Low-Carbohydrate Diets: Assessing the Science and Knowledge Gaps, Summary of an ILSI North America Workshop

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On April 12 and 13, 2005, the International Life Sciences Institute (ILSI) North America Technical Committee on Carbohydrates sponsored a workshop on low-carbohydrate diets at the ILSI offices in Washington, DC. Over 50 participants from academia, government, industry, and scientific associations assembled to discuss and review the current science, regulatory, and health impacts of low-carbohydrate diets.

The goals of the workshop were to assess the state of the science, to address and clarify definitions and behavioral questions regarding low-carbohydrate diets, and to identify research gaps relative to improving public health. The workshop consisted of presentations and discussions organized into three major themes: Perspectives, Mechanisms, and Gap Analysis. Perspectives provided information on efficacy and definitions regarding "low-carbohydrate" diets from the perspective of the researcher/clinician, the consumer, and the regulator. The Mechanisms session addressed hypotheses of the efficacy and other possible effects of low-carbohydrate diets. The third and final session, Gap Analysis, enabled attendees to consider scientific and consumer perspectives to determine areas of agreement, identify data gaps, and identify ways to improve communication of this information. The purpose of this article is to relate the key points of the workshop to dietetics professionals.

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PERSPECTIVES ON EFFICACY

Adult Populations

Few published studies have adequately assessed the efficacy of low-carbohydrate diets, particularly for longer than 6 months. It is difficult to compare studies because the level of carbohydrates can fluctuate from 1% to 25% of total energy intake (1), the intervention diet is not always well defined, subject characteristics vary, and the degree of subject compliance is often unclear. However, despite their shortcomings, six recent randomized controlled trials provide data regarding possible health effects of low-carbohydrate diets (Table 1) (2-7) compared with more conventional low-calorie, low-fat diets in obese (body mass index [BMI]>30) subjects.

As shown in Table 1, subjects on the low-carbohydrate diets lost between 3% and 13% of their body weight at 5 months, whereas those on the low-calorie, low-fat (control) diet lost between 1.4% and 7% . However, by 1 year, the differences in weight loss did not persist (2,4). For example, Foster and colleagues observed weight regain in both groups by 1 year, with a greater regain in the low-carbohydrate group (4). In the study by Stern and colleagues, the low-fat group continued to lose weight after 6 months, resulting in similar weight losses by 1 year (6). Only three studies assessed dietary intake (2,6,7), so it is difficult to assess study protocol compliance to link dietary factors to the apparent success. These limited findings suggest that a low-carbohydrate approach may be more efficacious than conventional (eg, low-calorie, low-fat) approaches for short-term weight loss. Beyond 6 months, more data are needed.

Pediatric Populations

If there are few studies rigorously designed to test the long-term effects of low-carbohydrate interventions in obese adults, there exist even fewer such studies in overweight or obese children. One recent trial compared a low-carbohydrate, high-protein diet (similar to those discussed for adults) with a low-fat diet for weight loss in 30 overweight adolescents (mean age 14 years; BMI 35.5) (8). After 12 weeks, those on the low-carbohydrate diet lost more weight than those on the low-fat diet (9.9±9.3 kg vs 4.1±4.9 kg, $P<0.05$) (8), even though their caloric intake was greater (according to self report). Other investigations of low-carbohydrate diets for weight loss in children tested extreme

Table 1. Weight loss reported by randomized trials comparing low-carbohydrate diets with conventional low-calorie, low-fat diets at 6 months and 1 year in adults[a]

