UNDER APPRECIATED ISSUES IN THE TREATMENT OF CHRONIC ILLNESS – LOW GRADE, CHRONIC ACIDOSIS COMBINED WITH POTASSIUM DEFICIENCY – PART V – POTASSIUM METABOLISM AND CLINICAL APPLICATION OF POTASSIUM SUPPLEMENTS

INTRODUCTION

Over the last few months I have devoted the Moss Nutrition Report to my cause of increasing awareness in the clinical nutrition community that, even with the new treatment vistas that have been opened to us through genomics, new generation functional medicine tests and supplements, and exciting dietary protocols such as intermittent fasting and the ketogenic diet, addressing basic issues such as muscle and protein metabolism, acid/alkaline balance, and optimal potassium intake still has significant clinical utility. In this installment, I would like to go back to the subject of potassium and explore in depth its metabolism and application in terms of supplementation. To do this I will first review an excellent paper that provides some of the often ignored and under-appreciated fine points of potassium metabolism. Then I will provide an overview of three papers that consider three important aspects of potassium supplementation – improving bone health, retarding systemic protein breakdown, and deciding which form of potassium supplementation is best.

AN IN-DEPTH REVIEW OF POTASSIUM METABOLISM

During the last ten years or so I have been spending a good deal of time searching the literature for clinically useful published papers on potassium metabolism. Even though it was published 15 years ago in 2004, I still feel that “Protective effects of high dietary potassium: Nutritional and metabolic aspects” by Demigne et al (1) is one of the best if not the best. The first quote I would like to feature from this paper gives the authors’ thoughts as to why, as I have repeatedly stated, potassium does not get the attention it deserves:

“In contrast to other major cations, potassium (K+) is rarely considered to be a critical dietary constituent whose supply should be optimized for better health. This relative lack of interest likely reflects the fact that K+ deficiencies of nutritional origin are uncommon because this element is quite ubiquitous, at least when diets are based on nonpurified foods. Nevertheless, due to the extensive use of processed foods, a significant fraction of the population in Westernized countries might suffer from a discrete but relevant K+ depletion, resulting in moderate chronic hypokalemia.”

Before continuing, I would like to reinforce some key points made in the above quote. First, one reason, historically, potassium has not received the attention it deserves is that, up until the time that ingestion of processed, refined foods became prevalent, which is most of human history, potassium deficiency was a non-issue because the element is found in significant amounts in virtually all plant-based whole foods. Therefore, consideration of potassium deficiency only has relevance because of modern society’s reliance on diets containing large amounts of processed foods. Lastly, dietary potassium deficiency probably does not get the attention it deserves because it rarely leads to the gross potassium deficiency scenarios discussed in conventional medicine and nutrition textbooks. Rather, it leads to, as noted by Demigne et al (1), a “moderate chronic hypokalemia” where serum potassium may appear normal or low-normal based on usual laboratory analyte ranges.

Why is high potassium intake important? Even though I have discussed this question in previous
installments of this series, I would like to share the way Demigne et al (1) answer this question:

“It is now well established that a high K⁺ intake plays a protective role against hypertension, stroke, cardiac dysfunctions, renal damage, hypercalciuria, kidney stones, and osteoporosis. In fact, optimization of dietary K⁺ is indicated not only in association with the above pathologic states, but also in connection with various other physiologic processes such as the acid-base status, and control of carbohydrate metabolism or energy balance.”

Carbohydrate metabolism? Like many of you, I was not aware of the potassium-carbohydrate connection, at least until I read the Demigne et al (1) paper. More on that when I near the end of the review of this paper.

Next, the authors comment on dietary potassium sources. As you will see in the following quote the usual green leafy vegetables and fruits such as bananas are far from the only sources:

“Potassium is the most abundant cation in eukaryotic cells…and is thus amply supplied when intact or moderately altered tissues are consumed from plant (vegetables, legumes, or fruits) or animal foods (muscles or offal such as liver, heart, kidneys). In addition, some other foods such as milk (breast milk or cow’s milk: 50 or 160 mg/100 g, respectively) and cereals also contain significant amounts of K⁺.”

