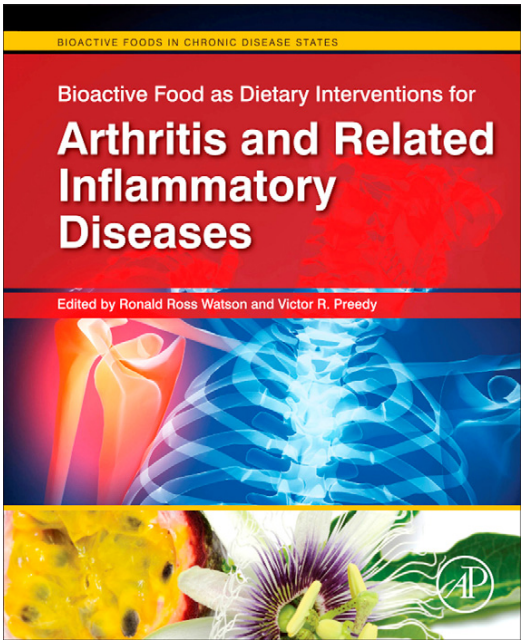

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CHAPTER 7

The Alkaline Way: Integrative Management of Rheumatoid Arthritis and Other Autoimmune Conditions

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Decades of research on immune function have shown that healthy immune systems are tolerant, resilient, responsive, and competent. Conversely, unhealthy immune systems tend to be intolerant, restricted, indiscriminate, and imbalanced. Yet at present, despite our expanded knowledge of immune function, autoimmune (AI) disorders and chronic illness are becoming more and more prevalent. In the United States, for example, more than half of all adults and a rapidly growing proportion of children experience some type of health condition that reflects immune compromise (Hoffman et al., 1996).

Rheumatoid arthritis (RA) is a classic AI condition, characterized by persistent synovitis, systemic inflammation, and autoantibodies (particularly to rheumatoid factor and citrullinated peptide). In industrialized countries, RA affects 0.5–1.0% of adults, with 5–50 new cases per 100 000 annually (Scott et al., 2010). RA is usually seen more frequently in women and in the elderly. Up to 50% of the risk for RA may be attributable to genetic factors, associated with a susceptibility to other AI conditions (Barton et al., 2009; Kurreeman et al., 2010; Zhernakova et al., 2007). Smoking is the primary environmental or epigenetic risk (Franceschi et al., 2005). Hormone disrupters, essential protective nutrient deficit, and distress are other epigenetic contributors.

In RA, unhealthy immune responses are focused on certain joints and repair deficits are reflected in pain, inflammation, and tissue pathology. New criteria for diagnosing RA, established in 2010 by the American College of Rheumatology and the European League against Rheumatism include (1) the confirmed presence of synovitis in at least one joint, (2) the absence of an alternative diagnosis better explaining the synovitis, (3) elevated symptoms, including the number and site of involved joints, serological abnormalities, elevated acute-phase response, and symptom duration (Aletaha et al., 2010).

1. AN INTEGRATIVE APPROACH

Integrative sciences focus on causes of RA and associated AI conditions in contrast to the conventional symptom driven care. The goal of this approach is to remove obstacles to

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recovery. This includes identification of antigen load on the immune system through advanced cell culture tests. In addition, individual needs for essential nutrients are verified through predictive tests of core physiologic functions.

Diet is another important aspect of clinical intervention. To determine the importance of diet in the treatment of RA, Swedish researchers analyzed data from three RA studies and concluded "Statistically significant correlations were found between diet and three disease outcome variables—acute-phase response, pain score, and physical function. Body weight was ... not significant when diet was taken into account" (Sköldstam et al., 2005).

This approach emphasizes physiology 1st. Clinical strategies include improving cell acid–alkaline balance, increasing antioxidant sufficiency, thus lowering oxidative stress, enhancing repair ability, and minimizing inflammation. Sustained remission based on oral tolerance and homeostasis is the goal of this integrative approach, sometimes summarized as the Alkaline Way to sustainable health. This program has achieved impressive rates of remission in conditions that are more difficult to manage, including diabetes (Jaffe et al., 2006), fibromyalgia (Deuster and Jaffe, 1998), and osteoporosis (Jaffe and Brown, 2000), thus demonstrating how forgiving and responsive the human body can be when biochemical balance and immune tolerance are restored. Our case experience is that this Alkaline Way works as well for RA as for any AI or immune dysfunction situation.

1.1 Evaluating Markers of Inflammation, Detoxification, and Immune Function

The goal of these evaluations is to assess underlying causal factors in illness rather than pathologic consequences. In ill health, tolerance and homeostatic resilience are reduced, and in some cases, they are lost. AI and immune dysfunction occurs commonly, and commonly together. They reflect the impairment or loss of immune defenses and repair tolerance and competences.