								Mean Weight Loss (% Change)			
								6 mo		1 y	
Author (reference)	n	Age±SD[b] (y)	BMI[c]±SD	Health status of subjects	Control diet (low-calorie, low-fat) carbohydrate:protein:fat, %	Low-carb diet carbohydrate:protein:fat, %	Intervention protocol	Control	Low-carbohydrate	Control	Low-carbohydrate
Brehm and colleagues (2)	53	44±7	34±2	Healthy	Goal: 55:15:30 Report: 53:18:29	Goal: carbohydrate ≤20 g/d for initial 2 weeks, increase to 40-60 g/d Report: 30:23:46	3 months counseling, individual and group, weekly 3-d food records	4.2	9.3	Not tested	Not tested
Dansinger and colleagues (3)	80	49±11	35±3.9	Hypertension, dyslipidemia, or fasting hyperglycemia	Weight Watchers	Atkins	Group counseling, cookbook	3.6	3.2	3.1	2.1
Foster and colleagues (4)	63	44±8	34±4	Healthy	Goal: 55:15:30	Goal: carbohydrate ≤20 g/d for initial 2 weeks, then increase until weight stable	Self-help based on provided books	3.2	7.0	2.5	4.4
Samaha and colleagues (5), Stern and colleagues (6)[d]	132	54±9	43±7	39% DM,[e] 43% metabolic syndrome	Goal: 55:15:30 Report: 50:16:34	Goal: carbohydrate ≤30 g/d Report: 30:18:52	Some guidance	1.4	4.5	2.3	3.9
Yancy and colleagues (7)	120	45±10	34±5	High total cholesterol, LDL,[f] triglycerides	Goal: 55:15:30 Report: 52:19:29	Goal: carbohydrate ≤20 g/d for initial 2 weeks, then increase until weight stable Report: 8:26:68	Group meetings, exercise recommended	6.7	12.9	Not tested	Not tested

[a]Results reported were those presented to workshop attendees (intent-to-treat analysis by primary authors). When available, the goal and reported dietary composition are included. See reference for thorough protocol details.
[b]SD=standard deviation.
[c]BMI=body mass index; calculated as kg/m^2.
[d]The 6-month and 1-year time points from same weight loss trial reported in two publications.
[e]DM=diabetes mellitus.
[f]LDL=low-density lipoprotein.

versions of low-carbohydrate diets such as protein-sparing modified fasts (9-11) or severely energy restricted (600 to 800 kcal) plans (9-11). Although weight loss was reported, it is unclear how to interpret these findings.

In summary, the data available are not yet generalizable to adult or pediatric populations and do not warrant modification of the current clinical recommendations for weight loss with a reduced-calorie, moderately low-fat (<30%) diet. The evidence does suggest, however, that low-carbohydrate diets should be studied as a potentially viable alternative for weight loss in obese adults. Additional studies evaluating low-carbohydrate diets with less severe energy restriction in youth and adolescents are needed.

Consumer Perspectives

Consumer attention to carbohydrates is reflected in consumer attitudes, industry actions, and media coverage. As concern about carbohydrates increased through 2003 (12), the food industry responded by developing a variety of new no-carbohydrate, low-carbohydrate, or reduced-carbohydrate products (13). Concurrently, sales flattened or declined for traditional "high-carb" foods. Concern about sugar and carbohydrates and the number of adherents to a low-carbohydrate lifestyle declined by 2005 (14,15). As a result, "low-carb" product introductions decreased sharply in the fourth quarter of 2004 and early 2005 (13). Similarly, the content of media stories shifted from articles touting the popularity of low-carbohydrate diets throughout 2004 to those proclaiming "low-carbohydrate" to be a fad and the increasing favor of "good" carbohydrates by the end of 2005 (14).

There is also confusion regarding carbohydrates. Consumers associate carbohydrates with positive attributes (they give you energy; they provide fiber and nutrients; and they are found in nutritious whole grains, fruits, and vegetables), and with negative qualities (they make you fat, raise insulin levels, and slow down your metabolism) (14). However, most consumers cannot articulate why they think certain carbohydrates are healthful or not. Although some consumers recognized carbohydrate restriction as an easy way to lose weight (14), the degree of carbohydrate restriction and which carbohydrates were eliminated varied greatly. For some, cutting out seemingly healthful foods was counterintuitive; many consumers believe that restricting foods does not provide a long-term path to a more healthful weight or a healthful diet. Although others acknowledged that low-carbohydrate diets may not be healthful, the desire for weight loss compelled many to try low-carbohydrate diets. Unfortunately for many consumers, eating for health and eating for weight control are two separate practices (14).

