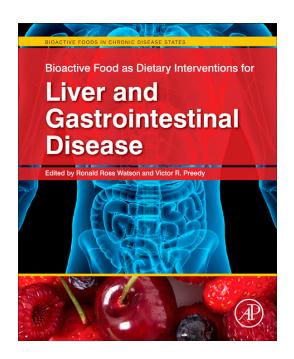
Provided for non-commercial research and educational use. Not for reproduction, distribution or commercial use.

This chapter was originally published in *Bioactive Food as Dietary Interventions for Liver* and Gastrointestinal Disease published by Elsevier, and the attached copy is provided by Elsevier for the author's benefit and for the benefit of the author's institution, for noncommercial research and educational use including without limitation use in instruction at your institution, sending it to specific colleagues who you know, and providing a copy to your institution's administrator.



All other uses, reproduction and distribution, including without limitation commercial reprints, selling or licensing copies or access, or posting on open internet sites, your personal or institution's website or repository, are prohibited. For exceptions, permission may be sought for such use through Elsevier's permissions site at:

http://www.elsevier.com/locate/permissionusematerial

Jaffe R. (2013) The Alkaline Way in Digestive Health. In: Watson RR and Preedy VR (eds.) *Bioactive Food as Dietary Interventions for Liver and Gastrointestinal Disease*, pp. 1-21. San Diego: Academic Press.

© 2013 Elsevier Inc All rights reserved.



# The Alkaline Way in Digestive Health

## R. Jaffe

Health Studies Collegium, Ashburn, VA, USA

The biochemical consequences of diet are the greatest influence on overall metabolism for most patients. Food choices clearly affect the course of common pathophysiological errors such as insulin resistance, metabolic syndrome, and their sequella. However, these dynamics can also be considered a leverage point – an opportunity to reverse immune reactivity through practical interventions that patients can implement in their daily lives.

# **1. DIETARY FACTORS IN METABOLISM**

The intestinal tract plays a key part in nutrient absorption, immune defense against foreign invaders, physiologic repair from wear and tear, growth, neurohormone regulation and stress management. Disorders anywhere in the gastrointestinal system can affect the function of the entire body and overall health. Digestive competence tends to predict survival and the capacity to thrive years to decades later.

# 1.1 Profile: Metabolic Acidosis as a Major Cause of Chronic Disease

Toxin accumulation in the body can result from a diet that promotes metabolic acidosis (net acid excess after metabolism) as shown by low levels of buffering minerals such as potassium and magnesium. A number of large research studies involving thousands of participants have reported about the association between metabolic acidosis and insulin resistance (Jaffe and Mani, 2006; Souto et al., 2011), type 2 diabetes (Jaffe and Mani, 2006; Schulze et al., 2003), cardiometabolic risk (Murakami et al., 2008), coronary heart disease (Liu et al., 2000), and osteoporosis (Jaffe and Brown, 2000; Jehle et al., 2006), as well as cancer (Tavani et al., 2000). A typical American diet provides insufficient minerals and fiber to counter or buffer the buildup of metabolic acids and to help displacement of toxic wastes. As a result, alkaline cellular reserves within the body reduce and deplete as the intracellular environment becomes progressively acidic, mineral depleted and proton rich (Lim, 2007; Zeidel and Seiffer, 1986).

## 1.1.1 Associated signs and symptoms

The symptoms associated with metabolic acidosis include malaise and fatigue, metabolic syndrome and diabetes, osteopenia and osteoporosis, and depression. Metabolic acidosis is associated with a broad range of clinical conditions in the body because of the

#### 2 R. Jaffe

biochemical reduction of the proton gradient, upon which cell energy depends. The ratio of ATP: ADP is a measure of cell energy. A ratio of 100:1 is healthy. A ratio less than 80 begins to shift cells from an elective protective, proactive, and prevention mode to a survival mode.

#### 1.1.1.1 Fatigue

Low energy is the major complaint that patients report to their primary care physician. Energy production and the ability to remove toxins safely are compromised when even minor increases in acidity occur. Metabolic acidosis has also been linked to chronic fatigue immune dysfunction syndrome (Jaffe and Brown, 2000). Fibromyalgia and chronic muscle pain that is unresponsive to pain medication have been documented to produce acidic end products that directly irritate and inflame nerve muscle end plates (Deuster and Jaffe, 1998). We observe restoration of vitality and quality of life when metabolic acidosis is corrected comprehensively using predictive tests compared to best outcome reference ranges thus incorporating personalized biochemical individuality into primary care.

#### 1.1.1.2 Osteopenia and osteoporosis

Excess acid within the cells is also a key factor in osteoporosis (Maurer et al., 2003). One of the best examples of this metabolic sensitivity is the influence of acid–alkali balance on skeletal structure, health, and integrity. Skeletal muscles are the largest storehouse of available minerals in the body and are thus exquisitely sensitive to small changes in pH. Even a 10% reduction in pH increases osteoclastic activity while inhibiting osteo-blastic function, inducing amplified bone mineral loss (Jehle et al., 2006). For the past 20 years, we have consistently observed 2–10% new bone growth confirmed by DEXA scores after just 2 years.

#### 1.1.2 Relevant evaluations

One of the most useful assessments in the management of metabolic acidosis is self-testing for pH, which can be performed simply by the patient in their home. After 6 h of rest, we find the urine pH is equilibrated with the urinary tract cells. Costing pennies per day, this is a useful self-care test that motivates better compliance with healthier choices. Another assessment involves laboratory testing for reactive food antigens. In tandem, these tests can be pivotal in correcting metabolic acidosis and repair deficits often called inflammation and their myriad sequellae.

#### 1.1.2.1 Self-evaluation: Testing for pH

The hazard of metabolic acidosis is that it requires additional minerals to buffer and remove excess acids from the body, stripping out needed minerals with potential harm to the kidneys and urinary tract. The role of metabolic acidosis in chronic kidney disease has been extensively documented (Sahni et al., 2010).

3



Figure 1.1 Picture of pH strips.

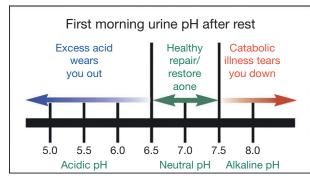


Figure 1.2 Interpretation of first, morning-urine measurements.

A pH assessment of the first morning urine provides a clinically useful measure of metabolic acidosis risk. The urine pH is a predictive indicator of the body's mineral reserves, as well as acid/alkaline status (Whiting and Bell, 2002). Typically pH balance is restored during sleep and rest when excess acids are excreted (Shafiee et al., 2002). This capacity varies widely based on the specific toxic load and the individual's ability to make energy, deactivate toxins, and excrete those toxins as reported by Bazhin (2007) (see Figure 1.1, pH strips and Figure 1.2, reference range for urine measurement).

