

Invited Review

Low-Carbohydrate Diet Review: Shifting the Paradigm

Adele H. Hite, MAT; Valerie Goldstein Berkowitz, MS, RD, CDE; and
Keith Berkowitz, MD, MBA

Financial disclosure: none declared.

Low-Carbohydrate Diet Review: Shifting the Paradigm

Adele H. Hite, MAT; Valerie Goldstein Berkowitz, MS, RD,
CDE; and Keith Berkowitz, MD, MBA

Financial disclosure: none declared.

What does a clinician need to know about low-carbohydrate (LC) diets? This review examines and compares the safety and the effectiveness of a LC approach as an alternative to a low-fat (LF), high-carbohydrate diet, the current standard for weight loss and/or chronic disease prevention. In short-term and long-term comparison studies, ad libitum and isocaloric therapeutic diets with varying degrees of carbohydrate restriction perform as well as or better than comparable LF diets with regard to weight loss, lipid levels, glucose and insulin response, blood pressure, and other important cardiovascular risk markers in both normal subjects and those with metabolic and other health-related disorders. The metabolic, hormonal,

and appetite signaling effects of carbohydrate reduction suggest an underlying scientific basis for considering it as an alternative approach to LF, high-carbohydrate recommendations in addressing overweight/obesity and chronic disease in America. It is time to embrace LC diets as a viable option to aid in reversing diabetes mellitus, risk factors for heart disease, and the epidemic of obesity. (*Nutr Clin Pract.* 2011;26:300-308)

Keywords: weight loss; reducing diet; carbohydrate-restricted diet; fat-restricted diet; diabetes mellitus; cardiovascular diseases

A low-carbohydrate (LC) diet is not a new dietary concept. In 1825, Jean Brillat-Savarin published *The Physiology of Taste*, in which he offered a solution to obesity. His solution was to restrict everything that contained starch or flour. Since then, clinicians have adopted a similar approach for their patients. A LC diet limits daily carbohydrate intake to 30-130 g/d. A low-fat (LF) diet restricts daily fat intake to 10%-15% of total calories. Recent short-term and long-term randomized controlled trials—considered the gold standard of research—have shown that LC diets perform as well as or better than LF diets with regard to weight loss, glucose and insulin response, and important cardiovascular risk markers in both normal subjects and those with metabolic and other health-related disorders. These results, and the fact that longitudinal studies have found limited benefit of the LF dietary approach for preventing chronic disease,¹⁻⁴ make a LC approach an attractive dietary option.

Given the underlying cause of carbohydrate intolerance, it is frequently surprising to clinicians and patients alike that there is any question that some forms of reduction in dietary

carbohydrate is the first line of attack against diabetes and metabolic syndrome. The American Diabetes Association concurs that a LC diet is an acceptable approach for weight loss for up to 1 year. This recommendation also cites evidence that markers of cardiovascular disease (specifically serum levels of triglycerides [TG] and high-density lipoprotein cholesterol [HDL-C]) are improved with LC diets compared with LF diets (Figure 1) and acknowledges the benefit of carbohydrate restriction for glycemic control.⁵ Taking the 1-year mark at face value, the clinician is confronted with the question, “What diet do I recommend on day 366?” If a patient is doing well on a LC diet for a year, is there a reason to return the patient to his or her previous, presumably less beneficial, diet after a year? It is also important to understand that glycemic control in patients with diabetes⁶ and lipid profiles in normal people⁷ are improved by carbohydrate restriction even in the absence of weight loss.

The argument may be made that it is not the LF diets that have failed but the will of the American people to follow them. From a clinician’s perspective, we prefer not to blame patients but to assist them; in fact, Americans are clearly aware of the purported dangers of fat and have made a substantial attempt to alter the content of their diets.^{8,9} That the increase in calories in the American diet over the past 30 years is almost entirely due to an increase in carbohydrate intake should be reason enough to consider carbohydrate reduction a principal target for improving the health of Americans (Figure 2).⁹ First demonstrated by LaRosa et al¹⁰ in 1980 and confirmed many times

From ¹the Department of Nutrition, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; and ²the Center for Balanced Health, New York, New York.

Address for correspondence: Valerie Goldstein-Berkowitz, 7 West 51st Street, New York, NY 10019; e-mail: Valerie@centerforbalancedhealth.com.

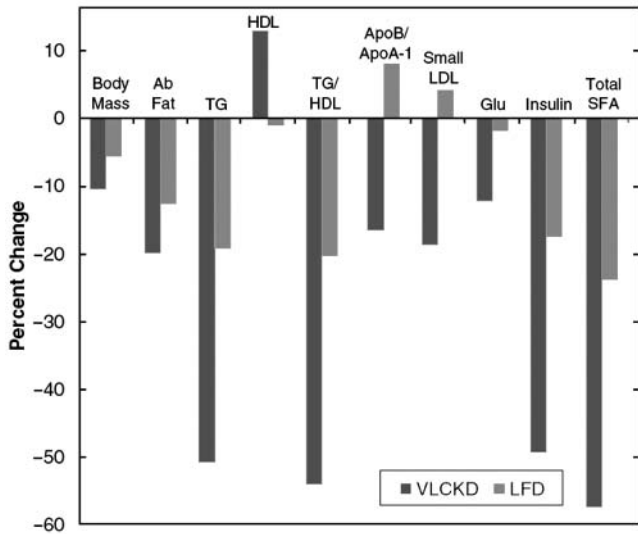


Figure 1. Comparison of low- and high-carbohydrate diets at 12 weeks. Results from trial in which 40 subjects with atherogenic dyslipidemia were randomly assigned to either diet²². Ab, abdominal; ApoA-1, apolipoprotein A-1; ApoB, apolipoprotein B; Glu, glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SFA, saturated fatty acids; TG, triglycerides. LFD, low-fat diet. Adapted from Jakobsen MU, O’Reilly EJ, Heitmann BL et al. Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies. *Am J Clin Nutr.* 2009;89:1425-1432 with permission from the American Society for Nutrition.

since,¹¹ LC diets do not, by necessity, require higher fat or protein intakes, as a spontaneous decrease in overall calorie consumption frequently results in little protein or fat added back in for the carbohydrate that is removed. Although the “one-size-fits-all” approach to diet is universally disavowed, there is nevertheless a tendency for healthcare providers to recommend a single approach even when this approach may not work for many patients.

