REVIEW ARTICLE

Nutritional Aspects of Detoxification in Clinical Practice

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ABSTRACT

Detoxification is a vital cellular task that, if lacking, can lead to early morbidity and mortality. The process of detoxification involves the mobilization, biotransformation, and elimination of toxicants of exogenous and endogenous origin. This article discusses the phase I and phase II detoxification and biotransformation pathways and promotes using food to support these highly complex processes. The author identifies the comprehensive elimination diet as a useful therapeutic tool for clinicians and patients to use to achieve detoxification. Using this diet, the patient removes the most common allergenic foods and beverages from the diet and replaces them with nonallergenic choices for a period of 4 wk, gradually adding back the eliminated foods and observing their effects. Another effective clinical tool that the author discusses is the detox-focused core food plan, which identifies the variety of foods required to supply key nutrients that can maximize the effectiveness of detoxification. Finally, the author provides a case study in which these tools were used to help a patient suffering from major, debilitating illnesses that resulted from exposure to malathion, including severe vomiting and diarrhea, headaches, night sweats, severe arthralgias and myalgias, episcleritis, and shortness of breath. The article details the interventions used and the clinical results (ie, successful resolution of most issues after 3 mo). (*Altern Ther Health Med.* 2015;21(3):54-63.)

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Detoxification is a vital cellular task that, if lacking, can lead to early morbidity and mortality.[1] The process of detoxification involves the mobilization, biotransformation, and elimination of toxicants of exogenous and endogenous origin. Human cells expend large amounts of energy to ensure that detoxification pathways continue to do their work. A variety of macronutrients and micronutrients are required on a continuous basis to construct the multitude of enzymes for the various oxidation, reduction, hydrolysis, and conjugation pathways, as well as the provision of enzymatic cofactors, phytochemical antioxidants, and fiber.[2] Patients often request a detoxification program and are surprised to learn that it is not a program that is required, but rather a detoxification lifestyle that needs to be adopted. Components of this lifestyle include (1) avoidance of environmental toxicants such as heavy metals, persistent organic pollutants, and electromagnetic radiation; (2) mobilization or elimination of toxicants via loss of excessive fat and use of saunas, chelation therapy, and exercise[3]; (3) optimal gastrointestinal health; (4) excellent nutrition and hydration[1]; (5) attention to stress and resilience and to relational health[4]; and (6) adequate sleep and relaxation.[5] It is important for health practitioners to model the detoxification lifestyle, which then encourages patients to adopt similar health practices. This article reviews the nutritional aspects of detoxification for use in clinical practice.

DETOXIFICATION AND BIOTRANSFORMATION PATHWAYS

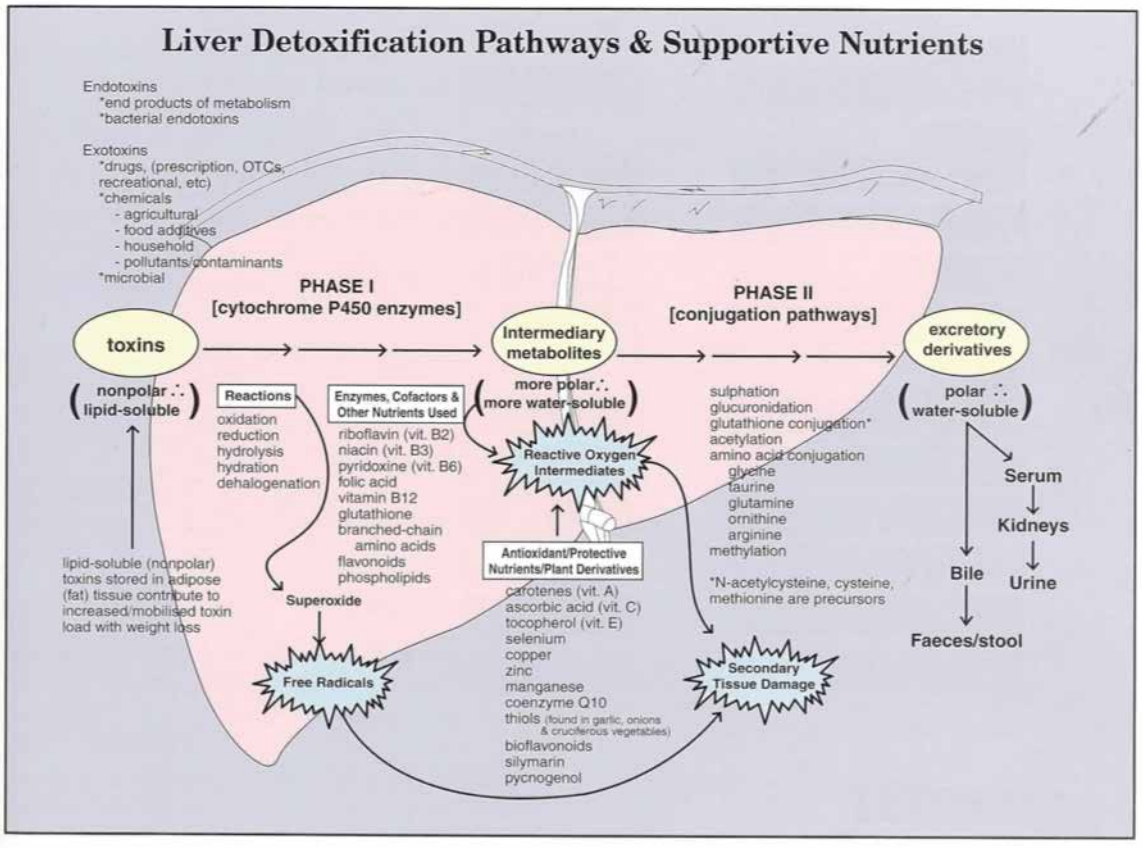
The process of detoxification involves multiple steps in the biotransformation of primarily nonpolar, lipid-soluble toxicants into polar, water-soluble, and excretable derivatives, as originally postulated by R. T. Williams in his monograph *Detoxification Mechanisms* followed by his paper "Detoxication

