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The Evolution-Informed Optimal Dietary Potassium Intake of Human Beings Greatly Exceeds Current and Recommended Intakes

Anthony Sebastian, Lynda A. Frassetto, Deborah E. Sellmeyer, and R. Curtis Morris Jr

An organism best fits the environment described by its genes, an environment that prevailed during the time period (millions of years) when evolution naturally selected the genes of its ancestors—those who survived to pass on their genes. When an organism's current environment differs from its ancestral one, the environment's mismatch with the organism's genome may result in functional disadvantages for the organism. The genetically conditioned nutritional requirements of human beings established themselves over millions of years in which ancestral hominins, living as hunter-gatherers, ate a diet markedly different from that of agriculturally dependent contemporary human beings. In that context, we sought to quantify the ancestral-contemporary dietary difference with respect to the supply of one of the body's major mineral nutrients: potassium. In 159 retrojected Stone Age diets, human potassium intake averaged 400 ± 125 mEq/d, which exceeds current and recommended intakes by more than a factor of 4. We accounted for the transition to the relatively potassium-poor modern diet by the fact that the modern diet has substantially replaced Stone Age amounts of potassium-rich plant foods (especially fruits, leafy greens, vegetable fruits, roots, and tubers), with energy-dense nutrient-poor foods (separated fats, oils, refined sugars, and refined grains), and with potassium-poor energy-rich plant foods (especially cereal grains) introduced by agriculture (circa 10,000 years ago). Given the fundamental physiologic importance of potassium, such a large magnitude of change in potassium intake invites the consideration in human beings of whether the quantitative values of potassium-influenced physiologic phenomena (eg, blood pressure, insulin and aldosterone secretion rates, and intracellular pH) currently viewed as normal, in fact disaccord with genetically conditioned norms. We discuss the potential implications of our findings in respect to human health and disease.
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KEYWORDS dietary potassium, human evolution, diet net acid load

Nothing in biology makes sense except in the light of evolution.
—Theodosius Dobzhansky[1]
Nature is the cure of illness. Leave thy drugs in the chemist's pot if thou can heal the patient with food.
—Hippocrates, 460-370 BC

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An organism's structure, physiology, and metabolism best serve the organism's primary biological imperatives (survival and mating) when the organism lives in the environment described by its genes.[2] For our hominin species, *Homo sapiens*, that propitious environment prevailed during the time period (millions of years) when evolution naturally selected the genes of its hominin ancestors—more specifically, those hominins so adapted that they survived to pass on their genes. In areas in which the current environment of *Homo sapiens* differs from the ancestral one to which evolutionary forces adapted the species, the environment's mismatch with the organism's genetic adaptations may result in structural, physiologic, and metabolic disadvantages.[3]

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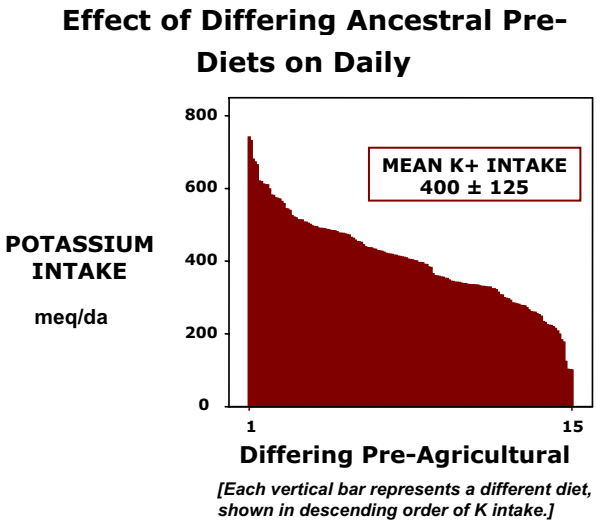

Figure 1 Daily potassium intake for differing ancestral hominin preagricultural diets. Each vertical bar represents a different diet, in descending order of potassium intake from left to right. See Sebastian et al[29] for details of the criteria for selecting the daily menus of wild animal-source foods and uncultivated plant-source foods. (Color version of figure is available online.)

