

**ADJUSTABLE**

**You have tried  
everything to lose**

**weight**

You've tried the latest and greatest diet or fat-melting workout. You may have tried weight loss supplements or prescription medications but you are now heavier than ever. Sound familiar?

Humans are very successful as a species because we can store energy (fat) very efficiently and have multiple ways to store this energy. Thus, for long-term success physicians must look at the metabolic and endocrinological factors leading to weight gain and not assume it is a matter of will-power to eat less and exercise more. Here at Holtorf Medical Group we identify the underlying causes of the inability to lose weight, including hormonal deficiencies, thyroid imbalance, leptin resistance, insulin resistance, mitochondrial dysfunction, metabolic insufficiency, set-point abnormalities and vitamin deficiencies. We have a wide-range of methods to treat these conditions, ultimately leading to weight loss. Diet and exercise is rarely successful for long-term weight loss if such metabolic disturbances are left untreated.

## Leptin

The hormone leptin has been found to be a major regulator of body weight and metabolism and dysfunctional leptin signaling results in one of many vicious-cycles that prevents individuals from losing weight. With increased weight, leptin is secreted as a signal to the body to stop storing fat. Leptin stimulates metabolism, reduces appetite and signals the body to burn fat. Studies are finding, however, that the majority of overweight individuals that are having difficulty losing weight have varying degrees of leptin resistance. The leptin is unable to produce its normal effects of weight loss, with the severity correlating with the degree of obesity and difficulty losing weight.

This leptin resistance results in a leptin deficiency in the hypothalamus, which is sensed as starvation, so multiple

mechanisms are activated to increase fat stores, as the body perceives a state of starvation. Baseline leptin levels and the degree of leptin resistance is shown to be a good predictor of a person's likelihood of achieving successful weight loss with dieting. Leptin levels above 12 ng/dl indicates there is leptin resistance and, as with insulin, the higher the leptin the more resistance is present.

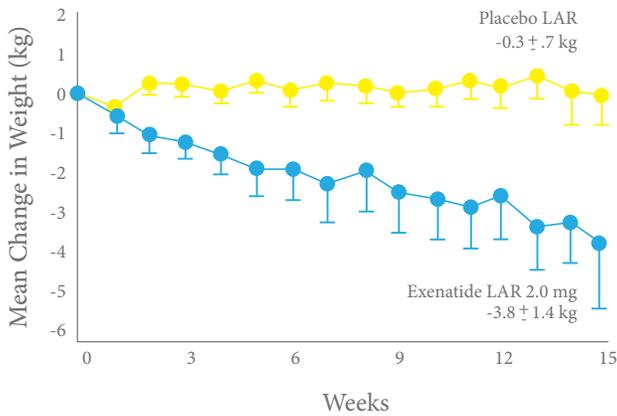
Leptin resistance also results in cellular hypothyroidism that is not detected by standard thyroid function tests, including the TSH, free T4 and free T3 levels. The metabolic effects of leptin resistance include a diminished TSH secretion, a suppressed T4 to T3 conversion, an increase in reverse T3, an increase in appetite, an increase in insulin resistance and an inhibition of lipolysis (fat breakdown). Thus, with leptin resistance, significant hypothyroidism may exist despite the fact that standard thyroid tests look "normal". If a person is not able to lose weight despite dieting, there is usually a problem with leptin resistance that needs to be diagnosed and treated. With treatment, dramatic weight loss can be obtained.

A newly published study presented at the annual Obesity Society meeting demonstrated that new therapies treating leptin resistance are very effective for weight loss in overweight individuals with or without diabetes. In a randomized, double-blind placebo controlled, cross-over trial, it was found that short-term use (less than 4 months) of the leptin sensitizing medication, resulted in significant weight loss in 65% of individuals. In the responders, 48% lost significant weight in two to four weeks with no change in diet. Individuals also experienced increased satiety vs. placebo. There were no reported side-effects with treatment. Studies also show significant improvements in cardiovascular risk factors.

