Chapter X: The Pharmacology of Weight Management

compiled by Jeff Russell

The Pharmacology of Weight Management:
Introduction

The storied tale of pharmacological agents used for weight management really begins in the late 1940's and early 1950's. Before this time, obesity was considered to simply be caused by overeating. However, in 1954, with the publication of A.T.W. Simeon's study in the British medical journal, The Lancet, regarding the inclusion of Human Chorionic Gonadotrophin (hCG) as a useful pharmaceutical in the fight against obesity, the issue of obesity and weight management began to be characterized as "a disorder of energy metabolism." At the same time, in the late 1950's, the FDA also approved the use of several prescription appetite suppressants to assist in weight management.

Interestingly, appetite suppressants and hCG protocols flourished during the 1960's, and then in the early 1970's, following a series of unfavorable studies refuting the effectiveness of hCG in weight loss, hCG use fell from credibility. Equally, the use of appetite suppressants in the class of amphetamines also fell from favor. An excessive proliferation of disreputable "fat clinics" and over prescribing of these agents resulted in an increased rate of clinical complications.

However, today physicians appreciate weight management as a multifaceted disorder. Pharmacological solutions are paired with diet, exercise, technology and other advancements to develop weight management protocols tailored to individual patient needs. This chapter provides an introduction to the key players in the pharmacological arsenal used in diverse weight management programs.
Human Chorionic Gonadotropin (hCG)

What it is

Human Chorionic Gonadotrophin (hCG) was first discovered by researchers Ascheim (1927), Zondek (1931), and in the Friedman test (1931), and the Xenopus laevis test (Shapiro, 1934), respectively, in the urine of pregnant women. hCG is specifically the glycoprotein hormone normally secreted by trophoblastic cells of the placenta during pregnancy. Today, most hCG on the market, such as Pregnyl, is synthetic.

Interestingly, some researchers do not consider hCG a "true hormone." The term hormone was coined by Banting and Best in 1915 and was used to denominate those substances that are produced in one organ and their actions are performed elsewhere in the organism. Thus, testosterone is a hormone, because it is produced in the testicles, exerting its action on skin, brain, etc. However, hCG has been found in every human tissue, and is found in males and both pregnant and non pregnant females. (http://oralhcg.com)

Therapeutically, thousands of articles have been published regarding its action on gonads, but comparatively few have investigated its vast therapeutic potentialities, including its effects on: Kaposi sarcoma, asthma, mood and psychiatric disorders, artheriopaties, thalassemia, osteopenia, glaucoma, and most recently obesity.

The first report on hCG and obesity was published in 1954 in The Lancet, by British physician, Dr. A.T.W. Simeons. Previous to this, hCG was reported to be a useful drug for the treatment of certain clinical presentations of adolescent obesity, except Frohlich's syndrome. After Simeons publication, hCG was advocated for several years as a useful approach to obesity. The pendulum of its popularity swung back and forth until a series of studies in the early and mid 1970's espoused that hCG was "of no use" to weight management. However, since the 1994 publication of "Utility of an oral presentation of hCG for the management of obesity. A double-blind study," by Drs. Daniel Belluscio, Leonor Ripamonte, and Marcelo Wolansky Ph.D, the medical community is again investigating the use of hCG as an aid in the fight against obesity. And finally, since the 2007 publication of Kevin Trudeau's controversial monograph, The Weight Loss Cure, dozens of new websites and numerous hCG offerings at weight clinics and from weight loss practitioners are appearing.

How it works: hCG's proposed mechanisms of action

In layman's terms, hCG is said "to perform a metabolic recovery, where the hypothryoid is said to be reset, boosting the metabolism and increasing the person's ability to burn fat at a much higher rate. hCG is also said to break down body fat, causing rapid weight loss by mass even before registering on a scale. Simultaneously, it is said to protect the endogenous fat and muscle which the body needs to stay healthy, but also avoiding sagging and loose skin known of excessive of weight loss." (C. Jones, hCG and The Weight Loss Cure, 2007).

Several researchers have studied how hCG displays a metabolic action on adipose tissue metabolism, via an inhibitory effect on lipogenesis.

Fleigelman concluded that the administration of hCG in rats decreased the activity of alfa-

Yanagihara reported that hCG accelerates "not only the mobilization of fat from fat deposits, but also its utilization in peripheral tissues. hCG increased the metabolism of injected fat emulsions, suggesting the acceleration, not only of fat oxidation, but also increased ketone production in the liver and its utilization in peripheral tissues," (Yanagihara Y. "Carbohydrate and lipid metabolism in pregnant albino rats during starvation after loading with gonad-stimulating hormones." Nippon Sanka Fujinka Gakkai Zasshi, 1966 Dec;18(12):1379-84).

Finally, administration of hCG to humans appears to increase the release of fatty acids which varies with the age of the subject. Melichar demonstrated that hCG causes a marked FFA release in newborn infants. Equally, in adults, a single dose of hCG caused a marked FFA release by p > 0.05 when compared to placebo-treated subjects.

Consequently, after significant research, physicians have hypothesized that hCG might act upon adipose tissue metabolism through some mediators secreted at the hypothalamic level.


**Why it works: The Pro's of hCG**

If obesity can be defined as an excess of body fat, then it follows that any pharmacological intervention on the disease should assess whether the drug in question can mobilize fat from fat deposits.

