

GOODHORMONEHEALTH NEWS

VOLUME 5-January 2016

www.goodhormonehealth.com

The purpose of GOODHORMONEHEALTH NEWS is to disseminate new information to Dr. Friedman's patients and others who signed up to receive his newsletter. 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 for GOODHORMONEHEALTH NEWS or to schedule an appointment.

Order your "I've been to see the Cushing's Wizard" car magnets and sweatshirts and other Cushing's gift items at <http://www.cafepress.com/sk/zebraesque>.

Dr. Friedman and Dr. Dae, a Naturopath in Washington DC (healthydaes.com) hosted a videoconference on "Eating Well to Reverse and Prevent Diabetes, Hormone Imbalances, Fatigue and Obesity" on Sunday January 10, 2016. The webinar will be posted on goodhormonehealth.com

Dr. Friedman hosted his videoconference on Hormones and Weight Loss on Sunday December 13, 2015. The webinar is available at http://www.goodhormonehealth.com/hormones_wt_loss_20151214_0202_1.mp4.

Read Dr. Friedman's interview with Dr. Dae on The Many Benefits of Drinking your Fruits and Veggies at <http://www.empowher.com/weight-loss/content/many-benefits-drinking-your-fruits-and-veggies>

Read Dr. Friedman's interview on Redbookmag.com, [7 Foods That Balance Your Sex Hormones](#).

Ellen, Paul and Abby: heartwarming story of a challenging but rewarding pregnancy

Ellen and Paul just welcomed their first baby, Abby. Not such unusual news except this baby was the result of 10 years of dreaming, patience and persistence. Ellen and Paul both have pituitary failure. Ellen had pituitary surgery and a bilateral adrenalectomy to treat Cushing's disease, while Paul had pituitary surgery for Cushing's disease, as well as radiation therapy for cancer as a teen. These health issues made getting and staying pregnant more challenging. In addition to constant hormone tweaking by Dr. Friedman, they consulted a reproductive endocrinologist but multiple cycles of in vitro fertilization (IVF) failed, as did three separate adoption attempts. Almost out of hope, they made one last return to IVF and little Abby was born. Ellen shares her experience:

Educate yourself ahead of time about pregnancy with endocrine disease. The more you know, the more you can help your medical team to keep you healthy. For my pituitary failure and Addison's disease I started with this article (Yuen et al, Adrenal insufficiency in pregnancy: challenging issues in diagnosis and management, Endocrine, Feb 2013) and used the references for even more information: <https://goo.gl/p489QR>

- 1 I had to learn to listen carefully to my body. It took some experimenting, with the help of my doctors, to find what medication doses felt best.



- 2 A balanced thyroid is so important for a successful pregnancy! I was surprised at how much thyroid function was affected by pregnancy hormones, even up to my third trimester.
- 3 I enjoyed the extra boost I got from pregnancy hormones—bonus estrogen, progesterone and growth hormone helped me to feel wonderful. Surprisingly, I slept better and had more energy.
- 4 Pregnancy with pituitary failure and Addison's involves a leap of faith. There are no great lab tests to check and see how things are going with regard to hormone status (except thyroid). Doctors may or may not have a complex understanding of your unique needs. Don't be afraid to advocate for yourself by voicing your concerns or seeking new medical team members. Of course, Dr. Friedman has significant experience in balancing hormones during pregnancy and a visit to him may be worthwhile.
- 5 Persistence in IVF pays off. A new study (<http://goo.gl/JyJxzj>) just showed that each additional round of IVF is associated with progressively higher success rates (up to nine

cycles). Don't give up! Look into insurance plans that offer your money back if you don't have success after a set number of cycles—this may allow you to try again.

- 6 Research not only success rates with IVF clinics (http://www.sart.org/Find_A_Clinic/) but also clinics that are more affordable. You want high success at a reasonable cost. Consider that traveling for care may ultimately save you money.
- 7 If you have concerns about the risk of passing on genetic diseases, consider donated embryos, eggs and/or semen.
- 8 You may be able to nurse your baby even if you have some pituitary damage. Again, medication balance is critical for success. It's hard enough for Mom and baby to learn how to work together in those first few weeks but hormone fluctuations post pregnancy can make it even tougher.
- 9 Be patient with your recovery after having a baby. It takes time and tinkering to get those hormones balanced again.