A value of 7.0 indicates a neutral state, a balance of acid, and alkaline elements. The first morning urine pH goal of 6.5–7.5 shows healthy mineral balance. Neutral or low-level acid excess reflected in lower pH values indicates that metabolic chemistry is appropriately alkaline and that the small amounts of metabolic acids built up from daily metabolism have been easily concentrated and excreted. Cell cytoplasm or 'cell juice' functions in an exquisitely narrow, slightly alkaline optimum functional pH range (De Young, 1994; Zeidel and Seifter, 1986).

#### 1.1.2.2 Laboratory evaluation: Reducing immune reactivity

Immune responses directly and indirectly generate substantial amounts of acidic products. For the at-risk individual with impaired dietary buffering capacity, it is especially important to avoid immune reactions due to antigen reactivity or other causes that can contribute to additional cell acidity in the system (Jaffe et al., 2006). A lymphocyte response assay (LRA) can identify delayed allergic reactivity. Substitution of immune reactive substances lowers acid loads.

#### 1.1.3 Clinical interventions: the alkaline way

Reduction of hyperacidity in the body can be achieved through a nutrient-rich alkaline diet, targeted supplementation with alkaline nutrients, and the inclusion of buffered fats.

#### 1.1.3.1 Alkaline diet

The Alkaline Way diet is a health-promoting, fiber-rich diet that consists primarily of whole foods based on individual food tolerances and sensitivities. Preference is given to locally, vine-ripened, organic, or biodynamic sources of foods. Mineral-rich water is the preferred beverage. Reducing the net excess cell acidity supports a range of health benefits.

**1.1.3.1.1 Enhancing immune defenses** Alkalinizing foods improve immune defense and repair functions (Lee and Shen, 2008) by reducing host hospitality to chronic infections. This reduced infectious challenge results in lower levels of inflammation, more resources for anticancer surveillance, and enhanced repair capacity. Clinical strategies that accompany an alkaline diet include a rotation or a substitution diet to reduce exposure to reactive foods coupled with health-promoting food choices, fresh fruits and vegetables, pulses and grasses, whole grains, minimal animal protein, and a program of individualized nutritional supplements to fully meet biochemical needs.

**1.1.3.1.2 Buffering cellular chemistry** A metabolically alkaline diet means that food has a buffering or cell acid neutralizing effect on *in vivo* cellular chemistry, *in vivo* (Budde and Crenshaw, 2003). The effects of specific food responses within the body can differ from that food's test tube chemistry (Gonick et al., 1968). For example, citrus fruits are alkalinizing in the body because citrate, malate, succinate, and fumarate all promote the generation of more than twice as much bicarbonate as the acid contributed from the total amount of food metabolized (Brown and Trivieri, 2006). This means that citrus fruits and similar foods are acidic in a test tube environment, yet alkaline forming in the body.

Figure 1.3 reflects this real-time perspective on metabolism – assessing nutrition for *in vivo* efficacy rather than merely evaluating the ash residue of the food as has been historically performed in nutrient assays. The foods listed here are categorized based

# Author's personal copy

						ennear Balan		
Most Alkaline Baking Soda	More Alkaline Spices/Cinnamon	Low Alkaline	Lowest Alkaline White Willow Bark	Food Category Spice/Herb	Lowest Acid Curry	Low Acid Vanilla	More Acid Nutmeg	Most Acid Pudding/Jam/Jelly
Baking Soua		<ul> <li>Herbs (most): Arnica,</li> </ul>		Spice/ Herb	Gurry		Nutmeg	Pudding/Jam/Jelly
	Valerian	Bergamot, Echinacea	Slippery Elm			Stevia		
	Licorice	Chrysanthemum,	Artemesia Annua					
	<ul> <li>Black Cohash</li> </ul>	Ephedra, Feverfew,						
	Agave	Goldenseal, Lemongrass						
		Aloe Vera						
		Nettle						
		Angelica						
Sea Salt			Sulfite	Preservative	MSG	Benzoate	Aspartame	Table Salt (NaCL)
Mineral Water	<ul> <li>Kambucha</li> </ul>	<ul> <li>Green or Mu Tea</li> </ul>	Ginger Tea	Beverage	Kona Coffee	Alcohol	Coffee	Beer , 'Soda'
						Black Tea		Yeast/Hops/Malt
	Molasses	Rice Syrup	<ul> <li>Sucanat</li> </ul>	Sweetner	Honey/Maple Syrup		Saccharin	Sugar /Cocoa
	Soy Sauce	Apple Cider Vinegar	<ul> <li>Umeboshi Vinegar</li> </ul>	Vinegar	Rice Vinegar	Balsamic Vinegar	Red Wine Vinegar	White/Acetic Vinegar
<ul> <li>Umeboshi Plum</li> </ul>		•Sake	<ul> <li>Algae, Blue Green</li> </ul>	Therapeutic		Antihistamines	Psychotropics	Antibiotics
			<ul> <li>Ghee (Clarified</li> </ul>	Processed Dairy	Cream/Butter	Cow Milk	<ul> <li>Casein, Milk</li> </ul>	Processed Cheese
			Butter)				Protein,Cottage	
							Cheese	
			Human Breast Milk	Cow/Human	Yogurt	Aged Cheese	New Cheese	Ice Cream
				Soy		Soy Cheese	Soy Milk	
				Goat/Sheep	Goat/Sheep Cheese	Goat Milk		
		•Quail Egg	<ul> <li>Duck Egg</li> </ul>	Egg	Chicken Egg			
				Meat	Gelatin/Organs	Lamb/Mutton	Pork/Veal	Beef
				Game	<ul> <li>Venison</li> </ul>	Boar/Elk/-Game Meat	Bear	
				Fish/Shell Fish	Fish	Mollusks	<ul> <li>Mussel/Squid</li> </ul>	Shell Fish (Processed)
						Shell Fish (Whole)		Lobster
				Fowl	Wild Duck	Goose/Turkey	Chicken	Pheasant
			Oat		<ul> <li>Triticale</li> </ul>	Buckwheat	Maize	Barley
			'Grain Coffee'	Grain	Millet	Wheat	Barley Groat	Processed Flour
			•Quinoa	Cereal	Kasha	<ul> <li>Spelt/Teff/Kamut</li> </ul>	Com	
			Wild Rice	Grass	Brown Rice	Farina/Semolina	Rye	
			•Amaranth		Diowiiiilioo	White Rice	Oat Bran	
			Japonica Rice				out bruit	
	Poppy Seed	Primrose Oil	Avocado Oil	Nut	Pumpkin Seed Oil	Almond Oil	Pistachio Seed	Cottonseed Oil/Meal
Pumpkin Seed	Cashew	Sesame Seed	Seeds (most)	Seed/Sprout	Grape Seed Oil	Sesame Oil	Chestnut Oil	Hazelnut
i unipkin oeeu	Chestnut	Cod Liver Oil	Coconut Oil	OII	Sunflower Oil	Safflower Oil	Lard	Walnut
	Pepper	Almond	Olive/Macadamia Oil	•	Pine Nut	Tapioca	Pecan	Brazil Nut
	1 appai	•Sprout	Linseed/Flax Oil		Canola Oil	<ul> <li>Seitan or Tofu</li> </ul>	Palm Kernel Oil	Fried Food
entil	Kohlrabi	Potato/Bell Pepper	Brussel Sprout		Spinach	Split Pea	Green Pea	Soybean
				Beer				
Brocoflower	Parsnip/Taro	Mushroom/Fungi Cauliflower	Beet Chive/Cilantro	Bean	Fava Bean	Pinto Bean White Bean	Peanut Snow Pea	Carob
Seaweed	Garlic			Vegetable	Kidney Bean		onow Pea	
Noril Kombu Wakame Hijiki Onion/Miso	Asparagus Kala (Paralau	Cabbage	Celery/Scallion Okra/Cucumber	Lamma	Black-eyed Pea String/Wax Bean	Navy/Red Bean Aduki Bean	Leaumee (ether)	
	Kale/Parsley	Rutabaga		Legume			Legumes (other)	
Daikon/Taro Root	Endive/Arugula	<ul> <li>Salsify/ Ginseng</li> </ul>	Turnip Greens	Pulse	Zucchini	Lima or Mung Bean	Carrot	
Sea Vegetables (other)	Mustard Greens	Eggplant	Squash	Root	Chutney	Chard	Chick Pea/Garbanzo	
Dandelion Greens	Jerusalem Artichoke	Pumpkin	Artichoke		Rhubarb			
<ul> <li>Burdock/•Lotus Root</li> </ul>	Ginger Root	Collard Greens	Lettuce					
Sweet Potato/Yam	Broccoli		Jicama					
Lime	Grapefruit	Lemon	Orange	Citrus Fruit	Coconut			
Nectarine	Canteloupe	Pear	Apricot		Guava	Plum	Cranberry	
Persimmon	Honeydew	Avocado	Banana		<ul> <li>Pickled Fruit</li> </ul>	Prune	Pomegranate	
Raspberry	Citrus	Apple	Blueberry		Dry Fruit	Tomato		
Vatermelon	Olive	Blackberry	Pineapple Juice	Fruit	Fig			
langerine	<ul> <li>Dewberry</li> </ul>	Cherry	Raisin, Currant		Persimmon Juice			
No	Loganberry	Peach	Grape	1	<ul> <li>Cherimoya</li> </ul>			
Pineapple								

