Standardizing Terminology for Estimating the Diet-Dependent Net Acid Load to the Metabolic System

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ABSTRACT

Contemporary Western diets contain acid precursors in excess of base precursors, yielding a daily systemic net acid load of varying amounts, depending on the specific composition of the diet. Increasing evidence suggests that differences in daily net acid load, resulting predominantly from differences in dietary intake, can have deleterious health consequences, with a stepwise increase in severity with increasing magnitude of the net acid load.

The daily net acid load's magnitude (in part by influencing systemic acid–base status) has been shown to induce renal losses of calcium, magnesium, and nitrogen and adversely affects numerous endocrine functions. Investigations have shown detrimental clinical outcome effects for axial and peripheral bone health, particularly in elderly subjects (1) and postmenopausal women (2), as well as healthy children (3,4).

Although physiological and biochemical principles support negative effects on bone architecture, muscle wasting, and nephrolithiasis, quantifying clinical outcomes is not straightforward. The long latency period required for subclinical changes to be clinically relevant and the lack of precision of current technology have posed challenges for researchers. For example, dual energy X-ray absorptiometry does not detect moderate changes in architectural-related bone strength parameters thus requiring long-term follow-up or large sample sizes.

Additionally, terminological confusions result from investigators’ use of different algorithms for estimating the diet’s daily net acid load, even when the estimates derive essentially from the same input variables. For this reason, a number of plenary speakers at the 2nd International Acid-Base Symposium held in Munich, (8–9 September 2006) tried to reach agreement on terminology related to estimating the diet’s daily net acid load from the composition of the diet, based on accepted physiological principles.

The group discussions yielded the following: under ordinary physiological conditions, differences in the amount of net acid produced by the metabolic system per day, which is referred to as the daily net endogenous acid production (NEAP), results predominantly from differences in the relative amounts of the diet’s acid and base precursors absorbed by the gut. Although investigators have devised several algorithms for estimating NEAP from the composition of the diet (see below), the group agreed to refer to the estimated diet-dependent net acid load as “estimated NEAP” and to always specify the algorithm used to obtain the estimated NEAP.

For example, Frassetto et al. (5) estimated the diet’s net acid load from the diet’s contents of protein (an acid precursor) and potassium (an index of base precursors from organic anions). They would then specify:

Estimated NEAP (mEq/d) = [0.91 × protein (g/d)] – [0.57 × potassium (mEq/d)] + 21, or

Estimated NEAP (mEq/d) = [54.5 × protein (g/d)] / potassium (mEq/d) – 10.2.

This equation was developed based on chemical analyses of diets fed research participants. With cost being the limiting factor, the equations were developed using the most complete data available. This algorithm provided the opportunity to estimate NEAP when nutrients and mineral content of the diet is limited.

Remer et al. (6,7) estimate the net acid load from average intestinal absorption rates of ingested protein and additional minerals as well as an anthropometry-based estimate for organic acid excretion:

Estimated NEAP (mEq/d) = PRAL (mEq/d) + OAest (mEq/d),

whereby PRAL denotes dietary potential renal acid load and OAest denotes estimated urinary organic anions, with the 2 components calculated as follows:

PRAL (mEq/d) = 0.49 × protein (g/d) + 0.037 × phosphorus (mg/d) – 0.021 × potassium (mg/d) – 0.026 × magnesium (mg/d) – 0.013 × calcium (mg/d);

OAest (mEq/d) = individual body surface area9 × 41/1.73.

The various ions are listed in millequivalents (mEq) rather than mg because most acid-base physiologists use mEq, as these are ions in solution that interact according to their charge. To calculate mEq from mg, divide by the molecular weight of the ion to get millimoles (mmol), and then multiply by the charge of the ion in solution.

Body surface area was calculated according to the formula of Du Bois and Du Bois (11) as follows: body surface area (m²) = [0.007184 – height (cm)0.725 – weight (kg)0.425].


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This equation was based on nutrients obtained from nutrient values from diet composition tables. The equation was developed for adults (6) and modified for children (7) residing in Germany. These equations should be evaluated or confirmed in populations that may rely on nutrient values published for different countries or cultures.

Sebastian et al. (8) estimated NEAP with an algorithm similar to that published by Remer et al. (6), with the following exceptions: they calculated the sulphuric acid content of each individual food item in the diet, from reported values of the sulfur-containing amino acids, methionine and cystine, \(^{11}\) in each item; they estimated urine organic anion excretion as a function of the unmeasured anion content of the total diet, \(^{11}\) after Kleinman and Lemann (9), so that urine organic anion excretion [milliequivalents per day \((\text{mEq/d})\)] = 32.9 + 0.15 \times \text{diet unmeasured anion content (mEq/d)}, where the latter term calculates as

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\text{[sodium + potassium + calcium + magnesium – chloride – phosphorus]},
\]

and each constituent is expressed in mEq/d. This equation was based on nutrient values obtained by chemical analyses of foods provided in a feeding study. If applied to data obtained from diet composition tables, the equation may not hold because of the difficulty in estimating Na and Cl from many processed foods.

The Frassetto et al. (5), Remer et al. (6, 7), and Sebastian et al. (8) algorithms yielded reasonable estimates of NEAP, primarily dependent on the availability of the respective diet composition and/or anthropometric data (10).

The authors would like to point out that investigators can best estimate NEAP by collecting 24-h urines and measuring renal net acid excretion (RNAE) \(^{\text{11}}\) in mEq/d, where:

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\text{estimated NEAP (mEq/d)} \approx \text{NAE} = \text{TA} + \text{NH}_4 - \text{HCO}_3, \\
\text{and TA, NH}_4, \text{and HCO}_3 \text{ (each constituent expressed in mEq/d) denote 24-h urinary excretion rates of titratable acid, ammino-nium, and bicarbonate, respectively (7,10). One should keep in mind that NAE may progressively deviate from NEAP at high positive values of NAE, as the body increases its utilization of bone base to titrate NEAP, at least for the relatively short durations in which investigators have studied the relation.}
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We point out that, in trying to standardize terminology for estimating the diet net acid load (i.e., estimated NEAP), we do not address the issue of the accuracy of the estimates given by the exemplified algorithms, nor do we address the issue of the accuracy of the estimates given by the methodologies used in measuring the variables for NEAP or NAE algorithms (12–14), but also that additional endocrine and metabolic effects may interfere with endogenous acid generation and buffering (15,16).

We emphasize that different investigators have developed different algorithms for estimating NEAP from the composition of the diet whether or not those estimates approach true NEAP as classically determined from the differences in composition of the diet and the stool (17). In doing so, however, those investigators have used different terminologies for designating estimated NEAP, causing confusion in the minds of attendees of the symposium; our objective in this article was to standardize the terminology to a common term, viz., “estimated NEAP.” We hope this proposed standard terminology contributes to a more straightforward use of estimates to determine the diet-dependent daily net acid load.

### Literature Cited


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10 To calculate mEq for methionine and cysteine, calculate the mmol of sulfur (methionine contains one S and cystine 2) and multiply that number by 2 to get mEq.

11 \([0.15 \times \text{unmeasured diet anion content} + 32.9]\) would be the equivalent of the OAest used in the Remer et al. (6) equations.