The low-carbohydrate fad increased awareness of carbohydrates, and the new/reformulated products enabled consumers to personalize their definition and approach for low-carbohydrate dieting. Research is needed to identify the extent to which low-carbohydrate lifestyles were adopted and what foods are included in such approaches. Nutrition communicators need the tools and resources to convey the facts about carbohydrate foods and the message that eating for health and eating for weight loss are one and the same. As these gaps are narrowed, consumers will likely select nutrient-rich carbohydrate-containing foods such as whole grains, fruits, and vegetables, as recommended by the Dietary Guidelines for Americans (16).

PERSPECTIVES ON REGULATIONS, DEFINITIONS, AND ANALYSIS OF "LOW CARBOHYDRATE"

Regulations

In 2004 and early 2005, terms such as low carb, net carb, available carb, impact carb, carb lite, and carb simple were found throughout the global marketplace to describe the level of carbohydrate content of a food. For the manufacturer, the plethora of terms to describe the level of carbohydrates in foods has no regulatory labeling status in many countries. Although US regulations have quantitatively defined "no" or "low" for a number of nutrients [eg, fat and cholesterol (16), sodium (17), and calories (18)], presently, "low-carbohydrate food" and "low-carbohydrate diet" are not terms defined by the US Food and Drug Administration (FDA). The FDA does not have a guidance on these terms, thus they cannot be placed on packaging. However, the lack of objection to the use of the terms net carb or available carbs does not constitute an opinion that their use is appropriate. The USDA Food Safety and Inspection Service guidance related to meat and poultry products states that such label terms must be accompanied by specific information telling the consumer the meaning and usage of such terms and providing the calculation necessary to determine the number of carbohydrates included by the term (19). In the United States, these terms may be used in ad copy or labeling only in conjunction with terms to describe a diet or lifestyle (not a level of carbohydrate in a particular food or product), provided they are truthful and not misleading.

It became common practice by most manufacturers to measure the total nonglycemic or nondigestible carbohydrates (typically dietary fiber, resistant starch, and sugar alcohols) and subtract this quantity from the calculated quantity of total carbohydrates (Figure 1). Because of warning letters and position papers, American food producers generally gravitated toward the use of the terms net carbohydrates, available carbohydrates, or net available carbohydrates to indicate the levels of carbohydrate present in a product, but each manufacturer has created its own scheme for applying the designations.

Several petitions for proposed nutrient content claims such as carbohydrate-free, low-carbohydrate, reduced-carbohydrate, good source of carbohydrates, and excellent source of carbohydrates have been received by the FDA. These are under review, as are comments regarding guidelines for the use of the term net carbohydrate on food labels. The FDA is presently gathering information about the science surrounding low-carbohydrate labeling so that appropriate actions are taken.

Definitions

In an effort to harmonize terms describing foods of relatively low-carbohydrate content, the Board of Directors of AACC International (formerly the American Association of Cereal Chemists) formed an ad hoc committee charged with developing a science-based, measurable definition(s) for glycemic carbohydrates (20), which would contribute to the low-carbohydrate dialogue. Accepted definitions would enable manufacturers to communicate how the carbohy-