Definition of Low-Carbohydrate

Diets are frequently characterized by percentage composition, although this method does not address the threshold effects of absolute amount of carbohydrate reduction—reflecting a point at which lowered insulin levels shift the body away from an anabolic state and toward fat oxidation. Although not universally accepted, standardized definitions for discussing carbohydrate reduction have been proposed.¹¹

The following definitions are used to quantify fat allowances in various carbohydrate-reduced diets:

1. Reduced-carbohydrate diet: >130 g of carbohydrate per day, up to 45% of total calories

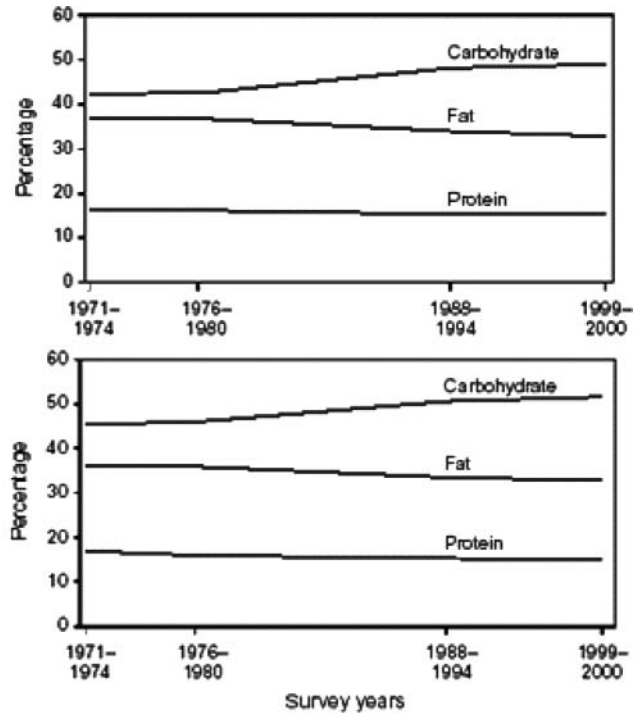


Figure 2. Percentage of kilocalories from macronutrient intake among men (top) and women (bottom) aged 20-74 (age-adjusted), by survey years. Data from National Health and Nutrition Examination (NHANES), United States, 1971-2000.⁹

2. LC diet: 30-130 g of carbohydrate per day
3. Very low-carbohydrate ketogenic (VLCK) diet: <30 g of carbohydrate per day; will usually permit ketosis to occur

A low-fat diet contains 10% to 15% of total calories as dietary fat.

Body Weight

The biochemistry that relates LC nutrition to weight loss and chronic disease rests on the well-known response of the pancreas to dietary carbohydrate. Insulin release is directly related to the amount of glucose in the bloodstream and has a large effect on fatty acid metabolism and storage. Insulin increases fatty acid synthesis via stimulation of acetyl-coA carboxylase and increases triacylglycerol synthesis in the liver through lipoprotein lipase. Cholesterol synthesis increases via activation of hydroxymethylglutaryl-CoA reductase. Storage of fatty acids is favored because insulin inhibits the release of fatty acids from the cell through the activation of the hormone-sensitive lipase. Reducing carbohydrate appears to create a metabolic milieu that can positively affect appetite and reduce fat storage as well as or more effectively than other dietary strategies.¹²⁻¹⁵

Experimental Studies

A recent meta-analysis by Hession et al¹⁶ compared the effects of LC diets with LF diets on weight loss and coronary disease risk factors. A total of 13 studies conducted from 2002 to 2007 that lasted at least 6 months fulfilled the inclusion criteria, with a total of 1,222 participants. The weighted mean difference at 6 months between diets was -4.02 kg in favor of the LC diet group. After 12 months, this difference fell to -1.05 kg. In addition, higher attrition rates were found in the LF group compared with the LC group. Finally, the LC diet demonstrated favorable changes in serum levels of HDL-C and TG as well as systolic blood pressure.

Another study conducted by Gardner et al¹² in 2007 randomized 311 overweight premenopausal women to 1 of 4 popular diets for a 12-month period: Atkins (<20 g CHO/d; no calorie restriction), Zone (40% CHO; calorie-restricted), LEARN (55%-60% CHO, calorie-restricted), and Ornish ($<10\%$ fat; no calorie restriction). The mean 12-month weight change was -4.7 kg for those on the Atkins diet, -1.6 kg for those on the Zone diet, -2.2 kg for those on the LEARN diet, and -2.6 kg for those on the Ornish diet. The Atkins group experienced the most improved metabolic effects, with positive changes in HDL-C, TG, and systolic blood pressure.

More recently, a 2-year trial was conducted by Shai et al¹³ in which 322 moderately obese individuals were randomized to 1 of 3 diets: a VLC diet with no calorie restrictions; a calorie-restricted Mediterranean diet (MED); or a calorie-restricted LF diet. The mean weight change was -4.7 kg for the VLC group, -4.4 kg for the MED group, and -2.9 kg for the LF group. The ratio of serum total cholesterol to HDL-C decreased in all groups, with the LC group showing the greatest improvement with a relative decrease of 20% compared with the LF group with a decrease of 12%.

These studies show that the LC dietary approach, despite unrestricted caloric intake, is at least as effective as other dietary plans with regard to weight loss. There is some indication that the complexity of human metabolism goes beyond a simple energy balance equation. Some of the most intriguing examples of this are diet studies where calories are held constant and weight loss differs between groups, with greater weight loss observed in the LC group.¹⁷⁻²⁰ This suggests the possibility that the weight loss may be due to specific metabolic or hormonal advantages of a LC diet. These could include a metabolic advantage with regard to energy expenditure related to increased metabolic rate due to metabolic inefficiencies, increased thermogenesis, and/or increased spontaneous activity. Not mutually exclusive, a spontaneous decrease in calorie consumption is frequently noted in LC diet groups, possibly related to increased satiety effects of

protein and/or fat and a restoration of intrinsic appetite control.

