

## Diet to Prevent and Reverse Insulin Resistance and Type 2 Diabetes

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- I. The first step to using dietary means to prevent the development of type 2 diabetes is the early identification of those patients who have a genetic propensity to develop insulin resistance (IR).
  - A. People who have a family history of type 2 diabetes mellitus (DM) are more likely to have genetic traits that predispose them to also develop type 2 DM.
    1. Analysis of data from the Bogalusa Heart Study found that many of the metabolic abnormalities associated with insulin resistance start to show up in childhood or early adulthood in the offspring of parents with type 2 diabetes.<sup>1</sup>
    2. But heredity is not necessarily destiny.
  - B. Nearly all patients who ultimately develop type 2 diabetes had IR for many years before their blood sugar (BS) level rose high enough for a diagnosis of type 2 DM.
  - C. The metabolic changes associated with IR are now called the “metabolic syndrome” (formerly called “syndrome X”). It has also been called the “insulin resistance syndrome”, the “deadly quartet” and the “dysmetabolic syndrome”. IR is associated with an increased risk of developing both type 2 diabetes mellitus (DM) and cardiovascular disease (CVD).
  - D. The metabolic syndrome appears to result primarily from IR and its metabolic sequelae. These metabolic changes are characterized initially by increased fasting insulin levels and a delayed clearance of a glucose load from the blood. Most people with the metabolic syndrome have elevated serum triglyceride levels, increased small dense LDL particles and decreased HDL-C levels, increased blood pressure (BP), and increased fasting blood sugar (BS) level. These metabolic abnormalities are believed to result largely from IR.<sup>2</sup>
  - E. Most of the people who have the metabolic syndrome have an increased amount of abdominal fat and have a high risk of eventually developing type 2 DM.
    1. The metabolic syndrome also greatly increases the risk of cardiovascular disease (CVD).
    2. Many patients with the metabolic syndrome who were headed towards type 2 diabetes succumb to a heart attack or stroke and die before ever being diagnosed with diabetes.
    3. Clearly there is a need to identify those at risk early in life and intervene to prevent the accumulation of excess body fat stores that bring on the insulin resistance.
  - F. There still is no routine laboratory test widely available to measure IR directly.
    1. However, the new National Cholesterol Education Program (NCEP) guidelines established 5 risk factors common among patients with the Metabolic Syndrome.<sup>3</sup>
    2. A patient with 3 or more of these 5 risk factors listed in **Table 1** below are now to be characterized as having this metabolic syndrome.