Therefore, it seems that hCG can accelerate fat mobilization from certain fat deposits in the course of a weight reduction program coupled with a Very Low Calorie Diet (VLCD).

Subcutaneous adipose tissue reduction could be accomplished by lipogenesis inhibition at the level of the fat cell membrane. Since administered hCG accumulates at the hypothalamic region, it has been hypothesized by Dr. Belluscio et al., that hCG metabolic actions could be exerted through the release of a lipolytic substance located in that area.

Adipose tissue reduction should be the goal to reach in any weight reduction program, more than appetite or anxiety reduction. Belluscio's study suggests that the oral use of hCG helps to mobilize fat from certain fat deposits, but poses several as yet unsolved questions:

- Why was circumference reduction similar in both groups while the hCG treated group significantly decreased the amount of subcutaneous body fat? The hypothesis is that they gained total body water and/or lean mass.
- Why did hCG treated volunteers not lose more weight despite a significant reduction in subcutaneous fat?. Dr. Belluscio has no explanation for this data.

Finally, Dr. Belluscio's study postulates that only a fraction of hCG is absorbed, and this fraction might be responsible for the metabolic activity we have observed in patients. Therefore, perhaps hCG has no direct action upon fat cells.


**Possible complications: The Con's of hCG**
**Blood Clots:** hCG can cause clotting issues. Symptoms include pain, warmth, redness, numbness, or tingling in your arm or leg; confusion, extreme dizziness, or severe headache.

**Ovarian Hyperstimulation:** Some women using this medicine have developed a condition called ovarian hyperstimulation syndrome (OHSS), especially after the first treatment cycle. OHSS can be a life-threatening condition. Symptoms include: severe pelvic pain, swelling of the hands or legs, stomach pain and swelling, shortness of breath, weight gain, diarrhea, nausea or vomiting, and urinating less than normal.

**Early Puberty in Boys:** hCG can cause early puberty in young boys. Symptoms include a deepened voice, pubic hair growth, and increased acne or sweating.

**Fertility related Effects:** Using hCG can increase one's chances of having a multiple pregnancy (twins, triplets, quadruplets, etc). A multiple pregnancy is a high-risk pregnancy for the mother and for the babies. Equally, although HCG can help you become pregnant, this medication is in the FDA pregnancy category X. This means that using the medication once you are pregnant can cause birth defects in the baby. Do not use this medication if you are pregnant. Tell your doctor right away if you become pregnant during treatment.

**Allergic Reactions:** Some patients will experience allergic reactions to hCG, including signs such as: hives; difficulty breathing; swelling of your face, lips, tongue, or throat.

**Links to Cancer:** Finally, studies out of Fox Chase Cancer Center have established a link between the presence of human chorionic gonadotropin (hCG), and a decrease in the likelihood to develop breast cancer when exposed to a known carcinogen. However, other studies have suggested that there may be a link between hCG and developing ovarian or prostate cancers.

**Interactions:** hCG has known to have adverse interactions with herbal or dietary supplements, like blue cohosh, black cohosh, or chasteberry.

**FDA and Medical Community Issues**

The FDA states that, "HCG is a hormone extracted from urine of pregnant women. It is approved by FDA for treatment of certain problems of the male reproductive system and in stimulating ovulation in women who have had difficulty becoming pregnant. No evidence has been presented, however, to substantiate claims for HCG as a weight-loss aid."


"In 1962, the Journal of the American Medical Association warned against the Simeons diet, saying "continued adherence to such a drastic regimen is potentially more hazardous to the patient's health than continued obesity."

In 1974, the Food and Drug Administration required producers of HCG to label the drug with a warning against using it for weight loss or fat redistribution. In Canada, the Task Force on the Treatment of Obesity warned that the use of the hormone "touches on possible malpractice." Nevertheless, a few diet doctors continued with the treatment -- "it is legal for physicians to prescribe medications for purposes that are not approved by the FDA -- often handing the patients the drugs and injection equipment so they could administer it themselves."


Since these concerns have prevailed, the FDA now requires all labeling and advertising of HCG used in a weight management program, to include the following notice:

"THESE WEIGHT REDUCTION TREATMENTS INCLUDE THE USE OF hCG , A DRUG WHICH HAS NOT BEEN APPROVED BY THE FOOD AND DRUG ADMINISTRATION AS SAFE AND EFFECTIVE IN THE TREATMENT OF OBESITY OR WEIGHT CONTROL. THERE IS NO SUBSTANTIAL EVIDENCE THAT hCG INCREASES WEIGHT LOSS BEYOND THAT RESULTING FROM CALORIC RESTRICTION, THAT IT CAUSES A MORE ATTRACTIVE OR "NORMAL" DISTRIBUTION OF FAT, OR THAT IT DECREASES THE HUNGER AND
DISCOMFORT ASSOCIATED WITH CALORIE-RESTRICTIVE DIETS."

Why it may work for everyone

Both proponents and critics alike are adiment that hCG is not "a magic wand." Proponents emphasize that a "daily injection of hCG gives optimum results only when used in a rational weight reduction program. Therefore, strict observation to the complete protocol is mandatory," for success. (Belluscio, D and Trudy Vogt. "Controversies in Plastic Surgery: Suction-Assisted Lipectomy (SAL) and the hCG (Human Chorionic Ganadotropin) Protocol for Obesity Treatment." Aesthetic Plastic Surgery. 11:131-156, 1987.)

