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Part Six - Medication and Weight Control

In general, when we are aroused, vigilant, or alert and especially when in a “fight or flight” mode our appetite is suppressed. The brain transmitters serotonin, norepinephrine, dopamine, and histamine decrease appetite, and being in a relaxed vegetative state increases appetite and low blood sugar causing carbohydrate craving. During physical activity appetite suppression occurs, but after activity hormones stimulate appetite to replace the energy depleted energy sources. When stress causes depletion of brain serotonin we eat to raise serotonin levels, or stress stimulates appetite by raising cortisol and insulin. When we’re bored eating raises dopamine levels.

Inactivity as in hibernation causes excessive eating, and eating because of stress or boredom causes excessive intake of calories. Eating sweets increases insulin, and insulin stimulates low blood sugar, carbohydrate craving and the roller coaster of high blood sugar and low blood sugar levels. Intermittent acute stress leads to intermittent release of adrenaline, which causes the liver to dump sugar into the blood stream. This high level of insulin then causes the low blood sugar cycle.

Weiging the Risk Vs. Benefits of Medications that Affect Weight

Managing stress and eating the right foods is of preeminent importance in combatting the blood sugar cycling. Further, some medications protect against these negative cycles, while helping you to lose or control your weight. Many patients gain weight from certain medications, many of these patients feel a lot of guilt and shame because of their weight gain. Lack of self discipline and self indulgence can be a problem but for many patients it’s out of their control. Some medications change brain functioning, and like a person with genetic obesity, they begin to save every extra calorie as extra fat. Weight gained on medication sometimes comes off fairly easily with discontinuation of the medicine when no longer needed, but sometimes it seems the medication resets the weight-o-stat making it difficult to return back to previous weight.

When using medications to lose weight, especially those that work by decreasing appetite or increasing control of eating, it is important to realize that stopping them could lead to the gaining the weight back. Frequently with a couple of extra pounds for good measure. In other words, there’s no medication that can be taken just to lose weight that effectively helps keep the weight off after it is discontinued. Because of this, it only makes sense to use medication for weight control if you need it for another condition, like stimulants for ADHD or thyroid medication for low thyroid. Sometimes long term use of pure appetite suppressants is useful just because the risks associated with obesity versus the relative long term safety of appetite suppressants is greater.

Fenfluramine (Pondimin) and d-fenfluramine (Redux) were used for 10 years in France and an additional 3-4 years in the U.S. before discovery that they caused serious

complications, especially heart valve abnormalities and/or pulmonary hypertension, and especially when used in combination with phentermine. The reason for this is because Fenfluramine increases serotonin activity and Phentermine increases norepinephrine activity, both which can constrict arteries. The combination fen-phen was never promoted by any pharmaceutical company but became popular after a paper was published by a doctor who had good success with this combination. After realizing the harmful effects of the combination, Fenfluramine was taken off the market, and since then many law suits have been filed. Though there is not doubt that this combination can be dangerous, claims of damage most likely exceed actual damage. The lesson learned from phen-fen is the same as the one recently learned from Vioxx. Controlled studies of most medications are relatively short term. There is always some potential risk with the long term use of medications, so it is always important to ask, “What are the Potential Benefits vs. the Potential Risks”?

Medications and Weight Control From the Worst to the Best

The following medications are commonly used in treating stress disorders. I will list them starting with the worst for weight management (the one most likely to cause weight gain) and end with the best medication for weight management.

1. **Zyprexa**
2. **Clozaril**
3. **Symbyax**
4. **Remeron**
5. **Seroquel**
6. **Risperdal**
7. **Lithium**
8. **Depakote**
9. **Neurontin**
10. **Anafranil**
11. **SSRI's**
12. **Abilify**
13. **Geodon**

Clozaril, Zyprexa & Symbyax: Symbyax is a combination of Prozac and Zyprexa, and these three are tied for the most likely to cause weight gain. They block the serotonin receptor associated with satiety. In addition they block histamine, some dopamine, and increase the hormone prolactin. Both medications are considered a high risk for causing metabolic syndrome, and patients taking these medications should have blood work done regularly to check their lipids and glucose.

Remeron: This antidepressant blocks histamine and the satiety receptor, but because it also increases serotonin and norepinephrine, it is not as bad as Zyprexa and Clozaril.

Seroquel: This atypical medication poses moderate risk for metabolic syndrome and sometimes causes substantial weight gain, because it acts strongest as an antihistamine.