**Table 1. NCEP Guidelines for Clinical Identification of the Metabolic Syndrome.**

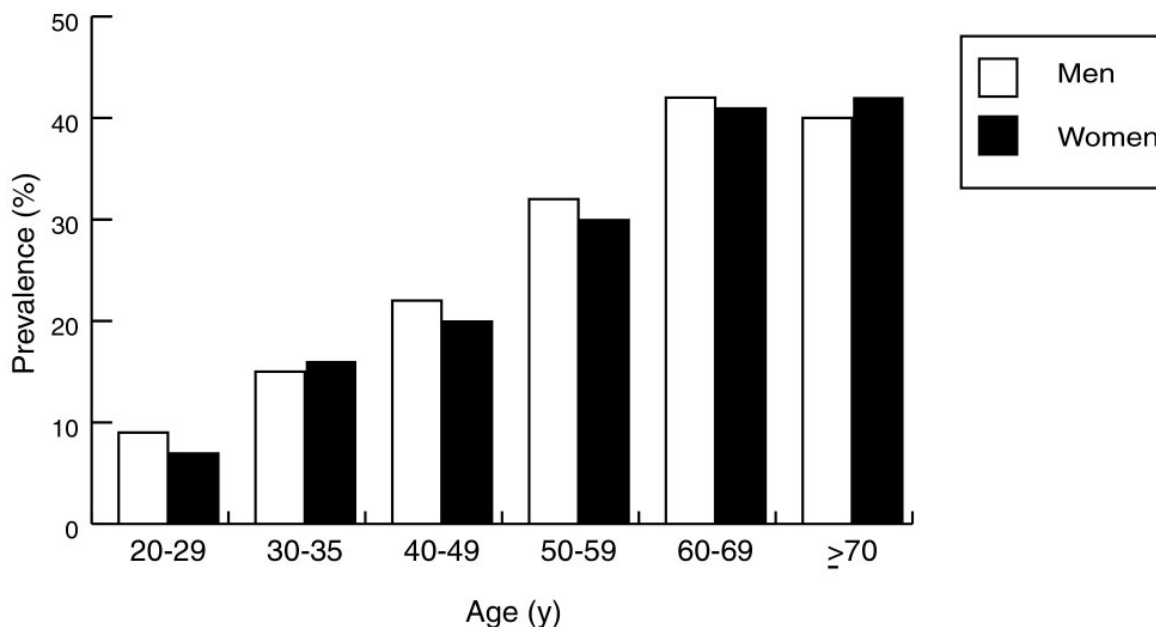
<u>Risk Factor</u>	<u>Defining Level</u>
1. Abdominal Obesity Waist circumference	
Men	≥40 in.
Women	≥35 in
2. Triglycerides	≥150mg/dl
3. High-density lipoprotein cholesterol	
Men	<40mg/dl
Women	<50mg/dl
4. Blood pressure	≥130/≥85mm Hg
5. Fasting glucose	≥100mg/dl*

\* Based on Latest American Diabetes Association Reclassification of Impaired Fasting BS Cutpoint

G. The prevalence of the metabolic syndrome for US adults in different age groups using the NCEP guidelines<sup>4</sup> is shown in **Figure 1** below.

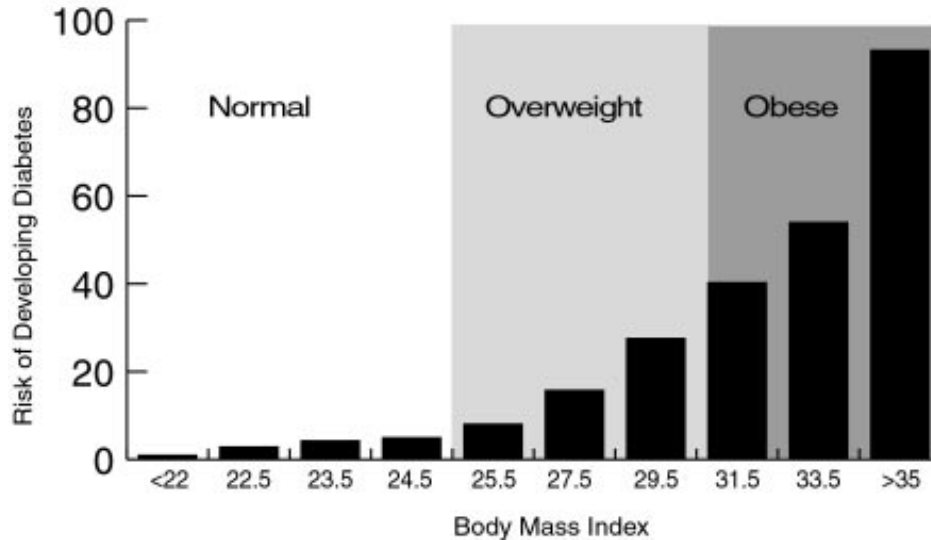
**Figure 1.**

**Age-Specific Prevalence of the Metabolic Syndrome Among U.S. Adults**



- H. Note that **Figure 1** shows the prevalence of the metabolic syndrome increasing with age. It seems likely that most of this increase reflects the increasing BMI and body fat stores in middle-aged and older adults in the US.
- I. Data from the Nurses' Health Study are shown in **Figure 2** clearly demonstrate that the risk of developing type 2 DM increases markedly with increasing BMI.<sup>5</sup> The data show the relative risk of developing type 2 DM over a 14y follow-up period in middle-aged (35-59y) women at the start of the study.