Equally, Dr. Fred Bloem refutes the many studies that have indicated that hCG is not an effective tool in weight management, on the grounds that:

- The dietary protocol that the researchers recommended was not consistent with the one that Dr. Simeons prescribed for his patients.
- The daily caloric intake that the research recommended exceeded 500 Calories.
- The research subjects deviated from the dietary protocol that the researchers and/or Dr. Simeons recommended.
- The amount of HCG used for the research subjects was not consistent with Dr. Simeons's recommendations.
- The HCG was not prepared, administered, or stored properly.
- The study was performed by researchers who had no prior experience or skill in treating patients with the Dr. Simeons HCG Protocol and who were not expert in recognizing and addressing the patients' individual needs and concerns.
- Researcher bias or pressure from industry or political circles.

(Source: http://www.drbloem.com/hcgfaqs.htm#research)

Summary of the Simeons hCG Protocol: 5 Key Points to the Program

Brief Overview of Complete Protocol

- 125 iu of hCG is administered daily (with the exception of menstruation.)
- Until 3rd injection the patient eats excessively.
- Following the third injection, the 500 calorie diet (VLCD) and personal care product restrictions are applied and continue through 72 hours after the last injection. This portion of the protocol takes no more than 40 days.
- For the continuing 3 weeks, all foods are allowed except sugar and starch- this includes sweet fruits.
- After the 3 weeks starches are introduced into the diet in very small quantities and weight is monitored to ensure weight maintenance.

1. hCG Injections

Pursuant to the Simeons protocol, Hcg Injections are administered daily. The dose for the Simeons protocol is 125 iu administered daily, for no more than 40 days.

When treating only one or two cases simultaneously, vials containing a small number of units say 1000 I.U. should be used. The 10 cc. of solvent which is supplied by the manufacturer is injected into the rubber- capped bottle containing the hCG, and the powder must dissolve instantly. Of this solution 1.25 cc. are withdrawn for each injection. One such bottle of 1000 I.U. therefore furnishes 8 injections. When more than one patient is being treated, they should not each have their own bottle but rather all be injected from the same vial and a fresh solution made when this is empty.
Patients who need to lose 15 pounds or, 7 kilos or less require 26 days treatment with 23 daily injections. The VLCD is continued for 3 days following the end of the injections to avoid weight regain.

Time and hCG Shots

When a patient has more than 15 pounds to lose the treatment takes longer but the maximum we give in a single course is 40 injections, nor do we as a rule allow patients to lose more than 34 lbs. (15 Kg.) at a time. The treatment is stopped when either 34 lbs. have been lost or 40 injections have been given. The only exception we make is in the case of grotesquely obese patients who may be allowed to lose an additional 5-6 lbs. if this occurs before the 40 injections are up.

hCG Diet Injections and the Female Cycle

No injections during menstruation on the hCG diet, however the VLCD is continued. Once menstruation is over, dieters must reinstate the daily hCG injections.

Belluscio's Oral hCG™ Method

Dr. Belluscio's Oral hCG Protocol is a medically designed program, based on the Simeon’s weight loss protocol, however, it differs in one key area: oral administration of hCG vs. injection.

In his 1991 study, Dr. Belluscio et al. found that sub-lingual administration of hCG was a safe and effective procedure on obese treated volunteers (83 female volunteers). No side effects were observed in the course of their study, and no reports were found in the literature regarding this administration route to compare to his findings. Further, Belluscio postulated that the administration route may influence the biological activity of a drug. He noted that all previous studies were performed with an hCG preparation administered by injections. In Belluscio's study, it was theorized that an increase in dose and a shifting in hCG administration to a sub-lingual route may modify the pharmacological activity of hCG.

Oral Dosage:

Study subjects were divided into 3 groups: Group 1, Group 2 and Group Placebo.

Volunteers from group G1 were administered a diluted solution of hCG (125 IU) b.i.d. (twice daily; total: 250 IU). One of the doses was taken before breakfast (fasting).

Volunteers from group G2 were given twice the amount of group G1: 250 IU b.i.d (a total of 500 IU daily).

2. Very Low Calorie Diet (VLCD)

Simeons advocated that the 500 calorie limit must always be maintained.

Breakfast:

Tea or coffee in any quantity without sugar. Only one tablespoonful of milk allowed in 24 hours. Saccharin or Stevia may be used.

Lunch:

1. 100 grams of veal, beef, chicken breast, fresh white fish, lobster, crab, or shrimp. All visible fat must be carefully removed before cooking, and the meat must be weighed raw. It must be boiled or grilled without additional fat. Salmon, eel, tuna, herring, dried or pickled fish are not allowed. The chicken breast must be removed from the bird.

2. One type of vegetable only to be chosen from the following: spinach, chard, chicory, beet-greens, green salad, tomatoes, celery, fennel, onions, red radishes, cucumbers, asparagus, cabbage.
3. One breadstick (grissino) or one Melba toast.

4. An apple, orange, or a handful of strawberries or one-half grapefruit.

*Dinner:*

The same four choices as lunch (above.)

*Substitutions:*

2 small apples are not an acceptable exchange for “1 apple.”

Very occasionally the protocol allows egg - boiled, poached or raw - to patients who develop an aversion to meat, but in this case they must add the white of three eggs to the one they eat whole.

Cottage cheese made from skimmed milk is available and 100 grams may occasionally be used instead of the meat

The fruit or the breadstick may be eaten between meals instead of with lunch or dinner, but not more than four items listed for lunch and dinner may be eaten at one meal.

