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Very-low-carbohydrate weight-loss diets revisited

ABSTRACT

Much scientific and anecdotal data demonstrate favorable metabolic responses to very-low-carbohydrate diets. We believe that very-low-carbohydrate diets merit further study for weight loss, and that criticisms of these diets lack scientific evidence.

KEY POINTS

Most studies have found that people lose more weight on very-low-carbohydrate diets than on standard weight-loss diets.

Mechanisms of weight loss on these diets may go beyond water loss and include suppression of appetite, increasing the metabolic rate, decreasing metabolic efficiency, and shunting of nutrients away from fat storage.

Weight loss is usually associated with small to moderate reductions in lean tissue, but low-energy, very-low-carbohydrate diets may have a protein-sparing effect compared with low-fat diets.

These diets may also have favorable effects on specific risk factors for cardiovascular disease (eg, fasting and postprandial triglyceride levels, high-density lipoprotein levels, and low-density lipoprotein particle size).

IN THE SEARCH for an effective method of losing weight, many people have adopted various diets that limit carbohydrate intake, commonly called *ketogenic diets* or *very-low-carbohydrate diets*.

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Experts have criticized this dietary approach in several articles, including one recently published in the *Cleveland Clinic Journal of Medicine*,¹ on the grounds that it jeopardizes health. Indeed, very-low-carbohydrate diets are an easy target for criticism, since they are diametrically opposed to the low-fat/high-carbohydrate dietary recommendations put forth by national organizations such as the National Cholesterol Education Program.²

Our hypothesis is that there is a lack of scientific evidence for the criticisms commonly laid against very-low-carbohydrate diets, especially regarding the metabolic mechanisms involved. Quite the contrary, we feel there is a significant amount of scientific and anecdotal data demonstrating favorable metabolic responses to very-low-carbohydrate diets. A recent US Department of Agriculture review has called for further research into the safety and efficacy of low-carbohydrate diets.³

This review provides a slightly different perspective on very-low-carbohydrate diets, based on scientific data and clinical experience. We hope this overview provides a background on which to formulate ideas and testable hypotheses, stimulating further discussion and research in this area.

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■ DEFINITIONS

Diets that limit carbohydrate intake have been called *low-carbohydrate*, *very-low-carbohydrate*, *high-protein*, *high-fat*, and *ketogenic*. For the purpose of this review, we use the term *very-low-carbohydrate diet*, defined as less than 50 g of carbohydrate per day.

Not all very-low-carbohydrate diets are high-protein diets, and vice versa. For example, a mixed diet with “high protein” would not be a very-low-carbohydrate diet if it contained more than 50 g of carbohydrates per day. In general, the studies presented in this review examined very-low-carbohydrate diets that contained less than 10% carbohydrate, 25% to 35% protein, and 55% to 65% fat (TABLE 1).

■ IMPORTANT QUESTIONS

Important questions need to be addressed concerning the advantages and disadvantages of very-low-carbohydrate diets. Hard data are limited but suggest that these diets are not harmful in the short term and may have therapeutic value for weight loss and certain other medical conditions.

Physicians should be open to this possibility and stay abreast of the research in this area. The challenge will be to link the metabolic advantages commonly associated with short-term consumption of very-low-carbohydrate diets to long-term outcomes.

Are all calories equivalent?

The basic principle behind all weight-loss diets is to reduce dietary energy intake below the energy needs of the body. Whether the relative distribution of protein, carbohydrate, and fat can influence the magnitude of weight loss achieved remains unclear, however.

According to the first law of thermodynamics, changes in energy store equal energy intake minus energy expenditure.