The word *hominin* refers to the group (technically a tribe) of bipedal primate species ancestral to *Homo sapiens*, including *Homo sapiens* and earlier *Homo* species, and *Australopithecus* species. It replaces the older word *hominid*, which now includes both the hominin tribe and all the great apes, extant and ancestral.

As evolutionary biologist Richard Dawkins[2] stated:

> *Living organisms are beautifully built to survive and reproduce in their environments. Or that is what Darwinians say. But actually it isn't quite right. They are beautifully built for survival in their ancestors' environments. It is because their ancestors survived—long enough to pass on their DNA—that our modern animals [including humans] are well-built. For they inherit the very same successful DNA. The genes that survive down the generations add up, in effect, to a description of what it took to survive back then. And that is tantamount to saying that modern DNA is a coded description of the environments in which ancestors survived. A survival manual is handed down the generations. A Genetic Book of the Dead.*

As evolutionary biologist George C. Williams[4] stated:

> *A population living in a predictable environment does little evolving. When the environment changes significantly, quantitative changes evolve quickly toward new optima. The 'quickly' must be understood to relate to an evolutionary time scale on which anything taking a few thousand generations is 'quick'. All our ancestors of three hundred generations ago were hunter-gatherers. Nothing resembling big cities existed more than two hundred generations ago. Many of the foods we eat today and other aspects of current lifestyles are just one or a few generations old. We must assume that evolution has not been able to do much to adapt us to the environments we inhabit today.*

Human Nutritional Requirements: Evolutionary Development

The lineage of our species' goes back perhaps as many as 5 to 7 million years of hominin evolution before we can recognize an ancestor that we have in common with our closest relatives—chimpanzees and gorillas (however, see articles by Pennisi[5] and Patterson et al[6]). The environmental changes of the entire period of evolution beginning with the first hominins undoubtedly made important contributions to our present genetic composition, with dietary patterns counting as major genetically determining aspects of the environment. To paraphrase the colorful expression by the Oxford historian, Felipe Fernandez-Armesto,[7] a species' most intimate contact with its natural environment occurs when the species eats it.

The nutritional requirements for human survival and reproduction thus established themselves, at least in part,[8] through the natural selection of genes over millions of years. Ancestral *Homo* species first appeared at the beginning of the Stone Age about 2 million years ago—the Stone Age (also known as the Paleolithic epoch) extended from approximately 2 million years ago to the beginnings of agriculture approximately 10 thousand years ago. During that period ancestral *Homo* species (*Homo habilis*, *Homo erectus*, *Homo ergaster*, *inter alia*) adapted to a profile of diets markedly different from that of the diets of contemporary human beings.[9]

When agriculture began about 10,000 years ago, *Homo sapiens* began giving up their lifestyle as hunter-gatherers, a lifestyle in which they ate only wild animal and plant foods, and began settling down as farmers and animal husbanders, and began introducing foods to which they or their hominin

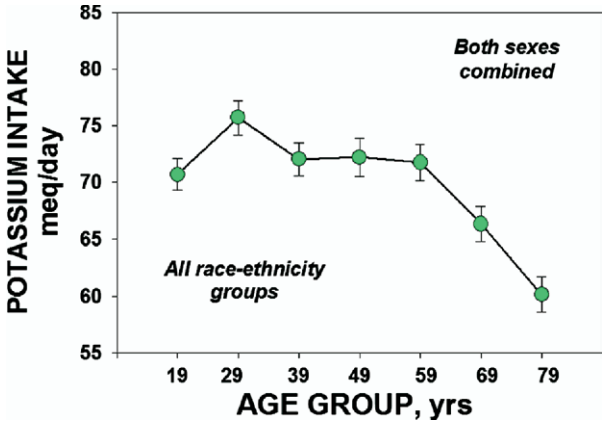

Figure 2 Average potassium intake of the US population (NHANES III, 1988-1991) by age group, both sexes, and all ethnicity groups combined. (Color version of figure is available online.)

