

## REPORT

### The Seven Pillars of Successful Weight Loss

By William Faloon



The Life Extension Foundation has a 28-year track record of identifying novel methods to address the health concerns of aging humans. For example, Life Extension warned long ago that atherosclerosis was caused by more than a dozen independent correctable risk factors, with cholesterol and LDL being only two of them.<sup>1</sup>

When it comes to weight loss, mainstream medicine has recommended “diet and exercise” for so long that this phrase has become more of a cliché than any kind of momentous scientific communication.

The fact is that aging people need to do a lot more than reduce calorie intake and increase physical activity if they are going to lose and keep off excess body fat.

In this article, we succinctly address the seven steps that most overweight aging people should follow if they are to achieve optimal removal of surplus body fat. This multi-step program is analogous to the “drug cocktails” that doctors now use to control HIV infections in a way that enables patients to live for decades instead of less than one year, as was the case when the disease first manifested.

The Seven Pillars of Successful Weight Loss are also analogous to what progressive oncologists are doing to cure cancer today by administering multiple therapies designed to neutralize the numerous survival mechanisms cancer cells use to escape eradication.

In some respects, the uncontrolled proliferation and size of adipocytes (fat cells) in the aging body is like a benign tumor growing in our abdomens, buttocks, and other areas of the body where it is unwanted.

Just like most Life Extension members understand that they often have to correct several vascular disease risk factors if they are to protect against heart attack and stroke, those seeking to lose weight should consider making these Seven Pillars of Successful Weight Loss a regular part of their health-maintenance program.

#### **PILLAR NUMBER 1: RESTORE INSULIN SENSITIVITY**

Normal aging causes the insulin receptors on cell membranes to lose their youthful sensitivity or functionality. The result is a pathological condition called “insulin resistance” that impairs the ability of cells to efficiently take up glucose and utilize it for energy production. Glucose not taken up by energy-producing cells prompts the release of excess insulin. Hyperinsulinemia, a condition of high circulating insulin levels, is associated with a significantly increased risk of heart disease. In fact, a recent study showed that patients with heart disease had significantly higher plasma levels of blood sugar and circulating insulin.<sup>2</sup>

There are several ways to restore insulin sensitivity to our cell membranes. For example, nutrients such as chromium,<sup>3,4</sup> magnesium,<sup>5</sup> cocoa polyphenols,<sup>6</sup> and fish oil<sup>7,8</sup> can help.



A low-cost prescription drug called metformin can also significantly enhance insulin sensitivity.<sup>9-11</sup> While it is approved only as a treatment for type 2 diabetes, published scientific studies indicate it can help reduce body fat.<sup>12</sup> The dose range for those seeking to enhance their insulin sensitivity and reduce body weight can vary from 250 mg three times daily with meals up to 850 mg three times daily with meals. Consult with your prescribing physician to make sure that metformin is right for you. As you will read later in this section, restoring free testosterone to youthful ranges markedly enhances insulin sensitivity in aging men.

The absolute most effective way of restoring insulin sensitivity is to reduce calorie intake. Severe calorie restriction to under 1,500-1,800 calories/day significantly enhances insulin sensitivity, as

documented by dramatic lowering of fasting glucose and insulin blood levels.<sup>13-17</sup> Even a moderate cutback of excess calories can markedly improve insulin sensitivity.

So the first pillar to successful long-term weight loss should involve a moderate reduction in calorie intake, at least long enough to restore insulin receptor sensitivity to more youthful ranges. The use of nutrients, hormones, and drugs that enhance insulin sensitivity should also be considered. As you probably know already, a lot more than just eating less is needed to lose weight.

## PILLAR NUMBER 2: RESTORE YOUTHFUL HORMONE BALANCE

Most overweight human beings have suffered the agonies of calorie deprivation (dieting), but have failed to achieve any kind of sustained fat reduction. While eating less addresses some of the underlying causes of weight gain, the high failure rate of dieting is partially attributable to the severe alteration in hormone levels that occurs as part of normal aging.

A large percentage of men today suffer from abdominal obesity—the most dangerous kind of body fat. It is often difficult, if not impossible for aging men to lose inches off their waistline if they are deficient in free testosterone, especially in the presence of excess estrogen.<sup>18-20</sup> Low levels of dehydroepiandro-sterone (DHEA) can also contribute to undesirable fat accumulation in men and women.<sup>21</sup>



A comprehensive blood test panel can reveal free testosterone and estrogen (estradiol) levels so that a physician can prescribe a topical testosterone cream and an aromatase-inhibiting drug (if necessary) to restore a man's sex hormone profile to a youthful range. The same blood test panel can also detect DHEA blood levels to enable one to take the proper dose of this over-the-counter dietary supplement.

