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Just a Little Excess Weight Increases Insulin Levels, Risk of Health Problems

Elevated blood levels of insulin are one of the hallmarks of prediabetes, diabetes, and overweight and obesity. Insulin levels increase in response to high blood sugar, the consequence of eating too many refined sugars and other processed carbohydrates. Quality protein and high-fiber foods generally lower both blood sugar and insulin levels.

But physicians are often confused by insulin levels, and researchers have been uncertain as to what occurs first – elevated insulin (leading to what’s called insulin resistance) or overweight. Now, a team of researchers from Germany has unraveled part of what happens, and other recent research adds to the health dangers of elevated insulin levels.

Johannes Erdmann, MD, and his colleagues at the University of Munich, studied the effect of weight gain on 10 healthy men in their twenties. Erdmann asked the subjects, who were all thin, to increase their food consumption by 300 to 500 calories daily for four and one-half months. The objective was a relatively modest 2-point increase in their body mass – roughly, about 10 pounds.

It turned out that the men did not secrete more insulin secretion while eating the extra calories. Instead, they lost their ability to remove insulin from the blood – a sign of insulin resistance.

Insulin is widely regarded as the fat-storage hormone, but Erdmann found that the higher insulin concentration resulted from the weight gain – in other words, the weight gain came first. “Insulin resistance already develops during weight gain within the normal range of body weight,” he wrote.

In a separate study, conducted in Quebec, Canada, researchers found that people with the highest insulin levels gained an average of 10 pounds over six years, compared with people who had the lowest insulin levels. In addition, people eating the diets lowest in fat had the highest insulin levels.

New research also suggests more serious health hazards from elevated insulin levels – beyond those

of just overweight and an increased risk of diabetes.

T. Keith Blackwell, MD, PhD, of the Joslin Diabetes Center, Boston, analyzed the effect of insulin on the SKN-1 protein in *C. elegans*, a microscopic worm. Despite the worm’s size, studies have generally found direct bearing on people (because people share many of the same genes).

The SKN-1 protein is considered a “master” regulator of genes, and increased SKN-1 protein activity lengthens lifespan. But Blackwell found that insulin inhibits SKN-1 activity, in effect shortening lifespan. The finding is similar to research conducted in the 1990s showing that elevated insulin levels inhibit FOXO, another “master” regulator of genes involved in diabetes and suppressing tumors.

Finally, Philipp Stawowy, MD, of the German Heart Center, Berlin, reported that insulin stimulated the activity of mononuclear cells, a family of immune cells that includes monocytes, macrophages, and lymphocytes. He wrote that high levels of insulin may facilitate the infiltration of immune cells – resulting in inflammation – in body fat and blood vessel walls.

Editor’s note: Although most physicians do not routinely test for fasting insulin levels, they will probably do so if asked. Ideal fasting insulin levels are less than 7 mcIU/ml, and levels above 11 mcIU/ml are suggestive of prediabetes.

References: Erdmann J, Kallabis B, Oettel U, et al. Development of hyperinsulinemia and insulin resistance during the early stage of weight gain. *American Journal of Physiology, Endocrinology, and Metabolism*, 2008;294:E568-E575. Chaput JP, Tremblay A, Rimm E, et al. A novel interaction between dietary composition and insulin secretion: effects on weight gain in the Quebec family study. *American Journal of Clinical Nutrition*, 2008;87:303-309. Tullet JMA, Hertweck M, An JH, et al. Direct inhibition of the longevity-promoting factor SKN-1 by insulin-like signaling in *C. elegans*. *Cell*, 2008;132:1025-1038. Kappert K, Meyborg H, Clemenz M, et al. Insulin facilitates monocyte migration: a possible link to tissue inflammation in insulin-resistance. *Biochemical and Biophysical Research Communications*, 2008;365:503-508. □

More research summaries on next page

Perspectives

Nutricide and Pharmacide

As I look at the increasingly bizarre world around us, I think two new words seem appropriate: *nutricide*, the killing of people by serving them junk foods; and *pharmacide*, the killing of people by over-prescribing pharmaceutical drugs.

