Review

Cardiovascular Disease Resulting From a Diet and Lifestyle at Odds With Our Paleolithic Genome: How to Become a 21st-Century Hunter-Gatherer

James H. O'Keefe, Jr, MD, and Loren Cordain, PhD

Our genetic make-up, shaped through millions of years of evolution, determines our nutritional and activity needs. Although the human genome has remained primarily unchanged since the agricultural revolution 10,000 years ago, our diet and lifestyle have become progressively more divergent from those of our ancient ancestors. Accumulating evidence suggests that this mismatch between our modern diet and lifestyle and our Paleolithic genome is playing a substantial role in the ongoing epidemics of obesity, hypertension, diabetes, and atherosclerotic cardiovascular disease. Until 500 generations ago, all humans consumed only wild and unprocessed food foraged and hunted from their environment. These circumstances provided a diet high in lean protein, polyunsaturated fats (especially omega-3 [ω-3] fatty acids), monounsaturated fats, fiber, vitamins, minerals, antioxidants, and other beneficial phytochemicals. Historical and anthropological studies show hunter-gatherers generally to be healthy, fit, and largely free of the degenerative cardiovascular diseases common in modern societies. This review outlines the essence of our hunter-gatherer genetic legacy and suggests practical steps to realign our modern milieu with our ancient genome in an effort to improve cardiovascular health.

Mayo Clin Proc. 2004;79:101-108

HDL = high-density lipoprotein; LDL = low-density lipoprotein

Humans evolved during the Paleolithic period, from approximately 2.6 million years ago to 10,000 years ago. Although the human genome has remained largely unchanged (DNA evidence documents relatively little change in the genome during the past 10,000 years),[1] our diet and lifestyle have become progressively more divergent from those of our ancient ancestors. These maladaptive changes began approximately 10,000 years ago with the advent of the agricultural revolution and have been accelerating in recent decades. Socially, we are a people of the 21st century, but genetically we remain citizens of the Paleolithic era.

Today most of us dwell in mechanized urban settings, leading largely sedentary lives and eating a highly processed synthetic diet. As a result, two thirds of Americans are overweight or obese.[2] The lifetime incidence of hypertension is an astounding 90%,[3] and the metabolic syndrome is present in up to 40% of middle-aged American adults.[4] Cardiovascular disease remains the number 1 cause of death, accounting for 41% of all fatalities, and the prevalence of heart disease in the United States is projected to double during the next 50 years.[5] Despite remarkable pharmacological and technological advances, the pandemic of cardiovascular disease continues. At least for today, the genes we are born with are those that we will live and die with. Thus, the most practical solution for reducing the incidence of chronic degenerative diseases such as atherosclerosis is to realign our current maladaptive diet and lifestyle to simulate the milieu for which we are genetically designed.

Living organisms thrive best in the milieu and on the diet to which they were evolutionarily adapted; this is a fundamental axiom of biology. All of the food consumed daily by our ancient ancestors had to be foraged or hunted from wild plants and animals in their natural world. In many respects, that Paleolithic world is gone forever, but insights gained from a wide array of disciplines are providing a clear picture of the ideal diet and lifestyle for humans. The hunter-gatherer mode of life became extinct in its purely non-westernized form in the 20th century.[6] At the beginning of the 21st century, we are the first generation to have the genetic and scientific understanding to allow us to reconstruct the essence of this lifestyle and the means to afford it.

Historical and archaeological evidence shows hunter-gatherers generally to be lean, fit, and largely free from signs and symptoms of chronic diseases.[7] When hunter-gatherer societies transitioned to an agricultural grain-based diet, their general health deteriorated.[8,9] Average adult height was substantially shorter for both men and women who consumed cereals and starches compared with

From the Mid America Heart Institute, Cardiovascular Consultants, Kansas City, Mo (J.H.O.); and Department of Health and Exercise Science, Colorado State University, Fort Collins (L.C.).