# Food & Chemical Effects on Acid / Alkaline Body Chemical Balance<sup>TM</sup>

itic, gourment, or exotic Prepared by Dr. Russell Jaffe, Fellow, Health Studies Collegium. Reprints

e from Health Studies Collegium, 44621 Guilford Drive, #150, Ashburn, VA 20147, 800.328.7372. Sources include USDA food data base (Rev 9 & 10),

on influence effect intensity. Thanks to Hank Liers for his original work.

Food & Nutrition Encyclopedia; Nutrition Applied ©R Jaffe, 1990-2013

Figure 1.3 Food and chemical effects on acidic/alkaline body chemical balance.

Personally , by M. Walczak; Acid & Alkaline by H. Alhara. Food growth, transport, storage, processing, preparation, combination, & ass

#### 6 R. Jaffe

on an empirical formula calculated from the actual composition of the foods' total protein, fat, carbohydrates, minerals, cofactors, and fiber contents (Jaffe, 1987).

#### 1.1.3.2 Alkaline nutrients

A diet high in acidic foods tends to be less-nutrient-dense and fiber-rich than an alkaline forming, whole foods, immune tolerant diet. Once mineral depletion occurs, cells become progressively more acidic and less energetic. The cell cytoplasm proton gradient is required for the cellular power centers, mitochondria, to work effectively. When the cell becomes acidic, the proton gradient is reduced and cells become dependent on anaerobic "survival" metabolism. This is a less efficient form of energy production. Lower energy production shifts cells into minimal function survival mode until adequate mineral buffers are restored.

**1.1.3.2.1 Buffering minerals** Minerals are required to activate enzyme catalysts within cells; lack of specific minerals has been linked to numerous specific types of enzyme deficits. Supplementation at maintenance levels includes a healthy balance of calcium and magnesium, as well as copper and zinc, and all of the divalent cations that perform essential buffering minerals needed for healthy function. These minerals are required supplements for individuals suffering from metabolic acidosis (also known as net acid excess) because buffered minerals neutralize metabolic acids to maintain healthy pH homeostasis inside the cell.

**1.1.3.2.2 Buffering fats** Short-chain and medium-chain fatty acids with less than 16 carbons such as octanoate and decanoate are alkalinizing. Found in palm kernel oil, coconut oil, and ghee (clarified butter), these short and medium chain fatty acids can accept acetate molecules.

#### 1.1.4 Individual essential nutritional supplementation

Additional functional strategies in clinical management include the reduction of oxidative stress, support of detoxification processes (through healthy methylation), and reduction of risks such as homocysteine. We find a healthier, least risk goal value for homocysteine to be <6  $\mu$ mol/l. With a combined 20-fold risk difference between a homocysteine of <26 versus <6  $\mu$ mol/l, healthier homocysteine levels are a major clinical opportunity.

#### 1.1.4.1 Antioxidants: Ascorbate to zinc

Ascorbates are the principal antioxidants in eukaryotic cells. As one of but three species that are unable to convert glucose to ascorbate, people are vulnerable to chronic as well as acute scurvy. Ascorbates uniquely set the cell redox electrochemical potential. Ascorbates recycle and regenerate vitamins E, taurine, glutathione, alpha lipoic acid and can even salvage mitochondrial cytochromes. Cumulative antioxidant deficits become repair

7

deficits observed clinically as inflammation, in turn is associated with metabolic acidosis. Antioxidant supplements are provided to protect against oxidative damage, restore cell energy production, rehabilitate mitochondria, and reset homeostatic mechanisms (Jaffe and Brown, 2000). We suggest a functional personalized assessment of ascorbate need (www.PERQUE.com).

#### 1.1.4.2 B-complex vitamins to support methylation

Impaired methylation is commonly reflected in elevations in homocysteine above the healthy value of  $<6 \ \mu mol \ l^{-1}$ . Problems with cell communication, detoxification, and transport result from such impaired methylation. This reframes these common states in physiologic rather than pathologic terms, and offers integrative approaches to care as evidence-based options to be included as first-line comprehensive care.