Table 1 Potassium Intake and Diet Net Acid Load of a Hypothetical Paleolithic Diet*

Food Group	% of Daily Energy	NEAP meq/day	Protein g/day	Potassium meq/day
Paleolithic Diet (animal-to-plant energy = 35%-to-65%; animal-fat energy = 26% animal-food energy)				
Meat	35.0		178	71
Nuts	10.8		7	8
Leafy greens	10.8		30	116
Vegetable fruit	10.8		24	113
Tubers	10.8		6	33
Roots	10.8		10	65
Fruit	10.8		5	28
Totals	100.0	−77.7	258	435

*For simplicity, we divided non-animal-source energy intake equally among the food groups. Abbreviation: NEAP, net endogenous acid production

ancestors had no or negligible exposure to such as cereal grains, legumes, animal milk and milk products, and fatty meats.[10] But the 10,000-year (300-generation) interval between the beginnings of agriculture and the present time provided natural selection too little time to produce the comprehensive restructuring of our physiology and metabolism for optimal functioning in the face of such a major shift in dietary patterns. Not to mention the even shorter period natural selection has had to adapt us to dietary novelties since the more recent industrial and fast-food revolutions that further drastically changed our dietary environment.

Agricultural food sources actually did not dominate the human food supply until about 7,000 years ago.[11]

"Natural selection can never redesign a mechanism. It can only bring about slight quantitative shifts in its parameters."[4]

"Constraints due to history: Perhaps a different arrangement of leg muscles and bones would produce cheetahs that run faster—however, the basic body form of mammals is already laid out in their genes and development in such a mutually constrained way, that is unlikely to be altered. There really may be "no way to get there from here."[12]

With respect to integrated metabolic and physiologic functioning, *Homo sapiens'* genome therefore has remained fundamentally unchanged since agriculture began. Accordingly, we need to look to our hominin ancestral diets, especially during the Paleolithic epoch, and compare them with our modern diets to see if we can discover similarities that presumably would favor optimal functionality, or to see if we find important differences that might render aspects of our metabolism and physiology maladapted.

"Stone-Agers in the Fast Lane"

Eaton refers to contemporary inhabitants of westernized countries as "Stone agers in the fast lane."[3] Accumulating evidence suggests that the large-scale mismatch between our modern diet and the nutritional requirements set by our Paleolithic genome[13] play a substantial role in the pathogenesis of obesity, hypertension, diabetes, certain forms of cancer, atherosclerotic cardiovascular disease, kidney stones, age-related muscle wasting, and osteoporosis.[14-19]

With those considerations in mind, our research group sought to quantify the dietary difference between Paleolithic and modern diets with respect to the provision of one of the body's major mineral nutrients: potassium.

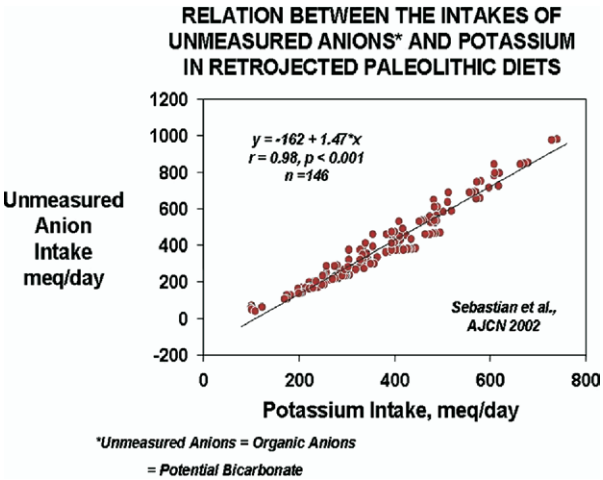

Figure 3 The relationship between the intake of unmeasured anions (eg, organic anions or potential bicarbonate) and potassium intake in the 146 of the 159 diets shown in Figure 1 for which adequate data permitted calculation. (Color version of figure is available online.)

