

GOODHORMONEHEALTH NEWS
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The purpose of GOODHORMONEHEALTH NEWS is to disseminate new information to Dr. Friedman's patients and others who signed up to receive his newsletter before posting on his website. We encourage you to visit www.goodhormonehealth.com and to make an appointment to see Dr. Friedman to discuss your medical condition. Please contact his office at mail@goodhormonehealth.com to suggest a future topic or to schedule an appointment. Be sure to schedule a follow-up appointment. Follow-up appointments are available in person, by telephone (20 min.), drive by (15 min.), email or FaceTime. Please see the first page of www.goodhormonehealth.com for more details on FaceTime appointments.

Dr. Friedman talked on hypopituitarism and Cushing's syndrome at the Magic Foundation Adult Convention (for patients with pituitary problems) on Sunday, April 21 in Las Vegas. This year more than 100 patients attended, the most ever and many of them were Dr. Friedman's patients. The talks were entitled "The Ins and Outs of Pituitary Hormone Replacement", "Nuances of Cushing's Syndrome" and "Grill the professor- pituitary hormone replacement including GH". Slides for the first two lectures will be posted on www.goodhormonehealth.com shortly.

The Ins and Outs of Glucocorticoid Replacement

Patients with adrenal insufficiency, either due to a pituitary problem or an adrenal problem, need glucocorticoid replacement. Patients with adrenal causes of adrenal insufficiency, such as those who have had an bilateral adrenalectomy for Cushing's disease, need both glucocorticoid and mineralocorticoid replacement. Glucocorticoid replacement is usually given in the form of hydrocortisone, of which the brand name is Cortef. Other possibilities include prednisone or dexamethasone, but hydrocortisone, because it has a relatively short half-life is more physiological, and is usually recommended. The body makes most of its cortisol in the morning and the proper way to replace cortisol is to give most of it in the morning in the form of hydrocortisone, which is a relatively short-acting glucocorticoid. Many physicians used to give too much glucocorticoid to a patient with adrenal insufficiency; however, more recently it is recognized that the body makes about 10-12 mg of hydrocortisone. Because not all of the hydrocortisone is not absorbed, doses around 15 mg to 20 mg of hydrocortisone are needed, with a higher dose in patients who are heavier and a lower dose in patients who are more petite. In general, patients with pituitary causes of adrenal insufficiency need less replacement than those with adrenal causes. In most of the hydrocortisone given in the morning, the common replacement might be 12.5 mg in the morning and 2.5 mg in the afternoon. Brand Cortef is often preferable to generic hydrocortisone

Dr. Friedman, when he was a fellow at the NIH in the 1990s, published a paper in the *Journal of Clinical Endocrinology and Metabolism* on the timing of giving glucocorticoids to patients with Addison disease. This paper involved sleep studies, and Dr. Friedman found that a small dose of hydrocortisone given at bedtime helped the patients with Addison disease go into REM sleep while if the glucocorticoids were withheld for 1-1/2 days, the patient did not go into REM sleep. It is commonly known that excess glucocorticoids give trouble sleeping, but this paper showed

that glucocorticoid insufficiency is also associated with poor sleep and that it might be beneficial to give a small amount of glucocorticoids at bedtime.

Another question that Dr. Friedman is often asked is, "When do I increase my hydrocortisone?". Patients who have permanent glucocorticoid insufficiency and need lifelong hydrocortisone should be on the lowest dose possible and should find a stable dose. Patients who are weaning off glucocorticoids who had Cushing disease and are cured, may be able to decrease their dose progressively to get off the glucocorticoids. For those on a chronic dose, again, the lowest dose is desirable; however, if the patient has a fever greater than 100.5 or is nauseous and vomiting, I recommend the patient double their hydrocortisone dose. If they still cannot take down hydrocortisone (such as if they have a stomach flu) it could be an emergency and they should go to the emergency room and/or give themselves an IM injection of Solu-Cortef at 100 mg. I do provide patients with a letter to take to the emergency room. If patients are doing strenuous exercise or are under rather severe stress, they can add an extra 2.5 mg to 5 mg of hydrocortisone, but this should only be done for a short period of time. In general, the principle is to take the least amount of glucocorticoids over a long period of time, although for a short period of time, extra can be taken.

