**Letters to the Editor**

**Paleolithic diet, sweet potato eaters, and potential renal acid load**

Dear Sir:

In a recent article in the Journal, Sebastian et al (1) provided a detailed analysis of the probable effect of ancestral preagricultural diets on systemic acid load (net endogenous acid production, or NEAP) and compared this with the average acid load of contemporary diets. The NEAP was calculated for retrojected preagricultural diets for which compositions were suggested by Eaton and Konner (2). Current food tables served to estimate the respective nutrient content. Final computation was based on an existing calculation model (3, 4) that was modified to more accurately estimate those food-dependent acid loads that lead to endogenous production (and renal excretion) of sulfate and organic acids (OAs).

This modified approach, which considers individual dietary sulfur-containing amino acids (instead of average protein content) and dietary determinants of OA production, offers an important improvement to existing estimation models for net acid excretion. However, we do not fully agree with Sebastian et al, who argue that food-dependent endogenous OA production can be sufficiently predicted (with specific formulas) from the same nutrients (sodium, potassium, calcium, magnesium, chlorine, and phosphorus) that are needed to estimate the major food-dependent component (apart from sulfur-containing amino acids) of NEAP or of potential renal acid load (PRAL). It is highly probable that the renal excretion of different OAs is dependent on diet. Aromatic organic acids are a dietary component, not mentioned by Sebastian et al, that may have a particularly strong effect. For example, phenolic and benzoic acids, which are found in considerable amounts especially in fruit (5, 6), are metabolically inactivated (detoxified) and excreted (mainly via the kidney) as acids, largely in the form of hippuric acid. Interestingly, in the highlands of New Guinea, some Papuan tribes consume a low-protein vegetarian diet consisting predominantly of sweet potatoes. These sweet potato eaters excrete extremely high amounts of hippuric acid (31 mmol/d on average compared with 4 mmol/d in European control subjects), which adds substantially to their basal (not primarily food-dependent) renal OA excretion (7). Basal OA excretion can be estimated from average anthropometric data as follows (3, 4):

\[
\text{Basal OA excretion = body surface area (m}^2\times 41 \text{ mEq} \times \text{d}^{-1} \times (1.73 \text{ m}^2)^{-1}
\]

As a result, 36 mEq/d is yielded for sweet potato eaters [young adult males weighing 53 kg, 1.55 cm tall, and with a body surface area of 1.5 m\(^2\); (7)], which together with their hippuric acid output amounts to 67 mEq total OA excretion/d.

The reported data (7) on average daily food intake and 24-h urinary excretion of sodium (7 mmol/d), chloride (4 mmol/d), potassium (180 mmol/d), and total nitrogen (2.6 g/d) allowed us to estimate the NEAP and PRAL of the sweet potato eaters. Urinary excretion rates not given in the original article (7) were calculated (3, 4) from the corresponding daily intakes of magnesium (443 mg/d), calcium (728 mg/d), and phosphorus (936 mg/d). They were obtained from the reported food consumption by using food tables (8) and yielded values of 12, 9, and 34 mEq/d, respectively. Urinary sulfate output (11 mEq/d) was estimated from protein degradation, ie, from total nitrogen excretion (see above), corresponding to an absorbed amount of 16.3 g protein/d. The nutrient-dependent PRAL (sulfate + phosphate + chloride – sodium – potassium – magnesium – calcium) was then calculated as 159 mEq/d. Because the NEAP corresponds to PRAL + OA, an average overall endogenous acid production of 88 mEq/d was finally yielded. This NEAP, directly calculated for “modern” stone age farmers by using measured (ie, hard) data for the intake and renal excretion of nutrients, is nearly identical to the average NEAP (88 mEq/d) found by Sebastian et al for 159 retrojected preagricultural diets. However, the protein intake of the sweet potato eaters was very low (22 g protein/d, as estimated from urinary nitrogen output under the assumption of 75% net absorption), whereas protein intakes of 200 g are assumed for most ancestral diets (1, 9).

If the protein intake of sweet potato eaters was to isonenergetically increase by only 100 g/d (with protein replacing carbohydrates), the NEAP would increase (ie, net base production would fall) to 43 mEq/d. Therefore, it appears to us that the average net base production of 88 mEq/d (ie, the absolute figure) calculated by Sebastian et al may be too high for Stone Age persons with high protein intakes. This is also confirmed if the average PRAL and NEAP are calculated from the average nutrient intakes of Stone Age persons as recently published by Eaton and Eaton (9). Using their figures on daily nutrient intakes, we estimated a negative PRAL of −39 mEq/d, leading to an NEAP of 22 mEq/d, which is markedly lower than current net acid excretion (64 mEq) in the United States (Table 1).