But are all calories equivalent? With one exception,⁴ most studies^{5–9} have reported that people lost more weight on very-low-carbohydrate diets than on diets that contained the same number of calories but more carbohydrates. The experimental diets in these studies contained from 600 to 1,900 calories and 46 to 115 g of protein per day. Subjects included

TABLE 1

Typical day's menu on a very-low-carbohydrate diet

Breakfast

Ham and cheese omelet	
Whole eggs	3
Cheddar cheese	2 ounces
Ham	2 ounces
Bacon	2 slices
Coffee	1 cup
Cream	2 tablespoons

Lunch

Chicken salad	
Tossed greens	2 cups
Chicken breast	4 ounces
Mozzarella cheese	1.5 ounces
Ranch dressing	3 tablespoons
Almonds	1 ounce
Diet soda	1 cup

Dinner

Grilled salmon	4 ounces
Green beans	1 cup
Tossed greens	1 cup
Vinegar and oil dressing	4 tablespoons
Sugar-free gelatin	1 cup
Red wine	4 ounces

Daily nutrient content

Kilocalories	2,000
Carbohydrate	10%
Fat	58%
Protein	28%
Alcohol	4%

obese men and women, and the diets were consumed for 10 to 63 days.

In the only study that did not demonstrate greater weight loss with the very-low-carbohydrate diet,⁴ the energy content of the diet was low (600 kcal/day) and the subjects were morbidly obese (> 45 kg of excess body weight).

Is the weight loss from water?

The greater weight loss is presumed to be from water.¹ However, several other possibilities exist:

- Very-low-carbohydrate diets may alter the metabolic rate by preserving more lean body mass⁹
- They may decrease metabolic efficiency, resulting in greater loss of heat¹⁰

TABLE 2

Very-low-carbohydrate diets decrease fat mass, spare lean body mass

STUDY	YEAR	DIET	SUBJECTS	DURATION (DAYS)	ENERGY (KCAL)	CHO (G)	BODY MASS CHANGE (KG)	FAT MASS CHANGE (KG)	LEAN BODY MASS CHANGE (KG)	METHOD
Benoit et al ¹¹	1965	Fasting VLCD	7 M, obese	10	0	0	−9.6	−3.4	−6.2	UWW
				10	1,000	10	−6.6	−6.4	−0.2	
Young et al ⁹	1971	VLCD	2 M, obese	63	1,800	104	−11.2	−8.4	−2.8	K40
		VLCD	3 M, obese	63	1,800	60	−12.3	−10.2	−2.1	
		VLCD	3 M, obese	63	1,800	30	−15.6	−14.9	−0.7	
Phinney et al ²²	1980	VLCD	5 F, 1 M, obese	42	500–750	0	−10.6	−7.1	−3.5	UWW
Willi et al ¹²	1998	VLCD	6, obese	56	650–725	25	−15.4	−16.8	1.4	DXA
Volek et al ¹³	2002	VLCD	12 M, lean	42	2,335	46	−2.2	−3.3	1.1	DXA
		Control	8 M, lean	42	2,190	330	0.4	0.0	0.4	DXA

CHO = carbohydrate, M = male, F = female, UWW = underwater weighing, VLCD = very-low-carbohydrate diet, K40 = potassium-40, DXA = dual-energy x-ray absorptiometry

Very-low-carb diets:

- < 10% carbs
- 25%–35% protein
- 55%–65% fat

- They may promote loss of energy in the form of ketones in urine, feces, and sweat
- They may also result in partitioning of nutrients away from fat storage and toward accumulation of lean tissue. The few studies that have assessed body composition on a very-low-carbohydrate diet suggest a preferential loss of fat mass and preservation of lean body mass (TABLE 2).^{9,11,12}

We recently used dual-energy x-ray absorptiometry to examine the change in body composition in subjects who switched from their habitual diet (48% carbohydrate, 32% fat) to a very-low-carbohydrate diet (8% carbohydrate, 61% fat) for 6 weeks.¹³ Surprisingly, fat mass decreased significantly (−3.3 kg) and lean body mass increased significantly (+1.1 kg), despite no change in physical activity. There were no significant changes in the control group.

These results suggest that a very-low-carbohydrate diet favors loss of fat. Water may account for some of the initial rapid weight loss, but it appears that fat loss accelerates and lean tissue is preserved over longer periods. There is no evidence that prolonged very-low-carbohydrate diets cause chronic dehydration.

Do these diets increase the risk of cardiovascular disease?

The possibility that very-low-carbohydrate diets increase the risk of cardiovascular disease has received widespread attention. Although no single diet is appropriate or ideal for everyone, our experience is that very-low-carbohydrate diets may improve the cardiovascular risk profile in selected individuals, even without significant weight loss.