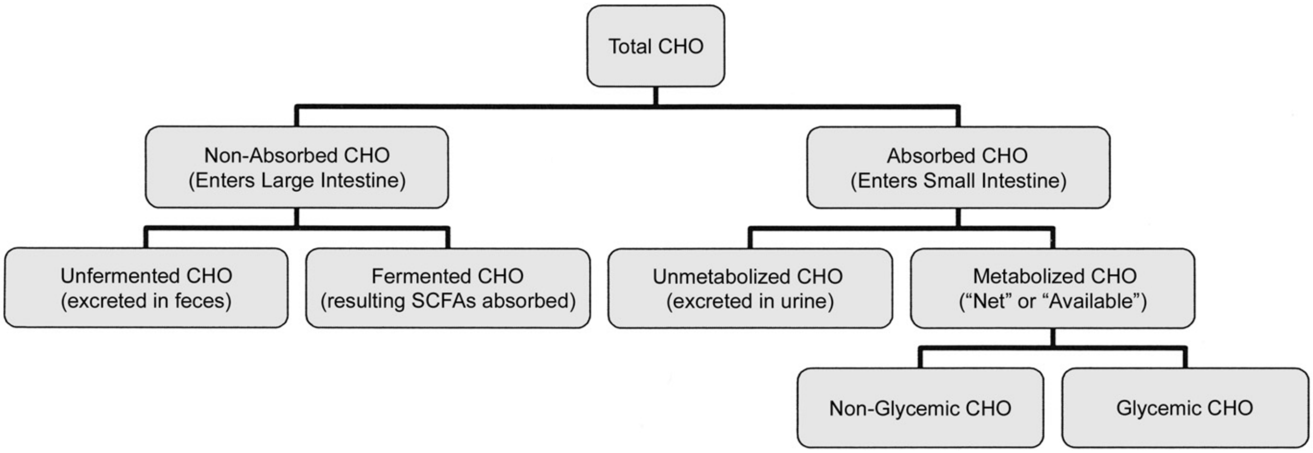

Figure 1. Carbohydrate (CHO) classification scheme. This flow chart shows the relationships between different types of carbohydrates organized by metabolic fate. It was presented at the International Life Sciences Institute North America Workshop on Low-Carbohydrate Diets to illustrate the scheme the AACC International Committee referenced as it proposed definitions of carbohydrates (Figure 2). Developed from work by Steve Brooks, Health Canada, Ottawa, Ontario, and Stuart Craig, Danisco USA, Inc, Ardsley, NY.

Available carbohydrate in a food can be absorbed as monosaccharides and metabolized by the body. Net carbohydrate is equivalent to available carbohydrate.

Glycemic response is the change in blood glucose concentration induced by ingested food.

Glycemic impact is the blood glucose response of a serving of food relative to that of an equivalent weight of glucose.

Figure 2. Proposed AACC International definitions related to glycemic carbohydrates. (Information current as of submission. See www.aaccnet.org for more information related to the process of arriving at definitions.)

drate content of a certain amount of a given food will affect blood glucose levels and possible risk of chronic disease, thus standardizing calculations to unify label claims across products and manufacturers. The AACC International Committee is presently reviewing three interconnected definitions (Figure 2) developed with the aid of a flow chart (Figure 1), public comments, and revisions.

Analysis

There are two related philosophies for quantifying the glycemic effect of carbohydrates. The first is to measure and report the portion of carbohydrate known to elicit a glycemic effect (the available/net carbohydrate). As long as the meaning of net carbohydrate is agreed on, analytical methods currently exist to determine this quantity in foods (21), although alternative approaches are being investigated (22). The second philosophy is to indicate the physiological glycemic effect that the food produces. To measure the glycemic effect of carbohydrates currently requires in vivo methods, although in vitro methodology is being researched. The most widely used in vivo measurement is the glycemic index (GI). Compared with other routine analytical procedures, GI measurements are extremely variable (Table 2), not only with regard to the calculated ratios to the standard food, and among individuals, but with regard to the individual's blood glucose response when the individual consumes replicate samples of the same food (23). The effects of processing and mixtures of foods on the overall glycemic impact also remains a methodological challenge. Derivative methods of the GI, such as glycemic load and glycemic glucose equivalents, will all show the same shortcomings because of the difficulties with the basic measurement.