A comprehensive blood test panel should also measure prostate-specific antigen (PSA) in men to help rule out prostate cancer. Those with prostate cancer cannot restore these hormones until the cancer is completely eradicated. Some men are able to reduce excess estrogen while simultaneously boosting free testosterone by taking nutrient formulas that contain plant extracts to help inhibit the aromatase enzyme (which converts testosterone into estrogen) and decrease levels of sex hormone-binding globulin (which binds free testosterone). It should be noted one reason that the application of testosterone creams does not always promote belly fat loss in aging men is that the testosterone converts (or aromatizes) to estrogen, ergo the need for aromatase-inhibiting drugs or nutrients, in addition to follow-up blood tests to measure blood levels of these hormones and PSA.

A substantial percentage of aging women (and many aging men) have less-than-optimal thyroid levels, thus predisposing them to weight gain. Thyroid hormone is needed to maintain healthy metabolic rates. Those who are deficient in thyroid hormone should be prescribed thyroid medication to maintain or improve their overall health, as well as to provide this hormone involved in the regulation of body composition. Drugs to consider are Armour® natural thyroid complex (containing both T4 and T3) or Cytomel® (containing T3). Trying to lose weight in the face of thyroid hormone deficit can be particularly challenging.

Aging women are often confronted with a condition termed “estrogen dominance,” whereby they have too much estrogen in relation to their progesterone levels. Excess estrogen can cause women to gain weight and make it difficult to keep excess weight off. Restoring hormone balance in aging females requires the intervention of a health care practitioner with specialized expertise in prescribing bioidentical hormone replacement therapy. Men are more fortunate in that almost any doctor can prescribe the proper dose of testosterone (and aromatase-inhibiting drugs, if needed).

## WHAT YOU NEED TO KNOW: THE SEVEN PILLARS OF SUCCESSFUL WEIGHT LOSS

- Simply eating less and exercising more is not enough to help most people remove excess body fat and keep it off. A comprehensive program is necessary to aggressively target the many factors that contribute to excess body fat.
- Excess body fat is not only unsightly, it can be deadly, increasing the risk for heart disease, diabetes, and cancer.

Abdominal fat is particularly dangerous.

- A comprehensive fat-loss program includes improving insulin sensitivity, achieving youthful hormone balance, controlling the rate of carbohydrate absorption, increasing physical activity, normalizing brain serotonin, restoring energy expenditure rate, and adopting a long-term healthy eating strategy.
- Nutritional supplements offer important support for reducing appetite, promoting satiety, and enhancing fat-burning.
- The rewards of removing excess body fat go far beyond a slim physique to the promise of a lengthy, disease-free life.

### PILLAR NUMBER 3: CONTROL RATE OF CARBOHYDRATE ABSORPTION

We already know that too much blood glucose (and the subsequent insulin spike) predisposes people to gaining unwanted fat pounds. By taking just five grams of soluble fiber before or with each meal, one can significantly blunt the glucose-insulin surge.<sup>32</sup>

Fiber may protect against unwanted weight gain via several mechanisms that involve both effects on satiety and glucose-insulin responses.<sup>32-34</sup> For example, research has shown that vegetarians weigh significantly less than non-vegetarians, whether measured by body mass index or body weight.<sup>35</sup> Some experts believe that vegetarians' lower average body weight is linked to one factor: the high fiber content of the plant foods consumed.<sup>36</sup> Plant fiber fills you up quickly, and studies indicate that this results in less snacking and binging later in the day.

The Seven Countries Study provides additional evidence linking a high-fiber diet with lower body weight. Researchers found that people living in countries with high fiber intake weighed less than those living in countries where fiber intake is low.<sup>37</sup> Higher fiber intake is also associated with lower average body weight in the US. In the famous Nurses' Health Study, those who ingested more dietary fiber consistently weighed less than those who consumed less fiber.<sup>34</sup>

Finally, in the Coronary Artery Risk Development in Young Adults Study examining how heart disease develops in adults, researchers linked higher dietary fiber intake with lower body weight and waist-to-hip ratios, along with a reduction in markers of heart disease risk. Higher fiber consumption predicted less weight gain more strongly than did total or saturated fat consumption.<sup>36</sup>

Not all fibers are created equal. Beta-glucans (derived from oats and barley) are particularly effective in slowing the absorption of carbohydrates—enabling one to control blood sugar levels and induce the satiety needed to achieve healthy weight management. Studies show that when taken with meals, beta-glucan fibers markedly blunt post-meal elevations in blood sugar and insulin levels. Like other foods rich in soluble fiber, beta-glucans help improve blood glucose metabolism while also lowering serum lipid levels.<sup>38,39</sup>



Getting into the routine of taking five grams of a neutral-tasting beta-glucan fiber mix before or with each meal would provide optimal weight loss effects via this mechanism (i.e., controlling rate of carbohydrate absorption). Alternatively, taking fiber capsules (containing the highly viscous fiber glucomannan, which promotes healthy glycemic status) before each carbohydrate-rich meal would also help reduce the glucose-insulin surge that contributes to obesity.