Triglycerides. The most dramatic and consistent lipid response to a very-low-carbohydrate diet is a moderate to large decrease in fasting triglyceride levels and postprandial triglyceride responses to a fat-rich meal,¹⁴ both independent risk factors for cardiovascular disease.^{15,16}

Total cholesterol. Studies that examined blood lipid responses indicate that very-low-carbohydrate diets generally result in small increases in total cholesterol,^{14,17–21} which can be prevented or even reversed if significant weight loss occurs.^{7,12,22}

LDL and HDL. Although the data are limited, very-low-carbohydrate diets tend to result in moderate increases in low-density lipoprotein (LDL) and high-density lipopro-



tein (HDL), but the ratio of total cholesterol to HDL is not altered significantly.^{14,18,23}

Further work is warranted to examine the effects of a very-low-carbohydrate diet in different populations over longer periods.

Atherogenic lipoprotein phenotype. An impaired ability to clear circulating triglyceride-rich lipoproteins during the postprandial period is the driving force underlying the lipid abnormalities of the *atherogenic lipoprotein phenotype*: increased hepatic production of very-low-density lipoprotein (VLDL), reduced HDL, and a predominance of small LDL particles.²⁴ Approximately 25% of adult men have this constellation of lipid abnormalities, which confers increased risk of cardiovascular disease upon otherwise-healthy people.²⁵

Paradoxically, a low-fat/high-carbohydrate diet exacerbates atherogenic dyslipidemia if the patient does not lose a significant amount of weight or increase his or her level of physical activity.^{26,27} However, a very-low-carbohydrate diet improves all aspects of atherogenic dyslipidemia, decreasing fasting and postprandial triglyceride levels, increasing HDL, increasing LDL size, and decreasing insulin, independent of weight loss.^{14,23}

We have studied the response to a very-low-carbohydrate diet in a group of healthy subjects with the atherogenic lipoprotein phenotype (fasting triglyceride level > 150 mg/dL and peak postprandial triglyceride level > 400 mg/dL).¹⁴ These subjects consistently demonstrated significant improvements in fasting and postprandial triglyceride levels (**FIGURE 1**), HDL levels, and LDL particle size.

We also recently examined the effects of a 6-week very-low-carbohydrate diet on fasting and postprandial serum lipid levels in healthy, normal-weight, normolipemic men who switched from their habitual diet (17% protein, 47% carbohydrate, 32% fat) to a very-low-carbohydrate diet (30% protein, 8% carbohydrate, 61% fat).²⁸ There were significant decreases in fasting serum triglycerides (–33%), postprandial lipemia after a fat-rich meal (–29%), and fasting serum insulin concentrations (–34%). Fasting serum total and LDL cholesterol and oxidized LDL were unaffected, and HDL cholesterol tended to be increased (+11.5%). In subjects with a predominance of small LDL particles (“pattern

A very-low-carbohydrate diet lowers triglyceride levels

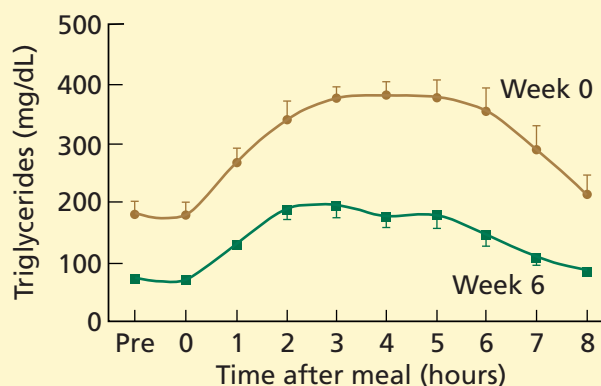


FIGURE 1. Data from nine subjects in two previous studies of very-low-carbohydrate diets performed in our laboratory^{14,28} who had elevated fasting triglyceride levels greater than 150 mg/dL and exaggerated postprandial lipemia. Serum triglyceride responses to the same fat-rich meal were determined after their habitual high-carbohydrate diet and after 6 weeks of a very-low-carbohydrate diet.

