogen deficiency in women, testosterone and estrogen deficiency in men, and the results of the aging process. However, there are other conditions, not truly disorders of bone, which make the bones more fragile and increase your fracture risk. When this occurs it is referred to as secondary osteoporosis, which may arise at any age and affect men and women equally.

In order to determine if secondary osteoporosis is present, the diagnosis of osteoporosis first needs to be established. This can be achieved through several methods of testing. A T score compares your bone density to that of young people who are at their peak (best) bone density and lowest fracture risk. The more your score differs from their score, the more you are at risk for fracture. A score of less than or equal to a -2.5 on a dual-energy x-ray (DEXA) – which is a means of measuring bone mineral density – or clinical assessment and use of a fracture risk assessment tool (FRAX) – a diagnostic tool used to evaluate the 10-year probability of bone fracture risk – are used to establish the diagnosis of osteoporosis and judge the risk of fracture. FRAX scores are calculated based on your medical history and include such factors as your gender, whether you smoke, alcohol intake, personal history of fracture, parents’ history of fracture, steroid use and most recent T score; a score greater than or equal to 20 percent for major risk and greater than or equal to three percent in the hip would also help identify if you are at risk for a fracture. A FRAX score is only applicable for patients not currently on drugs that reduce the excessive removal of old, hardened bone (some removal of bone happens normally when bones repair wear-and-tear damage) or other medications for treatment of osteoporosis.

Sixty percent of men and 50 percent of premenopausal women diagnosed with osteoporosis will have at least one secondary cause. This article provides an overview of secondary causes of osteoporosis such as endocrine disorders, blood cell disorders, connective tissue disorders, medications, malabsorptive disorders (difficulty absorbing nutrients from food), genetic disorders and others.

ENDOCRINE DISORDERS

Endocrine disorders that can be linked to secondary osteoporosis include: hyperparathyroidism [hi-per-par-a-thi-royd-ism], an overproduction of a hormone that can lead to high calcium levels; Cushing’s [kush-ings] syndrome, a condition that is associated with high levels of steroid; hyperthyroidism [hi-per-thi-royd-izm], a condition in which the thyroid gland produces too much thyroxine hormone; hypogonadism [hi-po-go-nad-izm], a condition in which the body doesn’t produce enough of the male hormone testosterone; prolactinoma [pro-lak-ti-no-ma], a non-cancerous tumor of the pituitary gland which produces a hormone called prolactin; diabetes mellitus, a condition in which the pancreas no longer produces enough insulin or cells stop responding to the insulin that is produced, so that glucose in the blood cannot be absorbed into the cells of the body; acromegaly [ak-row-meg-a-le], a long-term condition in which there is too much growth hormone and the body tissues get larger over time; and other causes of estrogen deficiency (chemotherapy or primary ovarian failure).

In men, hypogonadism is still the most common cause of osteoporosis. The exact relationship between testosterone, estrogen and bone mineral density is unclear, but it is known that the depletion of either hormone is related to a decrease in body mass density (BMD) in both men and women. For men with proven hypogonadism (a testosterone level of less than 200
MEDICATIONS

Disorders that weaken formation of bone by associated deficiency. Most of these conditions are related to genetic and tissues having a lot of flexibility, and vitamin C include Ehler-Danlos syndrome, a condition of skin as discussed above. Other connective tissue diseases are also related to osteoporosis. There is some suggestion that chronic blood loss is also related to osteoporosis. There are many conditions and medications that can contribute to the development of osteoporosis. A careful history and medication list can exclude many of the above causes. Most women of postmenopausal age will have primary osteoporosis, but in men, premenopausal women and perimenopausal women, other conditions should be evaluated as the discovery would change medical management options.

BLOOD CELL DISORDERS

Multiple myeloma, a cancer of plasma cells, is a type of white blood cell normally responsible for producing antibodies; mastocytosis, a disorder caused by too many mast cells in your body; leukemia; cancer of the blood or bone marrow; lymphoma, cancer of the lymphatic system; sickle cell disease, an inherited blood disorder that turns normal, round blood cells into crescent-shaped cells; lipidoses, harmful amounts of fats accumulating in some of the body's cells; and polycythemia, a blood disorder in which your bone marrow makes too many red blood cells, all represent disorders in the blood cell lines that are also related to osteoporosis. There is some suggestion that chronic blood loss is also related to osteoporosis.