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**The 500 Calorie VLCD vs. 400 or 800 Calories**

A Very Low Calorie Diet is defined as a diet of between 400 - 800 calories per day. On the Simeons and Belluscio's protocols, 500 calories per day is the standard, however, there a many different versions of the HCG diet, though none of them included more than 800 calories. Determination of total calorie intake is a decision to be made between the doctor, the patient and in consideration of the patient's weight loss goals and time frame for weight loss.

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3. **Drinks and Seasonings**

The juice of one lemon daily is allowed for all purposes.

Salt, pepper, vinegar, mustard powder, garlic, sweet basil, parsley, thyme, marjoram, etc., may be used for seasoning, but no oil, butter or dressing.

Tea, coffee, plain water, or mineral water (2 liters of water per day is recommended) are the only drinks allowed, but they may be taken in any quantity and at all times.

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4. **Medications and Cosmetics and Personal Care**

Generally, no medicines or cosmetics other than lipstick, eyebrow pencil and powder may he used without special permission.

We do permit the use of powder and such lotions as are entirely free of fatty substances. We also allow brilliantine to be used on the hair but it must not be rubbed into the scalp. Obviously sun-tan oil is prohibited.

Aspirin and birth control are allowed on the Simeons hCG Diet.

No massage of any kind.

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5. **Maintenance**
When three days of dieting after the last injection are over, the patients are told that they may now eat anything they please, except sugar and starch (this includes sweet fruits). This continues for 3 weeks.

After the 3 weeks, starches are introduced into the diet in very small quantities and weight is monitored daily (in the morning after the bladder is emptied) to ensure weight maintenance.

During this period patients must realize that the so-called carbohydrates, that is sugar, rice, bread, potatoes, pastries, etc, are by far the most dangerous. If no carbohydrates whatsoever are eaten, fats can be indulged in somewhat more liberally and even small quantities of alcohol, such as a glass of wine with meals.

Source: http://www.hcgdietinfo.com

Key Supporting Documentation on hCG: Studies and Websites

Proponents: There are two key clinician proponents of the hCG protocol as part of a weight loss regime: Dr. Simeons and Dr. Belluscio. (Kevin Trudeau has also written on the use of hCG in weight management, but his writings are very controversial).


Dr. Belluscio's professional resources page: Research and studies for the hCG protocol for weight loss.

Trudeau, Kevin. The Weight Loss Cure They Don't Want You to Know About. 2007.

Critics: There are several studies that indicated that hCG is not effective in the treatment of obesity or weight management. The following is a selection of key studies concerned with an hCG approach:


US Based Compounding Pharmacies for hCG

Physicians seeking compounding pharmacies to fill their patients’ prescriptions for hCG should seek out pharmacies accredited by the Pharmacy Compounding Accreditation Board (PCAB).

For a list of PCAB Accredited compounding pharmacies in a specific state, including a summary of each
Appetite Suppressants and Lipase Inhibitors

What they are and Why they work

Drugs prescribed for weight loss can be divided into two categories, based on their putative mechanisms of action: appetite suppressants and lipase inhibitors.

Appetite suppressants can be further subdivided, based on the neurotransmitters on which they are believed to exert their effects.

Appetite Suppressants
Medications have been prescribed for their ability to suppress appetite for over half a century. The first prescription appetite suppressants were the sympathomimetic amphetamine derivatives, so described because they exert their effects by stimulating the sympathetic nervous system. Some of the newer appetite suppressants exert their effects by mimicking the sympathetic nervous system.

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Names</th>
<th>DEA Schedule</th>
<th>Approved Use</th>
<th>Year Approved</th>
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<tr>
<td>Orlistat</td>
<td>Xenical</td>
<td>None</td>
<td>Long-term</td>
<td>1999</td>
</tr>
<tr>
<td>Sibutramine</td>
<td>Meridia</td>
<td>IV</td>
<td>Long-term</td>
<td>1997</td>
</tr>
<tr>
<td>Diethylpropion</td>
<td>Tenulate</td>
<td>IV</td>
<td>Short-term</td>
<td>1973</td>
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<tr>
<td>Phentermine</td>
<td>Adipex, Ionamin</td>
<td>IV</td>
<td>Short-term</td>
<td>1973</td>
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<tr>
<td>Phendimetrazine</td>
<td>Bontril, Prelu-2</td>
<td>III</td>
<td>Short-term</td>
<td>1961</td>
</tr>
<tr>
<td>Benzphetamine</td>
<td>Didrex</td>
<td>III</td>
<td>Short-term</td>
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Sibutramine is a combined norepinephrine and serotonin reuptake inhibitor. Its putative effect on weight loss is attributed to appetite suppression and increased thermogenesis, secondary to stimulation of brown adipose tissue. Sibutramine was approved for use in conjunction with a low calorie diet as an aid to weight loss in 1998.

Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) that was originally approved to treat depression. The original manufacturer submitted an New Drug Application for use of fluoxetine as a weight loss drug in the early 1990s; however, approval was not given, and the application was eventually withdrawn.

Sertraline, like fluoxetine, is a SSRI. In the early 1990s, it was noted that sertraline administered to laboratory animals resulted in weight loss.
**Phentermine** is a sympathomimetic amine of the β-phenethylamine family. It was approved for use by the FDA in 1959 as a short term aid to weight loss in conjunction with a low calorie diet and exercise. Unlike use of sibutramine, use of phentermine leads to the development of tolerance.