Pregnancy was a miraculous experience for me. Parenting can be exhausting, yes, but I wouldn't trade it for the universe. I adore our daughter and am so happy I braved the challenges. Feel free to contact me through Dr. Friedman if I can answer any questions you might have about my personal experience.

HORMONES AND WEIGHT LOSS

Dr. Friedman was taught in medical school that weight gain is due to taking in more calories than expending calories, although it is not so simple. Weight gain is a complex process that depends on hormones, other medical conditions, sleep, stress, mood and the motivation to stick to lifestyle changes. There are certain hormones that are specifically involved in weight control. The most important one is cortisol. Cortisol is elevated in stress, sleep deprivation, in people who have social jet lag which means their circadian rhythm is different from society's and the disease called Cushing's syndrome. Also, weight gain can be due to low thyroid hormone, low growth hormone (mediated by low IGF-1), high insulin, low leptin, low testosterone, low estrogen and possibly low oxytocin.

The first question is how does **cortisol** lead to weight gain. Cortisol especially leads to visceral or central obesity, which is the detrimental fat that is in your abdomen. Some studies have suggested that elevated nighttime cortisol may be more detrimental than daytime cortisol. Some studies have suggested that cortisol increases appetite, but I am not sure as my Cushing's patients really do not eat that much. It also may affect the type of food eaten in that people with high cortisol may prefer comfort foods, which are foods like your mother used to make such as macaroni and cheese and mashed potatoes. Cortisol stimulates enzymes that are involved in fat storage. These enzymes are in the visceral fat which is why cortisol leads to weight gain there. Cortisol leads to storage of triglycerides and decreased breakdown of fat. Cortisol also leads to larger fat cells (adipocytes). Growth hormone, testosterone and estradiol act oppositely to the combination of cortisol and insulin and they stimulate fat breakdown. Cortisol also inhibits other axes such as the thyroid, growth hormone and reproductive axis. All of these axes when they are turned off, lead to further weight gain. Cortisol stimulates glucose production which leads to more fat. Cortisol increases the hormone called NPY, which is a brain hormone that is involved

in appetite. I am not really sure why nighttime cortisol leads to higher weight gain as people do not really eat that much at night, but I do know when I put my patients with Cushing's syndrome that have high cortisol at night on the medicine called ketoconazole, and I give it usually at night, they lose a lot of weight. Ketoconazole lowers cortisol for a few hours after its given.

How else does cortisol lead to weight gain? Cortisol decreases muscle strength that makes it harder to exercise. Cortisol leads to fatigue by unknown mechanisms. Cortisol leads to poor sleep that encourages people to eat more and especially more higher preference for a high fat and sugary foods. The poor sleep itself leads to high cortisol. Although it is hard to avoid stress and it is better to deal with it, stress reduction is one thing everybody can do to lower their cortisol.

Insulin is also involved in weight gain. Cortisol increases insulin. Insulin converts energy into fat and is a rainy day hormone that stores fat and leads to weight gain. When your insulin levels drop, your body starts to burn fat and weight loss occurs. In insulin resistance which occurs in obesity, your insulin does not bind to the insulin receptor properly and does not signal properly so you fail to sense you are full. Foods that are high in glycemic index, especially carbohydrates, lead to release of insulin. When you eat foods that raise your insulin, you also get more dopamine release in the reward centers of the brain, so you become addicted to food. Try to eat more high fiber foods and this will prevent release of insulin. The medicine metformin also reduces insulin levels and can lead to mild weight loss.

The hormone **leptin** is made in your fat cells and the more fat cells you have, the higher your leptin is. High leptin tells you not to eat anymore and low leptin tells you to eat more, so it sounds like it should be good that if you are obese that you should not eat that much. Unfortunately, most obese people are leptin resistant, so the leptin does not work properly and doesn't tell you to stop eating. It is like insulin resistance in that the insulin does not work properly, so you still eat even if though you are full. If you have leptin resistance, both the starvation and reward signals occur making it especially hard to lose weight.