CONNECTIVE TISSUE DISORDERS

Osteogenesis imperfecta is a disorder that causes secondary osteoporosis due to a high level of calcium, the same as hyperparathyroidism, as discussed above. Other connective tissue diseases include Ehler-Danlos syndrome, a condition of skin and tissues having a lot of flexibility, and vitamin C deficiency. Most of these conditions are related to genetic disorders that weaken formation of bone by associated effects with connective tissue.

MEDICATIONS

Glucocorticoids, often referred to as steroids, are the most common cause of secondary osteoporosis. Conditions that require frequent exposure to steroids, such as rheumatoid arthritis, organ transplants, chronic pulmonary disease and inflammatory bowel disease, have strong associations with osteoporosis as well. Steroids are known to inhibit formation of osteoblasts and osteoclasts over time as well as decrease the lifespan of these cells. Osteoblasts and osteoclasts are the two cells involved in bone formation. The duration of glucocorticoid use is not well defined, but it is known that short bursts of taking the medication such as those seen in treatment of COPD (chronic obstructive pulmonary disease) and asthma exacerbations do not have the same detrimental effects on bone such as the long-term effects of bone metabolism resulting from lifelong immunosuppression for transplant patients.

Other medications associated with increased risk of osteoporosis include some anti-seizure medications, some anticoagulants (an agent used to prevent the formation of blood clots), immune system-suppressing medications, some hormones, some antidepressants and aluminum-containing antacids.

MALABSORPTIVE AND NUTRITIONAL DISORDERS

Calcium and vitamin D supplementation is the key component to the prevention of progression from osteopenia, a condition where bone mineral density is lower than normal, to osteoporosis. Calcium and vitamin D deficiencies alone are risk factors for osteoporosis. The problem with malabsorption syndromes such as inflammatory bowel disease, chronic liver disease, alcoholism, celiac disease (an autoimmune digestive disease that interferes with absorption of nutrients from food), eating disorder anorexia nervosa [an-uh-RECK-see-uh nur-VOH-suh], chronic use of total parenteral nutrition (feeding of a person intravenously), and patients that have had a gastrectomy, a partial or total surgical removal of the stomach, is that they absorb vitamin D poorly. The same was thought to be true of steroid-related osteoporosis. Vitamin D deficiency is exceedingly common, with an overall prevalence of 46.1 percent in the U.S. population. Though not always caused by a gastrointestinal disease, vitamin D deficiency should be treated aggressively to maintain a normal level.

ADDITIONAL DISORDERS

Other disorders associated with increased risk of osteoporosis include some listed above that require the use of medications that affect osteoblast or osteoclast function or inhibit the body's absorption of calcium and vitamin D, which are essential for bone health. These conditions include rheumatoid arthritis, chronic obstructive pulmonary disease, organ transplantation, immobilization, idiopathic hypercalciuria [hi-per-kal-se-yu-ree-a] (high calcium concentrations in the urine), multiple sclerosis, mastocytosis and end-stage kidney disease. In conditions involving defects in the body's ability to eliminate calcium, the risk to bones actually originates from the kidneys' inability to reabsorb calcium. There are many conditions and medications that can contribute to the development of osteoporosis. A careful history and medication list can exclude many of the above causes. Most women of postmenopausal age will have primary osteoporosis, but in men, premenopausal women and perimenopausal women, other conditions should be evaluated as the discovery would change medical management options.

Cory Wilczynski was born in Moline, IL. She was diagnosed with type 1 diabetes at the age of 3. She started going to a diabetes camp, Camp Herkko Hollow in Boone, Iowa. She eventually became a camp counselor and acting physician when in medical school. Cory finished her undergrad at Knox College in Galesburg, IL. She then went to Rush Medical College and graduated in 2010. She finished her Internal Medicine residency at Saint Louis University in 2013. Currently she is an Endocrinology Fellow at Loyola University in Maywood, IL.
What You Should Know About Acromegaly

By C. Rachel Kilpatrick, MD and Julie M. Silverstein, MD

What Is Acromegaly?

