

Low-grade chronic metabolic acidosis:

How an acid promoting diet and lifestyle contributes to poor quality of life in chronic illness

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www.thealkalinediet.org

The Alkaline Diet Will Transform Your Health Forever...



The thing is most of the people have been eating the **wrong** way. The 'balanced' diet that taught us about the food pyramids, balanced meal and healthy food, are the culprits in making us obese, disease, and ill. And this is because the balanced diet that contains all the meat, dairy, vegetables, grains and fruits is an acidic meal.

Being acidic means that our body's pH level is less than optimal (**optimal pH level is around 7.35-7.45, slightly alkaline**). When our blood level is acidic, our cells and immune system would not be able to rebuild its tissues efficiently. And when this acidic condition persists for a long time, it would lead to many diseases like stroke, high blood pressure, obesity, heart disease and many other common diseases.

To restore our health and body, we would need to focus on our diet to balance the pH level. And to do that, an alkaline diet can help you achieve a healthy pH level, rebuild your cells and your tissues, and eventually leading to a healthy body.

These Alkaline Supplements Can Dramatically Improve your Health

Why would you need alkaline supplements? If your body pH is too acidic, and you're finding it difficult to eat all the right foods necessary to turn it around.

Or you want to balance your pH as quickly as possible so you can start feeling better sooner.



These products below were spe quickly and naturally.

This particular brand, pHion, is by far my favorite. I've used their products for years and have always been impressed by their quality.

pHion is the category leader when it pertains to pH balancing of the body. Their products range from pH Testing Devices, Alkaline Water Supplements, Green Drinks to Pre-Package Programs designed to create and maintain optimal health and wellness.

pHion products are backed by a "no questions asked" 30 day guarantee and supported by second to none educational content on how to best maximize results.

There are a lot of supplements listed here - so if you're not sure which ones to choose, check out pHion's alkalizing program kits.

These kits give maximum results at a substantial savings.

Feel free to contact me with questions regarding any of these alkaline supplements

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Causes of low grade chronic metabolic acidosis in chronic illness

- Dietary imbalance of acidifying and alkalinizing foods and electrolytes such as sodium, chloride, potassium, and magnesium.
- ***Metabolic imbalances seen with chronic illness***

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- Resolving low grade chronic metabolic acidosis in chronically ill patients involves the following:
 - Optimizing dietary intake of acidifying and alkalizing foods
 - Optimizing dietary intake of fluid and key electrolytes
 - ***Optimizing key metabolic imbalances seen with chronic illness***

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Key metabolic imbalances seen with chronic illness that contribute to an acidotic state

- Loss of lean body mass (sarcopenia)
- Insulin resistance
- Increased innate immunity and decreased adaptive immunity (Inflamm-aging)
- Suboptimal caloric intake and carbohydrate:protein ratio (Refeeding syndrome)
- Gastrointestinal dysfunction
- Deficiency of key nutrients such as vitamin D, zinc, selenium, and sleep

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Summer of Work Exposes Medical Students to System's Ills - NYTimes.com Page 1 of 3

The New York Times

September 9, 2009

Summer of Work Exposes Medical Students to System's Ills

By KEVIN BAKER

SEATTLE — This summer, medical students from the University of Washington took a long look under the hood of the health care system they are about to inherit, and many returned to campus last week with their eyes wide open and their idealism tempered.

Jacob R. more m...
enched...
Olgard...
treatme...

Summer of work exposes medical students to system's ills, *The New York Times*, September 9, 2009

The students learned not only to deliver babies and suture wounds, but also to order unnecessary tests as protection against lawsuits, to hector specialists into seeing Medicaid patients, to match patients with prescriptions on Wal-Mart's \$4 list. And they saw firsthand what Mr. Olgard called "a tidal wave of chronic disease" — diabetes, hypertension, obesity, depression — that left many questioning how much any one physician could really accomplish.

"I often wondered what we were actually doing to help people," Mr. Olgard said.

Not sur...
evaluat...

"...a tidal wave of chronic illness..."

"You ha...
reimbur...
treatme... they can avoid early mortal or waning until there's a catastrophic surgery, it's pretty simple.

For 10 years, the University of Washington School of Medicine has dispatched its rising second-year students across the Northwest to provide primary care in rural or underserved areas. The monthlong program is elective, but a record number of students took part this year — 117 from a class of 245.

The school has a cooperative agreement to train medical students from Alaska, Idaho, Montana and Wyoming, none of which has a medical college of its own. The summer program is one of several vehicles, along with loan forgiveness enticements, designed to lure students back to their home states to practice in areas with a shortage of primary care givers.

This year, the students set out as negotiations were intensifying in Washington over wholesale changes to the health care system they will soon be joining. Whether there will be improvements to the system remains to be seen, but few students returned thinking there was little to fix.

http://www.nytimes.com/2009/09/09/health/policy/09medschool.html?_r=1&th=&mc=th&... 9/9/2009

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Oxford Journals Life Sciences & Medicine The Journals of Gerontology: Series B Volume 66B, Issue 1, pp. 75-86

LIFESTYLE CALL FOR ABSTRACTS DUE MARCH 15, 2011

Mortality and Morbidity Trends: Is There Compression of Morbidity?

Eileen M. Crimmins and Hiram Beltrán-Sánchez
• Author Affiliations

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Received July 28, 2010.
Accepted October 25, 2010.

Abstract

Objective: This paper reviews trends in mortality and morbidity to evaluate whether there has been a compression of morbidity.

Keywords: Compression of morbidity, mortality trends, morbidity trends

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Crimmins EM & Beltran-Sanchez H. Mortality and morbidity trends: Is there compression of morbidity? *The Journals of Gerontology: Series B*, Vol. 66B, No. 1, pp. 75-86, 2010

"Empirical findings do not support recent compression of morbidity when morbidity is defined as major disease and mobility functioning loss."

75-86

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**Nestlé Nutrition Workshop Series
Clinical & Performance Program, Vol. 8**

Nutrition and Critical Care

**Luc Cynober
Frederick A. Moore**




Baracos VE. Overview on metabolic adaptation to stress, pp. 1-13.

“An understanding of the nature of stress is fundamental to the rational design of nutrient mixtures to feed patients whose homeostasis has been altered by one or more stressors.”

“All stresses may be presumed to be associated with characteristic modifications in the metabolism of lipids, carbohydrates, amino acids, and micronutrients.”

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Clinical Nutrition (2004) 23, 1256-1266



REVIEW

Acute and “chronic” phase reaction—a mother of disease

Stig Bengmark

Department of Surgery and Liver Institute, UCL, London, UK

Received 23 July 2004

KEYWORDS

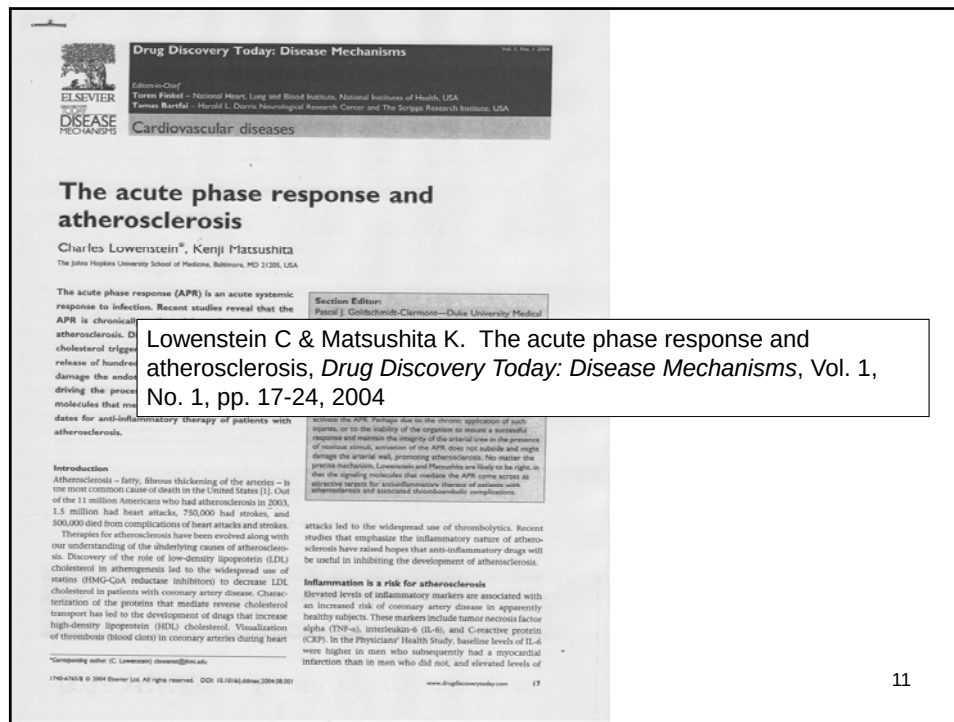
Acute phase response;
Chronic phase response;
Metabolic syndrome;
Cellular membranes;
Endothelial cells;
Abdominal obesity;
Insulin resistance;
Growth hormones;
Free fatty acids;
Alzheimer disease;
Parkinson disease;
Neurodegenerative disease;
Atherosclerosis;
Coronary-vascular disease;
Cancer;
Breast cancer;
Colorectal cancer;
Prostatic cancer;
Diabetes;
Crimson;
Fatty liver;
Gallbladder disease;
Chronic renal disease;

Summary The world is in diseases. Almost half of the mortality is due to these chronic diseases. And they are these diseases are associated consumption of calorie and also under-consumption of a function of the innate immune changes induced in response the subsequent development chronic diseases. The endo importance, and the function of the underlying cells; their ability to obtain nutrients and antioxidants and to eliminate waste products. The abdominal adipocytes seem to play a key role, as they have the ability to in stressful situations release much of proinflammatory cytokines, PGE-1 and free fatty acids compared to elsewhere in the body. The load on the liver of these various substances in often of greater magnitude than the liver can handle. Some of the most common chronic diseases and their potential association with acute and “chronic” phase responses and metabolic syndrome are discussed separately. The need for studies with lifestyle modifications is especially emphasized.