B”), there were significant increases in mean and peak LDL particle diameter and in the percentage of large LDL particles after the very-low-carbohydrate diet.

These findings suggest that a very-low-carbohydrate diet does not have a deleterious effect on the cardiovascular risk profile in the short term and may improve the lipid disorders characteristic of atherogenic dyslipidemia.

Do dietary carbohydrates or fat lead to obesity?

Obesity is multifactorial; its causes include both excess energy intake and inadequate energy expenditure. A great deal of controversy exists about the role of dietary carbohydrate and fat in contributing to obesity. Current dietary guidelines focus on lowering dietary fat and increasing carbohydrate intake.²⁹

Americans have steadily reduced their reported intake of dietary fat, yet we are in the midst of a national epidemic of obesity. The prevalence of obesity has risen progressively from the mid-1970s to the mid-1990s, and

Americans have lowered their fat intake but keep getting fatter

Ketone bodies may be the perfect fuel for dieters

over 50% of Americans are overweight, defined as a body mass index greater than 25 kg/m².³⁰ These statistics suggest that the cause of obesity is probably not related to consumption of dietary fat.

Several long-term intervention studies have examined whether high-fat diets promote weight gain and whether low-fat diets can lead to weight loss.³¹ Generally, the weight loss was small (< 1 kg) in studies of up to 1 year, leading us to conclude that the effects of diets differing in macronutrients on energy intake and body fatness remain unclear.

How might a low-fat/high-carbohydrate diet promote weight gain? Consumption of carbohydrates with a high glycemic index (a measure of how quickly and how high specific foods raise the blood sugar level) promotes a short-term increase in energy intake,³² although no studies have linked this to long-term changes in body weight.

In theory, the stimulatory effect of increased carbohydrate intake (especially sugar or processed carbohydrates) on insulin concentrations provides a sound biological mechanism linking high-glycemic carbohydrate diets to weight gain, given the potent antilipolytic effects of insulin at physiologic concentrations.³³ In contrast, very-low-carbohydrate diets result in lower insulin concentrations,^{13,34} in addition to suppressing appetite, both of which could enhance long-term weight loss and weight maintenance.

Are ketones bad?

During prolonged fasting or adherence to a very-low-carbohydrate diet, whole-body metabolism gradually shifts toward obtaining a greater percentage of energy from lipid sources, which can result in the production of ketone bodies in the liver. Clinically, ketone body production indicates that lipid metabolism has been accelerated and that all the enzymes involved in metabolic pathways of lipid metabolism (eg, lipolysis, fatty acid transport, beta-oxidation, and ketogenesis) are operational.

During starvation or periods when carbohydrate intake is very low, ketone bodies serve as an alternative oxidative fuel for peripheral tissues to spare carbohydrate and protein. In this sense, ketone bodies could be considered

the perfect fuel for dieters.

Catabolism of protein is reduced by ketones,³⁵ which probably explains the preservation of lean tissue observed during very-low-carbohydrate diets.^{9,11,12} The small amount of glucose required by the brain and red blood cells can easily be met via gluconeogenesis from protein and fat. There are no direct data from which we can ascertain whether the low level of ketosis accompanying this diet is harmful or harmless.

Do very-low-carbohydrate diets cause insulin resistance?

Despite concern that very-low-carbohydrate diets, especially if high in saturated fat, might lead to insulin resistance, the link between saturated fat and insulin resistance is tenuous. Further, data from three recent studies that used the insulin clamp technique indicate that very-low-carbohydrate diets do not have an adverse effect on glucose metabolism or insulin resistance.^{36–38}

Collectively, these studies indicate that very-low-carbohydrate diets alter the effects of insulin on oxidative and nonoxidative glucose disposal, favoring storage of glucose as glycogen in muscle. They also appear to prevent insulin-stimulated inhibition of lipid oxidation.

Data from these studies do not support the notion that very-low-carbohydrate diets exacerbate the risk of type 2 diabetes and insulin resistance; rather, they actually show a potential favorable effect as evidenced by decreased basal endogenous glucose production and improved insulin-stimulated nonoxidative glucose disposal.

Do very-low-carbohydrate diets suppress appetite?