Before continuing, please note again that the key to optimal dietary intake of potassium is not so much the source since it is quite prevalent. Rather the key to optimal ingestion is dining on unprocessed foods. However, with the above mind, as noted in the following quotes, there is still a hierarchy in terms of which are the best unprocessed foods to eat to optimize potassium intake. This is due to the fact that different unprocessed foods have different densities of potassium content per unit volume. The authors comment:

“…the nutritional density…is generally lower in cereals and animal foods than in fruits and vegetables, with the exception of low-fat fishes…”

Another key aspect of this hierarchy is the fact that certain unprocessed foods such as animal products and cereals demonstrate a scenario where the potassium is connected to an acid-forming anion. In contrast, potassium in fruits and vegetables tends to be connected to an alkalizing anion:

“…the accompanying anions for K⁺ are chiefly phosphate and chloride in animal products and cereals, whereas in fruits and vegetables, they are largely represented by organic anions such as citrate, malate, and to a lesser extent, oxalate or tartrate…”

In turn:

“…the organic acidity of vegetables is more completely neutralized, giving them greater alkalizing potency…”

The next key point that Demigne et al (1) make about food sources of potassium is that, unlike sodium, calcium, and magnesium, water is a poor source:

“…in contrast to Na⁺, Ca²⁺, and Mg²⁺, most mineral waters are low in K⁺, and drinkable water is rarely a significant source of K⁺.”

However, other dietary liquids can be excellent sources of potassium:

“Other beverages such as fruit juices, coffee, and tea, or liquid foods such as soups provide substantial quantities of K⁺…”

How, specifically, does food processing and preparation affect potassium content? The authors state:

“…food processing often alters nutritional density; for example, highly refined wheat flour contains less than half of the K⁺ level of complete flour. Food processing such as boiling is probably a cause of K/organic salt losses, especially for vegetables because fruits are generally consumed uncooked. Steam cooking or brief frying are likely to maintain greater concentrations of K/malate or K/citrate than cooking procedures that lead to extensive leaching.”

Absorption of potassium

The next few quotes I would like to feature from the Demigne et al (1) paper address absorption of potassium. As you will see, unlike minerals such as
calcium and magnesium where optimal absorption is a concern, potassium is absorbed very efficiently:

“Potassium salts are intrinsically very soluble and the conditions prevailing in the upper part of the digestive tract afford the release of the major fraction of dietary K\(^+\) in the luminal water. The small intestine is the major site of K\(^+\) absorption (~90% of dietary K\(^+\)). Because K\(^+\) is present in salivary, gastric, biliary, and pancreatic secretions, actual K\(^+\) absorption is higher than intake/output calculations might suggest.”

Another reason potassium is so easily absorbed is that, unlike many nutrients that require active transport mechanisms to cross the intestinal lining into the systemic circulation, potassium crosses the intestinal barrier via passive diffusion:

“…it is generally accepted that the dominant force for K\(^+\) absorption is passive diffusion. Presumably, passive diffusion occurs via the leaky tight junction pathway in the small intestine.”

**Potassium metabolism**

The first quote I would like to feature from this section points out what most of you already know – only a small amount of potassium is present outside of the cellular environment:

“Extracellular K\(^+\) represents only ~2% of the total K\(^+\) body and this extracellular pool is of the same magnitude as K\(^+\) daily intake (70 mEq vs. 80-100 mEq/d).”

(One mEq of potassium equals 40 mg)

Which foods provide enough potassium to approximate the extracellular pool? The authors comment:

“Some commonly consumed meals may provide >50 mEq K\(^+\) if they contain high-K\(^+\) plant foods (potatoes, various vegetables, fruits.”

Given the high absorption rate of potassium and the high potassium content of certain foods, it would be logical to ask why we do not develop severe hyperkalemia after a high potassium meal. The reason is that the body is very adept at storing excessive dietary potassium:

“To match a massive K\(^+\) supply, several tissues have the capacity to transiently remove K\(^+\) from the extracellular fluid, i.e., the muscles, in particular, and to a lesser extent the liver.”

Before continuing, please note again, as I have pointed out in previous newsletters, the important role of muscle in maintaining optimal serum levels of potassium. Given that many of our chronically ill patients suffer from loss of muscle mass and function (sarcopenia), the ability to maintain optimal potassium metabolism may be compromised in these patients.

The next quote addresses what I mentioned above about potassium and carbohydrate metabolism, the important vastly under-appreciated relationship between potassium and insulin.

“Potassium uptake is also controlled by insulin, which circulates in portal blood at concentrations much higher than in peripheral blood.”