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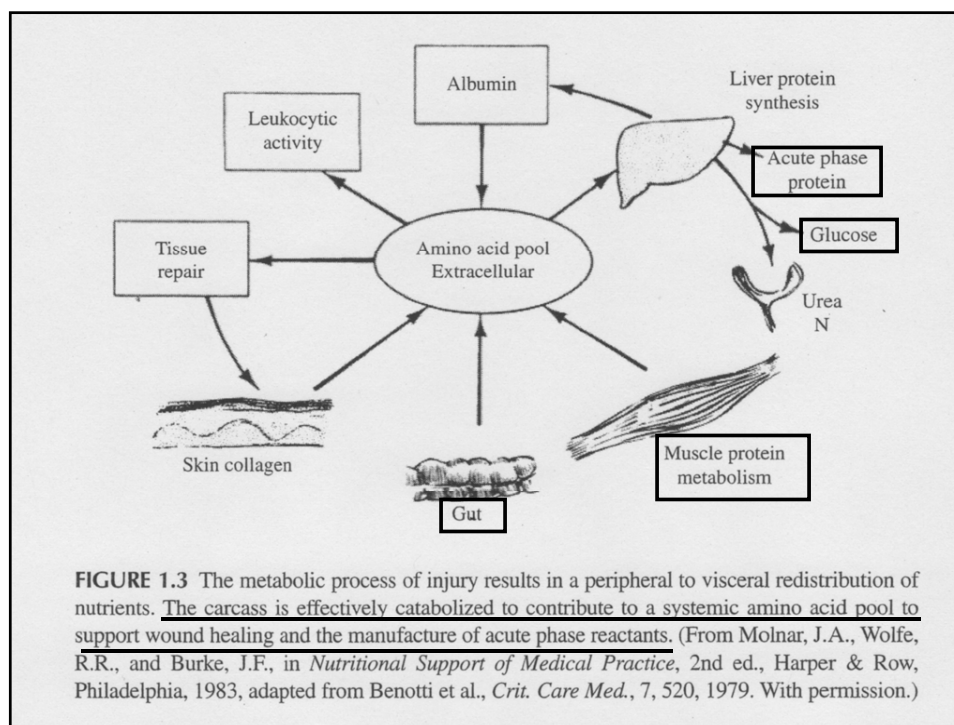
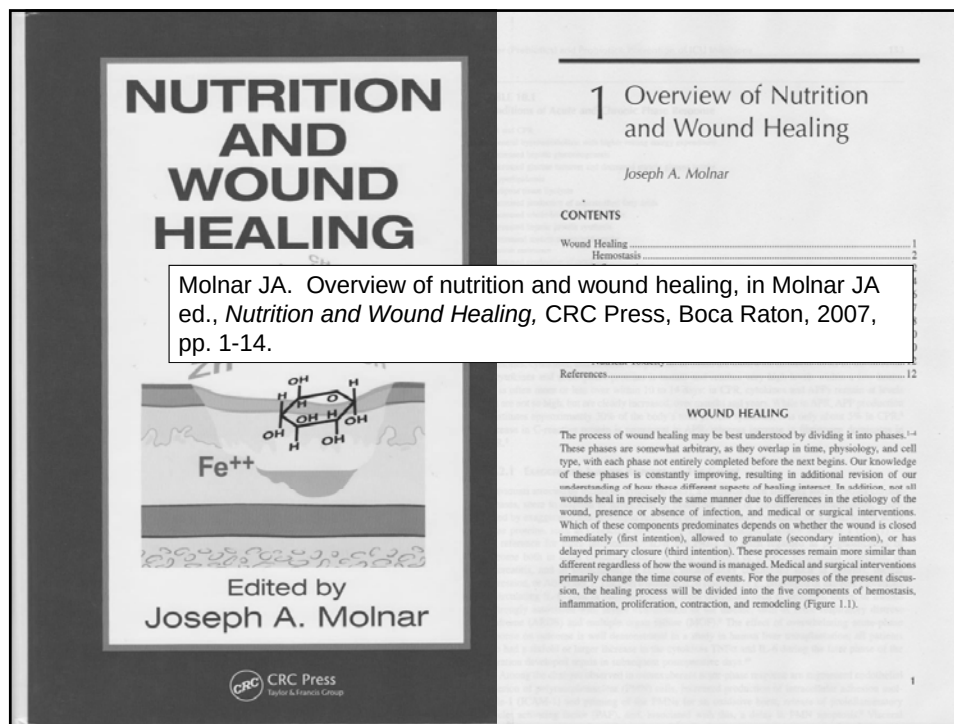
Bengmark S. Acute and “chronic” phase reaction – a mother of disease, *Clin Nutr*, Vol. 23, pp. 1256-66, 2004

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Key metabolic imbalances seen with the acute phase response

- Metabolic acidosis
- Loss of lean body mass (sarcopenia, GI mucosal atrophy)
- Insulin resistance
- Inflamm-aging (Increased innate immunity and decreased adaptive immunity)
- Suboptimal caloric intake and carbohydrate:protein ratio (Refeeding syndrome)
- Gastrointestinal dysfunction
- Deficiencies of key micronutrients such as zinc, selenium, and vitamin D



NEURO-SIGNALS

Invited Review

Neurosignals 2009;17:144-152
DOI: 10.1159/00018682

Received: April 26, 2009
Accepted after revision: June 5, 2009
Published online: February 4, 2009

Biological Mechanism of Antidepressant Effect of Omega-3 Fatty Acids: How Does Fish Oil Act as a 'Mind-Body Interface'?

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Key Words
Major depressive disorder · Depression · Docosahexaenoic acid · Arachidonic acid · Prostaglandins · Thromboxanes · Leukotrienes · Cyclo-oxygenase

Abstract
The unsatisfactory results of monoamine-based antidepressant therapy and the high occurrence of somatic symptoms and physical illness in patients with depression imply that the serotonin hypothesis is insufficient to approach the aetiology of depression. Depressive disorders with somatic presentation are the most common form of depression. Somatization, the bodily symptoms without organic explanation, is similar to cytokine-induced sickness behaviour. Based on recent evidence, omega-3 polyunsaturated fatty acids (n-3 PUFAs, or n-3 fatty acids) are enlightening a promising path to discover the unsolved of depression, sickness behaviour and to link the connection of mind and body. The PUFAs are classified into n-3 (or omega-3) and n-6 (or omega-6) groups. Docosahexaenoic acid and arachidonic acid, the major bioactive components of n-3 PUFAs, are not efficiently synthesized in humans and should therefore be obtained directly from the diet, particularly by consuming fish. Docosahexaenoic acid deficiency is associated with dysfunctions of neuronal membrane stability and transmission

prostaglandin E₂ synthesis, which might be linked to the somatic manifestations and physical comorbidity in depression. The role of n-3 PUFAs in immunity and mood function supports the promising hypothesis of psychoneuroimmunology of depression and provides an excellent interface between 'mind' and 'body'. This review is to provide an overview of the evidence about the role of n-3 PUFAs in depression and its common comorbid physical conditions and to propose mechanisms by which they may modulate molecular and cellular functions.

Introduction
Major depressive disorder (MDD) is a serious psychiatric illness with a high lifetime prevalence rate [1]. However, the current treatment for this high burden disease is not satisfactory. Less than 50% of patients achieve full remission with optimized medication treatment [2] despite that more than 40 antidepressants with mechanisms related to serotonin, noradrenaline and/or dopamine

Su KP. Biological mechanism of antidepressant effect of omega-3 fatty acids: How does fish oil act as a 'mind-body interface'? *Neurosignals*, Vol. 17, pp. 144-152, 2009

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Table 1. Overlapping of symptoms of acute sickness behaviour associated with IFN- α therapy and the somatic symptoms in MDD

Symptoms	Prevalence in IFN- α therapy ^a , %	Prevalence in MDD ^b , %
Fatigue/asthenia	39–90	73
Headache	27–67	33 ^c
Gastrointestinal symptoms	50 ^{c, 1}	34–47 ^f
Psychomotor slowing	40 ^c	59–65 ^f
Insomnia	20–39 ^d	63
Irritability	35 ^d	50
Arthralgia	9–36	31 ^e
Musculoskeletal pain	26–32	62–80 ^{g, 2}
Abdominal pain	15–20	21 ^e
Anorexia	13–19	40
Anxiety	13–18 ^d	57
Poor concentration	14 ^d	51

^a [46], unless otherwise specified; ^b [99], unless otherwise specified; ^c [100]; ^d [101]; ^e [102]; ^f [103]; ^g [104].

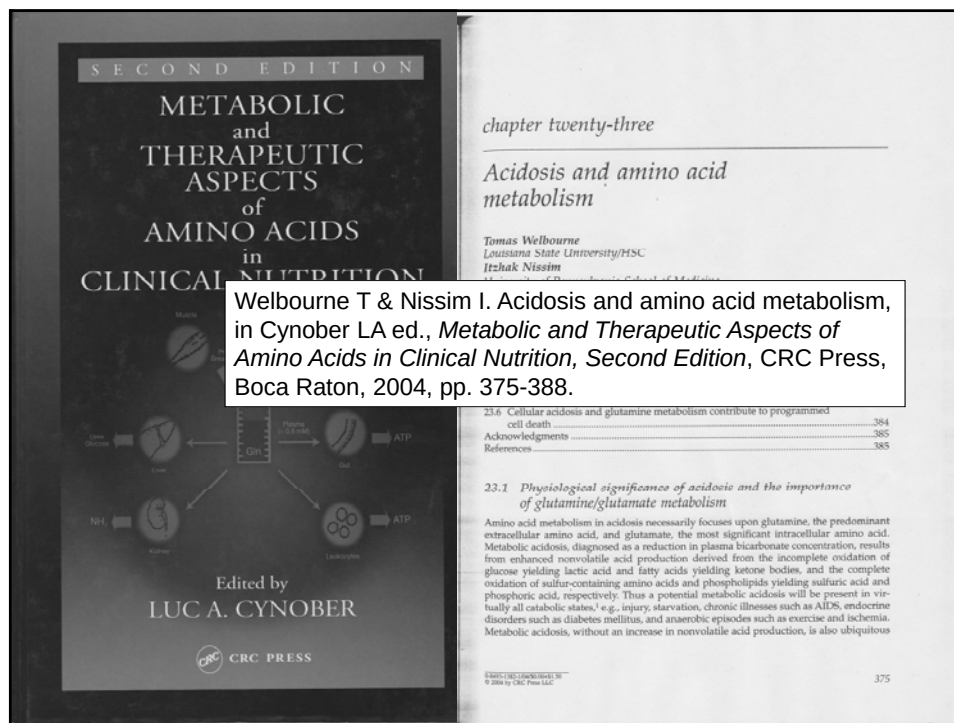
¹ Nausea, vomiting, bowel problems.

² Result from depressed inpatient population.

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Why does chronic illness lead to acidosis?

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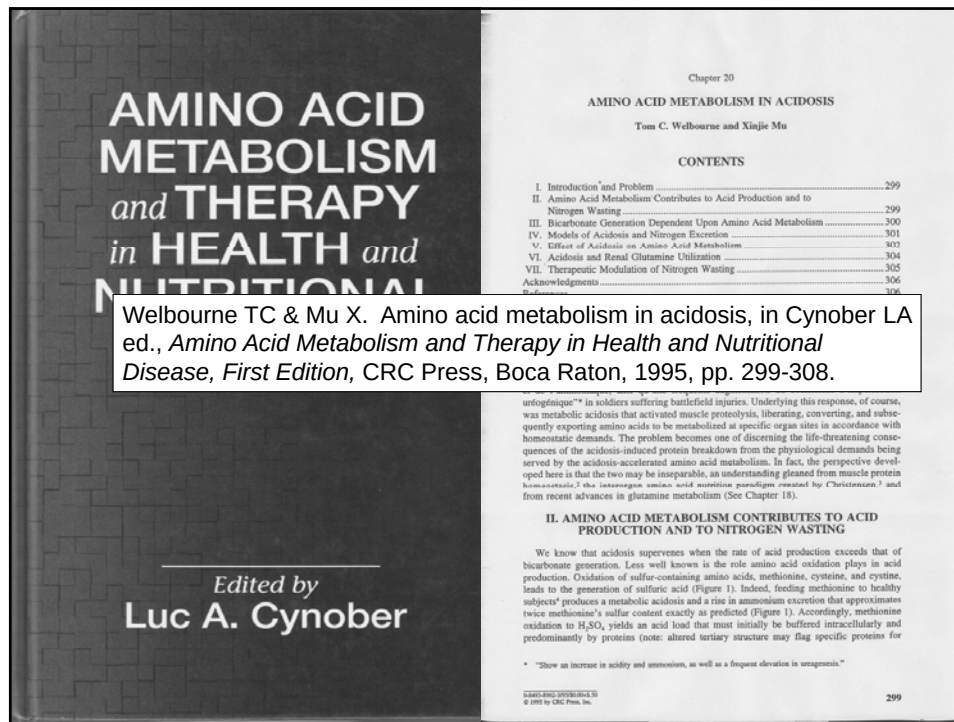


- “Metabolic acidosis, diagnosed as a reduction in plasma bicarbonate concentration, results from enhanced nonvolatile acid production derived from the incomplete oxidation of glucose yielding lactic acid and fatty acids yielding ketone bodies, and the complete oxidation of sulfur-containing amino acids and phospholipids yielding sulfuric acid and phosphoric acid, respectively.”

