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Low-Carbohydrate Diets and Weight Loss

PART I OF A SERIES ON DIET AND WEIGHT LOSS

By Dónal P. O'Mathúna

THE INCIDENCE OF OBESITY CONTINUES TO RISE IN THE UNITED States and most of the developing world. Effective strategies for long-term weight reduction elude most, yet less than a quarter of those trying to lose weight adhere to the two well-established requirements: reduce caloric intake and increase exercise. Instead, Americans spend about \$33 billion each year on weight-loss products and services.¹ The Atkins diet is one of the most popular current approaches, with an estimated 20 million people worldwide embracing this low-carbohydrate diet.² Dr. Robert C. Atkins' book was on the *New York Times* bestsellers' list for several years, though the same basic principles are used in other popular diets (the Zone, Carbohydrate Addict's, and Sugar Busters diets).³ With so many people shunning carbohydrates and loading up on protein and fat, practitioners must be aware of recent studies so they can advise their patients.

Background

The Atkins diet advocates avoiding carbohydrates, initially recommending they constitute only 5% of one's daily intake. People can eat unrestricted amounts of high-protein, high-fat foods, like meat, eggs, fish, cheese, olives, and nuts. After the initial two-week induction period, small amounts of complex carbohydrates are allowed (primarily vegetables and fruits), but breads, pastas, and starchy foods should be considered a thing of the past. The goal is to keep carbohydrate intake below 20 g/d.³

The Atkins diet flies in the face of the conventional low-fat approach to dieting. Dr. Atkins points out that while Americans have decreased their proportion of dietary fat from 40% to about 32%, obesity has become a pandemic.⁴ Atkins concludes that fat is not to blame. However, while the proportion has decreased, the actual per capita fat consumption has increased by 10 lbs/yr since 1975, and the consumption of simple carbohydrates (like sugar, syrup, and processed flour and rice) has increased per capita by 20 lbs/yr.⁵ A diet that adds even more fat seems questionable, especially in light

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of calls to reduce fat intake to promote cardiovascular health.

Mechanism of Action

A number of metabolic processes are believed to contribute to weight loss on low-carbohydrate diets.² When carbohydrate consumption is severely restricted, glycogen stores are depleted along with associated bound water. Early weight loss may thus be due to fluid loss. Depletion of glycogen leads to ketotic acidosis, which may suppress appetite. Atkins claims that weight is lost because a high-protein, high-fat diet is thermogenic and requires increased energy expenditure. Evidence to support this is lacking, but even if significant thermogenesis occurs it is unlikely to cause more than very minimal weight loss. Protein's greater satiating effect may also help people feel full quicker and for longer, thus making overeating and snacking less likely. In this way, the Atkins diet can be a low-calorie diet, though this is often not measured in studies because people are free to consume as much protein as they desire.

Clinical Studies

A systematic review of studies involving low-carbohydrate diets conducted prior to 2003 uncovered 94 tri-

als.³ Of these, only 13 examined diets with the carbohydrate level recommended by Dr. Atkins (< 20 g/d). None of these trials lasted longer than 90 days and few included control groups. Weight loss was found to be associated with restricted caloric intake and study duration, but not with restricted carbohydrate intake.

During 2003 and 2004, four randomized controlled trials (RCTs) of the Atkins diet were published. The first assigned 53 obese women (mean BMI = 33.6 kg/m²) to either the Atkins diet or a calorie-restricted diet meeting the American Heart Association recommendations (*see Figure and insert*).⁶ After six months, those on the Atkins diet lost more weight (8.5 vs. 3.9 kg; P < 0.001) and more body fat (4.8 vs. 2.0 kg; P < 0.01) compared to those on the low-fat diet. Mean levels of blood pressure, lipids, fasting glucose, and insulin improved in both groups over the course of the study, with no statistical differences between the groups at three or six months.

Another study randomly assigned 63 obese men and women (mean BMI = 34 kg/m²) to the Atkins diet or a conventional diet (high-carbohydrate, low-fat, low-calorie).⁷ Drop-out rate was high (41%) and not statistically different between the two diets. Those on the Atkins diet had significantly more weight loss at three months (6.8% vs. 2.7% body weight; P = 0.001) and six months (7.0% vs. 3.2% body weight; P = 0.02), but not after 12 months. Healthy changes in blood pressure and insulin sensitivity occurred in both groups and were not significantly different. Ketone levels were significantly elevated for those on the Atkins diet for only the first three months. No correlation was found between weight loss and ketosis.

Serum lipoprotein changes were more complicated. Total cholesterol and LDL levels initially increased for those on the Atkins diet, but had returned to baseline after 12 months. The levels initially decreased for those on the conventional diet, but were not significantly lower after 12 months. In contrast, total triglycerides and HDL-cholesterol levels remained unchanged on the conventional diet, while the Atkins diet led to significant lowering of total triglycerides and elevation of HDL levels (P < 0.05).