Individual reprints of this article are not available. Address correspondence to James H. O'Keefe, Jr, MD, Mid America Heart Institute, Cardiovascular Consultants, 4330 Wornall Rd, Suite 2000, Kansas City, MO 64111 (e-mail: jhokeefe@cc-pc.com).

Table 1. **Comparison of Diets**

	Hunter-gatherer	Low-carbohydrate (Atkins diet)	Traditional low-fat (Ornish diet)	Traditional Mediterranean
Protein (%)	High (19-35)	Moderate (18-23)	Low (<15)	Moderate (16-23)
Carbohydrates (%)	Moderate (22-40)	Low (4-26)	High (80)	Moderate (50)
Total fat (%)	Moderate (28-47)	High (51-78)	Low (<10)	Moderate (30)
Saturated fat	Moderate	High	Low	Low
Monounsaturated fat	High	Moderate	Low	High
Polyunsaturated fat	Moderate	Moderate	Low	Moderate
Omega-3 fat	High	Low	Low	High
Total fiber	High	Low	High	High
Fruits and vegetables	High	Low	High	High
Nuts and seeds	Moderate	Low	Low	Moderate
Salt	Low	High	Low	Moderate
Refined sugars	Low	Low	Low	Low
Glycemic load	Low	Low	High	Low

their hunter-gatherer ancestors who consumed lean meats, fruits, and vegetables.[10] Furthermore, studies of bones and teeth reveal that populations who changed to a grain-based diet had shorter life spans, higher childhood mortality, and a higher incidence of osteoporosis, rickets, and various other mineral- and vitamin-deficiency diseases.[8,9] When former hunter-gatherers adopt Western lifestyles, obesity, type 2 diabetes, atherosclerosis, and other diseases of civilization become commonplace.[11,12]

This review outlines the essence of the hunter-gatherer lifestyle and diet and suggests practical steps to realign our modern milieu with our ancient genome in an effort to improve cardiovascular health, vigor, and longevity.

THE IDEAL HUMAN DIET

Perhaps no scientific topic has generated more controversy and confusion in recent times than the question of the ideal human diet. Medical experts espouse divergent views of human nutrition with evangelical zeal, each citing scientific data to validate their respective contradictory conclusions. This confusing dialogue is epitomized by the Atkins[13] vs Ornish[14] debate. The Atkins diet includes high protein, high saturated fat, and avoidance of nearly all carbohydrates. In contrast, the Ornish diet consists of 80% carbohydrates and minimized consumption of all animal protein fats. Proponents of both diets insist theirs is the answer to the American epidemics of obesity and cardiovascular disease; however, the advice for these diets is mutually exclusive and diametrically opposed.

In truth, the ideal diet is neither of these extremes nor what many medical professionals now promote. In a recently published large review of approximately 150 studies on the link between diet and cardiovascular health,[15] the authors concluded that 3 major dietary approaches have emerged as the most effective in preventing cardiovascular events: (1) replacing saturated and *trans*-fats with monounsaturated and polyunsaturated fats; (2) increasing consumption of omega-3 (ω-3) fats from either fish or plant sources such as nuts; and (3) eating a diet high in various fruits, vegetables, nuts, and whole grains and avoiding foods with a high glycemic load (a large amount of quickly digestible carbohydrates). Despite common misperceptions, this report found no strong evidence for a link between risk of cardiovascular disease and intake of meat, cholesterol, or total fat.

These broad characteristics are consistent with the diet that Paleolithic humans evolved eating. This is the diet that our hunter-gatherer ancestors thrived on until the advent of the agricultural revolution. Through the millennia, our genome and physiology became adapted to this diet. Of course, this diet varied by paleontological period, geographic location, season, and culture, but many characteristics remained consistent until recent times (Table 1).