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- ***“Thus a potential metabolic acidosis will be present in virtually all catabolic states, e.g., injury, starvation, chronic illnesses such as AIDS, endocrine disorders such as diabetes mellitus, and anaerobic episodes such as exercise and ischemia.”***
- “Metabolic acidosis, without an increase in nonvolatile acid production, is also ubiquitous in the aged population, apparently reflecting diminished renal acid secretion and a reduced bicarbonate threshold.”

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- "...acid production increases following glucocorticoid doses mimicking the catabolic state, resulting in a metabolic acidosis..."
- "Importantly, the sources of this acidosis were accelerated keto and sulfuric acid production, not unlike what is observed in catabolic illnesses."

***The key to resolution of acidosis
in many if not most chronically ill
patients is optimizing dietary
acid/alkaline balance, optimizing
intake of fluid and key
electrolytes***

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Plus...

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Key metabolic imbalances seen with chronic illness that contribute to an acidotic state

- Loss of lean body mass (sarcopenia)
- Insulin resistance
- Increased innate immunity and decreased adaptive immunity (Inflamm-aging)
- Suboptimal caloric intake and carbohydrate:protein ratio (Refeeding syndrome)
- Gastrointestinal dysfunction
- Deficiency of key nutrients such as vitamin D, zinc, selenium, and sleep

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How, specifically, does low-grade chronic metabolic acidosis and other key metabolic imbalances create catabolic physiology?

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TRANSACTIONS OF THE AMERICAN CLINICAL AND CLIMATOLOGICAL ASSOCIATION, VOL. 111, 2000

MECHANISMS ACCELERATING MUSCLE ATROPHY IN CATABOLIC DISEASES

WILLIAM E. MITCH
ATLANTA, GEORGIA

INTRODUCTION

Loss of lean body mass, predominantly muscle, is a serious complication for patients afflicted with virtually any disease because protein malnutrition in hospitalized patients is associated with excessive morbidity and mortality (1). The potential causes of protein malnutrition include an inadequate diet but the mechanism(s) leading to loss of muscle mass in such patients is not so simple since feeding more

Mitch WE. Mechanisms accelerating muscle atrophy in catabolic diseases, *Transactions of the American Clinical and Climatological Assoc*, Vol. 111, pp. 258-270, 2000

protein stores (Figure 1). In fact, the major cause of the decline in muscle mass that occurs in catabolic illnesses is an acceleration of protein degradation. Recent discoveries using animal models of catabolic illnesses have provided insights into the mechanisms stimulating muscle protein degradation: in all the conditions studied to date, common mechanisms when muscles atrophy (3).

PHYSIOLOGIC IMPORTANCE OF PROTEIN DEGRADATION

The information depicted in Figure 1 shows that the rates of protein degradation must be highly regulated to match changes in the rates of protein synthesis precisely in widely varied proteins (in terms of half-lives) in order to maintain protein balance. In some ways, the daily loss of so much protein in processes of protein degradation seems counterproductive but in fact, the continual destruction of cellular proteins serves several important homeostatic

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Supported in part by NIH R01 DK67171 and R01 DK64097.

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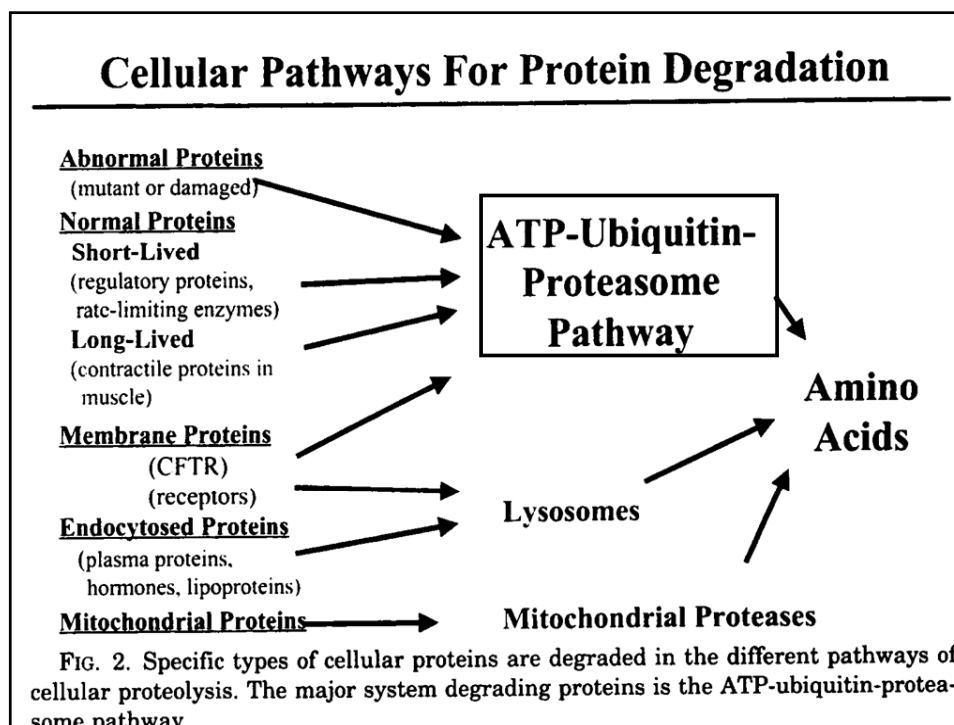
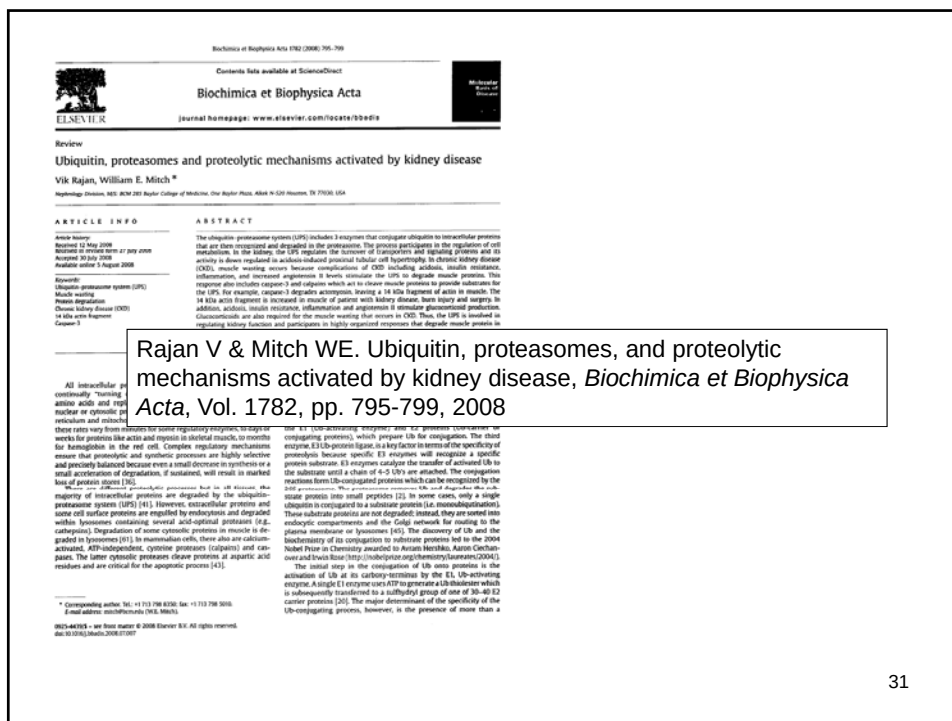


TABLE 1 <i>Muscle Protein Turnover and the ATP-Ubiquitin-Proteasome Pathway</i>	
Experimental Model	Human Disease
fasting	eating disorders
metabolic acidosis	renal tubular defects, diabetes
kidney failure	acute and chronic uremia
muscle denervation	neuromuscular disease, immobilization
thermal injury	burns
endotoxins	sepsis, AIDS
tumor implantation	cancer cachexia
glucocorticoids	Cushing's Disease
thyroid hormone	Graves' Disease
insulinopenia	diabetes
Studies of experimental models of human diseases reveal that loss of muscle mass involves a common pathway, the ubiquitin-proteasome system. In all of these models, there is evidence of increased degradation of muscle proteins in the ubiquitin-proteasome pathway and increased levels of mRNAs encoding components of the pathway.	

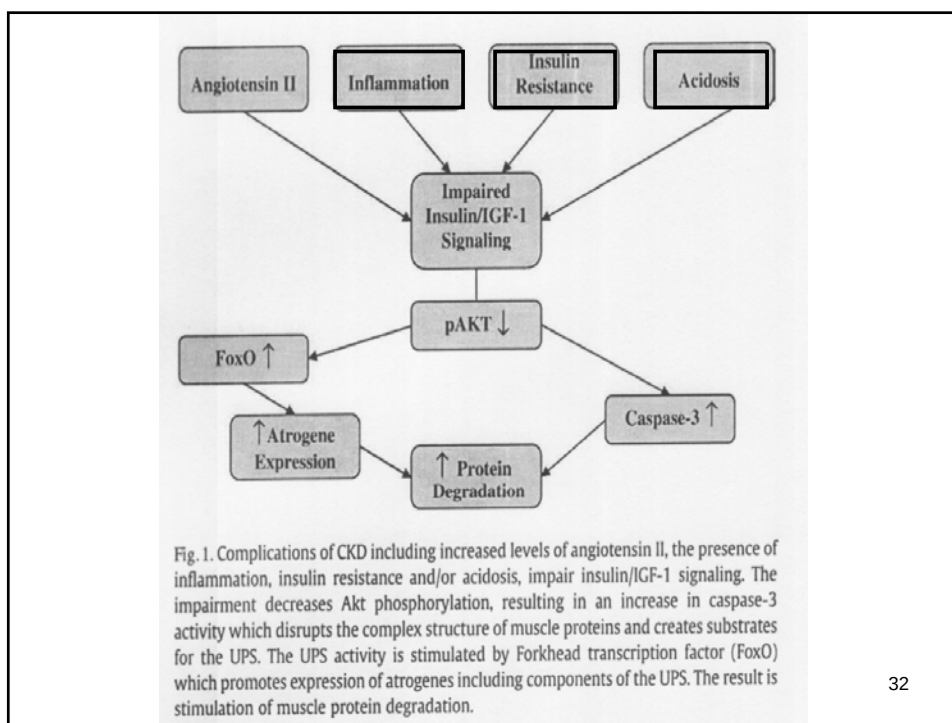
“Signals that could activate muscle protein degradation by this system...include metabolic acidosis, impaired response to insulin and high circulating levels of cytokines. The activation mechanism also involves glucocorticoids.”

