COMMENTARY

WESTERN DIET AND INFLAMMATION

by John Neustadt, ND

The prevalence of chronic, degenerative diseases attributable wholly or in part to dietary patterns is the most serious threat to public health in the United States. These diseases include cardiovascular disease (CVD), cancer, type 2 diabetes mellitus, and overweight/obesity. The numbers are truly staggering. One third of American adults (more than 71 million people) have one or more types of CVD, including 13.2 million cases of coronary heart disease (CHD) and 65 million cases of high blood pressure (HBP, defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg).[1] CVD, the number-one cause of mortality in the United States, accounted for 37.3% of all US deaths in 2003, and was "an underlying or contributing cause" for approximately 58% of deaths in 2002.[1]

Cancer is responsible for 25% of US deaths and is the second leading cause of mortality.[2] Research suggests that about one-third of all cancer deaths are attributable to poor nutrition, physical inactivity, and overweight or obesity;[2] and these risk factors may account for up to 80% of large bowel, breast, and prostate cancers.[3,4] Overweight (defined as body mass index [BMI] of 25-29.9) and obesity (BMI ≥30) are at epidemic levels, with 65% of US adults classified as overweight or obese.[5] Nearly one-third of US children are either at risk for being overweight or are already overweight or obese.[5] Obesity contributes to more than 280,000 deaths each year in the United States,[6] and in the coming decades may erode the national gains in life expectancy.[7]

A common factor that may contribute to the development and progression of these illnesses is chronic inflammation, which can be caused and modified by diet.[8-13] In fact, several pathologies that were once viewed as unrelated are now grouped by some researchers and clinicians into the category of "inflammatory disease," including atherosclerosis, dementia, arthritis, vasculitis, diabetes, and autoimmune diseases.[14] This article reviews the role diet plays in creating inflammation in the body.

THE WESTERN DIETARY PATTERN

Since the Agricultural Revolution approximately 10,000 years ago, dietary and lifestyle patterns have dramatically changed. Prior to the revolution, people consumed an enormous variety of wild plants and animal foods. This diet, commonly called the Paleolithic diet or Hunter-Gatherer diet, had predominated for about 2 million years. According to AP Simopoulos, a leading researcher into the effects of polyunsaturated fatty acids on health and disease, the Paleolithic diet contained 19% to 36% protein and 22% to 46% carbohydrates; daily intakes of 520 mg cholesterol, 100 to 150 g fiber, 690 mg sodium, 1500 to 2000 mg calcium, and 400 mg vitamin C; and a polyunsaturated-to-saturated fatty acid ratio of 1.41.[15,16] Additionally, this diet contained a potassium-to-sodium ratio of approximately 10:1.[17] The Paleolithic diet, of course, was devoid of all processed foods.[16,18]

In contrast, the post-Agricultural Revolution Western diet, also called the Standard American diet (SAD), is radically different from our ancestors' diet. Today's Western dietary pattern is characterized by a high intake of saturated fatty acids, trans fatty acids, and processed foods; and low intakes of mono- and polyunsaturated fatty acids, dietary fiber, and micronutrients. The foods most commonly consumed in the Western dietary pattern are grain-fed beef, processed meat (eg, deli meats or hotdogs), refined-grain products, eggs, French fries, high-fat dairy products, and sweets and other desserts.[19,20]

In contrast with the Paleolithic diet, which contained no refined sugar, in 2000 the consumption of all refined sugars in the US was 69.1 kg, up from 55.5 kg in 1970.[21] In addition, the typical Western diet has been estimated to contain 16 to 30 times more omega-6 fat than omega-3 fat[15,22] and has a potassium-to-sodium ratio of 1:1.25–3.75.[17] The potassium, found primarily in plant foods, is mostly in the form of potassium bicarbonate ($KHCO_3$), while sodium in the Western diet is in the form of sodium chloride (NaCl) from processed foods. Therefore, the imbalance of potassium to sodium in the Western diet is also accompanied by elevated dietary chloride consumption and decreased dietary bicarbonate consumption.[17] Additionally, in the year 2000, cereal grains, such as wheat and rye, were consumed at a rate of 200 pounds per person per year in the United States.[21]

Summarizing the major differences between ancestral diets and the Western diet, Simopoulos writes, "Today industrialized societies are characterized by (1) an increase in energy intake and decrease in energy expendi-

ture; (2) an increase in saturated fat, omega-6 fatty acids and trans fatty acids, and a decrease in omega-3 fatty acid intake; (3) a decrease in complex carbohydrates and fiber; (4) an increase in cereal grains and a decrease in fruits and vegetables; and (5) a decrease in protein, antioxidants, and calcium intake."[15] (See Table 1.)