REAL FOOD, NOT SYNTHETIC FOOD

Our remote ancestors consumed only natural and unprocessed food foraged and hunted from their environment. This subsistence strategy provided a diet of lean protein that was high in fiber, vitamins, minerals, antioxidants, and other beneficial phytochemicals[16] (Table 2). The typical Paleolithic diet compared with the average modern American diet contained 2 to 3 times more fiber, 1.5 to 2.0 times more polyunsaturated and monounsaturated fats, 4 times more ω-3 fats, but 60% to 70% less saturated fat. Protein intake was 2 to 3 times higher, and potassium intake was 3 to 4 times higher; however, sodium intake was 4 to 5 times lower.[17] Finally, the Paleolithic diet contained no refined grains and sugars (except for seasonally available honey). Clearly, the ongoing epidemic of cardiovascular diseases is at least in part due to these striking discrepancies between the diet we are designed to eat and what we eat today.

In growing season, abundant fruits, berries, and vegetables were consumed. The one variable on which nearly all nutritional experts can agree is the need for increased intake of fruits and vegetables in our modern diet. We do not fully understand all the health-promoting components of unprocessed whole-plant foods; thus, the only way to ensure the benefits is to consume these foods regularly in their natural and unprocessed state. Most experts recommend an intake of 5 servings of fruits and vegetables per day; studies indicate that only 16% of adults are meeting this goal.[18] However, approximately 8 or more daily servings of fresh fruits and vegetables (avoiding potatoes and bananas because of their high glycemic loads) are necessary to replicate the dietary composition that we evolved eating[17] and to lower the risk of coronary heart disease.[19]

Large randomized controlled trials recently have shown antioxidant supplements to be ineffective in improving cardiovascular outcomes.[20,21] In contrast, many epidemiological studies have shown cardiovascular protection from diets that contain foods naturally high in antioxidants, such as vitamins A, C, and E.[19,22] The hunter-gatherer diet is high in beneficial phytochemicals and antioxidants, thus rendering multivitamin and mineral supplements superfluous.[17]

Table 2. **Fundamentals of the Hunter-Gatherer Diet and Lifestyle**

Eat whole, natural, fresh foods; avoid highly processed and high-glycemic-load foods
Consume a diet high in fruits, vegetables, nuts, and berries and low in refined grains and sugars. Nutrient-dense, low-glycemic-load fruits and vegetables such as berries, plums, citrus, apples, cantaloupe, spinach, tomatoes, broccoli, cauliflower, and avocados are best
Increase consumption of omega-3 fatty acids from fish, fish oil, and plant sources
Avoid *trans*-fats entirely, and limit intake of saturated fats. This means eliminating fried foods, hard margarine, commercial baked goods, and most packaged and processed snack foods. Substitute monounsaturated and polyunsaturated fats for saturated fats
Increase consumption of lean protein, such as skinless poultry, fish, and game meats and lean cuts of red meat. Cuts with the words *round* or *loin* in the name usually are lean. Avoid high-fat dairy and fatty, salty processed meats such as bacon, sausage, and deli meats
Incorporate olive oil and/or non–*trans*-fatty acid canola oil into the diet
Drink water
Participate in daily exercise from various activities (incorporating aerobic and strength training and stretching exercises). Outdoor activities are ideal

Caloric Intake

Throughout most of human history, food consumption (energy intake) was obligatorily linked to food acquisition (energy output). Accordingly, our ancient ancestors expended more energy finding and obtaining food calories than do typical sedentary, westernized citizens for whom there is virtually no connection between energy intake and energy expenditure.

Our cravings for calorie-dense foods, such as fats, sweets, and starches, are legacies of our Paleolithic ancestors, who sought these foods because they conferred positive survival value in an environment in which these food types were scarce. These cravings betray us in our modern world, where calorie-dense foods are abundant and inexpensive, and most people die of caloric excess manifested as obesity, the metabolic syndrome, hypertension, and cardiovascular disease. Compounding the issue is the fact that our genome became adapted to an environment in which caloric intake was often sporadic and sometimes inadequate. This promoted efficient energy use and storage, commonly referred to as the *thrifty gene hypothesis*. Although this genetic adaptation (which results in storage of excess calories as intra-abdominal fat) provides a survival advantage in an environment of scarcity, it becomes a liability in the setting of long-term excessive caloric intake.