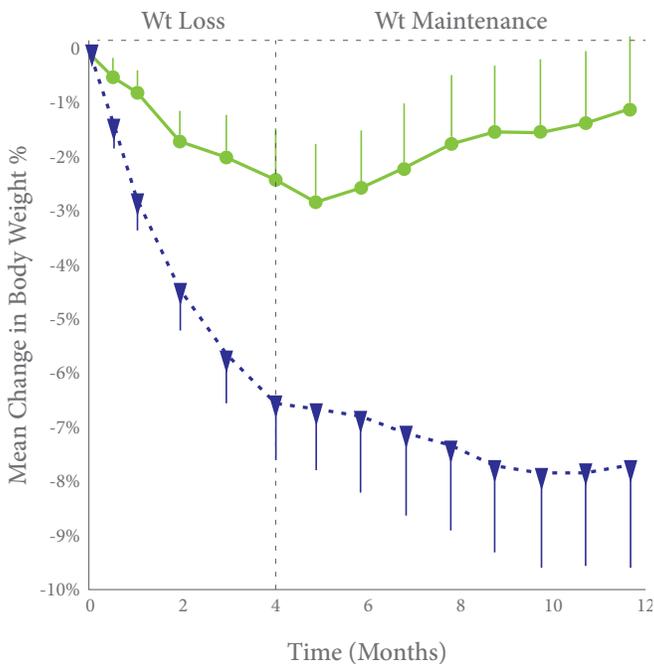
Many doctors are not aware of this class of medications or believe they are only useful to control blood sugar in diabetic

patients. As the studies have shown, we have found this class of medications to be very safe and effective for weight loss in both diabetic and non-diabetic patients, especially for patients who have leptin resistance.

### Exenatide for Weight Loss



### Pramlintide for Weight Loss



## Have you wrecked your metabolism with too much dieting or exercise?

You never eat fast food, let alone supersize anything. To the contrary, you are constantly depriving yourself and doing regular rigorous exercise. But you can't seem to lose weight or keep it off. You starve yourself and run extra miles per week—wow a quarter pound lighter. As soon as you go back to your

normal diet routine, the weight comes back. You swear you have no metabolism but your doctor says everything is normal. Your friends recommend yet another fat burning diet but nothing seems to work. Sound familiar?

Could you be doing too much exercise or eating too little? Such a thought is often met with skepticism and eye rolling, as it is assumed you are eating Ding Dongs in the closet at midnight. But it may be that too much exercise or dieting may be to blame. Really, say it isn't so. All that work for nothing?

Studies show that if you chronically diet or “over exercise” your body may turn on you and reduce your metabolism by suppressing thyroid levels. The body normally produces an inactive thyroid hormone called T4, which is then converted to T3. The T3 is the active substance that is responsible for your body's metabolism. When it is low or suboptimal, your metabolism is low. When it is high, your metabolism is high.

When the body senses excessive dieting or exercise this normal sequence of events is altered. Instead of converting T4 to the active T3, the body then converts the T4 into a substance called reverse T3 instead of into T3. This causes the metabolism to drop and it is shown to often not return to normal even after regular eating or exercise is resumed. You have now wrecked your metabolism.

A study published in American Journal of Physiology, Endocrinology and Metabolism found that 25 days of dieting reduced T4 to T3 conversion by 50% while a study in the journal Metabolism found that chronic dieting dramatically lowers metabolism that stays depressed even after resuming normal food intake. This dramatic reduction in tissue T3 levels (and increased reverse T3) that results in hypometabolism is not detected by the standard blood tests used by 99% of physicians and endocrinologists.

Mirroring the results of the above study, our center has found that a reduced basal metabolic rate is a consistent finding in those who chronically diet, with many such individuals having a 20-40% lower metabolism than expected for their body mass index (BMI). With such a reduced metabolism, you must eat 500-1000 less calories per day or burn that many calories to just stay even and not gain weight. While diet and exercise are important components of successful weight loss, they will certainly fail to achieve long-term success if metabolic abnormalities are not addressed.

The question is how much exercise or dieting is too much. The answer is, “it depends” because everyone is different. Women are much more prone to this syndrome of exercise or diet induced hypothyroidism than men. And those that do intense yo-yo dieting and have lost and gained significant weight in the past or only eat one meal a day are at particular

risk. It is important to determine the extent that a suppressed metabolism is contributing to the inability to lose weight. This is done in our center with in-house metabolic testing and the measurement of tissue thyroid levels, as well as extensive metabolic and hormonal laboratory testing to determine the physiologic basis of the inability to lose weight.