FOOD AND INFLAMMATION

Inflammation is a dynamic, immune-mediated response to noxious stimuli (eg, environmental factors, food, or microbial antigens; or vascular endothelial damage) that involves leukocytes (eg, mast cells, eosinophils, basophils, and neutrophils) as well as signaling molecules produced by these cells such as interleukins (eg, IL-1, IL-6), leukotrienes (eg, LTB_4), and prostaglandins (eg, PGE_2). Other inflammatory molecules are produced by the endothelium [eg, E-selectin, intercellular adhesion molecule 1 (ICAM-1) and vascular cell adhesion molecule 1 (VCAM-1)] and the liver [eg, C-reactive protein (CRP), fibrinogen]. Additionally, the immune system requires reactive oxygen species (ROS) to kill pathogens, but these free radicals can also induce inflammation. All of these, as well as other, inflammatory mediators are relatively short lived and are part of the acute inflammatory response. In this response, vessel diameter and permeability are altered, which permits plasma proteins and leukocytes to migrate out of the blood vessel and into a lesion.

Chronic inflammation occurs when damage continues and acute inflammatory mediators remain elevated or become elevated too often. This state is characterized by an infiltration of mononuclear cells (lymphocytes and monocytes), inflammatory cell–mediated tissue destruction, and increased angiogenesis at the foci of active tissue repair.[23] A complete discussion of the pathology and biochemistry of inflammation is beyond the scope of this paper; however, a partial list of inflammatory mediators is provided in Table 2.

TABLE 1 NUTRIENT CONTENT OF PALEOLITHIC AND WESTERN DIETS[15-18, 21]

Dietary component	Western diet	Paleolithic
Calories (calories/d)	3,900	↓*
Protein (% of total calories)	11	19-35
Meat (% of total calories)	12 (mostly conventionally raised beef)	45–60 (wild game)†
Carbohydrates (% of total calories)	50	22-46
Carbohydrate quality	Mostly refined, rapidly absorbed	Mostly complex, slowly absorbed
Refined sugars (kg/yr)	69.1	0
Water, relative consumption	↓ (mainly in calorie containing soft drinks)	_
Fat, total (% total daily calories)	39	21 (mostly unrefined, plant based)
Saturated fat (% total daily calories)	32	↓
Polyunsaturated-to-saturated fat ratio	0.67	1.41
Cholesterol (mg/day)	430	520
trans fatty acids (g/day)	5.3	0
Total long-chain omega-6 + omega-3 (g/day)	0.2	2.3
Ratio of omega 6:3	12	2.4
Fiber (g/day)	24	100-150
Fiber from vegetables and fruit (%)	40	100
Sodium (mg/day)	1,330	690
K:Na	2.81	_ (Potassium intake was 3 to 4 times higher than today)
Riboflavin mg/d	1.34-2.08	6.49
Folate mg/d	0.149-0.205	0.357
Thiamin mg/d	1.08-1.75	3.91
Carotene mg/d	2.05-2.57	5.56
Vitamin A mg/d	7.02-8.48	17.2
Vitamin C mg/d	77-109	440-604
Vitamin E mg/d	7-10	32.8

*Up and down arrows are used when exact numbers are not known, and denote relatively higher or lower amounts, respectively.
†Conventionally-raised beef has a higher fat content than wild game, and the fat in conventionally-raised beef has a relatively high omega-6 to omega-3 ratio compared to wild game.

TABLE 2 SOME INFLAMMATORY MEDIATORS

IL-1
IL-6
TNF-alpha
Fibrinogen
LTB4
PGE2
Cyclooxygenase-2 (COX-2)
ICAM-1
VCAM-1
CRP
Nuclear factor-_B

The influence of diet on inflammation results from a combination of food quantity and quality, and genetic susceptibility. James O'Keefe, Jr, MD, of the Mid America Heart Institute, co-authored a review article on the effects diet has on cardiovascular disease. He concluded that it results from a diet and lifestyle "at odds with our Paleolithic genome."[16] Several features of the modern diet have been studied extensively for their effects on inflammation. Specifically, excessive consumption of refined carbohydrates, low dietary fiber intake, and a high omega-6 to omega-3 ratio are strongly associated with the pro-

duction of pro-inflammatory molecules.[24-26] Additionally, antioxidants decrease inflammation, and the low intake of antioxidants in the form of vitamins (eg, C and E) and flavonoids found in fruits and vegetables contributes to a chronic, pro-inflammatory state that initiates, maintains, and exacerbates disease.[19,27,28] (See Table 3 for a list of dietary patterns or components and their relationship to inflammatory mediators.)

