ACID-ALKALINE BALANCE: ROLE IN CHRONIC DISEASE AND DETOXIFICATION

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Several researchers have noted that the contemporary Western diet has increased in net acid load relative to diets of the ancestral pre-agricultural *Homo sapiens*.[1-3] Quite possibly, this shift occurred because of the agricultural revolution and the ubiquity of processed grains and shelf-stable food products devoid of essential nutritional components. In addition to this underlying foundational change in diet, there is the overlay of various nutritional fads that have risen and fallen over the past few decades. Most recently, the latest diet trend has been an interest in high-protein foods accompanied by a compensatory decrease in the phytochemical load from fresh fruits and vegetables. Indeed, high-protein diets increase net dietary acid load and acidify the urine pH.[2-5] Conversely, diets high in fruits and vegetables have been proposed to be associated with a greater degree of alkalinity.[4,6] Remer and Manz calculated the potential renal acid loads of certain food groups and reported that alkaline-forming foods were primarily vegetable and fruits, whereas acid-forming foods were derived from cheese, meat, fish, and grain products (Table 1).[4]

TABLE 1 Average Potential Renal Acid Loads (PRAL) of Specified Foods[4]

Food	PRAL* (mEq)
Fats and oils	0
Fish	7.9
Fruits and fruit juices	-3.1
Grain products	3.5-7.0
Meat and meat products	9.5
Milk and dairy products	1.0-23.6
Vegetables	-2.8

*PRAL = mEq of Cl + PO4 + SO4 – Na – K – Ca – Mg)

Over time, ingestion of a high dietary acid load can progress to a chronic low-grade level of metabolic acidosis. The incidence of low-grade acidosis resulting from our modern diet has been well documented.[1-3,6] A chronic acidic load can cause a number of health conditions such as osteoporosis, kidney disease, and muscle wasting.[1,7] Sebastian et al articulates this cause and effect relationship eloquently: "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 to bone, muscle wasting, kidney stone formation, and damage to the kidney."[1(p1308)]

In order to maintain acid-alkaline balance throughout the various body systems, one system may be required to support another. For example, the bone matrix contains a substantial alkaline reserve such as calcium and magnesium cations that are released from the bone to balance an overly acidic dietary load in the event of inadequate buffering capacity in the blood. However, repeated borrowing of the body's alkaline reserve in response to a consistent increased (dietary) acid load can be potentially detrimental. In humans, hypercalciuria and negative calcium balance due to calcium efflux from bone may lead to metabolic bone disease and calcium nephrolithiasis.[2,8,9] In the chapter titled "Potassium" of its report *Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate*, the Institute of Medicine Food and Nutrition Board states the following:

> *In the setting of an inadequate intake of bicarbonate precursors, buffers in the bone matrix neutralize the excess diet-derived acid, and in the process, bone becomes demineralized. Excess diet-derived acid titrates bone and leads to increased urinary calcium and reduced urinary citrate excretion. The resultant adverse clinical consequences are possibly increased bone demineralization and increased risk of calcium-containing kidney stones.*[7(p187)]

Conversely, dietary modification can positively influence bone metabolism. A diet favoring neutralization of net endogenous acid production increases calcium and phosphate retention, reduces bone resorption markers, and increases markers of

bone formation in postmenopausal women.[10] Furthermore, studies have demonstrated a positive association between a high intake of alkali-rich fruits and vegetables with preservation of bone mineral density.[6,11,12]

PHYSIOLOGY OF ACID-ALKALINE BALANCE

From a physiological perspective, the body has compartmentalized organ systems operating within specific pH ranges (Table 2).[13] The "potential of hydrogen," or "pH," is based on a logarithmic scale, meaning that there is a 10-fold difference between each number going from 1 to 14. The lower numbers (1-6.99) represent the acid (or H+ donating) range, and the higher numbers (7.01-14) represent the alkaline (or H+ accepting) range. For the most part, body tissues remain within the neutral pH of 7. Some body systems such as the blood (7.35-7.45) are more tightly regulated than others (eg, urine pH ranges from 4.5-8.0), and any extended disturbance in acid-alkaline balance may upset cell functioning via its transport and signaling processes.[14-16] The human body has several means whereby it is able to regulate acid-alkaline balance, including the following: (1) at the cellular level via chemical reactions generating or consuming H+; (2) in the blood with the assistance of bicarbonate, amino acids, albumin, globulin, and hemoglobin; and (3) systemically through the release of carbon dioxide from the lungs and hydrogen ions from the kidney.[17]

TABLE 2 pH of Selected Body Tissues[13,17]

Body Tissue	pH
Blood	7.35-7.45
Muscle	6.1
Liver	6.9
Gastric juice	1.2-3.0
Saliva	6.35-6.85
Urine	4.5-8.0
Pancreatic juice	7.8-8.0