Scientific and anecdotal evidence clearly indicate that very-low-carbohydrate diets reduce appetite and caloric intake.^{14,39} This may be partially due to the fewer food choices available on the diet, but a more likely explanation is the higher satiety value of fat and protein or the anorectic effect of ketosis.⁴⁰

Increased circulating levels of beta-hydroxybutyrate (the primary ketone in the blood) act as a satiety signal.⁴¹ Given that most people who lose weight find it difficult to



keep the weight off, the high level of appetite satiation associated with very-low-carbohydrate diets could enhance successful adherence to a long-term low-energy diet.

Do these diets decrease athletic performance?

Several studies have shown that chronic consumption of very-low-carbohydrate diets leads to several metabolic and hormonal adaptations that facilitate increased fat oxidation and promote a glycogen-sparing effect within muscle.⁴²

The effects of a very-low-carbohydrate diet on prolonged exercise performance are unclear; studies have produced inconclusive results. Although high-carbohydrate diets have historically been considered superior to high-fat diets for this type of exercise, studies have shown that very-low-carbohydrate diets may result in improved⁴³ or maintained⁴² endurance exercise performance.

Are there other possible adverse effects?

Although research on very-low-carbohydrate diets is limited, information about potential adverse effects may come from two different but related dietary approaches: the ketogenic diet and the protein-sparing modified fast.

The ketogenic diet, a treatment for epilepsy, consists of high fat intake, low carbohydrate intake, and low protein intake.⁴⁴ Side effects of the ketogenic diet in children have included calcium oxylate and urate kidney stones (from 0.5% to 5.0% incidence over 1 year), vomiting, amenorrhea (21%), hypercholesterolemia, and water-soluble vitamin deficiencies.^{45,46}

The protein-sparing modified fast is a specific type of very-low-calorie diet, with extreme limitation of carbohydrate and calories (< 800 kcal daily).^{47,48} Because the currently popular very-low-carbohydrate diets typically provide more than 800 kcal daily, they may not cause the side effects seen with the much more stringent protein-sparing modified fast.

Another criticism relates to the potential adverse health effects of reducing intake of foods generally recognized as healthy, including fruits, vegetables, and whole grains. This is a legitimate concern; however, a very-low-carbohydrate diet can include a wide range of vegetables (eg, tomatoes, cucumbers, peppers) and even small amounts of fruit. It would also be prudent to take a multivitamin/mineral supplement to ensure adequate intakes of all essential micronutrients.

MORE RESEARCH NEEDED

Substantial evidence from short-term controlled studies indicates that very-low-carbohydrate diets are effective for weight loss. Because research methods and techniques have advanced since many of these studies were done, several research teams are revisiting very-low-carbohydrate diets in view of the urgent need for effective therapies for obesity and other metabolic disorders.

Because there are very few ad libitum ("free-living") outpatient studies and no controlled studies longer than 8 weeks, no conclusion can be made yet regarding the long-term safety and efficacy of this approach.

**Ketosis
suppresses
appetite,
helping keep
weight off**

REFERENCES

1. Blackburn GL, JC, Morreale S. Physician's guide to popular low-carbohydrate weight-loss diets. *Cleve Clin J Med* 2001; 68:761-774.
2. National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Bethesda, MD: National Heart, Lung and Blood Institute and National Institutes of Health, 2001 (NIH publication no. 01-3670).
3. Freedman MR, King J, Kennedy E. Popular diets: a scientific review. *Obesity Res* 2001; 9(suppl 1):1s-40s.
4. Vazquez JA, Adibi SA. Protein sparing during treatment of obesity: ketogenic versus nonketogenic very low calorie diet. *Metabolism* 1992; 41:406-414.
5. Rabast U, Vornberger KH, Ehl M. Loss of weight, sodium and water in obese persons consuming a high- or low-carbohydrate diet. *Ann Nutr Metab* 1981; 25:341-349.
6. Rabast U, Schonborn J, Kasper H. Dietetic treatment of obesity with low and high-carbohydrate diets: comparative studies and clinical results. *Int J Obes* 1979; 3:201-211.
7. Rabast U, Kasper H, Schonborn J. Comparative studies in obese subjects fed carbohydrate-restricted and high carbohydrate 1,000-calorie formula diets. *Nutr Metab* 1978; 22:269-277.
8. Yang MU, Van Italie TB. Composition of weight lost during short-term weight reduction. *J Clin Invest* 1976; 58:722-730.
9. Young CM, Scanlan SS, Im HS, Lutwak L. Effect on body composition and other parameters in obese young men of carbohydrate level of reduction diet. *Am J Clin Nutr* 1971; 24:290-296.
10. Kasper H, Thiel H, Ehl M. Response of body weight to a low carbohydrate, high fat diet in normal and obese subjects. *Am J Clin Nutr* 1973; 26:197-204.
11. Benoit FL, Martin RL, Watten RH. Changes in body composition during weight reduction in obesity. *Ann Intern*