A Health Studies Collegium estimate is that the loss of tolerance and homeostasis accounts for one-third of all chronic diseases. These are the inflammatory conditions, the conditions of cumulative repair deficit that reduce life quality and increase costs of primarily palliative care. Inflammatory lab markers that indicate repair deficit include elevations of the following:

- Sedimentation rate
- Unexplained elevation of fibrinogen, ferritin, and microalbumin, among other inducible "inflammatory" proteins
- High-sensitivity C-reactive protein
- Tumor necrosis factor (TNF)
- Oxidative stress markers such as oxidized low-density lipoprotein/high-density lipoprotein LDL/HDL and 8-oxo-guanine

- Prealbumin in urine
- Elevated interleukins: IL-2, IL-6, and IL-12, among other cytokines

1.2 Testing for Delayed Antigen Reactions to Food and Chemicals

The extent of inflammatory immune activity in RA is well documented. Clinical trials, genetic research, and animal studies have been conducted to explore both AI and allergenic processes in RA.

- *Genetic aspects of AI reactivity*. Specific locations in the genome associated with RA have been identified that "increase the risk of other autoimmune conditions" (Zhernakova et al., 2007). Diseases associated with RA at various genetic loci include AI thyroid conditions, celiac disease, juvenile RA, psoriatic arthritis, systemic lupus, and type 1 diabetes (Barton et al., 2009; Kurreeman et al., 2010).
- *Food sensitivities*. The effects of diet on RA are reflected in a German study at an integrative medicine hospital, which compared the effects of a Mediterranean diet and an 8-day fasting period (Michalsen et al., 2005). Researchers found clinical improvement in the fasting group but not with the Mediterranean diet. Improvement in RA with fasting has been reported in other studies and holds implications for the role of antigen stimulation in these conditions.
- *Nonspecific allergens*. In other studies, researchers have noted a broad range of nonspecific allergenic tendencies in arthritic populations. For example, "self-reported and observed cutaneous abnormalities are more common in patients with rheumatoid arthritis than in controls with non-inflammatory disease" (Douglas et al., 2006).

In the context of this inflammatory profile, strategies to reduce antigen load can be an important step in clinical management. Various clinical tests are currently in use for assessing an individual's adverse response to environmental antigens. Antibodies capable of inciting a delayed response include IgA, IgG, or IgM. We suggest the Lymphocyte Response Assay (LRA) by ELISA/ACT tests and associated Health Assessment Questionnaire (HAQ) to personalize care plans and improve outcomes.

1.2.1 Antibody assays

Antibody assays are frequently performed to evaluate for immunoglobulin G (IgG; Laevy, 2006). These IgG antibodies reflect the immunologic memory of the individual. However, there are challenges in the clinical interpretation of IgG antibodies against a specific antigen. Four subclasses of IgG have been identified, which have different biologic functions and vary independently under different clinical conditions. For example, only IgG4 is cytophilic for mast cells. Thus, some IgG antibodies are protective and others reflect an adverse response.

In fact, most IgG antibodies are neutralizing and protective; only a minority of antibodies is actually harmful. It is only when antibodies are reactive that they provoke symptoms (Lux et al., 2010). However, IgG tests record all antibody activity and do not differentiate between helpful and harmful stimuli.

Measurement of IgG antibodies also omits information about IgA (Woof and Kerr, 2006), as well as IgM reactors, requiring multiple subclass assays to provide the most accurate clinical information.

1.2.2 Immune complexes

Immune complexes can also be assayed through a variety of techniques, each with its own methodological limitations. Measurement of this and other aspects of cell-mediated immune response can be particularly useful in immune complex disorders (see Table 7.1).

1.2.3 Lymphocyte response assays

This lymphocyte response assays (LRA) were developed to evaluate the underlying functional *causes* of autoimmunity, including exposures to foods or chemicals to which the body has become hypersensitive, marked by unhealthy reactions involving harmful antibodies, immune complexes, and/or T-cell lymphocyte responses.

1.2.3.1 Reducing immune reactivity

LRAs have been successfully tested in controlled outcome studies on fibromyalgia muscle pain and chronic fatigue syndrome (Deuster and Jaffe, 1998), diabetes (Jaffe et al., 2006), and osteoporosis (Jaffe and Brown, 2000). Clinical data indicate that all AI conditions tested to date have responded to this approach, which involves identifying person specific antigens that are potential burdens on the immune defense system for that individual. The implications of antigen load extend beyond defensive activity, since the immune system is also responsible for repair from wear and tear, deleting cancer cells, and systemic communication.

1.2.3.2 Evaluating lymphocyte response

Through this technology, it is possible to evaluate the responses of living white blood cells (lymphocytes), enabling them to react in the laboratory just as they do in the body. This *ex vivo* procedure can be used to identify immune responses to more than 490 food and chemical substances on one ounce of blood. These reactions indicate true delayed allergies or hypersensitivities, based on the body's long-lived memory carrying white blood cells reacting just as they do in the body yet under controlled laboratory conditions.

1.2.4 Comparative methodology

Limitations of other testing systems such as antibody measurement and particle size determination have been reported elsewhere (Hodsdon and Zwickey, 2010). Clinical strategies based on these tests usually involve simple avoidance. Avoidance often provides transient symptom remission. New sensitivities and symptoms tend to emerge within months if the underlying *causes* of maldigestion are not addressed. Comprehensive care management also includes restoring essential nutrient deficits and significantly reducing oxidative stress.