**Diethylpropion**, like phentermine, is a sympathomimetic agent prescribed for short-term weight loss when used in conjunction with diet and exercise. Diethylpropion is similar in chemical structure to bupropion, which is approved as an antidepressant and as a smoking cessation aid and has also been tested as a weight loss aid.

**Zonisamide** was approved by the FDA in 2000 for the treatment of partial (focal) seizures in adults with epilepsy, in conjunction with other anticonvulsants. Although the precise mechanism of action is unknown, it may exert its effects by acting as a sodium or calcium channel blocker. Because one of zonisamide's side effects is appetite suppression, its use as a weight loss drug has been tested.

Topiramate is also an anticonvulsant, approved in the mid 1990s for the treatment of refractory seizures in conjunction with other anticonvulsants. In the process of testing topiramate for treatment of mood disorders, it was discovered that the agent might mitigate the weight gain often observed with antidepressant treatment, and a dose-ranging study established it does so in a dose-dependent manner.

### Other U.S. Food and Drug Administration–Approved Appetite Suppressants, 1947–1997

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<tr>
<th>Generic Name</th>
<th>Trade Name</th>
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<td>Desoxyephedrine</td>
<td>Hydrin, Desoxyn</td>
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<td>Phenmetrazine</td>
<td>Preludin</td>
<td>1956</td>
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<td>Diethylpropion</td>
<td>Tenuate</td>
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<td>Phentermine</td>
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<td>Phendimetrazine</td>
<td>Bontril, Plegine</td>
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<td>Benzphetamine</td>
<td>Didrex</td>
<td>1960</td>
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<tr>
<td>Fenfluramine</td>
<td>Pondimin</td>
<td>1973</td>
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<td>Mazindol</td>
<td>Sanorex</td>
<td>1973</td>
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<tr>
<td>Dexfenfluramine</td>
<td>Redux</td>
<td>1996</td>
</tr>
<tr>
<td>Sibutramine</td>
<td>Meridia</td>
<td>1997</td>
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In the United States, appetite suppressants don’t have to be approved by the FDA when they are based on a 100% natural basis. There are all kinds of natural appetite suppressants (supplements) on the market helping people to control and limit their food intake. Most common natural appetite suppressants are based on **hoodia** a genus of 13 species in the flowering plant family Apocynaceae, under the subfamily Asclepiadoideae. Also widely used as a basis is green tea with other plant extracts to limit calorie intake. A lot of appetite suppressants are based on a mix of natural ingredients mostly using green tea as its basis with a combination/mix of other plant extracts like fucoxanthin, found naturally in seaweed.

**Lipase Inhibitors**

Lipase inhibitors putatively aid weight loss by reversibly binding to the active center of the enzyme lipase, preventing the digestion and absorption of some dietary fats.

**Orlistat (Xenical)** was approved in the late 1990s and is currently the only lipase inhibitor approved
for weight loss. Orlistat inhibits approximately 30 percent of fat absorption, including the absorption of fat-soluble vitamins.


Possible complications

The Agency for Healthcare Research Report, cited the following side effects were consistent with this class of drugs:

- palpitations,
- tachycardia,
- elevation of blood pressure,
- central nervous system effects, and
- gastrointestinal effects.

Also noted were:

- dry mouth,
- insomnia, and
- nausea.

(Case reports of stroke in persons taking phentermine for weight loss have been reported.) (Sertraline patients reported fatigue, nausea, difficulty concentrating, and problems urinating. Of note is that insomnia, headache, nausea, and fatigue were reported by approximately half of all sertraline-treated patients.)

Lipase Inhibitors

Most common adverse effects for lipase inhibitors is oily spotting, flatus with discharge, fecal urgency, fatty oily stool, oily evacuation, increased defecation and fecal incontinence. Orlistat is contraindicated for patients with chronic malabsorption syndrome or cholestasis, and patients with an organic cause of obesity (e.g. hypothyroidism) should not consider this treatment. Also, orlistat is not recommended for pregnant or nursing mothers. and there is a risk of drug interaction with orlistat and cyclosporine.

FDA Issues

Appetite Suppressants

Nowhere has the question of risk versus benefit come under greater scrutiny than with anorectics. After the approval in the 1940s and 1950s of a number of amphetamine and amphetamine-like compounds for the treatment of obesity, the U.S. Food and Drug Administration struggled to define the efficacy and safety of these agents. Labeling restrictions on duration of use and warnings about abuse and addiction ultimately contributed to the reduced use of anorectics.

That trend continued until the mid-1990s, when the off-label use of fenfluramine plus phentermine (fen-phen) and the approval of dexfenfluramine gave rise to widespread, long-term use of anorectics to treat obesity. The adverse effects that came to be associated with fenfluramine and dexfenfluramine, leading to their eventual withdrawal from the market, gave pause to regulators, physicians, patients, and drug companies alike.

Sibutramine, the latest anorectic to enter the market, is now the focus of a landmark trial that is examining, for the first time, whether drug-induced weight loss reduces the risk for fatal and nonfatal cardiovascular disease.
Orlistat

In 1999, the FDA approved Orlistat (Xenical: Roche) 120 mg capsules, a new drug to treat obesity. Orlistat is the first drug in a new class of non-systemically acting anti-obesity drugs known as lipase inhibitors.