Although the key to weight loss is simply the daily consumption of fewer calories than are expended, it is easier to moderate caloric intake in a diet that has adequate quantities of protein and fat because of superior satiety compared with a high-carbohydrate, low-fat diet.[15,23,24] This strategy in part accounts for the success of the Atkins diet in inducing weight loss,[25] but its high levels of saturated fat, low levels of antioxidants, and net metabolic acidosis, which may promote osteoporosis and atherosclerosis, make this a suboptimal eating style.[26,27] A growing consensus indicates that a diet containing moderate amounts of beneficial fat and protein in addition to carbohydrates consisting exclusively of low-glycemic-load foods (nonstarchy vegetables and fruits) in conjunction with daily exercise is the most effective way to achieve and maintain ideal body weight and prevent cardiovascular disease.[15,23,24,26] This approach was the eating pattern and lifestyle of prehistoric humans.

ω-3 Fats

The polyunsaturated fats are classified as ω-6 (generally proinflammatory) and ω-3 (anti-inflammatory with several other inherent cardioprotective effects). ω-3 Fats were abundant in the diet of our Paleolithic ancestors.[28] In the natural world, the broad base of the food chain is composed of ubiquitous algae in the sea and of grasses and leaves on land. The small amount of fat in algae, grasses, and leaves is rich in ω-3 fatty acids, which become more concentrated in larger animals up through both the land and marine food chains, especially in fish and larger grazing animals. Today, meat from domesticated animals is low in ω-3 fats because these animals are generally grain-fed or corn-fed rather than grass-fed.[29] This and other issues have resulted in much lower intake of ω-3 fats today compared with our remote ancestors.[28,29]

The correction of this ω-3 deficiency in the modern diet is a key step to improving the cardiovascular risk in our

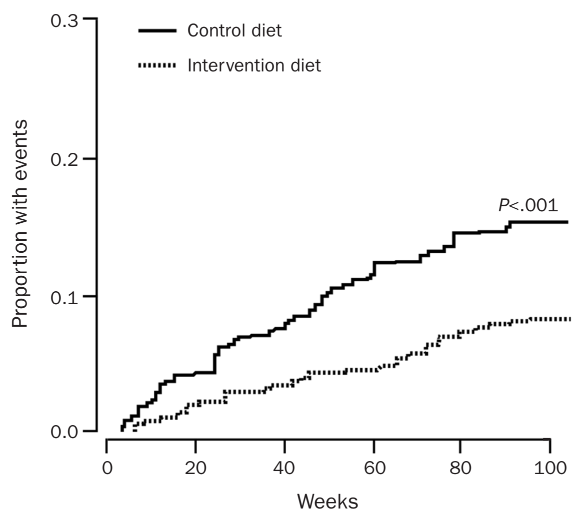

Figure 1. The Indo-Mediterranean Diet Heart Study[32] showed a reduction of cardiac deaths and myocardial infarctions in patients on the intervention diet (a traditional Mediterranean diet high in omega-3 fats, fruits, and vegetables and low in saturated fat) compared with a standard American Heart Association (control) diet.

population.[30] Two randomized trials, the Lyon Diet Heart Study,[31] which involved 600 postinfarction patients, and the Indo-Mediterranean Diet Heart Study[32] (Figure 1), which involved 1000 coronary heart disease patients, evaluated a standard low-fat American Heart Association

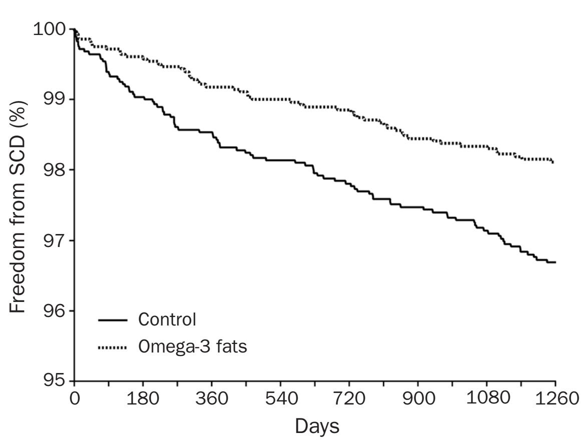

Figure 2. The Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico Prevenzione study[33] showed a 45% reduction in sudden cardiac death (SCD) among patients receiving a concentrated fish oil supplement containing approximately 850 mg of omega-3 fats.