Because of these limitations, it is difficult to apply GI values in a meaningful manner to aid individuals in food selection. For example, oat porridge has a GI of 58, carrots a GI of 92, and chocolate cake with chocolate frosting a GI of 38. If GI were on the label, a consumer who might select foods purely on the basis of GI might believe that frosted cake is a better choice than oatmeal or carrots. Future research is needed to improve methods of measuring the glycemic effect of carbohydrates, which may be translated to consumers through possible labeling designations.

MECHANISMS FOR EFFICACY OF LOW-CARBOHYDRATE DIETS

There are several hypotheses related to how reduced-carbohydrate strategies may promote weight loss. These involve behavior and ease of compliance, changing macronutrient distribution and use, and inducing satiety. Factors influencing satiety include the level or type of carbohydrate, effects of hormones, the level or type of protein, or the overall dietary energy density. These elements, each having complex regulatory pathways, may also interact with one another.

Dieting Behavior

Although reducing caloric intake decreases weight, it is challenging for individuals to achieve weight loss by trying to control calories on their own. There is general agreement that a comprehensive weight-loss treatment should focus on health and self-esteem and incorporate self-monitoring, realistic goal-setting, physical ac-

Table 2. Variability of the glycemic index (GI)[a]

Food sample	GI result (mean±SD)[b]	95% confidence interval	99% confidence interval
White bread	72.5±35.8	1.1-143.9	−22.3-167.3
Instant mashed potatoes	84.5±32.7	19.3-149.7	−2.09-171.1
Long-grain rice	71.1±38.2	−5.1-147.3	−30.1-172.3
White spaghetti	46.9±26.7	−6.3-100.1	−23.8-117.6
Pot barley	34.7±24.7	−14.5-84.0	−30.7-100.1

[a]Results of a multicenter trial in which 68 participants (28 male, 40 female) consumed the white bread sample in triplicate and the remaining foods in singlet. As can readily be seen the variability of the measurements is so great that individual results for each food significantly overlap across the GI range and include zero and negative numbers in the confidence intervals in every case. Table presented during the workshop was adapted from reference 24.
[b]SD=standard deviation.

tivity, nutrition education (including portion control), stress management, and social support (24-26).

Research shows that subjects instructed to follow a low-carbohydrate diet (without guidance on calorie reduction) spontaneously decrease their caloric intake (2,6,7). Decreasing intake of high-carbohydrate foods may offer an easy-to-follow, prescriptive strategy for decreasing total caloric intake (4). There is enough variety in most low-carbohydrate plans, particularly with the new and reformulated products, that an individual is unlikely to feel deprived. In addition, low-carbohydrate dietary patterns that emphasize fruits and vegetables may actually improve an individual's dietary nutrient profile. Because the pounds drop faster than with a "low-fat" diet in the short term, there is increased incentive, and this may lead to enhanced compliance and efficacy.

Ketosis vs Calories

It was theorized that low-carbohydrate diets put the body into a state of ketosis, thereby conferring a metabolic advantage that permits more rapid weight loss. This implies that calories do not count, but rather that the source of the calories does, and that greater weight loss can be gained from a low-carbohydrate diet than from a high-fiber diet with available carbohydrates at traditional levels (~55% kcal). If ketosis were contributing to weight loss, one would expect an increase in ketone production to be associated with weight loss of individuals on a low-carbohydrate diet, but this was not the case in two studies (2,4) in which ketone levels were assessed. On closer inspection, low-carbohydrate diets are almost always hypocaloric in comparison to the control diet. This concept was tested in subjects consuming isocaloric 1,000-kcal low-carbohydrate or normal-carbohydrate diets (low-fat) over 6 weeks, and results showed that weight loss did not differ between the two groups (27,28). Therefore, calories apparently are the more relevant factor.

