



Mythbusters: Pharmacy Edition



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Please enjoy our
"mythbusters"
edition.

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Myth: The human chorionic gonadotropin (hCG) is a weight loss miracle cure

By Elina Baskina, PharmD (Valley View Clinical Pharmacy)

Finding: BUSTED

Explanation:

The "hCG diet" (as it's commonly known) was developed by a British endocrinologist Dr. Albert T.W. Simeons in the 1950s. He believed in the use of hCG as a treatment modality for adiposogenital dystrophy – a pituitary disorder that causes severe obesity and a delay in puberty in young men. Dr. Simeons went on to perfect his hCG weight loss protocol and his method was largely sought after by the society's elite and old Hollywood. The tenets of the "hCG diet" are as follows: duration of 3.5-6 wks; fat-free, 500 kcal/day diet; daily injections of 125 IU of hCG. It is claimed that the followers of the diet will lose weight quickly, not feel weak, not experience hunger, and lose fat from the "trouble" spots – stomach, hips, thighs, and upper arms.

A meta-analysis was conducted to assess scientific validity for the aforementioned claims by Lijesen et al in 1995. Majority of the studies published on the subject are poorly designed – the authors identified only 14 randomized controlled trials. Authors concluded that hCG has no place in weight loss therapy. Although there is no scientific basis for the use of hCG, those on the diet do lose weight. This is entirely attributable to the highly re-

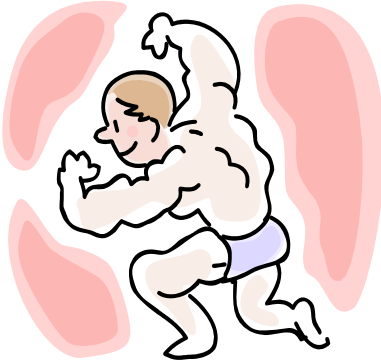
stricted caloric intake. Proponents of the diet claim that although calories are highly re-stricted, it is the hCG that prevents patients from feeling hungry and weak. If this were true, a greater drop out rate would have been noted in the placebo arm of the randomized trials. However, as the authors of the meta-analysis noted, this was not the case.

The hCG diet should not be recommended to patients. There is no data backing the efficacy of hCG as a weight loss supplement. The highly restrictive diet puts the patient at risk for malnutrition. Sustainable weight loss must be maintained through a combination of a nutritious, well-balanced diet and exercise. Fad diets, such as the "hCG diet", are quick solutions at best, and life-threatening at worst.

Encourage patients interested in weight loss to consult with a dietician and steer them away from diet fads propagated by the media but unsubstantiated by science.

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Lijesen, et al. "The effect of the human chorionic gonadotropin (hCG) in the treatment of obesity by means of the Simeons therapy: a criteria-based meta-analysis". *British Journal of Clinical Pharmacology* 1995; 40: 237-243.



Testosterone Mini-Myths

By: Joseph Lents, PharmD (Tulalip Pharmacy)

Taking testosterone improves fertility⁴.

BUSTED. When used chronically, testosterone can lead to sterilization and may cause testicles to shrink or become soft.

Obesity is not related to low testosterone levels⁵.

BUSTED. Superfluous adipose, particularly around the waist, absorbs, and stores testosterone, pulling it out of the bloodstream. When this happens, the amount of biologically active hormone is reduced, leading to decreases in libido, energy, and secondary sex characteristics.

Men can raise their testosterone levels by exercising vigorously⁵.

PLAUSIBLE: Moderate exercise can raise testosterone, but excessive vigorous exercise can drop testosterone levels. Of note, low testosterone yields low-energy, making it harder to exercise, leading to cyclic inactivity and low-testosterone levels.

Testosterone supplements are safe because they have to be approved by the FDA⁷.

BUSTED. The FDA does not regulate the sale or use of products containing pro-testosterone hormones such as prasterone (5-DHEA) or androstenedione (Andro). These products have potential long-term risks similar to anabolic steroids, including shrinking testicles, gynecomastia, breast cancer, hirsutism, male pattern baldness, hypercoagulability, and acne. Testosterone and its precursors should only be used under a doctor's supervision and testosterone levels should be raised only to normal physiological levels.

Low testosterone causes depression⁹.

CONFIRMED. Depression can lower testosterone levels. Unfortunately, many patients do not recognize the signs of depression in themselves or are reluctant to seek help treating it. The testosterone-depression relationship is a two way street: sometimes repleting testosterone levels will alleviate symptoms of depression, other times treating the depression with psychotherapy and/or antidepressants will increase testosterone levels.

Erectile dysfunction medications (PDE5 inhibitors) work whether a man has normal testosterone levels or not.