So what do you do if you have high cortisol and are insulin and leptin resistance? Exercise is the first choice. Although exercise raises cortisol while you exercise, it lowers cortisol throughout the day. Exercise prevents insulin resistance and improves clearance of fat from the liver. It helps you deal with stress. You should also try to avoid the simple carbohydrates that stimulate insulin release.

Thyroid hormones also play a crucial role in metabolism. Patients who have an underactive thyroid have slower metabolism and are more tired. They have fluid retention, have a harder time exercising and the liver does not metabolize glucose properly. Patients that are hypothyroid can gain weight, but it is usually modest. Patients who have an overactive thyroid often have an increased appetite, so I usually do not recommend thyroid hormone for weight loss in someone with normal thyroid tests.

Another crucial hormone is **growth hormone** which tells the liver to release a hormone called IGF-1. Growth hormone itself can lead to diabetes and insulin resistance. IGF-1, however, is the active hormone that increases metabolism and often improves diabetes and insulin resistance. IGF-1 decreases fat stores and leads to increased muscle mass. In patients with normal IGF-1 levels who are not growth hormone deficient, growth hormone has minimal effects on weight and increases the risk of cancer. However, in patients who are growth hormone deficient determined by a growth hormone stimulation test, growth hormone treatments lead to increased energy, increased muscle mass, better sleep, decreased abdominal fat and weight loss. There is a

supplement called Serovital, which is a blend of amino acids that does stimulate growth hormone and may be a good choice in people who have a low IGF-1 but are not found to be growth hormone deficit.

Testosterone is also helpful for weight loss in both men and women with low testosterone. Testosterone replacement increases muscle mass, decreases abdomen fat and blocks some of the detrimental effects of cortisol in fat, but it is not recommended in patients with normal testosterone levels.

Estrogen plays a crucial role in weight regulation. Weight gain is common in perimenopausal and menopausal women, and it may be related to the worsening mood and poor sleep that menopausal women have. Low estrogen may lead to fat storage. Estrogen replacement is often beneficial for weight control in perimenopausal and menopausal women.

Another very interesting hormone that has not been well studied is **oxytocin**, which is made by the posterior pituitary like arginine vasopressin. It is the only pituitary hormone that we do not test for and that we do not replace, and it may have a role in bonding, intimacy, orgasm, GI issues, trust, generosity, pain and energy. A 2015 Endocrine Society abstract showed that oxytocin given to men caused weight loss. It needs to be studied more, but I think oxytocin may be helpful to facilitate weight loss.

So why it is hard to lose weight? It is because most people gain weight as they age and because of something called the thrifty gene hypothesis. Humans lived for millions of years in times of scarcity, therefore, their hormones, such as leptin, insulin and cortisol, have evolved to prevent starvation. Also, the thyroid, reproductive and growth hormone axes are programmed to shut down in times of starvation. Now food is abundant, but we still have the hormones designed to prevent starvation. There is an abundance of high caloric and unhealthy foods, healthy foods are more expensive, people have less time to exercise, they live sedentary lifestyles, they have a lot of stress and are sleep deprived. For all of these reasons, it makes it very hard to lose weight.

For patients to try to lose weight, I recommend a low or no carbohydrate diet, with mostly vegetables and lean protein, and avoid processed foods. Get an app on your phone and track your food intake. You should eat about 1200 or 1400 calories a day for women and 1400 to 1600 calories a day for men. Avoid eating at night, avoid stress eating and avoid eating out at fast food restaurants. You should try and exercise 30 to 60 minutes a day or longer if you can. Eat a high fiber low glycemic diet, get at least 7 to 8 hours of sleep at night and avoid and learn to deal with stress.

So who should come see me for weight gain and hormonal testing? Somebody who has unexplained weight gain after being on the same diet and exercise pattern. If you have a dramatic weight gain over a short period of time and if you have other symptoms including fatigue, irregular periods in premenopausal women or hair loss. I will test patients for hormonal causes of weight gain by testing for Cushing's syndrome, growth hormone deficiency, hypothyroidism, testosterone and estrogen deficiency, hypopituitarism, polycystic ovarian syndrome which is marked by high testosterone and insulin resistance making it hard to lose weight, insulin resistance in general, vitamin D deficiency and iron deficiency.