In a cross-sectional study of 732 women (43-69 years old, average 56 years) participating in the Nurses' Health Study, researchers analyzed the correlation between dietary patterns and inflammatory markers. Two dietary patterns were identified using food frequency questionnaires: the "prudent pattern" diet and the Western diet. The prudent pattern diet was much closer to a Paleolithic diet than the Western diet in that the prudent pattern diet contained larger amounts of vegetables, fruit, legumes, whole grains, fish, and poultry. The Western diet pattern in this cohort contained more red meat, processed meat, refined grains, sweets and other desserts, French fries, and high-fat dairy products. Inflammatory markers showed a positive relation with the Western diet, including significantly greater concentrations of CRP (P<0.001), IL-6 (P=0.006), E-selectin (P<0.001), sICAM-1 (P<0.001), and sVCAM-1 (P=0.008) in the highest quintile of those following the Western diet, compared with the lowest quintile. In comparison, there was a modest but statistically significant decrease in these same inflammatory markers in the highest quintile of the prudent pattern diet compared with the lowest quintile.[29]

Similar to the prudent pattern diet, the Mediterranean diet stresses exercise, whole grains, fruits, vegetables, legumes, and nuts.[30] In a single, blind, 2-year clinical trial, 180 volunteers (mean age approximately 44 years) diagnosed with metabolic syndrome were randomized to follow a Mediterranean diet (n=90) or a control diet (n=90) containing 50% to 60% carbohydrates, 15% to 20% proteins, and less than 30% total fat. Volunteers in the Mediterranean diet group were given the same percent recommendations as in the control group, but were also instructed to eat less than 10% saturated fat and less than 300 mg/day cholesterol; to consume at least 250 to 300 g/day fruits, 125 to 150 g/day vegetables, 25 to 50 g/day walnuts, and 400 g/day whole grains (defined in this study as legumes, rice, maize, and wheat); and to increase olive oil consumption. End points, which included serum high-sensitivity C-reactive protein (hsCRP), IL-6, IL-7, and IL-18, were determined at baseline and after 2 years.

The researchers reported that after 2 years on the Mediterranean diet, volunteers "consumed a greater percentage of calories from complex carbohydrates and from polyunsaturated and monounsaturated fat; had a greater intake of fiber; had a lower ratio of omega-6 to omega-3 fatty acids; and had lower calories, levels of saturated fat, and levels of cholesterol than did controls. Total fruit, vegetable, nuts, and whole grain intakes, and olive oil consumption were also significantly higher." Compared with the control group, the Mediterranean diet group also had significantly greater improvement in all end points after the 2 years. In addition, only 40 patients in the Mediterranean diet group could still be classified as having metabolic syndrome at the end of the trial, compared with 78 volunteers in the control group (P<0.001).

Among other reasons, diet can alter inflammatory markers because of the quantity of food consumed, macronutrient and antioxidant content, glycemic load, and fatty acid ratio. Due to the high quantity of low-fiber processed foods in the Western diet, the glycemic load (GL) of food is higher than in the Paleolithic or Mediterranean diets. The GL indicates the relative effect a given quantity of food has on raising blood sugar. Unlike the glycemic index (GI), which denotes how rapidly a carbohydrate (eg, a potato) turns into glucose, the GL takes into account how much carbohydrate might be in a given serving of the food, and, therefore, how eating a specific quantity of that food affects blood sugar. Thus, a high-GI food, such as watermelon, may have a low GL if the person only eats a small serving. In diets containing refined foods low in fiber, people typically consume large amounts of high-GL foods. One result from this is blood fluctuations. Recently, acute postprandial fluctuations in blood glucose concentrations in patients with type 2 diabetes were shown to result in greater generation of oxidative stress than chronic, sustained hyperglycemia.[31] It is a sobering comparison, since, in itself, hyperglycemia has such deleterious effects because it produces ROS that damage mitochondria and activate nuclear factor kappa beta (NFkB), a nuclear transcription factor involved in the production of inflammatory mediators such as interleukins and TNF-alpha.[32,33] Consuming fructose, which is used to sweeten soft drinks, can also increase free-radical generation.[34]

Fat quality also plays a role in inflammation because it is incorporated into cell membranes and affects cell-signaling. Fatty acids are cleaved from the cell membrane by phospholipase A_2 (PLA_2) and then metabolized to prostaglandins or leukotrienes by either cyclooxygenase or lipoxygenase enzymes. The omega-6 series of fatty acids, such as arachadonic acid (20:4 omega-6) are converted by these enzymes into cytokines that are part of the pro-inflammatory cascade, such as PGE_2 and LTB_4. In contrast, fatty acids in the omega-3 series, such as eicosapentaenoic acid (EPA, 20:5 omega-3), are metabolized by these enzymes into cytokines that are part of the anti-inflammatory cascade, such as prostaglandin I3 (PGI_3) and thromboxane (TXA_3).