The next question that comes up is, "What about for surgery?". There was a landmark study from the NIH in the 1990s that used monkeys to show that replacement glucocorticoid dose is needed in monkeys who had an adrenalectomy to handle the stress of having their gallbladder removed. However, 10 times the amount of glucocorticoids was not needed. This shows that our common practice of giving extra glucocorticoids at the time of surgery is probably an overkill. However, doctors do not want patients to get sick when they have surgery so most doctors recommend giving extra glucocorticoids. In general, prior to general anesthesia, Dr. Friedman would recommend 100 mg of IV hydrocortisone before the surgery and 50 mg after; this would be for an extensive surgery like a gallbladder removal. In patients who are having minor surgery, 100 mg before the general anesthesia could suffice with regular dosing afterward. A patient going for a colonoscopy may also benefit from 50 mg of IV hydrocortisone before their colonoscopy. It is also important before going for surgery to drink a lot of fluids.

In addition to glucocorticoid replacement, patients with adrenal insufficiency need mineralocorticoid replacement. This is done using a medicine called fludrocortisone (Florinef). Florinef is no longer available as a brand, and the generic name is fludrocortisone. The dose of Florinef is very easily monitored in patients with adrenal insufficiency by use of a blood test called renin. When the renin is high, it means the patient needs more Florinef and when the renin is low, the patient needs less. Patients who are going for procedures such as a colonoscopy when they have to have their bowels cleaned out should double their Florinef dose the day before the colonoscopy.

Glucocorticoid replacement can be difficult, and I recommend you contact your doctor or Dr. Friedman with specifics regarding glucocorticoid replacement.

If you have any questions about Dr. Friedman's practice or want to make an appointment, please to go his website www.goodhormonehealth.com.

Best Tests To Predict Likelihood of a Fracture

Osteoporosis (or thin bones) is a major problem for older women, especially those who are on the thinner side. The problem with osteoporosis is it can lead to fractures, especially hip fractures, which are associated with high morbidity and mortality. A classic test to predict the risk of fractures is a bone density test called a DXA scan. This is often done at 2 or 3 regions, most likely in the hip and the lumbosacral area of the back and often it is done in the forearm as well. The patients' bone density is reported as both a Z score, which is how the bone density compares to a person who is the same age and gender as the patient, as well as a T score, which compares to a young person of the same gender. Most doctors use the T score, as they do not want people to have worsening bone density as they age. However, Dr. Friedman does not necessarily think this is correct, as you want to know what your bone density is for your chronological age, just like you want to know what your hormone levels are for a given age. The bone density test measures how thin your bones are, and this could reflect having thin bones many years ago or thin bones more recently.

Another test that is underutilized but gives very important complementary information to the DXA scan is called a urine N-telopeptide test. It is done on the second void in the morning. The values reported are the urine N-telopeptide concentration in nmol BCE (bone collagen equivalents) over the concentration of creatinine in mg/dL. The units are usually reported as nM BCE over mM creatinine and the range at LabCorp is 5 to 65. The higher the urine N-telopeptide, the more active bone turnover is occurring. If the value is about 55 or higher, it means the bones are being broken down frequently and a person is more likely to get a fracture. Lower values indicate a decreased rate of bone turnover and a lower risk for fractures. The urine N-telopeptide tells about how much bone is being broken down at the time the test was taken, so a person could have had good bones when they were younger and now are having a lot of bone turnover and the bone density would be normal but the urine N-telopeptide would be high, indicating active bone turnover. Therefore, these tests can be done together to give the risk for osteoporosis.

Dr. Friedman especially likes to use this test when he is trying to treat patients with thyroid medicine. One of the main side effects of giving too much thyroid medicine is increased breakdown of bone which would be manifested with a high urine N-telopeptide level. If the urine N-telopeptide level is not that high, Dr. Friedman feels more comfortable increasing the dose of the thyroid medicine until it is possibly in the upper range of normal with the TSH in the lower range of normal. However, if the urine N-telopeptide is high, Dr. Friedman would be more cautious about increasing the thyroid hormone dose.