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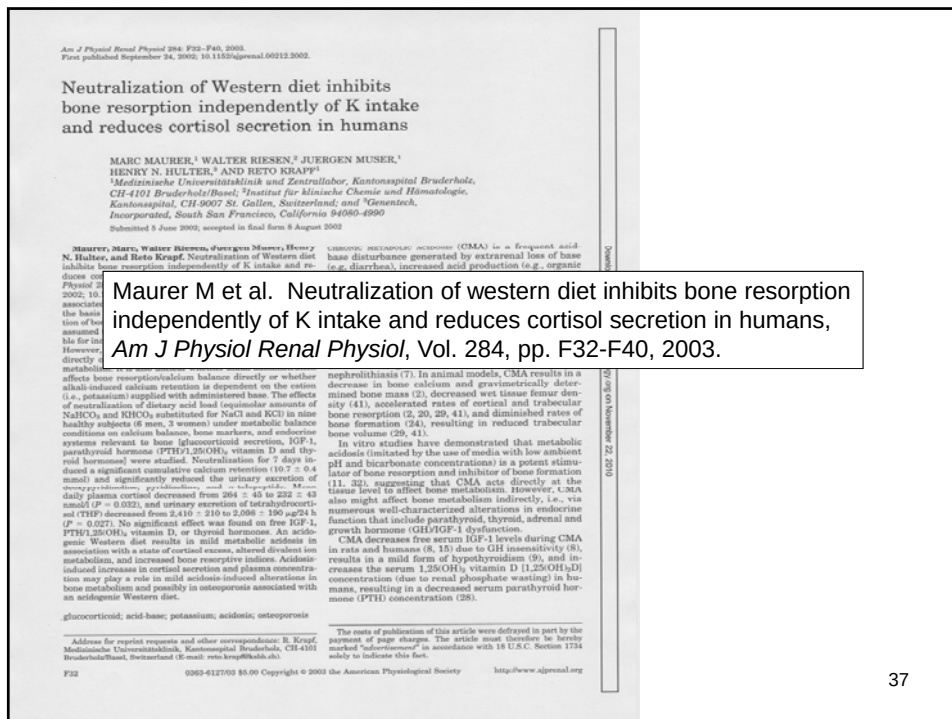
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Table 2 Metabolic acidosis in otherwise normal humans changed hormonal levels or responses to hormones	
Hormone	Acidosis-induced response
Growth hormone (GH) [80–84]	Suppressed GH secretion Lower IGF-1 response
Insulin [44, 85, 86]	Suppressed insulin-stimulated glucose metabolism
Insulin-like growth factor (IGF)-1 [81, 84, 87]	Decreased IGF-1 in plasma, and kidney and liver (but not in muscle)
Thyroid hormone [82, 88]	Decreased plasma T ₃ and T ₄ levels plus a higher plasma thyroid-stimulating hormone
Glucocorticoids [89]	Increased glucocorticoid production
Parathyroid hormone (PTH) [90, 91]	Decreased sensitivity of PTH secretion to changes in plasma calcium
Vitamin D [91]	Suppressed activation to 1,25 (OH) ₂ cholecalciferol

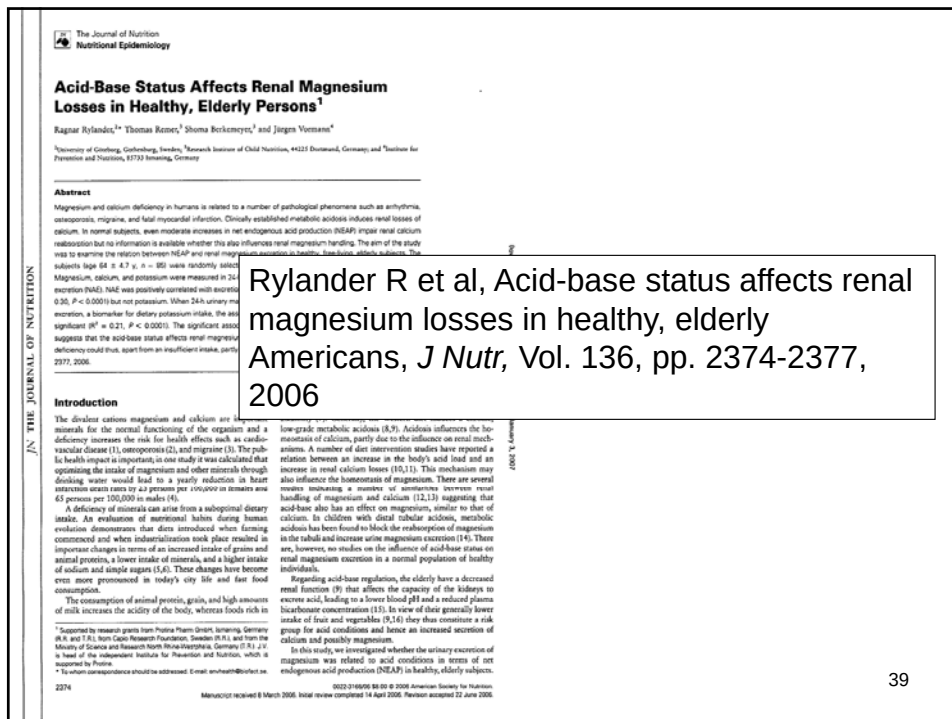
How diets high in acid-forming foods and low in key electrolytes such as potassium and magnesium contribute to low-grade chronic metabolic acidosis

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- “Although still within the broad range of normal values, plasma bicarbonate concentration decreases progressively when endogenous acid production is increased by menu changes among normal foodstuffs in normal subjects.”
- “...a very mild Western diet-induced CMA (a degree of acidosis that would not be recognized by applying diagnostic acid-base criteria found in textbooks) results in a state of increased cortisol secretion and plasma concentration...”



- “The consumption of animal protein, grain, and high amounts of milk increases the acidity of the body, whereas foods rich in minerals such as green vegetables and fruit increase the alkalinity.”
- “Generally, the western diet induces a chronic, low-grade metabolic acidosis.”
- “Acidosis influences the homeostasis of calcium, partly due to the influence on renal mechanisms.”

- “A number of diet intervention studies have reported a relation between an increase in the body’s acid load and an increase in renal calcium losses.”
- “This mechanism may also influence the homeostasis of magnesium.”
- “There are several studies indicating a number of similarities between renal handling of magnesium and calcium suggesting that acid-base also has an effect on magnesium, similar to that of calcium.”

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- “Regarding acid-base regulation, the elderly have a decreased renal function that affects the capacity of the kidneys to excrete acid, leading to a lower blood pH and a reduced plasma bicarbonate concentration.”

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- “The results demonstrated a close relation between net acid excretion as an indicator of net endogenous acid production and the excretion of both magnesium and calcium.”
- “It is known, however, that the amount of urinary calcium is not related to dietary calcium. Furthermore, magnesuria is only weakly associated with dietary magnesium.”

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Potassium and acid/alkaline balance

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Recent Advances in Nutritional Sciences

Protective Effects of High Dietary Potassium: Nutritional and Metabolic Aspects^{1,2}

Christian Demigne,¹ Houssé Sabatou, Christian Rémy, and Pierre Menetier¹

Metabolic Diseases and Micronutrients Unit, INRA Team/CNRS Clermont-Ferrand, 63122 St-Genès-Chantagnelle, France and ¹Public Health and Computing Department, School of Medicine (Bioscience)

except in subjects suffering terminal renal deficiencies or severe diabetes (1). Before the emergence of agriculture and later of agroindustry, humans consumed a diet high in K⁺ (>200 mmol/d) and generally low in Na⁺. The recent increase in the consumption of processed foods, together with a reduction in fruit and vegetable consumption, has dramatically depressed K⁺ intake, in some cases falling below 50 mmol/d, in the presence of a large Na⁺ excess (1-3).

It is now well established that a high K⁺ intake plays a protective role against hypertension, stroke, cardiac dysfunction, renal damage, hypercalcaemia, kidney stones, and cancer.

ABSTRACT largely overruled a transition to a substantial food habits, now have demonstrated pathologic effects on the bones. Additionally, fruits and vegetables contain K/organic anion salts (malate, citrate), which exert alkalinizing effects, through KHCO₃ generation, which serves to neutralize fixed acidity in the urine. Low-grade metabolic acidosis, when not properly controlled, may exacerbate various catabolic processes (bone Ca⁺⁺ mobilization, proteolysis), especially in the elderly.”

...fruits and vegetables contain K/organic anion salts (malate, citrate), which exert alkalinizing effects, through KHCO₃(-) generation, which serves to neutralize fixed acidity in the urine. Low-grade metabolic acidosis, when not properly controlled, may exacerbate various catabolic processes (bone Ca⁺⁺ mobilization, proteolysis), especially in the elderly.”

¹ Supported in part by ANR/INRA (Public Agency for Fresh Vegetable and Fruit Development), Paris, France.
² Manuscript received 8 August 2004.
³ To whom correspondence should be addressed.
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0022-3166/04 \$8.00 © 2004 American Society for Nutritional Sciences

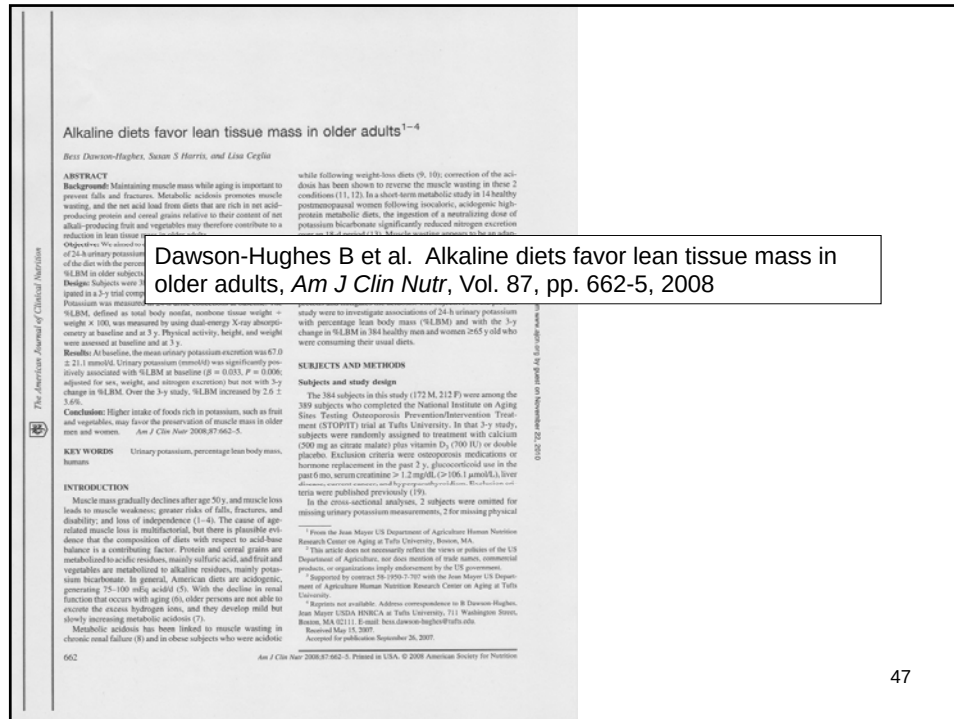
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- “Potassium and organic anions, through KHCO₃ generation...are very effective in neutralizing mineral acidity and favoring neutral or slightly alkaline urine pH.”
- “...K⁺ plays a crucial role in neutralizing excess sulfate ions (affluent sulfur amino acid provision, dietary sulfate)...”