Healthy alkaline cell balance is clinically assessed through first, morning-urine pH measurements. An increase in alkali-forming foods and supplements is recommended in proportion to individual need to reach the healthy goal range of 6.5–7.5 for first, morning-urine pH. Healthy methylation and detoxification is reflected in a plasma homocysteine of less than 6 mg dl<sup>-1</sup>. Other measures of detoxification such as glucarate, mercapturate, and hippurate urine excretion are discussed elsewhere (Jaffe, 2006). A slow, steady uptake of glucose by managing glycemic load is another important aspect of this approach.

# 2. GLYCEMIC LOAD AS A TOOL FOR BETTER DIGESTIVE AND CARDIOVASCULAR MANAGEMENT

Simple carbohydrates are easily taken up and cause a rapid rise of glucose in the bloodstream, which requires the release of insulin to return blood sugar levels to a safer level. Ongoing stress on the glucose–insulin–energy regulatory system frequently leads to high insulin levels of less functional insulin. Chronically elevated insulin is associated with a series of sequella with adverse long-term health effects. It is increasingly apparent that progress in treating chronic illness requires effective management of food glucose–insulin interaction. We suggest the Alkaline Way to improve insulin sensitivity through corrected metabolic acidosis, antioxidant, and mineral deficits and enhanced toxin removal.

#### 2.1 Associated Signs and Symptoms

The consumption of a high sugar, low fiber diet invites the continuum of weight gain, obesity, metabolic syndrome and diabetes. Associated risks include poor glucose management, with effects such as lipogenesis, loss of insulin sensitivity, development of insulin resistance, and a wide range of cardiovascular and systemic consequences.

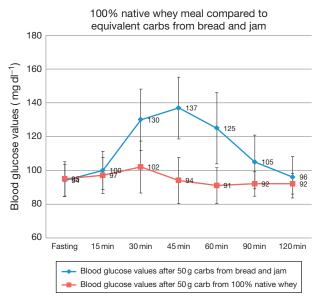


Figure 1.4 Comparison of glycemic response between 100% native whey meal and standard 50 g carbohydrate load from bread and jam.

# 2.2 Self-evaluation

Two tools useful in glycemic management by patients include the glycemic index and calculation of glycemic load.

#### 2.2.1 Glycemic index: Older and less useful

The glycemic index measures the effects of carbohydrates on blood sugar levels (Atkinson et al., 2008). A measure of 100 on the index reflects the typical metabolic response to white sugar (based on research-determined norms). Foods rated 55 or below on the index are identified as healthful because they require lower levels of insulin, defined as 'insulin-sparing' (Foster-Powell et al., 2002). Fructose, certain processed foods as well as the size, complexity and constituents of a meal, can provide conflicting glycemic index results.

#### 2.2.2 Glycemic load: Newer and more useful

The glycemic load is a better measure of the impact of carbohydrate consumption. It takes the glycemic index into account, but provides a fuller picture than the index alone (Murakami et al., 2007). Glycemic load indicates how rapidly a specific carbohydrate food raises blood sugar and factors in the actual amount of the particular carbohydrate being consumed (see Figure 1.4 for an ideal glycemic response to a low glycemic load meal that includes 100% whey). This is evident since the experimental meal was 2.5 times the basic carbohydrate load and still showed a small change in blood glucose. The contrast with the blood glucose change with 50g carbohydrate (bread + jam) was dramatic.

9

This chapter focuses on cellular metabolic acidosis and glycemic load as key clinical aspects of the Alkaline Way. Immune tolerance and delayed allergies are also discussed.

#### 2.3 Intervention: Low to Moderate Glycemic Diet

Glycemic management involves the reduction of refined food products in the diet – foods that trigger the release of high levels of insulin, resulting in lipogenesis and weight gain. By definition, these foods are high on the glycemic index and have a high glycemic load (Jenkins 2004; Riccardi et al., 2008). Foods containing a large proportion of simple carbohydrates include white flour and other refined grains, white rice, white potatoes, and corn, as well as cane sugar, corn syrup, fructose, honey, maple syrup, and other sweet-eners. The optimal diet is high in fresh fruits and vegetables, whole grains, and protein (De Natale et al., 2009; Jenkins, 2004; Riccardi et al., 2008). Note that this is essentially a more alkaline diet, so that the two systems can be used in tandem by both clinicians and consumers. For other reasons, we suggest a minimum non-caloric sweeteners.

# 3. NATIVE WHEY-BASED MEALS AND GASTROINTESTINAL HEALTH

Research suggests that high amounts of animal protein can cause undesirable gastrointestinal issues. Excessive amounts of protein from meat and fish have the potential to increase disease risk as high as threefold in the development of inflammatory bowel disease and ulcerative colitis (Jantchou et al., 2010). A large Italian study of more than 10000 individuals demonstrated a significant association between meat intake and the development of cancer (Tavani et al., 2000).

In selecting optimal protein sources, a quality whey protein provides essential amino acids, such as glutamine and cysteine, and fatty acids, such as conjugated linoleic acid (Belobrajdic et al., 2003). The high cysteine content of whey has been found a superior means of supporting glutathione levels and, therefore, antioxidant function, a finding reported by Bounous (2000).

For healthy glycemic control, a balance of all food groups is essential with an emphasis on nutrients from fiber-rich whole foods that maintain stable blood glucose levels.

#### 4. FOOD ALLERGIES AND SENSITIVITIES

Immune responses to specific foods, chemicals, or contaminants can take the form of classic allergies or of delayed sensitivities. For decades, the conventional approach to allergy focused on histamine immunoglobulin E or IgE reactions, which can trigger a harmless case of hives or life-threatening anaphylactic shock. However, it is now widely recognized that reactivity can be driven by type 1 allergies (typical skin tests or radioallergosorbent (RAST) IgE reactions), or by type 2 antibody reaction (IgA, TgG, or IgM reactive antibodies), type 3 immune complexes, and type 4: T-cell mediated responses. In contrast, helpful neutralizing antibodies are often misunderstood when conventional ELISA or EIA IgG tests are done.

# 4.1 Associated Signs and Symptoms

Eighty percent of food reactions are not IgE-type reactions – rather, they are delayed types of reactions. Reactive antibodies can cause symptoms that become apparent from hours to weeks later, so that they are frequently difficult to identify. Given the range of potential antigens and the various types of responses, a comprehensive food assessment is vital. IgE tests do not measure delayed reactions.

## 4.1.1 The link between allergies and digestive competence

Food intolerance and allergies result from impaired digestion. All of the following issues typically develop before food allergies or intolerances occur:

- *Maldigestion* results in partially digested digestive remnants that are recognized as foreign antigens – thus evoking immune responses to neutralize the foreign invader.
- Infectious and noninfectious foreign antigens (partially digested food) invade the gastrointestinal mucosa/are treated equally as invasive antigens. This means that with increased presence of digestive remnants, the individual has fewer immune defense and repair resources to defend against infection or repair from daily wear and tear. This results in a loss of immune tolerance and emergence of delayed hypersensitivities with a shift from homeostasis to self-attacking immune responses. The Alkaline Way restores homeostasis and tolerance by personalized diagnostics and including therapeutic monitoring to assess how much of the healthy goal states have been achieved.