**Figure 2. Relative risk of developing Type 2 DM in middle-aged US women**

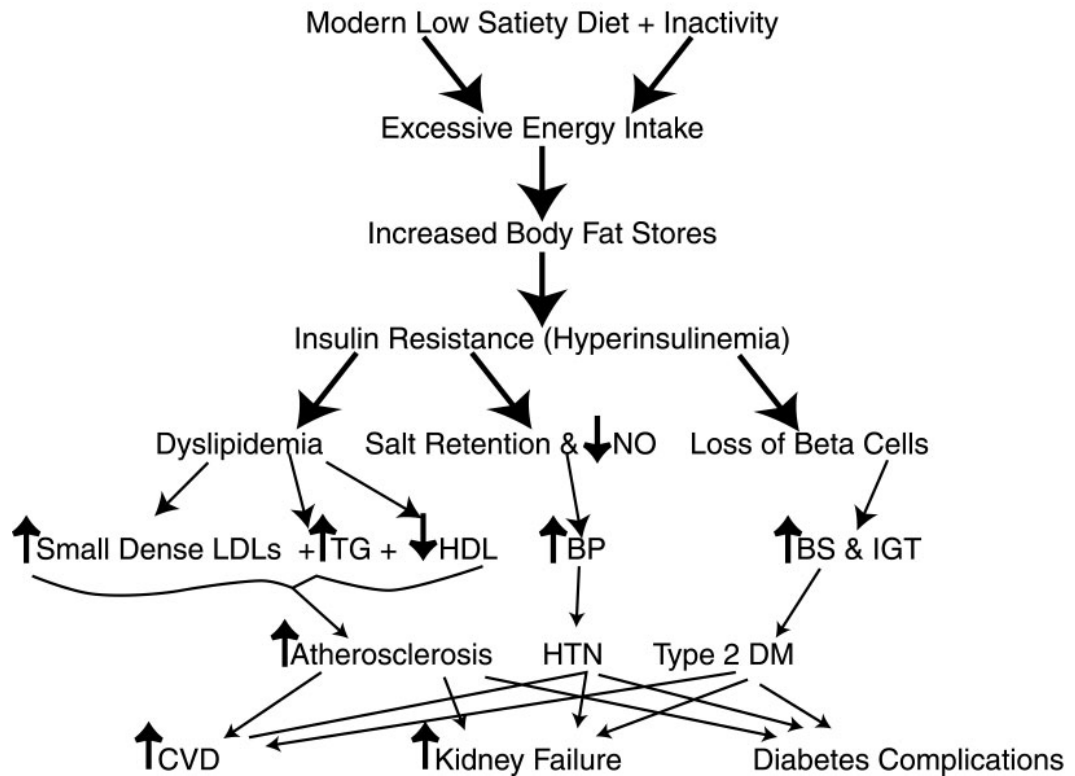


Colditz GA, et al. Ann Intern Med 1995;122:481

- II. How does a typical modern diet coupled with a sedentary lifestyle promote IR, the metabolic syndrome and ultimately type 2 DM and/or CVD?
- A modern diet high in fat and especially Saturated fatty acids (SFA) and processed meats promotes excessive energy intake, the accumulation of increased body fat stores and an increased risk of developing type 2 DM.<sup>6,7</sup>
  - As body fat stores expand beyond a certain point, which varies between people and with age, it leads to the development of IR.
  - This IR leads eventually to the development of type 2 DM and CVD as outlined in **Figure 3**.
  - Over time insulin resistance and perhaps the increased flux of free fatty acids (FFA) from adipocytes appears to damage beta-cells. Over time this reduces insulin production capacity to the point where the beta-cells can no longer produce sufficient insulin to overcome the impact of insulin resistance on blood sugar removal. As the beta-cells fail both fasting and postprandial B.S. levels begin to rise into the IGT and eventually type 2 DM ranges.<sup>8</sup>