Lipids

When a patient is advised to lower the fat content of his or her diet for reasons of cardiovascular health, the fat is most often replaced by carbohydrate. For most patients, this leads to elevation in fasting serum TG levels and a concomitant decrease in HDL-C.^{21,22} Reducing dietary carbohydrate reliably reduces serum TG, increases HDL-C, and can improve other aspects of the lipid profile. This was true even in studies where there was no change in weight.

Experimental Studies

In 2009, Volek et al²³ compared the effects of 2 hypocaloric diets on 40 subjects with atherogenic dyslipidemia: a carbohydrate-restricted (CR) diet (12% CHO) and a LF diet (56% CHO). After 12 weeks, subjects on the CR diet had more favorable TG (-51%), HDL-C (13%), and total cholesterol/HDL-C ratio (-14%) responses. In addition, the CR group showed more favorable responses in alternative indicators of cardiovascular risk, including low-density lipoprotein (LDL) particle distribution. Despite a 3-fold intake of dietary saturated fat in the CR group, saturated fatty acids in TG and cholesterol esters were significantly decreased compared with the LF group.

These results were similar to those of Yancy et al¹⁴ in 2004, who randomized 120 overweight adults to either a LC diet with no calorie restriction or a calorie-restricted, LF diet. After 24 weeks, the LC diet group had a greater decrease in serum TG levels as well as a greater increase in HDL than the LF group. Changes in the LDL-C levels were not statistically significant. Of note, 76% of LC diet group completed the study versus 57% of the LF diet group.

In another study, Sharman et al²⁴ compared the effects of 2 calorie-restricted diets on serum lipid levels in

15 overweight men: a VLC diet and a LF diet. Subjects were randomized to 1 of the diets for a 6-week period, after which they crossed over to the other diet for another 6 weeks. Both diets had the same effect on total cholesterol and neither diet changed HDL-C. LDL-C was reduced only by the LF diet (-18%), whereas the fasting serum TG level was only reduced by the VLC diet (-44%). Significant increases in large LDL-1 particles and decreases in smaller, more atherogenic LDL-3 and LDL-4 particles were seen only after the VLC diet was ingested.

Although diets tend to lower serum LDL-C and total cholesterol levels, there is substantial variation. More reliable are the effects of LC diets: improvement in

HDL-C, TG, and, most importantly, LDL particle size. The possibility that it is not LDL-C that is atherogenic but rather the predominance of small, dense LDLs (the so-called pattern B phenotype) is a possible reconciliation of the different risk factors and bears on current questioning of the use of LDL-C as the only focus for predicting cardiovascular disease risk.²⁵⁻²⁷

Blood Glucose and Insulin

Basic biochemistry, agreed-upon knowledge of human physiology, clinical experience, and common sense all concur: high dietary carbohydrate intake will raise blood sugar, and reducing dietary carbohydrate will lower it. Similarly, although also sensitive to other macronutrients, fluctuations in insulin are reduced with LC diets. This is the logical starting point for discussion of hyperglycemia and hyperinsulinemia as seen in diabetes mellitus and other metabolic states. In practice, weight loss improves diabetes mellitus and glucose control, but the mechanism is unknown and may involve de facto reduction in dietary carbohydrate. Emphasis on weight loss as the primary effect of LC diets on glucose control is disingenuous; as noted below and elsewhere,⁶ LC diets improve glycemic control in the absence of weight loss.

Experimental Studies

In 2008, Westman et al²⁸ found significantly greater improvements in hemoglobin A1c (HbA1c) levels, body weight, and HDL-C levels of subjects with obesity and type 2 diabetes following a VLCK diet with no calorie restriction compared with those eating a calorie-restricted, low-glycemic index (LGI) diet. Diabetes medications were reduced or eliminated in 95.2% of participants following the VLCK diet versus 62% of LGI diet participants.

Yancy et al²⁹ evaluated the effect of a VLCK diet with no calorie restriction on blood glucose and medication use in individuals with type 2 diabetes. After 16 weeks, the 21 individuals who completed the study demonstrated a 16% decrease in mean HbA1c and only 2 subjects requiring diabetes medication did not reduce dosage; 7 subjects discontinued their medications entirely.

Gannon and Nuttall³⁰ examined the effect of 2 isocaloric diets on blood glucose control in 8 men with type 2 diabetes randomized to a 5-week crossover study: either a high-carbohydrate control diet or a LC diet. At the end of the diet intervention period, mean 24-hour serum glucose was 198 mg/dL for the control diet and 126 mg/dL for the LC diet, whereas HbA1c was 9.8 ± 0.5 and 7.6 ± 0.3 , respectively. In addition, serum insulin levels were decreased on the LC diet.

Recently, the intensive insulin therapy arm of the ACCORD trial was terminated because of significantly increased mortality, raising concerns about the benefits of tight glucose control. However, the intensive control was entirely drug-based; deaths might have been attributable to the method of targeting glucose rather than the value of the target itself. A LC diet is an alternative to medication (or at least an adjunct to less intensive pharmacology) and can give patients the opportunity to control glucose levels without the risk of hypoglycemic reactions.^{31,32}

Blood Pressure

Obesity has been strongly associated with increased blood pressure. The increased size of the vascular bed leads to impaired outflow of blood from the heart and increased pressure in large arteries. In addition, the high circulating levels of insulin that accompany insulin resistance related to obesity have been associated with sodium retention, proliferation of vascular smooth muscle, increased sympathetic nervous system activity, and diminished release of nitric oxide from the endothelium.³³⁻³⁵ Frequently, the improvements seen in blood pressure with patients eating a LC diet are attributed to the weight loss effects of the diet,^{12,14} but recent results demonstrate that improvements in blood pressure may be independent of weight loss and related to other mechanisms, as noted below.

Experimental Studies

Yancy et al³⁶ evaluated changes in blood pressure in their 2010 comparison study of 146 overweight males randomized to either a VLC diet with no calorie restrictions or a calorie-restricted, diet plus orlistat, a weight-loss medication (LF+O). After 48 weeks, the VLC diet group had greater improvement in both systolic and diastolic blood pressure despite similar weight loss in both groups. Systolic blood pressure decreased by 5.9 mm Hg in the VLC group and increased by 1.5 mm Hg in the LF+O group. Diastolic blood pressure decreased by 4.5 mm Hg in the VLC group and increased by 0.4 mm Hg in the LF+O group.