Mechanisms in Man".[6] Since then, a large body of literature has been published, leading to the current understanding of how detoxification can be used in the prevention and treatment of disease in clinical practice.[7] Figure 1 shows an important tool that summarizes the phase I and phase II detoxification and biotransformation pathways and provides a conceptual framework for clinicians and patients.[8] Toxicants originate from exogenous sources such as drugs (pharmaceutical and recreational); heavy metals; chemicals, such as herbicides, pesticides, insecticides, food additives, household cleaners, and other pollutants; and microbials. Toxicants also originate from endogenous sources, such as bacterial endotoxins and the end products of metabolism.[1] It is important to realize that steroid hormones and fat-soluble vitamins are also metabolized through these pathways.

Phase I Detoxification

The majority of the detoxification and biotransformation processes occur in the liver and in the enterocytes that line the intestine, colon, and appendix. Detoxification and biotransformation are done to a lesser extent in other tissues, such as the brain, lungs, kidneys, and skin. The phase I system comprises at least 57 pathways known as the cytochrome P450 (CYP) family of mixed-function oxidases.[9] Nine of the most commonly used CYP enzymes are 1A1, 1B1, 2A6, 2B6, 2C9, 2C19, 2D6, 2E1, and 3A4. In phase I, toxicants are transformed to more polar, less lipid-soluble forms through oxidation, reduction, hydrolysis, hydration and dehalogenation reactions. For the P450 enzymes to be present and conformationally active, an individual must consume high-quality, bioavailable protein as well as a host of phytonutrients, botanicals, minerals, fats, and carbohydrates.[2] These nutrients are required for epigenetic influence (ie, changes in gene expression, during transcription and production of the various CYP enzymes as well as enzymatic cofactors and energy). After going through the phase I processes, the activated toxicants are often more toxic than their parent compounds. If these activated, intermediate metabolites are not further metabolized via the phase II conjugation pathways; they can cause cellular damage by

Figure 1. Liver detoxification pathways and supportive nutrients.[8] Lipid-soluble (nonpolar) toxicants, whether endogenous or exogenous in origin, are metabolized through phase I cytochrome P450 enzymes into intermediary metabolites, which are often more toxic than the parent compound. These metabolites are further biotransformed through the phase II conjugation pathways, leading to water-soluble (polar) toxicants, which are readily excreted via the bile and stool pathway or the kidney and urine pathway. By-products of the biotransformation processes are free radicals and reactive oxygen species. A large number of nutrients are required for these pathways to function properly.



covalently binding to various proteins, lipids, and nucleic acids within cells.[2] Reactive oxygen species are also a by-product of phase I activity. Therefore, to quench the propagation of free-radical activity, adequate protection from antioxidant nutrients is required using a number of plant derivatives,[10] including (1) the carotenes—lycopene, β-carotene, lutein, zeaxanthin, and astaxanthin; (2) ascorbic acid; (3) tocopherol (vitamin E); (4) selenium; (5) copper; (6) zinc; (7) manganese; (8) coenzyme Q_{10}; (9) thiols, found in garlic, onions, and cruciferous vegetables; (10) bioflavonoids; (11) silymarin; and (12) pycnogenol (Figure 1). Other nutrients include (1) *N*-acetylcysteine; (2) α-lipoic acid; (3) polyphenols such as pomegranates, green tea, and raspberries; (4) anthocyanins found in blueberries and blackberries; and (5) curcumin.[11]

Phase II Detoxification

The majority of intermediate metabolites progress to the phase II conjugation pathways, where they are joined to constituents such as glucuronide; sulfate; glutathione; various amino acids, such as taurine, glycine, arginine, glutamine, serine, and proline; and acetyl and methyl groups. The biotransformed polar and water-soluble toxicants are then excreted via the bile and feces or the serum, kidneys, and urine. As the various nutrients required for conjugation are bound to the toxicants, they potentially can become depleted unless an ongoing dietary supply exists.[1] Therefore, excellent nutrition is imperative for a detoxification lifestyle.