CLINICAL DETERMINATION OF ACID-ALKALINE BALANCE

Although it is not common, blood pH levels can shift to the side of excessive acidity or alkalinity, in which case several clinical symptoms will appear. Acidosis can lead to symptoms of lethargy, progressing to stupor and coma, while alkalosis can lead to a host of nervous conditions such as cramps, muscle spasms, irritability, and hyperexcitability. Clinical determination of a high systemic acid load can be accomplished by a number of methods, including a review of the diet diary for at least 3 to 7 days to gauge the degree of processed food and animal protein intake relative to fruit and vegetable consumption and a measurement of urine pH using narrow-range indicator paper. Urine pH is a good indicator of the net dietary acid load, as reported by Remer and Manz, who observed an inverse relationship between the two variables.[4] The urine compartment appears to be well suited for measuring the effect of acute and chronic factors. In our clinical experience, we have noted that the urine pH responds to a dietary intervention in as little as 2 hours. Additionally, the fact that the urine pH range spans a greater continuum (4.5-8.0) indicates that it has more potential to reflect systemic pH changes. From our testing, it was determined that due to the wide pH range of the urine, it is important to take a fasting urine sample and to control for water intake during the fasting period. Intra- and inter-individual variability can be further reduced if the same person is determining the pH readings consistently.

URINARY ALKALINIZATION

The concept of acid-alkaline balance in the field of medicine is not entirely novel, as it has been embraced by several groups within the medical community. Naturopathic medicine has used the acid-alkaline balance as a theoretical model to explain the foundation of many diseases. Allopathic medicine has examined pH modulation in specific organ systems such as the kidney to control the formation of stones and the elimination of toxins. For example, urine alkalinization has been part of the medical protocol for the management and prevention of uric acid stones.[18,19]

Another aspect of the acid-alkaline balance is its role in detoxification, via either the acute removal of a drug or poison due to overdose or a nutritional protocol to support metabolic detoxification and decrease dietary toxins. Urinary pH alkalinization is a method employed under acute medical settings for the enhanced elimination of toxins in the event of a severe overdose. Conversely, acidification of urine also increases the elimination of specific toxins, although to a seemingly lesser degree.[20,21] The method by which urine alkalinization works to enhance toxin elimination is by the medically recognized process of "ion trapping," which is the ability to enhance urinary excretion of weak acids in alkaline urine, preventing the reabsorption of xenobiotics by renal tubules.[22,23] Proudfoot et al published a position paper on urine alkalinization, approved by the American Academy of Clinical Toxicology, which describes the use of urine alkalinization to ≥7.5 via intravenous sodium bicarbonate administration for acute poisoning and toxicity.[22] In this extensive review, the effect of urine alkalinization on the excretion of various pharmaceuticals and environmental toxins is elucidated. This report states that "urine alkalinization increases the urine elimination of chlorpropamide, 2,4-dichlorophenoxyacetic acid, diflunisal, fluoride, mecoprop, methotrexate, phenobarbital, and salicylate."[22] The potential of urine alkalinization to enhance toxin excretion is exemplified by the work of Blank and Wolffram, wherein they modulated urine pH in pigs with 2% dietary sodium bicarbonate, changing the urine pH from 5.7 ± 0.2 to 8.3 ± 0.1, and favorably impacted the excretion of ochratoxin A, a mycotoxin, from 9.3 ± 1.9% to 22.2 ± 4.3% of the dose.[24] Also, experimental and clinical studies confirm that urine alkalinization is effective for salicylate poisoning.[23,25,26] Garrettson and Geller showed in humans that an increase in urine pH from 6.1 to 8.1 changed the renal clearance of salicylate from 0.08 ± 0.08 L/h to 1.41 ± 0.82 L/h.[23]

Therefore, if the rapid removal of toxins can be achieved to a large extent with increasing urine pH 2 points on the pH scale

(which corresponds to a 100-fold decrease in H+ ions), it would follow that smaller quantities of toxins may be removed on a prolonged basis if there were a subtle increase of urine pH in the alkaline direction. Due to the logarithmic pH scale, a small change in urine pH could have a disproportionately large effect on drug and xenobiotic clearance.[22] The concept of "progressive" versus rapid alkalinization of urine may be useful as an adjunct for integrative health approaches employing metabolic detoxification using specific (nutritional) protocols. Traditionally, functional medicine has addressed detoxification or the removal of harmful endo- or exogenous substances, from the aspect of upregulating hepatic phase I and phase II enzymes to enable the chemical biotransformation of toxins into water-soluble metabolites for excretion in the urine. With the added clinical procedure of urine alkalinization, the removal of these compounds from the body is accelerated. There are many dietary agents to assist in progressive alkalinization. Foods that are high in potassium are noteworthy (Table 3).[27] One approach to clinically implementing these strategies for metabolic detoxification involves initiating the patient on an elimination diet high in whole fruits and cruciferous vegetables and low in animal protein. In addition to potassium, cruciferous vegetables contain myriad phytochemicals, such as indole-3-carbinol and sulforaphane, which are essential for facilitating toxin biotransformation.[28-30] Additionally, these vegetables can favorably alkalize urine pH. In a pilot trial with 5 volunteers, we found that a 200 g serving of cooked broccoli, carrots, and cauliflower (with broccoli as the predominant vegetable) resulted in an increase in urine alkalinization for up to 4 hours afterwards (baseline pH = 6.20 ± 0.51; after vegetables = 6.91 ± 0.45, P=.01). Thus, the simple instruction to alter diet to include cruciferous vegetables can promote detoxification by upregulating phase II enzymes and by alkalizing urine, resulting in enhanced excretion of toxins.