Acromegaly [ak-row-meg-a-le] is a disorder characterized by overproduction of growth hormone and is most commonly caused by a benign tumor of the pituitary gland that secretes excess growth hormone. Growth hormone is one of seven different hormones made by cells within the pituitary, a pea-sized gland which lies in a small bony pocket between the sinuses of the face and the base of the brain. Normally, growth hormone is partially responsible for maintaining adequate growth in children. Excess growth hormone in children, however, causes abnormally rapid growth which results in gigantism [ji-gan-tizm], a condition characterized by excessive growth and height significantly above average. In adults, because growth in one’s height has stopped, excess growth hormone causes acromegaly, with overgrowth of small bones such as in the hands, in soft tissues and organs, such as the heart.

I Seem to Be Getting Bigger

Fortunately, acromegaly is uncommon and affects only about one person in 300,000. However, because the signs and symptoms of acromegaly develop slowly over time and may be subtle, there can be a delay in making the diagnosis. Most of the symptoms of acromegaly are due to the effects of excessive amounts of growth hormone on the body. The physical findings can include the growth of skin tags, thickening of the skin, excessive sweating, and enlargement of the hands and feet, which might cause an increase in ring or shoe size, certainly something that could be normal with aging. Other findings can include an enlarged forehead, nose and jaw and an increase in the space between the bottom teeth due to growth of the facial bones. Sometimes it is helpful to compare the face to an old photograph to see these changes.

Acromegaly also may cause soft tissue swelling which, when present in the hands, can cause carpal tunnel syndrome, pinching of the median nerve at the wrist, or neuropathy (nerve irritation). Soft tissue swelling in the back of the throat can cause snoring and sleep apnea, leading to disturbed sleep and daytime sleepiness. Acromegaly can also cause insulin resistance and diabetes, heart problems or heart failure, or arthritis, and it increases the risk of developing benign, non-malignant tumors.

People with acromegaly may have symptoms due to the pituitary tumor itself. Large pituitary tumors can cause headaches and change in vision (especially loss of peripheral vision, the ability to see to the sides). In addition, pituitary tumors may disrupt the normal production of hormones from the pituitary and cause symptoms related
to hormone deficiencies, such as fatigue, decreased energy, lack of menstruation and low libido.

**IS THERE A TEST FOR ACROMEGALY?**

The single best test for diagnosing acromegaly is insulin-like growth factor-1 (IGF-1) level, which is a simple blood test that can be done at any time during the day and is increased in people with acromegaly. A growth hormone level can also be checked, but growth hormone levels vary widely throughout the day based on food intake, exercise and sleep. If there is evidence of acromegaly based on elevated IGF-1 and growth hormone levels and symptoms, then an MRI scan of the brain should be done to evaluate the pituitary gland, specifically to look for a pituitary tumor. Sometimes the diagnosis of acromegaly is made when an MRI done for another reason shows a pituitary tumor.

**HOW IS ACROMEGALY TREATED?**

First-line therapy for acromegaly is generally surgery. Surgery is performed under general anesthesia and is done by making a small incision into the nasal cavity into an area called the sinuses. This allows easy access to the pituitary gland using a special device called an endoscope. The surgery is usually performed by both a neurosurgeon (brain surgeon), who operates directly on the pituitary gland, as well as an otorhinolaryngologist [ot-o-ri-no-lar-en-gal-e-jest] (ear, nose, and throat surgeon), who operates on the back of the nasal passage. The surgery usually requires a two-to-three-day hospital stay if there are no complications. Complications of the surgery are rare when done by an experienced pituitary surgeon, but can include leakage of spinal fluid from the nose, meningitis (an infection of the covering of the brain) and hormone deficiencies.