After conjugated toxicants exit the liver via the bile, they are excreted into the feces. One component of bile is the variety of bile acids that are necessary to emulsify and solubilize dietary fats. In the distal small bowel, 90% to 95% of the bile acids are reabsorbed and returned to the liver, thus recycling and conserving them. This cycling of bile acids occurs approximately 12 times each day and is known as *enterohepatic circulation*.[12] Microbes found in the intestinal lumen contain enzymes, such as β-glucuronidase, that can cleave conjugated toxicants, reactivating them and allowing them to reabsorb into the portal system which returns them to the liver. The enterohepatic circulation allows essential compounds, such as estrogen and vitamin D, to be conserved.[13,14] Some evidence in animal models shows that the alginate *Chlorella* has the potential to inhibit the absorption of certain heavy metals and organic pollutants across the intestinal mucosa, thus decreasing the enterohepatic circulation of these toxicants.[15,16]

"LET FOOD BE THY MEDICINE"

"Let food be thy medicine," as taught to us by Hippocrates, is as true today as it was in 400 BC. Using a focus on food to support the highly complex processes of detoxification and biotransformation is the wise approach. If an apple contains at least 700 different phytochemicals, it is better to eat the apple as one of a variety of foods than to try to replicate its benefits with single nutritional supplements. A recent review[17] of this subject stated this concept succinctly:

> It is very difficult to imagine how a single phytochemical—[that is] selected as representative of a whole food, such as lycopene in tomatoes, resveratrol in grapes, sulforaphane in broccoli, and beta-carotene in carrots—would offer an advantage [when] used as a food supplement, because a variety of fruit and vegetables seems necessary to provide the mixture of vitamins and minerals that appear to favor protection against neoplasia. Ingesting whole fruits and vegetables exposes the digestive milieu to enzyme-modulating components of varying amounts and proportions in which unpredictable synergistic and /or antagonistic (or both depending on the enzyme involved) interactions occur among thousands of different chemicals in their natural matrix.—How can we imagine that these benefits could be reproduced just by supplements of single representative phytochemicals? The beneficial or harmful outcomes of a single compound can be quite different from those elicited by the same compound within complex mixtures.[17,18]

