BIOACTIVE FOOD AS DIETARY INTERVENTIONS FOR LIVER AND GASTROINTESTINAL DISEASE

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Edited by

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PREFACE: LIVER AND GASTROINTESTINAL HEALTH

Optimum functioning of the liver and gastrointestinal systems is critical for health. They are critical for the digestion and absorption of nutrients and foods to produce growth. Nutrient and non-nutrients are important modulators of the liver function. The symptoms related to liver dysfunction include both physical signs and symptoms of abnormal absorption of fat, changes in blood sugar, and altered metabolism. This book provides evidence that foods and their compounds can modify some of these diseases. Expert reviews are provided on liver function as people mature and mechanisms of fatty liver as modified wild and bioactive foods for hepato-protection and digestion. The data supporting actions of bioactive, and especially Chinese foods, to prevent and treat liver diseases are defined by experts. Specific individual foods and herbs have shown specific liver disease benefits including: betal leaf, selected Indian herbs, gooseberries, and curcumin. Non-botanical materials in reviews show promise, including probiotics. In defining mechanisms including antioxidant capacity of antocyanins, extracts of pomegranate and medicinal plants as well as specifically their carotenoids show benefits in modifying liver function in reviews. Phytochemicals' involvement in liver and gastrointestinal health is concisely defined.

More diverse information is provided about bioactive foods in the therapy of gastrointestinal diseases and functions, which are many and important in health. In this book the gastrointestinal focuses on the stomach and intestine. It releases hormones that help regulate the digestive process and is subject to many diseases and problems. An overview reviews functional assessment of gastrointestinal tract function and alkaline in digestive health. Reviews generally define the protective effects of bioactive botanical foods. The human microbiome diseases are defined in a metagenomic approach. Specific classes and types of foods are reviewed for selected gastrointestinal diseases. For example, a chapter defines the role of milk bacteria in gastrointestinal allergies. Then selected reviews of prebiotics and probiotics documented their value in irritable bowel syndrome, mucosal immunity, and viral infections. Their lactic acid and its stimulation of folate production are reviewed as mechanisms of probiotic gastrointestinal health. The actions of non-bioactive fiber on bowel health are reviewed. Several additional reviews focus on polysaccharides from soy sauce and fiber from apples, sources readily available to the public. Dietary fibers and cholelithiasis are shown to be important in lipid lowering. Specific small molecules and defined substances are important in gastrointestinal health. Omega 3 fatty acids are shown to be an interesting story of biotechnology leading to health. One review describes fatty acids in inflammatory bowel diseases. Black plum has a long research history, which is summarized on its phytochemicals in health, as do bioactive

polyphenols on other mucosal diseases of the lung. Indian plants have a historical application to health such as spices in treatment of ulcerative colitis. Ginger and basil are reviewed as an ancient remedy, while another expert gives an overview of medicinal plants in gastrointestinal diseases. Finally not all bioactive materials are safe. Therefore the dangers of herbal weight loss supplements and alcohol on gastrointestinal functions are reviewed. Bioactive foods however, as reviewed, appear to have a role in preventing the epidemic on non-communicable diseases. Clearly bioactive herbs, foods and their extracts can play key roles in liver function and gastrointestinal health.

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CHAPTER 1

The Alkaline Way in Digestive Health

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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 Seifter, 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

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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 osteoblastic 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).

Figure 1.1 Picture of pH strips.

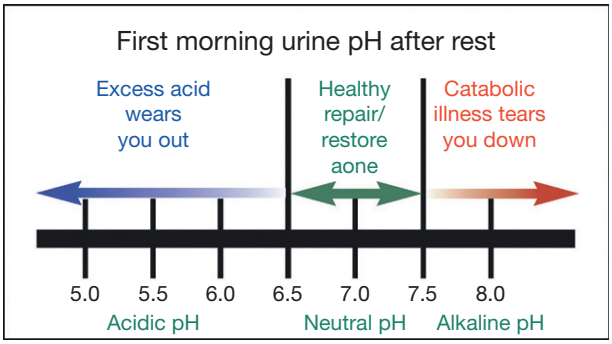

Figure 1.2 Interpretation of first, morning-urine measurements.