TABLE 3 Potassium Content of Selected Foods[27]

Food	Serving	Potassium (mg)
Potato, baked with skin	1 medium	721
Prunes, dried	½ cup	633
Raisins	½ cup	598
Prune juice	6 fl oz	530
Lima beans, cooked	½ cup	478
Banana	1 medium	467
Acorn squash, cooked	½ cup (cubes)	448
Tomato juice	6 fl oz	400
Orange	1 medium	237

Moreover, alkalinization during metabolic detoxification may be particularly useful, as it is believed that cellular pH and the blood buffering system shift to the acid side of ideal pH reserve during detoxification due to increased circulation of xenobiotics and organic acids (eg, glucuronic acid). Furthermore, organic cation transporters that are responsible for the transport of xenobiotics in and out of the cell are pH-sensitive.[31,32]

ALKALIZING AGENTS

In addition to dietary changes, nutritional supplementation for a short-term course of 3 to 4 weeks with select botanicals can facilitate metabolic detoxification. It would be appropriate to include specific alkalizing agents, such as potassium, within this nutritional regimen (Table 3). Unfortunately, the mainstream American diet is poor in potassium, as it often lacks sufficient fruits and vegetables. The adequate intake (AI) established by the Food and Nutrition Board of the Institute of Medicine for potassium is 4.7 g daily,[7] which is the same amount that is encouraged by the Dietary Approaches to Stop Hypertension (DASH) diet to maintain lower blood pressure levels, decrease the effects of salt intake, decrease the risk of kidney stones, and possibly reduce the incidence of bone loss. Current median intakes of potassium in the United States are roughly 35% and 50% below the AI for men and women, respectively.[7] African Americans would particularly benefit from increased potassium intakes due to their relatively low potassium intakes and high prevalence of elevated blood pressure and salt sensitivity.[7] For the healthy population, intake of potassium at levels higher than the AI is not of particular high risk due to the ability of the kidney to excrete excess amounts.[7] However, potassium intakes should be closely monitored for patients with acute or chronic renal failure and pre-existing heart disease and for those on medications that increase potassium reserves in the body, such as potassium-sparing medications.[7]

Various potassium salts are available to alter urine pH. Studies using sodium bicarbonate administration reveal little effect on urinary calcium excretion in contrast to studies that used potassium bicarbonate or potassium citrate supplementation and found significant reductions.[33,34] Potassium citrate, a therapeutic regimen to prevent kidney stones, can effectively alkalize urine. Doses of 4 to 8 g daily for 2 weeks in patients with homozygous cystinuria have effectively alkalized urine.[35] Additionally, there are a number of studies on the use of potassium citrate to counteract bone resorption caused by chronic acidemia of protein-rich diets.[36-38]

The effects of potassium depend on its accompanying anion.[7] Potassium chloride, commonly used in processed food products, does not appear to have the same alkalizing ability as potassium citrate.[7] In a recent study, Jehle et al demonstrated that potassium citrate was more efficacious than potassium chloride in increasing bone mineral density in postmenopausal women with osteopenia.[39] Furthermore, potassium chloride led to decreased bone mineral density in the lumbar spine. Potassium citrate supplementation in these subjects resulted in a sustained and significant reduction in urinary calcium excretion and an increase in urinary citrate excretion, indicating that alkalinization had occurred.[39,40]

Additionally, the citrate anion may be especially relevant for detoxification since it is an intermediate of the Krebs cycle and can potentially play a role in energy production. As many clinicians acknowledge from their experience, lack of energy is a common side effect of the first stages of metabolic detoxification.

Therefore, eating foods that are high in citrate, such as certain fruits and vegetables, may be beneficial. It is also worth noting that citrate is metabolized to bicarbonate in the body, thereby further adding to the buffering potential.[7]

SUMMARY

In conclusion, the increasing dietary acid load in the contemporary diet can lead to a disruption in acid-alkaline homeostasis in various body compartments and eventually result in chronic disease through repeated borrowing of the body's alkaline reserves. Adjustment of tissue alkalinity, particularly within the kidney proximal tubules, can lead to the more effective excretion of toxins from the body. Metabolic detoxification using a high vegetable diet in conjunction with supplementation of an effective alkalizing compound, such as potassium citrate, may shift the body's reserves to become more alkaline.

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