In a study by Frisch et al,³⁷ 165 subjects were assigned to either a LC diet or a LF diet, both of which were calorie-restricted. Although both diets resulted in similar weight loss, systolic blood pressure was significantly lower in the LC group (-5 mm Hg) compared with the LF group (-1 mm Hg) at 12 months.

In the studies evaluated, compared with a LF diet, a LC diet was found to produce greater improvements in blood pressure independent of weight loss.

Other Therapeutic Benefits

It has been proposed^{11,23,38} that carbohydrate restriction creates a unique metabolic environment from which multiple effects may radiate. In preliminary studies, the range of health effects for which there is evidence of benefit of carbohydrate restriction includes polycystic ovarian syndrome,³⁹ gestational diabetes,⁴⁰ cancer,⁴¹⁻⁴⁴ gastroesophageal reflux disease,^{45,46} schizophrenia,⁴⁷ nonalcoholic fatty liver disease,⁴⁸ epilepsy,⁴⁹⁻⁵¹ and age-related macular degeneration.⁵²

Carbohydrate Reduction for Life

Carbohydrate reduction has advantages that go beyond VLC therapeutic diets. For patients who are being treated successfully on a LC diet, this way of eating can be extended in a more flexible form to a long-term dietary pattern. Studies support the use of LC diets for weight loss, diabetes, and cardiovascular health for periods of more than a year.^{13,53,54} Members of the general population who have not yet reached clinically significant levels of metabolic dysregulation may need guidance in preventing deterioration in health; for some, a LC diet may be a more effective approach than a LF one.

One Diet Does Not Fit All

Various genetic and metabolic profiles may predispose certain patients to adverse risks of an LF diet or, conversely, to improved response to a LC one. Although reducing dietary fat can reduce LDL-C, for portions of the population it can also result in increases in reduced LDL particle size, a more atherogenic lipid profile.⁵⁵ This effect is heritable and suggests that caution should be used in suggesting population-wide dietary fat reductions.⁵⁶ When dietary fat is reduced, it is often replaced by carbohydrate. Individuals who may be more susceptible to dyslipidemia related to this dietary change include those with a higher fasting insulin concentrations and higher body weight.²¹ Low serum HDL-C, accompanied by elevated TG levels, is often the predominant lipid abnormality in obese or diabetic patients hospitalized with cardiovascular disease.⁵⁷ This population may benefit from the lipid profile improvements related to a LC diet.

LC diets have a positive impact on obesity, elevated serum TG levels, reduced serum HDL-C levels, impaired glucose metabolism, and hypertension, a cluster of medical disorders used to define the clinical criteria for metabolic syndrome (MetS).⁵⁸ Insulin resistance is thought to

be the common denominator underlying the expression of each of these markers.⁵⁹ Carbohydrate restriction addresses all of the features of MetS and is the logical therapy for those diagnosed with the syndrome.^{23,60,61}

Most studies demonstrate that the incidence of MetS is lower in African American adults than in Caucasians, despite the fact that the individual clinical outcomes predicted by MetS—stroke, myocardial infarction, and type 2 diabetes—are more frequent in African Americans, a fact that cannot be adequately explained by social and economic differences in these populations.^{62,63} Recent developments in understanding reduced expression of several genes and transcription factors related to carbohydrate metabolism in African Americans may explain this disconnect.⁶⁴ In this light, a diet that reduces carbohydrate impact on metabolism may be especially appropriate for this population.

Appetite and Satiety

Certain food types may stimulate feeding whereas others produce satiety. These influences should be taken into account when recommending a long-term dietary approach. LC, high-fat diet studies frequently demonstrate a spontaneous reduction in caloric intake on an ad libitum diet.¹²⁻¹⁵ Although this effect has been attributed to boredom with the diet,⁶⁵ the appetite-driving and/or satiety effects of various macronutrients may be below conscious awareness and should be considered in light of our current food environment.⁶⁶

The satiety effects of protein are well-documented,^{60,67} although carbohydrate reduction does not always result in significantly increased protein consumption. Carbohydrate restriction may also work through changes in interaction of gastrointestinal sensory signals that are only now being elucidated. In practice, a comparison between a breakfast of eggs (22% CHO) and a breakfast of bagels (72% CHO) resulted in reduced energy intake over 24 hours for subjects who had eggs for breakfast.⁶⁸ In addition, subjects reported increased hunger 3 hours after the bagel breakfast. In a 6-week weight loss intervention, 28 overweight premenopausal women were randomized to either a LC diet with no calorie restriction or a calorie-restricted, LF diet. Despite having no calorie restrictions, the LC group spontaneously reduced energy intake to a level similar to that of the calorie-restricted group. At the same time, self-rated hunger scores decreased in the LC diet group compared with the LF group.⁶⁹ Controlling calorie intake without hunger is an important part of weight management and health maintenance. A diet that assists people in doing so can be part of a preventive care approach.