Read the labels of almost every supermarket food sold in a box, can, jar, bottle, or bag, and you'll find that they contain far too many ingredients that serve large-scale processing but are slowly lethal to consumers ingesting them. I'm referring to various sugars, trans fats, interesterified fats, excess salt, and soybean oil as the top offenders. The fast-food companies are no better, serving up their breaded, deep-fried, hydrogenated goodies.

The folks at McDonald's, KFC, Coca-Cola, Kraft, Campbell, and so many other makers of processed food are killing people by way of overweight, diabetes, and heart disease. They're guilty of *nutricide*.

Unfortunately, some so-called health food and natural food products aren't much better. I recently attended the Natural Foods Expo show in Anaheim, California, where more than 3,000 companies showed their products to over 50,000 visitors. Many of the products were great – meats from organically raised animals, organically grown produce, and even relatively healthy snack foods.

But there were also too many attempts at feel-good knockoffs of conventional junk foods: "health food" soft drinks with as much sugar as a Pepsi, energy bars with as much sugar as a Snickers, chocolate soy milk with more sugar and calories than regular chocolate milk, *ad nauseam* (a term that seems particularly appropriate). And people wonder why two-thirds of Americans are overweight.

Meanwhile, the pharmaceutical industry has cooked up their own solution to the ills caused by all these unhealthy foods: heavily advertised drug panaceas that, in most cases, have side effects worse than the disease itself. Each year, more than 700,000 people get hospitalized because of adverse reactions to drugs, and more than 100,000 people in hospitals die from their medications, all of which are approved for use by the Food and Drug Administration. They're all guilty of *pharmacide*.

Abram Hoffer, MD, PhD, a pioneer in nutritional medicine, recently pointed to the debate about whether anti-depressant drugs were really better than placebos. "This is a phony debate, almost like trying to figure out how many angels are dancing on the head of a pin," he told me. "Even if the drugs are 10 percent better, they are so much more toxic than any placebo that a placebo should be preferred." –JC

B-Vitamins Regulate Genes, May Prenatally Prevent Disease

Folic acid is known to regulate the activity of genes and alter their programming, all without changing the hardwiring of the genetic code. Several years ago, studies in mice showed that extra amounts of B vitamins during pregnancy could actually turn off a gene involved in making offspring overweight.

Mice are mice, of course, and people are people. But a new study – this time in sheep, a higher mammal – has found that these nutrients play a similar role in gene regulation, and that low levels of these nutrients at the time of conception predisposes offspring to a host of health problems.

Lorraine E. Young, PhD, of the University of Nottingham, United Kingdom, deprived ewes of folic acid, vitamin B12, and methionine from eight weeks before conception until six days after conception. These nutrients help create "methyl groups," which attach to genes and alter the genes' usual programming. Such alterations in gene programming is the focus of epigenetics, a relatively new branch of genetics. Meanwhile, a separate group of ewes were given a normal sheep diet.

The offspring of the vitamin-deprived sheep received a typical diet, but by adulthood, they were heavier and fatter, were insulin resistant (prediabetic), had elevated blood pressure, and also had altered immune responses suggestive of allergies.

Both male and female offspring of vitamin-deprived ewes tended to be fatter, compared with the offspring of ewes fed a normal diet. Male offspring really tipped the scales – they were 25 percent fatter and had less muscle mass, compared with offspring of the ewes that had received a normal diet.

Both sexes developed signs of glucose intolerance, but the effect was stronger in male offspring. Likewise, male offspring of the vitamin-deprived ewes had substantially higher blood pressure.

Reference: Sinclair KD, Allegrucci C, Singh R, et al. DNA methylation, insulin resistance, and blood pressure in offspring determined by maternal periconceptional B vitamin and methionine status. *Proceedings of the National Academy of Sciences*, 2008;doi/10.1073/pnas.0707258104. □

Veggies and Some Supplements Help Prevent Muscle Loss

If you're in your 60s or older, you can take a couple steps toward preventing age-related muscle loss, also known as sarcopenia: eat lots of veggies and take amino acid supplements, according to two recent studies.