GI and Insulin

The theory that weight loss can be achieved by selecting foods that minimize postprandial insulin secretion is predicated on the belief that carbohydrates, through insulin, increase hunger. Proponents of such diets often do not distinguish between normal insulin responses to meals and disordered adaptive responses existing in insulin resistance states. Foods with a low GI value, in theory, could reduce the insulin response. However, studies of the effect of GI on insulin response and satiety are few, often are not rigorous, and taken together are inconclusive (29). Epidemiologic studies show no effect of GI or glycemic load on insulin response in people with BMIs below 23 (30-33). Central adiposity is associated with increased circulating insulin, and insulin sensitivity is inversely related to BMI (34,35). Further, during normal insulin signaling, reduced glucose-stimulated insulin secretion predicts greater future weight gain (36); therefore, increased insulin secretion in response to meals is unlikely to contribute to weight gain and obesity.

Furthermore, considerable evidence supports that insulin signaling in the brain actually decreases food intake, acting as a negative feedback signal of recent energy intake and body adiposity (37). Reduced insulin delivery into the central nervous system or disruption of insulin signaling pathways results in weight gain and development of obesity in animals. Insulin also facilitates leptin secretion; thus, meals higher in carbohydrate tend to increase not only insulin levels, but also leptin levels to signal satiety. Research is needed to clarify how dietary carbohydrates and GI affect satiety and eating behaviors through a myriad of hormones including insulin.

Protein

Several lines of evidence suggest that the higher protein level consumed on low-carbohydrate diets is key in regulating food intake and body weight. It is generally accepted that proteins suppress food intake and are more satiating than fats or carbohydrates and by a greater percentage than can be accounted for by energy content alone (38,39). Compared with fat and carbohydrate, protein delays the return of hunger (40) and reduces the amount of calories consumed at a second meal (41). There is also limited data that indicate that the protein source, not just the quantity, impacts satiety (42,43). For example, subjects reported higher feelings of satiety after consuming 50 g protein as lean fish compared with beef or chicken, although this study did not investigate the impact of this protein meal on subsequent meal intake (44). Short-term studies with 1.5 g protein/kg and moderate-low carbohydrate (up to 200 g per day) increased satiety, increased thermogenesis, spared loss of muscle protein, and enhanced glycemic control compared with low-protein, high-carbohydrate diets. The effects of moderate protein and lower carbohydrate intake may contribute to decreasing postprandial increases in blood glucose and insulin response, while increasing substrates for gluconeogenesis (45). Protein in the diet helps maintain lean body mass and, therefore, increases resting energy expenditure.

Several mechanisms may explain how protein affects satiety and overall intake (46,47). Bioactive peptides activated during protein digestion act on centers within the digestive tract that in turn signal the brain. Free

Low-carbohydrate diets result in weight loss in the short term (6 months), but there was no difference in weight loss after 1 year between low-carbohydrate and other more traditional approaches.

Calories are calories, and calories do count.

Low-carbohydrate diets lower blood triglycerides and raise high-density lipoprotein in both short-term and long-term studies.

Low-carbohydrate diets increase low-density lipoprotein in short-term weight loss studies and during weight maintenance.

To fully compare and evaluate dietary effects of various studies, details surrounding the diet protocol, subjects, and dietary composition need to be accurate and complete.

Figure 3. Scientific points of agreement identified at the International Life Sciences Institute North America Workshop on Low-Carbohydrate Diets.

Atkins-type diets are easy to comprehend and therefore to follow.

Calories are too hard to count.

The low-carbohydrate diet has enthusiastic supporters and is palatable for many.

There are carbohydrates with different effects on health (like fats).