However, as noted by Demigne et al (1), muscle is much more important than insulin in maintaining optimal potassium status:

“…the highest capacity to keep pace with a rapid rise in K\(^+\) absorption is clearly located in muscles.”

The next quote discusses the relationship between insulin and muscle in maintaining optimal potassium status:

“…the transfer of K\(^+\) into the muscle intracellular compartment takes place against a considerable concentration gradient and depends on active transport mediated by the Na\(^+\)/K\(^+\)-ATPase. This process is stimulated by hormones such as insulin (postprandial period) or catecholamines (after exercise, for example).”

Could excessive insulin production (as seen with high refined carbohydrate diets) and excessive catecholamine production (as seen with high levels of chronic stress), lead to too much muscular uptake of potassium with a resultant state of hypokalemia? As pointed out in my potassium and sudden cardiac death series, a large body of research on refeeding syndrome and other disorders indicates that this is a definite possibility.

What about losses of potassium via the kidney? Generally, potassium is reabsorbed to a great extent:
“A large fraction of filtered K\(^+\) is reabsorbed along the proximal tubule and the loop of Henle.”

What promotes excretion of potassium versus reabsorption? The authors state:

“Factors promoting K\(^+\) secretion in the distal parts of the nephron include affluent K\(^+\) intake/aldosterone/tubular fluid flux, and alkalosis.”

More information on the relationship between potassium and acid/alkaline balance

The first quote I would like to feature in this section discusses the important role of potassium in neutralizing one of the main acid-forming metabolites in the body, sulfate, which is the end-product of sulfur amino acid metabolism:

“…K/organic salts that generate \(\text{KHCO}_3\) play an important role in neutralizing anions excreted in urine such as sulfate, an end-product of sulfur amino acid metabolism.”

Of course, as has been mentioned in previous newsletters, potassium is an excellent promotor of a neutral or slightly alkaline state:

“Potassium and organic anions, through \(\text{KHCO}_3\) generation or glutamine sparing, are very effective in neutralizing mineral acidity and favoring neutral or slightly alkaline urine pH.”

In turn, the alkalizing impact of potassium favors citrate excretion in the urine, which helps prevent calcium kidney stone formation:

“Alkalosis and K\(^+\) were also identified as major positive effectors of citrate excretion, with citrate considered to be a major crystallization inhibitor of calcium stone formation.”

The impact of potassium on other minerals

Over the years I have discussed in detail the relationship between potassium and magnesium. Certainly, as you might guess, Demigne et al (1) have much to say on this issue, which I will cover shortly. First, though, I would like to share the authors’ thoughts on the relationship between potassium and calcium. Concerning loss of calcium in the urine, conventional nutritional thinking suggests that the main focus should be on optimization of calcium absorption. According to Demigne et al (1), addressing potassium status will provide much better results than efforts to address calcium absorption:

“Factors affecting the amounts of Ca\(^{++}\) lost in urine, such as organic K\(^+\) salts, may be more effective than factors altering intestinal Ca\(^{++}\) absorption. Thus, Appel et al. observed a 30% decrease in urinary Ca\(^{++}\) excretion when fruit and vegetable intake increased from 3.6 to 9.5 daily servings.”

Of course, any discussion on calcium metabolism inevitably leads to thoughts of bone health. The next quote features an interesting comment on the relationship between osteoblastic/osteoclastic activity and acid/alkaline balance:

“Cell function, including that of osteoblasts, is normally impaired by acid; the stimulatory effect of acid on osteoclasts may represent a primitive ‘fail-safe’ that evolved with terrestrial vertebrates to correct systemic acidosis by ensuring release of alkaline bone mineral when the lungs and kidneys are unable to remove sufficient H\(^+\) equivalent.”

Thus, the authors suggest increased osteoclastic activity is not so much a cause of osteoporosis as much as it is an effort by the body to release alkalizing minerals from bone such as calcium to correct an acidic situation that cannot be addressed by corrective efforts by the lungs and kidneys alone.

Then, of course, a logical extension of this train of thought is that alkalizing factors will help maintain bone. The authors comment:

“From an epidemiologic point of view, Tucker et al. reported that dietary components such as K\(^+\) contributed to the maintenance of bone density, and New showed that fruit consumption was a predictor of greater bone density in postmenopausal women.”