### WHERE'S THE FAT?

The location of body fat stores is directly related to disease risk factors. People with excess levels of abdominal fat are at markedly increased risk of chronic illnesses such as cardiovascular disease and type 2 diabetes—both of which are closely related to the metabolic syndrome.<sup>22,23</sup> Direct entry of fats from abdominal stores into the liver may trigger increased insulin resistance, accounting for the relationship with type 2 diabetes.<sup>24</sup>

Recent studies have also shown that the potent endocrine function of abdominal body fat may explain the relationship between abdominal fat and cognitive decline, such as that seen in Alzheimer's and other neurodegenerative diseases.<sup>25</sup>

Abdominal fat is not just a problem in adults—new studies have established a relationship between fat distribution in early childhood and adolescence and serious chronic disease in early to mid-adulthood.<sup>26,27</sup> Responsible doctors now include abdominal circumference measurements at routine visits as a means of identifying these risk factors.<sup>28</sup>

Even within the abdomen, the location of fat stores matters. People with excessive amounts of fat in their livers (fatty liver disease) are at even higher risk for all of these chronic conditions, compared with those who have lower levels of liver fat.<sup>29</sup>

Indeed, damage to liver cells, as measured by increased levels of liver-based enzymes in the bloodstream, is closely associated with decreased insulin sensitivity and is a risk factor for development of type 2 diabetes.<sup>30,31</sup>

## PILLAR NUMBER 4: INCREASE PHYSICAL ACTIVITY

Most people think the only weight-loss benefit of exercise is to use up more stored body fat calories. In reality, exercise induces many beneficial changes at the cellular level that contribute to better weight control. Increased physical activity itself improves insulin sensitivity and mimics the effect of certain antidiabetic drugs (such as the PPAR-gamma agonists), which can have a favorable effect on body fat contouring.<sup>42</sup>

The type and intensity of physical activity will vary considerably among individuals. The purpose of making increased physical activity one of the Seven Pillars of Successful Weight Loss is to encourage everyone seeking to achieve optimal fat loss to engage in some form of increased physical activity.

It is our opinion that people who could follow a good exercise program to keep fat pounds off would do so if they saw rapid and meaningful weight loss results. Even a modest increase in physical activity, as a component of the Seven Pillars of Successful Weight Loss, should produce a reduction of fat mass (especially in the abdomen) remarkable enough to motivate even sedentary individuals to find ways to become more consistently physically active.



## FAT AND OXIDATIVE STRESS

Because of its chemical nature, fat is readily oxidized by free radicals—and it is the oxidized form of many lipids that triggers the blood vessel damage and eventual plaque formation that leads to atherosclerosis and its deadly consequences. Obesity is closely associated with increased oxidative stress,<sup>40</sup> while loss of body fat is associated with decreasing levels of molecules associated with oxidation.<sup>41</sup> The bottom line is that people with excessive adipose tissue are walking “oxidant factories” whose bodies must cope with enormous loads of these violently destructive molecules.

## FAT AND INFLAMMATION

The metabolic syndrome and its related conditions all derive from increased levels of inflammatory molecules called cytokines—and inflammatory cytokines are more prominent in people with excessive stores of body fat.<sup>23,43</sup> Indeed, physicians now commonly measure certain markers of inflammation such as C-reactive protein (CRP) as a means of screening for people at risk for cardiovascular disease.<sup>44</sup> Fortunately, reductions in body fat content (through exercise, diet, and appropriate supplementation) are associated with healthy reductions in inflammatory markers such as CRP—and that means a reduction in the many risk factors associated with obesity-related inflammation.<sup>45-47</sup>

## PILLAR NUMBER 5: RESTORE BRAIN SEROTONIN

When the brain is flooded with serotonin, satiety normally occurs. A serotonin deficiency has been associated with the carbohydrate binging that contributes to the accumulation of excess body fat.<sup>48</sup> Obese individuals have low blood tryptophan levels, which indicate that their overeating patterns may be related to a serotonin deficiency in the brain.<sup>49,50</sup>

In addition, cutting-edge research reveals that chronic inflammation and immune system overactivation appear to play critical roles in obesity.<sup>50,51</sup> As you will read in next month’s issue of Life Extension magazine, inflammatory cytokines like interferon-gamma (IFN-gamma) are made and released in body fat. An enzyme called indoleamine 2,3-dioxygenase is activated by IFN-gamma, which then degrades tryptophan in the body. Tryptophan is needed to produce serotonin in the brain.