If acromegaly is not cured by surgery or if someone is not a candidate for surgery, other treatment options include radiation and medication. The goal of radiation is to decrease tumor size and decrease growth hormone production. Since the effects of radiation therapy take time to work (sometimes up to 10 years), people are often treated with medication in addition to radiation. Some people may also require medical therapy because they are not candidates for radiation therapy due to the location of their tumor.

Medical therapy is generally administered by an endocrinologist [en-do-kri-nol-o-jist] (hormone doctor) who will monitor the effects of treatment over time. The medications include lanreotide [lan-REE-oh-tide], octreotide [ok-TREE-of-tide], pegvisomant [peg-VEE-so-mant] and cabergoline [ca-BER-goe-leen]. Lanreotide and octreotide are somatostatin analogues and are taken as a shot and decrease the release of growth hormone from the tumor. Pegvisomant is a growth hormone receptor antagonist that is also taken as a shot and blocks the effects of growth hormone on the body. Cabergoline is taken as a pill and has a similar mechanism of action as lanreotide and octreotide medication, but is less effective at decreasing growth hormone production. The choice of medication depends on the specific individual situation and how effective each treatment is for the patient. Sometimes, more than one medication is required.

**COULD THE TUMOR COME BACK AFTER SURGERY?**

All patients, regardless of which treatment is used, need lifelong monitoring, as acromegaly can recur. Sometimes patients who are not initially cured by surgery will require a second surgery to decrease the tumor size and to control symptoms. It is very important that there is continued follow-up both with an experienced endocrinologist and a neurosurgeon who can monitor IGF-1 and growth hormone levels and follow changes on brain MRI.
CUSHING’S SYNDROME: When Too Much Is Too Much

BY AHMET BAHADIR ERGIN, MD

Have you ever heard of Cushing’s syndrome? As a physician, I hear from people that their dog got it somehow. But this disease can happen in humans. Which leads to the question: what is Cushing’s Syndrome?

Significant weight gain in a short time, round face, excessive body hair, pink or purplish stretch marks, maybe a fat pad between the shoulders, easy bruising, or weakness in your thighs or arms. These are some symptoms of Cushing’s syndrome. Frightening isn’t it? In addition, flushing of the skin, excessive hair growth, and weight gain with abdominal distension (bloating) often occur. What about high blood pressure, elevated blood glucose or osteoporosis that developed relatively fast when you were otherwise healthy? These are also conditions that accompany Cushing’s. Additional features of Cushing’s syndrome can occur, such as irregular periods in women, decreased sex drive in men, acne, slow healing of cuts or wounds, frequent or unusual infections, depression, psychosis, headaches and visual disturbances.

Cushing’s syndrome is the result of elevated hormone levels in the body, specifically a hormone called cortisol. Cortisol is a very important steroid hormone produced in our adrenal glands, which is a gland that sits on top of each of the kidneys. It helps us regulate our blood pressure, blood glucose (sugar), immune system and strength. But too much of a good thing is not so good, as excessive cortisol can lead to serious health consequences such as hypertension, diabetes and osteoporosis. Most of the time the detrimental effects of cortisol are gradual and patients may have some or all of the features of this syndrome.

The most common reason for this syndrome is the use of cortisol or cortisol-like drugs, commonly known as steroids. These drugs are mostly used in the treatment of diseases such as arthritis or asthma. They are also used after organ transplants and with chemotherapy. Prednisone is the most commonly prescribed steroid.

The second reason for Cushing’s syndrome is excessive production of cortisol by the body due to a tumor in the adrenal glands. Adrenal glands are responsible for normal daily cortisol production. Any tumor inside the adrenal gland that results in overproduction of cortisol can cause Cushing’s syndrome.

A third cause of Cushing’s syndrome is overproduction of adrenocorticotropic hormone (ACTH) by the pituitary gland, a part of the brain that is located at eye level in the head. The pituitary gland controls secretion of many hormones, including cortisol. A tumor in the pituitary that secretes excessive amounts of a hormone that stimulates the adrenal (ACTH) will cause the gland to secrete too much cortisol. This results in Cushing’s syndrome, more specifically called Cushing’s disease. This is the most common disease state causing Cushing’s syndrome.