The effects of orlistat on weight loss, weight maintenance, and weight regain and on a number of obesity-related illnesses were assessed in seven long-term multicenter, clinical trials. Of the patients who completed one year of treatment, 57 percent of the patients treated with orlistat lost at least 5 percent of their baseline body weight.

Because orlistat reduces the absorption of some fat-soluble vitamins and beta carotene, patients should take a supplement that contains fat soluble (A, D, E, and K) vitamins and beta carotene.

In February 2007, the FDA approved orlistat 60 mg capsules as an over-the-counter (OTC) weight loss aid for overweight adults (Alli: GlaxoSmithKline).

Key Supporting Documentation on Appetite Suppressants and Lipase Inhibitors: Studies and Websites

Agency for Healthcare Research and Quality of the U.S. Department of Health and Human Services, Pharmacological and Surgical Treatment of Obesity, July 2004


Hormones

Building upon the discussion of the role hCG might play in a successful weight loss program, other hormones should be examined relative to their influences in weight management.

What they are

Insulin

High levels of insulin may contribute to our fatness. Insulin, the blood sugar regulator, is pumped out in excessive amounts as it tries to reduce the abnormally high blood sugar that results from a high carbohydrate, low protein diet. Patients inevitably gain weight and become fat, and the cells become resistant to insulin and fat loss.

Cortisol

High insulin also increases the secretion of cortisol, our stress hormone. High cortisol causes a corresponding drop in the hormone dehydroepiandrosterone (DHEA), which, among other actions, helps to increase muscle mass. More muscle mass is needed for fat loss, as it increases fat burning and reduce insulin.

Chronic stress also activates all fat cells to store fat. The central fat cells, found mainly deep in the abdominal wall, have four times the cortisol receptors on their cell membranes. Each time we are
stressed the cortisol-fat mechanism turns on and our body stores more fat.

**Leptin**

Another hormone - leptin, produced by body fat - is critical in telling the body when to eat and when we are satisfied. Scientists have learned that in some people the message of satiety is not heard and fat cells send out more and more leptin, causing resistance to leptin, increased food cravings, and the desire to continue eating. In other people, leptin levels are low due to zinc deficiency.

**Serotonin**

The hormone serotonin, a neurotransmitter in the brain made from the amino acids found in proteins, is also involved in signalling satisfaction. Low serotonin levels cause depression, obesity, lethargy, a preference for refined carbohydrates, and overeating because the brain senses it is starving. A diet that restricts protein-rich calories causes serotonin levels to plummet. People who are hyper-secretors of cortisol also exhibit suppressed serotonin levels.

**Thyroid**

Low thyroid - called hypothyroidism - affects approximately 30 percent of the population. Low thyroid reduces the fat burning rate and causes fatigue, inhibiting energy levels.

**Estrogen and Testosterone**

Estrogen and testosterone are more commonly known for influencing the development of physical traits that distinguish the female and the male genders, respectively, but these sex hormones also regulate fat storage. Estrogen promotes the storage of fat, while testosterone stimulates fat burning. "Estrogen dominance" occurs when the natural balance between estrogen and progesterone is disrupted. This phenomenon is often caused by high doses of synthetic estrogen.


Further, Dr. Richard Foxx, MD, owner, CEO and Medical Director of the Medical and Skin Spa, who has extensively studied the implications of other hormones in weight management suggests that the following hormones should also be considered in a comprehensive approach to late-onset obesity:

- DHEA;
- Parathyroid;
- Melatonin and
- Pituitary hormone.

**Ghrelin**

Finally, there is some evidence that an increase in the hormone ghrelin was positively correlated with the extent of weight loss in various studies. (T.K Hansen et al. "Weight loss increases circulating levels of ghrelin in human obesity", Clinical Endocrinology 56(2): 3203-206, 2002).

**Why they work**

Studies have examined the metabolic effects of combined hormone replacement therapy showing that "combined hormone replacement therapy not only prevented weight-gain, but favored weight-loss by significantly increasing lipid oxidation. It also favourably influenced the insulin response, plasma lipids and energy expenditure." (Chmouliovsky L., Habicht F., James R.W., Lehmann T., Campana A., Golay A. "Beneficial effect of hormone replacement therapy on weight loss in obese menopausal women." Maturitas. 1999 Aug 16;32(3):147-53).
Possible complications

FDA Issues

Why they may not work for everyone

Key Supporting Documentation


Vitamins: B12 and B6

Vitamin B12

What Is It and How it works?

Vitamin B12, also called cobalamin, is important to good health. It helps maintain healthy nerve cells and red blood cells, and also is needed to make DNA, the genetic material in all cells. Vitamin B12 is bound to the protein in food. Hydrochloric acid in the stomach releases B12 from protein during digestion. Once released, B12 combines with a substance called intrinsic factor (IF) before it is absorbed into the bloodstream.

All of these B vitamins help the body in converting carbohydrates into glucose or sugar, which is burned in order to produce energy for proper body function. These are often referred to as B complex vitamins, and are essential for the breakdown of fats and proteins. They help maintain muscle tone, protect the mucus lining in the digestive tract and mouth, and promote upkeep of nervous system and the organs like the liver, skin, hair, and eyes. Cobalamine is an excellent anti-stress vitamin since it is believed to enhance the health functioning of the immune system and improve the body's ability to fight stressful conditions.

12 injections have been found to frequently improve energy levels and general well-being. They also support thyroid function to regulate energy levels. B12 also reduces water retention owing to its diuretic attributes.