The research team in charge of the third RCT published separate reports after six⁸ and 12 months.⁹ Of 132 severely obese subjects (mean BMI = 43 kg/m²), 79 returned for six-month evaluations, and 87 were examined after 12 months. The low-carbohydrate diet restricted carbohydrate intake to 30 g/d with fruits and vegetables as recommended carbohydrate sources. After six months, weight loss was significantly greater for those on the low-carbohydrate diet compared to the conventional low-fat diet (5.8 vs. 1.9 kg; P = 0.002). At 12 months,

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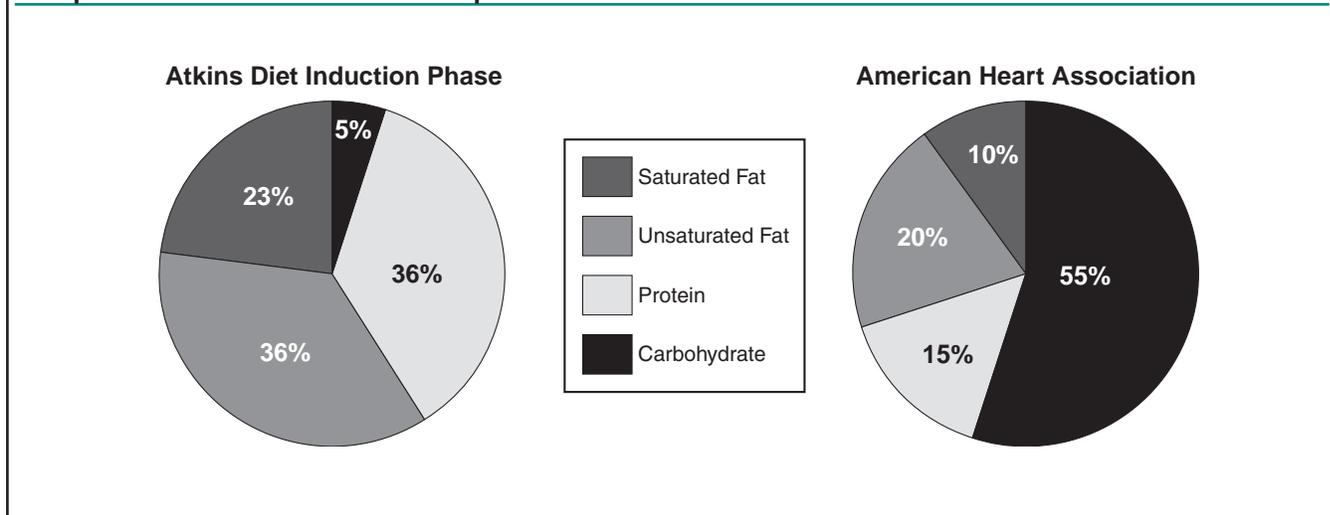
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Comparison of Atkins diet induction phase and American Heart Association recommendations



however, the weight losses were no longer statistically different. Total triglyceride levels were significantly lower with the low-carbohydrate diet after six and 12 months. Cholesterol levels were not significantly different after six months, but after 12 months the HDL values were lower with both diets, with significantly greater reductions with the conventional diet ($P = 0.028$).

The most recent RCT involved 120 healthy subjects (mean BMI = 34 kg/m²) randomly assigned to either the Atkins diet or a conventional reduced-calorie diet.¹ All participants were provided with a support group and exercise recommendations, and those on the Atkins diet also took the Atkins-recommended dietary supplements. One-third of the participants did not complete the study. After 24 weeks, weight-loss was greater on the Atkins diet (12.9% vs. 6.7% body weight; $P < 0.001$). The Atkins diet also led to significantly greater reduction in triglyceride levels ($P = 0.004$) and elevation of HDL levels ($P = 0.001$).

Adverse Effects

Concerns about the Atkins diet have centered around the high fat content and low plant and fiber content. Much of the additional protein comes from animal meats that are high in cholesterol. One study reported that the Atkins diet increased intake of cholesterol from 215 mg to 461 mg and then to 285 mg (at baseline, three months, and six months, respectively).⁶ These were significantly higher than those on the conventional diet: 273 mg, 169 mg, and 182 mg, respectively.

Studies have thus far reported improvements in some cardiovascular risk factors. The elevated HDL levels are sometimes cited as evidence of the Atkins diet being heart-healthy. However, elevated HDL levels can result

from needing to remove additional cholesterol in the diet, and reduced HDL level can result from less cholesterol in the system. As Dean Ornish, a critic of the Atkins diet, put it, “Eating a stick of butter will raise HDL-C in those who are able to do so, but that does not mean that butter is good for the heart.”⁵

The long-term effects of sticking with the Atkins diet are not well understood. Short-term adverse effects are less serious, but relatively common. One study funded by the Atkins Center found that among those using the Atkins diet for six months, 70% were constipated, 65% had halitosis, 54% had headaches, and 10% had hair loss.¹⁰ Reduced fruit, vegetable, and whole-grain consumption may explain these adverse effects.

Conclusion

Controlled studies of the Atkins diet support its greater effectiveness than a low-fat, reduced-calorie diet over six months, but not over 12 months. Such findings can be explained by the depletion of stored glycogen resulting in fluid loss, and the satiety effect of protein and ketosis. The resulting rapid weight loss, and the diet’s novelty, can be highly motivating. However, the big question is whether people can tolerate the high-protein diet over long periods—and whether it is safe, long term.

The improved lipid profiles found in RCTs are surprising given the large proportion of fat being consumed. However, even minor weight loss can markedly improve lipid profiles and glucose tolerance.² In addition, the Atkins diet includes nutritional supplements that contain multivitamins and essential oils (flaxseed, borage seed, and fish oils; each 1,200 mg daily).¹ Studies have not taken into account their use and impact on

lipid profiles. Of great concern also is the long-term cardiovascular impact of consuming the high-fat, low-fiber diet.