**Figure 3.**

### Pathophysiology of Insulin Resistance and its metabolic sequelae



- III.** The development of IR, the metabolic syndrome and ultimately type 2 DM is the result of both genetic and environmental factors.
- A. In genetically susceptible animals, research has shown that simply offering them a diet high in fat and refined carbohydrate leads to overeating and the rapid induction of insulin resistance (IR) within just a few days.<sup>9</sup>
  - B. In genetically susceptible people a diet high in fat and refined carbohydrate coupled with a sedentary lifestyle also triggers the development of IR and the metabolic disturbances associated with it primarily because it causes the accumulation of excessive fat stores.<sup>10</sup>
  - C. Most research suggests that a diet higher in SFA and sucrose/fructose and lower in omega-3 polyunsaturated fatty acids (PUFA) is more likely to promote increased ad libitum energy intake and IR than a diet higher in unrefined carbohydrate.<sup>11 12</sup>
  - D. Weight loss lowers FFA levels, improves insulin sensitivity, and blood lipids.<sup>13</sup>
- IV.** So how does the NCEP justify its recommendation for increasing dietary fat in people characterized as having the metabolic syndrome?

A. The newest NCEP guidelines now recommend a 35% fat diet for people identified with 3 or more of the 5 metabolic characteristics of the insulin resistant syndrome.

1. Many studies have shown that high-carbohydrate diets do indeed lead to higher BS levels, higher insulin levels and/or adverse effects on blood lipids when compared to diets higher in unsaturated fat and lower in carbohydrate.<sup>14 15 16</sup>
2. However, all of the studies that have shown these presumably adverse metabolic effects on the higher carbohydrate diet compared to the higher fat diet required the test subjects to consume the same number of calories (and/or maintain the same body weight) on both the high-fat and high-carbohydrate diets.
3. In one of these studies the authors stated that they had difficulty getting people to eat as many calories on the high-carbohydrate diet as they ate willingly on the higher fat diet.<sup>17</sup>
4. When a high-carbohydrate diet was compared to a high monounsaturated fat diet but both diets were fed ad libitum in addition to at the same energy level the negative metabolic effects attributed to the high-carbohydrate diet were shown to largely disappear. If anything when fed ad libitum, the high-carbohydrate diet appeared to be superior to the higher monounsaturated fat diet for reducing CVD disease risk factors because it reduced energy intake.<sup>18 19</sup>
5. There is little disagreement about the role of excessive energy intake and inactivity in promoting the development of IR and the metabolic syndrome. All researchers seem to agree that this syndrome occurs in genetically susceptible individuals primarily as the result of the accumulation of excessive body fat stores.
6. There is also general agreement that IR and the metabolic syndrome is a precursor to the development of type 2 DM.<sup>20</sup>
7. However, there is reason to believe that the short-term (presumably) beneficial impact of a diet higher in unsaturated fat compared to one higher in carbohydrate on some of the metabolic abnormalities associated with insulin resistance may not persist in the longer term.<sup>21</sup> This is largely because it is more difficult to lose weight if the satiety value of the higher fat diet is less than that of a diet with less fat.

V. Studies of the US population suggest certain characteristics of a modern diet increase the risk of developing insulin resistance and ultimately type 2 DM. These characteristics include relatively little cereal fiber and relatively large amounts of fat (especially saturated and hydrogenated) and refined carbohydrates (especially sugar).