Risperdal: This medication also poses moderate risk for metabolic syndrome. The moderate risk for weight gain may be related to the fact that it has a strong blocking effect on dopamine and is the most likely of the newer medications to increase the hormone prolactin which may contribute to increased appetite.

Lithium and Depakote: These medication are generally used to treat Bipolar disorder and they pose a moderate risk for increased weight over the long haul.

Neurontin and Anafranil: Neurontin and the tricyclic antidepressant Anafranil (Clomipramine) can also lead to significant weight gain over time.

SSRI's: The most commonly prescribed medications for depression and also commonly used for anxiety are the group referred to as SSRI's (selective serotonin reuptake inhibitors). These include Prozac, Zoloft, Paxil, Lexapro, and Celexa and low doses of Effexor. The first one (Prozac) has been available since 1987. Again, to quote Einstein, "*keep it as simple as possible, not simpler*". The effect of SSRI's on weight is complicated because there are 3 different phases in the mechanism of action. To simplify this process, here is a breakdown of the phases:

Phase 1 By blocking the reuptake of serotonin into the sending cells, Serotonin builds up in the synapses and stimulates multiple receptors on adjacent cells. This happens within 24 hours and goes on for several days. This immediate boost in serotonin can help premature ejaculation, decrease carbo craving and can help premenstrual dysphoric disorder. It can also destabilize bipolar disorder.

Phase 2 After one week on Effexor, 10 days on Lexapro, 2 weeks on Celexa, Prozac and Paxil or 3 weeks on Zoloft, the effects of the increase in serotonin begin to modulate activity within adjacent cells and will begin to change receptor activity on the sending cells also. These modulating effects help clinical anxiety and depression.

Phase 3 The least well understood phase of SSRI activity occurs after several weeks. Because most controlled studies of SSRI's only last 6-8 weeks, the information on how they work long-term is limited. However, the proof that changes continue to take place can be explained when used to treat Obsessive Compulsive Disorder, because it usually takes 12 weeks to see positive changes. The down regulation of serotonin activity in the brain presumably causes the change, because when serotonin levels increase a messages goes from the brain to the cells and says "we have enough, you can decrease production".

This mechanism may explain how SSRI's help anxiety and panic disorder by decreasing serotonin release where there is hypersensitivity to serotonin. A common phenomenon seen in patients on SSRI's has been referred to as "poop out". It is not clear whether this is due to excessive down regulation of serotonin release or if it is due to the fact that

serotonin causes a decreased release of dopamine which is the drive and motivation system. Symptoms of “poop out” include feeling "blah", blunting of normal emotions, sexual dysfunction and weight gain that can occur due to decreased serotonin activity and/or decreased dopamine release. Because the weight gain doesn't occur until several weeks or months of being on an SSRI most doctors and patients don't see the cause and effect relationship. In some cases, it may be correctible by decreasing the dose.

Unfortunately more often the "blahs" are seen as a return of the depression so the dose is raised, which temporarily helps by raising serotonin but eventually down regulates serotonin even lower. Sometimes lowering the dose or stopping the SSRI causes return of severe anxiety, OCD, or depression. Adding Wellbutrin XL or a stimulant may help.

Finding a different medication that is as effective for anxiety and depression that does not cause weight gain is difficult, sometimes impossible.

Of the SSRI's Paxil seems to be the most likely to cause weight gain but any of them can be a problem in the long term. Effexor XR is mainly an SSRI at 37.5-75mg but does have some norepinephrine effect even at the lower doses, which may help protect against the “poop out” syndrome. Doses of more than 150mg of Effexor XR and Cymbalta are not as likely to cause long term weight gain presumably because of the combined serotonin and norepinephrine modulation, but weight gain does occur in some patients over the long term.

Abilify and Geodon: These atypicals have the least likelihood of causing metabolic syndrome and tend to be weight neutral. Thin people may gain a little weight on these meds long term, but overall they don't pose a huge risk of weight gain.

Hormones - Some women gain weight on the hormones estrogen and or progesterone. Estrogen, especially estradiol, may be a particular problem if taken orally.

