Commentary

Dietary Changes and Their Influence in the Development of Kidney Disease

Artemis P. Simopoulos

The Center for Genetics, Nutrition and Health, 4330 Klingle Street NW, Washington, DC 20016, USA; cgnh@bellatlantic.net; Tel.: +1-(202)-462-5062

Abstract: Human beings evolved on a diet that was balanced in omega-6/omega-3 fatty acids, and was rich in fruits and vegetables with a ratio of animal to vegetable intake of 35:65. Such a diet is a base-producing anti-inflammatory diet and one in which our genes have been programmed to respond. Current Western diets are acid-producing diets and are also high in omega-6 fatty acids, leading to a proinflammatory state. From an evolutionary perspective a mild systemic metabolic alkalosis, resulting from chronic net-base loading, is the natural and optimal systemic acid–base homeostasis of humans. Western diets that lead to a metabolic acidosis increase susceptibility to kidney disease as has been shown from the proinflammatory biomarkers that produce a cytokine storm. Healthy dietary patterns, including the Dietary Approach to Stop Hypertension (DASH) Study, and Mediterranean diets, such as the diet of Crete, both of which have a healthy dietary pattern, are associated with a lower incidence of chronic kidney disease and may prevent or decrease albuminuria and improve the estimated glomerular filtration rate (eGFR).

Keywords: omega-6/omega-3 fatty acid balance; acid–base homeostasis; chronic kidney disease; Dietary Approach to Stop Hypertension (DASH) diet; Mediterranean diet; healthy dietary patterns; evolutionary aspects of diet and exercise

1. Introduction

Chronic kidney disease (CKD) is a major public health problem. Kidney failure leads to high cardiovascular disease and mortality. Non-diabetic CKD is related to hypertension, and many patients with diabetes develop end stage kidney disease. Obesity is increasing worldwide, and visceral adiposity is associated with reduced estimated glomerular filtration rate (eGFR) in normal weight people with hypertension [1]. Obesity is an independent risk factor for the development of CKD [2–4]. The focus of CKD prevention is usually overlooked in populations with normal weight because of their “safe range” of BMI. It is, therefore, important to identify the risks of CKD among normal weight individuals [1].

Hypertension is associated with kidney disease, and both represent an inflammatory state, which could respond to dietary modifications. Hypertension is a multifactorial disorder involving gene-nutrient interactions and other factors. Different mechanisms appear to be involved, operating at variable proportions based on the organ involved or the cause of hypertension. Changes have been reported in eicosanoid metabolism, renin concentration, vascular reactivity, blood viscosity, loss of sodium, potassium content in cells (increase), and intracellular calcium (decrease), among others [5–7].

In this commentary, I will discuss the dietary changes that have taken place in the past 10,000 years with an emphasis on the last 150 years in terms of the evolutionary aspects of diet relative to the high omega-6/omega-3 fatty acid ratio; the increase in foods that increase net endogenous production of acid (NEAP) leading to a state of metabolic acidosis, the decrease in foods that are base producing (buffer—alkaline foods); and the importance of healthy dietary patterns in the prevention and/or management of chronic kidney disease.
2. Evolutionary Aspects of Diet and Exercise

During evolution, human beings began to develop hunting skills that resulted in an increase in protein intake. Cultivation of plants occurred at about 20,000 years ago and agricultural practices were developed at about 15,000–10,000 years ago. Their diet was based on eating the meat of wild animals and wild fruits and plants at a ratio of 35/65 meat/vegetables [8]. People before the Agricultural Revolution and present-day hunter-gatherers typically used many species of wild plants for food. Roots, beans, nuts, tubers, and fruit were eaten regularly, providing a balance between omega-3 and omega-6 fatty acids and a base-producing or alkaline diet. Small cereal grains made a minor contribution to man’s overall diet prior to the Agricultural Revolution. Such a diet is anti-inflammatory and consistent with good health [8–14].