In fact, human studies suggest that obese patients have decreased plasma tryptophan levels that remain low, independently of weight reduction or dietary intake.<sup>49,50</sup> This altered tryptophan metabolism reduces serotonin production and contributes to impaired satiety, which in turn contributes to increased caloric intake and obesity.

When obese patients were given 1,000 mg, 2,000 mg, or 3,000 mg doses of L-tryptophan one hour before meals, a significant decrease in caloric consumption was observed. The majority of the reduction in caloric intake was in the amount of carbohydrates consumed and not the amount of protein consumed.<sup>52</sup>

In a double-blind, placebo-controlled study, obese patients on protein-rich diets who received tryptophan (750 mg twice daily orally) had significant weight loss, compared with a placebo group.<sup>53</sup>

For the past 18 years, tryptophan dietary supplements have been restricted. The good news is that pharmaceutical-pure tryptophan supplements are once again available to Americans.

Those seeking to embark on a comprehensive weight-loss program should consider adding this safe form of tryptophan to their daily program in starting doses of 500 mg before meals, two to three times per day.

## FAT AND CANCER

Excess body fat not only increases the risk of cardiovascular disease, it also increases the risk of deadly cancers. In one large European study, increasing body mass index was associated with a significant increase in the risk of cancer for 10 out of 17 specific types examined.<sup>62</sup>

Specific recent studies have shown a powerful association between body fat content and kidney and liver cancers.<sup>63,64</sup> By now, it should be no surprise to learn that weight loss, specifically body fat reduction, can lead to lowered risks for cancers just as it does for other devastating conditions.<sup>65,66</sup> One study has estimated a reduction of 45% in the risk of breast cancer in women who lost more than about nine pounds.<sup>66</sup>

## PILLAR NUMBER 6: RESTORE RESTING ENERGY EXPENDITURE RATE

Up until now, it was difficult for aging humans to lose significant body fat stores, even when following a low-calorie diet, restoring youthful hormone balance, ingesting fiber, and aggressively exercising. The missing link for successful long-term weight loss was a safe method to boost resting energy expenditure, i.e., to burn off stored body fat.

With the availability of fucoxanthin and pomegranate seed oil, aging humans can safely boost their metabolic rate and, for the first time, obtain meaningful results when following sensible steps to maintain a healthy body weight.<sup>54,55</sup>

## PILLAR NUMBER 7: EAT TO LIVE A LONG AND HEALTHY LIFE

No one should embark on a weight-loss program by trying to follow a fad diet that cannot be adhered to over the long term. At the same time, aging individuals have to make choices as to what is more important, i.e., ingesting foods that are known to promote weight gain (and cause horrendous diseases) or selecting healthier foods that facilitate weight loss and protect against illness.



Five years ago, Life Extension published an article about the dangers of eating foods cooked at high temperatures (over 250 degrees). Overcooked foods damage our body's proteins, while foods cooked at lower temperatures have been shown to facilitate weight loss. So just changing how your foods are prepared could help you shed body fat and, at the same time, protect against age-related disease (see "Eating food cooked at high temperature accelerates aging," Life Extension, May 2003).

Solid scientific evidence shows that excess calorie ingestion accelerates the onset of degenerative disease and the aging process itself—in addition to promoting the unsightly accumulation of body fat. Women in the fucoxanthin studies consumed 1,800 calories/day and still lost considerable body weight over a relatively short time period. With the help of the various elements described in this Seven Pillars of Successful Weight Loss, the rapid reduction in body fat one may see should provide a strong motivational basis to initiate more sensible food intake patterns.

It's never too late to change one's lifestyle in a manner that promotes better health while melting away excess body fat. Now that

a safe and proven method of boosting resting metabolic rate (using fucoxanthin) is finally available, aging humans can embark on a fat-reduction program with a high degree of confidence of enjoying long-term results.