BUSTED. Testosterone provides the necessary impulse to have sex that erectile dysfunction meds cannot give. Studies show that erection-enhancing medications work best in men with testosterone levels within the normal range⁸.

Testosterone therapy is just cosmetic medicine for the middle-aged man⁹.

BUSTED. Low testosterone levels left untreated can lead to other increased risk factors for frailty, osteoporosis, heart disease, and perhaps, Alzheimer's disease¹⁰.

Only old men suffering from andropause have low testosterone^{2,9}.

BUSTED. The older the patient, the more likely they are to have low testosterone. However, this condition can affect men of any age. Conditions such as varicoceles, undescended testicles, and certain genetic problems can cause below-normal testosterone levels which need to be diagnosed and corrected as quickly as possible.

Testosterone shots are the only way to increase testosterone levels.

BUSTED. There are many routes to administer testosterone aside from injections. For example there are creams, gels, ointments, subcutaneous pellets, buccal adhesives, transdermal patches, and even a topical solution that is applied to the axilla.

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Myth: Probiotics prevent antibiotic-associated diarrhea*By: Theresa Hagen, PharmD (Valley View Clinical Pharmacy)***Finding:** Confirmed**Explanation:**

Patients are commonly instructed to eat yogurt or take over-the-counter probiotic capsules to prevent diarrhea associated with antibiotics. It makes physiologic sense that the "good" microbes would recolonize the gut flora with probiotics, thus preventing the common side effect of many antibiotics, diarrhea. Many providers make this recommendation, but it is unclear which probiotic product should be recommended and how it should be taken. Is one yogurt per day enough?

Evidence shows that probiotics may be helpful in reducing incidence of antibiotic-associated diarrhea. Products supported by clinical studies to recommend to patients include Culturelle (*Lactobacillus GG*), DanActive (*Lactobacillus/Strep thermophilus*), or Florastor (*Saccharomyces boulardii*). Patients should take the probiotic throughout the course of antibiotic treatment and for up to one week after antibiotic discontinuation. The probiotic is most likely to survive and provide the most benefit if taken two hours after each antibiotic dose. (Of note, there is currently not good evidence for use of probiotics to prevent yeast infections following antibiotic use. Probiotics should not be relied upon for this use.)

Probiotics are regulated as dietary supplements, which raises concerns about product quality and standardization. Well-studied products such as Culturelle (\$0.60 per capsule) and Florastor (\$0.90 per capsule) may be worth the extra cost. Floranex Granules (*Lactobacillus*) is covered by Molina insurance.

As with any medication choice, consider the cost versus benefit for the patient. There is not much harm from taking a probiotic supplement. If the cost of probiotics is not a barrier for the patient, why not try it?

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Myth: Do B-vitamins increase energy?*By: Sheila Song, PharmD (Bartell Pharmacy)***Finding:** Plausible**Explanation:**

Vitamin B is a water soluble vitamin that plays a role in cell formation and DNA synthesis. It is present in some foods, supplements, and prescription medications. There are eight different forms of B Vitamins, but B12 most thought of when trying to increase energy. B vitamins are found in unprocessed foods, such as various meats, whole grains, beans, and milk products. Vitamin B deficiency can result in fatigue, weakness, constipation and even neurologic changes. Specifically with Vitamin B12 deficiency, macrocytic anemia can occur- causing numbness in hands and feet, poor memory, and depression.

So why do people equate increasing vitamin B to increased energy? Because low vitamin B levels can cause lethargy and general tiredness. But there is no evidence that state taking more than the Recommended Dietary Allowance (RDA) of Vitamin B increases normal energy. The Institute of Medicine published the RDA for vitamin B12 at 2.4 micrograms a day and vitamin B6 at 1.7 mg a day. If a patient is concerned whether they have adequate levels of vitamin B, a blood test can be done. A range of 200-1,000pg/ml is an acceptable range which indicates little chance of anemia.

Decreased energy can be blamed to many things, not just vitamin B levels. Age, diet, and various medical history/conditions, can cause fatigue. Regular checkups, well-balanced diet, along with physical activity and sleep- are recommended to stay healthy and energy levels high.