A fourth cause of Cushing’s syndrome is a tumor
outside the pituitary that oversecretes ACTH and stimulates the adrenal to oversecrete cortisol. This is referred to as ectopic [ek-top-ik] Cushing’s and is the rarest form of Cushing’s syndrome.

Although the severity of signs and symptoms may be much less remarkable, obesity can partly mimic some features of this syndrome. Obesity is becoming an epidemic in our country, given that 30 percent of the U.S. population is obese and 60 percent is overweight. On the other hand, Cushing’s syndrome due to a tumor inside the body is quite rare.

Diagnosis of Cushing’s syndrome can be a challenge for clinicians. Because of the difficulty making a diagnosis, if Cushing’s syndrome is suspected, your physician will usually refer you to a specialist, an endocrinologist, for evaluation.

The endocrinologist will order screening tests for suspected Cushing’s syndrome. If the tests are positive, then confirmatory tests and even further tests are obtained to determine where the cause of the Cushing’s is located. These tests may take days to complete. It is very important that patients follow instructions provided by clinicians to ensure the correct interpretation of these tests. And it is not unusual to be asked to repeat testing when the result is borderline or unclear. So be prepared to be patient!

Imaging is the final step in confirming the location of disease after biochemical tests are completed. Sometimes even imaging may not totally localize the disease. Then, in some cases, trying to find the source of the problem might require specialized testing of your internal veins to measure where the excess cortisol might be coming from.

If Cushing’s syndrome is caused by steroid drugs, then simply stopping the use of steroids may reverse signs of Cushing’s syndrome. If the disease is located in the adrenal gland, surgical removal of the adrenal tumor is indicated and may be done with laparoscopic surgery or with a more traditional surgical approach.

If the patient has an ACTH-producing tumor in the pituitary, a surgical procedure to remove the tumor through an incision through the nose is performed. The size and degree of tumor invasiveness and surgeon’s experience play a role in the success of surgery.

The cure rate is high if a single tumor is located in one of the adrenal glands, provided that the whole adrenal gland on that side is totally removed by the surgeon. When the tumor is in the pituitary gland, chance of cure is between 60 to 90 percent. The disease may recur even after many years of surgery. Thus, lifetime follow-up is necessary. When recurrence or relapse happens in pituitary tumors, alternative treatments can include repeating the surgery, radiation therapy, medical therapy or a combination of these treatments. Radiation therapy takes months or even years to work, and you may need medication treatment in the meantime. Medications used to treat Cushing’s syndrome include cabergoline [ca-BER-goe-leen], pasireotide [pas-i-REE-oh-tide], ketoconazole [KEE-toe-KON-a-zole] and metyrapone [me-TIR-a-pone]. Some of these medications, however, have limitations and restrictions by the FDA in their use. What might or might not be of benefit to you should be discussed with your endocrinologist. When surgery is not possible, even initially, then radiation or medical treatment might be recommended.

Some treatment side effects that are acceptable to one patient may not even be an option for another patient. The decision is generally based on your medical team composed of surgeons, endocrinologists and radiologists and you as to best approach and with regard to your input and comfort level. The bottom line, Cushing’s syndrome is treatable and often curable. No one should go untreated due to the grave consequences of excessive cortisol for the body.

On the other end of the spectrum, those who become Cushingoid [kush-ing-oyd] during their medical treatment due to steroid drugs may experience adrenal insufficiency at the same time or shortly after stopping the treatment. During times of stress, such as when undergoing surgery or experiencing infection, if you have used steroid drugs for a long time, you may need extra cortisol.

Most of the symptoms or signs of the disease will go away after successful treatment of Cushing’s syndrome. Of course, the earlier that you are diagnosed and treated, the better the chances are for complete recovery. In the early stages of recovery, be prepared to feel aches and pains because of relative cortisol deficiency after a long period of excessive cortisol exposure. Your endocrinologist will help you balance your cortisol level for a smooth recovery. During recovery, start exercising slowly and eat sensibly to help lose the cortisol weight gain and to improve your bone density. Your endocrinologist might recommend a bone density test called a DEXA to look at whether the cortisol has had an effect on your bones. Support groups also may be helpful during the treatment and recovery process. Be sure to ask your endocrinologist about resources that are available in your community.