Food intake and energy expenditure changed as human beings progressed from a very active lifestyle of being hunter-gatherers to a less active one that involved the domestication of animals and the development of agriculture. Even greater changes have occurred over the past 100 years in the food supply, and in energy intake and energy expenditure. Modern industrialized societies are characterized by a very sedentary existence, and an abundant, calorie-dense food supply that is acid producing (metabolic acidosis), whereas the Paleolithic diet is base producing (alkaline) (Table 1).

| Characteristics               | Hunter-Gatherer Lifestyle            | Western Lifestyle                  |
|-------------------------------|--------------------------------------|------------------------------------|
| Physical Activity level       | high                                 | low                                |
| Diet                           | anti-inflammatory base producing     | proinflammatory acid producing     |
| Energy density                 | low                                  | high                               |
| Energy intake                  | moderate                             | high                               |
| Protein                        | high                                 | low-moderate                       |
| animal                         | high                                 | low-moderate                       |
| vegetable                      | very low                             | low-moderate                       |
| Carbohydrate                   | low-moderate (slowly absorbed)       | moderate (rapidly absorbed)        |
| Fiber                          | high                                 | low                                |
| Fat                            | low                                  | high                               |
| animal                         | very low                             | moderate                           |
| vegetable                      | low, polyunsaturated                 | high, saturated                    |
| Total ω-6 / ω-3 ratio          | low (0.79)                           | high (18.75)                       |
| linoleic to linolenic acid ratio| low (0.70)                           | high (16.74)                       |
| long chain ω-6 / ω-3 PUFA ratio| low (1.79)                           | high (3.33)                        |
| Potassium                      | high                                 | low                                |
| Sodium                         | low                                  | high                               |
| Calcium                        | high (normal)                        | low                                |
| Vitamin C                      | high (normal)                        | low                                |
| Vitamin D                      | high (normal)                        | low                                |
| Vitamin E                      | high (normal)                        | low                                |

It is estimated that at the turn of the 20th century, 30% of energy expenditure was due to muscular work, whereas it is now 1% [15].

During man’s evolution, genetic variants that protected human beings against famine, infectious agents, and a hostile environment increased in prevalence, because of natural selection. Coronary heart disease, essential hypertension, obesity, diabetes mellitus, and chronic kidney disease have a high prevalence in the populations of industrialized societies [10,16]. The genetic variants responsible for the increase of the common polygenic disorders contributed to the survival of our hunter-gatherer ancestors by maintaining cholesterol and blood sugar concentrations, as well as blood pressure, and body weight during periods of famine [10,11].

Today, industrialized societies are characterized by:

1. An increase in energy intake and decrease in energy expenditure;
(2) An increase in saturated fat and in omega-6 fatty acids but a decrease in omega-3 fatty acid intake, Vitamin C, D, and E, and antioxidants;
(3) A decrease in complex carbohydrates and fiber;
(4) Acid-producing diet leading to metabolic acidosis, whereas during evolution the diet was base-producing alkaline.

All of the above lead to a proinflammatory state in humans, whereas during evolution humans were in an anti-inflammatory state.

3. Genetic Differences in Populations

Nutritional health depends on food availability and intake, with absorption, transport, metabolism, transformation, and excretion controlled by enzymes, receptors, and other proteins that are in turn genetically controlled. Although man has evolved being able to feed on a variety of foods and to adapt to them, certain genetic adaptations and limitations have occurred in relation to the diet. Because there are genetic variations among individuals, however, changes in the dietary patterns impact on a genetically heterogeneous population, although populations with similar evolutionary background have more similar genotypes [10,11]. Therefore, to be successful, dietary interventions must be based on knowing the frequency of genes whose effects we are attempting to control or modify.

4. Evolutionary Aspects and the Omega-6:Omega-3 Balance

Precise information does not exist about man’s diet prior to the development of agriculture 10,000 years ago. Human beings usually ate wild plants, wild animals, and fish from the rivers, lakes, and oceans. The green leaves of wild plants are good sources of the omega-3 fatty acid alpha-linolenic acid (ALA), whereas cultivated plants are poor in omega-3 fatty acids and the seeds of plants are high in omega-6 fatty acids [17]. Wild animals and birds who feed on wild plants are very lean with a carcass fat content of only around 4% and contain about five times more polyunsaturated fat per gram than is found in domestic livestock. Most importantly, 4% of the fat of wild animals contains eicosapentaenoic acid (an omega-3 fatty acid), whereas domestic beef contains very small or undetectable amounts, since cattle are fed grains that are rich in omega-6 fatty acids and poor in omega-3 fatty acids [8]. Deer, on the other hand, that forage on ferns and mosses contain omega-3 fatty acids in their meat. Recent studies in the fatty acid composition of eggs from free-ranging chickens indicate that the ratio of omega-6/omega-3 is 1.3, whereas the ratio for the supermarket egg is 19.4 [18]. Supermarket eggs are produced by hens in cages fed commercially developed feed high in linoleic acid, an omega-6 fatty acid.