Figure 4. Consumer points of agreement identified at the International Life Sciences Institute North America Workshop on Low-Carbohydrate Diets.

amino acids activate neurochemical systems within the brain to terminate eating as well as to impact macronutrient choice. Also, the end products of protein metabolism (amino acids, ammonia, and urea) signal excess intake and probably play a role in determining meal intervals. Although the roles of cholecystokinin, insulin, glucagon, leptin, ghrelin, peptide YY (PYY), and glucagon-like peptide-1 (GLP-1) in appetite regulation are becoming elucidated, how proteins, especially as mixtures in the diet, impact satiety via these hormone signaling pathways to regulate food intake and weight is not completely understood. The evidence suggests that increasing protein to 26% of energy (from the average of 15% to 18%) is enough to reduce appetite. The higher-protein (lower-carbohydrate), energy-restricted diets seem to be more satiating and result in better weight loss, contributing to adherence.

Energy Density

A growing body of laboratory-based, clinical-based, and epidemiology-based data suggest that low-energy-density diets can reduce body weight in the short term (48). Energy density (measured in kcal/g) is primarily impacted by water, which adds weight and volume with no calories; thus, it lowers the energy density of foods, even high-fat foods. Fruits and vegetables tend to have low energy densities because of both their high water and their high fiber contents. It has been postulated that satiety is increased when energy density decreases because foods high in water and fiber are associated with enhanced satiety, reduced energy intakes and body weight, and better diet quality. Hence, consumption of high volumes of low-energy-density foods is associated with lower total caloric intake and enhanced satiety (49). Consuming food preloads with high water content and low energy density, such as soups or salads, enhances satiety and reduces overall energy intake at the meal. In a study in which the energy density of a meal was reduced by 30% and the subjects consumed the same weight of food, caloric intake was reduced by 30% (50). Perhaps some low-carbohydrate diet regimens are satiating due to the inclusion of foods with lower energy densities.

Cardiovascular Disease Risk and Other Considerations

A principal concern regarding low-carbohydrate diets is that the (relatively) high fat content of the diet may adversely affect serum lipids and the risk of cardiovascular disease. Paradoxically, preliminary findings challenge this argument. If the dietary fatty acid composition is known, mathematical equations predict that large increases in low-density lipoprotein cholesterol (LDL) with low-carbohydrate diets should only be realized in extreme cases in which carbohydrates are replaced almost exclusively with saturated fatty acids (51). Furthermore, virtually any implementation of a low-carbohydrate diet should produce beneficial changes in high density lipoprotein (HDL) and triglyceride levels and the ratio of total cholesterol to HDL cholesterol. Clinical research generally supports these models. There were no differences in total cholesterol or LDL concentrations between groups across four studies at 6 or 12 months. Low-carbohydrate diets consistently decreased triglycerides (2,4,5,7) and tended to increase HDL, and no studies showed an increase in LDL. One study reported decreases in HDL in participants following a low-carbohydrate diet, but the decrease was less than the decrease in the low-calorie group (6). No adverse effects on the lipid profile were observed in the sole pediatric study (8). Furthermore, no significant differences in blood pressure were observed between groups in these studies. Alhough results should be interpreted cautiously, because means may obscure important individual differences, low-carbohydrate diets seem to be less harmful than might be anticipated in terms of traditional measures of cardiovascular disease risk.

At 6 months, any improvement in triglyceride or HDL levels may be confounded by weight loss, because losing weight decreases triglyceride levels. However, decreasing carbohydrate intake reduced triglyceride levels more than diets with the same level of fat and higher levels of protein (52). When carbohydrates are exchanged for protein, there is no effect on LDL and the effects on HDL are inconsistent, but all studies show a decrease in triglycerides because of the independent effect of carbohydrates on very-low-density lipoprotein synthesis and, therefore, triglycerides (52-55). Although there may be additional beneficial effects of low-carbohydrate diets, such as decreased postprandial lipemia and prevalence of low LDL levels, not all of the effects of a “low-carb lifestyle” diet on cardio-

Develop definition of "low carbohydrate."

Document composition and determine nutritional quality of multiple low-carbohydrate dietary patterns to understand changes in energy and macronutrient intake in research settings.