Bess Dawson-Hughes, M.D., and her colleagues at Tufts University, Boston, studied 384 men and women ages 65 years or older for three years. The subjects were part of a study investigating the roles of calcium and vitamin D in health. But Dawson-Hughes also looked at their muscle mass and potassium levels.

She found that potassium excretion – an indicator of potassium intake – was strongly associated with muscle mass.

The major dietary sources of potassium are fruit and vegetables, which together maintain a slightly alkaline (and healthy) body pH. An alkaline pH helps maintain muscle and bone, whereas an acidic pH triggers the breakdown of muscle and bone to buffer the acidity.

Dawson-Hughes wrote that “the ingestion of potassium-rich alkaline foods such as fruits and vegetables relieves the mild metabolic acidosis that occurs with the ingestion of a typical American diet that is rich in protein, cereal grains, and other net acid-producing foods.”

Meanwhile, Elisabet Borsheim, PhD, of the University of Texas Medical Branch, Galveston, and her colleagues asked 12 glucose-intolerant (prediabetic) men and women, who had an average age of 67 years, to take “free” amino acid supplements, each containing 11 grams of eight essential amino acids and arginine (a nonessential amino acid). The subjects took the supplements twice daily for 16 weeks.

By the 12th week, subjects gained an average of 2.5 pounds in muscle mass. This muscle mass decreased by the 16th week, though the subjects still had an average gain of 1.3 pounds in muscle mass.

The amino acids also led to a 22 percent increase in leg strength after 16 weeks, faster walking speed, and better physical functioning.

References: Dawson-Hughes B, Harris S, Ceglia L. Alkaline diets favor lean tissue mass in older adults. *American Journal of Clinical Nutrition*, 2008;87:662-665. Borsheim E, Bui QUT, Tissier S, et al. Effect of amino acid supplementation on muscle mass, strength and physical function in elderly. *Clinical Nutrition*, 2008: doi:10.1016/j.clnu.2008.01.001. □

Low Levels of Vitamin B1 Plague People with Type 1 & 2 Diabetes

People with either type 1 or type 2 diabetes tend to have very low levels of vitamin B1, also known as thiamine. The vitamin is required in carbohydrate metabolism.

Paul J. Thornally, PhD, of the University of Essex, United Kingdom, and his colleagues measured vitamin B1 levels in 26 people with type 1 diabetes,

48 people with type 2 diabetes, and 20 healthy subjects.

The people with diabetes had vitamin B1 blood levels that were about one-fourth of normal, compared with healthy subjects. Thornally found that the people with diabetes had faster “clearance” of the vitamin through their kidneys, and subsequent excretion, which contributed to their low levels.

He also reported that erythrocyte transketolase activity, which is used to measure of vitamin B1 levels, appeared normal. However, high levels of thiamine transporters (molecules that transport vitamin B1 in the blood) masked the abnormalities in transketolase activity.

Vitamin B1 is needed to make dehydrogenases, a family of enzymes involved in carbohydrate metabolism. High intake of carbohydrates increases requirements for both dehydrogenases and vitamin B1.

Reference: Thornalley PJ, Babaei-Jadidi B, Al Ali H, et al. High prevalence of low plasma thiamine concentration in diabetes linked to a marker of vascular disease. *Diabetologia*, 2008;50:2164-2170. □

N-Acetylcysteine Reduces Risk of Heart Problems After Surgery

Physicians have discovered that N-acetylcysteine (NAC), one of the most versatile of all antioxidants, has a new benefit: it significantly lowers the risk of atrial fibrillation, a type of dangerous heart-rhythm abnormality, after coronary artery bypass or valve surgery.

Mehmet Ozaydin, MD, of the Suleyman Demirel University School of Medicine, Turkey, provided intravenous NAC or standard saline solution, in addition to conventional medications, to 115 patients after heart surgery.

“Postoperative atrial fibrillation is the most frequent arrhythmia after cardiac surgery with the incidence ranging from 10 to 65 percent,” Ozaydin wrote. It greatly increases the risk of complications, hospital stays, and death.

Patients received IV NAC at a dose of 50 mg/kg (3,500 mg for a 150-pound person) for one hour before surgery, and then received the same amount daily for two days after surgery.