Recommendation

Current evidence supports the use of low-carbohydrate diets like Atkins for short-term weight loss. Some risk factors for cardiovascular disease may also improve, but precisely how requires further research. Beyond six months, low-carbohydrate diets are no more effective than conventional, low-fat, reduced-calorie diets. Frequent constipation and headaches may lower compliance, resulting in one more “failed diet” that may discourage people from making necessary lifestyle and dietary changes. The long-term nutritional quality of low-carbohydrate diets, and their impact on long-term cardiovascular risk factors, remains a major concern. ❖

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Cholesterol- and Glucose-Lowering Effects of Fenugreek

By Susan T. Marcolina, MD, FACP

THE ROLE OF DIET HAS LONG BEEN RECOGNIZED AS THE cornerstone of therapy for the treatment of both diabetes and hypercholesterolemia, well-known risk factors for coronary artery disease, the leading cause of death worldwide in both men and women. Recent studies have elucidated the benefits of dietary fiber in both of these chronic medical conditions.¹ Pereira et al showed that for each 10 g/d of dietary fiber consumption, there was a 14% lower risk of coronary disease events and a 27% risk reduction of fatal coronary events.² The seeds of the herb fenugreek, *Trigonella foenum graecum* L., a condiment regularly used in East Indian, Mediterranean, and African cuisines, are a rich source of fiber and as such may be a useful adjunct in dietary management of these conditions.

Botanical Characteristics

Fenugreek is an annual leguminous plant extensively grown in India, Egypt, and Middle Eastern and Mediterranean countries. Its leaves are generally used as vegetables while its seeds, which mature in long pods, are ground and used as culinary condiments and for medicinal uses.^{3,4}

Fenugreek is one of the oldest medicinal plants. In ancient Egypt, fenugreek was used in embalming processes, for incense, and as a supplement added to wheat and corn flour for bread-making. The first recorded use of fenugreek in the Ebers papyri, which have been dated to 1500 BCE, was for labor induction during childbirth. Latin and Greek pharmacopoeias describe the antidiabetic effects of fenugreek seeds.^{5,6}

Widespread medicinal use has been somewhat limited by the pungent odor and bitter taste attributed to the presence of sotolone, a volatile chemical concentrated in the testa, the hard outer coat of the seed. As a result, solvent or physical extraction methods to isolate the biologically active compounds in a debittered, defatted product have been developed to mitigate this feature.⁵

Chemical Composition

Table 1 gives the nutritional composition of fenugreek seeds compared to other legumes.⁷ The dietary fiber of fenugreek seeds is dispersed throughout the seed coat and the endosperm (nutritive tissue of the plant seed). Analyses of fenugreek seed samples grown

throughout the world have shown that dietary fiber constitutes up to 48% of the dry weight.^{8,9} Chemical analysis of the fiber content of fenugreek revealed high concentrations of hydrocolloids or water-soluble gums called galactomannans, which have a unique structure of mannose and galactose monomers grafted in a 1:1 ratio. This accounts for its high water solubility in comparison to the galactomannans contained in other legumes.¹⁰

Mechanism of Action

The glucose-lowering effects of fenugreek have been attributed to several mechanisms. Sauvaire et al showed in vitro that the amino acid, 4-hydroxyisoleucine, unique to the *Trigonella* species, increased glucose-induced insulin release in human and rat pancreatic islet cells.¹¹ Amin et al demonstrated in human studies that fenugreek's hypoglycemic effects were due to stimulation of glucose-dependent insulin secretion from pancreatic beta cells, as well as by inhibition of the activities of alpha amylase and sucrase, intestinal enzymes involved in carbohydrate digestion.¹² The viscous galactomannan gel fraction of fenugreek appears to be an effective hypoglycemic agent and significantly inhibited glucose absorption from perfused rat small intestine by decreasing digestate transit time. These soluble dietary fibers are active in both ground whole seeds and as a purified galactomannan isolate.^{13,14} In addition, this gel fraction inhibits cholesterol absorption from the small intestine and bile acid resorption from the terminal ileum, thus increasing bile acid excretion. Fenugreek also contains saponins which, when ingested, form micellar complexes with bile salts, thereby minimizing their absorption and increasing fecal excretion.⁶

Pre-Clinical Animal Studies

Madar and Shomer isolated galactomannan from fenugreek seeds and demonstrated that this fraction decreased digestion and absorption of starch and uptake of bile salts by the rat intestinal mucosa.¹⁰ Similarly, Evans et al found that addition of fenugreek galactomannans, in contrast to guar gum and locust bean gum galactomannans, to the diet of rats lowered liver and plasma cholesterol levels and the rate of hepatic cholesterol synthesis.¹³ Ribes et al demonstrated that the galactomannan extract from fenugreek seeds decreased hyperglycemia and glucosuria in alloxan-induced diabetic

Table 1
Comparative nutritional composition* of several legumes⁷

Nutrient	Fenugreek	Chickpeas	Lentils	Mung Beans
Protein (g)	23	19	28	24
Total lipid (g)	6	6	1	1
Carbohydrate (g)	58	61	57	63
Fiber, total dietary (g)	25	17	31	16
Calcium (mg)	176	105	51	132
Iron (mg)	34	6	9	7
Magnesium (mg)	191	115	107	189
Potassium (mg)	770	875	905	1,246
Folate (mg)	57	357	433	625

* Value per 100 g of mature seeds

dogs.¹⁵ Stark showed that defatted fenugreek seeds, a gum isolate rich in dietary fibers, and a crude saponin extract each decreased cholesterol levels in rats to the same extent as did whole ground fenugreek seeds.¹⁶

Human Studies—Antidiabetic Effects

Gupta et al conducted a randomized, controlled, double-blind trial to evaluate the effect of fenugreek seeds on glycemic control in 25 patients with newly diagnosed Type 2 diabetes.¹⁷ The patients received either 1 g daily of debittered fenugreek seeds or dietary discretion and exercise for two months. After the study period, although mean fasting glucose levels and mean glucose tolerance test values were reduced in both groups, there were no significant intergroup differences. Despite the fact that study design and methods were not well described, it suggested that both fenugreek and diet/exercise improve glycemic control.