- A. Epidemiological data from US women and men have found a diet with more hydrogenated fat and saturated fat from animal products are associated with the development of IR and the metabolic syndrome whereas a diet higher in unrefined carbohydrate appears protective.<sup>22 23</sup>
- B. Of course epidemiological studies finding a correlation do not prove cause and effect. That requires more definitive studies such as randomized clinical trials.
- C. Two studies have now shown that a healthier diet, exercise and weight loss can slow the progression from IGT to type 2 DM.
  1. In the Finnish study 522 obese subjects with IGT were randomized to receive either routine diet and exercise counseling (control group) or a more intensive individualized instruction about weight loss, a healthy diet and exercise (intervention group). After a 3.2-year follow up those in the intervention group were 58% less likely to have progressed to type 2 DM than those in the control group.<sup>24</sup>
  2. The DPP trial involved 3,234 subjects with IGT (about 45% from minority groups). The subjects were randomly assigned to the Glucophage (metformin) therapy group, the intensive dietary and exercise counseling group or simply a placebo group. After 2.8 years there was a 58% reduction in the progression to type 2 DM in the intensive diet and

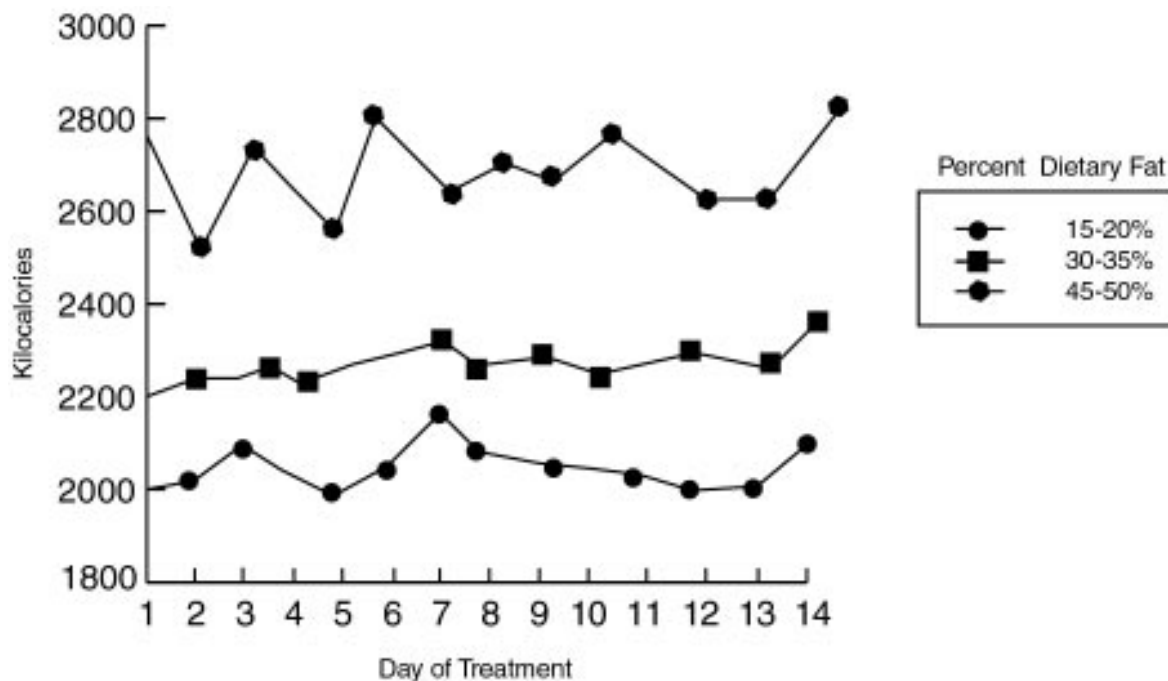
exercise group than in the placebo group. This was much better than the 31% reduction in the progression to type 2 DM in the Glucophage group.<sup>25</sup>

3. These two randomized clinical trials have now clearly demonstrated that a diet low in saturated fat and high in legumes, pulses, fruits, vegetables and whole grains in conjunction with an exercise program resulted in modest weight loss and a dramatic reduction in the progression from IGT to type 2 DM.
4. Surgical treatment of obesity that resulted in a 16% reduction in initial body weight after 8 years cut the risk of developing type-2 DM by more than 6-fold compared to control subjects who did not get the surgery or lose weight.<sup>26</sup>
5. It seems logical to assume intervening even earlier in the course of the disease process would be even more effective at preventing or at least delaying the development of type 2 DM. This is why identifying patients with IR and the metabolic syndrome even sooner before IGT develops is important. At this point beta cell function is even less impaired than it is with IGT patients. It is likely a healthier diet and exercise program that leads to a reduction in body fat stores would prevent them from ever developing type 2 DM and also dramatically cut their risk of CVD.