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- “Muscle mass gradually declines after age 50 y, and muscle loss leads to muscle weakness; greater risk of falls, fractures, and disability; and loss of independence.”
- “The cause of age-related muscle loss is multifactorial, but there is plausible evidence that the composition of diets with respect to acid-base balance is a contributing factor.”
- “Protein and cereal grains are metabolized to acidic residues, mainly sulfuric acid, and fruit and vegetables are metabolized to alkaline residues, mainly potassium bicarbonate.”
- “In general, American diets are acidogenic, generating 75-100 mEq acid/d. With the decline in renal function that occurs with aging, older persons are not able to excrete the excess hydrogen ions, and they develop mild but slowly increasing metabolic acidosis.”

- ***“...much of the loss of lean tissue mass that occurs with aging can likely be prevented by increasing the intake of alkaline potassium salts to the recommended level.”***

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Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents¹⁻³

Lynda A. Fralsetto, Karen M. Todd, R. Curtis Morris Jr., and Anthony Sebastian

[illegible]

KEY WORDS: Endogenous acid production, renal net acid excretion, potassium, protein, diet, metabolic acidosis

INTRODUCTION

Normal adult humans eating typical American diets characteristically have chronic, low-grade metabolic acidosis (3-4). The persisting perturbation of systemic acid-base equilibrium occurs because metabolism of the diet releases noncarbonic acids into the systemic circulation (eg, sulfuric acid from metabolism of protein) in amounts that exceed the amounts of base released concomitantly (eg, bicarbonate from combustion of organic acid salts of potassium in vegetable foods) (5, 6). The size of the discrepancy between acid and base production determines the net endogenous acid production rate (ie, the net acid load of the

diet), which in turn determines the degree of perturbation of systemic acid-base equilibrium (1, 2, 4). Under normal physiologic circumstances, the net endogenous acid production rate and the degree of the attendant low-grade metabolic acidosis are deter-

With advancing age, the severity of diet-dependent acidosis increases independently of diet (3, 4). That occurs because kidney function declines steadily and substantially with age, resulting

Estimation of net end products from diet potassium

676-83, 1998).

Frassetto LA et al. Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents, *Am J Clin Nutr*, Vol. 68, pp. 576-83, 1998.

¹From the Department of Medicine and General Clinical Research Center, University of California, San Francisco.

¹Supported in part by the General Clinical Research Center, UCSF (grant M01 00079); the National Institutes of Health (grants P01DK 39964 and R01HL47943); the University of California Research Evaluations and Allocation Committee (grant MSC-72); a grant from the UCSF Academic Senate; and gifts from Church & Dwight Co. Inc. and the Emil Mosbacher, Jr. Foundation.

²Address reprint requests to A. Sebastian, Box 0126, University of California, San Francisco, CA 94143. E-mail: sebastian@gcrc.ucsf.edu.
Received November 7, 1997.
Accepted for publication February 23, 1998.

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Am J Clin Nutr 1998;68:575-83. Printed in U.S.A. © 1998 American Society for Clinical Nutrition

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- “Potassium bicarbonate is a natural base that the body generates from the metabolism of organic acid salts of potassium (eg, potassium citrate), whose density (ie, mmol K/kJ food item) is greatest from fruits and vegetables.”
- “Long-term supplementation of the diet with potassium bicarbonate has numerous anabolic effects.”
- “In postmenopausal women for example, calcium and phosphorus balances improve, bone resorption markers decrease, bone formation markers increase, nitrogen balance improves, and serum growth hormone concentrations increase.”
- “These findings suggest that the adverse effects of chronic, low-grade, diet-dependent acidosis are not inconsequential and may contribute to such age-related disturbances as bone mass decline, osteoporosis and muscle wasting.”

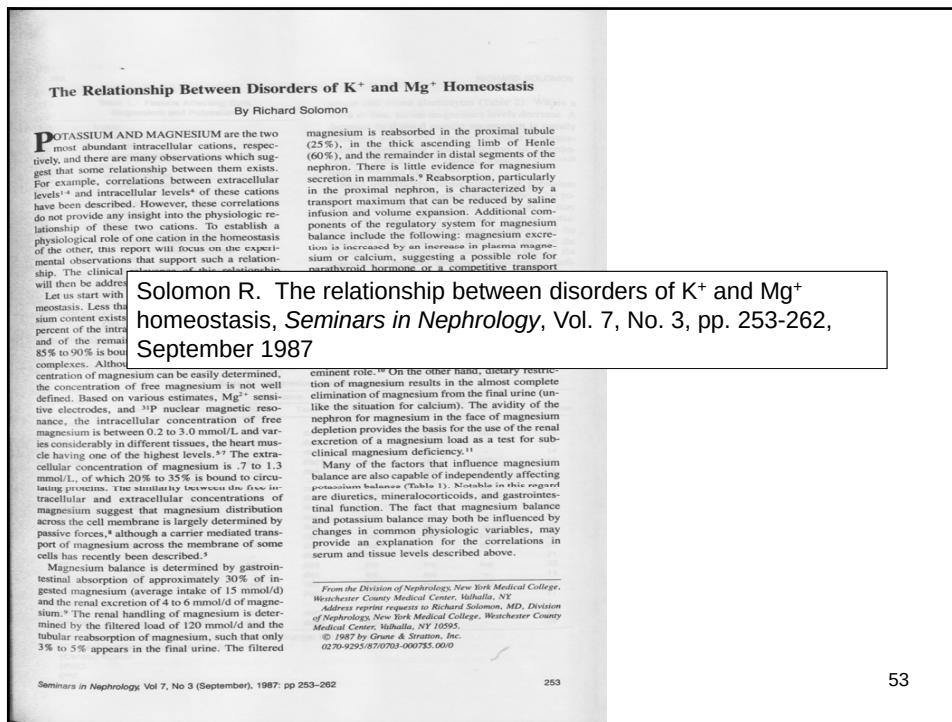
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***The impact of magnesium
deficiency on the creation of
low-grade metabolic acidosis***

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- "...primary disturbances in magnesium balance, particularly magnesium depletion, produce secondary potassium depletion."
- "This appears to result from an inability of the cell to maintain the normally high intracellular concentration of potassium, perhaps as a result of an increase in membrane permeability to potassium and/or inhibition of Na⁺-K-ATPase."
- "As a result, the cells lose potassium, which is excreted in the urine."
- "Repletion of cell potassium requires correction of the magnesium deficit."

***The impact of low-grade
chronic metabolic acidosis on
magnesium status***

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Acidosis and magnesium

“Chronic acidosis...leads to urinary magnesium wasting, which, as with acute acidosis, may be partially corrected by the administration of bicarbonate.”

Quamme GA & De Rouffignac C. Renal magnesium handling, in Selden DW & Giebisch G eds., The Kidney: Physiology & Pathophysiology, Volume II, Third Edition, Lippincott Williams & Wilkins, Philadelphia, 2000, pp. 1711-1729.

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Acidosis and magnesium

“Metabolic acidosis diminishes magnesium absorption...”

Quamme GA & De Rouffignac C. Renal magnesium handling, in Selden DW & Giebisch G eds., The Kidney: Physiology & Pathophysiology, Volume II, Third Edition, Lippincott Williams & Wilkins, Philadelphia, 2000, pp. 1711-1729.

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Acidosis and magnesium

“...potassium depletion, phosphate deficiency, and metabolic acidosis may be additive.”

Quamme GA & De Rouffignac C. Renal magnesium handling, in Selden DW & Giebisch G eds., The Kidney: Physiology & Pathophysiology, Volume II, Third Edition, Lippincott Williams & Wilkins, Philadelphia, 2000, pp. 1711-1729.

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Diagnostic considerations

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Nutrition 21 (2005) 961–963

Brief communication

Measurement of net acid excretion by use of paper strips

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Received July 30, 2004; accepted January 24, 2005.

Abstract

Objectives: Net endogenous acid production, reflected in the steady state as net acid excretion (NAE), is implicated in bone loss because it is positively associated with urinary calcium loss. Protein is one of the main sources of dietary acid load, whereas fruit and vegetables provide alkaline potassium salts that counteract the dietary acid load. This study investigated whether a pH paper strip measurement of overnight (i.e., first voided urine) would reflect 24-h NAE, measured as excretion rate of titratable acid minus bicarbonate plus ammonium.

Methods: Twenty-three subjects collected 24-h urine in two parts: day (7–11 am to 11 pm) and overnight (11 pm to 7 am). At first void, subjects recorded pH using paper strips. Subjects recorded intake and 20 subjects provided fasting urine collected from 7 to 9 am.

Results: The pH paper strip measurements of first void urine was significantly correlated with 24-h titratable acid minus bicarbonate ($r = -0.466$, $P < 0.05$) but not with 24-h NAE. We examined the association of dietary protein, potassium, protein:potassium ratio, and sodium with NAE, with fasting morning urinary calcium excretion, as indirect measurement of bone loss, and with urinary creatinine, a direct measurement of bone resorption. Of these, only sodium intake (measured in 24-h urine excretion) and urine potassium:sodium ratio showed a significant relation (with fasting calcium excretion).

Conclusions: We did not find that the first void urine pH by paper strip measurement provided an index of daily net endogenous acid production as reflected in 24-h NAE. In our sample of young adults, daily sodium intake positively correlated with bone resorption, as reflected in fasting urine calcium, whereas daily NAE did not. © 2005 Elsevier Inc. All rights reserved.