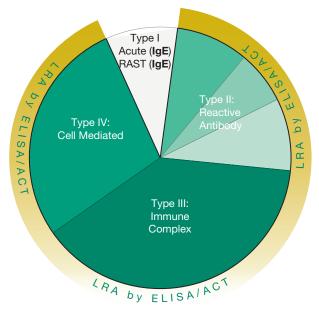


Figure 1.5 Wheel of immune response mechanisms.

#### 4.1.2 Lactose intolerance

With this type of functional impairment, the enzyme that digests milk sugar – lactase – is either not produced or available in such low levels that milk cannot be completely digested. This intolerance is almost always acquired as a byproduct of maldigestion and enteropathy.

#### 4.1.3 Gluten or casein intolerance or sensitivity

Casein is one of the major proteins in milk. Gluten is a protein from grains like wheat. Both are among the most difficult foods to digest. Intolerance to casein or gluten can occur when digestive ability is impaired. Upper abdominal discomfort and alternating constipation and diarrhea sometimes accompany this condition. Functional hypochlorhydria, maldigestion, dysbiosis, and enteropathy are typically the underlying causes.

Gluten intolerance results from maldigestion, food intolerance, or delayed allergic hypersensitivity. Advanced ex vivo LRAs can be employed to measure all delayed allergy pathways.

## 4.2 Evaluation: LRA by ELISA/ACT Tests

Testing for delayed, acquired sensitivities focuses on the type of functional antibody and the specific reactive allergens. Sensitivities reflect the variety of immune reactions present (see Figure 1.5). Older technologies, such as IgG antibody assays, have proven at best only temporarily helpful in the treatment of chronic autoimmune conditions. The tests do not distinguish helpful from harmful antibodies. Newer functional tests such as LRAs are recommended because they detect only the reactive antibodies. These antibodies are indications of a burdened immune system. LRA lab tests can measures reactions just as they occur in the body *(ex vivo)*. This type of functional testing targets antibodies that cannot be distinguished by standard antibody detection systems.

Assessing delayed allergy or hypersensitivity to foods or other chemicals provides an 'immunologic fingerprint' of the foods, chemicals, and medications to which the individual is tolerant and those which their lymphocytes react against. Tests such as the LRA by ELISA/ACT<sup>TM</sup> can sensitively, specifically, and predictively identify underlying causes of immune burdens and increased hospitality to infection, as well as accelerate degenerative, chronic, and autoimmune conditions with less than 3% variance day to day (Jaffe and Kruesi, 1992). These tests have been employed to identify the epigenetic burdens on a given individual's immune system. The causes of autoimmunity are typically provoked by exposures to specific foods or chemicals to which the person has acquired hypersensitivity. Substituting other food choices for reactive items and minimizing chemical exposure, while evoking human healing responses is part of the Alkaline Way. With over 50,000 cases in our database, we suggest this technology helpful in

Nutrient		symptoms of deficiency
Vitamins		
Vitamin A, from mixed natural carotenoids including beta carotene which requires retinol binding protein and zinc for transport into cells; available as a specific supplement and in cod liver oil	Major factor in the growth and healing of the gastrointestinal (GI) tract, intestinal lining, and other mucous membranes in the body; production of protective mucus and SIgA (the primary antibody protecting the GI tract); antioxidant; antibacterial; and	Beta carotene conversion is reduced by intestinal disease, diabetes, hypothyroidism, exposure to toxic metals or chemicals. Symptoms include inflammation and slower healing, rough skin on elbows or underside of forearms, reflux-like symptoms
Thiamine (B <sub>1</sub> )	antimicrobial; DNA synthesis Builds red cells; antioxidant protection; mental focus	Constipation and bloating; cognitive changes
Riboflavin (B <sub>2</sub> )	Energy production; antioxidant activity through glutathione production	Altered iron metabolism; magenta tongue
Niacin (B <sub>3</sub> )	Lowers LDL cholesterol and triglycerides; regulates gene expression	Chronic diarrhea, cracked lips, and mental confusion
Pantothenic acid (B <sub>5</sub> )	Anti-inflammatory, antiviral properties, and wound- healing action; given after abdominal surgery to restart bowel motility	Sluggish motility and bloating; headache, fatigue, insomnia, compromised immune defenses and repair
Pyridoxine (B <sub>6</sub> )	Amino acid metabolism and neurotransmitter synthesis; reduces homocysteine	Irritable Bowel Syndrome (IBS), high blood sugar, and prediabetes; deficiencies can result in lactose intolerance, allergies, or internal bleeding; incomplete conversion of amino acids to neurotransmitters such as serotonin, causing depression or confusion; microcytic anemia; reflux-like symptoms; peripheral neuropathy; potential liver damage
Biotin (B <sub>7</sub> )	Biosynthesis of fatty acids and gluconeogenesis; DNA replication; improves glucose	Accelerated aging, hair loss, brittle nails; accelerated graying; muscle pain

 Table 1.1 Major Nutrients Noted for Beneficial Effects in Digestive Health

 Nutrient
 Metabolic function
 Symptoms of deficiency

Nutrient	Metabolic function	Symptoms of deficiency
Inositol (B <sub>8</sub> ) (hexaphosphate) Folate (B <sub>9</sub> and B <sub>11</sub> ) – low folate can be caused by low levels of activated thyroid (T <sub>3</sub> ), selenium, and trace minerals and by irritation in the upper duodenum due to wheat or gluten sensitivity, low intake of fruits and vegetables, a genetic disorder	tolerance and decreases insulin resistance Essential for fat transport; feeds brain cells Instrumental in healing the GI tract; minimizes periodontal infections; supports immune function; protective against yeast and parasitic infections; strengthens connective tissue; key in methylation and moderation of homocysteine levels; DNA synthesis;	Gastritis; alopecia Deficiency can be caused by impaired absorption and leaky gut syndrome. Can play a role in chronic GI inflammation; bleeding gums; reflux-like symptoms, sinusitis, or frequent colds. Low levels can result in high homocysteine. Anemia resulting in weakness
that interferes with folate absorption, malabsorption, or microscopic parasites; restored in part by supplementing selenium and folic acid; available in activated sublingual form as folinic acid or as injectable folate; must be supplemented at the same time as B <sub>12</sub> ; acts in concert with riboflavin, niacin, vitamin C, zinc, and serine	support of T cell production healing processes	or fatigue, depression, loss of appetite, and weight loss; forgetfulness, irritability; sore red tongue. Potential liver damage.
Betaine, trimethylglycine (B $_{10}$ and B $_{15}$ )	Especially protective, lowering homocysteine by recycling it into methionine; prevents fatty liver; characterized by high triglycerides; acts as a digestive aid	Protein maldigestion and high homocysteine; potential liver damage
Hydroxocobalamin (B12) – essential nutrient in metabolism, absorbed in the ileum and reduced by ileitis, celiac disease, bacterial and parasitic infections, chronic IBS, Crohn's disease, low intrinsic factor (genetic disorder), or a strict vegan diet; available in meats or through sublingual	Instrumental in healing the GI tract and a source material for competent GI defenses; key factor in methylation, lowering homocysteine levels; essential for enzyme production and energy production, DNA synthesis, and health of the nervous system	Deficiency can be caused by impaired absorption and leaky gut syndrome. Symptoms include impaired protein digestion, digestive disorders, high or low stomach acid, peptic ulcers, fatigue, or weakness, bloating, diarrhea, or anemia. Additional symptoms: numbness, tingling of hands and feet; pernicious

