

# Dietary Modulation of Insulin and Glucose in Prediabetes

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**Abstract** *Prediabetes is usually intertwined with overweight, and both conditions presage type 2 diabetes, coronary artery disease, and many other common diseases. Early signs of prediabetes include abdominal adiposity, mood swings, sugar and carbohydrate cravings, and feeling tired or mentally fuzzy after eating. Standard measures of glucose intolerance, such as fasting glucose, may reveal a "false normal" when a person is actually prediabetic. Combined with tests for glucose, fasting insulin becomes a powerful predictor of type 2 diabetes and sequelae 10 to 15 years before glucose becomes elevated. Such an early warning provides a window to implement dietary changes to restore normal glucose tolerance. Adopting a Paleolithic-style diet that emphasizes fresh, low-fat animal proteins and high-fiber vegetables can usually reverse prediabetes. Furthermore, dietary supplements can enhance insulin sensitivity and/or glucose control. These supplements include alpha-lipoic acid, chromium, biotin, silymarin, vitamin D3 combined with calcium, and vitamin K. Prediabetes is an opportunity to improve health, and it is wise to seize this opportunity. Not doing so will eventually lead to type 2 diabetes, which is far more difficult to reverse and almost always requires some form of pharmaceutical intervention.*

## Introduction

Prediabetes, not influenza, is the true pandemic. It is intertwined with overweight, and both conditions presage type 2 diabetes mellitus and many other health problems. In fact, prediabetes (glucose intolerance) could be considered "ground zero" in many of today's chronic health problems.

Overweight and obesity are the most common preludes to type 2 diabetes, and the statistics are nothing less than alarming. In the United States, three-fourths of American adults are currently overweight or obese. Half of those are obese, and one in every 20 adults is morbidly obese. One-third of children are also overweight and obese. Meanwhile, 24 million Americans have type 2 diabetes, and an estimated 100 million have some form of prediabetes. Each

year, one million Americans graduate from prediabetes to type 2 diabetes. Similar trends are occurring in Canada.<sup>1</sup>

Depending on the diagnostic test used, prediabetes may be referred to as impaired fasting glucose, impaired glucose tolerance, insulin resistance, hyperinsulinemia, metabolic syndrome, syndrome X, and hypoglycemia. Each of these diagnoses points to a deleterious metabolic response to carbohydrates, particularly refined sugars and starches.

One might argue that a diagnosis of prediabetes medicalizes an illness that does not yet exist, much the way some physicians have argued in favor of treating prehypertension or moderately elevated cholesterol. However, disease processes are not black and white, with patients being healthy one day and sick the next. Rather, prediabetes is part of the

progression from healthy to sick, and early treatment (not merely the masking of symptoms) is far more likely to achieve a complete reversal compared with later treatment.

### **The Health Consequences of Prediabetes**

Which occurs first—prediabetes or overweight? Or is the question a chicken-or-egg conundrum?

Although hyperinsulinemia exists in one-fourth of thin people,<sup>2</sup> a recent clinical trial suggests that gaining a very modest amount of weight initiates metabolic changes that lead to prediabetes.<sup>3</sup> In the trial, researchers asked 10 healthy, thin men in their twenties to increase their food consumption by 300 to 500 calories daily for four and one-half months. The objective was to track the metabolic consequences of a modest two-point increase in body mass, approximately 10 pound in weight. With the increased weight, the men did not secrete more insulin compared with baseline levels, but they did lose their ability to remove insulin from the blood, one of the signs of insulin resistance. Because insulin is lipogenic, the inability to clear the hormone from the blood likely promotes further weight gain and an exacerbation of insulin resistance.

One of the current determinations of prediabetes—having a fasting glucose between 100 to 125 mg/dL—ignores the risks associated with relatively small increases in the normal range of blood sugar. For example, men with a fasting glucose of 87 mg/dl are far more likely to develop type 2 diabetes, compared with men who have a fasting glucose of 81 mg/dL.<sup>4</sup> In other words, a moderately high-normal glucose is a risk factor for type 2 diabetes.

Furthermore, prediabetes is strongly associated with more than just an increased risk of type 2 diabetes. The intertwining of prediabetes, type 2 diabetes, overweight, and obesity are also associated with an increased risk of coronary artery disease, cancer, Alzheimer's disease, serious eye diseases, kidney disorders, sleep problems, gynecomastia in men, elevated blood lipids, hypertension,

inflammatory diseases, hypercoagulation, premenstrual syndrome, early puberty, polycystic ovary syndrome, sleep apnea, erectile dysfunction, food cravings, anxiety, depression, mood swings, cognitive impairment, and many other health problems.<sup>5</sup>

Recent studies have provided a clearer picture of how prediabetes affects cognitive function. Insulin resistance can occur in the brain, not just in muscle tissue.<sup>6</sup> In addition, elevated glucose levels have been shown to slow thinking processes and to increase the number of errors on tests.<sup>7</sup> Elevated glucose levels inhibit production of orexins, a family of peptides involved in alertness.<sup>8</sup> Decreased activity of orexins may partly explain postprandial tiredness, another sign suggestive of hyperglycemia and prediabetes.