VI. What is the best dietary approach for patients with the metabolic syndrome?

- A. The current NCEP guidelines emphasize a diet that is higher monounsaturated fat (35% en.) for patients identified as having the metabolic syndrome.
- B. When the fat content of foods was manipulated covertly and palatability was held constant, human subjects were shown to increase their ad libitum caloric intake and gain weight as dietary fat increased at the expense of carbohydrate.<sup>27</sup> Figure 4 below shows the results of this study.

Figure 4. Impact of increasing dietary fat on ad libitum energy intake.



Lissner L, Levitsky DL, Strupp BJ et al. Dietary fat and the regulation of energy intake in human subjects. *Am J Clin Nutr* 1987;46:886-92

C. As **Figure 4** shows the ad libitum energy intake increased 658kcal per day on average on the high-fat diet compared to the low-fat diet. It seems likely that the addition of more fat to low-fat foods reduces satiety and increases ad libitum calorie intake and promotes weight gain. Likewise, the failure to remove fat from high fat foods like milk and meat will likely result in less satiety per calorie and so a greater ad libitum calorie intake.

D. However, high-fat diets do not invariably lead to increased calorie intake compared to higher carbohydrate diets if the energy density (ED) of the two diets is held constant.<sup>28</sup>

E. It has been shown that on both a 20% and 40% fat diet that at least in the short-term it is primarily variation in the ED of the diet that leads to differences in ad libitum caloric intake.<sup>29 30</sup> It appears that the main reason ad libitum calorie intake tends to increase when the percent of calories from fat is higher is that more fat usually means a higher ED.

F. The addition of fat to foods invariably increases the food's ED and most naturally occurring high-fat foods have a high to very high ED so it is very difficult to consume a high-fat but low ED diet.

G. By contrast, fresh fruits, vegetables, many whole grain foods, non-fat dairy products and most seafood have a very low to moderate ED. It is precisely because diets higher in fat are generally more calorie dense that they are also more likely to lead to excessive caloric intake, weight gain and metabolic problems, including metabolic syndrome when compared to diets higher in carbohydrate but with a lower ED.

H. A study that compared a low ED diet consisting primarily of minimally processed plant high in fiber and low in fat to a typical high-fat, Western diet found that the ad libitum caloric intake was dramatically lower on the low ED diet (3000 vs. 1570 Cal/day).<sup>31</sup> In this study the satiety ratings of the high and low ED diets were similar, as was food acceptance. In this study, the high ED diet had 681 cal/lb and the low ED diet had only 318 cal/lb.

I. It appears that a high fat and energy dense diet coupled with a sedentary lifestyle that promotes obesity.<sup>32</sup> Excess body fat stores leads to insulin resistance and the associated metabolic problems in genetically predisposed individuals.

J. It is challenge to plan acceptable meals that average about 300-400 calories per pound and are high in fiber.

1. Such meal plans require more nutrition knowledge than most Americans possess. They also require more culinary skill than most Americans possess to make them palatable. This is because the palatability of foods tends to decrease with decreasing ED even though ED is the primary determinant of ad libitum caloric intake.<sup>33</sup>
2. Nevertheless, a high-fiber and low ED meal plan is probably more comparable to what our ancient ancestors consumed and what the human body is biologically designed to handle.<sup>34</sup>
3. Returning to a less processed and refined diet with far less concentrated calories and markedly increasing daily activity may be necessary for most people to lose 30 or more pounds and keep it off long-term without chronic hunger.<sup>35 36</sup>
4. The Pritikin diet and exercise program has been shown to reverse many of the metabolic disturbances associated with insulin resistance. This very low fat, high-fiber, near vegetarian diet combined with exercise has been shown to dramatically lower serum TG, hsCRP, LDL-C, BP and promote weight loss in most people when calorie intake is ad libitum. In people with insulin resistance it has been shown to lower serum insulin levels. In people with type 2 DM it has been shown to improve blood sugar regulation and reduce or completely eliminate the need for oral hypoglycemic agents.<sup>37 38 39 40 41</sup>

K. Refining and processing of foods usually increases both the GI and the ED. Therefore, the consumption of highly refined and processed foods may contribute to the development of weight gain and the metabolic syndrome.