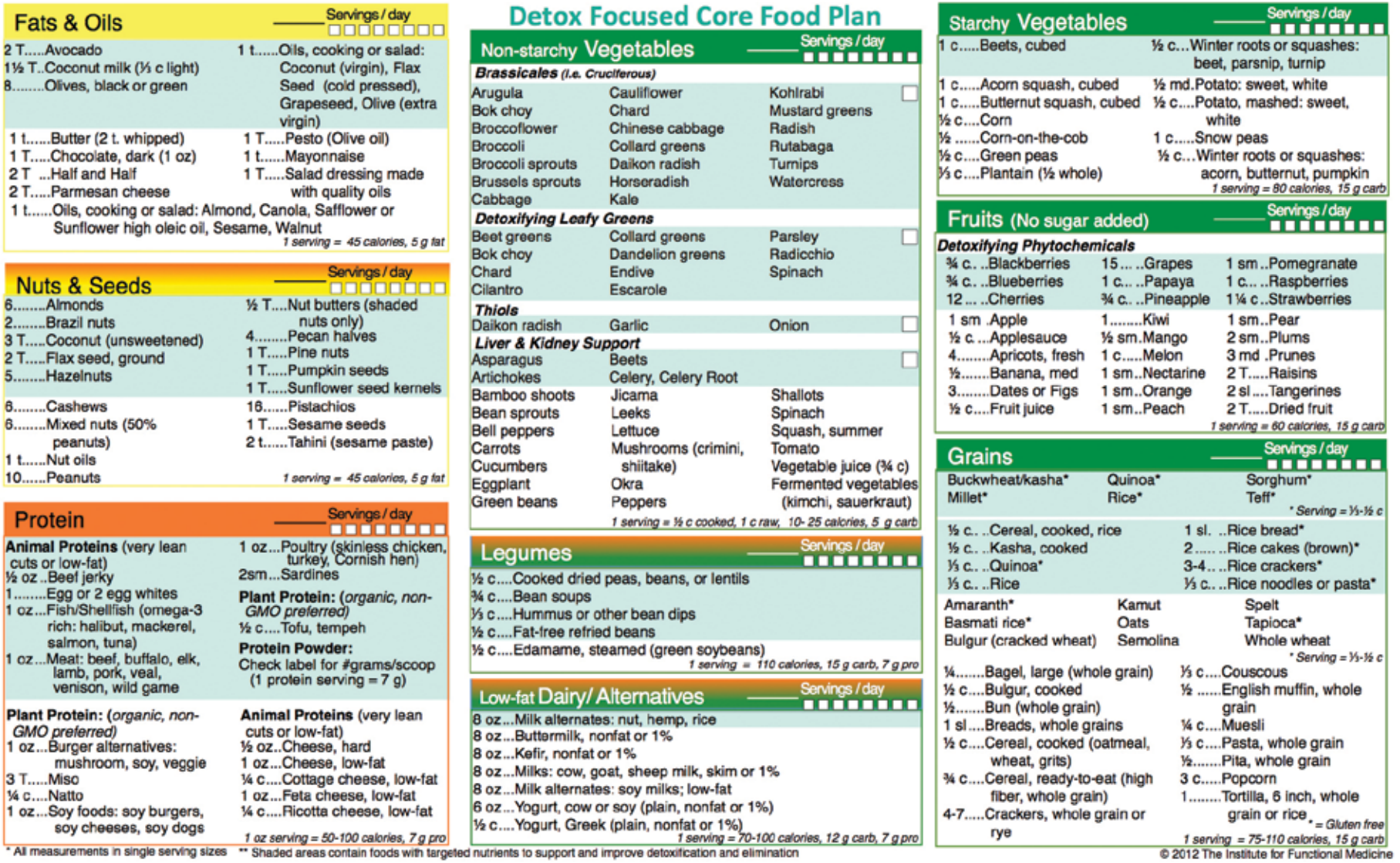
Nutritional Aspects of Detoxification

The first step in the use of nutritional support to promote detoxification is to remove foods and beverages from the diet that may be contributing to the total body burden of toxicants. Examples include removing (1) foods containing petrochemical residues from farming practices; (2) foods containing polycyclic aromatic hydrocarbons such as charbroiled meat; (3) trans fats; and (4) water contaminated with metals and chemicals. Next, it is important to add foods to the diet that nourish the organs of detoxification, providing substrates and cofactors for optimal detoxification, as well as foods that positively modify genetic expression and cell signaling.[19] A useful therapeutic tool is the comprehensive elimination diet, in which the most common allergenic foods and beverages are removed from the diet and replaced with nonallergenic choices for a 4-week period. The allergenic foods and beverages are then added back to the diet every 4 days, one food group at a time. The patient is instructed to observe the reactions of his or her body carefully to note any adverse changes in health. This approach helps patients to become their own medical detectives in discovering the foods or beverages that cause their bodies to react.[2] This diet can be used under the direction of a registered dietician, certified clinical nutritionist, or physician, with menus and recipes provided. Another effective clinical tool is the detox-focused core food plan (Figure 2), which includes the variety of foods required to supply key nutrients to maximize the effectiveness of detoxification.

Detox-focused Core Food Plan

A cursory look at the detox-focused core food plan reveals the various macronutrient food groups, beginning with fats and oils in the upper left corner, and gives examples of nuts and seeds, protein, legumes, low-fat dairy products or alternatives, grains, fruits, and starchy vegetables. In the center of the diagram is the nonstarchy vegetable group. Patients who need to focus on a detoxification lifestyle will want to emphasize eating the foods in the green shaded areas

Figure 2. Detox-focused core food plan. Used with permission from the Institute for Functional Medicine.[20]



of each food group. By doing so, they will consume the thousands of micronutrients and phytochemicals known to support balanced phase I and phase II detoxification. Within each food group, each individual food item has beside it the amount that constitutes 1 serving. A person on this plan should consume a minimum of 4 servings of fruit and vegetables and at least 1 serving from each of the 4 nonstarchy vegetable groups. Forty percent of the daily calories should come from carbohydrates and 30% from proteins and fats. Although water is not listed, it is of the utmost importance to consume adequate high-quality water throughout each day—0.5 fluid ounce (14.8 mL) of water per pound (0.45 kg) of ideal body weight per day. Figure 3 shows the health professional's companion guide[20] to the detox-focused core food plan. The important foods to avoid and the foods to emphasize for phases I and II are reviewed; the tool highlights the 4 primary phase II pathways of conjugation: (1) glucuronidation, (2) sulfation, (3) methylation, and (4) glutathione support.

Each food group within the detox-focused core food plan contains foods that are selected for their unique array of phytonutrients.

Fats and Oils. These foods are important because they provide excellent sources of energy for the detox and biotransformation processes. The selected oils in the green shaded area are high in medium-chain triglycerides.

Nuts and Seeds. The highlighted nuts and seeds provide excellent sources of energy as well as fiber that assists in proper excretion and elimination. They also have a positive impact on reduction of bacterial deconjugating enzymes.

Proteins. High-quality, bioavailable protein is important as a source of amino acids for the production of the phase I CYP enzymes as well as the provision of substrates for phase II enzymes, particularly glycine, L-glutamine, methionine, L-cysteine, and taurine. Protein is also a good source of inorganic sulfate.