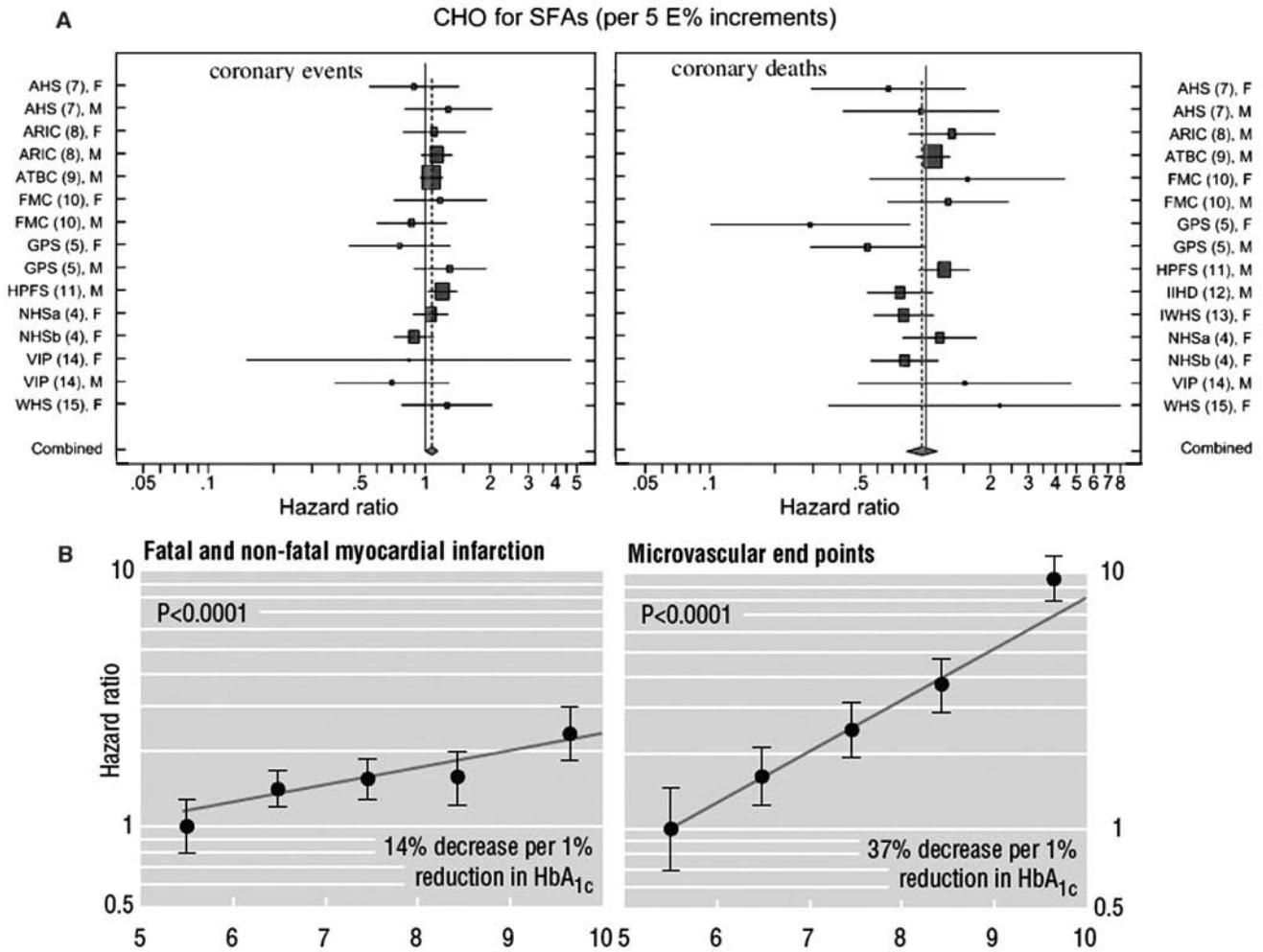


Figure 3. Effect of change in dietary saturated fatty acid (SFA) intake and hemoglobin A1c levels on cardiovascular events. (A) Hazard ratio for coronary events or deaths for increments of replacement of SFA with CHO. Figure redrawn from Jakobsen et al. Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies. *Am J Clin Nutr.* 2009;89:1425-1432. (B) Hazard ratio for macro- or microvascular end points as a function of HbA1C (%). Figure redrawn from Stratton et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ.* 2000;321:405-412. Error bars show 95% confidence intervals. Note: Hazard ratios <1.5 (>0.66) are considered weak, and data for which confidence intervals cross 1 are considered to show no effect. Reproduced from Stratton IM, Adler AI, Neil AW, et al. Association of glycaemia with macrovascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *Brit Med J.* 2000;321:405-412 with permission from BMJ Publishing Group Ltd.

Barriers to Acceptance

As clinicians, we must evaluate all possible solutions to improvement in patient care, recognizing that the majority of our population is overweight or obese. We must at times step back from academic research and focus on basic physiology, common sense, and—most importantly—the patient. Observational studies are no substitute for a patient with a glucometer. Conventional scientific and medical thinking has been wrong before;

consider the response to Semmelweis's call for hygiene in birthing wards, and, more recently, the effects of hormone replacement therapy to reduce heart disease in women. Although Americans have changed their eating habits toward the recommended lower fat and higher carbohydrate intake, the current epidemic of obesity and diabetes would suggest that these recommendations have had little impact on improving health.⁷⁰ It is time to move beyond outdated notions that persist far beyond any scientific evidence to support

them, the clinical versions of “urban myths,” and put the patient first.

Clinical Myths

Concerns that reducing carbohydrate intake will have an adverse effect on kidney function have been answered many times. It should be noted that LC intake does not imply high protein intake. The Dietary Reference Intakes support a wide range of protein intake, from 10% to 35% of calories; only diets above this range can accurately termed “high protein.” In any case, it is established that higher protein diets do not have an adverse effect on healthy kidneys.⁷¹⁻⁷⁵ In fact, improvements in hypertension that can be achieved by carbohydrate reduction may assist in protecting kidney function.

Another concern is that fiber intake will fall below recommended levels. The major sources of dietary fiber in the American diet are white flour and potatoes,⁷⁶ foods with a high blood sugar impact and little nutritive value. Information from the Active Low-Carbers Forum, an on-line support group for people who have chosen a low-carbohydrate eating pattern, shows that one of the primary dietary changes that takes place when switching to a LC diet is a large increase in consumption of leafy green vegetables.⁷⁷ A diet that shifts eating patterns away from white flour and potatoes toward leafy green vegetables is considered beneficial to overall health.