Stress, sleep deprivation and social jet lag: the 3 Ss of how cortisol leads to weight gain

In December, 2015, I gave a webinar (http://www.goodhormonehealth.com/hormones_wt_loss_20151214_0202_1.mp4) on the hormonal effects on obesity, that was one of my most popular webinars. Everybody wants to learn about how hormones are related to body weight and food intake. I talked a lot about how cortisol is involved in weight gain. I would like to explore the topic further by writing about the three Ss of obesity that are all cortisol mediated. These are **stress**, **sleep deprivation** and **social jet lag**.

Stress definitely have negative effects on health, and it seems like everybody is stressed. Stress is defined as anything that is a threat either "real" or "imaginary" to homeostasis. Homeostasis is your hormonal balance. A real stress would be seeing a tiger escaping from the zoo and about to eat you. An imaginary stress would be giving a talk about a topic you are not familiar with. Both of these stresses are harmful. Several studies have shown that stress is correlated with weight gain, and one of the main mechanisms is that stress activates the hypothalamic-pituitary-adrenal axis that gives a higher level of cortisol. The high cortisol leads to weight gain predominantly in the abdominal area. However, stress also causes increased food intake even when people are not necessarily hungry. A study was done where they fed people until they were no longer hungry, then had them do a stressful task and then gave them a tray of snacks. They ate more if they were stressed even though they were not hungry, so there is something about stress that leads to overeating, especially comfort foods. These are foods that your mother used to make for you and includes mashed potatoes and macaroni and cheese.

The second area that is leading to the obesity epidemic is lack of **sleep**. Over the past 50 years, we went from sleeping about 8-1/2 hours a night to 7 hours or less. This happened about the same time as the obesity epidemic has blossomed and now more people are staying up later using their electronics. Studies have shown that people who sleep less than 7 hours a night have higher levels of cortisol and are more likely to be overweight and get diabetes than those who sleep at least 8 hours. In addition to sleep quantity, sleep quality is also important; therefore, a good night's sleep is essential for proper cortisol levels and to prevent weight gain. There are apps that can track how many hours a night you sleep and how many times you wake up, and these apps can be quite helpful in determining your quality of sleep.

The third area is called **social jet lag**. Social jet lag is a term meaning that your circadian rhythm (body's own clock) is different from what the real world expects from you (society's social clock). Some people are nighttime persons and some people are morning persons. If a nighttime person had his choice, he might go to bed at 6 in the morning and sleep until 3 in the afternoon; however, society forces him to go to bed around 10 or 11 at night and wake up around 6 in the morning to get to work at 8 in the morning. This is called social jet lag when there is a disconnect between the body's own circadian rhythm and what society imposes on the person. Social jet lag seems also to raise cortisol levels and leads to obesity. When the person who is a night owl but goes to bed at a regular time during the week followed by the weekend, when he resumes his normal circadian rhythm and can go to bed much later, his body shifts to a different circadian rhythm on the weekend. Then on Monday, when he has to return back to work, he has mini jet lag and is suffering from social jet lag. These patients have activation of the hypothalamic-pituitary-adrenal axis.

You may think that there is not that much to do to overcome these physiological effects leading to weight gain--stress, sleep and social jet lag. However, although nobody has a stress-free life, the trick is not to let stress effect you. Be one of those people that have the stress just bounce off you. Also, avoid stressful situations. In terms of sleep, try to get both a good quality and a good quantity of sleep and try to avoid alcohol and caffeine at night as well. Finally, for the social jet lag, you may need to get a job that can accommodate your circadian rhythm. You can try to adjust your circadian rhythm in that if you are a night owl you can try to be exposed to sunlight in the morning and avoid sunlight in the evening. Trying to tackle the three Ss and controlling your cortisol level is the key to good hormone health.

Blending or Juices: What is Better for Your Hormones?