diet vs a traditional Mediterranean diet (similar in composition to our ancestral hunter-gatherer diet; Table 1). The patients on the Mediterranean diet rich in ω-3 and monounsaturated fats, fruits, vegetables, legumes, and nuts experienced 50% to 70% reductions in risk of cardiovascular events during long-term follow-up.

The Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico Prevenzione study[33] randomized more than 11,000 myocardial infarction survivors to 1 g/d of an 85% ω-3 supplement or control. The ω-3 group experienced a 45% reduction in sudden cardiac death and a 20% decrease in all-cause mortality during a 3 1/2-year period[33] (Figure 2). Prospective studies indicate that increased intake of fat in the form of ω-3 fatty acids from either plant sources (α-linolenic) or fish oils (eicosahexanoic acid and docasahexanoic acid) will reduce cardiovascular risk up to 32% to 50%.[29-34] Recently, for the first time, the American Heart Association recommended that a nutrient, ω-3 fatty acids, be consumed as a supplement if the diet contained an insufficient amount of this fat.[35]

Monounsaturated Fats

Monounsaturated fats made up approximately half of the total fat in the diets of most hunter-gatherers.[36] Monounsaturated fats reduce cardiovascular risk, especially when substituted for easily digestible starches and sugars.[37] Nuts are a valuable source of monounsaturated fats and have been shown to be cardioprotective in at least 6 epidemiological studies.[15,22,38] Our hunter-gatherer ancestors relied on nuts as an easily accessible source of calorie-dense, highly nutritious food that was often available in nonsummer months. The calories in nuts typically are 80% from fat, but most of this is in the form of healthy monounsaturated and polyunsaturated fatty acids (including some ω-3 fat). Epidemiological studies show that frequent nut consumption (5 or more times per week) is associated with up to a 50% reduction in risk of myocardial infarction compared with the risk of people who rarely or never eat nuts.[38] Other studies show that nut consumption reduces the risk of developing type 2 diabetes,[39] lowers the atherogenic low-density lipoprotein (LDL) cholesterol level without lowering the high-density lipoprotein (HDL) level,[40] and provides plant-based protein and other potentially cardioprotective nutrients such as vitamin E, folate, magnesium, copper, zinc, and selenium. Because of their high levels of fiber, protein, and fat, nuts also provide better and longer-lasting satiety compared with high-glycemic-load snack foods typically consumed today. Oleic acid is the major monounsaturated fat in our diets and is found in meats, nuts, avocados, dark chocolate, and olive oil. Although some of these foods were not part of the ancient ancestral diet, they can improve the cardiovascular risk profile when substituted for sugar, starches, *trans*-fats, and saturated fats that are prevalent in the modern diet. Studies suggest that replacing saturated fat with monounsaturated fat would result in a 30% reduction in risk, or 3 times the risk reduction achieved by replacing saturated fat with carbohydrates.[37]

Vegetarian vs "Breaditarian"

All evidence points to the fact that hunter-gatherers were omnivorous.[41] Strictly vegetarian diets are difficult to follow and are not necessarily associated with better health. A study of 2 groups of Bantu villagers in Tanzania compared 618 people who lived on a lakeshore and consumed large amounts of fish to 645 people who lived in the nearby hills and were vegetarians.[42] The lifestyles, gene pools, and diets (except for the fish) were similar in the 2 groups. The fish-consuming group had lower blood pressure levels; lower triglyceride, cholesterol, and leptin levels; and higher plasma ω-3 fat levels than the vegetarian group.[42,43]