Table 7.1 Autoimmune Syndromes and Antigen Source Overlap

	Antigen site in cell or tissue					
Disorder	**Intracellular**	**Receptor**	**Membrane**	**Extracellular**	**Plasma protein**	**Hormone**
AIDS/ARC	+		+			+
Addison's	+					
Anemias	+		+			+
Arthritis, rheumatoid			+		+	
Asthma		+		+	+	
Bronchitis			+	+		
Cirrhosis	+					
Collagen diseases	+					
Diabetes, type 1	+	+				+
Diabetes, type 2	+	+	+			
Enteropathy	+					
Glomerular nephritis				+	+	
Graves', thyroiditis	+	+				
Hepatitis	+				+	
ITP			+			
Infertility (AI)			+			
Lupus (SLE)	+		+		+	
Multiple sclerosis			+			
Myasthenia gravis		+				
Neutropenia		+				
Pemphigus vulgaris			+	+		
Pneumonitis			+	+		
Polymyositis	+		+			
Sjogren's	+	+			+	
Thyroiditis	+	+				+
Vitilago	+					

1.2.5 Accuracy of functional immunology tests

Ex vivo LRAs are unique, in that they concurrently measure all hypersensitivity pathways, which allow more true positive reactions to be identified. The pathways for evaluating both acute and delayed allergy are depicted in the 'wheel of allergy' (Figure 7.1), and

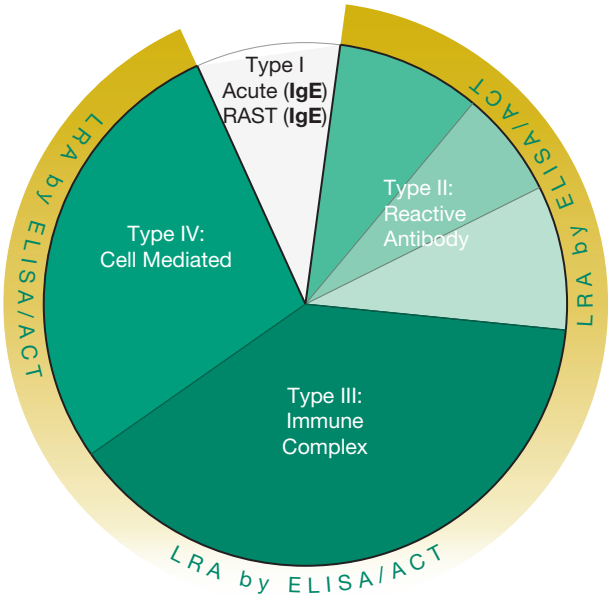

Figure 7.1 Wheel of immune response mechanisms.

are types of delayed hypersensitivity immune pathways described by Gel et al. (1963, 1975):

- Reactive humoral antibodies (IgA, IgG, and IgM: Type 2 reactions)
- Immune complexes (IgM anti-IgG antigen complexes)
- Cellular responses by T-cells (direct immune responses)

The LRAs provided by ELISA/ACT™ are specific (accurate) and sensitive (avoid false positives). The ELISA or enzyme amplification occurs on the surface of lymphocyte cells. The LRA functional tests provided by ELISA/ACT have a 97% accuracy rate, which is higher than nonfunctional IgG testing and other automated cytotoxic, particle-size procedures (Figure 7.1). Our clinical estimate is 99.9% sensitive, 99% specific, and less than 3% variance day to day on split samples.

2. RESTORING ALKALINE BALANCE

The *Alkaline Way* program focuses on evaluating and improving the individual's metabolic balance. This is a complementary approach that includes a health-promoting diet, which consists primarily of fresh, organic whole foods that are rich in nutrients, minerals, and fiber. Targeted supplementation is based on individual need with the goal of further restoring buffering mineral, essential antioxidants, and cofactors sufficient to keep the person well hydrated (www.PERQUE.com). Priority is given to locally grown,

vine ripened, organic, or biodynamic sources of immunocompatible foods. Mineral-rich water is the primary beverage (Figure 7.2).

2.1 The Alkaline Diet

Large research studies involving thousands of participants have reported on the association between metabolic acidosis and health disorders, which include insulin resistance (Souto et al., 2011), type 2 diabetes (Schulze et al., 2003), increased hypertension and cardiometabolic risk (Murakami et al., 2008), coronary heart disease (Liu et al., 2000), lean muscle wasting (Abramowitz et al., 2011), osteoporosis (Jehle et al., 2006), and cancer (Tavani et al., 2000).

A metabolically alkaline diet assures that the food has a buffering effect on cellular chemistry. The goal of this approach is to reverse intracellular acidosis, which impairs electron transport, reduces energy production, and impedes detoxification. Immune responses directly and indirectly generate substantial amounts of acidic products. In the vulnerable patient with impaired buffering capacity, it is especially important to avoid as many sources of acid formation as possible because of their adverse effects on cell metabolism. We find this approach helpful in RA while providing multiple systemic benefits as well.