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Dr. Friedman's Guide to New And Old Weight Loss Drugs

Dr. Friedman's initial approach as an Endocrinologist regarding weight loss is to first rule out any endocrine problems, such as hypothyroidism, Cushing's syndrome, or growth hormone deficiency, that may lead to weight gain. He then encourages the patient to consume a low-calorie diet, and he often recommends eating an increasing amount of vegetables, as they are low

in calories with a large amount of nutrition, as well as to increase exercise. However, many patients need a jumpstart for the weight loss, and this is where weight loss medicine comes into play. There are 2 new weight loss medicines that have been FDA approved in 2012, although it is unclear whether these medicines have an advantage over existing weight loss medicine. Prior to these two FDA approvals, the only weight loss medicine FDA approved for long-term use is Orlistat which is also available over-the-counter as Alli. The prescription version contains 100 mg of Orlistat and is usually given 3 times a day while the over-the-counter form, Alli, contains 50 mg of the drug and the patient can take 1 to 2 pills before each meal. Orlistat works by decreasing fat absorption so in a patient who is consuming a high-fat diet, that fat will not be absorbed and the patient will not get those calories. The patient will also experience diarrhea when eating a high-fat diet, and this may condition the patient not to eat a high-fat diet. However, most of Dr. Friedman's patients know about eating a low-fat diet and therefore, this drug is not that helpful for most of the patients.

The second drug that has been around for over 50 years is FDA approved for short-term but not for long-term weight loss. This is Phentermine of which the brand name is Adipex. Phentermine was part of the Fen-Phen combination that was quite popular about 20 years ago. Fenfluramine, the drug that is abbreviated Fen, was pulled from the market in 1997 due to valve and lung problems. However, the Phentermine, which is the Phen drug, has remained in use and is actually a quite-effective weight loss medicine. Phentermine works by decreasing appetite and also may have some effects on increased metabolism and is in the family of amphetamine-like drugs. Therefore, the side effects of Phentermine include feeling hyper or jittery, rapid heart beat, increased blood pressure, and trouble sleeping. The drug works quite well short-term in reducing food intake and can often be given before lunch and dinner. The tablets are 37.5 mg in dose and therefore, Dr. Friedman often gives 1/2 tablet before lunch and dinner. In some patients, this keeps them awake at night and therefore, Dr. Friedman may give them a full pill to take in the morning. However, as the drug is only FDA approved for short-term use, Dr. Friedman usually gives this for a period of 2 to 4 months.

One of the 2 new drugs the FDA approved is called Qsymia, which contains Phentermine plus extended-release Topiramate. The Phentermine in the drug is actually a lower dose than in Phentermine itself and is usually given as either 15 mg or 7.5 mg of Phentermine compared to the 37.5 mg which is available as Phentermine alone. Topamax is a drug that was originally developed as a seizure drug that was found to have weight loss properties; however, this drug has a lot of side effects and is actually nicknamed "Stupamax" as it often makes people have decreased memory. Qsymia came out in 2012 and has only recently been used. It is available, but there is some difficulty getting it and it is about \$160/month, with only about 1 out of 5 prescriptions covered by insurance. Dr. Friedman does not see any advantage of this drug over Phentermine itself. Therefore, Dr. Friedman has not started using Qsymia in his patients.

The other new drug is called Belviq, of which the generic name is lorcaserin. This is a serotonin 5HT_{2C} receptor agonist that is similar to the fenfluramine that was removed from the market; however, fenfluramine was a 5HT_{2B} receptor agonist and Belviq is a 5HT_{2C} receptor agonist. Therefore, this is likely to be much more safe than the fenfluramine which was removed from the market. However, as of April 2013, this drug is not yet clinically available in the United States

due to issues related it being a controlled substance. This drug does seem quite promising, and Dr. Friedman would be interested in prescribing this drug once it becomes available.

In summary, weight loss medicines can be used to help patients lose weight who have already tried diet and exercise and have already had their endocrine problems treated. The drug that is most successful as a weight loss medicine is Phentermine, although the new medicine, Belviq, looks promising.

It's not *what* you eat but *how* you eat: A Hormonal Guide to Weight Management

<http://goodhormonehealth.com>

America has a serious weight problem, with more than 60% of adults classified as overweight or obese. Starting at age 30, most people gain about a pound per year despite efforts to keep it off. We are bombarded with countless books, articles and infomercials touting the latest fad diet. Despite all of this advice, the average overweight adult finds losing weight a difficult and unpleasant task and nothing has succeeded in making us thinner. Americans are actually eating healthier foods, but they are consuming more calories. The sheer amount of food we eat is a large part of the problem.

Why is it so difficult to lose weight?