Some of the other early signs of prediabetes include abdominal adiposity, mood swings, and sugar and carbohydrate cravings. Skipping breakfast (or consuming a high-sugar or high-starch breakfast) and eating large, late dinners are also commonly associated with prediabetes.

### **The Importance of Measuring Insulin Levels**

Although health-care practitioners tend to use glucose (fasting glucose, glucose-tolerance test, or hemoglobin A1c;HbA1c) to diagnose prediabetes and type 2 diabetes, the addition of a fasting insulin test can provide a clearer—and earlier picture—of prediabetes. Combined with tests for glucose, fasting insulin becomes a powerful predictor of type 2 diabetes. Hyperinsulinemia may exist 10 to 15 years before glucose levels become elevated and physicians diagnose type 2 diabetes.<sup>9</sup> Such an early warning provides a window to implement dietary changes to restore normal glucose tolerance.

There are many health consequences of hyperinsulinemia (as opposed to hyperglycemia per se). In addition to being indicative of insulin resistance, hyperinsulinemia can:

- Trigger reactive hypoglycemia
- Promote abdominal obesity
- Increase activity of 3-hydroxy-3-methylglutaryl coenzyme A activity

- Elevate triglycerides and low high-density lipoprotein
- Increase sodium retention and magnesium depletion
- Increase arachidonic acid production
- Increase production of interleukin-6
- Contribute to polycystic ovary syndrome
- Promote aromatase activity
- Increase the risk of breast and other cancers,
- Increase the risk of gastric reflux

The measurement of fasting (or postprandial) insulin is not a new or novel concept. The first research to identify the role of hyperinsulinemia in prediabetes (which was also termed "occult diabetes" and "diabetes mellitus in situ") was published in 1975.<sup>10</sup> Like so many studies in nutritional medicine, this one has been largely lost to the dusty pre-internet shelves of medical libraries. In this seminal study, Dr. Joseph R. Kraft described patterns of glucose and insulin in 3,650 men and women and noted that many subjects had normal glucose levels but abnormally elevated insulin levels. He proposed that prediabetes existed in subjects whose fasting insulin levels was 13 mIU/ml or higher—a level fairly consistent with the views of many contemporary orthomolecular physicians.

By measuring fasting insulin, clinicians can reduce the risk of obtaining a "false normal" from measuring only fasting glucose, postprandial glucose, or HbA1c. For example, an apparently normal fasting glucose of 87 mg/dl combined with a fasting insulin of 15 mIU/ml would be suggestive of prediabetes. In terms of clinical guidelines, a fasting glucose of 90 mg/dl or higher should justify testing for hyperinsulinemia, and any patient with significant abdominal obesity should also be tested for hyperinsulinemia.

Although the standard laboratory range for normal fasting insulin is 6 to 35 mIU/ml, this range is too broad to be clinically meaningful. A fasting insulin of less than 10 mIU/ml is excellent, and less than 7 mIU/ml would be ideal. Another useful tool for assessing patients is the Homeostasis Assessment Model for Insulin Resistance

(HOMA-IR) calculator. The HOMA-IR calculator is simple to use and can be downloaded without cost from [www.dtu.ox.ac.uk/index.php](http://www.dtu.ox.ac.uk/index.php). Simply input a patient's fasting glucose (in mg/dl or mmol/l) and insulin (in mc/dl or pmol/l) into the HOMA-IR calculator. The results of the HOMA-IR calculator correlate closely with those of the euglycemic clamp, which is difficult to use in a clinical (nonresearch) setting. As a generally rule, a HOMA-IR of 3.5 or less is considered good, and a HOMA-IR of 1.0 if considered normal for a 35-year-old male. The lower the number, the more insulin sensitive a patient is; the higher the number, the more insulin resistant.

### Dietary Causes of Prediabetes

Prediabetes (including overweight) is a nutritional disease, and in most cases it is best treated nutritionally. The diagnosis can be frightening for many people, but the negative impact can be balanced with a positive—that prediabetes is an opportunity to improve one's health. The nutritional causes have been described in many articles and books, and they include the consumption of too many calories, too many refined sugars and sugarlike carbohydrates (mostly from grains), too many trans fats, and too many "junk" cooking oils, such as soybean and corn oils. Genetics appears to play only a minor role in the risk of prediabetes and type 2 diabetes, although epigenetics may play a greater role in children and in the multigenerational risk of these diseases.