Legumes. Legumes provide a good source of soluble and insoluble fiber as well as a variety of amino acid precursors for phases I and II and antioxidant phytochemicals.[2]

Low-fat Dairy and Alternatives. These foods provide amino-acid substrates for the phase II pathways as well as inorganic sulfate and selenium.

Fruits. The foods in the shaded area provide a wide variety of phytonutrients, such as β-carotene, lutein, and anthocyanins that have protective antioxidant properties. Fruits are also a good source of soluble and insoluble fiber, promoting healthy intestinal transit of toxicants. Fruits in general are high in water content, which aids in detoxification.

Grains. Grains supply excellent sources of soluble and insoluble fibers that are vital for healthy intestinal transit.

Vegetables. Starchy vegetables provide excellent sources of fiber and phytonutrients similar to fruits. The nonstarchy vegetables, including the *Brassica* genus, provide a wide variety of phytochemicals that impact detoxification and biotransformation. They directly impact many of the phase I CYP pathways in the metabolism of estrogens, favoring production of the 2-hydroxy estrogens. Many of the phytochemicals also provide antioxidant support to quench reactive oxygen species. They also increase the flow of bile as well as the alkalinity of urine. *Coriandrum sativum* (cilantro) has a direct chelating effect on a number of heavy metals such as mercury[21] and lead.[22]

The spectrum of phytochemicals outlined in the food groups listed above provide broad and comprehensive tools for individuals to support phase I and II detoxification processes to benefit their health.

CASE STUDY

The Patient

A 45-year-old, single businesswoman (MBA), gravida 0, came to the author with a 1-year history of (1) episodic, severe vomiting and diarrhea, with blood in the stools; (2) cramps in the central lower abdomen; (3) nonthrobbing headaches; (4) night sweats; (5) severe arthralgias and myalgias, particularly in the wrists and ankles; (6) episcleritis; (7) sensitivity to light; and (8) shortness of breath with gasping episodes. She was a nonsmoker and had been relatively healthy until 1 year prior to development of her symptoms.

Each episode was more severe than the previous one, causing several admissions to a hospital through the emergency room, with no underlying diagnosis achieved. Most of the symptoms cleared within a few months of each episode. On her last hospital admission, a chest X-ray revealed evidence of pulmonary edema, and she was treated with intravenous furosemide. Her joints were transiently swollen and painful, with her initial level of C reactive protein (CRP) elevated at 211 mg/L (normal < 5.0). Joint aspirations were within normal limits and revealed no evidence of microbial growth. Nevertheless, she was given intravenous antibiotics.

A rheumatologist concluded that she had inflammatory arthritis of unknown origin and prescribed prednisone, nonsteroidal anti-inflammatory medication, and analgesics. At the time of her first visit to the author's clinic, she was taking 24 × 200 mg of ibuprofen per day. An ophthalmologist concluded that she had episcleritis of possible autoimmune origin. An allergist suggested that she had acute urticaria, possibly postviral.

Physical Examination and Testing

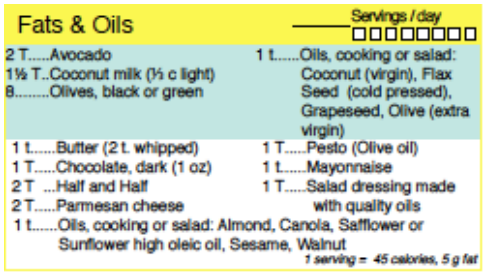
Using the Institute for Functional Medicine's model of critical thinking (Functional Medicine Matrix and Functional Medicine Timeline), the author queried this client about any unusual events that had occurred shortly before she became so ill. She replied that 1 or 2 days before each episode, she had sprayed her trees and shrubs with malathion. Malathion is a broad-spectrum organophosphorus insecticide and acaricide.

On physical examination, the author found (1) a pleasant woman in no acute distress, who was able to move well; (2) her right medial conjunctiva was inflamed; (3) her blood pressure was 82/60 right and 80/60 left; her pulse was 84 and regular; and her heart sounds were normal; (4) she did not

Figure 3. Companion guide for the detox food plan. Used with permission from the Institute for Functional Medicine.[20]

Companion Guide for the Detox Food Plan

The Detox Food Plan calls attention to what one could eat to incorporate natural and whole foods to support, modulate, induce, or inhibit various biological processes related to optimal detoxification and elimination. It is modified from the Core Food Plan. This version identifies the key foods known to improve the metabolic cleansing process and aid biotransformation.



Not all food is created equal, especially when viewed through the metabolic detoxification lens. When making dietary choices to support detoxification, it is best to choose the shaded areas within each food grouping because they indicate preferred foods.

The foods listed below are organized based on the specific detoxification pathway they influence. These lists are helpful for choosing foods that support specific biotransformation and detoxification processes.