## HCG Injection for Weight Loss

HCG, which stands for human chorionic gonadotropin, is a hormone produced during pregnancy. Research has shown that a small amount injected everyday can aid in weight loss. While most studies were done in combination with a very low calorie diet, it can aid in the selective reduction of fat and reduce appetite, increasing the effectiveness of any sensible diet. Thus, it is not necessary to do a very restrictive diet to see results. There is also evidence that it may reduced the risk of breast cancer and improve prostate health.

## Has your set-point malfunctioned?

The basic premise of the set-point theory is that the body has a built in weight regulating mechanism that will tend to keep your weight in a physiologically established comfortable range. Have you felt that despite initial weight loss success, your body will tend to go back to your “normal” increased weight despite significantly reducing calories and/or increasing exercise?

There are numerous medications that can result in an increase in the body’s weight set point and stimulate weight gain. These medications include antidepressants such as Zolft, Paxil, Celexa and Lexapro; SNRI’s, such as Effexor, Cymbalta and Savella; mood modulators such as Seroquel and Abilify; anti-seizure/pain medication such as Lyrica and Neurontin; birth control pills; synthetic hormone replacement; diabetic medications that stimulate insulin such as glyburide and Amaryll; many blood pressure medications; and many more. There are, however, medications that have the opposite effect and lower the body’s weight set. Thus, they can be used to aid in weight loss.

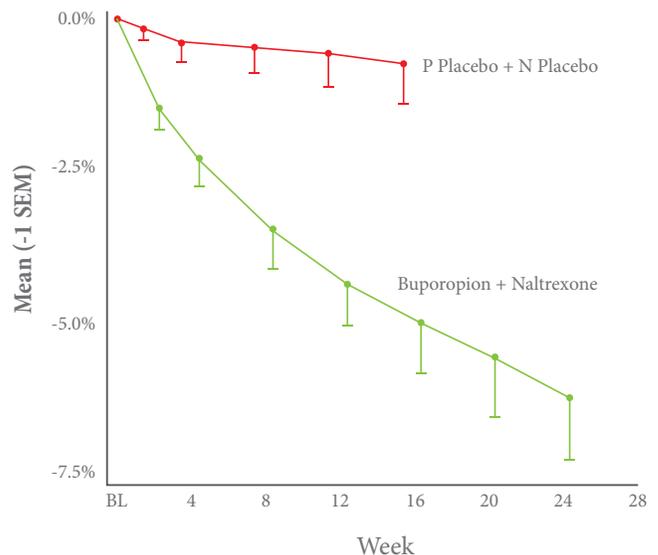
The most recent medication that has been shown to decrease the body’s set-point is naltrexone. This medication

blocks a particular type of opioid receptor and has been used for many years to as treatment for a narcotic overdose and to reduce the incidence of relapse in alcoholism and opiate addiction.

At lower dose, however, naltrexone has very different effects. At very low dose it is an immune modulator and has shown to be effective for autoimmune diseases such as Lupus, rheumatoid arthritis, Hashimoto’s and Crohn’s disease as well as conditions associated with immune dysfunction such as chronic fatigue syndrome, Lyme disease and fibromyalgia. At low doses, but higher than the immune modulation doses, it is shown to reduce the body’s set point and cause significant weight loss. The effect is enhanced when used with bupropion (Wellbutrin). In a recent trial, this combination was shown to result in significant weight loss over twice the rate of placebo with an average weight loss of over 17 pounds. Studies also show an increased reported sense-of-well-being and quality-of-life with this combination. There are other medications that can be used to lower the body’s set point, as well.

We have found the combination of naltrexone and bupropion to be effective in a significant number of patients with few side-effects. This combination will soon be available in one pill for weight loss, but can now be given as separate prescriptions.

## Use of Bupropion and Naltrexone for weight loss



23456 Hawthorne Boulevard, Suite 160, Torrance, CA 90505 (310) 375-2705  
48 N El Molino Ave, Suite 201, Pasadena, CA 91101 (626) 796-7500  
1065 East Hillsdale Blvd, Suite 108, Foster City, CA 94404 (650) 638-1141  
491 Allendale Rd, Suite 222, King of Prussia, PA 19406 (610) 265-0500