Compare varying degrees of carbohydrate restriction to understand potential threshold/dose effects on weight and other endpoints.

Determine what risk factors should be included in analysis of the efficacy and safety of low-carbohydrate diets.

Investigate short-term and long-term use of low-carbohydrate diets in more population subgroups (healthy adults and children as well as those with chronic diseases and a range of risk factors) to obtain data on multiple safety end points and to identify weight-loss responders.

Elucidate mechanisms of short-term weight loss success of low-carbohydrate diets. Consider factors related to satiety (protein, fat, fiber, energy density), behavior (structure, perceptions, palatability), role of ketones, and glucose, among others.

Determine why low-carbohydrate diets seem to lose efficacy over the longer term.

Explore possible health benefits, beyond benefits attributed to weight loss, of following a low-carbohydrate diet.

Understand how the source(s) of carbohydrate(s) impacts the rate of glucose absorption.

Research glycemic index methodology(ies) to reduce variability and improve applicability.

Determine the degree of comfort clinicians have in recommending low-carbohydrate diets in the short term and long term and delineate their reservations, if any.

Figure 5. Scientific research gaps identified at the International Life Sciences Institute North America Workshop on Low-Carbohydrate Diets.

Explore what "low-carbohydrate food" and "low-carbohydrate diet" mean to consumers. What are individuals actually eating on a low-carbohydrate diet?

Assess composition and quality of personalized low-carbohydrate dietary approaches of consumers.

Determine what consumers understand "energy density" to mean.

Clarify role of label messages and images, advertising copy, and product claims for low-carbohydrate foods and determine whether and how such designations impact consumer perceptions, behavior, and health.

Investigate strategies that will enable consumers to understand the negative impacts of excess calories instead of a focus on carbohydrates.

Figure 6. Consumer gaps identified at the International Life Sciences Institute North America Workshop on Low-Carbohydrate Diets.

vascular disease risk are necessarily mediated through changes in macronutrient composition.

Not all low-carbohydrate diet studies investigated possible side effects. Minor side effects including constipation, halitosis, and muscle cramps occurred more frequently in subjects consuming the low-carbohydrate diet compared with the low-calorie diet according to Yancy and colleagues (4). Some less desirable immediate effects, such as enhanced lean body mass loss, increased urinary calcium loss, increased plasma homocysteine levels, and increased LDL levels, have been reported (45). Results of these and other studies should be interpreted with caution given the relative small sample sizes, varied subject characteristics, high attrition rate, and short duration of treatment.

Research is needed to evaluate the short-term and long-term safety and effectiveness of dietary management of carbohydrates for weight loss. Future studies, some of which are underway, should assess the effects of the diet on other clinical endpoints (ie, renal function, bone health, exercise endurance, and cognitive function) and in larger study populations, and should distinguish between the impact of weight loss and dietary factors on metabolic outcomes in both adults and children. Additional effort is needed to translate the findings to the general population.

GAPS ANALYSIS

After the data were presented, workshop participants were challenged to consider what information is agreed on from both a scientific and a consumer perspective (Figures 3 and 4) and to identify questions that remain to be answered (Figures 5 and 6). Research to bridge the gaps in knowledge between scientists and consumers will enable effective translation of the science of low-carbohydrate diets to the public so that dietary choices can be made to optimize the health of the individual.

ILSI North America Statement of Purpose

The North American branch of the International Life Sciences Institute (ILSI NA) is a public, nonprofit scientific foundation. ILSI NA advances the understanding and application of scientific issues related to the nutritional quality and safety of the food supply as well as health issues related to consumer self-care products. The organization carries out its mission by sponsoring relevant research programs, professional education programs and workshops, seminars, and publications, as well as providing a neutral forum for government, academic, and industry scientists to discuss and resolve scientific issues of common concern for the well-being of the general public. ILSI NA also strives to foster the career development of outstanding new scientists. ILSI NA's programs are supported primarily by its industry membership.

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