Two randomized, controlled, crossover studies in patients with Type 2 diabetes were conducted by Sharma and Raghuram.¹⁸ Fifteen patients in the first study had their diabetic drugs decreased 20% and were stabilized on diet and medication for a week prior to beginning the study. Seven of the 15 subjects ate meals with 100 g of defatted fenugreek seed powder divided into two equal daily doses for 10 days. They then crossed over to no fenugreek supplementation without a washout for the next 10 days. The other eight patients did the converse.

The second study had a similar design but only five patients participated, three of them receiving the fenugreek supplementation first. Significant improvements in mean fasting blood glucose levels, oral glucose tolerance tests, and 24-hour urinary glucose excretion were seen in the fenugreek-treated patients. In addition, these patients reported improvements in polyuria and polydipsia symptoms.

Human Studies—

Hypocholesterolemic Effects

Sharma et al conducted a study of 10 healthy, non-obese subjects with serum cholesterol levels above 240 mg/dL.¹⁹ Each subject was assigned to receive a control diet and an experimental diet, which was supplemented with defatted fenugreek seed powder over two successive time periods, each lasting 20 days. During the experimental period, 100 g of defatted fenugreek powder was divided into two equal parts and incorporated into chapatti (unleavened bread) for lunch and dinner. For the control period, the chapatti contained no fenugreek. Both diets were isocaloric and nutritionally similar except for the higher dietary fiber content of the experimental group. Physical activity was stable during the study. After ingestion of the fenugreek diet, eight of the 10 subjects experienced a 25% reduction in serum cholesterol. The fenugreek significantly reduced the LDL and VLDL fractions without altering the HDL levels. After 20 days of the control diet, the serum cholesterol and triglyceride levels were unchanged from baseline.

Sharma et al performed a long-term study of 60 diabetic patients, 40 of whom were taking one or more antidiabetic medications.²⁰ Each subject was initially placed on a control diet for seven days, followed by placement on an experimental diet for 24 weeks. During this experimental diet, 25 g of the fenugreek seed powder was divided into two equal parts and consumed in soup 15 minutes prior to lunch and dinner. Blood tests were drawn at the end of the control period and at weeks 4, 8, 12, and 24 of the experimental period. After 24 weeks of fenugreek, the mean total cholesterol level decreased 14% from baseline, a highly statistically significant result ($P < 0.001$). The decrease was primarily in LDL, triglyceride, and VLDL fractions, with HDL levels showing a small increase that was not statistically significant.

Dosage

Fenugreek seeds, called methi, can be obtained in markets that sell East Indian foods. One tablespoon is approximately 6 g of seed. It can be ground into powder and incorporated into breads, curry dishes, and other foods to augment their nutritional value. The typical intake range for diabetes or cholesterol lowering is 5-30 g of the powdered seeds with each meal.²¹ The German E Commission monograph recommends a daily intake of 6 g. Due to the bitter taste of the fenugreek

Table 2
Products containing standardized fenugreek galactomannan extract

Product	Dosage	Health Focus	Manufacturer
FenuMax	500 mg capsule	Blood glucose, cholesterol health	Nutra Science Sedona Labs Cottonwood, AZ
Fenugreek extract	350 mg capsule	Glucose, cholesterol health	Solaray Brand Neutraceutical Corp. Park City, UT

seeds, debittered seeds or encapsulated extract products are preferred.⁴

The galactomannan extracts, which contain the active principals, can be taken in lower doses than the seeds. One such product, FenuLife, manufactured by Acatris, Inc., is a patented dietary source of odorless galactomannan fiber extract from fenugreek. It is standardized to contain at least 85% total fiber, 75% of which is the soluble galactomannan hydrocolloid. Table 2 lists some products on the market which contain this extract.²²

Adverse Effects

Ingestion of more than 100 g of fenugreek seeds daily can cause intestinal cramping, diarrhea, and nausea. Study patients taking fenugreek initially reported mild gastrointestinal complaints consisting of diarrhea and excess flatus, which resolved within 3-4 days.²³

Fenugreek should not be used in pregnant females because it causes uterine tonic activity and can be an abortifacient.⁵ It is folklore practice, however, to use fenugreek to augment lactation in nursing women. Schanler et al support the use of fenugreek for this purpose in the medical literature.²⁴

Korman described a case of pseudo maple syrup urine disease (MSUD) in a healthy full-term male infant, secondary to fenugreek ingestion by his mother in the form of a spicy paste called "hilbe" during the early hours of labor. The infant was noted to have the characteristic urinary odor several hours after birth. However, clinical examination was normal and plasma amino acid analysis revealed normal levels of branched chain amino acids without detection of alloisoleucine, a derivative of isoleucine, which is elevated specifically in MSUD.⁵

Patients on anticoagulants should avoid taking fenugreek as it contains coumarin-like substances that may potentiate their effects.²⁵ Patients on oral hypoglycemics or insulin should have blood sugars closely monitored as fenugreek can significantly potentiate their glucose-lowering effects.

Patients with a documented peanut allergy should not take fenugreek due to the possibility of cross reactivity. Rare allergic reactions to fenugreek have been described and those patients who experienced such a reaction should avoid its use.²⁶

Conclusion

Legumes are functional foods that promote good health because they are low in sodium and an excellent source of low-glycemic carbohydrate, dietary fiber, protein, and minerals. Animal and human clinical research thus far suggests fenugreek has the potential to be a useful dietary intervention. However, more studies involving larger numbers of patients with fenugreek products standardized to specific galactomannan content must be performed to strengthen the evidence for its utility as a routine dietary intervention. Its use is contraindicated in persons who are pregnant, have a documented peanut allergy, or are taking anticoagulant medicines. Blood sugars should be carefully monitored in patients on insulin or oral hypoglycemics.