Many current vegetarians would be more appropriately labeled "breaditarians." Modern vegetarian diets often rely heavily on processed carbohydrates such as white rice, potatoes, and white flour and sugars. The *South Asian paradox* refers to the relatively high prevalence of coronary heart disease despite low levels of LDL cholesterol and low prevalence of obesity in urban vegetarians from India who consume a diet high in refined carbohydrates.[32] In westernized societies, sugar intake has increased substantially during the past 2 centuries (Figure 3[44]). A recent study showed that a high-glycemic-load diet is the most important dietary predictor of HDL level (as an inverse relationship).[45] A high-glycemic-load diet predisposes a person to the metabolic syndrome and cardiovascular disease and is one of the most atherogenic features of our modern eating pattern.[45-48]

Can Meat Be Cardioprotective?

Comprehensive studies of diverse hunter-gatherer populations show that these people typically derived 45% to 60% of their calories from animal food.[36,41] Only 14% of hunter-gatherer societies obtained more than 50% of their calories from plant sources.[36,41] Paleolithic humans often lived in temperate climates and were confronted with winters during which most plant-based food was unavailable. Early humans adapted to these conditions by eating meat, organs, marrow, and fat from animals during the winter months. Paradoxically, these meat-based hunter-gatherer diets were nonatherogenic.[36,41] Although increased meat consumption in Western diets has been associated with increased cardiovascular risk, the hunter-gatherer societies were relatively free of the signs and symptoms of cardiovascular disease.[7]

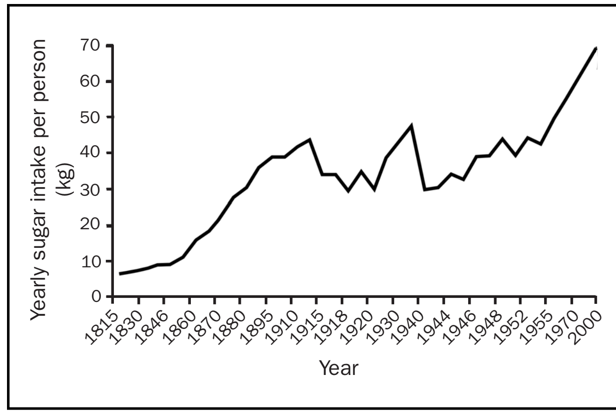

Figure 3. Average per capita consumption of sugar in England (1815-1970) and in the United States (1970-2000).[44]

The flesh of wild game is typically about 2% to 4% fat by weight and contains relatively high levels of monounsaturated and ω-3 fats compared with fatty grain-produced domestic meats, which can contain 20% to 25% fat by weight, much of it in the form of saturated fat.[27] Wild game meat is not widely accessible today, and many people do not prefer the "game" taste, which is at least in part conferred by a higher ω-3 content and by aromatic oils from plant foods consumed by the herbivore. The modern-day alternative is to choose animal protein sources that are low in saturated fat, such as skinless poultry, fish, eggs (especially high–ω-3 varieties), and lean cuts of red meat with visible fat trimmed.

It is not the amount of meat eaten but rather the composition of the meat and cooking methods that determine the health effects of this food. Accumulating scientific evidence indicates that meat consumption is not a risk for cardiovascular disease, but instead, the risk is secondary to high levels of saturated fat typically found in the meat of most modern domesticated animals.[44,49] Diets high in lean protein can improve lipid profiles and overall health, especially if care is taken to trim any visible fat from the meats and to allow the fat to drain when cooking.[50-55] Lean animal protein eaten at regular intervals (with each meal) improves satiety levels,[56-58] increases dietary thermogenesis,[56,59,60] improves insulin sensitivity,[55,61,62] and thereby facilitates weight loss[51,63,64] while providing many essential nutrients.[65] However, cooking red meats at high temperatures produces charring and high levels of heterocyclic amines, which have been implicated in the risk of gastrointestinal and prostate cancers.[66] Highly salted and preserved meats may also contain carcinogens. Lean, fresh meat cooked appropriately is a healthy and beneficial component of a varied diet, especially in conjunction with a high intake of vegetables and fruits.[65]