## FAT AND CARDIOVASCULAR DISEASE

High body fat is of course strongly associated with cardiovascular disease—but the relationship is more complicated and subtle than we used to think. Atherosclerosis is clearly the result of the cycle of lipid oxidation, inflammation, and vascular injury, as mentioned above, but fat tissue causes other risks that are independent of plasma lipid levels. Acting as an endocrine organ, fat tissue can increase the flow of hormones (known as adipokines) involved in blood pressure control,<sup>24</sup> potentially accounting directly for some of the hypertension we used to attribute simply to “stiff blood vessels” and “extra force needed to pump blood.”<sup>56</sup> Again, it seems to be specifically the accumulations of abdominal fat that produce these remarkable and deadly effects.<sup>57</sup> And again, it is fortunate that adequate reduction in body fat content through lifestyle changes, diet, and supplementation has been associated with decreased risk for cardiovascular catastrophes, such as heart attacks and strokes.<sup>58-61</sup>

## CONCLUSION

Lifestyle changes are clearly critical to safe and responsible loss of weight and body fat and provide additional quality-of-life benefits that vastly exceed simple reduction in disease risk. Clinicians and patients who are truly committed to attaining a long and happy life will always include responsible diet and moderate exercise programs in their long-term plans. The introduction of fucoxanthin to safely boost resting energy expenditure should be seen as a way to augment, not replace, sensible lifestyle strategies.

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370.

## CONTROLLING BODY FAT CONTENT SAFELY

Despite the obvious dangers of obesity and specifically, elevated abdominal body fat content, most Americans have a hard time losing weight. Many turn to “quick-fix” solutions such as bariatric surgery (“stomach stapling”), which actually does provide some benefit in extreme cases,<sup>67</sup> or to “diet pills” that are usually ineffective and often dangerous.<sup>68-72</sup> The best and safest approaches to weight loss continue to be a modest reduction in caloric intake coupled with a careful increase in energy expenditure.

---

## References

---

1. Available at: [http://www.lef.org/magazine/mag96/aug\\_new\\_therapies.html](http://www.lef.org/magazine/mag96/aug_new_therapies.html). Accessed January 2, 2008.
2. Yamasa T, Ikeda S, Koga S, et al. Evaluation of glucose tolerance, post-prandial hyperglycemia and hyperinsulinemia influencing the incidence of coronary heart disease. *Intern Med.* 2007;46(9):543-6.
3. Rodriguez-Moran M, Guerrero-Romero F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects: a randomized double-blind controlled trial. *Diabetes Care.* 2003 Apr;26(4):1147-52.
4. Yasmin T, Shara M, Bagchi M, Preuss HG, Bagchi D. Toxicological assessment of a novel niacin-bound chromium, known to ameliorate the symptoms of metabolic syndromes. *J Amer College Nutr.* 45th Annual Meeting, Abs 77. (Long Beach, California.) 2004 Oct;76(2):272-5.
5. Anderson RA, Cheng N, Bryden NA, et al. Elevated intakes of supplemental chromium improve glucose and insulin variables in individuals with type 2 diabetes. *Diabetes.* 1997 Nov;46(11):1786-91.
6. Grassi D, Necozione S, Lippi C, et al. Cocoa reduces blood pressure and insulin resistance and improves endothelium-dependent vasodilation in hypertensives. *Hypertension.* 2005 Aug;46(2):398-405.
7. Ebbesson SO, Risica PM, Ebbesson LO, Kennish JM, Tejero ME. Omega-3 fatty acids improve glucose tolerance and components of the metabolic syndrome in Alaskan Eskimos: the Alaska Siberia project. *Int J Circumpolar Health.* 2005 Sep;64(4):396-408.
8. Wilkins C, Long RC, Jr., Waldron M, Ferguson DC, Hoenig M. Assessment of the influence of fatty acids on indices of insulin sensitivity and myocellular lipid content by use of magnetic resonance spectroscopy in cats. *Am J Vet Res.* 2004 Aug;65

(8):1090-9.