2.1.1 The importance of reducing acidity in the body

Acid-forming diets are those that contain more than 25% of calories from fat and more than 75 g of protein intake daily. Clinical trials have tracked the effects of diets higher in protein and fat.

- *Risk of diabetes*. Harvard data on over 90 000 US women of ages 26–46 years found that those consuming *processed* meat five times a week or more had about twice the risk of diabetes. Those who consumed red meat (beef, lamb, or pork) had ~50% increased risk (Schulze et al., 2003).
- *Cardiometabolic factors*. A study by the National Institute of Health and Nutrition in Tokyo assessed the health of more than 1000 female students of age 18–22, evaluating the potential acid load on the kidneys due to high-dietary protein and low-mineral levels. Acid-forming diets were associated with elevated hypertension, higher total and LDL cholesterol, and increased body mass index and waist circumference (Murakami et al., 2008).
- *Cancer incidence*. An Italian study correlated diet with the incidence of cancer in 18 000 patients seen in a large urban hospital in Milan. Researchers found that those who consumed red meat seven times a week or more had a 50% higher risk of cancers of the stomach, pancreas, and bladder. The risk of colon cancer was almost doubled (Tavani et al., 2000).

Food and 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 Valerian Licorice •Black cohash Agave	•Herbs (most): arnica bergamot, echinacea chrysanthemum ephedra, feverfew goldenseal lemongrass aloe vera nettle angelica	White willow bark Slippery elm Artemesia annua	Spice/Herb	Curry	Vanilla Stevia	Nutmeg	Pudding/Jam/Jelly
Sea salt Mineral water	•Kambucha	•Green or Mu tea	*Sulfite* Ginger tea	Preservative Beverage	*MSG* *Kona coffee*	*Benzoate* *Alcohol* Black tea	*Aspartame* *Coffee*	*Table salt (NaCl)* *Beer, 'soda'* Yeast/Hops/Malt
	Molasses Soy sauce	Rice syrup Apple cider vinegar	•Sucanat •Umeboshi vinegar	Sweetner Vinegar	Honey/Maple syrup Rice vinegar	Balsamic vinegar	*Saccharin* Red wine vinegar	Sugar/Cocoa 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 Soy Goat/Sheep	Yogurt Goat/Sheep cheese	Aged cheese Soy cheese Goat milk	New cheese Soy milk	Ice cream
		•Quail egg	•Duck egg	Egg	Chicken egg			
				Meat Game Fish/Shell fish	Gelatin/organs •Venison fish	Lamb/Mutton Boar/Elk/•game meat Mollusks Shell fish (whole)	Pork/veal Bear •Mussel/squid	Beef Shell fish (processed) •Lobster
				Fowl	Wild duck	Goose/turkey	Chicken	Pheasant
			Oat 'Grain coffee' •Quinoa wild rice •Amaranth Japonica rice	Grain Cereal Grass	•Triticale Millet Kasha Brown rice	Buck wheat Wheat •Spelt/Teff/Kamut Farina/Semolina White rice	Maize Barley groat Corn Rye Oat bran	Barley Processed flour
Pumpkin seed	Poppy seed Cashew Chestnut Pepper	Primrose oil Sesame seed Cod liver oil Almond •Sprout	Avocado oil Seeds (most) Coconut oil Olive/Macadamia oil Linseed/Flax oil	Nut Seed/sprout oil	Pumpkin seed oil Grape seed oil Sunflower oil Pine nut Canola oil	Almond oil Sesame oil Safflower oil Tapioca •Seitan or tofu	Pistachio seed Chestnut oil *Lard* Pecan Palm kernel oil	*Cottonseed oil/Meal* Hazelnut Walnut Brazil nut Fried food
Lentil Brocoflower •Seaweed nori|kombu|wakame|hijiki onion/miso •Daikon/taro root •Sea vegetables (other) Dandelion greens •Burdock/•Lotus root Sweet potato/Yarm	Kohlrabi Parsnip/Taro Garlic Asparagus Kale/parsley Endive/arugural Mustard greens Jerusalem artichoke Ginger root Broccoli	Potato/Bell pepper Mushroom/Fungi Cauliflower Cabbage Rutabaga •Salsify/Ginseng Eggplant Pumpkin Collard greens	Brussel sprout Beet Chive/Cilantro Celery/Scallion Okra/cucumber Turnip greens Squash Artichoke Lettuce Jicama	Bean vegetable Legume pulse root	Spinach Fava bean Kidney bean Black-eyed pea String/Wax bean Zucchini Chutney Rhubarb	Split pea Pinto bean White bean Navy/Red bean Aduki bean Lima or mung bean Chard	Green pea Peanut Snow pea Legumes (other) Carrot Chickpea/Garbanzo	Soybean carob
Lime Nectarine Persimmon Raspberry Watermelon Tangerine Pineapple	Grape fruit Canteloupe Honeydew Citrus Olive •Dewberry Loganberry Mango	Lemon Pear Avocado Apple Blackberry Cherry Peach Papaya	Orange Apricot Banana Blueberry Pineapple juice Raisin, currant Grape Strawberry	Citrus fruit Fruit	Coconut Guava •Pickled fruit Dry fruit Fig Persimmon juice •Cherimoya date	Plum Prune Tomato	Cranberry Pomegranate	

•Therapeutic, gourmet, or exotic items

Italicized items are NOT recommended

Figure 7.2 Food and chemical effects on acid/alkaline body chemical balance.