Overall, 15 patients developed atrial fibrillation. Only three patients (5 percent) in the NAC group developed atrial fibrillation, compared with 12 patients (20 percent) in the placebo group.

Reference: Ozaydin M, Peker O, Erdogan D, et al. N-acetylcysteine for the prevention of postoperative fibrillation: a prospective, randomized controlled pilot study. *European Heart Journal*, 2008;29:625-631. □

Quick Reviews of Recent Research

• Eating faster linked to insulin resistance

Japanese researchers investigated the relationship between eating meals quickly and weight gain and insulin resistance, a sign of glucose intolerance. They analyzed eating speed and calorie consumption for one month in 3,465 middle-age and nondiabetic men and 761 women. In both sexes, body mass index (a measure of overweight) increased with eating more quickly. In men, an increase in insulin resistance was related to habitually eating meals faster.

Otsuka R. *Preventive Medicine*, 2008;46:154-159.

• Low vitamin B6 is factor in arthritis

Low levels of vitamin B6 has long been associated with rheumatoid arthritis. In the latest study along these lines, researchers from Arizona State University and Oregon State University compared vitamin B6 levels in 18 patients with rheumatoid arthritis and 33 healthy subjects. Patients with rheumatoid arthritis were deficient in vitamin B6 and also had elevated homocysteine levels, a risk factor for heart disease and stroke.

Woolf K. *Journal of the American Dietetic Association*, 2008;108:443-453.

• Prilosec use affects vitamin B12 levels

Researchers in New York City tracked the use of proton-pump inhibitor drugs (e.g., Prilosec, Prevacid, and Nexium) and H2 blockers (e.g., Tagamet and Zantac), which are widely used to treat heartburn and gastric reflux. Vitamin B12 levels decreased with prolonged proton-pump inhibitor use, but not with H2 blockers. The researchers wrote that “concomitant oral B12 supplementation slowed but did not prevent the decline in B12 use...”

Dharmarajan TS. *Journal of the American Medical Directors Association*, 2008;9:162-167.

• Omega-3 fish oils improve heart rate

The omega-3 fish oils are increasingly recognized for their heart benefits, particularly in reducing triglycerides and arrhythmias. Australian researchers gave either 6 grams of fish oil supplements or placebos to 65 overweight and sedentary adults. Half of each group also began a moderate exercise program. After 12 weeks of supplements, heart rate variability improved and resting heart rate decreased.

Ninio DM. *British Journal of Nutrition*, 2008;13: epub ahead of print.

• Garlic’s benefits may be related to its odor

Garlic, which yields a rich trove of beneficial sulfur-containing chemicals, has been used for its health benefits for centuries. Researchers from the University of Alabama in the United States recently

reported that one of garlic’s chief compounds, allicin, is quickly metabolized to hydrogen sulfide, which sometimes gives garlic an unpleasant odor. In turn, hydrogen sulfide relaxes blood vessels and increases blood flow.

Benavides GA. *Proceedings of the National Academy of Sciences*, 2008;doi:10.1073/pnas.0705710104.

• Malnutrition common in UK hospitals

A recent British government report noted that 140,000 people were discharged from hospitals with clear signs of malnutrition in the past year. In an editorial in the *British Medical Journal*, doctors wrote that the incidence of malnutrition increased by 85 percent over the past 10 years, and that 70-80 percent of malnourished patients currently enter and leave hospitals without any action being taken to treat their nutritional problems.

Lean M. *British Medical Journal*, 2008;336:290.

• Broccoli compound boosts immune health

Discovered in broccoli in 1992, sulforaphane increases activity of the body’s phase 2 detoxification enzymes, which enable the liver to dispose of toxins and also appears to lower the risk of cancer. Researchers at the University of California, Los Angeles, administered either sulforaphane or N-acetylcysteine (NAC) to both young and old laboratory mice for five days before challenging them with an infection, with the supplements continuing for another 11 days. Both of the supplements boosted immune activity in the mice. The older mice had age-related depressions in immunity at the start of the study, but both of the supplements enhanced their immune systems – to the level of the young mice.

Kim HJ. *Journal of Allergy and Clinical Immunology*, 2008: epub ahead of print.

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