9. Emral R, Koseoglu O, Tonyukuk V, et al. The effect of short-term glycemic regulation with gliclazide and metformin on postprandial lipemia. *Exp Clin Endocrinol Diabetes*. 2005 Feb;113(2):80-4.
10. Deutsch JC, Santhosh-Kumar CR, Kolhouse JF. Efficacy of metformin in non-insulin-dependent diabetes mellitus. *N Engl J Med*. 1996 Jan 25;334(4):269-70.
11. Charles MA, Eschwege E. Prevention of type 2 diabetes: role of metformin. *Drugs*. 1999;58 Suppl 1:71-3.
12. Paolisso G, Amato L, Eccellente R, et al. Effect of metformin on food intake in obese subjects. *Eur J Clin Invest*. 1998 Jun;28(6):441-6.
13. Henry RR, Wiest-Kent TA, Scheaffer L, Kolterman OG, Olefsky JM. Metabolic consequences of very-low-calorie diet therapy in obese non-insulin-dependent diabetic and nondiabetic subjects. *Diabetes*. 1986 Feb;35(2):155-64.
14. Larson-Meyer DE, Heilbronn LK, Redman LM, et al. Effect of calorie restriction with or without exercise on insulin sensitivity, beta-cell function, fat cell size, and ectopic lipid in overweight subjects. *Diabetes Care*. 2006 Jun;29(6):1337-44.
15. Bodkin NL, Ortmeyer HK, Hansen BC. Long-term dietary restriction in older-aged rhesus monkeys: effects on insulin resistance. *J Gerontol A Biol Sci Med Sci*. 1995 May;50(3):B142-7.
16. Gumbs AA, Modlin IM, Ballantyne GH. Changes in insulin resistance following bariatric surgery: role of caloric restriction and weight loss. *Obes Surg*. 2005 Apr;15(4):462-73.
17. Nakai Y, Taniguchi A, Fukushima M, et al. Insulin sensitivity during very-low-calorie diets assessed by minimal modeling. *Am J Clin Nutr*. 1992 Jul;56(1 Suppl):179S-81S.
18. Abate N, Haffner SM, Garg A, Peshock RM, Grundy SM. Sex steroid hormones, upper body obesity, and insulin resistance. *J Clin Endocrinol Metab*. 2002 Oct;87(10):4522-7.
19. Vermeulen A, Kaufman JM, Goemaere S, van Pottelberg I. Estradiol in elderly men. *Aging Male*. 2002 Jun;5(2):98-102.
20. Marin P, Krotkiewski M, Bjorntorp P. Androgen treatment of middle-aged, obese men: effects on metabolism, muscle and adipose tissues. *Eur J Med*. 1992 Oct;1(6):329-36.
21. Villareal DT, Holloszy JO. Effect of DHEA on abdominal fat and insulin action in elderly women and men: a randomized controlled trial. *JAMA*. 2004 Nov 10;292(18):2243-8.
22. Haffner SM. Abdominal adiposity and cardiometabolic risk: do we have all the answers? *Am J Med*. 2007 Sep;120(9 Suppl 1):S10-6.
23. Despres JP, Lemieux I. Abdominal obesity and metabolic syndrome. *Nature*. 2006 Dec 14;444(7121):881-7.
24. Bergman RN, Kim SP, Hsu IR, et al. Abdominal obesity: role in the pathophysiology of metabolic disease and cardiovascular risk. *Am J Med*. 2007 Feb;120(2 Suppl 1):S3-S8.
25. Whitmer RA. The epidemiology of adiposity and dementia. *Curr Alzheimer Res*. 2007 Apr;4(2):117-22.
26. Lee CD, Jacobs DR Jr, Schreiner PJ, Iribarren C, Hankinson A. Abdominal obesity and coronary artery calcification in young adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Clin Nutr*. 2007 Jul;86(1):48-54.
27. Botton J, Heude B, Kettaneh A, et al. Cardiovascular risk factor levels and their relationships with overweight and fat distribution in children: the Fleurbaix Laventie Ville Santé II study. *Metabolism*. 2007 May;56(5):614-22.
28. Connelly PW, Hanley AJ, Harris SB, Hegele RA, Zinman B. Relation of waist circumference and glycemic status to C-reactive protein in the Sandy Lake Oji-Cree. *Int J Obes Relat Metab Disord*. 2003 Mar;27(3):347-54.
29. Arslan U, Türkoğlu S, Balcioglu S, Tavil Y, Karakan T, Cengel A. Association between nonalcoholic fatty liver disease and coronary artery disease. *Coron Artery Dis*. 2007 Sep;18(6):433-6.