Phase I Detoxification

Induce (avoid): Charbroiled meats, high caffeine- and alcohol-containing beverages

Inhibit (minimize): Grapefruit (naringenin), high saturated and hydrogenated fat diets, low animal protein or a lack of complete proteins

Activate (promote): Cruciferous vegetables, diets adequate in protein (meat, fish, eggs, and plant-based foods that provide complementary essential amino acids)

Phase II Detoxification

Glucuronidation (promote):
α- and β-carotene-rich foods: (highest to lower): pumpkin, carrot, squash sweet potato, collards, red peppers, spinach, mustard greens, chard, dandelion greens, cantaloupe, romaine lettuce
Quercitin-rich foods: apple, onion, kale, cherry, red wine, extra virgin olive oil, beans, broccoli, tea
High chrysin and luteolin-rich foods: (highest to lower): broccoli, chili pepper, celery, rosemary, honey
High D-glucaric-acid-rich foods: (highest to lower): apple, grapefruit, alfalfa sprouts, broccoli, Brussels sprouts, adzuki beans, tomato, cauliflower, mung beans, cherries, apricots, spinach, oranges
Citrus foods: grapefruit, orange, tangerine
Watercress and turmeric (curcumin)
Dietary plant fibers
Magnesium-rich foods: (highest to lower) halibut, almond, cashew, soybean, spinach, oatmeal,potato, peanut, wheat bran, black-eyed peas, baked beans, brown rice, lentils, avocado, pinto beans

Sulfation (promote): **Sulfur-rich foods:** (highest to lower) scallop, lobster, crab, peanut, shrimp, veal, mussel, chicken, Brazil nuts, haddock, sardine, cod, oyster, beef, dried peach, egg, turkey, almond, cheddar, Parmesan cheese, dried skim milk, spinach, onion, cabbage, Brussels sprouts, chickpeas, figs, beans/peas, leeks, endive, potato

Methylation (promote): **Folic acid-rich foods:** liver, chicken giblets, egg yolk, dried beans, lentils, split peas, soybean, almonds, whole wheat, potato, sweet potato, spinach, beet root, Brussels sprouts, broccoli, cauliflower, kale, cabbage, bok choy, asparagus, banana, orange, peach
B_{12}-rich foods: liver, beef, chicken, pork, ham, fish, egg, milk, cheese, yogurt, clam, rainbow trout, salmon, haddock, tuna

Glutathione Support: **Cysteine-rich foods:** duck, yogurt, egg yolk, whey protein, ricotta cheese, cottage cheese, yogurt, red pepper, garlic, onion, broccoli, Brussels sprouts, oat, granola, wheat germ, sprouted lentils

Bifunctional Modulators

Adapts Phase l & ll Detoxification to Variable Exposures: pomegranate, turmeric (curcumin), cruciferous vegetables, green tea, artichoke heart

have a fever; (5) her skin was dry, and her fingertips were cracked; (6) in her mouth, she had 3 amalgams, with many composites, but no root canals; (7) she had nasal turbinates with chronic swelling and a coated tongue, but no nodes were palpable; (8) her chest excursion and breath sounds were within normal limits; (9) her radial and pedal pulses were normal, (10) she had no edema; (11) in her abdomen, she had no organomegaly, and her liver edge was smooth and nontender; (12) no abnormalities were detected in her central nervous system and peripheral nervous system; and (13) her wrists and ankles were warm to the touch, were nontender, and had a full range of motion.

Laboratory findings included results from the following measures: (1) red blood cells—3.73 tera/L (3.8-4.8); (2) hemoglobin—110 g/L (120-150); (3) CRP—37.8 mg/L (<5.0), at follow-up after hospital discharge; (4) ferritin—15 µg/L (15-180); (5) iron—5 µmol/L (10-33); (6) total iron-binding capacity—57 µmol/L (37-72); (7) transferrin saturation—0.09 (0.20-0.55); (8) 25 hydroxy vitamin D—29 nmol/L (75-150); (9) calcium—2.3 µmol/L (2.10-2.55); (10) AM cortisol—521 nmol/L (140-690); and (11) PM cortisol—315 nmol/L (50-300).

Her complete blood count was otherwise within normal limits, and her electrolytes, magnesium, creatinine, liver enzymes, serum immunoglobulin A (sIgA), antitissue transglutaminase, thyroid stimulating hormone, follicle stimulating hormone, C3, C4, and serum creatine kinase MB were also within normal limits.

The author performed a Metametrix GI Effects Comprehensive Profile Stool Analysis (Duluth, GA, USA). The testing provided the following results: (1) *Lactobacillus* species, low; (2) *Bifidobacterium* species, low; (3) total short-chain fatty acids (SCFAs), low-normal; (4) lactoferrin, elevated; (5) fecal sIgA, high-normal; (6) antigliadin sIgA, low; (7) occult blood, positive; (8) markers for digestion—elastase 1, triglycerides, and putrefactive SCFAs, well within normal ranges; (9) markers for absorption—long-chain fatty acids, total fat, and cholesterol, well within normal ranges.