Recommendation

Fenugreek in various forms, including whole ground seeds, defatted seed powder, and standardized galactomannan extracts, can be safely consumed in divided daily doses of 5-30 g to achieve glucose and cholesterol lowering. Fenugreek is an inexpensive, low-risk, food-based addition to the dietary armamentarium that may be useful for certain patients with diabetes and hypercholesterolemia. ❖

Dr. Marcolina is a board-certified internist and geriatrician in Issaquah, WA.

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Got Calcium?

Practical Clinical Pearls

By David Kiefer, MD

DO YOU EVER FIND YOURSELF HALFWAY THROUGH A glass of milk, knowing your mother would have been proud because it is so good for your bones and teeth? This public health message continues and has expanded to include numerous at-risk groups that may need to augment their dietary calcium intake. These recommendations have spawned an explosion in the types of calcium supplements available to meet our preventive health needs, but this may be confusing for patients and practitioners alike. What, literally, is the scoop?

Physiology

Calcium, as the most abundant mineral in the human body, functions in nerve conduction, muscle contraction, hemostasis, cell membranes, and, of course, forming bones and teeth. Ninety-nine percent of the body's calcium is stored in the skeletal system and the rest is in an exchangeable pool.¹ Calcium either exists in the serum in the metabolically active ionized form or as protein-bound complexes, and serum levels are under tight control by parathyroid hormone, calcitonin, and vitamin D.¹

The average calcium intake for adults in the United States is less than 800 mg of elemental calcium per day,² well below the estimated prehistoric intake of 1,900 mg/d.¹ This is despite recent surveys in the United States that report an increase in daily calcium supplement use from 6% to 11% between 1987 and 2000.³

Foods high in calcium include sardines, dairy products (especially ricotta cheese, yogurt, milk), tofu, sesame seeds, collard greens, and soybeans. (For detailed information about nutrient contents for specific foods, visit the Food and Nutrition Information Center web site at www.nal.usda.gov/fnic/.)

Absorption/Excretion

Calcium absorption is variable and depends upon a number of factors. When calcium intake is in the average range (750 mg/d), humans absorb 25-50% of what is ingested;¹ the fraction of calcium absorbed increases in low-intake situations and vice versa.⁴ There is also a variation in absorption percentage with age: Absorption is highest (about 60%) in infants, dropping to about 25% in young adults, with small peaks in early puberty and the last two trimesters of pregnancy.⁴ Calcium also behaves as a "threshold" nutrient, where beyond a certain intake (e.g., 1,000 mg/d for young adult females), there is no further effect on the body's calcium balance.⁵

There are many additional factors that affect the absorption of calcium (see Table 1). Absorption occurs in the duodenum and proximal jejunum, where there is a saturable and vitamin D-dependent system more important in low-intake situations, and throughout the small bowel (especially the ileum), involving a passive and non-saturable system more important when calcium intake is high.^{1,4} Caffeine (such as the amount in two cups of coffee per day) may decrease both calcium absorption and increase renal calcium excretion in situations when calcium intake is less than 800 mg/d.

Calcium is lost through the skin (< 20 mg/d), and in urine (40-200 mg/d) and feces (80-120 mg/d).⁶ Urinary excretion of calcium may increase with diets high in sodium or protein, but it remains unproven how this translates into clinically important endpoints such as bone mineral density, osteoporosis, or fractures.^{4,6}

Basic Intake Recommendations

Recommended intakes of vitamins and minerals were published from 1941 to 1989 as Recommended Dietary Allowances (RDA), values that were meant to meet the requirements of approximately 98% of healthy individuals of a certain age and gender.⁷ RDA values are useful in setting goals for individuals. More recently, the Institute of Medicine expanded on RDAs by establishing

Table 1

Factors affecting the absorption of calcium from the gastrointestinal tract²²

Calcium absorption enhanced by:

Food, probably via gastric acid
Lactose
Adequate vitamin D (either dietary or from sunlight exposure)

Calcium absorption decreased by:

Insoluble fiber
Phytates (high in such foods as unleavened bread, raw beans, seeds, nuts and grains, and soy)
Oxalate (high in such foods as spinach, sweet potatoes, rhubarb, and beans)
High calcium intakes (> 500 mg in one dose)
Caffeine
Advancing age (approximately 0.20% less per year)

Dietary Reference Intakes (DRI), four listings that include the Recommended Dietary Allowance (RDA); the Estimated Average Requirement (EAR), a value that ensures adequacy in 50% of a particular group; the Adequate Intake (AI), used if there is not sufficient evidence to set the EAR or RDA, and representing an estimate of the average intake by a certain group of healthy people; and the Tolerable Upper Intake Level (UL), the highest level below which there is no harm to the individual.⁴ The National Institutes of Health (NIH) also published guidelines for the optimal intake of calcium, based upon the input of experts from many medical disciplines.⁸

For calcium, the Adequate Intake (AI) recommendations, compared with NIH Consensus Statement recommendations, are listed in Tables 2 and 3. The UL for calcium (all individuals, including those who are pregnant or lactating) is 2,500 mg/d; there was not enough evidence to establish an UL for infants 0-12 months old.

Calcium Supplement Formulations

There are many different types of calcium supplements that differ in amount of elemental calcium, bioavailability, and cost. Calcium, a cation, needs to be paired with an anion carrier molecule to make a stable tablet for human consumption. There are many anions used for this purpose (i.e., carbonate, citrate, gluconate, sulfate, citrate-malate); it is the weight of the anion molecule that determines what percentage of a calcium product is the elemental calcium. For example, carbonate is relatively light, so 40% of calcium carbonate tablets are elemental calcium, compared to 24% for calcium citrate, or 9.3% for calcium gluconate.⁵ To avoid confusion, when reading a product label, focus on the amount (mg) of elemental calcium for a given tablet of each product.