When fat and protein intake increases above the body's needs, the healthy ratio of dietary fiber and essential nutrients is reduced, insulin resistance is usually induced, cell energetics is impaired, and joint repair reduced.

2.1.2 Reducing inflammation

An anti-inflammatory diet low in arachidonic acid was compared with a 'normal Western diet' in a German study that also evaluated the use of fish oil supplements for RA. The most significant improvement was seen with the anti-inflammatory diet in combination with fish oil, which resulted in a 28% improvement in joint tenderness and 34% reduction in swelling, compared with 11% and 22%, respectively, for the Western diet with fish oil supplements alone (Adam et al., 2003).

2.1.3 Increasing nutrient levels

The effects of fresh raw fruits and vegetables on arthritic symptoms were evaluated in a Finnish study. Blood tests showed highly increased levels of β- and α-carotenes, lycopene, and lutein, increases in vitamin C and vitamin E, and higher levels of polyphenolic compounds such as quercetin, myricetin, and kaempferol compared with omnivorous controls. For both patients with RA and those with fibromyalgia, the diet resulted in decreased joint stiffness and pain, and improvement in quality of life (Hänninen et al., 2000).

2.1.4 Improving health, functionality, and symptoms

Another interesting finding on diet comes from a Scandinavian study that tracked the health of patients randomly assigned to a vegan diet (gluten-free) or a well-balanced nonvegan diet. After 1 year, results showed that more than 40.5% in the vegan group fulfilled the ACR-20 improvement criteria, compared with only 4% in the nonvegan group (Hafström et al., 2001). Other researchers have found a gluten-free vegan diet atheroprotective and anti-inflammatory (Elkan et al., 2008).

2.1.5 Enhancing immune defenses

The substantial reduction in immunologic load in combination with an anti-inflammatory diet of alkalinizing foods can improve immune-defense performance. This provides the basis for reduced or eliminated host susceptibility to chronic infection. This also means enhanced repair and better anticancer surveillance. Substitution for reactive items is coupled with health-promoting diet substitutions and targeted supplementation.

2.2 Alkaline Nutrients

When dietary consumption patterns provide insufficient minerals and alkaline amino acids to buffer metabolic acids, this depletes cell alkaline reserves, and the intracellular

environment becomes more acidic. First morning urine pH is the predictive clinical tool to assess overall risk of net acid excess also known as metabolic acidosis.

- *Buffering minerals*. Deficits of minerals have been linked to reduced energy production and impaired ability to safely remove toxins, especially relevant to the patient with chronic fatigue. Minerals activate specific enzyme catalysts.
- *Alkalinizing short- and medium-chain fats*. Fats with less than 16 carbons are alkalinizing because acetate molecules can be added, thus reducing acetic acid (acetate).

Several other major groups of nutrients play important roles in supporting comprehensive nutrition.

- *Antioxidants*. Protect from oxidative damage, restore cellular energy production, rehabilitate mitochondria, and reset homeostatic mechanisms. Another goal of repletion is to reverse cumulative antioxidant deficits often observed clinically in inflammation.
- *B-complex nutrients*. Support methylation, to reduce homocysteine when levels rise above the healthy value of $<6\ \mu mol\ l^{-1}$ (linked to impaired detoxification). Impaired methylation is reflected in problems with cell communication, detoxification, and transport. This reframes these common states in physiologic rather than pathologic terms and offers integrative strategies to be included as first line comprehensive care.
- *Healthy fats and other nutrients*. Omega-3 fatty acids (EPA and DHA), gamma linolenic acid, selenomethionine, and vitamins E and C, essential cofactors and therapeutic herbs that stimulate joint repair, round out the program.

Table 7.3 offers a brief account of these supplemental therapies and their potential utility in an intervention for RA.

2.3 Self-Testing for Alkaline Status

A pH assessment of the first morning urine, after six or more hours of rest to allow equilibrium between cellular and bladder urine status, provides a surprisingly good measure of metabolic acidosis risk (Whiting and Bell, 2002). The urine pH is an effective indicator of the body's mineral reserve and its acid/alkaline state. The body routinely uses overnight rest time to excrete excess acids. This capacity varies based on toxin load and individual ability to make energy, to inactivate toxins, and to excrete those toxins.

Using specialized pHydrion test strips (Figure 7.3) can usually give a reliable assessment of the body's acid or alkaline balance. A value of 7.0 indicates the neutral state, neither acid nor alkaline. Ideally, the first morning urine pH should be in a pH range of 6.5–7.5. Cell cytoplasm or 'cell juice' functions best in a narrow, slightly alkaline range. A neutral or slightly acidic pH indicates that the overall cellular pH is healthy and that the small amounts of acids built up from normal metabolism have been easily concentrated in the urine for excretion (Figure 7.4).