Detoxification Genome Profile

The author also performed a detoxification genome profile for single nucleotide polymorphisms (SNPs) using DetoxiGenomic Profile (Genova Diagnostics, Asheville, NC, USA).[23,24] In detoxification, an individual's genetic predisposition to severe effects from toxin can be determined by measuring his or her SNPs in the key phase I and II, detoxification, and biotransformation pathways. A number of situations exist where this test can be quite useful, such as for patients who have (1) paradoxical or multiple reactions to pharmaceuticals or herbs, (2) illness related to food or chemical sensitivity, (3) refractory mood disorders, (4) chronic fatigue syndrome, (5) fibromyalgia, and (6) other chronic pain syndromes. For the patient in the current case study, this test provided invaluable information and a roadmap to help prevent future health crises.

In the current case, test results revealed 2 SNPs in the phase I CYP enzymes, CYP1B1 and CYP2C19. The CYP1B1 enzyme is responsible for the 4-hydroxylation of estrogen and activation of environmental toxicants, such as polycyclic aromatic hydrocarbons, polychlorinated biphenyls, and aflatoxin B1. Multiple medications and herbs can act as substrates, inhibitors, and inducers.[25] An SNP in this pathway conveys capacity for damage due to toxicant exposure. Hyperinduction of this pathway can increase oxidative stress and the 4-hydroxyestrogens may convert to quinine compounds, resulting in DNA damage to breast tissue.[26] To minimize risk, it is advisable to avoid cigarette smoke, decrease exposure to xenobiotics and xenoestrogens, and be cautious with long-term hormone replacement therapy, avoiding the equine estrogens. It is also advisable to eat a diet rich in antioxidants. To redirect estrogen metabolism away from 4-hydroxylation, individuals should liberally ingest foods such as cruciferous vegetables as well as add the nutritional supplements resveratrol,[27] indole-3-carbinol or di-indole methane,[28] fish oils, and rosemary to their diets.

In the current case study, the woman's results also showed a SNP in the enzyme CYP2C19, which is responsible for the metabolism of many drugs as well as some herbs.[29] A SNP in this pathway conveys a slower rate of metabolism, resulting in drug side effects at commonly prescribed dosages. To minimize risk, it is advisable that smaller dosages of pharmaceutical drugs and certain herbs should be used. In addition, a number of SNPs were detected in the woman's phase II conjugation enzymes, including a complete absence of pathways for glutathione-*S*-transferase M1 (GSTM1), with genetically intact pathways for glutathione *S*-transferase P1 (GSTP1). GSTM1 is found in the liver and kidneys, and GSTP1 is found in the brain and skin. Glutathione conjugation is one of the most important pathways whereby environmental toxicant, such as solvents, herbicides, fungicides, and lipid peroxides, and heavy metals, such as lead, mercury, and cadmium are biotransformed and excreted.[30] Decreased glutathione *S*-transferase capacity can increase the overall toxic burden, oxidative stress, and risk of various cancers.[31] To minimize risk, it is advised that people with this SNP avoid toxicant exposure as much as possible. A diet rich in colorful vegetables and fruits, cruciferous vegetables, onions, and garlic should be emphasized,[32] with added vitamins C and E, *N*-acetylcsysteine, and silymarin.

In the current case study, the woman had a homozygous SNP present in the phase II methylation pathway that uses the catechol-*O*-methyltransferase (COMT) enzyme. This pathway is responsible for the methylation and inhibition of the neurotransmitters dopamine, epinephrine, and norepinephrine as well as the catechol estrogens. A polymorphism in this pathway results in reduced COMT activity, leading to increased risks of certain neuropsychiatric disorders such as anxiety, panic disorder, depression, and ultrarapid-cycling bipolar disorder.[33,34] Risk is also increased for fibromyalgia, breast cancer, hypertension, and acute coronary events. To minimize risk, people with this SNP

should avoid elevated homocysteine, amphetamines, catechol drugs, and equine estrogens. The diet should be high in antioxidant foods as well as have adequate supplementation with trimethylglycine and vitamins B_{12}, B_6, and folate.[35]

She also had homozygous SNPs in the phase II pathway for superoxide dismutase 2 (SOD2). SOD2 is found in the mitochondria and is the primary antioxidant enzyme.[36] A SNP in this pathway results in decreased SOD2 activity and an increased risk for a higher level of oxidation within the mitochondria. To minimize risk, it is advised that people with this SNP consume a diet high in antioxidants, with colorful vegetables and fruits and a wide array of antioxidant nutritional supplements. Because manganese is the cofactor for SOD2, it should be added through the diet or with supplementation.