With respect to bioavailability, adult absorption efficiencies from most supplements average 30%-32%. One calcium form, calcium citrate-malate, is used to fortify some foods such as orange juice, and has an absorption efficiency around 35%. Several clinical trials have compared the absorption of calcium carbonate and calcium citrate. One trial found no difference in absorption when 24 postmenopausal women (23 white, one African-American; average age 56 years) were randomized to take 500 mg of elemental calcium, either as carbonate or citrate, plus 200 IU of vitamin D.⁹ Of note, the

women were also asked to avoid all dairy to keep food calcium ingestion below 400 mg; low calcium intake situations may lead to a situation of overall enhanced calcium absorption.

In a small trial of 11 people with achlorhydria, absorption from calcium citrate was significantly better than from calcium carbonate. In the comparison group of nine people with normal gastric acid, there was no difference between citrate and carbonate absorption.¹⁰ For these reasons, some sources recommend that people who have achlorhydria either use calcium citrate or take calcium carbonate supplements with a meal.⁴

Another randomized study compared the effects of 1,000 mg of calcium citrate vs. calcium carbonate in 40 postmenopausal women (mean age 73 years) by measuring several physiological parameters meant to indicate bone turnover.¹¹ Calcium citrate caused a significant decrease in all four markers of bone resorption when compared to calcium carbonate; there was no difference in serum PTH levels or urinary calcium excretion.

A recent trend has been to use calcium supplements from coral calcium (which contains calcium carbonate) obtained from the reefs off Okinawa. There are concerns

Table 2 Recommended daily intake of elemental calcium (mg) for different age groups		
Age Group (both sexes)	Adequate Intake	NIH Consensus Statement
0-6 months	210	400
7-12 months	270	600
1-3 years	500	800
4-5 years	800	800
6-8 years	800	800-1,200
9-10 years	1,300	800-1,200
11-18 years	1,300	1,200-1,500
19-24 years	1,000	1,200-1,500
25-50 years	1,000	1,000
51-65 years	1,200	1,000
> 65 years	1,200	1,500

Table 3 Recommended daily intake of elemental calcium (mg) for special populations		
Group	Adequate Intake	NIH Consensus Statement
Pregnancy/lactation (≤ 18 years)	1,300	1,200-1,500
Pregnancy/lactation (19-50 years)	1,000	1,200-1,500
Postmenopause (on estrogen)	1,200	1,000
Postmenopause (not on estrogen)	1,200	1,500

about the possibility of high amounts of lead and mercury in some of the coral calcium products, as well as no proof of the other health benefits often touted with this type of calcium.¹² Furthermore, other sources recommend avoiding oyster shell calcium, bone meal calcium, and dolomite calcium due to concerns about lead contamination.¹

Clinical Trials

Clinical research has shown a benefit with calcium supplementation in several disease states: osteoporosis and osteoporotic fractures, colorectal cancer, and breast cancer. Calcium supplementation appears to increase bone density. One meta-analysis showed that calcium was more effective than placebo in reducing rates of bone loss in postmenopausal women.¹³ There was also a trend toward improvement in vertebral fracture risk. One review of clinical trials found that increased intake of calcium in postmenopausal women led to a slight decrease in fracture risk: With approximately 1,000 mg of supplemental calcium per day there was a 30% reduction in fracture risk, including a 24% decrease in hip fracture risk.¹⁵ Furthermore, one placebo-controlled trial of 1,200 mg of calcium triphosphate plus 800 IU cholecalciferol in 3,270 women (mean age 84 years) demonstrated a decreased risk (odds ratio 0.70) of fracture, including hip and other non-vertebral fractures, over 36 months of follow-up.¹⁶ The effects of calcium on bone mineral density are mediated through other variables, such as body mass index (BMI), muscle strength, gender, and age.¹⁴ For example, these variables interact in such a way that the effects of dietary calcium are most pronounced in people with a low BMI.

The associations between high calcium intake and lower cancer risks are conflicting. One double-blind, randomized, controlled trial of 930 people found a slight reduction in recurrent colorectal adenomas over four years of supplementation with calcium carbonate (1,200 mg of elemental calcium daily).¹⁷ However, a review of the epidemiological evidence of association between calcium, vitamin D, and colorectal cancer failed to find anything more than a weak, non-significant inverse relationship between calcium and colorectal cancer rates.¹⁸

For breast cancer, a cohort analysis of 88,691 women in the Nurses' Health Study found that a high intake of low-fat dairy foods was associated with a lower risk of breast cancer in premenopausal women; this same connection was not statistically significant for postmenopausal women.¹⁹ It was difficult to determine, however, if the calcium in these dairy foods was independently associated with reduced breast cancer risks. Animal studies have demonstrated that low calcium

intake can lead to increases in breast cancer depending on the type of diet: In low-fat diets, increased breast cancer rates only occur when dietary calcium is very low, but in a high-fat diet, even moderately low calcium intakes (such as found in the normal Western diet) could lead to higher breast cancer rates.²⁰

Adverse Effects

Most calcium supplements are well tolerated, and clinical trials often report side effects as being minimal.¹¹ Calcium carbonate can cause constipation, bloating, and gas, symptoms that can be avoided by increasing fluid intake or switching to a different preparation.² For any calcium supplement, there may be a risk to people with calcium-containing urinary stones or with absorptive hypercalciuria, though low calcium intakes may actually increase the risk for stones (via increased urinary oxalate).² One clinical trial studied calcium citrate (400 mg twice daily) in 18 healthy, stone-free postmenopausal women, and found no increased risk of stone formation.²¹