- Med 1965; 63:604–612.
12. **Willi SM, Oexmann MJ, Wright NM, Collop NA, Lyndon L.** The effects of a high-protein, low-fat, ketogenic diet on adolescents with morbid obesity: body composition, blood chemistries, and sleep abnormalities. *Pediatrics* 1998; 101:61–67.
13. **Volek JS, Sharman MJ, Love DM, et al.** Body composition and hormonal responses to a carbohydrate-restricted diet. *Metabolism* 2002; 51:864–870.
14. **Volek JS, Gómez AL, Kraemer WJ.** Fasting and postprandial lipoprotein responses to a low-carbohydrate diet supplemented with n-3 fatty acids. *J Am Coll Nutr* 2000; 19:383–391.
15. **Austin MA, Hokanson JE, Edwards KL.** Hypertriglyceridemia as a cardiovascular risk factor. *Am J Cardiol* 1998; 81(4A):7B–12B.
16. **Patsch JR, Miesenböck G, Hopferwieser T, et al.** Relation of triglyceride metabolism and coronary artery disease: studies in the postprandial state. *Thrombosis* 1992; 12:1336–1345.
17. **Rickman F, Mitchell N, Dingman J, Dalen JE.** Changes in serum cholesterol during the Stillman Diet. *JAMA* 1974; 228:54–58.
18. **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.
19. **Phinney SD, Bistrian BR, Wolfe RR, Blackburn GL.** The human metabolic response to chronic ketosis without caloric restriction: physical and biochemical adaptations. *Metabolism* 1983; 32:757–768.
20. **Newbold HL.** Reducing the serum cholesterol level with a diet high in animal fat. *South Med J* 1988; 81:61–63.
21. **Westman EC, Yancy WS, Edman JS, Tomlin KF, Perkins CE.** Effect of 6-month adherence to a very low carbohydrate diet program. *Am J Med* 2002; 113:30–36.
22. **Phinney SD, Horton ES, Sims EAH, Hanson JS, Danforth E Jr, LaGrange BM.** Capacity for moderate exercise in obese subjects after adaptation to a hypocaloric, ketogenic diet. *J Clin Invest* 1980; 66:1152–1161.
23. **Campos H, Dreon DM, Krauss RM.** Associations of hepatic and lipoprotein lipase activities with changes in dietary composition and low density lipoprotein subclasses. *J Lipid Res* 1995; 36:462–472.
24. **Austin MA, King MC, Vranizan KM, Krauss RM.** Atherogenic lipoprotein phenotype. A proposed genetic marker of coronary heart disease risk. *Circulation* 1990; 82:495–506.
25. **Austin MA, Breslow JL, Hennekens CH, Buring JE, Willett WC, Krauss RM.** Low density lipoprotein subclass patterns and risk of myocardial infarction. *JAMA* 1988; 260:1917–1921.
26. **Dreon DM, Fernstrom HA, Williams PT, Krauss RM.** A very-low-fat diet is not associated with improved lipoprotein profiles in men with a predominance of large, low-density lipoproteins. *Am J Clin Nutr* 1999; 69:411–418.
27. **Parks EJ, Hellerstein MK.** Carbohydrate-induced hypertriglyceridemia: historical perspective and review of biological mechanisms. *Am J Clin Nutr* 2000; 71:412–433.
28. **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.
29. **US Department of Health and Human Services.** Dietary Guidelines for Americans, 5th ed. Washington, DC: USDA, 2000.
30. **Kuczmarski R, Flegal KL, Campbell SM, Johnson CL.** Increasing prevalence of overweight among US adults—The National Health and Nutrition Examination Surveys, 1960 to 1991. *JAMA* 1994; 272:205–211.