Metabolic Pathways for Malathion

An excellent source of reliable information regarding malathion and other toxic substances is available at the Agency for Toxic Substances and Disease Registry. The toxicological profile for malathion is 327 pages long.[37]

Malathion is an organophosphate pesticide used to kill insects found on agricultural crops, golf courses, home gardens, and nurseries where trees and shrubs are grown. It is also used in killing mosquitoes, Mediterranean fruit flies, fleas on pets, and head lice on humans. Malathion is first metabolized through the CYP2B oxidation pathway and is then biotransformed into the highly toxic intermediate malaoxon, an acetylcholinesterase inhibitor. Interestingly, the phase II pathway used to biotransform malaoxon is the GSTM1 pathway, which was genetically absent in the current case study's patient.

Therefore, with the absence of this phase II pathway, the highly toxic intermediate malaoxon was released into the patient's body. A review of the multiple symptoms associated with malaoxon exposure reveals that they are related to the inhibition of acetylcholinesterase at the nerve terminals of the central, peripheral, somatic, and autonomic divisions of the nervous system. This type of release leads to symptoms and signs involving several of the body's systems including, but not exclusive to, the nervous, respiratory, cardiovascular, and gastrointestinal systems. Potential effects of malathion exposure include difficulty breathing, chest tightness, vomiting, cramps, diarrhea, blurred vision, sweating, headaches, dizziness, loss of consciousness, and death.[37]

INTERVENTIONS

Based on the history, physical examination, standard laboratory work, gastrointestinal functional profile, and detoxification genetic SNP profile for phases I and II of the woman in the current case study, the following interventions were recommended: (1) a comprehensive elimination diet, as outlined in the *Textbook of Functional Medicine*[2]; and (2) a diet high in antioxidants and foods to support detoxification pathways, such as cruciferous vegetables (broccoli, cauliflower, cabbage, kale, Brussels sprouts, radish sprouts) and *Allium* vegetables (onions, leeks, and garlic); (3) the addition of a medical food product to enhance and support phase I and phase II pathways in the gastrointestinal tract, liver, and kidneys; (4) probiotics, 200 billion organisms daily; (5) pharmaceutical grade fish oil with eicosapentaenoic acid, 3600 to 4000 mg daily; (6) vitamin D_3, 4000 IU daily; (7) manganese, 25 µg daily; (8) curcumin, 750 mg twice daily with food; (9) liposomal glutathione daily; (10) an excellent whey powder twice daily, with precursors of glutathione such as *N*-acetylcysteine; (11) conformity with all instructions resulting from the genomics testing; and (12) avoidance of further exposure to malathion or other chemicals or metals.

CLINICAL RESULTS

At the 1-month follow-up visit, the woman reported that she was feeling much better in general. Her wrist and ankle pain and swelling had improved by 95%. The myalgias in her arms had resolved, and she was now gaining strength. Her night sweats had resolved, and her gastrointestinal function was back to normal, with no further blood in the stool. Her appetite had fully returned, and her sinuses were much clearer than they had been in years. Her headaches were occurring occasionally, but she was rarely taking any ibuprofen or analgesics. Her eye symptoms were still present but were gradually subsiding. More important, she recommenced her exercise routines, and she returned to work.

Three months after the author first met her, the patient followed up and reported that she felt "ridiculously well." She continued to experiment with the addition of foods into her diet and found that she seemed to tolerate small amounts of gluten every few days. If she increased the intake beyond that she would develop abdominal bloating and discomfort. The author suggested that she should continue to avoid gluten. He found that this woman was highly motivated to get well because she had become deathly ill with her exposures to malathion. She was compliant with what the author asked her to do. She found that the change in diet and the introduction of key nutritional supplements, such as liposomal glutathione, curcumin, and fish oil, was most helpful. As well as obtaining the knowledge of how she was designed genetically for detoxification, she had also learned important information about the lifelong modification of her environmental exposures.

CONCLUSIONS

It is increasingly important for each one of us to develop a detoxification lifestyle as a strategy in maintaining excellent health. Components of such a lifestyle include avoidance of environmental toxicants, excellent nutritional strategies, optimal gastrointestinal health, attention to stress/resilience and relational health, adequate sleep and relaxation, and the mobilization, biotransformation, and elimination of toxicants. This article has reviewed the importance of the phases I and II model of detoxification and biotransformation, emphasizing the food-as-medicine approach to supplying the body with a myriad of macro- and micronutrients as well

as the phytochemicals required to keep those highly complex processes functioning in a balanced fashion. A useful tool, the detox-focused core food plan, has been presented to help health practitioners enhance clinical acumen and improve patient compliance. In this article, the case of a 45-year-old woman with acute joint pain, episcleritis, and shortness of breath has been reviewed, demonstrating dramatic improvement through application of the functional medicine model of critical thinking, together with the use of new investigative tools and the therapeutic power of nutritional interventions to support detoxification processes.

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