On still another related manner, excess sodium intake is also a contributor to loss of bone mass. Could potassium have a positive impact on this issue?

“High salt intake is also a factor that can increase bone resorption in postmenopausal women, and high K\(^+\) intake ameliorates this adverse effect.”
Finally, as I suggested above, Demigne et al (1) do have some thoughts on the relationship between potassium and magnesium:

“Magnesium is frequently provided by high-K+ foods because both cations represent major intracellular cations in eukaryotes. Although Mg++ and K+ have distinct cellular roles they may be subject to similar disturbances such as cell leakage, for example, in the case of metabolic acidosis.”

More importantly from a clinical standpoint, the two nutrients tend to function in tandem where potassium requires optimal magnesium status to function at the highest level:

“…various metabolic effects of K+ are modulated and/or amplified by Mg++. This tight connection is illustrated in the study of Humphries et al., which focused on a possible protective role of dietary Mg++ in insulin resistance; their data also demonstrated a high degree of correlation of dietary K+ with insulin sensitivity. In fact, it was proposed that abnormalities in cellular ion homeostasis may be a major link between cardiovascular and metabolic diseases.”

**Potassium and glucose tolerance**

In the next section of their paper Demigne et al (1) continue their discussion on the relationship between potassium and insulin by addressing blood sugar metabolism:

“It is well established that cellular uptake of K+ is tightly dependent on insulin, and that hyperglycemia is a potent stimulator of K+ uptake in normal subjects, with enhanced involvement of passive transfer processes. Short-term K+ deprivation leads to a nearly complete insulin resistance for cellular K+ uptake, preceding changes in muscle Na+/K+-ATPase expression. Insulin’s actions on glucose uptake and K+ uptake is independently regulated by dietary fat and K+ content, respectively. Diabetes decreases the amount of Na+/K+-ATPase in skeletal muscles heart, and nerves and these changes may be important in the physiopathology of diabetes. K+ supplementation was shown to increase muscle Na+/K+-ATPase (improving extrarenal K+ homeostasis), and dietary K+ could therefore play a preventive role against diabetes as illustrated by a prospective epidemiologic study of 84,360 U.S. women over 6 y showing that high K+ intake was associated with a lower risk of developing type 2 diabetes.”

It is fairly well known that magnesium plays an important role in insulin metabolism, thus making optimal magnesium intake essential for diabetic patients. As noted by Demigne et al (1), what is less well known is that the inability of cellular pumps to efficiently bring potassium into the muscle cell may be a major pathophysiologic contributor to the creation of the diabetic state. Furthermore, potassium supplementation may be helpful in improving the ability of cellular pumps to bring potassium into the muscle cell, and, accordingly, positively affect diabetes incidence.

Demigne et al (1) conclude their paper by making dietary recommendations that would optimize potassium intake on a population basis:

“Ensuring a daily K+ supply of 2.5-3.5 g from fruits and vegetables (chiefly as citrate or malate) requires a daily intake of 0.6 – 0.8 kg, which is in line with the ‘5-10 servings per day’ recommendations. Achieving high daily intake of K+ would probably be beneficial, but this will require further efforts to achieve the following: 1) identification of the most effective sources of K+ in the diet; 2) optimizing food processing (especially for vegetables); 3) limiting the intake of empty calories; and 4) containing the cost of fruits and vegetables (a current WHO priority), major sources of K/organic anions.”

**POTASSIUM SUPPLEMENTATION AND BONE HEALTH**

As was noted above by Demigne et al (1), maintenance of optimal bone health can be greatly assisted through minimizing an acidic metabolism via optimal potassium intake. I would now like to examine this important relationship in more depth by highlighting some quotes from the paper “The effect of supplementation with alkaline potassium salts on bone metabolism: a meta-analysis” by Lambert et al (2). The first quote I would like to feature emphasizes the point made above that acidosis has a major detrimental impact on bone health:
“Severe acute and chronic metabolic acidosis have well-established physiological effects on bone, which provides a large reserve of alkaline calcium salts. These are released in response to the increased acid load. Whilst bicarbonate and other anions buffer the increased circulating H\(^+\), the excess calcium and other cations released are excreted in the urine. In vitro and in disease states with severe metabolic acidosis, the rise in extracellular acid concentrations promotes an increase in osteoclastic activity and a decrease in osteoblast activity.”