 Table 1.1 Major Nutrients Noted for Beneficial Effects in Digestive Health—cont'd

 Nutrient
 Metabolic function
 Symptoms of deficience

Nutrient	Metabolic function	Symptoms of deficiency
supplements or injections; must be supplemented at the same time as folate; acts in concert with riboflavin, niacin, vitamin C, zinc, and serine		anemia linked to autoimmune conditions; smooth tongue, beet red; potential liver damage; premature aging and a form of irreversible dementia
Para amino benzoic acid (Bx)	Metabolism and utilization of amino acids; supports folates production	Irritability, depression, skin problems, eczema, headaches digestive disorders, and hair prematurely gray
Choline as citrate	Important in moderating homocysteine levels	Deficiency linked to high homocysteine; insomnia, fatigue; in the extreme, heart disease, liver and kidney dysfunction
Choline citrate	Works with inositol to balance communication between cells	Impaired digestion of fat; low acetylcholine; reduced mental clarity
Ascorbate (vitamin C) as buffered ascorbate (calcium, magnesium, potassium, zinc ascorbate)	Controlling inflammation and immune resistance. Collagen and structural protein formation; antioxidant; glutathione enhanced; antihypertensive; detoxifying agent for heavy metals	Immune suppression; inflamed and bleeding gums, chronic GI infection or inflammation, especially in the gut wall; leaky gut, including bloating, soreness, malabsorption, toxicity, delayed gastric emptying, and resulting free radical damage
Cholecalciferol (vitamin D) – hormone adhesion molecule	Anti-inflammatory; regulates calcium homeostasis and absorption, compromising function of glands, impairing digestion; supports cognitive health; vital in production of digestive enzymes	Increased vulnerability to infection; impaired mineral metabolism, particularly calcium; compromised digestion; poor blood sugar regulation; altered bone and joint health; diabetic conditions
Tocopherols and tocotrienols (vitamins E)	Primary backup when cellular antioxidants are compromised due to inflammation; protects cell membrane from oxidative damage; antiatherogenic and neuroprotective	Fat malabsorption; vitamin E deficiency anemia in infants; peripheral neuropathy
	Supports appropriate blood clotting	Deficiencies rare, except in the case of heavy antibiotic

Table 1.1	Major Nutrients Noted for Beneficial Effects in Digestive	Health—cont'd
Nutrient	Metabolic function	Symptoms of deficier

Nutrient	Metabolic function	Symptoms of deficiency
Vitamin K, fat-soluble nutrients produced in the large intestine <b>Cofactors</b>		usage, malabsorption, or major damage to the intestines
Coenzyme Q <sub>10</sub>	Antioxidant; cardioprotective; neuroprotective	Periodontal disease; impaired ATP energy production; statin medication typically reduces $CoQ_{10}$ by 50%.
Fatty Acids		
Omega 3 essential fatty acids, EPA/DHA – available in fish oil and in those able to convert it, in flax oil	Resistance to infection; anti- inflammation effects; supports cell hydration and functionality, preventing brittle cell walls; regulates calcium metabolism; turns on inflammatory and anti- inflammatory defenses at the cellular level through prostaglandins; lower triglycerides. EPA has antithrombotic effects; DHA is vital for normal brain	Increased susceptibility to infection and inflammation; increased allergies; symptoms from dry skin, rashes, and hair loss to incontinence; deficiencies can result in either constipation or diarrhea; a factor in inflamed nerves and neurological disorders
Omega 6s – a source of linoleic acid, which is the basis for gamma linoleic acid	development and function Regulate metabolism; promote the growth of skin and hair; play a role in brain function	Deficiency – increased susceptibility to infection; thinning hair and dry skin, dandruff or eczema; poor concentration, learning disabilities Excess – contribute to inflammatory conditions due to the buildup of arachidonic acid
Short-chain fatty acids such as butyrate – found in butter and cream; also made from starches and proteins by digestive flora	The preferred fuel for cells in the colon lining and major factor in digestive health	Increased risk of chronic colitis and eventually cancer
GABA	Calms and stabilizes nervous system	Loss of mental clarity; more aberrant thought
<b>Minerals</b> Calcium – as the principle mineral in the teeth, essential	Essential to muscle growth and function, including heart	Deficiency – unformed stools, increased risk of colon cancer;

Table 1.1	Major Nutrients Noted for Beneficial Effects in Digestive	e Health—cont'd
Nutrient	Metabolic function	Symptoms of deficiency

Nutrient	Metabolic function	Symptoms of deficiency
to mastication in order to prepare food for digestion	beat; transmission of nerve impulses	weakened teeth and bones Excess – muscle and
Copper – trace mineral Iron – mineral	Reduces hyperacidity; required in various enzyme processes; assists in the absorption of iron; intracellular antioxidant Required for the production of red blood cells and the transport of oxygen to cell; resistance to infection; energy	abdominal pain; kidney stones Can become deficient with a diet high in sweets, resulting in hyperacidity, indigestion and dyspepsia; gastritis or ulcers Deficiency –anemia Excess – constipation, abdominal cramps, black stools
Magnesium – mineral	production Essential to appropriate motility and in some cases, an effective, inexpensive solution	Constipation; regurgitation due to constriction of lower esophagus
Manganese – trace mineral	to chronic constipation Useful in the treatment of digestive disorders; antioxidant; cofactor in enzyme, glucose, and lipid metabolism	Deficiency – a factor in the development of diabetes; the development of myasthenia gravis (muscle weakness) Excess – hypertension; symptoms resembling Parkinson's
Selenium as selenomethionine – trace minerals found in whole grain breads and cereals	Reduces hyperacidity; improves immune resistance and healing of all kinds of GI problems; supports production of both folate and T3; antioxidant	Hyperacidity; chronic indigestion; increased risk of gastric cancer
Zinc – trace mineral	Paired with vitamin A, essential to the production of secretory IgA (SIgA), the most prevalent antibody that protects the gut; antioxidant	Deficiency – Increased infection due to low SIgA levels Excess – hyperacidity, with indigestion and dyspepsia
Amino Acids		
Amino acids – derived from protein breakdown; provide the basis of protective antibodies	Essential for effective immune defenses; intracellular antioxidant	To perform antioxidant functions, requires trace minerals including selenium, zinc, copper, and manganese
Carnitine – specialized amino product, one of the most	Nourish the GI tract and gut lining; provide energy to transport micronutrients into	Chronic bowel irregularity; bloating; fatigue