Table 7.2 Nutrients and Botanicals Used in the Treatment of Rheumatoid Arthritis

Essentials	Role in rheumatoid arthritis
Nutrients	
Omega-3 fatty acids (James et al., 2010)	Suppress production of inflammatory mediators, including *n*-6 eicosanoids and proinflammatory cytokines
Gamma linolenic acid (Cameron et al., 2011; borage oil, evening primrose, black currant oils)	Symptom improvement: reduced pain intensity and improved mobility; assures healthy desaturase conversion of GLA to active DHA and EPA
Vitamin C (Pattison et al., 2004; buffered ascorbate)	Antioxidant, pro-repair of structural proteins and anti-inflammatory effect
Vitamin D (Merlino et al., 2004; cholecalciferol)	Immunomodulatory benefits when levels of 50–80 ng/ml are maintained
Vitamin E (Vasanthi et al., 2009; mixed natural tocopherols)	Decrease in oxidative stress that is higher in RA
Botanicals	
Quercetin dihydrate (Maria Mamani-Matsuda et al., 2006)	Modulate inflammatory response: inhibits macrophage-derived cytokines
Tripterygium wilfordii Hook F (TwF; Cameron et al., 2011)	Immunosuppressive, cartilage protective, and anti-inflammatory effect: Inhibits the expression of proinflammatory cytokines, proinflammatory mediators, adhesion molecules, and matrix metalloproteinases
Boswellia (Amon, 2006)	Inhibition of 5-lipoxygenase
Turmeric/curcumin (Cameron et al., 2011)	Anti-inflammatory/antioxidant activity by action on the production of anti-inflammatory cytokines, and activating the antioxidant defense system
Onions, Garlic and Feverfew (Ramadan et al., 2011)	Anti-inflammatory/antioxidant activity by action on production of anti-inflammatory cytokines, and activating the antioxidant defense system
Feverfew (Cameron et al., 2011)	Constituents of feverfew: sesquiterpene lactones, and particularly parthenolide, inhibit human blood platelet aggregation and secretory activity in platelets and polymorphonuclear leukocytes which are ↑ in RA
Dietary modifications	
Food sensitivities (Jaffe, 1989; as identified by LRA tests)	Decrease in immune load
Special diets: Fasting/vegetarian/ Mediterranean (Kjeldsen-Kragh, 1999)	Short-term management opportunity depending on individual; modalities cannot be explained completely as yet

Figure 7.3 Test strips for measuring first morning urine pH.

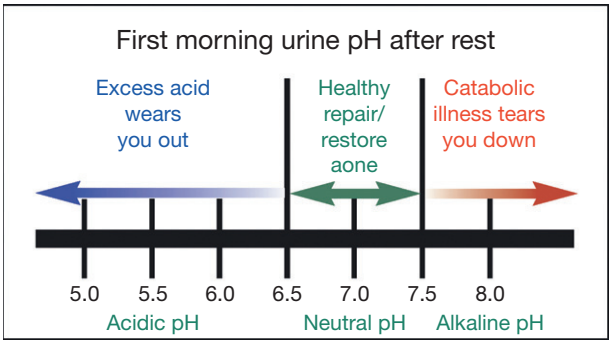

Figure 7.4 Interpretation of first morning urine measurements.

3. SELF-CARE

3.1 Physical Fitness and Immune Competence

Physical motion is necessary for physical health. This means that learning to move fluidly, to stretch easily and smoothly, to learn the links between breath and movement, and to move rather than be static is essential to physical well-being, and immune defense and repair competence. Exercise should be a pleasure, with a goal of adequate activity that is achievable rather than excessive activity that becomes a burden. Approaches reported in the literature to be beneficial and motivating for patients with RA include yoga, tai chi, chi gong, and strength training. Pilates, Trager Mentastics, Feldenkrais method and Alexander technique as also recommended over other massage and body work systems.

3.2 Mindfulness Practice and Immunity

In this program, a comprehensive, patient-centered, motivational approach is offered to promote long-term sustainable health practices that restore resilience. This means that if our thoughts or attitudes are unhealthy, they can be relearned in ways that promote rather than impair health. Distress is more about internal perception than external stress. Being at peace rather than anxious can be learned observationally through well-validated practices. Learning optimism is both possible and effective.

4. DISCUSSION

When routine wear-and-tear is not repaired, the integrity of the extracellular connective tissue scaffolding is impaired. This means the basement membranes glycoproteins, the structural collagens, and elastins are not being renewed and the most stressed spots wear out first. A result is increase in tissue permeability. Initially, damaged tissue hyperpermeability results in the entry of larger plasma proteins with platelets, dendritic first responder cells, and, when needed, lymphocytes, all seeking to enhance repair to 'put things right.' When incomplete, increase in blood–tissue permeability appears to be one of the factors that sets the stage for AI. This can be provoked by a variety of external *or* internal antigens perceived as foreign and thus overly burden immune responses. In the intestinal tract, hyperpermeability is clinically known as leaky gut syndrome. Research has also identified hyperpermeability of the blood–brain barrier, associated with arthritis and autoimmunity in an animal model (Nishioku et al., 2010).