Most men need only approximately 2,000 calories daily and most women need only approximately 1,600 calories daily, unless they regularly engage in exercise or other physical activities. However, according to recent estimates, the "average" American now consumes 3,900 calories per day. It is all too easy to consume an enormous quantity of mostly carbohydrate (and sugar) calories. A typical lunch at McDonald's contains 1,700 calories, some Pizza Hut 12-inch pizzas contain 2,640 calories, a Starbucks Frappuccino contains 730 calories, and a 64-ounce soft drink contains 800 calories and ap-

proximately one-half pound of sugars. These extremely high-calorie foods lead to weight gain, hyperinsulinemia, and hyperglycemia.<sup>5</sup>

Carbohydrates (especially sugars and sugarlike processed carbohydrates) have significantly different effects from those of protein on glucose and insulin. Graphs published in *Marks' Basic Medical Biochemistry* textbook clearly show the difference between a high-carbohydrate and high-protein meal on glucose and insulin levels. (*Marks'* did not describe the specific composition of the meals.) The high-carbohydrate meal promoted steep increases in both glucose and insulin levels, which could easily be considered indicative of prediabetes or type 2 diabetes. In contrast, the high-protein meal had no effect on glucose and produced only a slight increase on insulin levels.<sup>11</sup>

Is a low-glycemic diet the solution? It may not be if people are guiding by low-glycemic foods as opposed to low-glycemic nutritious foods. For example, fettuccini, spaghetti, ice cream, and M&M peanut candies are low-glycemic foods, but they are not very nutritious. A study of 23 apparently healthy men and women revealed fundamental flaws with low-glycemic foods. As a group, the subjects' average glycemic response to white bread was 70. (One might question why artifacts such as white bread and glucose are used as the benchmarks for measuring the glycemic index of foods.) However, the glycemic response to white bread ranged from 43 to 132 among the individual subjects, reflecting a range from very carbohydrate tolerant to very carbohydrate sensitive. Furthermore, the same individuals exhibited as much as an 18 percent variation in their glycemic responses on different days, with the difference likely related to what they consumed before the test meal. In addition, the researchers seemed to ignore that the baseline characteristics of some of the "healthy" subjects actually were suggestive of prediabetes.<sup>12</sup>

The ideal diet for preventing and reversing prediabetes may be a modern approximation of the diet human beings and their primate ancestors evolved eating. The Paleolithic diet emphasized quality animal

proteins and high-fiber vegetables, with a notable absence of grains, dairy products (other than mother's milk in infancy), and processed oils.<sup>13,14</sup>

The evolutionary diet was nutrient dense in that it supplied large amounts of vitamins, minerals, and vitaminlike nutrients with few if any empty (starch- or sugar-rich) calories, such as sugars or starches devoid of protein, essential fats, or micronutrients. In terms of reversing prediabetes and overweight, the Paleolithic diet is superior to the Mediterranean diet, which is often touted as a healthy diet. In one study, researchers compared the effects of a Mediterranean and a Paleolithic diet on 29 subjects with ischemic heart disease and either glucose intolerance or type 2 diabetes. After 12 weeks, the Mediterranean diet led to a 7 percent decrease in glucose and a 1.1-inch decrease in waist circumference. In contrast, the Paleolithic diet led to a 29 percent decrease in glucose and a 2.2 decrease in waist circumference.<sup>15</sup>

### Therapeutic Nutrition

How can a person translate the Paleolithic diet to current available foods? One of the keys is to emphasize fresh foods over most foods sold in boxes, cans, jars, bottles, and bags. Packaging is usually a sign of food processing and reduced nutritional value. Both protein and high-fiber produce improve glucose and insulin levels.<sup>16,17</sup> Fish, chicken, and grass-fed meats provide excellent sources of protein, and high-fiber vegetables and fruits provide a wealth of nutrients. (According to the Paleolithic nutrition data, no human culture had been entirely vegetarian.) Breakfast is the cornerstone meal of the day—consuming a protein-centered breakfast (e.g., with eggs), along with some vegetables, and fresh fruit quickly improves glucose and insulin levels, as well as energy levels. As a general rule, carbohydrates (starches) should be tailored to weight and physical activity.

Nutrients provide the chemical foundation of biochemistry, and many dietary supplements can also enhance insulin sensitivity and reduce glucose levels. These supplements strengthen weak biochemical pathways in-

volved in glucose tolerance, and some (e.g., biotin) have significant roles in regulating gene expression. Some of the most beneficial supplements include:

Alpha-lipoic acid and R-lipoic acid, 300 to 600 mg daily;  
Chromium, 1,000 mcg daily;  
Biotin, 3,000 to 5,000 mcg daily;  
Silymarin, 600 mg daily;  
Omega-3 EFAs, 1,000 to 3,000 mg daily;  
Vitamin C, 1,000 to 3,000 mg daily;  
Pycnogenol,<sup>®</sup> 150 to 300 mg daily;  
Resveratrol, 300 to 500 mg daily;  
Vitamin D3, 1,000 to 5,000 mg daily, combined with calcium, 500 to 1,000 mg daily;  
Vitamin K, 5,000 mg of vitamin K1 or K2 (MK-4) daily.

These dosages are suggestions, and they can probably be reduced when any of these supplements are used in combination.

All people, not just patients (or nutrition consulting clients), have a tendency to rationalize unhealthy food choices. The reasons may be due largely to the difficulty of changing one's habits and to the powerful grip of food addictions. Part of the clinician's role is to help motivate patients to make dietary and lifestyle changes that improve their health. Prediabetes is an opportunity to improve health, and it is wise to seize this opportunity. Not doing so will eventually lead to type 2 diabetes, which is far more difficult to reverse and almost always requires some form of pharmaceutical intervention.

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