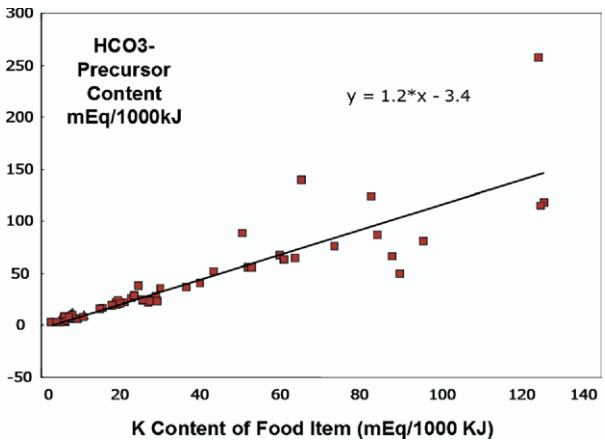

Figure 4 Relationship between bicarbonate-precursor content (unmeasured anions) and the potassium content of individual nongrain vegetables and fruits. (Color version of figure is available online.)

Table 2 Some Physiological Effects Of Potassium Bicarbonate And Bicarbonate-Generating Organic Anions That Have Positive Health Benefits

Established Associations
Stomach antacid[#]
Diuretic,* natriuretic,* chloruretic*
Increases serum potassium concentrations to evolutionary optima*
Corrects thiazide induced hypokalemia*[39]
Antihypertensive: reduces systolic & diastolic blood pressure*[40-44]
Optimizes endothelial function*[45]
Increases aortic compliance*[46]
Stroke prevention, independently of bp reduction*[47,48,49]
Reverses salt-induced (sodium chloride-induced) increases in blood pressure*[42,50]
Reverses salt-induced increases in urine calcium excretion*#[42,51]
Increases urinary citrate excretion*#[52–54]
Reduces kidney stone formation*#[55]
Reduces urine calcium excretion and improves negative calcium balance*#[56]
Reduces urine phosphorous excretion and improves negative phosphorus balance#[56]
Reduces urine nitrogen excretion#[57]
Inhibits osteoclastic bone resorptive activity#[58]
Stimulates osteoblastic bone formative activity#[58]
Decreases bone resorption markers in vivo#[56]
Reduces production of the reno-toxin, ammonia (NH_3)*#
Acts as vasodilator[59,60]
Reduces production of the reno-vasoconstrictor, thromboxane*[61]
Increases production of vasodilators, prostaglandins & nitric oxide*[62,63]
Reduces free radical formation (therefore anti-atherogenic)*[64]
Increases growth hormone blood levels in older individuals*[65]
Neutralizes the diet-induced endogenous acid load#[56]
Corrects the systemic metabolic acidosis caused by typical American diets#[56]
Increases plasma bicarbonate & reduces blood acidity#[56]
Lowers serum chloride concentrations#[56]
Increases serum phosphorus concentrations*[66]
Improves age-related declines in cognitive function*[67]

#predominantly a bicarbonate effect
*predominantly a pottasium effect
*#combined potassium and bicarbonate effect

Paleolithic Dietary Potassium

To estimate the potassium content of the human ancestral diet, we followed Eaton and Eaton[20] and Cordain et al[21] regarding which food groups Stone Age human beings and their hominin ancestors habitually ingested, and what ratio of animal-to-plant foods they consumed. By using standard nutrient databases, we computed the potassium contents for a series of retrojected Stone Age diets (n = 159 diets) and compared those with values for an average American diet (as taken from the Third National Health and Nutrition Examination Survey [NHANES III][22]). We reported the details of the methodology in a previous publication in which we estimated the systemic net acid load of Paleolithic diets.[23]

Within paleo-anthropologically accepted bounds of animal-to-plant food ratios and animal fat densities, the Stone Age human potassium intake averaged 400 ± 125 mEq/d (Fig 1),[24] which exceeds the NHANES III age-grouped averages (~60-85 mEq/d) by factors greater than 4 (Fig 2). We do not assume that our Paleolithic ancestors consumed such above-contemporary intakes on a daily basis, rather that they consumed differing amounts of potassium from day to day, perhaps over the range indicated in Figure 1.[22] It also exceeds the 120 mEq/d set for adequate intake by the Food and Nutrition Board of the Institute of Medicine in 2004[25] and 2006,[26] and the same value, 120 mEq/d, recommended by the US Department of Agriculture in 2005.[27]

What could account for that transition from our ancestral relatively potassium-rich preagricultural diet to our current relatively potassium-poor modern diet? We found that we could account for it by the fact that the contemporary diet has substantially replaced Paleolithic amounts of potassium-rich plant foods (especially fruits, leafy greens, vegetable fruits [also known as vine fruits], roots, and tubers) with energy-dense nutrient-poor foods (separated fats, oils, refined sugars, and refined grains), and with potassium-poor energy-rich plant foods (especially cereal grains) introduced by agriculture (ca. 10,000 years ago).