Vitamin B12 is naturally found in animal foods, including fish, milk and milk products, eggs, meat and poultry. Fortified breakfast cereals are an excellent source of vitamin B12 and a particularly valuable source for vegetarians. The table of selected food sources of vitamin B12 suggests dietary sources of vitamin B12.

The Recommended Dietary Allowance (RDA) is the average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97 percent to 98 percent) healthy individuals in each life-stage and gender group. The 1998 RDAs for vitamin B12 (in micrograms) for adults are 2.4 µg and the results of two national surveys, the National Health and Nutrition Examination Survey (NHANES III-1988-91) and the Continuing Survey of Food Intakes by Individuals (CSFII 1994-96) found that most adult men and women consume recommended amounts of vitamin B12.

Diets of most adult Americans provide recommended intakes of vitamin B12, but deficiency may still
occur as a result of an inability to absorb B12 from food. It also can occur in individuals with dietary patterns that exclude animal or fortified foods. As a general rule, most individuals who develop a vitamin B12 deficiency have an underlying stomach or intestinal disorder that limits the absorption of vitamin B12. Sometimes the only symptom of these intestinal disorders is anemia resulting from B12 deficiency.

Characteristic signs of B12 deficiency include fatigue, weakness, nausea, constipation, flatulence (gas), loss of appetite and weight loss. Deficiency also can lead to neurological changes such as numbness and tingling in the hands and feet. Additional symptoms of B12 deficiency are difficulty in maintaining balance, depression, confusion, poor memory, and soreness of the mouth or tongue. Some of these symptoms also can result from a variety of medical conditions other than vitamin B12 deficiency. It is important to have a physician evaluate these symptoms so that appropriate medical care can be given.

**Bariatric Surgeries**

Surgical procedures of the gastrointestinal tract such as surgery to remove all or part of the stomach often result in a loss of cells that secrete stomach acid and intrinsic factor. Surgical removal of the distal ileum, a section of the intestines, also can result in the inability to absorb B12. Anyone who has had either of these surgeries usually requires lifelong supplemental B12 to prevent a deficiency.

**The relationship between Vitamin B12 and Heart Disease?**

A deficiency of vitamin B12, folate or vitamin B6 may increase your blood level of homocysteine, an amino acid normally found in your blood. There is evidence that an elevated blood level of homocysteine is an independent risk factor for heart disease and stroke. The evidence suggests that high levels of homocysteine may damage coronary arteries [34] or make it easier for blood-clotting cells called platelets to clump together and form a clot. However, there is currently no evidence available to suggest that lowering homocysteine level with vitamins will actually reduce your risk of heart disease. Clinical intervention trials are needed to determine whether supplementation with vitamin B12, folic acid or vitamin B6 can help protect you against developing coronary heart disease.

**Con's**

Vitamin B12 has a very low potential for toxicity. The Institute of Medicine states "no adverse effects have been associated with excess vitamin B12 intake from food and supplements in healthy individuals." The Institute recommends that adults older than 50 years of age get most of their vitamin B12 from supplements or fortified food because of the high incidence of impaired absorption of B12 from unfortified foods in this population.


**Vitamin B6**

**What Is It and How it works?**

Vitamin B6 is a water-soluble vitamin that exists in three major chemical forms: pyridoxine, pyridoxal and pyridoxamine. It performs a wide variety of functions in your body and is essential for your good health. For example, vitamin B6 is needed for more than 100 enzymes involved in protein metabolism. It also is essential for red blood cell metabolism. The nervous and immune systems need vitamin B6 to function efficiently, and it also is needed for the conversion of tryptophan (an amino acid) to niacin (a vitamin).

Hemoglobin within red blood cells carries oxygen to tissues. Your body needs vitamin B6 to make
hemoglobin. Vitamin B6 also helps increase the amount of oxygen carried by hemoglobin. A vitamin B6 deficiency can result in a form of anemia that is similar to iron deficiency anemia.

An immune response is a broad term that describes a variety of biochemical changes that occur in an effort to fight off infections. Calories, protein, vitamins and minerals are important to your immune defenses because they promote the growth of white blood cells that directly fight infections. Vitamin B6, through its involvement in protein metabolism and cellular growth, is important to the immune system. It helps maintain the health of lymphoid organs (thymus, spleen and lymph nodes) that make your white blood cells. Animal studies show that a vitamin B6 deficiency can decrease your antibody production and suppress your immune response.

Vitamin B6 also helps maintain your blood glucose (sugar) within a normal range. When caloric intake is low, your body needs vitamin B6 to help convert stored carbohydrate or other nutrients to glucose to maintain normal blood sugar levels. While a shortage of vitamin B6 will limit these functions, supplements of this vitamin do not enhance them in well-nourished individuals.

Vitamin B6 can help with weight loss through a stimulating effect of the thyroid. This can be especially helpful for hormone balance in women when water retention is an issue. Lastly, patients seem to find the pyridoxine alleviates cravings consistently.

Vitamin B6 is found in a wide variety of foods, including fortified cereals, beans, meat, poultry, fish, and some fruits and vegetables. The table of selected food sources of vitamin B6 suggests many dietary sources of B6.

The Recommended Dietary Allowance (RDA) is the average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97 percent to 98 percent) healthy individuals in each life-stage and gender group.

The 1998 RDAs for vitamin B6 for adults, in milligrams, are 1.3 mg for men and women ages 9-50 and 1.7 mg and 1.5 mg for men and women over the age of 51, respectively.