Dr. Ahmet Bahadir Ergin is a last year Fellow in Endocrinology at Cleveland Clinic. He graduated from Marmara University School of Medicine, Istanbul, Turkey. He completed his post-graduate training in Internal Medicine at Cleveland Clinic Fairview Hospital. Dr. Ergin’s clinical interests include pituitary/adrenal disorders as well as thyroid diseases, including thyroid cancer. He has worked on multiple research studies related to thyroid cancer and diabetes mellitus. His studies have been published in peer-reviewed medical journals. He is also currently authoring a book about dynamic endocrine testing in endocrinology. Dr. Ergin will be joining Jackson Clinic in Montgomery, Alabama this summer.
PROLACTINEMIA: Excess Quantities of Lesser-Known Hormone Causes Broad Range of Symptoms

BY MARISA CRUZ, MD

SO WHAT IS PROLACTIN ANYWAY?

Although we’re all aware that hormonal changes take place during and after pregnancy that allow women to breastfeed, most people are not familiar with the specific hormones involved and what happens when this hormonal system breaks down. Prolactin [pro-lak-tin] is the name of the main hormone involved in the production of breast milk, and it is made by a tiny gland called the pituitary that sits at the base of your brain. In men and non-pregnant women, the level of prolactin in your bloodstream is kept at low levels by another chemical produced by the brain called dopamine.

HOW WOULD I KNOW IF MY PROLACTIN LEVEL IS HIGH?

High levels of prolactin in women who have not yet gone through menopause can cause breast enlargement, absent menstrual periods and production of breast milk. The most common cause for increased levels of prolactin (also called hyperprolactinemia [hi-per-pro-lak-ti-ne-me-a]) is pregnancy, and in pregnancy, these symptoms are entirely normal! Outside of pregnancy and breastfeeding, however, young women should generally not be skipping periods, leaking breast milk, or having problems with fertility. If you develop these symptoms, you should think about visiting your doctor to have your prolactin level checked.

In both men and postmenopausal women, the symptoms of excess prolactin are not always obvious. Men may occasionally notice breast enlargement and leakage of breast milk, but more commonly report symptoms of erectile dysfunction, reduced energy levels, reduced interest in sex, and a decrease in amounts of facial or body hair. Postmenopausal women tend to have very few symptoms related to excess prolactin itself, and so are often only diagnosed if the hyperprolactinemia is related to a growth in the pituitary gland.

WHAT WOULD BE CAUSING A HIGH PROLACTIN LEVEL?

A prolactin level can be checked by your doctor with a simple blood test.

Small elevations in prolactin can be caused by many factors, including stress and exercise, but if your level is significantly
elevated, further testing might be needed to identify the cause of the excess hormone production. Your doctor will likely begin by confirming that you do not have any medical conditions that can cause hyperprolactinemia, including kidney disease and thyroid disorders. The doctor will also review your medication list, as multiple drugs ranging from estrogens to certain psychiatric and pain medications have been linked to high prolactin levels. Certain blood levels, such as those to check your thyroid function, can be helpful.

If those initial steps are not helpful in determining the cause of your elevated prolactin levels, your primary care doctor may refer you to an endocrinologist for additional testing and treatment. The next step in evaluation is usually a pituitary MRI, which is a specialized way of taking a picture of the brain to look specifically for abnormalities in the pituitary gland. A pituitary tumor called a prolactinoma [pro-lak-ti-no-ma] is the most common structural problem responsible for hyperprolactinemia and is caused by unregulated growth of the pituitary cells that make prolactin. Almost all prolactinomas are benign, meaning that they are not cancerous and do not spread to other areas of the body.