There are several meds or groups of meds that are essentially weight neutral:

- **Benzodiazepines** - Xanax (Alprazolam), Niravam (Alprazolam in wafer form), Klonopin wafers, Clonazepam, Tranxene, Valium
- **Sleep meds** - Ambien, Lunesta, Sonata, Rozerem (Although lack of sleep can contribute to weight gain, so it could be argued that the sleep medications help control weight)
- **Lamictal**
- **Gabapril**
- **Tenex (Guanfacine)**
- **Strattera (for ADHD)**
- **DHEA/testosterone**

Meds that can help with weight control:

- **Wellbutrin XL (antidepressant)** - not as good for anxiety as SSRI's. It works by enhancing norepinephrine and to a lesser extent dopamine

- **Thyroid** - especially Cytomel or Armour, but also Synthroid if at an adequate dose. People occasionally report weight gain on Thyroid and this is presumably due to taking too low a dose.
- **Meridia** - This medication is approved for weight loss. It has moderate effects on serotonin, norepinephrine, and dopamine. It may increase blood pressure. Effects aren't dramatic and it is not used very much.
- **Xenical** - is sometimes helpful. It reduces absorption of part of the fat consumed. It doesn't help if eating a low fat meal and it can be problematic if you eat a high fat meal as in diarrhea and "accidents". It is also not used much.
- **Phentermine** - part of the old fen-phen. It has been around for a long time. It shouldn't be used unless the plan is to take it long term. It may raise blood pressure and it may cause nervousness or irritability. Some people like it but it's not used by very many.
- **Didrex** - is like phentermine and neither one requires a triplicate prescription, which is an advantage.
- **Provigil** - increases alertness and usually leads to increased activity and more calories burned per day.
- **Stimulants**
- **Chromium picolinate** 400-600mgm [See Chromium Picolinate](#)

I have been prescribing medication for stress disorders since 1966, and over the long term, the medications that have been the most helpful in controlling weight are the amphetamines prescribed for ADHD. Although, when short acting forms of the stimulants are taken they sometimes cause rebound overeating in the evening and this can also occur on days when not taken. Despite popular belief, the efficacy of stimulants on weight loss is not due to appetite suppression, although appetite suppression occurs when initially starting some stimulants, especially in kids and teens, but I believe it mainly increases control and decreases impulsivity. This prevents eating out of stress or boredom. I have the most experience and success with Adderall XR, the long acting form, since tablets, the short acting form, are more likely to cause rebound. Dexedrine and Desoxyn also work, most likely by setting the "weight-o-stat" lower. The methylphenidate type stimulants are usually not as effective for controlling weight, and the longer acting Concerta (soon to be available), Focalin XR, Ritalin LA, and Metadate CD are better than short acting meds. Stimulant often increase energy and motivation, which may be another attribute associated with their weight loss efficacy.

ADHD and Weight Issues

ADHD increases an individuals risk of abusing alcohol or drugs because part of the physiology of ADHD is the need for more stimulation than the non-ADHD person. There are several different polymorphic genes more commonly seen in ADHD and nearly all result in low dopamine activity in the brain, specifically the nucleus accumbens. Every addictive substance or activity increases dopamine, and food is one of the strongest enhancers of dopamine. For this reason, being ADHD may result in overeating and excess body weight. In one study using Adderall XR in people who were ADHD and obese, they found the obese individuals lost a significant amount of weight. In contrast,

people who were ADHD but within normal weight range did not lose a significant amount of weight.

Summary

If you don't take care of your body, where are you going to live? - Anonymous

All of this is not say you need medication to control your weight. But if all of your efforts to maintain not only healthy weight but fitness have failed, you may consider trying medication. When contemplating the use of medication the question is always, “*what are the potential benefits vs. what are the potential risks*”? Nietzsche said “*first be a good animal*”. You can't be mentally healthy if you're not physically healthy. Two thirds of the U.S. population are overweight. Being overweight, especially abdominally, increases risk for cardiovascular disease, diabetes, stroke and other health problems, and it's not so good for self-esteem either. I believe the main reason weight has become a rising epidemic exists because we weren't made for this world. The world of hunting and gathering that we adapted to was a much more active lifestyle. Food was not always plentiful, and additives and refined foods did not exist. People were at the mercy of ice ages, droughts and Mother Nature and our brain conspires to protect us from food shortage by storing energy as fat. Unfortunately in today's world, genetics (polymorphism) and behavior (brain plasticity) conspire to make us overweight. There are behaviors to help you lose and behaviors that make you gain, including ironically, dieting just like there are medications that make it hard not to gain weight and medications that make it easier to lose weight. It's more important to be physically fit than to be within the ideal range of body fat, which is where in realizing your full potential you have to “first be a good animal”.

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