A persistent concern regarding carbohydrate diets is that carbohydrate removed from the diet will be replaced with saturated fat. The effect of saturated fat on heart disease is dependent on the overall characteristics of the diet and, in particular, the effects of carbohydrate on insulin that shift the metabolism toward fatty acid synthesis and storage.¹¹ Recent meta-analyses and epidemiologic studies show that replacement of carbohydrate with saturated fat is, if anything, beneficial for risk reduction; these results must be added to the failure of numerous large-scale population studies to show a correlation between dietary saturated fat and cardiovascular disease.⁷⁸⁻⁸² At the same time, clinicians are acutely aware of the health risks, including cardiovascular disease, which arise when HbA1c becomes elevated (Figure 3).⁸³

Research supports the safety of VLCK diets for humans.^{32,84-86} There are, however, certain populations in which reducing carbohydrate intake to very low levels may not be appropriate: patients with insulin-dependent diabetes, thyroid defects, inborn errors of metabolism, ketotic hypoglycemia of childhood, corticosteroid, or growth hormone deficiency, certain elderly populations, and individuals who consume excess amounts of alcohol or aspirin.⁸⁶ Although these people should avoid VLC diets, patient who are not responding to LF diets and those with genetic and metabolic risk factors, including

high serum levels of insulin, TG, and glucose, may benefit from carbohydrate restriction.

Conclusion

The shift in metabolism that occurs on a LC diet heralds a shift in our current dietary paradigm. Changing the macronutrient content of the diet changes the metabolic profile. Although increasing fiber and decreasing saturated fat intake may be of concern to those whose diets are high in carbohydrates, they may be of less concern to those whose diets are not. Increasing vegetable consumption and decreasing consumption of foods low in nutritional value is a dietary goal cited numerous times in the 2010 Dietary Guidelines recommendations.⁸⁷ Reducing dietary carbohydrate can accomplish this goal while improving glucose control, insulin response, atherogenic dyslipidemia, and other cardiovascular risk factors, in addition to reducing caloric intake without hunger. This makes carbohydrate reduction a sensible dietary approach to achieving and maintaining health.

References

1. Forouhi NG, Sharp SJ, Du H, et al. Dietary fat intake and subsequent weight change in adults: results from the European Prospective Investigation into Cancer and Nutrition cohorts. *Am J Clin Nutr.* 2009;90:1632-1641.
2. Tinker LF, Bonds DE, Margolis KL, et al. Low-fat dietary pattern and risk of treated diabetes mellitus in postmenopausal women: the Women's Health Initiative randomized controlled dietary modification trial. *Arch Intern Med.* 2008;168:1500-1511.
3. Howard BV, Van Horn L, Hsia J, et al. Low-fat dietary pattern and risk of cardiovascular disease: the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA.* 2006;295:655-666.
4. Howard BV, Manson JE, Stefanick ML, et al. Low-fat dietary pattern and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. *JAMA.* 2006;295:39-49.
5. American Diabetes Association. Clinical practice recommendations 2010. *Diabetes Care.* 2010;33:S11-S61.
6. Gannon MC, Nuttall FQ. Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition. *Nutr Metab (Lond).* 2006;3:16.
7. Sharman MJ, Kraemer WJ, Love DM, et al. A ketogenic diet favorably affects serum biomarkers for cardiovascular disease in normal-weight men. *J Nutr.* 2002;132:1879-1885.
8. Eckel RH, Kris-Etherton P, Lichtenstein AH, et al. Americans' awareness, knowledge, and behaviors regarding fats: 2006-2007. *J Am Diet Assoc.* 2009;109:288-296.
9. Centers for Disease Control and Prevention (CDC). Trends in intake of energy and macronutrients—United States, 1971-2000. *MMWR Morb Mortal Wkly Rep.* 2004;53:80-82.
10. Larosa JC, Fry AG, Muesing R, Rosing DR. Effects of high-protein, low-carbohydrate dieting on plasma lipoproteins and body weight. *J Am Diet Assoc.* 1980;77:264-270.
11. Accurso A, Bernstein RK, Dahlqvist A, et al. Dietary carbohydrate restriction in type 2 diabetes mellitus and metabolic syndrome: time for a critical appraisal. *Nutr Metab (Lond).* 2008;5:9.