We may live in the 21st century, but we have prehistoric genes that helped our ancestors survive countless feast-then-famine cycles. Over thousands of years of human development, genes that prevent weight loss became more advantageous than genes that prevent weight gain. Scientists call this the “thrifty gene hypothesis”. Early man benefited from genes that stored fat when food was plentiful and slowed metabolism when food was scarce. Our early ancestors also expended a large amount of energy hunting and gathering for the food they ate. Nowadays, “hunting and gathering” often means selecting an entree from the freezer and popping it in the microwave. Modern man is consuming more calories than he is expending, and our ancient genes, unaware that no famine will follow, turn this excess into fat.

What role do hormones play?

Hormones play an important role in how and when we eat. Mechanisms that prevent weight loss include signals telling you to eat when hungry, and signals telling your body to decrease its metabolism when food is scarce, such as when you diet. The hormones, leptin (an important hormone released from fat), ghrelin (a stomach hormone), NPY and aMSH, among others, signal the body that the person is hungry and should initiate eating. Other factors that may act to regulate metabolism include thyroid hormone, catecholamines and uncoupling proteins. Consequently, a myriad of hormonal signals act to prevent weight loss.

The act of eating also sends out signals to the body. Even early man needed signals, called satiety, to tell the brain when the stomach was full. These signals preserved a limited food

supply and prevented sluggishness and vulnerability associated with eating too large of a meal. Leptin has a role in satiety, but the main hormones involved in telling the body to stop eating are hormones released from the stomach and intestine. These include cholecystokinin (CCK), as well as glucagon-like-peptide-1 (GLP-1) and glucagon-like-peptide-2 (GLP-2). These hormones are activated after eating, but take time to signal the brain to halt the desire to eat more. The key point to remember is that we need to eat quite slowly to allow these signals to work. Our western eating habits are bypassing these important signals, so most individuals eat much larger meals than desirable or even necessary. Thus, weight gain is not caused by eating the wrong foods or not exercising, although these are important; rather we eat too much food at one sitting bypassing satiety signals.

One might think that eating several small meals throughout the day (grazing or noshing) would prevent weight gain. Can many small meals insure that my satiety signals are released and received by the brain? These are good questions, but the answer is probably no. People who snack all day usually do not eat nutritional foods. Typically they don't eat because they are hungry, they eat because they are bored/anxious/depressed. They go from slightly full to very full with each snacking episode and underestimate how much food they eat. Eating three regular meals a day ensures that you will eat only when hungry, focus on your food and develop conscious eating. Eating only when hungry at regular mealtimes will allow satiety signals to operate and lead to portion control.

What is the solution?

Americans rarely sit down for a leisurely meal. We eat on the run, in front of a television, at a fast food restaurant, in the car, in bed for a midnight snack, always while doing something else. Because eating is not our primary activity, we eat unconsciously and do not focus our attention on our food. In contrast, Europeans, for the most part, exercise less and eat more fat and caloric-laden foods than their American counterparts, yet there is much less obesity in Europe. One of the reasons is because Europeans eat smaller portions. Another reason is that Europeans take the time to enjoy their meal, allowing ample time for satiety signals to work. This act of focusing on eating and eating slowly has been called "mindful" eating. Our problem is not that we think about food too much, but rather we think about food too little.

The following 8 steps to conscious or "mindful" eating will work well for weight control. Coupled with exercise and good food choices, they will work better for weight loss than fad diets.

- 1) Savor your food. Enjoy each bite. Look forward to your meals.
- 2) Eat 3 meals a day. If you want to skip a meal, skip dinner (but no late night snacks to make up for it).
- 3) Eat only when hungry. Eat only enough to be no longer hungry (not to be full).
- 4) Eat only in your kitchen, dining room or lunch room table.
- 5) Don't do anything else when eating, besides talking to your family and friends. Don't read, work on the computer, talk on the phone or watch TV.
- 6) Eat slowly. Chew slowly. Take small bites. Put your utensils down between bites.

7) Put a small portion on your plate and remove the serving platter/cooking dish back to the kitchen. Never eat directly from the common pot (it is also unsanitary) and don't leave food in front of you. This is especially important at restaurants, where there is usually bread on the table. Ask for the bread to be removed.

8) Sip water between each bite. This will fill you up and slow down your eating.

Remember, it's not only what you eat, but how you eat.

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