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Myth: Cranberry juice reduces recurrence of UTI*By: Melissa Enriquez, PharmD (QFC Pharmacy)***Finding: Plausible****Explanation:**

Approximately 11% of all women aged >18 years have a urinary tract infection (UTI) each year. Approximately 5% of women with an initial UTI have multiple episodes within a year. The 6-month risk of recurrence following the first UTI is 24%.¹ Historically, cranberry juice has been suggested as a remedy for reducing the incidence of recurrent UTIs. Cranberries contain tannins that prevent the expression of P fimbriae of *E. coli*. P fimbriae are thought to be the most important virulence factor in causing UTIs. Blocking fimbrial adhesion prevents *E. coli* and other gram-negative bacteria from colonizing and adhering to uroepithelial cells.³



Some studies have shown that cranberry products significantly reduced the incidence of UTIs at 12 months compared with placebo in women. One trial gave 7.5g of cranberry concentrate (in 50 mL) and another gave 1:30 concentrate given in either 250 mL juice or in tablet form. The combined relative risk (RR) for cranberry juice versus placebo for a recurrence at 12 months was 0.62. For cranberry capsules, the RR was 0.56. There was no significant difference in the incidence of UTIs between cranberry juice versus capsules. Other studies showing efficacy of cranberries were limited by study design by being underpowered, not blinded, or by other design flaws.² The most recent, well-designed study done in 2011 showed that drinking 8 ounces of 27% cranberry juice twice daily did not decrease the 6-month incidence of a second UTI compared to placebo in otherwise healthy college women. Overall recurrence rate was 16.9%, which is lower than the expected 24% recurrence rate. However, the groups taking active cranberry juice presented with a slightly higher recurrence rate than placebo (20% vs. 14%).¹ Lastly, the mean annual cost of prophylaxis was \$642 and \$1400 for cranberry tablets and juice respectively. Cost-savings was greatest for patients experiencing greater than two UTIs per year.

From the current studies conducted, there is some evidence to recommend cranberry juice for the prevention of UTIs in women with recurrent symptomatic UTIs. Its effectiveness in other groups, including men and children, is understudied and less certain. There were a large number (20-55%) of dropouts from the studies. This could indicate that cranberry juice is not an acceptable therapy taken over a long period of time. Furthermore, the cost of consuming large amounts of cranberry may limit acceptance in the general population. There is no clear evidence as to the amount and concentration that needs to be consumed and the length of time for the treatment to be cost-effective. There are more studies showing effectiveness of cranberry concentrate versus cranberry juice cocktail for the prevention of recurrent UTIs. Further properly designed studies are needed to determine the effectiveness of cranberries for the prevention of UTI in susceptible populations.²

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Myth: Rebound acid hypersecretion occurs with discontinuation of short-term proton-pump inhibitor therapy

By: Cynthia Beckett, PharmD (Tulialip Pharmacy)

Finding: Confirmed

Explanation:

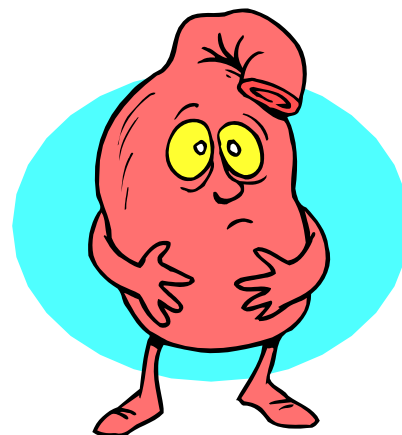
National and international guidelines support the use of short-term (4 to 8 week) proton pump inhibitor (PPI) therapy for empiric treatment of upper gastrointestinal (GI) symptoms.^{1,2} Some studies have reported that as many as 33% of patients who initiate PPI treatment continue to refill prescriptions beyond the short-term trial without an obvious indication for continued therapy.^{3,4} However, recent studies have demonstrated a clinically-significant rebound acid hypersecretion (RAHS) after withdrawal of a PPI after only a short-term course of therapy.^{5,6} Patients who are prescribed a PPI for mild or ambiguous symptoms may find it difficult to withdraw from therapy due to development of RAHS, thus creating a need for long-term therapy.

RAHS is defined as an increase in gastric acid secretion in excess of pretreatment levels that occurs within two weeks of antisecretory therapy discontinuation.³ Discontinuation of histamine-2 receptor antagonists (H2RAs) has also been associated with this syndrome.⁴ The mechanism of action is thought to be due to the hypertrophic effects of the drug-induced elevation of pH, leading to increases in circulating gastrin levels. This hypergastrinemia has been shown to produce functional and hyperplastic morphologic changes in parietal cells.⁷

A 12-week randomized, double-blind, placebo-controlled trial (n=120) in healthy volunteers found that 44% of patients experienced clinically significant GI-related symptoms (acid regurgitation, heartburn, dyspepsia) after discontinuing a 2-month course of esomeprazole 40 mg/day, compared with 15% after placebo (difference 29%; 95% CI, 15.2% to 47.4%; $p < 0.001$).³ Participants continued to report symptoms through the end of the study period. Thus, the full duration of RAHS was not established, but the authors suggested that it most likely lasts longer than three weeks.