It appears that human beings evolved on a diet that was rich in omega-3 fatty acids and that there was once a balance between omega-6 and omega-3 fatty acids, which is a more physiological state. However, over the past 100 years, the Western diet has shifted dramatically toward increased amounts of omega-6 fatty acids at the expense of omega-3 fatty acids (Table 1). It has been estimated that the present Western diet is “deficient” in omega-3 fatty acids with a ratio of omega-6 to omega-3 of 16–20:1 instead of a 1:1, as is the case with wild animals and presumably Paleolithic humans [8] (Tables 2 and 3).

Table 2. Sources of the omega-6 fatty acid linoleic acid (LA).

| Oils High in LA     | Amount of LA |
|---------------------|--------------|
| Safflower oil       | 78%          |
| Sunflower oil       | 71%          |
| Corn oil            | 59%          |
| Soybean oil         | 56%          |
| Cottonseed oil      | 53%          |
Table 3. Sources of the omega-3 fatty acid alpha-linolenic acid (ALA).

| Oils High in ALA   | Amount of ALA |
|-------------------|---------------|
| Chia oil          | 64%           |
| Perilla oil       | 58%           |
| Flaxseed oil      | 55%           |
| Canola oil        | 12%           |
| Rapeseed oil      | 10%           |

5. Evolutionary Aspects of Diet: Dietary Acid–Base Homeostasis

Sebastian et al. [16] through a series of studies estimated the net systemic load of acid (net endogenous acid production; NEAP) from retrojected ancestral preagricultural diets, which are characterized by an imbalance of nutrient precursors of hydrogen and bicarbonate ions that induce a lifelong, low-grade, pathogenically significant systemic metabolic acidosis. The mean (±SD) NEAP for 159 retrojected preagricultural diets was $-88 \pm 82$ mEq/d, and 87% were net base producing. The computational model predicted NEAP for the average American diet (as recorded in the third National Health and Nutrition Examination Survey) as 48 mEq/d, within a few percentage points of published measured values for free-living Americans. Therefore, the model was not biased toward generating negative NEAP values. The historical shift from negative to positive NEAP was accounted for by the displacement of high-bicarbonate-yielding plant foods in the ancestral diet by cereal grains and energy-dense, nutrient-poor foods in the contemporary diet—neither of which are net base producing. The authors concluded “The findings suggest that diet-induced metabolic acidosis and its sequelae in humans eating contemporary diets reflect a mismatch between the nutrient composition of the diet and genetically determined nutritional requirements for optimal systemic acid-base status”.

Although multiple homeostatic mechanisms operate to mitigate the resulting deviations in systemic acid–base balance, on average, blood acidity remains increased, and plasma bicarbonate concentrations remain decreased, in proportion to the magnitude of the daily net acid load [19,20]. Increasing evidence suggests that such persisting, albeit low-grade acidosis, and the relentless operation of responding homeostatic mechanisms, result in numerous injurious effects on the body, including dissolution of bone, muscle wasting, kidney stone formation, and damage to the kidney [21–26].

In comparison with the diet habitually ingested by preagricultural Homo sapiens living in the Upper Paleolithic period (40,000–10,000 years ago), the diet of contemporary Homo sapiens is rich in saturated fats, omega-6 fatty acids, simple sugars, sodium, and chloride and poor in omega-3 fatty acids, fiber, magnesium, and potassium. These and the most recent high intake of ultra-processed foods high in omega-6 fatty acids [27], and other post-agricultural dietary compositional changes (plant-based imitation meat, poultry, fish, etc.) have been implicated as risk factors in the pathogenesis of “diseases of civilization”, including atherosclerosis, hypertension, type 2 diabetes, CKD, osteoporosis, and certain types of cancer [14,28–33]. From an evolutionary perspective, a mild metabolic alkalosis resulting from chronic dietary net base loading is the natural and optimal systemic acid–base state in humans.