With the above in mind, the authors hypothesized the following:

“We hypothesized that supplementary potassium bicarbonate (KHCO\(_3\)) and potassium citrate (KCitr) would decrease urinary excretion of calcium and net acid excretion (NAE), as well as reducing bone turnover as observed by a decrease in urine and serum markers of bone formation and resorption.”

After reviewing 14 studies, the authors concluded the following:

“The results strongly favour evidence for a reduction in bone resorption following supplementation with KHCO\(_3\) or KCitr, as well as a reduction in calcium and net acid excretion, in support of our hypothesis.”

Furthermore:

“Moreover, our analysis also provides evidence for an inhibition of skeletal degradation with supplementation, with the majority of studies that measured bone turnover markers showing a decrease in bone resorption. In particular, we showed a significant overall reduction in NTX excretion with both KHCO\(_3\) and KCitr, with very low heterogeneity among these studies. Thus, there is clearly an effect of potassium or bicarbonate/citrate on osteoclastic activity.”

With the above in mind, the Lambert et al (2) conclude the following:

“In the present analysis, we show that, overall, administration of alkaline potassium salts, whether in the short- or long-term, leads to significant reduction in renal calcium excretion and acid excretion, compatible with the concept of increased buffering or neutralization of hydrogen ions by raised circulating bicarbonate. That this neutralization of dietary acid load has beneficial effects on bone is demonstrated by the reduction in bone resorption that this analysis confirms.”

Based on the above conclusions, what clinical recommendations can be made? The authors suggest the following:

“Thus, the effect of alkaline potassium salts on calcium, acid-base and bone metabolism that has been demonstrated in this meta-analysis has the potential to translate into preventative measures for osteoporosis. In particular, dietary measures which include increasing intakes of fruit and vegetables, and thus alkaline precursors, should be considered as valuable contributors to bone health.”

MORE INFORMATION ON POTASSIUM SUPPLEMENTATION AND ACIDOSIS AND MUSCLE HEALTH

As you have seen, much of this series has been devoted to the important and under-appreciated relationship between potassium status, optimal pH, and optimal muscle mass and function. I would now like review a study that considers this relationship from the standpoint of the excretion of a key constituent of muscle, nitrogen (N). In “Increasing alkali supplementation decreases urinary nitrogen excretion when adjusted for same day nitrogen intake” by Ceglia and Dawson-Hughes (3) 232 elderly patients (average age – approximately 67 years) were divided into three groups. 79 received a low dose potassium bicarbonate supplement, 74 received a high dose potassium bicarbonate supplement, and 79 received a placebo. The duration of supplementation was 84 days for all groups. The goal of the study was to see the impact of different doses of potassium bicarbonate supplementation on muscle mass via changes in nitrogen excretion. Ceglia and Dawson-Hughes (3) begin their paper by discussing the relationship between acidosis, muscle catabolism and loss of nitrogen in the urine:
“Chronic metabolic acidosis increases muscle catabolism and causes increased excretion of nitrogen (N) in the urine.”

The next quote I would like to feature points out that the loss of muscle mass with acidosis is not a disease per se but a response: to use muscle to correct the acidic condition:

“This muscle response is purported to mitigate acidosis by releasing amino acids like glutamine which provide ammonia which will facilitate renal acid excretion as ammonium ions.”

What was the reason for using potassium bicarbonate in this study? The authors note:

“A surrogate for alkalinogenic foods is an alkaline salt supplement such as potassium bicarbonate (KHCO₃).”

What were the results of the study? As you will see, potassium bicarbonate supplementation both reduced the acidotic state and reduced urinary N excretion:

“In this experimental intervention of generally healthy older men and postmenopausal women, we found that escalating doses of KHCO₃ supplementation to lower the dietary acid load led to a decline in urinary N excretion when expressed as a ratio to concomitant N intake.”

Of the two dosage levels, which was the most effective?

“In this study, we observed that the N sparing effect of KHCO₃ supplementation was more pronounced in the higher dose group than the lower dose group.”