The relative proportion of omega-6 and omega-3 fatty acids in tissues is modified by diet. High concentrations of omega-6 fats are found in red meat and dairy

products, while omega-3 fatty acids are found in the highest quantities in nuts, vegetables, and fish. As already noted, the Western diet is high in omega-6 and low in omega-3 fatty acids, which contributes to a pro-inflammatory state. As levels of EPA increase in macrophages, production of TNF-alpha and IL-1_ decrease.[35]

Trans fatty acids, which are present in fried and many processed foods, also contribute to inflammation. Using data from the Nurses' Health Study, Walter Willet, MD, showed 12 years ago in 1993 that trans fatty acid consumption increases the risk of CHD.[36] In a follow-up to the Nurses' Health Study, trans fat intake linearly correlated with plasma concentration of CRP (P=0.009). CRP was 73% higher among women in the highest quintile of trans fatty acid intake (3.7 ± 0.6 g/d) compared with those in the lowest quintile (1.5 ± 0.3 g/d).[37]

TABLE 3 DIETARY PATTERN OR COMPONENTS AND THEIR RELATIONSHIP TO INFLAMMATORY MEDIATORS

Diet or dietary components	Effects on inflammation
Western dietary pattern	Associated with increased CRP, IL-6, E-selectin, sICAM-1, sVCAM-1[29]
Prudent pattern diet	Associated with decreased CRP and E-selectin[29]
Mediterranean diet	Decreased CRP and IL-6[38]
Trans fatty acids	Associated with increased CRP[37]
Sugar-sweetened soft drink; refined grains; processed meat; diet soft drinks; vegetables other than green leafy vegetables, yellow vegetables, cruciferous vegetables, tomatoes, and legumes	Associated with increased CRP, IL-6, E-selectin, sICAM-1, and sVCAM-1[19]
Wine, coffee, cruciferous vegetables, yellow vegetables	Associated with decreased CRP, IL-6, E-selectin, sICAM-1, and sVCAM-1[19]
Omega-3 fatty acids	Decreases TXA2, PGE2, TNF-alpha, IL-1 beta.[35] Associated with decreased TNF-alpha receptor expression and CRP.[25]

CONCLUSION

Inflammation is a major contributor to the development and progression of the most prevalent chronic, degenerative diseases in the United States, and diet is the major contributor to inflammation. Our ancestors evolved while eating a predominantly plant-based diet that contained no processed foods. In contrast, the diet that predominates today is the opposite—low in fresh fruits, vegetables, and fiber, and high in meat, processed foods, and refined carbohydrates. The modern diet, also called the Western diet, is a pro-inflammatory diet, high in omega-6 fatty acids, excessive calories, and trans fatty acids.

Diet and lifestyle habits create the foundation for health. With the unique role we play in patients' lives, clinicians can help decrease the overwhelming burden of chronic degenerative diseases on our healthcare system by educating and encouraging patients to move in the direction of better health through better diet (see Table 4).

TABLE 4
HEALTHY DIET AND LIFESTYLE RECOMMENDATIONS[16]

Eat whole, natural, fresh foods.
Consume a diet high in fruits, vegetables, nuts, and berries; and low in refined grains and sugars.
Increase consumption of omega-3 fatty acids from fish, fish oil, and plant sources.
Avoid all trans fats and limit intake of saturated fats. Eliminate fried foods, hard margarine, commercial baked goods, and most packaged and processed snack foods. Substitute monounsaturated fats (eg, avocados, nuts and seeds) and polyunsaturated fats (eg, whole grains, fish—in particular herring, salmon, mackerel, and halibut—and soybeans) for saturated fats (eg, red meats and high-fat dairy products).
Increase consumption of lean protein, such as skinless poultry, fish, and game meats and lean cuts of red meat. Avoid high-fat dairy and fatty, salty processed meats, such as bacon, sausage, and deli meats.
Incorporate olive oil into the diet.
Drink water.
Participate in daily exercise through various activities (incorporating aerobic and strength training and stretching exercises). Outdoor activities are ideal.

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