Clinical signs of vitamin B6 deficiency are rarely seen in the United States. Many older Americans, however, have low blood levels of vitamin B6, which may suggest a marginal or sub-optimal vitamin B6 nutritional status. Vitamin B6 deficiency can occur in individuals with poor quality diets that are deficient in many nutrients. Symptoms occur during later stages of deficiency, when intake has been very low for an extended time. Signs of vitamin B6 deficiency include dermatitis (skin inflammation), glossitis (a sore tongue), depression, confusion and convulsions. Vitamin B6 deficiency also can cause anemia. Some of these symptoms also can result from a variety of medical conditions other than vitamin B6 deficiency. It is important to have a physician evaluate these symptoms so that appropriate medical care can be given.

The relationship between B6 and heart disease

A deficiency of vitamin B6, folic acid or vitamin B12 may increase your level of homocysteine, an amino acid normally found in your blood [28]. There is evidence that an elevated homocysteine level is an independent risk factor for heart disease and stroke. The evidence suggests that high levels of homocysteine may damage coronary arteries or make it easier for blood clotting cells called platelets to clump together and form a clot. However, there is currently no evidence available to suggest that lowering homocysteine level with vitamins will reduce your risk of heart disease. Clinical intervention trials are needed to determine whether supplementation with vitamin B6, folic acid or vitamin B12 can help protect you against developing coronary heart disease.

Con’s and other Issues Associated with B6

Too much vitamin B6 can result in nerve damage to the arms and legs. This neuropathy is usually related to high intake of vitamin B6 from supplements and is reversible when supplementation is stopped. According to the Institute of Medicine, "Several reports show sensory neuropathy at doses
lower than 500 mg per day". As previously mentioned, the Food and Nutrition Board of the IOM has established an Upper Tolerable Intake Level (UL) for vitamin B6 of 100 mg per day for all adults. "As intake increases above the UL, the risk of adverse effects increases."

Vitamin B6 is needed for the synthesis of neurotransmitters, such as serotonin and dopamine. These neurotransmitters are required for normal nerve cell communication. Researchers have been investigating the relationship between vitamin B6 status and a wide variety of neurologic conditions, such as seizures, chronic pain, depression, headache and Parkinson's disease.

Lower levels of serotonin have been found in individuals suffering from depression and migraine headaches. So far, however, vitamin B6 supplements have not proved effective for relieving these symptoms. One study found that a sugar pill was just as likely as vitamin B6 to relieve headaches and depression associated with low dose oral contraceptives.

Alcohol abuse can result in neuropathy, abnormal nerve sensations in the arms and legs. A poor dietary intake contributes to this neuropathy and dietary supplements that include vitamin B6 may prevent or decrease its incidence.

There are many drugs that interfere with the metabolism of vitamin B6. Isoniazid, which is used to treat tuberculosis, and L-DOPA, which is used to treat a variety of neurologic problems such as Parkinson's disease, alter the activity of vitamin B6. There is disagreement about the need for routine vitamin B6 supplementation when taking isoniazid. Acute isoniazid toxicity can result in coma and seizures that are reversed by vitamin B6, but in a group of children receiving isoniazid, no cases of neurological or neuropsychiatric problems were observed regardless of whether or not they took a vitamin B6 supplement. Some doctors recommend taking a supplement that provides 100 percent of the RDA for B6, which is usually enough to prevent symptoms of vitamin B6 deficiency, when isoniazid is prescribed. It is important to consult with a physician about the need for a vitamin B6 supplement when taking isoniazid.

Source:

**B12 and B6 Injections in Weight Management**

One of the key proponents of the use of B6 and B12 injections in a weight loss regimen is Dr. Stanley Bernstein. Dr. Bernstein has been running his weight loss clinics for 25 years, mainly in Ontario. The diet that bears his name is a unique program that includes injections and doesn't require exercise.

Bernstein says his diet is 100 per cent medically supervised and it's about more than just counting calories. "We use a lot of vitamins and minerals on our patients and we have a unique feature. Some of our vitamins are given by injection."

Clients are injected with a combination of Vitamin B6 and B12, three times a week. The idea is that the vitamins work to break down the fat. "The B vitamins make it easy for someone to stay on a diet," Bernstein said. "I find that they enhance the weight loss. Our patients are losing between four and five pounds a week." [That's the big draw: rapid weight loss. It comes with a price tag. The initial consultation ranges from $195 to $235. Add to that $100 per week for services and injections. Bernstein says an average patient who loses about 35 pounds will wind up paying about $1,000.]

Interestingly, Bernstein admits "there is not specific literature that will tell you that B vitamins are going to burn off fat," Bernstein said. "But there are a lot of articles about B vitamins being important for metabolizing food."
Harvard nutrition expert Dr. George Blackburn says the injections are like an electrical stimulus: "It's something to remind you that you're on this program and you want to be compliant to it. It's used as a motivator to make people adhere to the diet, in this case."

Equally, Dr. Kent Sharian suggests that, "If you get a patient to come to the office three times a week to be weighed, checked and have to be accountable for his weight, chances are that he or she will make an extra effort to show a weight loss. That has nothing to do with the injections that act primarily as a placebo to get the patient into the office."


**FDA and other Professional Concerns**

The American Society of Bariatric Physicians' position is that B12 injections are "no help with weight loss; there is no evidence that they work."