Key words: Calcium; Potassium; Sodium; Net acid excretion; pH

Introduction

Although dietary calcium is well known for its important role in ensuring healthy bone, other dietary factors are implicated in bone gain and bone loss. Experimental studies have found that increasing a subject's protein intake results in increased urinary calcium loss concomitant with an increase in net acid excretion (NAE) (1). NAE is estimated as the sum of excretion rates of titratable acid minus bicarbonate plus ammonium. Although some have attributed increased acidity primarily to protein intake (2), others have determined that protein and potassium contents of the diet could significantly predict the effect of diet on calcium retention and bone mass (3,4). Because people need to be able to monitor acid or base excretion, Brown (5) advocated a simple method that involves measuring first morning urine acidity using pH paper strips. Because pH paper strips measure H⁺ concentration (acidity) but not necessarily total acid content (ammonium and titratable acid minus bicarbonate), this method may not relate quantitatively to NAE. Our objective was to investigate whether a pH strip measurement of morning first voided urine could determine urinary net acid load by comparing it to net (24-h) NAE. We also determined relations between dietary factors, NAE, and bone loss, measured as fasting urine calcium excretion and as a bone resorption marker.

Materials and methods

Adult volunteers (19 women and 4 men) consumed their usual diets, which they reported for 24 h, during which time they made a 24-h urine collection. Subjects were instructed to begin collecting after rising (after discarding first void).

Whiting SJ & Muirhead JAB. Measurement of net acid secretion by use of paper strips, *Nutrition*, Vol. 21, No. 9, pp. 961-3, September 2005

“The pH paper strip readings of the first voided morning urine correlated with the net acid secretion (NAE) measured in the overnight urine collection.”

“The pH paper strip readings of the first voided morning urine did not correlate with the NAE measured in the 24-h urine collection.”

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INVITED REVIEW				F817
Table 2. Changes in body weight and in acid, mineral, and charge balances during KHCO_3 administration among 10 healthy adults eating otherwise constant diets (34)				
	Control	KHCO_3	Δ	P^a
Dose of KHCO_3 , mmol/day	0	61 ± 2^b	$+61 \pm 2$	Independent
Body wt, kg	68.60 ± 8.89	68.86 ± 8.68	$+0.26 \pm 0.99$	NS
Daily change in body wt, kg	-0.03 ± 0.06	0.04 ± 0.08	$+0.07 \pm 0.09$	$= 0.039$
Serum $[\text{HCO}_3^-]$, mmol/l	27.1 ± 0.8	27.3 ± 1.1	$+0.2 \pm 0.8$	NS
Diet unmeasured anion, meq/day ^c	57 ± 11	118 ± 11	$+61 \pm 2$	<0.001
Fecal K^+ , mmol/day	15 ± 3	15 ± 3	0 ± 2	NS
Fecal unmeasured anion, meq/day ^c	28 ± 7	27 ± 5	-1 ± 2	NS
Net intestinal absorption of unmeasured anion, meq/day ^d	29 ± 5	91 ± 7	$+62 \pm 3$	<0.001
Urinary unmeasured anion, meq/day ^c	33 ± 13	85 ± 16	$+52 \pm 11$	<0.001
Urinary unmeasured anion – measured intestinal absorption of unmeasured anion, meq/day	$+4 \pm 14$	-6 ± 14	-10 ± 10	$= 0.011$
Urinary SO_4 , meq/day	39 ± 7	37 ± 6	-2 ± 3	NS
Urinary organic anion, meq/day	35 ± 6	38 ± 7	$+2 \pm 4$	NS
Net fixed acid production, meq/day	45 ± 10	-17 ± 13	-62 ± 6	<0.001
Urinary pH	6.00 ± 0.13	6.68 ± 0.18	$+0.68 \pm 0.13$	<0.001
Urinary titratable acid, meq/day	21 ± 4	19 ± 4	-10 ± 2	<0.001
Urinary NH_4 , meq/day	37 ± 5	19 ± 5	-18 ± 4	<0.001
Urinary HCO_3^- , meq/day	3 ± 2	23 ± 8	$+20 \pm 6$	<0.001
Renal net acid excretion, meq/day ^c	55 ± 9	6 ± 13	-49 ± 9	<0.001
Acid balance, meq/day	-10 ± 10	-23 ± 14	-13 ± 11	$= 0.005$
Na^+ balance, meq/day	$+10 \pm 18$	$+11 \pm 16$	$+1 \pm 14$	NS
K^+ balance, meq/day	$+7 \pm 6$	$+18 \pm 14$	$+11 \pm 10$	$= 0.006$
Ca^{2+} balance, meq/day	-2.3 ± 1.9	-1.4 ± 1.9	$+0.9 \pm 0.8$	$= 0.009$
Mg^{2+} balance, meq/day	$+0.5 \pm 2.5$	$+2.0 \pm 3.4$	$+1.5 \pm 1.8$	$= 0.020$
Cl^- balance, meq/day	$+6 \pm 17$	$+9 \pm 17$	$+3 \pm 13$	NS
PO_4 balance, mmol/day	$+6.1 \pm 3.4$	$+8.4 \pm 4.6$	$+2.3 \pm 3.0$	$= 0.040$
PO_4 balance $\cdot 1.8$, meq/day	$+11.0 \pm 6.1$	$+15.1 \pm 8.3$	$+4.1 \pm 5.4$	$= 0.040$
Charge balance, meq/day ^f	-4 ± 14	$+6 \pm 14$	$+10 \pm 10$	$= 0.011$

^aProbability that the mean difference for the group is not different from zero using the *t*-test for paired data. ^bVariances throughout are shown as $\pm$ SD. ^cEstimated as $(\text{Na}^+ + \text{K}^+ + \text{Ca}^{2+} + \text{Mg}^{2+}, \text{meq/day}) - (\text{Cl}^-, \text{meq/day} + 1.8 \cdot \text{PO}_4, \text{mmol/day})$. ^dDifference between diet and fecal unmeasured anion, each estimated as $(\text{Na}^+ + \text{K}^+ + \text{Ca}^{2+} + \text{Mg}^{2+}, \text{meq/day}) - (\text{Cl}^-, \text{meq/day} + 1.8 \cdot \text{PO}_4, \text{mmol/day})$. ^eCalculated as $(\text{titratable acid} + \text{NH}_4 - \text{HCO}_3^-), \text{meq/day}$. ^fEstimated as $[(\text{diet}(\text{Na}^+ + \text{K}^+ + \text{Ca}^{2+} + \text{Mg}^{2+}), \text{meq/day}) - (\text{Cl}^-, \text{meq/day} + 1.8 \cdot \text{PO}_4, \text{mmol/day})] - [(\text{fecal} + \text{urine}(\text{Na}^+ + \text{K}^+ + \text{Ca}^{2+} + \text{Mg}^{2+}), \text{meq/day}) - (\text{Cl}^-, \text{meq/day} + 1.8 \cdot \text{PO}_4, \text{mmol/day})]$.

How do you know if your patient is acidotic? Routine laboratory and home/office analyses...

- First morning salivary and urine pH
 - Ideal 6.4 – 7.0
- Fasting glucose
 - Ideal <90
- Low normal serum potassium, high normal serum sodium
- Low or low normal serum CO_2 (18-22)
- High normal BUN (24-26) with normal creatinine

How do you know if your patient is acidotic? Routine laboratory and home/office analyses...

- Calcium to phosphorus ratio
Ideal 10:4
Catabolic physiology 3:1 (Ca 9.3–9.5, P 2.8-2.9)
- High normal globulin (3.6-3.8) (Possible food allergies)
- Total cholesterol (220 –280)
- High LDL, low HDL
- High triglycerides

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How do you know if your patient is acidotic? Routine laboratory and home/office analyses...

- Cholesterol to triglyceride ratio
Ideal 2:1
- High liver enzymes (ALT, AST, GGT)
- High WBC, high polys, high lymphs
- High CRP
- High or low TSH
Ideal 2.0
- High normal or low normal T₃ and/or T₄
- High blood pressure

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How do you know if your patient is acidotic? Routine laboratory and home/office analyses...

- High percent body fat
(Visceral adiposity)

Non-athlete male ideal 12% - 18%

Non-athlete female ideal 22% - 28%

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How do you know if your patient is acidotic? Non-routine laboratory analysis...

- High fasting insulin
- High or low salivary cortisol
- Elevated urinary catecholamine metabolites
- Low bone density
- High urinary sulfate (organic acid testing)

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How do you know if your patient is acidotic? Functional laboratory analysis...

- Dysbiosis
- Leaky gut
- Chemical toxicity - Abnormal phase I & II detox pathways
- High heavy metal levels (Hair, urine, serum)
- Genomic variations (Folate metabolism, low glutathione-S-transferase, etc.)

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How do you know if your patient is acidotic? Signs and symptoms...

- Fatigue
- Cravings
- Depression and/or anxiety
- Poor diet – high in acid-based, refined foods
- Lack of sleep or poor quality of sleep
- Too little or too much exercise
- Signs and symptoms of poor digestion and absorption
- Pain, trauma, infection

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Treatment considerations

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British Journal of Nutrition (2005), 94, 192–197
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DOI: 10.1017/S0005255805005474

Effect of potassium salts in rats adapted to an acidogenic high-sulfur amino acid diet

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(Received 14 April 2004; Revised 12 February 2005; Accepted 12 February 2005)

Low-grade metabolic acidosis, consecutive to recurrent ingestion of sulfur amino acids and a high dietary NaCl ratio, is a recurrent feature of Western food habits. This metabolic alteration may exert various adverse physiological effects, especially on bone, muscle and kidney. To assess the actual effects of various K salts, a model of the Western diet has been developed in rats, which provides essential (EAA) protein equivalent to non-essential amino acids (NEAA) K ratio. This diet resulted in acidic urine (pH 5.5) together with a high rate of distal renal tubular acidosis (RTA), especially in the distal tubule. A supplementation of 0.2% potassium citrate, without potassium bicarbonate or sodium bicarbonate and a concurrent increase in pH (up to 7.5), in parallel, citrate was strongly increased, together with 2-hydroxybutyrate excretion, by potassium bicarbonate or malate in the diet. Renal acid excretion, in the range of 1 mmol/d, was slightly increased in rats fed the potassium malate diet. The greater results of the greater metabolic acidosis indicate that potassium malate may be as effective as KHCY3, to counteract renal acidification, to limit distal renal tubular acidosis and to counter high chronic acidemia in urine.

Low-grade metabolic acidosis; Potassium; Magnesium; Sodium; Sulfate

Western diets are generally excessive in protein and NaCl and also frequently deficient in fruit and vegetables. Protein sulfur amino acid metabolism results in H₂S production, which is rapidly eliminated through renal excretion (Balla & Sirtori, 1991; Nakamura *et al.*, 2002). Bicarbonate volume may act to buffer chronic dietary acid load, mainly by neutralization from bone (Baron, 1992; Franceschini *et al.*, 2001; New, 2002) or glutamine oxidation in kidney, which yields HCO₃⁻ (neutralized to plasma together with NH₄⁺ ions released in urine (Ragotzke *et al.*, 1992). However, long-term periods of low-grade metabolic acidosis will lead to significant bone Ca wasting in rats and mice (Wan *et al.*, 1996; Montagna *et al.*, 2004), as well as in other muscle protein metabolism towards proteolysis (Gretchen & Mitch, 1992; Rasmussen, 1995). These effects contribute to sustain the propensity to osteoporosis and sarcopenia, all the more since the urinary excretion of K⁺ is generally increased in Western populations (Franceschini *et al.*, 1996; New, 2002).