Dr. Friedman runs a group obesity program at an inner city medical center in Los Angeles where he encourages participants to consume more vegetables. He finds that it is better to tell people what they should eat, rather than what they should not eat. Most people do not get eat enough vegetables and many people eat too much starches like bread, pasta, tortillas and rice. An excellent way to take in more vegetables is to blend them.

There is an important difference between blending and juicing. Juicing extracts the liquid from the vegetables and leaves behind the fiber. Blending, on the other hand, includes the fiber and you drink all of the fruit and vegetables. Drinks made in a blender can be called vegetable blends or vegetable smoothies. You can get a regular blender to do blending or you can get a high-powered blender that really breaks up the fruits and vegetables. Dr. Friedman uses the Ninja Professional blender which costs about \$100. The fiber in the fruits and vegetables is what is the most beneficial. Therefore, most people (unless they have problems with their digestive tract and can not handle fiber) should avoid juicing which is basically just the sugar, water and some of the other vitamins in vegetables and fruits.

The next question people ask Dr. Friedman is should you blend fruits or vegetables or both. Dr. Friedman especially recommends blending vegetables, with a small amount of fruit. Vegetables have a lot of nutrition, many micronutrients and very little calories. Therefore, they are quite filling. Fruit has more in sugar in it and fruit actually has fructose. However, a blended drink made only of vegetables probably does not taste too good, so Dr. Friedman does recommend people to add some fruit in it. The best fruits to add are berries, such as blueberries and cranberries that have a lot of antioxidants in them.

Fruits have fructose in them. It is becoming clear that high fructose corn syrup (55% fructose, 45% glucose) that is in soft drinks and many processed foods is very detrimental for people and may be involved in the obesity epidemic. Therefore, the question arises is why are fruits good for you (with 100% fructose) but high fructose corn syrup (with 55% fructose) is not good for you. This is because of the fiber in fruit. The fiber helps prevent the rapid absorption of the fructose from the proximal intestines into the liver and allows it to be absorbed more distally in the intestines where it allows for an even uptake of nutrients into the bloodstream and avoids blood sugar spikes. The fiber in blended drinks is the crucial part in changing them from an unhealthy drink to a healthy drink. There is some concern that the blending process breaks up the fiber; however, most of the time the blending leaves the majority of the fiber intact. This may be more of a concern with blending only fruit. There is both soluble and insoluble fiber in fruits and

vegetables and both are good for you and both are available when you blend your vegetables and fruits. Although there are postings on the internet of the harm of mixing vegetables and fruits, Dr. Friedman could not find scientific evidence against that and posits that the fiber in vegetables helps decrease the negative effects of fructose in fruit. It is important to use blends instead of more caloric, unhealthy foods and not in addition to them.

Dr. Friedman tries to drink 2 large 32 oz (1 liter) containers of a blended drink a day. He puts them in a BPA-free plastic container and brings them with him when he is seeing patients and writing his papers and grants. He blends kale, arugula, fennel, ginger, tomatoes and carrots as the vegetables and frozen berries such as blueberries, cranberries (bought before Thanksgiving and frozen) and blackberries and sometimes frozen mangos or pineapple as the fruit. He also adds a little bit of sunflower seeds, chia seeds or flaxseeds. These give it a nutty flavor and helps with satiety. He drinks his blend within 2 days of preparation.

Adding vegetables and fruit to your diet may help prevent chronic diseases, improve your bowel movements, give you increased energy and help with weight loss and control of high cholesterol and diabetes. Blending is definitely the way to go. Dr. Friedman recommends watching the movie *Fat, Sick and Nearly Dead* about an Australian man who weighed 300 pounds, had an autoimmune disease and was loaded up with steroids. He went on a blended holiday where he only did blended fruits and vegetables for 2 months and his health improved dramatically. He then convinced others to do the same. He was able to get off his steroids.