1. In general, more processed and refined foods have both a higher GI and ED than foods in their natural whole state and also provide less satiety.<sup>42</sup> But is it the higher insulin response or the greater ED of such foods that is primarily responsible for their lower satiety value?
2. The much-maligned potato does cause a relatively high glycemic response and insulin output compared to many other foods but it is also a very high satiety food.<sup>43</sup> It is unclear what the long-term impact of eating more or less potatoes might be on the development of type 2 DM but if they aid weight loss they would likely reduce the risk.
3. A food's ED and fiber content appear to be far more important than its GI in determining its satiety value. Because foods with a high satiety index are likely to lead to lower total calorie intake when consumed ad libitum, clinicians should perhaps focus more on a food's ED and satiety/calorie ratio than simply its GI.

## VII. Conclusions:

- A. The current NCEP guidelines suggest a diet higher in unsaturated fat is preferable to a diet higher in carbohydrate for treating patients characterized with the metabolic syndrome. This recommendation remains speculative because is not supported by well-designed clinical trials. There is also reason to believe that diets higher in fat will increase ED and promote excessive energy intake.<sup>44</sup>
- B. The best diet for improving insulin sensitivity is most likely to be an intensive one that promotes the greatest loss of excessive body fat stores.<sup>45</sup>
- C. Even if weight is not lost on a high-carbohydrate diet the type of high-carbohydrate foods consumed is important.
  1. A high-carbohydrate diet consisting largely of natural foods with a high-fiber content is preferable to a diet with more refined and processed foods because it will favorably impact blood lipids and blood sugar control.
  2. The results of one study that showed a drop in serum triglycerides (rather than a rise that is typically seen on high-carbohydrate diets). The authors conclude "there appear to be important cardiovascular benefits from choosing a plant-based diet over a convenience-food based diet for meeting national dietary guidelines."<sup>46</sup>
  3. Of course the main advantage of a high-fiber, low-fat and low-ED diets is that in most overweight or obese subjects it will reduce ad libitum energy intake and this in turn should improve insulin sensitivity.
- D. Preventing weight gain will largely prevent the development of IR and help prevent the development of type 2 DM and CVD in those genetically predisposed to develop IR and type 2 DM.
- E. Taken together the results of the Finnish study and the DPP trial clearly show that the progression from IGT to type 2 DM can be slowed significantly with about 30 minutes of exercise a day, a healthier diet and the loss of only 5-10% of body weight.
- F. Losing as much excess body fat as possible by adopting a healthier diet and exercise program will largely reverse IR and its metabolic abnormalities and greatly diminish the risk of developing type 2 DM and CVD.
- G. The best diet for promoting weight loss without inducing chronic hunger is one composed largely of minimally processed whole grains, fruits, vegetables and legumes. Modest amounts of nonfat dairy products and a little omega-3 rich seafood should also be part of the optimal diet. The overall diet should have a high-fiber content and a low energy density.
  1. Both saturated fat and partially hydrogenated fats promote weight gain and increase the risk of CAD. They should be minimized as much as possible in the diet.

2. Refined carbohydrates and particularly those containing fructose appear to promote weight gain and have adverse metabolic effects in those with the metabolic syndrome. It would be prudent to minimize the intake of refined fructose, sucrose and high-fructose corn syrup as much as possible in the diet of individuals with evidence of insulin resistance.<sup>47</sup>

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