30. Ruhl CE, Everhart JE. Determinants of the association of overweight with elevated serum alanine aminotransferase activity in the United States. *Gastroenterology*. 2003 Jan;124(1):71-9.
31. Vozarova B, Stefan N, Lindsay RS, et al. High alanine aminotransferase is associated with decreased hepatic insulin sensitivity and predicts the development of type 2 diabetes. *Diabetes*. 2002 Jun;51(6):1889-95.
32. McCarty MF. Glucomannan minimizes the postprandial insulin surge: a potential adjuvant for hepatothermic therapy. *Med Hypotheses*. 2002 Jun;58(6):487-90.
33. Available at: [http://www.ars.usda.gov/research/publications/publications.htm?SEQ\\_NO\\_115=181996](http://www.ars.usda.gov/research/publications/publications.htm?SEQ_NO_115=181996). Accessed January 9, 2008.
34. Liu S, Willett WC, Manson JE, et al. Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. *Am J Clin Nutr*. 2003 Nov;78(5):920-7.
35. Appleby PN, Thorogood M, Mann JI, Key TJ. Low body mass index in non-meat eaters: the possible roles of animal fat, dietary fibre and alcohol. *Int J Obesity Relat Metab Disord*. 1998 May;22(5):454-60.
36. Ludwig DS, Pereira MA, Kroenke CH, et al. Dietary fiber, weight gain, and cardiovascular disease risk factors in young adults. *JAMA*. 1999 Oct 27;282(16):1539-46.
37. Kromhout D, Bloemberg B, Seidell JC, Nissinen A, Menotti A. Physical activity and dietary fiber determine population body fat levels: the Seven Countries Study. *Int J Obes Relat Metab Disord*. 2001 Mar;25(3):301-6.
38. Reyna-Villasmil N, Bermudez-Pirela V, Mengual-Moreno E, et al. Oat-derived beta-glucan significantly improves HDLC and diminishes LDLC and non-HDL cholesterol in overweight individuals with mild hypercholesterolemia. *Am J Ther*. 2007 Mar;14(2):203-12.
39. Poppitt SD, van Druenen JD, McGill AT, Mulvey TB, Leahy FE. Supplementation of a high-carbohydrate breakfast with barley beta-glucan improves postprandial glycaemic response for meals but not beverages. *Asia Pac J Clin Nutr*. 2007;16(1):16-24.
40. Luo W, Cao J, Li J, He W. Adipose tissue-specific PPARgamma deficiency increases resistance to oxidative stress. *Exp Gerontol*. 2007 Nov 21.
41. Ziccardi P, Nappo F, Giugliano G, et al. Reduction of inflammatory cytokine concentrations and improvement of endothelial functions in obese women after weight loss over one year. *Circulation*. 2002 Feb 19;105(7):804-9.
42. Hawley JA, Lessard SJ. Exercise training-induced improvements in insulin action. *Acta Physiol (Oxf)*. 2008 Jan;192(1):127-35.
43. Bodary PF, Iglay HB, Eitzman DT. Strategies to reduce vascular risk associated with obesity. *Curr Vasc Pharmacol*. 2007 Oct;5(4):249-58.
44. Williams MJ, Williams SM, Milne BJ, Hancox RJ, Poulton R. Association between C-reactive protein, metabolic cardiovascular risk factors, obesity and oral contraceptive use in young adults. *Int J Obes Relat Metab Disord*. 2004 Aug;28(8):998-1003.
45. Kim YJ, Shin YO, Bae JS, et al. Beneficial effects of cardiac rehabilitation and exercise after percutaneous coronary intervention on hsCRP and inflammatory cytokines in CAD patients. *Pflugers Arch*. 2007 Sep 29.
46. Milani RV, Lavie CJ, Mehra MR. Reduction in C-reactive protein through cardiac rehabilitation and exercise training. *J Am Coll Cardiol*. 2004 Mar 17;43(6):1056-61.
47. Lee M, Aronne LJ. Weight management for type 2 diabetes mellitus: global cardiovascular risk reduction. *Am J Cardiol*. 2007 Feb 19;99(4A):68B-79B.
48. Leigh C. Serotonin and the Biology of Bingeing. *Eating Disorders: A Reference Sourcebook*. In: Lemberg R. Ed., Oryx Press; 1998:51.