A substantial part of K⁺ is lost by the kidney to maintain fluid acidity across from excretion in urine, especially in the glomerular area, of K⁺ organic anions (in contrasted anions) in fruits and vegetables. Citrate and malate anions are present in naturally mineral anions in protein of mostly consumed fruits and vegetables, where they are partly neutralized by K⁺ and Mg²⁺ (early less than 50% in fruits (Lévesque *et al.*, 1995) and 70–80% in vegetables (Danglade *et al.*, 2004a). Recently, few studies have addressed the respective importance of K⁺ and organic anions

(such as citrate or malate) in the effects of plant foods on acid-base status and metabolism, especially mineral homeostasis, whereas there are reports supporting the interest of K⁺ itself as a protective element (De Zeeuw *et al.*, 2001; Danglade *et al.*, 2004b). To further investigate this domain, models of low-grade metabolic acidosis in experimental animals are well suited and it must be noted that most of acid in diet, especially those based on AIN-93G recommendations, may be considered as oversuppressive in this respect (Ward *et al.*, 2003). In fact, the composition of these animal diets (especially meat anions) is more similar to that of the natural human diet (high in K⁺, poor in Na⁺ and rich in Ca and organic anions such as citrate) than of Western diets (with opposite characteristics). This type of rat diet leads to alkaline urine pH and moderate Ca and Mg excretion, and is a poorly suitable model to evaluate the effectiveness of high K⁺ intake in a Westernized rat diet was designed and evaluated, and its responsiveness to supplementation with different K salts (chloride, bicarbonate or malate) was assessed.

Materials and methods

Preparation of rat diets

The control diet contained 300 g/kg casein, 100 g/kg soybean oil, 100 g/kg maize, 100 g/kg wheat, 100 g/kg yeast, 100 g/kg molasses, 100 g/kg

Sabbab H *et al.* Effect of potassium salts in rats adapted to an acidogenic high-sulfur amino acid diet, *Br J Nutr*, Vol. 94, pp. 192–197, 2005

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- “Western diets are generally excessive in protein and NaCl and also frequently deficient in fruit and vegetables.”
- Protein sulfur amino acid catabolism results in SO_4 production, which is essentially eliminated through renal excretion.”
- Homeostatic systems may act to buffer excess dietary acid load, namely Ca mobilization from bone or glutamine catabolism in kidneys, which yields HCO_3^- transferred to plasma together with NH_4^+ ions released in urine.”

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- ***“However, long-term periods of low-grade metabolic acidosis will lead to significant bone Ca wasting in rats and man, as well as to shift to muscle protein metabolism towards proteolysis.”***

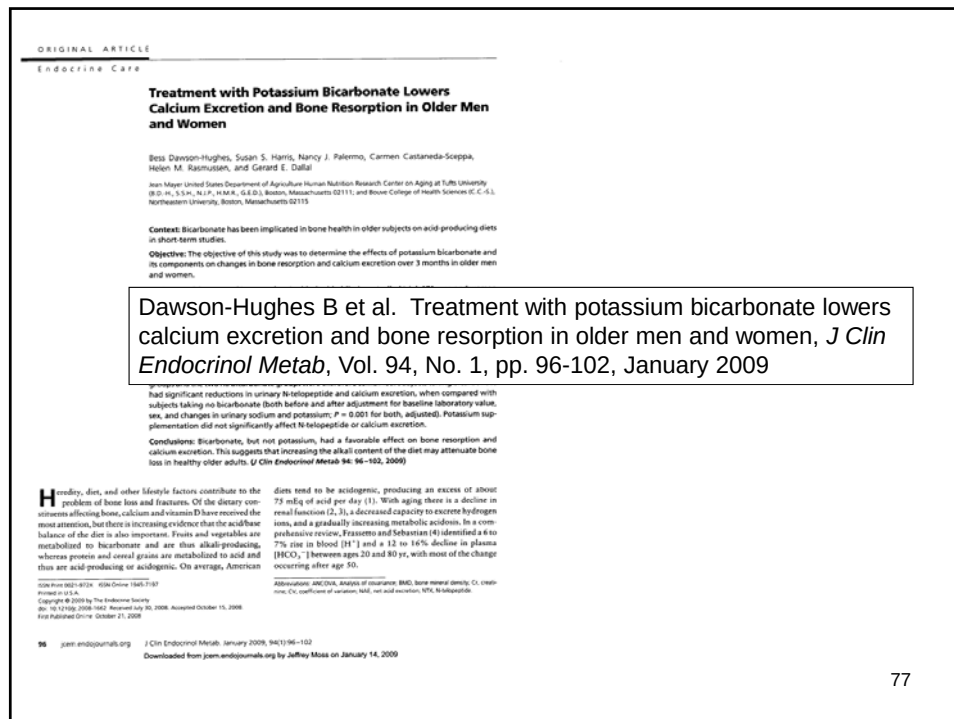
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- “The present results suggest that increasing dietary K is not effective against acidosis in the form of the Cl salt, as previously reported.”
- “In fact, acidosis may even be more pronounced with KCl in the diet, as reflected by the very high rate of Mg, Ca or H⁺ excretion.”
- “This point is noteworthy since KCl is frequently proposed as a substitute of NaCl in dietetic interventions aiming at lowering blood pressure and the risk of stroke.”

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- ***“In contrast to KCl, KHCO₃ or potassium malate were effective in alkalinising urine and counteracting various adverse effects of low grade acidosis such as excessive Ca and Mg elimination...”***

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- “Fruits and vegetables are metabolized to bicarbonate and are thus alkali-producing, whereas protein and cereal grains are metabolized to acid and thus are acid-producing or acidogenic.”
- “On average, American diets tend to be acidogenic, producing an excess of about 75 mEq of acid per day.”
- “With aging there is a decline in renal function, a decreased capacity to excrete hydrogen ions, and a gradually increasing metabolic acidosis.”

Key finding from the study

- “Bicarbonate, ***but not potassium***, had a favorable effect on bone resorption and calcium excretion.”
- “Treatment with potassium did enhance sodium excretion, as has been documented widely.”

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ORIGINAL INVESTIGATION

Joint Effects of Sodium and Potassium Intake on Subsequent Cardiovascular Disease

The Trials of Hypertension Prevention Follow-up Study

Nancy R. Cook, ScD; Eva Obazarenek, PhD; Jeffrey A. Cutler, MD; Julie E. Buring, ScD; Kathryn M. Rexrode, MD; Shiriki K. Kamanyika, PhD; Lawrence J. Appel, MD; Paul K. Whelton, MD;
for the Trials of Hypertension Prevention Collaborative Research Group

Background: Previous studies of dose-response effects of usual sodium and potassium intake on subsequent cardiovascular disease (CVD) have largely relied on suboptimal measures of intake.

Methods: Two trials of sodium reduction and other interventions collected 24-hour urinary excretions inter-

Results: Among 2974 participants, follow-up information was obtained on 2275 participants (76.5%), with 193 CVD events. After adjustment for baseline variables and

lifestyle changes, there was a nonsignificant trend in CVD risk across sex-specific quartiles of urinary sodium excretion (rate ratio [RR] from lowest to highest, 1.00, 0.99, 1.16, and 1.20; $P=.38$ for trend) and potassium excretion (RR, 1.00, 0.94, 0.91, and 0.64; $P=.08$ for trend) but a significant trend across quartiles of the sodium to potassium excretion ratio (RR, 1.00, 0.99, 1.15, and 1.30; $P=.07$).

that is associated with increased risk of subsequent CVD, with an effect stronger than that of sodium or potassium alone.

Arch Intern Med. 2009;169(1):32-40

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 Department of Biostatistics, University of Pennsylvania School of Medicine, Philadelphia (Dr. Karmali); Department of Epidemiology, University of Michigan, Ann Arbor (Dr. Selhub); Department of Epidemiology, University of California, Los Angeles (Dr. Wilhelmsen); and Department of Epidemiology, University of Minnesota, Minneapolis (Dr. Wilhelmsen).

OBSERVATIONAL DATA AND randomized trials have identified decreased blood pressure (BP) and reduced risk of hypertension among subjects with lower levels of sodium intake and higher levels of potassium intake.^{1,2} Recent evidence suggests

have not been definitively determined.³¹ The biologic interaction of sodium and potassium is of particular interest because it may have a dominant role in the pathogenesis of hypertension and in the development of CVD.³² Findings from several studies³³⁻³⁷ suggest that a high sodium to potassium excretion ratio is associated with

“A higher sodium to potassium excretion ratio is associated with increased risk of subsequent CVD, with an effect stronger than that of sodium or potassium alone.”

response relationships of sodium and potassium intake, as well as the sodium to potassium excretion ratio, with CVD intermittently during an 18-month period (TONP I) or during a 3-year period (TONP II). Therefore, we were able to as-

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Table 3. Linear Effect of Urinary Excretion on Total Cardiovascular Events After the Trials of Hypertension Prevention in the Nonsodium Interventions^a

Variable	Cardiovascular Events	Regression Coefficient		RR (95% CI) ^c
		β (SE)	P Value ^b	
Sodium excretion only				
Model 1	193	0.003 (0.004)	.04	1.32 (1.01-1.72)
Model 2	190	0.002 (0.002)	.19	1.22 (0.91-1.65)
Model 3	166	0.002 (0.002)	.18	1.25 (0.91-1.72)
Potassium excretion only				
Model 1	193	-0.007 (0.004)	.10	0.71 (0.48-1.06)
Model 2	190	-0.007 (0.004)	.12	0.71 (0.47-1.08)
Model 3	166	-0.004 (0.005)	.40	0.83 (0.53-1.29)
Both sodium and potassium excretion				
Model 1	193			
Sodium excretion		0.005 (0.002)	.002	1.61 (1.19-2.18)
Potassium excretion		-0.013 (0.005)	.006	0.53 (0.34-0.83)
Model 2	190			
Sodium excretion		0.004 (0.002)	.03	1.46 (1.05-2.03)
Potassium excretion		-0.011 (0.005)	.02	0.57 (0.36-0.91)
Model 3	166			
Sodium excretion		0.004 (0.002)	.05	1.42 (0.99-2.04)
Potassium excretion		-0.008 (0.005)	.12	0.67 (0.41-1.10)
Sodium to potassium excretion ratio				
Model 1	193	0.23 (0.06)	<.001	1.26 (1.12-1.42)
Model 2	190	0.19 (0.07)	.003	1.21 (1.07-1.38)
Model 3	166	0.21 (0.08)	.01	1.24 (1.05-1.46)

“...the sodium to potassium excretion ratio displayed the strongest statistically significant association, with a 24% increase in risk per unit of the ratio that was similar for CHD and stroke and was consistent across subgroups.”

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Journal of the American College of Cardiology
© 2004 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 43, No. 2, 2004
ISSN 0885-0666/04/\$30.00
doi:10.1016/j.amccard.2004.04.001

STATE-OF-THE-ART PAPER

What Is the Optimal Serum Potassium Level in Cardiovascular Patients?