31. **Roberts SB.** High-glycemic index foods, hunger, and obesity: is there a connection? *Nutr Rev* 2000; 58:163–169.
32. **Roberts SB, McCrory MA, Saltzman E.** The influence of dietary composition on energy intake and body weight. *J Am Coll Nutr* 2002; 21:1405–1455.
33. **Jensen MD, Caruso M, Heiling VJ, Miles JM.** Insulin regulation of lipolysis in nondiabetic and IDDM subjects. *Diabetes* 1989; 38:1595–1601.
34. **Volek JS, Gómez AL, Love DM, Avery NG, Sharman MJ, Kraemer WJ.** Effects of a high-fat diet on postabsorptive and postprandial testosterone responses to a fat-rich meal. *Metabolism* 2001; 50:1351–1355.
35. **Sherwin RS, Hendler RG, Felig P.** Effect of ketone infusions on amino acid and nitrogen metabolism in man. *J Clin Invest* 1975; 55:1382–1390.
36. **Cutler DL, Gray CG, Park SW, Hickman MG, Bell JM, Kolterman OG.** Low-carbohydrate diet alters intracellular glucose metabolism but not overall glucose disposal in exercise-trained subjects. *Metabolism* 1995; 44:1264–1270.
37. **Bisschop PH, de Metz J, Ackermans MT, et al.** Dietary fat content alters insulin-mediated glucose metabolism in healthy men. *Am J Clin Nutr* 2001; 73:554–559.
38. **Bisschop PH, Pereira Arias AM, Ackermans MT, et al.** The effects of carbohydrate variation in isocaloric diets on glycogenolysis and gluconeogenesis in healthy men. *J Clin Endocrinol Metab* 2000; 85:1963–1967.
39. **Yudkin J, Carey M.** The treatment of obesity by the “high-fat” diet. The inevitability of calories. *Lancet* 1960; 2:939–941.
40. **Bray GA, Davidson MB, Drenick EJ.** Obesity: a serious symptom. *Ann Intern Med* 1972; 77:779–795.
41. **Arase K, Fisler JS, Shargill NS, York DA, Bray GA.** Intracerebroventricular infusions of 3-OHB and insulin in a rat model of dietary obesity. *Am J Physiol* 1988; 255:R974–R981.
42. **Phinney SD, Bistrian BR, Evans WJ, Gervino E, Blackburn GL.** The human metabolic response to chronic ketosis without caloric restriction: preservation of submaximal exercise capacity with reduced carbohydrate oxidation. *Metabolism* 1983; 32:769–776.
43. **Lambert EV, Speechly DP, Dennis SC, Noakes TD.** Enhanced endurance in trained cyclists during moderate intensity exercise following 2 weeks adaptation to a high fat diet. *Eur J Appl Physiol* 1994; 69:287–293.
44. **Freeman JM, Vining EPG, Pillas DJ, Pyzik PL, Casey JC, Kelley MT.** The efficacy of the ketogenic diet-1998: a prospective evaluation of intervention in 150 children. *Pediatrics* 1998; 102:1358–1363.
45. **Ballaban-Gil K, Callahan C, O'Dell C, Pappo M, Moshe S, Shinnar S.** Complications of the ketogenic diet. *Epilepsia* 1998; 39:744–748.
46. **Herzberg GZ, Fivsh BA, Kinsman SL, Gearhart JP.** Urolithiasis associated with the ketogenic diet. *J Pediatr* 1990; 117:743–745.
47. **Palgi A, Read JL, Greenberg I, Hoefer MA, Bistrian BR, Blackburn GL.** Multidisciplinary treatment of obesity with a protein-sparing modified fast: results in 668 outpatients. *Am J Pub Health* 1985; 75:1190–1194.
48. **Bistrian BR.** Clinical use of a protein-sparing modified fast. *JAMA* 1978; 17:2299–2302.

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