**POTASSIUM BICARBONATE OR POTASSIUM CHLORIDE SUPPLEMENTATION: WHICH IS BETTER?**

The last study I would like to discuss in this newsletter is an older study that I initially reviewed four years ago. However, I still wanted to include it in this discussion on potassium supplementation because it addresses an important clinical controversy often encountered by both patients and practitioners: Which is the best form of potassium supplementation? Is it the most common and least expensive form that is almost universally recommended by virtually all medical doctors and nutritional practitioners for patients in need of potassium supplementation – potassium chloride? Or is it the much less common, slightly more expensive form – potassium bicarbonate? To answer these questions, I would like to reprint a portion of my August 2015 newsletter that reviewed the study “Comparative effects of potassium chloride and bicarbonate on thiazide-induced reduction in urinary calcium excretion” by Frassetto et al (4). Interestingly, this study is even more clinically relevant now than when I initially discussed it because so many of our middle-aged and older patients are now ingesting thiazide diuretics.

Below you will find my discussion on this study initially published four years ago:

One of the most important clinical decisions we must make almost every day is one that is rarely addressed in published research. What is the best form of a supplement for any given clinical situation? In the case of potassium, potassium chloride is the predominant form found in the marketplace. Is it the best for the needs of our patients? The paper “Comparative effects of potassium chloride and bicarbonate on thiazide-induced reduction in urinary calcium excretion” by Frassetto et al (4) answers this question in relation to a common scenario seen in many of our patients – loss of calcium in the urine.

In this paper 31 healthy men and women aged 50 or greater were evaluated for four weeks. The parameters of the study are as follows:

“After a baseline period of 10 days with three 24-hour urine and arterialized blood collections, subjects were randomized to receive either hydrochlorothiazide (HCTZ) 50 mg plus potassium (60 mmol daily) as either the chloride or bicarbonate salt. Another 19 women received potassium bicarbonate (60 mmol) alone. After two weeks, triplicate collections of 24-hour urines and arterialized bloods were repeated.”

(60 mmol of potassium equals 2400 mg)

What were the results of the study? As has been noted by several researchers, thiazide diuretics do reduce urinary calcium losses. By adding potassium supplementation to the diuretic, though,
the positive impact on urinary calcium was increased:

“Urinary calcium excretion decreased significantly in response to the administration of HCTZ in combination with either KHCO$_3$ or KCl and in response to the administration of KHCO$_3$ alone. Previous studies have shown that in normal, healthy people, thiazides decrease urine calcium excretion and that potassium alkali salts also decrease urine calcium excretion. Urine calcium excretion therefore decreased as expected in the KHCO$_3$ group and in both HCTZ groups. With respect to reducing urine calcium HCTZ + KHCO$_3$ should have been at least as effective as KHCO$_3$ treatment alone. In fact, the effects of the two treatments were additive so that treatment with HCTZ and KHCO$_3$ combined doubled the decrement in urinary calcium observed with either KHCO$_3$ treatment alone or that observed during combined treatment with HCTZ and KCl.”

How did potassium bicarbonate and potassium chloride compare in terms of reducing urinary calcium? As you will see in the concluding paragraph in the paper, potassium bicarbonate was clearly superior. Furthermore, potassium bicarbonate was superior in terms of reduction of acidity:

“In summary, in the present study, KHCO$_3$ was superior to KCl as an adjunct to HCTZ, not only inducing a twofold greater reduction in urine calcium excretion, but also completely neutralizing endogenous acid production and therefore correcting the pre-existing mild metabolic acidosis that normally accompanies ingestion of an acid-producing diet in older people. Accordingly, for stone disease and osteoporosis treatment and prevention, the combination of HCTZ + KHCO$_3$ may be preferable to that of HCTZ + KCl.”

Of all the important points made in the above study, one, for me, stands out. Due to the presence of the chloride portion of the molecule, potassium chloride, the most common form of potassium supplementation in this country, both in terms of what is found in most online and storefront retailers and what is recommended by many if not most health care practitioners, will not help correct the low-grade metabolic acidosis seen in so many of our patients. In fact, it will actually exacerbate the acidic state because most of our patients are already ingesting excessive amounts of chloride in the form of NaCl. Therefore, as I have tried to make clear in this newsletter and this whole series on metabolic acidosis and potassium, alkalizing potassium supplements such as potassium bicarbonate and potassium citrate are best. It is my hope that you will make every effort to educate patients and the public in general who tend to think all potassium supplements are the same so buy the cheapest.

In the next installment of this series I will discuss the fascinating, under appreciated body of research that considers a subject I touched upon only briefly in this newsletter, the relationship between metabolic acidosis and insulin metabolism.

REFERENCES