Most prolactin-producing pituitary tumors are microprolactinomas, or tumors that are smaller than one centimeter in diameter. These tumors usually cause symptoms that are related only to the high levels of prolactin in the bloodstream and typically do not increase in size over time. Macron prolactinomas are prolactin-producing tumors that are larger than one centimeter in diameter, and these tumors may cause additional symptoms related to the pressure that the tumor places on the pituitary and surrounding brain structures. In particular, patients may notice headaches, loss of vision and nausea. These tumors often grow larger over time and may require more aggressive treatment.

Occasionally, pituitary tumors that do not make hormones, or that make hormones other than prolactin, can also cause hyperprolactinemia. They do so by reducing production of dopamine [do-pa-men], the chemical that normally functions to keep prolactin levels in check. If you have high prolactin levels and are diagnosed with a pituitary tumor, your endocrinologist will likely perform additional blood tests to check for abnormalities in the levels of a variety of hormones produced by the pituitary.

HOW ARE HIGH PROLACTIN LEVELS TREATED?

High prolactin levels that are causing symptoms should be treated. If you are taking a medication that might cause hyperprolactinemia, your physician will likely ask you to switch to a different type of medication. Sometimes this makes all the difference. If your medication cannot be safely changed or discontinued, your endocrinologist may recommend that you be monitored and treated for the long-term side effects of excess prolactin, including weak bones and low levels of sex hormones.

If the elevated prolactin is due to a chronic medical condition or a pituitary tumor, the first line of treatment is usually a class of medications called dopamine agonists. The most commonly used dopamine agonist is a drug called cabergoline [ka-BER-goe-leen]. It is taken one to two times per week and generally has few side effects, though it can cause nausea in some people. In patients with prolactinomas, dopamine agonists can not only reduce prolactin levels, but can actually make the tumor smaller. You might see a drop in prolactin levels in just 2-3 weeks after starting your medication, though higher doses are sometimes required for prolactin levels to return to normal.

Medications alone are effective in treating about 90 percent of patients with prolactinomas, including both small and large tumors. While those are great odds for success with just drug therapy, about one in 10 patients will continue to have symptoms related to high prolactin levels or to the size of the tumor even after treatment. These patients are usually referred to a surgeon who specializes in the removal of pituitary tumors. In a few patients with very large tumors, radiation treatment may also be recommended after surgery.

If your prolactin level returns to normal with medications, your endocrinologist will likely try to lower your dose and eventually stop treatment after one to two years. As one of the few benefits of menopause, women who stop getting their periods can usually also discontinue treatment for hyperprolactinemia.

For some patients, the prolactin level increases again when the dose of medication is reduced. Fortunately, at the low doses used to control prolactin levels, using cabergoline for multiple years does not appear to cause significant side effects. High doses of cabergoline for long periods of time have been linked to leaky heart valves, so your endocrinologist may discuss with you obtaining an ultrasound of your heart if you are taking a higher dose than the average patient with hyperprolactinemia.

WHAT ELSE SHOULD I KNOW?

Women with prolactinomas can usually become pregnant and breastfeed without problems. Knowing about your plans to become pregnant is an important part of choosing the right treatment for you, however, so make sure that your endocrinologist is aware if you decide to start a family.
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THYROID AND DIABETES: OFTEN A DUO

Research from Germany looking at patients with diabetes mellitus type 2 (a diabetes that is the result of both the body’s own insulin not working as well as it should combined with a decrease in insulin production) showed that just over one in four people with diabetes also had thyroid disease.

The majority developed their thyroid condition after they had had diabetes diagnosed first. And many more women had a thyroid problem than men. These would not be surprising findings.

What was surprising was that if prior to diagnosed diabetes, thyroid disease was already present, or if diagnosed with thyroid disease in the same year as diabetes, there was an earlier need to start insulin. The time before starting insulin was 2.5 years versus 8 years. The researchers did add that their data might have included patients diagnosed as having type 2 diabetes, but really having a slower onset of type 1 diabetes – a condition called latent autoimmune diabetes in adults (LADA). This diagnosis is usually made by testing blood for the presence of antibodies to pancreatic tissue, but was not done in their study participants. This is important, as diseases that are the result of an autoimmune process (the body producing antibodies to its own tissues), typically cluster together, meaning if you have one autoimmune disease, your risk of having or developing another is higher. And many thyroid conditions are felt to be autoimmune system-related. So this is a possible factor that could make the numbers found different.