Trans-Fatty Acids

Trans-fatty acids are found in small quantities in the fat tissues of all ruminant animals. However, in recent decades, intake of *trans*-fatty acids has increased markedly because of their ubiquitous presence in commercially prepared foods. *Trans*-fatty acids are synthesized when hydrogen is applied to edible oils under high pressure and temperature in the presence of a catalyst. Hydrogenation of the edible oils is typically done in the prepared food industry to prolong shelf-life in commercial baked goods such as cookies, crackers, donuts, croissants, and processed snack foods. *Trans*-fatty acids are also found in shortenings, most margarines, and deep-fried foods, and recently in many brands of commercially available canola oils.[67] *Trans*-fats lower HDL levels, increase LDL levels, and increase risk of both cardiovascular disease and cancer.[24,37]

Studies indicate that replacing *trans*-fatty acids (typically 2% of total daily calories in the American diet) with the same amount of natural unsaturated fatty acids would result in a large (50%) decrease in risk of coronary heart disease.[37]

Beverages

Our Paleolithic ancestors drank water almost exclusively. Recent data suggest that generous water intake, 5 or more glasses daily, is associated with a lower risk of coronary heart disease.[68] This may be simply a function of the fact that water, when consumed frequently, displaces calorie-dense beverages such as sugared sodas from the diet. Or it may be that water provides adequate hydration and reduces blood viscosity better than other commonly ingested drinks. In any event, water is the beverage we are adapted to drink, and evidence suggests that it should remain the principal fluid we drink.

Sugared sodas are the predominant beverage consumed in America today. These are calorie-dense, nutritionally barren drinks that have contributed to the rise in obesity and insulin resistance. Generally, fruit juices are also high in sugar, and thus it is preferable to eat the whole fruit, which provides fiber and a lower glycemic load.[19,47]

Tea (*Camellia sinensis*) has been brewed for thousands of years as a favorite drink in several parts of the world. This beverage has been shown to be high in natural antioxidant phytochemicals (polyphenolic compounds). Drinking tea has been shown to reverse endothelial vasomotor dysfunction in people with coronary artery disease,[69] which may in part explain the inverse relationship between tea consumption and cardiovascular disease seen in observational studies. In 2 recent epidemiological studies, tea consumption (>2-3 cups per day) was associated with approximately half the risk of myocardial infarction compared with non–tea consumption.[70,71] Thus, tea appears to be a natural beverage that may help prevent cardiovascular disease, although more randomized prospective data are needed.

HUNTER-GATHERER FITNESS

Our Paleolithic ancestors exerted themselves daily to secure their food, water, and protection.[72,73] Although modern technology has made physical exertion optional, it is still important to exercise as though our survival depended on it, and in a different way it still does. We are genetically adapted to live an extremely physically active lifestyle. A sedentary existence predisposes us to obesity, hypertension, the metabolic syndrome, diabetes, and most types of cardiovascular disease, whereas regular exercise decreases the risks of developing all these diseases. Even in times of caloric excess, hunter-gatherers avoided weight gain in part because they were extremely physically active. Studies of obesity consistently show that the best way to maintain weight loss (regardless of the type of diet used) is by daily physical exercise.[74]

Our remote ancestors participated in various physical activities daily. They walked and ran 5 to 10 miles daily as they foraged and hunted for their food sources.[72,73] They also lifted, carried, climbed, stretched, leaped, and did whatever else was necessary to secure their sustenance and protection. Days of heavy exertion were followed by recovery days. In modern terms, these people cross-trained with aerobic, resistance, and flexibility exercises. According to recent data on physical activity, fitness programs that use various exercises are the most effective in preventing cardiovascular diseases.[75]

SUMMARY

The hunter-gatherer diet and lifestyle are the milieu for which we remain genetically adapted. Although it is neither practical nor even possible to replicate all prehistoric living conditions today, these general characteristics should serve as a template to design and test effective interventions to reduce the incidence of degenerative cardiovascular diseases.

We acknowledge Connie Smith for her assistance with the preparation of the submitted manuscript.

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