Table 1.1 Major Nutrients Noted for Beneficial Effects in Digestive Health—cont'dNutrientMetabolic functionSymptoms of deficiency

Nutrient	Metabolic function	Symptoms of deficiency
prevalent aminos in digestive tract	the bloodstream; supports mitochondria in conversion of fats into energy within the cell	
Cysteine – amino acid derived from methionine, from sulfurous vegetables, and animal proteins	Intracellular antioxidant	To perform antioxidant functions, requires trace minerals including selenium, zinc, copper, and manganese
Glutathione – peptide manufactured from glycine (a form of glutamine), glutamic acid, and cysteine found in sulfurous vegetables and animal protein	The primary antioxidant in the body; a major cellular defense; essential to energy production; detoxification of carcinogens; building DNA and proteins	Chronic fatigue; hemolytic anemia; metabolic acidosis
Glycine – metabolic byproduct of glutamine, nucleic acid precursor	One of the most important factors in gut health; detoxification; synthesis of bile acids, and of glutathione; construction of RNA and DNA	Deficiency – poor energy production Excess – fatigue People with kidney or liver disease should not consume
L-glutamine – the amino acid most prevalent in the digestive tract; recycled by Pyridoxal Alpha Ketoglutarate (PAK)	Nourish the digestive tract and gut lining, which enhances nourishment throughout the body	Chronic bowel irregularity; bloating; fatigue
Methionine – amino acid derived from sulfurous vegetables and animal proteins, which is converted to cysteine, a precursor of glutathione	Protein synthesis; methylation (a primary form of detoxification which occurs in every cell of the body); essential in the production of adrenaline and creatine, as well as choline and carnitine	Excess – With the intake of animal protein, methionine is converted into excess homocysteine. Chronic levels of homocysteine increase the risk for all major degenerative diseases
Taurine	Antioxidant, role in detoxification; improves insulin resistance by increasing the excretion of cholesterol	High homocysteine; reduced bile acids; gallstones, abdominal pain, intolerance of fat
Glucosamine and other sugar aminos – precursor in the synthesis of glycosylated proteins and lipids Probiotics and related factors	Enhances defenses by binding to and disposing of undesirable microbes	Deficiency occurs with aging; dietary sources often inadequate
Fiber – ideally 80% soluble fiber and 20% insoluble fiber	Lower carbohydrate content to food, and therefore, lower weight gain; cleansing	Slowed stool motility

 Table 1.1 Major Nutrients Noted for Beneficial Effects in Digestive Health—cont'd

 Nutrient
 Metabolic function
 Symptoms of deficient

Nutrient	Metabolic function	Symptoms of deficiency
	function; prevention of pathogen adherence to the gut wall; improved cholesterol levels; vitamin activation; improved elimination; toxin reduction	
Prebiotics – fibers, soluble and insoluble, FOS (fructooligosaccharides), non absorbable carbohydrates	Support the growth of flora and lactic acid; promote beneficial fermentation, reducing ammonia byproducts	Beneficial when signs of ammonia intoxication are present, such as headache and fatigue; FOS not well tolerated by those with sensitivities or are lactose or carbohydrate intolerance
Probiotics – beneficial flora	Production of nutrients such as butyrate; protection against pathogens; production of digestive enzymes; reduction of lipid levels; metabolism of nutrients such as folate	

 Mutrient
 Metabolic function
 Symptoms of deficiency

Source: Gaby A. Nutritional Medicine. Hendler, S.S., Rorvik, D.M., 2000. PDR for Nutritional Supplements, second ed. Thomson Reuters, New York; Jaffe, R., 2010. The Alkaline Way: Integrative management of autoimmune conditions. Townsend Letter for Doctors and Patients. November, pp. 44–51; Shils, M.E., Shils, M., Ross, A.C., Caballero, B., Cousins, R.J., 2005. Modern Nutrition in Health and Disease, tenth ed. Lippincott Williams and Wilkins, Philadelphia, PA.

all conditions where immune tolerance is lost. This includes all autoimmune and most chronic, degenerative ills.

# 4.3 Intervention: Hypoallergenic Diet

By avoiding offending food and chemical substances, following an alkalinizing diet, and utilizing targeted supplementation, the body can stimulate healing and induce repair. This concept has been successfully tested in controlled outcome studies on diabetes (Jaffe et al., 2004, 2006), as well as fibromyalgia and chronic fatigue syndrome (Deuster and Jaffe, 1998). Clinical data indicate that other autoimmune conditions respond to this approach as well. The Akaline Way includes the identification of acute and delayed food and chemical allergies and intolerances. This allows for a diet that can be digested, assimilated, and eliminated efficiently, while enhancing the individual's vitality and homeostatic competence. Mental and physical exercises are as important for gastrointestinal health as they are for any organ system. A high-nutrient, low-toxicity diet in the context of a lifestyle of mindfulness and gratitude rounds out the Alkaline Way to sustainable health.

## 5. THE ROLE OF SPECIFIC NUTRIENTS IN DIGESTIVE HEALTH

When chronic digestive disorders are present, the use of nutritional supplementation can improve clinical outcome. Thousands of research studies evaluating nutritional supplements have shown the benefits of specific nutrients in treating a wide range of complex conditions. The following table provides a brief overview of major nutrients that have been found to play an important role in digestive disorders. Supplementation with standardized ingredients makes it possible to provide nutrients at a level that will support active metabolic function, while improving compromised digestion and assimilation based on individual requirements revealed through their functional, integrative approach (Table 1.1).

## 6. CONCLUSION

The combined effects of individualized dietary programs, supplementation targeted to the specific needs of the patient, and reduction of allergenic stimulation offer the provider viable tools for conservative and effective clinical management of cardiovascular conditions. In this context, treatment strategy includes a detailed history of health, lifestyle, and diet. Laboratory assessment, development of a case-specific treatment plan that includes diet and nutritional supplements, and a long-term plan to support patient motivation and compliance, reinforced by ongoing caring and competence.