12. Gardner C, Kiazand A, Alhassan S, et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: the A TO Z Weight Loss Study: a randomized trial. *JAMA*. 2007;297:969-977.
13. Shai I, Schwarzfuchs D, Henkin Y, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *New Engl J Med*. 2008;359:229-241.
14. Yancy WS Jr, Olsen MK, Guyton JR, Bakst RP, Westman EC. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: a randomized, controlled trial. *Ann Intern Med*. 2004;140:769-777.
15. Brehm BJ, Seeley RJ, Daniels SR, D'Alessio DA. A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. *J Clin Endocrinol Metab*. 2003;88:1617-1623.
16. Hession M, Rolland C, Kulkarni U, Wise A, Broom J. Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities. *Obes Rev*. 2009;10:36-50.
17. Volek JS, Phinney SD, Forsythe CE, et al. Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. *Lipids*. 2009;44:297-309.
18. Buscemi S, Verga S, Tranchina MR, Cottone S, Cerasola G. Effects of hypocaloric very-low-carbohydrate diet vs. Mediterranean diet on endothelial function in obese women. *Eur J Clin Invest*. 2009;39:339-347.
19. Halyburton AK, Brinkworth GD, Wilson CJ, et al. Low- and high-carbohydrate weight-loss diets have similar effects on mood but not cognitive performance. *Am J Clin Nutr*. 2007;86:580-587.
20. Keogh JB, Brinkworth GD, Noakes M, Belobrajdic DP, Buckley JD, Clifton PM. Effects of weight loss from a very-low-carbohydrate diet on endothelial function and markers of cardiovascular disease risk in subjects with abdominal obesity. *Am J Clin Nutr*. 2008;87:567-576.
21. Parks EJ, Parks EJ. Changes in fat synthesis influenced by dietary macronutrient content. *Proc Nutr Soc*. 2002;61:281-286.
22. Parks EJ, Hellerstein MK. Carbohydrate-induced hypertriglycerolemia: historical perspective and review of biological mechanisms. *Am J Clin Nutr*. 2000;71:412-433.
23. Volek JS, Phinney SD, Forsythe CE, et al. Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. *Lipids*. 2009;44:297-309.
24. Sharman MJ, Gómez AL, Kraemer WJ, Volek JS. Very low-carbohydrate and low-fat diets affect fasting lipids and postprandial lipemia differently in overweight men. *J Nutr*. 2004;134:880-885.
25. Menown IB, Murtagh G, Maher V, Cooney MT, Graham IM, Tomkin G. Dyslipidemia therapy update: the importance of full lipid profile assessment. *Adv Ther*. 2009;26:711-718.
26. Rosenson RS. Biomarkers, atherosclerosis and cardiovascular events. *Expert Rev Cardiovasc Ther*. 2008;6:619-622.
27. Carmena R, Duriez P, Fruchart JC. Atherogenic lipoprotein particles in atherosclerosis. *Circulation*. 2004;109(23 suppl 1):III2-III7.
28. Westman EC, Yancy WS Jr, Mavropoulos JC, Marquart M, McDuffie JR. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. *Nutr Metab (Lond)*. 2008;5:36.
29. Yancy WS, Foy M, Chalecki AM, Vernon MC, Westman EC. A low-carbohydrate, ketogenic diet to treat type 2 diabetes. *Nutr Metab (Lond)*. 2005;2:34.
30. Gannon M, Nuttall F. Effect of a high-protein, low-carbohydrate diet on blood glucose control in people with type 2 diabetes. *Diabetes*. 2004;53:2375-2782.
31. Westman EC, Vernon MC. Has carbohydrate-restriction been forgotten as a treatment for diabetes mellitus? A perspective on the ACCORD study design. *Nutr Metab (Lond)*. 2008;5:10.
32. Gutierrez M, Akhavan M, Jovanovic L, et al. Utility of a short-term 25% carbohydrate diet on improving glycemic control in type 2 diabetes mellitus. *J Am Coll Nutr*. 1998;17:595-600.
33. Singer GM, Setaro JF. Secondary hypertension: obesity and the metabolic syndrome. *J Clin Hypertens (Greenwich)*. 2008;10:567-574.
34. Hsueh WA. Insulin resistance and hypertension. *Am J Nephrol*. 1991;11:265-270.
35. Passa P. Hyperinsulinemia, insulin resistance and essential hypertension. *Horm Res*. 1992;38:33-38.
36. Yancy WS Jr, Westman EC, McDuffie JR, et al. A randomized trial of a low-carbohydrate diet vs orlistat plus a low-fat diet for weight loss. *Arch Intern Med*. 2010;170:136-145.
37. Frisch S, Zittermann A, Berthold HK, et al. A randomized controlled trial on the efficacy of carbohydrate-reduced or fat-reduced diets in patients attending a telemedically guided weight loss program. *Cardiovasc Diabetol*. 2009;8:36.
38. Volek JS, Fernandez ML, Feinman RD, Phinney SD. Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome. *Prog Lipid Res*. 2008;47:307-318.
39. Mavropoulos JC, Yancy WS, Hepburn J, Westman EC. The effects of a low-carbohydrate, ketogenic diet on the polycystic ovary syndrome: a pilot study. *Nutr Metab (Lond)*. 2005;2:35.
40. Ilic S, Jovanovic L, Pettitt DJ. Comparison of the effect of saturated and monounsaturated fat on postprandial plasma glucose and insulin concentration in women with gestational diabetes mellitus. *Am J Perinatol*. 1999;16:489-495.
41. Fine EJ, Segal-Isaacson CJ, Feinman R, et al. Carbohydrate restriction in patients with advanced cancer: a protocol to assess safety and feasibility with an accompanying hypothesis. *Comm Oncol*. 2008;5:22-26.
42. Xu RH, Pelicano H, Zhou Y, et al. Inhibition of glycolysis in cancer cells: a novel strategy to overcome drug resistance associated with mitochondrial respiratory defect and hypoxia. *Cancer Res*. 2005;65:613-621.
43. Stattin P, Björk O, Ferrari P. Prospective study of hyperglycemia and cancer risk. *Diabetes Care*. 2007;30:561-567.
44. Sampathkumar SG, Jones M, Meledeo M, et al. Targeting glyco-sylation pathways and the cell cycle: sugar-dependent activity of butyrate-carbohydrate cancer prodrugs. *Chem Biol*. 2006;13:1265-1275.
45. Austin GL, Thiny MT, Westman EC, Yancy WS Jr, Shaheen NJ. A very low carbohydrate diet improves gastroesophageal reflux and its symptoms: a pilot study. *Dig Dis Sci*. 2006;51:1307-1312.
46. Yancy WS Jr, Provenzale D, Westman EC. Improvement of gastroesophageal reflux disease after initiation of a low-carbohydrate diet: five brief case reports. *Altern Ther Health Med*. 2001;7:120,116-119.
47. Kraft BD, Westman EC. Schizophrenia, gluten, and low-carbohydrate, ketogenic diets: a case report and review of the literature. *Nutr Metab (Lond)*. 2009;6:10.
48. Tandler D, Lin S, Yancy WS Jr, et al. The effect of a low-carbohydrate, ketogenic diet on nonalcoholic fatty liver disease: a pilot study. *Dig Dis Sci*. 2007;52:589-593.
49. Weber S, Mølgaard C, Karentaudorf, et al. Modified Atkins diet to children and adolescents with medical intractable epilepsy. *Seizure*. 2009;18:237-440.
50. Kossoff EH, Turner Z, Bluml RM, et al. A randomized, crossover comparison of daily carbohydrate limits using the modified Atkins diet. *Epilepsy Behav*. 2007;10:432-436.