Taken together, we also conclude that the average Paleolithic diet principally led to net base production (yielding a negative PRAL), but was possibly less alkaline than suggested by Sebastian et al. One of several uncertainties in this respect is obviously the intake of those OAs not metabolically combusted but renally excreted, eg, phenolic acid, which is excreted in the form of hippuric acid. Reasons for the historical shift from negative to positive PRAL are not only the displacement of alkali-rich plant foods in the ancestral diet by cereal grains and nutrient-poor foods in the temporary diet but also the modern processing and preparation of foods, which lead to considerable losses of base-forming nutrients such as potassium and magnesium.

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TABLE 1
Potential renal acid load (PRAL) and net endogenous acid production (NEAP) in the Paleolithic Age and today

<table>
<thead>
<tr>
<th></th>
<th>Paleolithic diet (3000 kcal/d)</th>
<th>US diet today (2500 kcal/d)</th>
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<tr>
<td></td>
<td>Protein/sulfate</td>
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<td>mEq/d</td>
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<tr>
<td>NEAP</td>
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</tr>
</tbody>
</table>

†Intake data from Eaton and Eaton (9), with protein intake calculated from given ratios of protein to potassium (0.84 g/mmol for Stone Age persons and 1.24 g/mmol for Americans).

‡Potential renal excretion, calculated according to references 3 and 4 by using the following conversion factors (g intake → mEq excretion): sulfate, 0.4888; phosphorus, 36.6; potassium, 20.5; calcium, 12.5; magnesium, 26.3.‡

§Basal organic acid excretion was calculated for a subject with a body surface area of 1.73 m² (41 mEq/d). A further diet-dependent organic acid excretion (eg, hippuric acid) value, assumed to be 20 mEq/d, was added for the Stone Age persons.

REFERENCES


Reply to T Remer and F Manz

Dear Sir:

In estimating net endogenous acid production (NEAP) in preagricultural humans and their hominin ancestors (1), we computed the contribution to the NEAP of the body’s total organic acid production as a function of the “unmeasured anion” content of the diet, on the basis of the following considerations. Ultimately, one must determine the contribution to the NEAP of total organic acid production as that fraction of organic acids produced whose dissociated organic anions escape into the urine, leaving behind the protons once associated with them (2). Those organic anions that do not so escape are metabolized to bicarbonate, which backtitrates the dissociated protons. As total organic acid production increases, so does the spillover of organic anions into the urine. Total organic acid production increases in response to increased bicarbonate input to the body—evidently a homeostatic response to mitigate the alkalization (3)—and as a result the excretion rate of the dissociated organic anions increases. The increase in lactic acid and ketoacid production, and the excretion of their anions, after alkali administration exemplifies that fact (3), as does the dose-dependent increase in total organic anion excretion in response to increased dietary bicarbonate precursors (4). The dose-dependent increase in citrate excretion in response to bicarbonate administration or to dietary bicarbonate precursors also exemplifies that fact (5, 6), which is contributed to by reduced reabsorption of citrate filtered at the renal glomerulus (3).

Accordingly, organic anion excretion increases in response to increases in the so-called unmeasured anion (UA) content of the diet—computed as Na⁺ + K⁺ + Ca²⁺ + Mg²⁺ − Cl⁻ – Pi, in mEq/d—because such UAs consist of organic anions largely metabolized to bicarbonate and thus are dietary bicarbonate precursors (4). Empirically, in adults eating a wide variety of diets, organic anion excretion correlates positively and quantifiably with the UA content of the diet (4, 6). Thus, in our study (1), we computed the contribution of organic acid production to the NEAP from the UA content of the diet by using the regression equation of Kleinman and Lemann (4).

Remer and Manz prefer to estimate organic anion excretion not from dietary UA but from body surface area (BSA) independent of diet composition. This approach ignores the physiology discussed above, in that persons with a given BSA may have markedly different organic anion excretion rates depending on the content of bicarbonate precursors in the diet. The BSA approach might identify a basal component of organic anion excretion independent of diet. However, our method accounts for any such base-line effect because the organic anion excretion intercept at zero diet UA content in the regression of the former on the latter among adult diets has a positive value, which is incorporated in the calculation for organic anion excretion (4). Moreover, because the UA content of contemporary Western diets is almost an order of magnitude lower than that in preagricultural diets (1), it has little influence on organic anion excretion relative to the diet-independent basal rate. This may explain why Remer and Manz’s BSA approach works reasonably well for contemporary diets, and why their approach may be questioned for preagricultural diets.

In part for the reasons cited above, we take exception to the estimation of the positive value of NEAP for the single retrojected preagricultural diet shown in Remer and Manz’s Table 1. We consider their estimation of organic acid production to NEAP in the table problematic, not only because it is based on an assumed BSA and thereby ignores the effect of the diet’s content of bicarbonate precursors independent of BSA but also because it posits an arbitrary diet-dependent substantial production of a nonmetabolized organic acid, hippuric acid, which might result from eating large amounts of noncombustible hippuric acid precursors in their undissociated acid form. Although a few plant foods (eg, cranberries and plums) do contain substantial amounts of noncombustible organic acids, such foods would substantially alter...