#### REFERENCES

- Atkinson, F.S., Foster-Powell, K., Brand-Miller, J.C., 2008. International tables of glycemic index and glycemic load values. Diabetes Care 31 (12), 2281–2283.
- Bazhin, N., 2007. Proton gradient energy in the catalytic ATP synthesis. Reaction Kinetics and Catalysis Letters 90, 401–404.
- Belobrajdic, D.P., McIntosh, G.H., Owens, J.A., 2003. Whey proteins protect more than red meat against azoxymethane induced ACF in Wistar rats. Cancer Letters 198, 43–51.
- Bounous, G., 2000. Whey protein concentrate (WPC) and glutathione modulation in cancer treatment. Anticancer Research 20, 4785–4792.
- Brown, S.E., Trivieri Jr., L., 2006. The Acid Alkaline Food Guide: A Quick Reference to Foods and Their Effect on pH Levels. Square One Publishers, Garden City Park, NY.
- Budde, R.A., Crenshaw, T.D., 2003. Chronic metabolic acid load induced by changes in dietary electrolyte balance increased chloride retention but did not compromise bone in growing swine. Journal of Animal Science 81, 197–208.
- De Natale, C., Annuzzi, G., Bozzetto, L., et al., 2009. Effects of a plant-based high-carbohydrate/high-fiber diet versus high-monounsaturated fat/low-carbohydrate diet on postprandial lipids in type 2 diabetic patients. Diabetes Care 32, 2168–2173.
- De Young, L., 1994. Mayo Clinic Diet Manual: A Handbook of Nutrition Practices, seventh ed. Mosby, St. Louis, MO.
- Deuster, P.A., Jaffe, R., 1998. A novel treatment for fibromyalgia improves clinical outcomes in a community based study. Journal of Musculoskeletal Pain 6, 133–149.
- Foster-Powell, K., Holt, S.H.A., Brand-Miller, J.C., 2002. International table of glycemic index and glycemic load values. American Journal of Clinical Nutrition 76, 55–56.

#### Author's personal copy

- Gonick, H.C., Goldberg, G., Mulcare, D., 1968. Reexamination of the acid-ash content of several diets. American Journal of Clinical Nutrition 21, 898–903.
- Jaffe, R., 2006. Managing toxic minerals, biocides, hormone mimics, solvents and chemical disruptors. In: Kohlstadt, I., (Ed.), Nutrition for Musculoskeletal Health. Marcel Dekker/CRC Press, New York (Chapter 30).
- Jaffe, R., Brown, S., 2000. Acid–alkaline balance and its effect on bone health. International Journal of Integrative Medicine 2, 7–18.
- Jaffe, R., Kruesi, O., 1992. The biochemical immunology window: a molecular view of psychiatric case management. Journal of Applied Nutrition 44, 26–43.
- Jaffe, R., Mani, J., DeVane, J., Mani, H., 2006. Tolerance loss in diabetics: association with foreign antigen exposure. Diabetic Medicine 23, 924–925.
- Jaffe, R., Mani, J., Trocki, T., Mehl-Madrona, L., 2004. First line comprehensive care: the diabetes continuum of insulin, glucose, energy dysregulation: better clinical management of causes improves outcomes, reduces risks and vascular complications. Original Internist 11, 11–27.
- Jantchou, P., Morois, S., Clavel-Chapelon, F., Boutron-Ruault, M.C., Carbonnel, F., 2010. Animal protein intake and risk of inflammatory bowel disease: the E3N prospective study. American Journal of Gastroenterology 105, 2195–2201.
- Jehle, S., Zanetti, A., Muser, J., Hulter, H.N., Krapf, R., 2006. Partial neutralization of the acidogenic western diet with potassium citrate increases bone mass in postmenopausal women with osteopenia. Journal of the American Society of Nephrology 17, 3213–3222.
- Jenkins, D.J., Kendall, C., Marchie, A., Augustin, L., 2004. Too much sugar, too much carbohydrate, or just too much? American Journal of Clinical Nutrition 79, 711–712.
- Lee, M.M., Shen, J.M., 2008. Dietary patterns using Traditional Chinese Medicine principles in epidemiological studies. Asia Pacific Journal of Clinical Nutrition 17 (Suppl. 1), 79–81.
- Lim, S., 2007. Metabolic acidosis. Acta Medica Indonesiana 39, 145-150.
- Liu, S., Willett, W.C., Stamfer, M.J., et al., 2000. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in women. American Journal of Clinical Nutrition 71, 1455–1461.
- Maurer, M., Riesen, W., Muser, J., Hulter, H.N., Krapf, R., 2003. Neutralization of Western diet inhibits bone resorption independently of K intake and reduces cortisol secretion in humans. American Journal of Physiology. Renal Physiology 284, F32–F40.
- Murakami, K., Sasaki, S., Okubo, H., et al., 2007. Dietary fiber intake, dietary glycemic index and load, and body mass index: a cross-sectional study of 3931 Japanese women aged 18–20 years. European Journal of Clinical Nutrition 61, 986–995.
- Murakami, K., Sasaki, S., Takahashi, Y., Uenishi, K., 2008. Japan dietetic students' study for nutrition and biomarkers group. Association between dietary acid–base load and cardiometabolic risk factors in young Japanese women. British Journal of Nutrition 100, 642–651.
- Riccardi, G., Rivellese, A.A., Giacco, R., 2008. Role of glycemic index and glycemic load in the healthy state, in prediabetes, and in diabetes. American Journal of Clinical Nutrition 87, 2698–274S.
- Sahni, V., Rosa, R.M., Battle, D., 2010. Potential benefits of alkali therapy to prevent GFR loss: time for a palatable 'solution' for the management of CKD. Kidney International 78, 1065–1067.
- Schulze, M.B., Manson, J.E., Willett, W.C., Hu, F.B., 2003. Processed meat intake and incidence of type 2 diabetes in younger and middle-aged women. Diabetologia 46, 1465–1473.
- Shafiee, M.A., Kamel, K.S., Halperin, M.L.A., 2002. Conceptual approach to the patient with metabolic acidosis application to a patient with diabetic ketoacidosis. Nephron 92 (Suppl. 1), 46–55.
- Souto, G., Donapetry, C., Calviño, J., Adeva, M.M., 2011. Metabolic acidosis-induced insulin resistance and cardiovascular risk. Metabolic Syndrome and Related Disorders 9 (4), 247–253.
- Tavani, A., La Vecchia, C., Galus, S., et al., 2000. Red meat intake and cancer risk: a study in Italy. International Journal of Cancer 86, 425–428.
- Whiting, S.J., Bell, J., 2002. First morning urine measured with pH paper strips reflects acid excretion. Proceedings of the American Society for Bone and Mineral Research. American Society for Bone and Mineral Research, Washington, DC.

Zeidel, M.L., Silva, P., Seifter, J.L., 1986. Intracellular pH regulation and proton transport by rabbit renal medullary collecting duct cells. Role of plasma membrane proton adenosine triphosphatase. Journal of Clinical Investigation 77 (1), 113–120.

#### **RELEVANT WEBSITES**

http://www.Healthstudiescollegium.org http://www.ELISAACT.com http://www.PERQUE.com http://www.PERQUEWheyGuard.com http://www.ncbi.nlm.nih.gov/pubmed