51. Dressler A, Stöcklin B, Reithofer E, et al. Long-term outcome and tolerability of the ketogenic diet in drug-resistant childhood epilepsy—the Austrian experience. *Seizure*. 2010;19:404-408.
52. Chiu CJ, Milton RC, Klein R, Gensler G, Taylor A. Dietary carbohydrate and the progression of age-related macular degeneration: a prospective study from the Age-Related Eye Disease Study. *Am J Clin Nutr*. 2007;86:1210-1218.
53. Nielsen J, Joensson Eva. Low-carbohydrate diet in type 2 diabetes: stable improvement of bodyweight and glycemic control during 22 months follow-up. *Nutr Metab*. 2006;3:22.
54. Lim SS, Noakes M, Keogh JB, et al. Long-term effects of a low carbohydrate, low fat or high unsaturated fat diet compared with a no-intervention control. *Nutr Metab Cardiovasc Dis*. 2010;20:599-607.
55. Dreon DM, Fernstrom HA, Miller B, Krauss RM. Low-density lipoprotein subclass patterns and lipoprotein response to a reduced-fat diet in men. *FASEB J*. 1994;8:121-126.
56. Dreon DM, Fernstrom HA, Williams PT, Krauss RM. Reduced LDL particle size in children consuming a very-low-fat diet is related to parental LDL-subclass patterns. *Am J Clin Nutr*. 2000;71:1611-1616.
57. Nam BH, Kannel WB, D'Agostino RB. Search for an optimal atherogenic lipid risk profile: from the Framingham Study. *Am J Cardiol*. 2006;97:372-375.
58. Pajunen P, Rissanen H, Härkönen T, Jula A, Reunanen A, Salomaa V. The metabolic syndrome as a predictor of incident diabetes and cardiovascular events in the Health 2000 Study [published online ahead of print July 27, 2010]. *Diabetes Metab*. 2010;36:395-401.
59. Reaven GM. Insulin resistance: the link between obesity and cardiovascular disease. *Endocrinol Metab Clin North Am*. 2008;37:581-601, vii-viii.
60. Layman DK. Dietary Guidelines should reflect new understandings about adult protein needs. *Nutr Metab (Lond)*. 2009;6:12.
61. Volek JS, Feinman RD. Carbohydrate restriction improves the features of metabolic syndrome: metabolic syndrome may be defined by the response to carbohydrate restriction. *Nutr Metab (Lond)*. 2005;2:31.
62. Sumner AE. Ethnic differences in triglyceride levels and high-density lipoprotein lead to underdiagnosis of the metabolic syndrome in black children and adults. *J Pediatr*. 2009;155:S7.e7-11.
63. Lindquist CH, Gower BA, Goran MI. Role of dietary factors in ethnic differences in early risk of cardiovascular disease and type 2 diabetes. *Am J Clin Nutr*. 2000;71:725-732.
64. Schisler JC, Charles PC, Parker JS, et al. Stable patterns of gene expression regulating carbohydrate metabolism determined by geographic ancestry. *PLoS One*. 2009;4:e8183.
65. Astrup A, Meinert Larsen T, Harper A. Atkins and other low-carbohydrate diets: hoax or an effective tool for weight loss? *Lancet*. 2004;364:897-899.
66. Cohen DA. Neurophysiological pathways to obesity: below awareness and beyond individual control. *Diabetes*. 2008;57:1768-1773.
67. Weigle DS, Breen PA, Matthys CC, et al. A high-protein diet induces sustained reductions in appetite, ad libitum caloric intake, and body weight despite compensatory changes in diurnal plasma leptin and ghrelin concentrations. *Am J Clin Nutr*. 2005;82:41-48.
68. Ratliff J, Leite JO, de Ogburn R, Puglisi MJ, VanHeest J, Fernandez ML. Consuming eggs for breakfast influences plasma glucose and ghrelin, while reducing energy intake during the next 24 hours in adult men. *Nutr Res*. 2010;30:96-103.
69. Nickols-Richardson SM, Coleman MM, Volpe JM, Hosig KW. Perceived hunger is lower and weight loss is greater in overweight premenopausal women consuming a low-carbohydrate/high-protein vs high-carbohydrate/low-fat diet. *J Am Diet Assoc*. 2005;105:1433-1437.
70. Hite AH, Feinman RD, Guzman GE, et al. In the face of contradictory evidence: report of the Dietary Guidelines for Americans Committee. *Nutrition*. 2010;26:915-924.
71. Brinkworth GD, Buckley JD, Noakes M, Clifton PM. Renal function following long-term weight loss in individuals with abdominal obesity on a very-low-carbohydrate diet vs high-carbohydrate diet. *J Am Diet Assoc*. 2010;110:633-638.
72. Pecoits-Filho R. Dietary protein intake and kidney disease in Western diet. *Contrib Nephrol*. 2007;155:102-112.
73. Kirby RK. Low-carbohydrate dieting. *Am Fam Physician*. 2006;73:1896,1901.
74. Eisenstein J, Roberts SB, Dallal G, Saltzman E. High-protein weight-loss diets: are they safe and do they work? A review of the experimental and epidemiologic data. *Nutr Rev*. 2002;60(7 pt 1):189-200.
75. Freedman MR, King J, Kennedy E. Popular diets: a scientific review. *Obes Res*. 2001;9(suppl 1):1S-40S.
76. Slavin JL. Position of the American Dietetic Association: health implications of dietary fiber. *J Am Diet Assoc*. 2008;108:1716-1731.
77. Feinman RD, Vernon MC, Westman EC. Low carbohydrate diets in family practice: what can we learn from an internet-based support group? *Nutr J*. 2006;5:26.
78. Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Saturated fat, carbohydrate, and cardiovascular disease. *Am J Clin Nutr*. 2010;91:502-509.
79. Hu FB. Are refined carbohydrates worse than saturated fat? *Am J Clin Nutr*. 2010;91:1541-1542.
80. Halton TL, Willett WC, Liu S, et al. Low-carbohydrate-diet score and the risk of coronary heart disease in women. *N Engl J Med*. 2006;355:1991-2002.
81. Halton TL, Liu S, Manson JE, Hu FB. Low-carbohydrate-diet score and risk of type 2 diabetes in women. *Am J Clin Nutr*. 2008;87:339-346.
82. Jakobsen MU, O'Reilly EJ, Heitmann BL, et al. Major types of dietary fat and risk of coronary heart disease: a pooled analysis of 11 cohort studies. *Am J Clin Nutr*. 2009;89:1425-1432.
83. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321:405-412.
84. Dashti H, Thazhumpal M, Hussein T. Long-term effects of a ketogenic diet in obese patients. *Exp Clin Cardiol*. 2004;9:200-205.
85. Veech RL, Chance B, Kashiwaya Y, et al. Ketone bodies, potential therapeutic uses. *IUBMB Life*. 2001;51:241-247.
86. Mitchell GA, Kassovska-Bratinova S, Boukaftane Y, et al. Medical aspects of ketone body metabolism. *Clin Invest Med*. 1995;18:193-216.
87. United States Department of Agriculture. Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans 2010. <http://www.cnpp.usda.gov/DGAs2010-DGACReport.htm>. Accessed July 2010.