49. Breum L, Rasmussen MH, Hilsted J, Fernstrom JD. Twenty-four-hour plasma tryptophan concentrations and ratios are below normal in obese subjects and are not normalized by substantial weight reduction. *Am J Clin Nutr.* 2003 May;77(5):1112-8.
50. Brandacher G, Hoeller E, Fuchs D, Weiss HG. Chronic immune activation underlies morbid obesity: is IDO a key player? *Curr Drug Metab.* 2007 Apr;8(3):289-95.
51. Xu H, Barnes GT, Yang Q, et al. Chronic inflammation in fat plays a crucial role in the development of obesity-related insulin resistance. *J Clin Invest.* 2003 Dec;112(12):1821-30.
52. Cavaliere H, Medeiros-Neto G. The anorectic effect of increasing doses of L-tryptophan in obese patients. *Eat Weight Disord.* 1997 Dec;2(4):211-5.
53. Heraief E, Burckhardt P, Wurtman JJ, Wurtman RJ. Tryptophan administration may enhance weight loss by some moderately obese patients on a protein-sparing modified fast (PSMF) diet. *Int J Eating Disord.* 1985;4(3):281-92.
54. Abidov M, Roshen S. Effect of Fucoxanthin and Xanthigen™, a phytomedicine containing fucoxanthin and pomegranate seed oil, on energy expenditure rate in obese non-diabetic female volunteers with non-alcoholic fatty liver disease: a double-blind, randomized and placebo-controlled trial. Submitted for publication. *Int J Obesity.* 2008.
55. Abidov M, Siefulla R, Ramazanov Z. The effect of Xanthigen™, a phytomedicine containing fucoxanthin and pomegranate seed oil, on body weight and liver fat, serum triglycerides, C-reactive protein, and plasma aminotransferases in obese non-diabetic female volunteers: a double-blind, randomized and placebo-controlled trial. Submitted for publication. *Int J Obesity.* 2008.
56. Safar ME, Czernichow S, Blacher J. Obesity, arterial stiffness, and cardiovascular risk. *J Am Soc Nephrol.* 2006 Apr;17(4 Suppl 2):S109-11.
57. Rosa EC, Zanella MT, Ribeiro AB, Kohlmann JO. Visceral obesity, hypertension and cardio-renal risk: a review. *Arq Bras Endocrinol Metabol.* 2005 Apr;49(2):196-204.
58. Rush EC, Chandu V, Plank LD. Reduction of abdominal fat and chronic disease factors by lifestyle change in migrant Asian Indians older than 50 years. *Asia Pac J Clin Nutr.* 2007;16(4):671-6.
59. Rokling-Andersen MH, Reseland JE, Veierod MB, et al. Effects of long-term exercise and diet intervention on plasma adipokine concentrations. *Am J Clin Nutr.* 2007 Nov;86(5):1293-301.
60. Nagao T, Hase T, Tokimitsu I. A green tea extract high in catechins reduces body fat and cardiovascular risks in humans. *Obesity (Silver Spring).* 2007 Jun;15(6):1473-83.
61. Slentz CA, Aiken LB, Houmard JA, et al. Inactivity, exercise, and visceral fat. STRRIDE: a randomized, controlled study of exercise intensity and amount. *J Appl Physiol.* 2005 Oct;99(4):1613-8.
62. Reeves GK, Pirie K, Beral V, et al. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. *BMJ.* 2007 Dec 1;335(7630):1134.
63. Setiawan VW, Stram DO, Nomura AM, Kolonel LN, Henderson BE. Risk factors for renal cell cancer: the multiethnic cohort. *Am J Epidemiol.* 2007 Oct 15;166(8):932-40.
64. Ahrens W, Timmer A, Vyberg M, et al. Risk factors for extrahepatic biliary tract carcinoma in men: medical conditions and lifestyle: results from a European multicentre case-control study. *Eur J Gastroenterol Hepatol.* 2007 Aug;19(8):623-30.
65. Campbell KL, McTiernan A. Exercise and biomarkers for cancer prevention studies. *J Nutr.* 2007 Jan;137(1 Suppl):161S-9.
66. Schapira DV, Kumar NB, Lyman GH. Estimate of breast cancer risk reduction with weight loss. *Cancer.* 1991 May 15;67(10):2622-5.
67. Khaitan L, Smith CD. Obesity in the United States: is there a quick fix? Pros and cons of bariatric surgery from the adult perspective. *Curr Gastroenterol Rep.* 2005 Dec;7(6):451-4.
68. Celio CI, Luce KH, Bryson SW, et al. Use of diet pills and other dieting aids in a college population with high weight and shape concerns. *Int J Eat Disord.* 2006 Sep;39(6):492-7.

69. Cohen PA, McCormick D, Casey C, Dawson GF, Hacker KA. Imported compounded diet pill use among Brazilian women immigrants in the United States. *J Immigr Minor Health*. 2007 Dec 9 [Epub ahead of print].

70. Fleming RM. The effect of ephedra and high fat dieting: a cause for concern! A case report. *Angiology*. 2007 Feb-Mar;58(1):102-5.

71. Rakovec P, Kozak M, Sebestjen M. Ventricular tachycardia induced by abuse of ephedrine in a young healthy woman. *Wien Klin Wochenschr*. 2006 Sep;118(17-18):558-61.

72. Blanck HM, Serdula MK, Gillespie C, et al. Use of nonprescription dietary supplements for weight loss is common among Americans. *J Am Diet Assoc*. 2007 Mar;107(3):441-7.

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

**LifeExtension**<sup>®</sup>

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.