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Dundee, United Kingdom

Humans are prone to sodium overload and potassium depletion. This electrolyte imbalance is important in the pathogenesis of cardiovascular disease and sudden cardiac death. Ameliorating hypokalemia is beneficial in several cardiovascular disease states including acute myocardial infarction, heart failure, and hypertension. The evidence highlighting the importance of potassium homeostasis in cardiovascular disease and possible mechanisms explaining potassium's benefits are reviewed. Targets for serum potassium concentration are suggested. (J Am Coll Cardiol 2004;43:155-61.)

Humans evolved ingesting diet, and mechanisms developed to excrete potassium (1). The human produces sodium (2). Hypokalemia corrected vascular disease, and many drugs aggravate hypokalemia from a constant, reversible cardiovascular disease. The balance in cardiovascular of potassium homeostasis is by renal excretion matching the amount consumed. Virtually all filtered potassium is reabsorbed in the proximal convoluted tubule. The remainder is excreted because potassium excretion is dependent on the distal nephron's secretory mechanism (sodium delivery) and concentration, and various sodium reabsorption potassium-ATPase potassium channels. Total body potassium is altered by renal and extracellular potassium-ATPase tension concentration gradient. It is a catecholamines, and

Macdonald JE & Struthers AD. What is the optimal serum potassium level in cardiovascular patients? *J Amer Coll Cardiol*, Vol. 43, No. 2, pp. 155-61, January 2004

“Humans evolved ingesting a potassium-rich, sodium-poor diet, and mechanisms developed to retain sodium and excrete potassium. The sodium-rich diet of modern humans produces sodium overload and potassium depletion.”

From the Department of Clinical Pharmacology, Ninewells Hospital, Dundee, United Kingdom.
Manuscript received July 4, 2003; revised manuscript received May 28, 2003; accepted June 17, 2003.

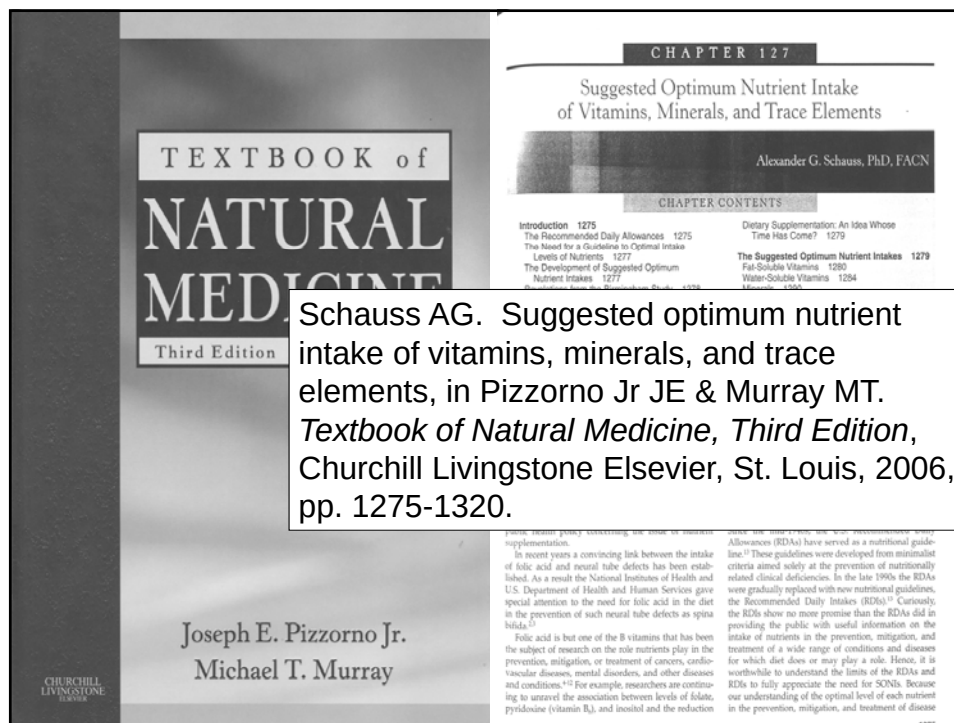
NO/CO synthesis pathway. Potassium partly mediates vasodilation via strong inwardly rectifying potassium channels and the sodium-potassium-ATPase pump of vascular

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Table 4. Clinical Evidence for Beneficial Effects of Potassium and Recommended Targets for Serum Potassium Concentration in Cardiovascular Disorders

Disorder	Recommended Level	Evidence
Hypertension	3.5–5.0 mmol/l	High K ⁺ diet ↓ BP Hypokalemia ↑ ventricular arrhythmia
Stroke	Unknown	High K ⁺ diet ↓ risk of stroke
Acute MI	4.5–5.5 mmol/l	Hypokalemia ↑ ventricular arrhythmia
Heart failure	4.5–5.5 mmol/l	Hypokalemia ↑ ventricular arrhythmia Increasing serum K ⁺ ↓ ventricular arrhythmia and ↓ QT and QT _d Serum K ⁺ level is inversely related to prognosis

BP = blood pressure; MI = myocardial infarction.



Schauss AG. Suggested optimum nutrient intake of vitamins, minerals, and trace elements, in Pizzorno Jr JE & Murray MT. *Textbook of Natural Medicine, Third Edition*, Churchill Livingstone Elsevier, St. Louis, 2006, pp. 1275-1320.

Table 127-23		Recommended intake of potassium (g)	
Gender	Age (yr)	RDA	Optimal
Male	11-14	2	2
	15-18	2	2
	19-24	2	3
	25-50	2	3
	51+	2	3
Female	11-14	2	2
	15-18	2	2
	19-24	2	3
	25-50	2	3
	51+	2	3

Optimal, Suggested Optimal Nutrient Intake; RDA, Recommended Daily Allowance.

Dietary considerations

- pH balanced diet
- Optimal caloric intake
- Optimal protein intake (1.2 – 1.8 g/kg/day)
- Hypoallergic
- Optimal carbohydrate:protein ratio
- Quality foods and liquids
- Eating behaviors (How fast; when, etc.)
- Medications (Hypertensive drugs, etc.)

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Product recommendations

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- Rule out significant renal dysfunction. The easiest way to accomplish this is to examine a recent blood chemistry for creatinine elevations. History can also be helpful in this regard. In addition, note serum potassium levels on the patient's blood chemistry to see if levels are approaching 5.5 mEq/L, which is usually considered to be the lower limit for hyperkalemia. Finally, determine if the patient is using any medications such as diuretics that may affect electrolyte metabolism. If any of these is determined to exist, this protocol should not be administered or only be administered with the consent of the patient's primary care physician, cardiologist, and/or urologist.

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- Have the patient start Epsom salt baths using one cup of Epsom salts in a full bath. Ideally, these baths should be done once per day for approximately 15 minutes. For elderly patients or others who have difficulty getting in and out of a bathtub, foot soaks are an adequate substitute. Finally, for those patients who are reluctant to perform either of these two procedures, use of the Designs for Health product **Magna-Derm** is recommended.

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- Determine, as best as possible, based on the patient's three day dietary history, the degree of nutritional deficiency:

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- **Significant:** Start with 1 **K Alkaline** and 1 **Magnesium Glycinate (Vital Nutrients)** before bedtime. Then have the patient check the urinary pH the next morning. If it is still below 6.4, have the patient take two of each of the above that night. Continue increasing the dose by one of each product on subsequent nights until the first morning urine pH is between 6.4 and 7.0. If the first morning urinary pH is too high (above 7.4) the next morning, simply decrease the dose of each product by one that night. Once the optimal dose has been determined, continue for at least 1-2 weeks. During this time continue to monitor first morning urinary pH on a daily basis as well as other signs, symptoms, and chief complaints. Also, institute at your discretion, other nutritional and lifestyle modifications as needed.

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- **Minor:** Use the same protocol as stated above except use **K Alkaline + Mg** instead of the two products mentioned.

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- **What if the patient reports diarrhea or loose stools with magnesium ingestion?** – For patients in both the “**Significant**” and “**Minor**” categories, use **K Alkaline** only.
- **What if the patient has digestive dysfunction to the extent that any supplements cause GI distress?** – Start with GI support as needed depending on the nature of the dysfunction. Then initiate the above mentioned protocol.

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Parting thought:

***Low-grade metabolic acidosis
is a metabolic disorder, not
just an issue of alkaline diets
and alkaline supplements***

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Editorial

Hypokalemia, Cardiac Failure, and Reporting NXY-059 Safety for Acute Stroke

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NXY-059, an alpha-phenyl-N-tert-butyl nitroxide derivative, is a free radical-trapping agent presently in late clinical trials as a potential neuroprotectant limiting reperfusion injury following acute stroke. Two recent trials suggest that NXY-059 causes hypokalemia and associated cardiac disturbances. With regard to the mechanism of such association, most investigators agree that potent trapping of free radicals leads to the 11 beta-hydroxysteroid dehydrogenase blockade in kidneys, diminishing renal hydrocortisone metabolism and increasing K⁺ ion urine excretion. Importantly, potassium deficiency represents the major avoidable cause of the array of serious cardiac adverse reactions (QT-prolongation, Torsades de

pointes and other life-threatening arrhythmias, and higher risks for perioperative cardiopulmonary resuscitation and cardiac death. Because a prime target for NXY-059 use will likely be acute strokes in the emergency room environment, the potential combination of the drug with intensive therapy including fluid infusions, particularly with diuretics, might be especially harmful because of the synergic depletion of potassium, which might also jeopardize the fate of the novel nitroxide neuroprotectant.

Keywords: hypokalemia; NXY-059; cardiac failures; safety; serious adverse events; clinical trials

The utmost need to go beyond thrombolysis stroke victims to also introduce novel strategies acknowledged, NXY-059, an nitroxide derivative, is a big presently in late clinical to protectant limiting reperfusion stroke. If, indeed, better acceptable safety profile is

Serebruany VL. Hypokalemia, cardiac failure, and reporting NXY-059 safety for acute stroke, *J Cardiovasc Pharmacol Ther*, Vol. 11, No. 4, pp. 229-231, December 2006.

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For instance, reduction of symptomatic intracranial hemorrhage and hemorrhagic stroke transformation in patients treated with NXY-059 are grossly inflated despite the point bias nature of the analysis. In addition, such promising statements were made based on a woefully small numbers of patients. In fact, hemorrhagic transformation occurred in 6 patients treated with NXY-059 versus 16 patients who received placebo.

On the other hand, almost identical severe numbers (NXY-059, n = 16; placebo, n = 7), favoring

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- “The problem that free-radical scavengers might cause hypokalemia and QT-interval prolongation is not new, and such adverse association is known for probucol, gossypol, and flavonoids.”
- “With regard to the mechanism of such association, most investigators agree that potent trapping of free radicals leads to the 11 beta-hydroxysteroid dehydrogenase blockade in the kidneys, diminishing renal hydrocortisone oxidation and increasing K⁺ ion urine excretion.”

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- ***“Importantly, potassium deficiency represents the major avoidable cause of the array of serious cardiac adverse reactions: QT prolongation, Torsades de pointes and other life-threatening arrhythmias, and higher risks for perioperative cardiopulmonary resuscitation and cardiac death are among just a few of the complications to be named.”***

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Thank you!!

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