Repair deficit can be enhanced by overproduction and imbalance of stress hormones such as cortisol and dehydroepiandrosterone (DHEA). Neurochemicals of distress such as adrenalin to serotonin imbalance add to hormone receptor resistance. Growth markers such as insulin (IGF1) go up when repair deficits increase and reduce when they are corrected. This makes them useful as clinical correlates of outcome. Buffering mineral *deficits* result in intracellular metabolic acidosis linked to reduced energy production and impaired ability to safely remove toxins or repair.

Too often, the lack of essential nutrients or burdens on the immune system prevent repair from being completed. Cumulative repair deficits are commonly known as inflammation. Appreciating them as repair deficit opens a variety of integrative care options.

5. CONCLUSIONS

Advances in molecular biology allow clinical information to be organized on the basis of physiologic causes rather than symptomatic, pathologic consequences. Organizing diagnosis by underlying biochemical disturbance with an emphasis on functional capacity and predictive tests provides earlier and more effective points of low-risk, low-cost

therapeutic entry. In clinical practice, this is outcome effective and cost-efficient. This approach is particularly valuable for the chronic illnesses that have become endemic in our time.

The Alkaline Way is an immune-strengthening, neurohormone balancing, detox-enhancing, health-restoring program that includes the following:

- Reduction of true immune reactive burden after predictive tests such as LRAs
- Reduction of toxicant exposure and enhancement of detoxification competencies
- Replacement of individually sufficient essential nutrient antioxidants, buffers, and required cofactors
- Mindfulness and relaxation response practices, active meditation, and therapeutic biofeedback as effective tools for increased awareness, more a witness to life than at the mercy of life's stresses
- A program of physical activity based on the needs and capacity of the individual

In essence, the enhancement of immune defense and repair system competences along with the restoration of tolerance and homeostasis, self-repair, and self-regulation.

One of the paradoxes of our time is that younger people are more and more often showing signs of chronic ill health – with symptoms that in previous decades were only observed in older people. These changes are occurring too quickly to be due to genetics. They are due in part to the losses in self-regulation/homeostasis and effective self-repair. Functionally, people are aging at earlier chronological ages on average. This is a drain on productivity and on quality of life.

The programs of the *Alkaline Way* are designed to restore tolerance, homeostasis, energetic balance, and resilience. Restoration of immune competence depends on identifying elements of both biochemistry and lifestyle that need strengthening and reducing elements that cause reactivity or stress on the system. These programs remove obstacles to recovery and are associated with sustained remissions in AI conditions such as RA.

REFERENCES

Abramowitz, M.K., Hostetter, T.H., Melamed, M.L., 2011. Association of serum bicarbonate levels with gait speed and quadriceps strength in older adults. American Journal of Kidney Diseases 58 (1), 29–38 [Epub ahead of print].

Adam, O., Beringer, C., Kless, T., et al., 2003. Anti-inflammatory effects of a low arachidonic acid diet and fish oil in patients with rheumatoid arthritis. Rheumatology International 23, 27–36.

Aletaha, D., Neogi, T., Silman, A.J., et al., 2010. Rheumatoid arthritis classification criteria: An American College of Rheumatology/European League against Rheumatism collaborative initiative. Annals of the Rheumatic Diseases 69, 1580–1588.

Amon, H.P., 2006. Boswellic acids in chronic inflammatory diseases. Planta Medica 72, 1100–1116.

Barton, A., Eyre, S., Ke, X., et al., 2009. Identification of AF4/FMR2 family, member 3 (AFF3) as a novel rheumatoid arthritis susceptibility locus and confirmation of two further pan-autoimmune susceptibility genes. Human Molecular Genetics 18, 2518–2522.

Cameron, M., Gagnier, J.J., Chrubasik, S., 2011. Herbal therapy for treating rheumatoid arthritis. Cochrane Database of Systematic Reviews 16 (2), CD002948.

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.

Douglas, K.M., Ladoyanni, E., Treharne, G.J., et al., 2006. Cutaneous abnormalities in rheumatoid arthritis compared with non-inflammatory rheumatic conditions. Annals of the Rheumatic Diseases 65, 1341–1345.

Elkan, A.C., Sjoberg, B., Kolsrud, B., et al., 2008. Gluten-free vegan diet induces decreased LDL and oxidized LDL levels and raised atheroprotective natural antibodies against phosphorylcholine in patients with rheumatoid arthritis: A randomized study. Arthritis Research and Therapy 2, R34.

Franceschi, C., Olivieri, F., Marchegiani, F., et al., 2005. Genes involved in immune response/inflammation, IGF1/ insulin pathway and response to oxidative stress play a major role in the genetics of human longevity: The lesson of centenarians. Mechanisms of Ageing and Development 126, 351–361.

Gell, P.G.H., Coombs, R.R.A., eds., (1963). Clinical Aspects of Immunology. 1st ed. Blackwell, Oxford, UK.

Gel, P.G., Coombs, R.R., Lachman, P.J., 1975. Clinical aspects of immunology. Wiley-Blackwell, Hoboken, NJ pp. 1399–1404.