An interview of Dr. Daemon Jones with Dr. Friedman is available on the EmpowHer website (<http://www.empowher.com/weight-loss/content/many-benefits-drinking-your-fruits-and-veggies>) entitled The Many Benefits of Drinking Fruits and Veggies

Drugs and Cortisol

Patients frequently ask me if taking a certain drug will affect cortisol levels, either in regarding to cortisol testing or if they want to raise or lower their cortisol. If a patient is undergoing testing for Cushing's Dr. Friedman recommends discontinuing the drug for a week before testing, especially drugs in **bold**. Although it may be a challenge, certain drugs can be used to raise (those with low cortisol) or lower (those with high cortisol) cortisol. Cortisol has a circadian rhythm, with the highest levels in the morning and low levels at night, Therefore, in general, cortisol-lowering agents should be taken at night and cortisol-raising agents should be taken in the morning.

Type of Drugs	Generic Name	Brand Name	Effect on cortisol	Comments
Cushing's Drugs	ketoconazole	Nizoral	↓	Most effective drug, should be given at night
	mifepristone	Korlym	↑	Blocks cortisol at the receptor, effective for Cushing's even though it raises cortisol
	somatostatin Analogues (octreotide, lanreotide, pasireotide)	Sandostatin, Somatuline, Signifor	↓	Lowers cortisol mildly with a high rate of diabetes
	metyrapone	Metopirone	↓	High rate of adrenal insufficiency
	etomidate	Amidate	↓	Can be given IV
	mitotane	Lysodren	↓	Destroys the adrenal gland

Antidepressant	citalopram	Celexa	↑	
	sertraline	Zoloft	↑	
	fluoxetine	Prozac	–	
	imipramine	Tofranil	↓	
	desipramine	Norpramin	↓	
	trazodone	Desyrel	↓	
	mirtazapine	Remeron	↓	
Antipsychotic	olanzapine	Zyprexa	↓	
	quetiapine	Seroquel	↓	
Anti-anxiety	temazepam	Restoril	↓	
	alprazolam	Xanax	↓	
	lorazepam	Ativan	↓/–	Anecdotal-lowers cortisol, literature no effect
Dopamine agents	cabergoline	Dostinex	↓	Variable effect
	bromocriptine	Parlodel	↓	Variable effect
	metoclopramide	Reglan	↑	
	methylphenidate	Ritalin	↑	Found in 1 study, but not another study
Anti-hypertensives	clonidine	Catapres	↓	
Opioids/anti-opioids	loperamide	Imodium	↓	
	morphine, methadone, codeine	various	↓	
	buprenorphine	Buprenex	↓	
	naloxone	Narcan	↑	
	naltrexone	Revia	↑	Unclear if low-dose naltrexone (LDN) has the same effect
Drugs of abuse	heroin		↓	
	cocaine		↑	
	alcohol		↑	
	Tobacco/nicotine		↑	
Hormones	progesterone	Provera, Prometrium	↓	Binds to the cortisol receptor, so Cushingoid features could occur, even though cortisol levels are decreased
	megesterol	Megace	↓	Used for weight gain
	growth hormone	various	↓	Increase breakdown of cortisol
	thyroid hormone	Synthroid, Levoxyl, Cytomel Armour, etc	↓	Increase breakdown of cortisol
	raloxifene	Evista	↓	Used for osteoporosis
	estrogens, birth control pills		–	Raises cortisol-binding protein and raises total cortisol, does not affect free cortisol
	DHEA		↓	
	desmopressin, oxytocin	DDAVP	↑	
Diabetes medications	rosiglitazone	Avandia	↓/–	Anecdotal reports of lowering cortisol
	pioglitazone	Actos	↓/–	Initial studies found a reduction in cortisol, not confirmed by additional studies
Supplements	phosphatidyl serine	Seriphos	↓	Effective at night, Seriphos and phosphatidyl serine are slightly

				different
	gingko bilabo		↓	
	St. John's wort		↑	
	rhodiola		↓	

Bold indicates substantial effect.

Reference: Ambrogio AG, Pecori Giralaldi F, Cavagnini F. Drugs and HPA axis. Pituitary 2008; 11:219-229

For more information about Dr. Friedman's practice or to schedule an appointment, go to www.goodhormonehealth.com or email us at mail@goodhormonehealth.com.

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