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

Food & Chemical Effects on Acid / Alkaline Body Chemical Balance™

Most Alkaline	More Alkaline	Low Alkaline	Lowest Alkaline	Food Category	Lowest Acid	Low Acid	More Acid	Most Acid
Baking Soda	Spices/Cinnamon	•Herbs (most): Arnica,	White Willow Bark	**Spice/Herb**	Curry	Vanilla	Nutmeg	Pudding/Jam/Jelly
	Valerian	Bergamot, Echinacea	Slippery Elm			Stevia		
	Licorice	Chrysanthemum,	Artemesia Annua					
	•Black Cohash	Ephedra, Feverfew,						
	Agave	Goldenseal, Lemongrass						
		Aloe Vera						
		Nettle						
		Angelica						
Sea Salt			*Sulfite*	**Preservative**	*MSG*	*Benzoate*	*Aspartame*	*Table Salt (NaCL)*
Mineral Water	•Kambucha	•Green or Mu Tea	Ginger Tea	**Beverage**	*Kona Coffee*	*Alcohol*	*Coffee*	*Beer , 'Soda'*
						Black Tea		Yeast/Hops/Malt
	Molasses	Rice Syrup	•Sucanat	**Sweetner**	Honey/Maple Syrup		*Saccharin*	*Sugar /Cocoa*
	Soy Sauce	Apple Cider Vinegar	•Umeboshi Vinegar	**Vinegar**	Rice Vinegar	Balsamic Vinegar	Red Wine Vinegar	White/Acetic Vinegar
•Umeboshi Plum		•Sake	•Algae, Blue Green	**Therapeutic**		*Antihistamines*	*Psychotropics*	*Antibiotics*
			•Ghee (Clarified Butter)	**Processed Dairy**	Cream/Butter	Cow Milk	•Casein, Milk Protein,Cottage Cheese	*Processed 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	•Duck Egg	**Egg**	Chicken Egg			
				Meat	Gelatin/Organs	Lamb/Mutton	Pork/Veal	Beef
				Game	•Venison	Boar/Elk/-Game Meat	Bear	
				Fish/Shell Fish	Fish	Mollusks	•Mussel/Squid	Shell Fish (Processed)
						Shell Fish (Whole)		•Lobster
				Fowl	Wild Duck	Goose/Turkey	Chicken	Pheasant
			Oat		•Triticale	Buckwheat	Maize	Barley
			'Grain Coffee'	**Grain**	Millet	Wheat	Barley Groat	*Processed Flour*
			•Quinoa	**Cereal**	Kasha	•Spelt/Teff/Kamut	Corn	
			Wild Rice	**Grass**	Brown Rice	Farina/Semolina	Rye	
			•Amaranth			White Rice	Oat Bran	
			Japonica Rice					
	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
	Chestnut	Cod Liver Oil	Coconut Oil	**Oil**	Sunflower Oil	Safflower Oil	*Lard*	Walnut
	Pepper	Almond	Olive/Macadamia Oil		Pine Nut	Tapioca	Pecan	Brazil Nut
		•Sprout	Linseed/Flax Oil		Canola Oil	•Seitan or Tofu	Palm Kernel Oil	*Fried Food*
Lentil	Kohlrabi	Potato/Bell Pepper	Brussel Sprout		Spinach	Split Pea	Green Pea	Soybean
Brocoflower	Parsnip/Taro	Mushroom/Fungi	Beet	**Bean**	Fava Bean	Pinto Bean	Peanut	Carob
•Seaweed	Garlic	Cauliflower	Chive/Cilantro	**Vegetable**	Kidney Bean	White Bean	Snow Pea	
Nori|Kombu|Wakame|Hijiki	Asparagus	Cabbage	Celery/Scallion		Black-eyed Pea	Navy/Red Bean		
Onion/Miso	Kale/Parsley	Rutabaga	Okra/Cucumber	**Legume**	String/Wax Bean	Aduki Bean	Legumes (other)	
•Daikon/Taro Root	Endive/Arugula	•Salsify/ Ginseng	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			
•Burdock/•Lotus Root	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		•Pickled Fruit	Prune	Pomegranate	
Raspberry	Citrus	Apple	Blueberry		Dry Fruit	Tomato		
Watermelon	Olive	Blackberry	Pineapple Juice	**Fruit**	Fig			
Tangerine	•Dewberry	Cherry	Raisin, Currant		Persimmon Juice			
Pineapple	Loganberry	Peach	Grape		•Cherimoya			
	Mango	Papaya	Strawberry		Date			

•Therapeutic, gourment, or exotic items *Italicized items are NOT recommended*

Prepared by Dr. Russell Jaffe, Fellow, Health Studies Collegium. Reprints available from Health Studies Collegium, 44621 Guilford Drive, #150, Ashburn, VA 20147, 800.328.7372. Sources include USDA food data base (Rev 9 & 10), *Food & Nutrition Encyclopedia; Nutrition Applied Personally* , by M. Walczak; *Acid & Alkaline* by H. Aihara. Food growth, transport, storage, processing, preparation, combination, & assimilation influence effect intensity. Thanks to Hank Liers for his original work.

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

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 μmol/l. With a combined 20-fold risk difference between a homocysteine of <26 versus <6 μmol/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

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^{-1}. 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.

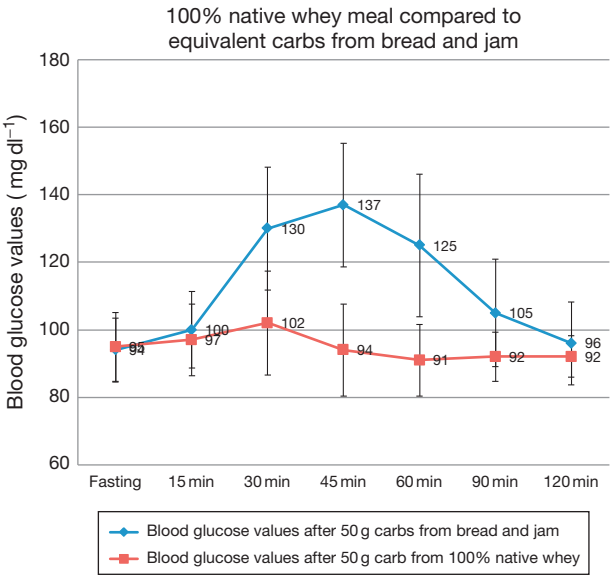

Figure 1.4 Comparison of glycemic response between 100% native whey meal and standard 50 g carbohydrate load from bread and jam.

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.