The over-use of calcium carbonate antacids (greater than approximately 4 g/d in people with impaired renal function, or 20 g/d in people with normal renal function) can lead to the "milk-alkali" syndrome, or high blood calcium levels, severe renal damage, metabolic alkalosis, and ectopic calcium deposition.⁸

Calcium may interfere with the absorption of many compounds including iron, zinc, bisphosphonates, and tetracycline,² as well as quinolone antibiotics,²² sotalol,²³ and levothyroxine,²⁴ either by forming complexes with the medications or by changing the acidity of the stomach (i.e., with calcium carbonate). It seems prudent to recommend that patients separate the timing of their calcium supplements and other medications. Thiazide diuretics may act to decrease the excretion of calcium.²⁵

There is some epidemiological evidence that calcium can increase the incidence of prostate cancer. The Physicians' Health Study (a cohort of 20,885 male U.S. physicians) demonstrated a trend toward increased prostate cancer risk with increased calcium intake as estimated from five dairy foods; the high calcium intake group (> 600 mg/d) had a 32% higher risk of prostate cancer than did the low calcium intake group (\leq 150 mg/d).²⁶ This result agrees with other epidemiological studies as well as with observations that countries with higher per capita dairy consumption also seem to have higher prostate cancer rates. The mechanism of this effect seems to be that a high calcium intake suppresses the formation of 1,25 dihydroxy vitamin D₃ levels, a vitamin that otherwise inhibits the proliferation of cells in the prostate.

Conclusion

Calcium is an important mineral for many physiological processes in the human body. The average intake in the United States is less than optimal, and recommendations have been made for the ideal daily intake of elemental calcium based on age, gender, and for certain medical situations. It is important to be aware of the different factors that can aid or hinder calcium absorption, as well as the form of calcium supplements. Calcium citrate is better absorbed in cases of achlorhydria, a common problem that occurs as people age. There are important connections between calcium intake and osteoporosis, fracture risk, and cancer rates, some of the specifics of which are still being elucidated.

Recommendation

The contribution of adequate calcium intake to health and the prevention of disease is important, especially for certain ages and at-risk populations. People should focus on consuming low-fat foods high in calcium, using supplements when necessary to achieve the intake of elemental calcium recommended by the NIH Consensus Panel (see Tables 2 and 3). Calcium citrate may be better absorbed and correlate with better clinical outcomes in people with achlorhydria; otherwise, cheaper supplements such as calcium carbonate may be adequate. ❖

Dr. Kiefer recently completed a fellowship at the Program in Integrative Medicine, College of Medicine, University of Arizona, Tucson.

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Clinical Briefs

With Comments from Russell H. Greenfield, MD

Manipulative Therapy for Shoulder Pain

Source: Bergman GJD, et al. Manipulative therapy in addition to usual medical care for patients with shoulder dysfunction and pain. *Ann Intern Med* 2004;141:432-439.

Goal: To assess the effectiveness of manipulative therapy of the shoulder girdle plus usual care in the treatment of shoulder dysfunction and pain.

Design: Randomized, controlled clinical trial.

Subjects: 150 adults with shoulder dysfunction and associated symptoms unrelated to trauma recruited from 50 general practices in the Netherlands.

Methods: All subjects received usual care from their general practitioners; the intervention group (n = 79) also received up to six manipulative therapy sessions over a period of 12 weeks. Primary outcome measure was patient-perceived recovery, and determinations were made at baseline, six weeks, and 12 weeks. Secondary outcomes included severity of complaints, shoulder pain, functional disability, and general health.

Results: By study's end, significantly more people who received manipulative

therapy reported full recovery or major improvement than those in the control group. At 26 and 52 weeks follow-up, the main complaint was significantly less severe in the intervention group.

Conclusion: Manipulative therapy of the shoulder girdle accelerates recovery of shoulder symptoms when combined with usual medical care.

Study strengths: Standardized treatment protocol; excellent follow-up.

Study weaknesses: Complete blinding not possible with manipulative therapies; no sham manipulation group; more than 20% of subjects in each group were missing data for at least one outcome variable; no limit on duration of symptoms; no range of motion determinations; outcomes were practitioner-dependent.

Of note: Usual care comprised use of oral analgesics or anti-inflammatory agents, corticosteroid injections, and physiotherapy (including shoulder exercises and massage); manual therapies were applied based on the therapist's preferred techniques (a total of eight therapists took part in the study); subjects in the intervention group received 3.8 ± 1.5 treatments lasting 23 ± 13 minutes; cost analysis is pending.

We knew that: The shoulder girdle is

composed of the cervicothoracic spine and adjacent ribs; up to 20% of people with shoulder symptoms have no shoulder joint dysfunction and are ultimately found to have shoulder girdle dysfunction; European data suggest that at one year more than 40% of people with shoulder complaints remain somewhat disabled.

Clinical import: Shoulder injuries are becoming increasingly commonplace and a growing number of orthopedists now specialize in care of the shoulder joint. Concomitantly, there has been a rise in interest in manipulative therapies, both chiropractic and osteopathic. A significant amount of data has been amassed addressing the use of manipulative therapies for back and neck complaints, but very little on their use for shoulder disorders. While reinforcing the idea that manual therapists are seeing more patients with shoulder and other joint disorders, and that such therapy may benefit select patients, the article does not effectively counter arguments that outcome may depend more upon a therapist's persona than upon the technique employed.

What to do with this article: Keep the abstract on your computer. ❖

CME Questions

CME Instructions: Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a certificate of completion. When an evaluation form is received, a certificate will be mailed to the participant.