Hafström, I., Ringertz, B., Spångberg, A., et al., 2001. A vegan diet free of gluten improves the signs and symptoms of rheumatoid arthritis: The effects on arthritis correlate with a reduction in antibodies to food antigens. Rheumatology (Oxford, England) 40, 1175–1179.

Hänninen, Kaartinen, K., Rauma, A.L., et al., 2000. Antioxidants in vegan diet and rheumatic disorders. Toxicology 155 (1–3), 45–53.

Hodsdon, W., Zwickey, H., 2010. NMJ original research: Reproducibility and reliability of two food allergy testing methods. Natural Medicine Journal 2, 8–13.

Hoffman, C., Rice, D., Sung, H.Y., 1996. Persons with chronic conditions: Their prevalence and costs. Journal of the American Medical Association 276, 1473–1479.

Jaffe, R., 1989. Improved immune function using specific nutrient supplementation and ELISA/ACT 'immunologic fingerprint' to detect late phase responses ex vivo. Journal of the American College of Nutrition 8, 424.

Jaffe, R., Brown, S., 2000. Acid–alkaline balance and its effect on bone health. International Journal of Integrative Medicine 2, 7–18.

Jaffe, R., Mani, J., DeVane, J., Mani, H., 2006. Tolerance loss in diabetics: Association with foreign antigen exposure. Diabetic Medicine 23, 924–925.

James, M., Proudman, S., Cleland, L., 2010. Fish oil and rheumatoid arthritis: Past, present and future. Proceedings of the Nutrition Society 69, 316–323.

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.

Kjeldsen-Kragh, J., 1999. Rheumatoid arthritis treated with vegetarian diets. American Journal of Clinical Nutrition 70, 594S–600S.

Kurreeman, F.A., Goulielmos, G.N., Alizadeh, B.Z., et al., 2010. The *TRAF1-C5* region on chromosome 9q33 is associated with multiple autoimmune diseases. Annals of the Rheumatic Diseases 69, 696–699.

Laevy, O., 2006. Unmasking IgG responses. Nature Reviews Immunology 6, 632.

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.

Lux, A., Aschermann, S., Biburger, M., Nimmerjahn, F., 2010. The pro and anti-inflammatory activities of immunoglobulin G. Annals of the Rheumatic Diseases 69 (Suppl. 1), i92–i96.

Maria Mamani-Matsuda, M., Kauss, T., Al-Kharrat, A., et al., 2006. Therapeutic and preventive properties of quercetin in experimental arthritis correlate with decreased macrophage inflammatory mediators. Biochemical Pharmacology 72, 1304–1310.

Merlino, L.A., Curtis, J., Mikuls, T.R., et al., 2004. Vitamin D intake is inversely associated with rheumatoid arthritis: Results from the Iowa Women's Health Study. Arthritis and Rheumatism 50, 72–77.

Michalsen, A., Riegert, M., Lüdtke, R., et al., 2005. Mediterranean diet or extended fasting's influence on changing the intestinal microflora, immunoglobulin a secretion, and clinical outcome in patients with

rheumatoid arthritis and fibromyalgia: An observational study. BMC Complementary and Alternative Medicine 22, 22.
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.
Nishioku, T., Yamauchi, A., Takata, F., et al., 2010. Disruption of the blood–brain barrier in collagen-induced arthritic mice. Neuroscience Letters 482, 208–211.
Pattison, D.J., Silman, A.J., Goodson, N.J., et al., 2004. Vitamin C and the risk of developing inflammatory polyarthritis: Prospective nested case–control study. Annals of the Rheumatic Diseases 63, 843–847.
Ramadan, G., Al-Kahtani, M.A., El-Sayed, W.M., 2011. Anti-inflammatory and anti-oxidant properties of Curcuma longa (turmeric) versus *Zingiber officinale* (ginger) rhizomes in rat adjuvant-induced arthritis. Inflammation 34 (4), 291–301.
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.
Scott, D.L., Wolfe, F., Huizinga, T.W., 2010. Rheumatoid arthritis. Lancet 376, 1094–1108.
Sköldstam, L., Brudin, L., Hagfors, L., Johansson, G., 2005. Weight reduction is not a major reason for improvement in rheumatoid arthritis from lacto-vegetarian, vegan, or Mediterranean diets. Nutrition Journal 4, 15.
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.
Vasanthi, P., Nalini, G., Rajasekhar, G., 2009. Status of oxidative stress in rheumatoid arthritis. International Journal of Rheumatic Diseases 12, 29–33.
Whiting, S.J., Bell, J., 2002. First morning urine measured with pH paper strips reflects acid excretion. Proceedings 2002 American Society for Bone and Mineral Research. ASBMR, Washington, DC.
Woof, J.M., Kerr, M.A., 2006. The function of immunoglobulin A in immunity. The Journal of Pathology 208, 270–282.
Zhernakova, A., Alizadeh, B.Z., Bevova, M., et al., 2007. Novel association in chromosome 4q27 region with rheumatoid arthritis and confirmation of type 1 diabetes point to a general risk locus for autoimmune diseases. American Journal of Human Genetics 81, 1284–1288.

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