So what is the take-home message?

If you have diabetes, ask if your thyroid function has been checked. If not, ask to have it checked, particularly if you are a female, as you do have a risk for developing a thyroid condition!

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HEMOGLOBIN A1C AND BLOOD SUGARS...NOT SO MUCH A DUO

The American Association of Clinical Endocrinologists’ (AACE) recommendations for the control of diabetes target an HbA1c (a measure of average blood sugars over the past three months) of 6.5 percent or less, while the American Diabetes Association suggests less than 7 percent, with both organizations acknowledging individualization depending on a variety of factors.

Day-to-day care of diabetes to get to a target HbA1c is supported by self-monitored blood glucose (sugar) values, obtained by fingersticks that create a tiny drop of blood that then can be absorbed by a chemically treated strip that is placed in a glucose meter.

What these fingerstick glucose targets should be has been a bit unclear. Your doctor might have given you a range of sugar values to aim for. Researchers in Boston wanted to see what these sugar ranges should be—premeal and at bedtime—to match a recommended HbA1c level. They looked at data from an earlier study, the ADAG (A1c-Derived Average Glucose), that used fingerstick glucose results, also a continuous glucose sensor with at the same-time HbA1c measures at specific time intervals. Study participants included 237 patients with type 1 diabetes and 141 with type 2 diabetes from the original ADAG study group. What was surprising were the glucose levels that seemed to match with HBA1c!

For example, you might have been told to aim for fasting blood glucose level of less than 120 mg/dL (milligrams per deciliter), and results from ADAG found that actual average fasting blood glucose to achieve HbA1c levels of 5.5 percent to 6.49 percent was 122 grams per liter. But for an HbA1c level of 6.5 percent to 6.99 percent, average fasting glucose was 142 grams per mg/dL. Postmeal sugars (defined as those checked at 90 minutes after starting a meal) averaged 144 grams per mg/dL for HbA1c of 5.5 percent to 6.49 percent and 164 grams mg/dL for a 6.5 percent to 6.99 percent range.

So what is the take-home message?

Discuss with your diabetes medical team what would be an appropriate HbA1c goal for you. Then discuss these recent findings to decide on what your fasting blood sugar target should be, as well as what your postmeal target should be. You might find that you safely could aim for a higher fasting sugar, but in contrast, a lower post-meal sugar!

FOOD AND DIABETES—NOT AT ALL A DUO

Finally, researchers from New York have reported that specific chemicals found at high concentrations in fried and grilled meats may raise the risk of diabetes and dementia. Mice raised on a diet that contained a high concentration of chemicals called glycotoxins showed early signs of diabetes. The mice also were found to have brain changes with symptoms similar to those seen in Alzheimer’s disease. The animals that ate a diet rich in a glycotoxin called advanced glycation end products, or AGEs, showed a build-up of protein called amyloid in their brains. Amyloid in the brain was not seen in mice raised on a low-AGEs diet. Amyloid presence is believed to be linked to Alzheimer’s dementia. Additionally, when the researchers looked at a small number of people over age 60, they found those with higher levels of glycotoxins in their circulation had more memory and other thought-process problems, as well as signs of insulin resistance, which can precede diabetes, when these people were followed over a relatively short period of time—nine months. Glycotoxins are very common in animal products, including meat and dairy produce, but levels increase considerably when food is fried, grilled, or smoked. Levels of glycotoxins go up when food is cooked dry at high temperature. The researchers suggest that how we prepare our food could make a substantial impact in lowering the risk of both diabetes and dementia.

So what is the take-home message?

Poach or boil your breakfast egg—skip the frying. Have a fresh muffin or bagel—skip toasting. And maybe skip the bacon altogether! ☞

News to EmPower You!

(Continued from page 27)
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