Vegetable fruits (also known as vine fruits) and fruits commonly referred to as vegetables (eg, cucumbers, squash, eggplant, tomato, and sweet pepper). All fruits come from flowering plants as ripened ovaries containing seeds. Cereal grains make up approximately 25% of the energy content of the American diet. The potassium contents of brown rice, wheat, whole-grain wheat flour, corn, and barley range from 1.9 to 3.1 mEq/100 kcal (mean, 2.3 mEq/100 kcal), compared with the potassium contents of oranges, bananas, carrots, squash, and spinach, which range from 8.8 to 61.0 mEq/100 kcal (mean, 28.4 mEq/100 kcal), introduced by agriculture (circa 10,000 years ago). Omitting energy-dense nutrient-poor foods and cereal grains from the diet in a hypothetic Paleolithic diet, as shown in Table 1, reveals the

Table 3 Some Physiological Effects Of Potassium Bicarbonate And Bicarbonate-Generating Organic Anions That Have Positive Health Benefits

Proposed, with Plausible Rationales
Epithelial cancer prevention*
Slows the normal age-related decline in glomerular filtration rate#
Slows progression of chronic renal disease#
Increases exercise capacity#
Counteracts some forms of male and female subfertility#
Extends lifespan*#

*predominantly a pottasium effect
#predominantly a bicarbonate effect
*#combined potassium and bicarbonate effect

Table 4 Effect of Prolonged Large Potassium Loads on Serum Potassium Concentration In Healthy Humans

Reference	No. of Subjects	How Diet K Was Increased	Baseline Diet K, mEq/d	Final Diet K, mEq/d	Duration of High K Diet, days	Baseline Serum K mEq/L*	Final Serum K mEq/L*
Rabelink et al.[68]	6	KCl supplement 300 mEq/d	100	400	20	3.75 ± 0.16	4.22 ± 0.12
Witzgall and Beh[69]	16	K-citrate/KHCO3 supplement 200 mEq/d	60	260	6	4.2 ± 0.3	4.6 ± 0.3
Dluhy et al.[70]	5	?	40	200		4.1 ± 0.1	4.3 ± 0.1
Sebastian et al.[56]	6	KHCO3 supplement 120 mEq/d	59	179	18	3.92 ± 0.15	4.15 ± 0.21
Jenkins et al.[71]	10	Grain-free vegetarian diet	98	341	14	4.26 ± 0.10#	4.03 ± 0.08#
Hene et al.[72]	6	K-citrate supplement 220 mEq/d	80	300	14	4.07 ± 0.27	4.48 ± 0.29

Abbreviations: K, potassium; KHCO3, potassium bicarbonate; K-citrate, potassium citrate; KCL, potassium chloride

potential for a markedly above-contemporary dietary potassium intake.

Given the fundamental physiologic and metabolic importance of potassium, such a large magnitude of change in potassium intake invites the question of whether in human beings the quantitative values of potassium-influenced physiologic phenomena (eg, blood pressure, insulin and aldosterone secretion rates, and intracellular pH) that currently are viewed as normal in fact are in disaccord with genetically conditioned norms. We must address that question, but before we can do so coherently we need to introduce a consideration of the anions that accompanied potassium in the Paleolithic diet.