50. Low-carbohydrate diets are *not* more effective than conventional, low-fat, reduced-calorie diets at:

- three months.
- six months.
- nine months.
- 12 months.

51. Although fenugreek may be safely used to achieve glucose and cholesterol lowering, it should be avoided in persons who:

- are pregnant.
- have a documented peanut allergy.
- are taking anticoagulant medicines.
- All of the above

52. Clinical research has shown a benefit with calcium supplementation in which of the following disease states?

- Osteoporosis and osteoporotic fractures
- Breast cancer
- Colorectal cancer
- All of the above

Answers: 50. d, 51. d, 52. d.

ALTERNATIVE MEDICINE ALERT™

The Clinician's Evidence-Based Guide to Complementary Therapies

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The American Heart Association Dietary Recommendations

THE EATING PLAN RECOMMENDED BY THE AMERICAN HEART ASSOCIATION (AHA) WAS designed with the goal of reducing three of the major risk factors for heart attack—high blood cholesterol, high blood pressure, and excess body weight. The recommendations incorporate the latest advice of medical and nutrition experts. Following this plan, according to the AHA, will help Americans achieve and maintain a healthy eating pattern, the benefits of which include a healthy body weight, a desirable blood cholesterol level, and a normal blood pressure. Many research studies have compared popular diet programs, including low-carbohydrate dietary plans, to the AHA dietary recommendations.

AHA Dietary Guidelines

The AHA plan is based on these dietary guidelines outlined in Table 1.

Table 1

AHA dietary guidelines

- Eat a variety of fruits and vegetables. Choose five or more servings per day.
- Eat a variety of grain products, including whole grains. Choose six or more servings per day.
- Include fat-free and low-fat milk products, fish, legumes (beans), skinless poultry and lean meats.
- Choose fats with 2 g or less saturated fat per serving, such as liquid and tub margarines, canola oil, and olive oil.
- Balance the number of calories you eat with the number you use each day. (To find that number, multiply the number of pounds you weigh now by 15 calories. This represents the average number of calories used in one day if you're moderately active. If you get very little exercise, multiply your weight by 13 instead of 15. Less-active people burn fewer calories.)
- Maintain a level of physical activity that keeps you fit and matches the number of calories you eat. Walk or do other activities for at least 30 minutes on most days. To lose weight, do enough activity to use up more calories than you eat every day.
- Limit your intake of foods high in calories or low in nutrition, including foods like soft drinks and candy that have a lot of sugars.
- Limit foods high in saturated fat, trans fat, and/or cholesterol, such as full-fat milk products, fatty meats, tropical oils, partially hydrogenated vegetable oils, and egg yolks. Instead choose foods low in saturated fat, trans fat, and cholesterol.
- Eat less than 6 g of salt (sodium chloride) per day (2,400 mg of sodium).
- Have no more than one alcoholic drink per day if you're a woman and no more than two if you're a man.

Source: American Heart Association. Available at: www.americanheart.org/presenter.jhtml?identifier=1330. Accessed on Nov. 12, 2004.

Table 2**Food groups and recommended servings**

Food Group	Recommended Servings
Lean meat, fish, skinless poultry, dry beans, eggs and nuts	2-3 servings per day; fish twice a week
Vegetables and fruits	5 or more per day
Fat-free and low-fat milk, yogurt and cheese	2-3 per day
Breads, cereals, pasta and starchy vegetables	6-11 per day
Saturated and trans fats, oils, salt and sweets	Use sparingly

Source: American Heart Association. Available at: www.americanheart.org/presenter.jhtml?identifier=4665. Accessed on Nov. 12, 2004.

Table 3**Recommendations for fat consumption**

Risk Category	Saturated Fat + Trans Fat Combined	Dietary Cholesterol
People without coronary heart disease, diabetes, or high LDL cholesterol	No more than 10% of total calories	Less than 300 mg per day on average
People with coronary heart disease, diabetes, or high LDL cholesterol	No more than 7% of total calories	Less than 200 mg per day on average

Source: American Heart Association. Available at: www.americanheart.org/presenter.jhtml?identifier=4665. Accessed on Nov. 12, 2004.

According to the AHA, this plan is an easy-to-follow guide to delicious eating—and does not require giving up favorite foods. Every meal doesn't have to meet all the guidelines; however, it is important to apply the guidelines to an overall eating pattern over several days.

With these guidelines, the American Heart Association hopes that good dietary choices will do more than improve heart health: These dietary recommendations may reduce the risk for other chronic health problems as well, including Type 2 diabetes, osteoporosis (bone loss), and some forms of cancer.

The American Heart Association can help consumers choose heart-healthy foods when grocery shopping. Hundreds of items throughout the grocery store have the American Heart Association special, red heart-check mark. Visit www.americanheart.org/FoodCertification/ for a list of certified foods.

Food Groups and Recommended Servings

Each of the basic food groups must be represented in an individual's diet to supply a balanced combination of

nutrients, vitamins, and minerals. Variety is the key to good nutrition. Table 2 outlines the basic food groups and recommended servings.

Some populations have a greater risk for chronic health problems. Table 3 shows recommended levels of saturated fat, trans fat, and dietary cholesterol for people in two categories of risk.

AHA also suggests balancing caloric input with 30-60 minutes of moderate-to-vigorous physical activity on most days to avoid gaining weight.

For More Information

For more information on the dietary recommendations of the American Heart Association, including a food certification list, menu planning tips, recipes, and nutrition labeling guidance, please visit: www.americanheart.org.

Source: American Heart Association. Available at: www.americanheart.org/presenter.jhtml?identifier=9203. Accessed on November 12, 2004.

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