6. What Are Healthy Dietary Patterns?

Dietary patterns are defined as the consumption of foods that reflect habitual dietary intake. A dietary pattern can be classified as “healthy” or “unhealthy.” Examples of healthy dietary patterns include the Mediterranean diet and especially the diet of Crete [34] and the Dietary Approach to Stop Hypertension (DASH), which is very similar to the diet of Crete [7]. Other dietary patterns that are considered healthy and have been studied, include vegetarian diets, diets based on dietary guidelines, and any approach to dietary intake that focuses on the overall pattern of eating as opposed to approaches targeting individual or multiple nutrients [35].

Typically, healthy dietary patterns share similar characteristics:
1. Higher consumption of whole grains, fruits, and vegetables which provide higher intake of fiber, Vitamin C, Vitamin E, and carotenoids and omega-3 fatty acids;
2. Lower consumption of saturated fats and omega-6 fatty acids, and a balanced omega-6 /omega-3 ratio;
3. Lower amounts of processed and ultra-processed foods, lower sodium and sugar, and lower dietary acid load-producing foods, and more base-producing foods (Table 4).

Table 4. Acid-producing and base-producing foods.

| Acid Producing Foods | Base Producing Foods |
|----------------------|----------------------|
| - Beef               | - Fruits and vegetables (spinach, lettuce, cabbage, broccoli, cauliflower, zucchini, squash, sweet potato, carrots, celery, raisins, apples, bananas) |
| - Poultry            |                      |
| - Cheese             | - Generally, all fruits and green leafy vegetables |
| - Yogurt             |                      |
| - Eggs               |                      |
| - Cereal grains      |                      |
| - Fish               |                      |

Unhealthy dietary patterns include Western diets and high fat and meat diets [36]. Western diets high in refined starches, saturated fats, omega-6 fatty acids, trans fatty acids (due to increased consumption of fried poultry and fried fish), and sodium, but lower in whole grains, fruit, vegetables, fiber, and omega-3 fatty acids increase the inflammatory response [37]. Elevations in inflammatory markers (IL-1, IL-6, TNFa, and IL-8), leading to cytokine storms, have been suggested as biomarkers for incident CKD [38]. A dietary approach which lowers inflammatory markers and dietary acid load may be important for reducing the incidence of CKD.

In a systematic review and meta-analysis, Bach et al. [39] evaluated the association between adherence to dietary patterns and incident CKD in adults without kidney impairment. The primary analysis demonstrated that adherence to a healthy dietary pattern was associated with lower odds of incident CKD and albuminuria over an average of 10.4 years of follow-up. These results add to the evidence supporting the benefits of adherence to healthy dietary patterns for chronic disease conditions, including those which are considered to be risk factors for the development of kidney disease, such as type 2 diabetes, hypertension, cardiovascular disease, and obesity. Earlier studies [40] based on meta-analyses have also supported the role of healthy dietary patterns, such as the Mediterranean diet [41], in the prevention of CKD progression.

Choi et al. [42] evaluated the association between plant-centered diet defined by the A Priori Diet Quality Score (APDQS), eGFR, and initial microalbuminuria over a 10-year period in participants in the Coronary Artery Risk Development in Young Adults (CARDIA) study. The study, based on an in-depth examination of the early stages of CKD risk in a healthy middle-age population, provides data on the effect of the diet, consumed throughout young adulthood, in influencing the course of CKD in a positive way. Those in the highest score returned to high normal albuminuria and less deterioration in kidney function and an attenuated decrease in eGFR. These results extend the findings from previous studies that have reported an inverse relationship between CKD outcomes and diet quality as measured by the DASH and the alternate Mediterranean diet [7,41].

7. Conclusions

It is evident that current Western diets are (1) proinflammatory due to high amounts of vegetable oils high in omega-6 fatty acids and low in antioxidants and vitamins and (2) acid producing due to low consumption of fruits and vegetables and high intakes of animal products and ultra-processed foods. Yet, we know what a healthy diet is, and we understand the importance of evolutionary aspects of diet and exercise, and how they shaped human health through their interaction with our genes. Our genes have
been programmed to respond to a diet, physical activity, and other environmental factors consistent with evolution. From an evolutionary perspective, a mild systemic metabolic alkalosis, resulting from chronic net-base loading, is the natural and optimal systemic acid–base homeostasis of humans. A healthy dietary pattern such as the Mediterranean diet [41] or the DASH diet [7] is associated with a lower incidence of CKD and may prevent or decrease albuminuria and improve eGFR.

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