Treatment with pantoprazole 40 mg/day for four weeks was shown to lead to more frequent upper GI symptoms during the first two weeks after discontinuation of therapy when compared with placebo during a randomized, parallel-group study (n=48) in otherwise healthy patients.⁴ One week after cessation of therapy, 44% of the PPI-treated patients reported dyspeptic symptoms compared with 9% of the placebo group ($p = 0.009$). In the second week post-treatment, 24% of the treatment group compared with none of the placebo group experienced dyspeptic symptoms ($p = 0.003$). The symptom scores did not differ significantly in weeks 3 through 6 of follow-up. Plasma gastrin levels were measured before the start of the treatment period, on the last treatment day, and at six weeks after treatment. Fasting and meal-stimulated plasma gastrin levels were found to be significantly higher in the PPI-treated group compared with the placebo group ($p < 0.001$) as measured during the last week of treatment, but not in the before-treatment or the 6-week post-treatment measures. The total symptom scores were found to be significantly associated with both the fasting gastrin levels ($p < 0.01$) and with meal-stimulated gastrin levels ($p < 0.001$) at the end of the treatment period.

PPI treatment should not be withheld from patients with a genuine need for therapy. However, clinicians should make an effort to restrict use of PPI therapy to those most likely to derive benefit. In patients prescribed PPIs as a diagnostic test for possible acid-related symptoms, a shorter course (1 – 2 weeks) may be appropriate to decrease the risk of inducing RAHS. A “step-up” rather than “step-down” approach to treating patients who present with symptoms assumed to be from acid reflux should also be considered. In addition, lifestyle modifications and “as-needed” agents, such as antacids or H2RAs, may be a preferable treatment alternative in patients with mild or infrequent upper GI symptoms.



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Myth: Do insulin analogues cause cancer?

By: Morgan Adams, PharmD (HealthPoint Pharmacy)

Result: Plausible**Explanation:**

In the summer of 2009, a wave of articles were published in the journal, *Diabetologica*, linking insulin analogues (specifically glargine) with increased risk of cancer. These studies concluded that insulin glargine use increased risk of cancer, especially breast cancer. Insulin glargine is a recombinant DNA analog of human insulin that has three amino acid substitutions. These amino acids result in 6-8 times greater affinity for insulin. Unfortunately, these amino acids also result in an increased affinity for insulin-like growth factor-1 (IGF-1). In vitro, glargine has also been shown to be more mitogenic than human insulin and also promotes the growth of certain tumor cells. One retrospective cohort study completed in Germany found a positive association between insulin (analogues and human) and cancer. The risk was found to be significantly higher for glargine than any other analog.¹ Another retrospective cohort study completed in Sweden showed a greater incidence of breast cancer in patients using glargine alone.²

As could be expected, these studies generated much concern amongst health care professionals treating patients with diabetes. Since that time, several studies have been completed to dispel these theories. As a disease state, type II diabetes is associated with an increased risk of colon, pancreas, and breast cancers. The studies that linked insulin glargine and cancer did not account for the possible association of BMI and dose on cancer risk. Also, many of the studies were conducted in Europe where glargine use is not as common as in the United States. Additionally, the published studies were based on administrative data from national health system databases and often did not account for possible confounding variables. A retrospective cohort study conducted in Scotland found no association between cancer and insulin glargine use and attributed other studies' results to allocation bias rather than effect of insulin.³ Another retrospective cohort trial in the UK showed a possible association of risk of cancer with insulin. However, this risk was almost eliminated when insulin was given concomitant with metformin, a standard of care therapy regimen in the US.⁴ A more recent retrospective cohort epidemiological study conducted in the United States found no significant increase of cancer among patients using insulin glargine. The study did, however, find an association between high dose (mean dose of 119 units per day) insulin glargine use and higher risk of breast cancer, especially among patients 75 and younger.⁵

In the midst of this conflicting data, clinicians should continue to prescribe insulin glargine as usual for patients with type II diabetes, supported by a 2010 consensus statement of the American Cancer Society and American Diabetes Association.⁷ It remains unclear whether there is a direct relationship between diabetes and cancer or if common risk factors (age, obesity, hyperinsulinemia, physical inactivity) account for some of this association. Diet, physical activity, and weight loss should be encouraged for all patients with diabetes not only to improve glycemic control, but also to decrease risk of cancer. While there are plausible physiological explanations for the increased risk of cancer with insulin glargine, at the current time, clinicians should not modify drug therapy choices based on cancer risk except for specific patients with high cancer risk due to other risk factors. Further prospective clinical trials are needed to further explore the relationship between cancer and insulin analogues.

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