Anions Charge-Balancing Potassium in Natural Foods

In natural diets not subjected to processing that includes the addition of potassium salts, typically potassium chloride, a variety of organic anions accompany food potassium in near-equivalent amounts. The body converts a large fraction of those organic anions to bicarbonate (base) as an end-product of metabolism. We can estimate the organic anion content of individual food items and of entire diets by determining the contents therein of the major inorganic cations and anions, and then calculating the difference, the so-called *unmeasured anion content*, typically a positive number, which reflects the organic anion content, or the potential bicarbonate yield on metabolism. Figure 3 shows how well the potential bicarbonate content of retrojected Paleolithic diets correlates with the potassium content of those diets.

In Figure 3, note that the equivalents of a diet's potential bicarbonate yield more than matches the equivalents of potassium in the diet (slope >1). The excess may in part represent organic anions not metabolizable to bicarbonate and in part errors in determining inorganic cation and anion contents. A similarly near-equivalent relationship exists for individual food items, as shown in Figure 4.

Not surprisingly, then, our Paleolithic ancestors consumed their large potassium loads, by contemporary standards, with near-equivalent amounts of bicarbonate precursors, the latter sufficient to render the Paleolithic diet net base-producing in contrast to the contemporary Western net acid-producing diet.[28,29]

Health Benefits of Potassium Organates

Supplementing a contemporary Western diet with potassium accompanied by bicarbonate or a bicarbonate-generating organic anion (eg, citrate) results in numerous physiologic effects with potential health benefits. Table 2 outlines some of the well-established effects, which include positive effects on blood pressure, cardiovascular dynamics, bone, and kidney, and preventive effects for stroke. Table 3 outlines effects for which one can generate a plausible rationale but require further research.

One obviously must exercise caution in supplementing potassium in individuals with certain underlying conditions, such as hyperkalemia, chronic renal insufficiency, adrenal insufficiency, aldosterone deficiency, and use of certain medications: angiotensin-converting enzyme inhibitors, angiotensin II–receptor blockers, potassium-sparing diuretics, cyclooxygenase-2 inhibitors, and nonsteroidal anti-inflammatory drugs. Individuals without such contraindications tolerate chronic large potassium loads without developing hyperkalemia (Table 4) because the human kidney excretes chronic potassium (and bicarbonate) loads with great facility and prodigious capacity.[30-33]

The Institute of Medicine has not set a Tolerable Upper Intake Level (UL) for potassium intake. They reported:

> *In otherwise healthy individuals (ie, individuals without impaired urinary potassium excretion due to a medical condition or drug therapy), there is no evidence that a high level of potassium from foods has adverse effects. Therefore, a UL for potassium from foods has not been set . . . Fruits and vegetables, particularly leafy greens, vine fruit [a.k.a., vegetable fruit] (such as tomatoes, cucumbers, zucchini, eggplant, and pumpkin), and root vegetables, are good sources of potassium and bicarbonate precursors. Although meat, milk, and cereal products contain potassium, they do not contain enough bicarbonate precursors to balance their acid-forming precursors, such as sulfur-containing amino acids.*

The Yanomamo Indians represent only one human culture in the contemporary world in which dietary potassium intake remains in the retrojected Paleolithic diet range. Denton[34] reports their mean 24-hour urine potassium excretion as 303 ± 105 mmol/d (see Table 27-7 in article by Denton[34]). The Yanomamo have a mean body weight of 55 ± 2 kg. If we consider an 85% gut absorption of consumed potassium, and extrapolate to a standard 70-kg body weight, potassium intake computed from the urine excretion rates would amount to 70*([303/0.85]/55) = 454 mEq/d.

Beyond Potassium

Americans would have difficulty increasing their daily potassium intake to levels greater than 200 to 250 mEq/d because they would have to substitute a large number of servings of fruits and nongrain vegetables (considerably more than current United States Department of Agriculture recommendations) in place of energy-dense nutrient-poor foods and relatively potassium-poor (per kilocalorie) plant foods. Giving up cereal grains, which are not only an acid-producing plant food but among the lowest of potassium densities of plant foods,[35] would require a major lifestyle change, but not an impossible one.[36-38] Such a change in dietary lifestyle could have numerous health benefits beyond those resulting from increased potassium intake.[3,35] As Ophelia says in Shakespeare's Hamlet, Act IV, Scene V: "We know what we are, but know not what we may be."

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