What is a “Detoxification Diet”? 

Jeffery S. Bland, Ph.D.

Detoxification is a fundamental metabolic process encoded by more than one hundred genes, expressing enzymes that comprise the phase 1, 2, and 3 detoxification processes. When discovered in the late 1960s, these enzymes were thought to be involved primarily in drug metabolism but were quickly recognized to be critically involved in both general xenobiotic metabolism and metabolic biotransformation of hormone and intermediary metabolites. As such, this system of biotransformation/detoxification enzymes is responsible for the control of intermediary metabolism, as well as protection of the organism against exposure to and adverse metabolic consequences of external (exo) and internal (endo) toxins, ranging from foreign chemicals to enteric bacteria-related endotoxins. The process of metabolic detoxification takes place primarily in the gastrointestinal and hepatic systems and is involved in the “first pass” detoxification of drugs, xenobiotics and substances produced in the gastrointestinal tract.

It is important to note that any substance that accumulates in the body’s tissues can potentially become a toxin and, above a certain threshold concentration, can impair metabolic function. An example of this is the cellular metabolite lactic acid. Under normal metabolic conditions, its concentration is controlled within cells, and it does not have a deleterious effect on the organism. However, under certain conditions, such as enhanced lactic acid production during extreme physical exertion, or slowed lactic acid metabolism as a side-effect of some drugs, lactic acid can build up in tissues, resulting in muscle pain, low energy, and central nervous system abnormalities.

Many potentially toxic substances are lipid soluble and can bioaccumulate in lipid-rich tissues. Through the phase 1 cytochrome P450 (CYP450) and phase 2 conjugation systems, these lipid soluble toxic substances are converted into water soluble metabolites that can be excreted in the urine or feces. The phase 1 CYP450 system is made up of nearly a hundred different enzymes, each with different affinities for specific substrates. The genes that both encode and control the expression of these CYP450 enzymes have been found to be highly polymorphic. In other words, numerous single nucleotide polymorphisms (SNPs) have been identified within this family of enzymes, which translates clinically into slow, intermediate and fast detoxification phenotypes. This has resulted in the concept of the “yellow canary syndrome” — the name applied to individuals with a genetically regulated slow metabolism of specific substances, thus increasing the potential for these individuals to have an adverse response at a lower level of exposure to the substances. Recent information suggests that the genetically controlled detoxification system demonstrates a larger inter-individual variation in function than any other metabolic process; the difference in first phase metabolism for a specific substance can vary as much as 1000-fold among healthy individuals.

The phase 2 conjugation reactions involved in detoxification include glucuronic acid conjugation, sulfation, amino acid conjugation, methylation, acetylation, and glutathione conjugation. The phase 2 enzymes convert the biotransformed intermediates produced by CYP450 metabolism into water soluble final products that can be safely excreted.

continued on page 69
The “total load” concept
There is potential for competition among different substrates for biotransformation by the same detoxification enzymes. This competition among various substances poses a risk for impaired detoxification due to overloading specific steps in the phase 1 or phase 2 processes, which then exceeds the capacity of the system to manage the “total load” of exposure. This has been observed clinically with various potential adverse drug-drug interactions, such as amiodarone for heart rhythm problems and simvastatin for elevated serum cholesterol. Another example—and the most common cause of emergency room visits for poisoning—is the consumption of alcohol while taking the over-the-counter drug acetaminophen.

The discovery that diet and specific foods influence detoxification
The field of detoxification/biotransformation took a big step forward in the 1970s with the recognition that diet could have an important impact on the phase 1 and 2 enzyme systems. It was first recognized that adequate calorie and protein consumption is necessary to support detoxification. Animal models indicated that certain constituents in vegetables and fruits stimulated intestinal drug metabolism. In 1978, it was reported that vegetarians had a more rapid first pass drug metabolism than omnivores, once again suggesting that certain dietary compositions and specific constituents of vegetable-rich diets were associated with increased detoxification. Controlled human dietary intervention trials have confirmed that consumption of vegetables at levels consistent with normal dietary intakes increases the rate of detoxification. It has also been shown that diets rich in plant foods that have an alkaline influence on the body enhance the excretion of biotransformed substances. Alkalization of the urine can be achieved by consuming a diet that is high in alkaline ash foods, including vegetables, fruits and legumes. In contrast, diets high in animal proteins, sugars, fat and processed foods are known to result in acidification of the urine, which is associated with a delayed excretion of biotransformed substances.

From these discoveries, researchers have recognized that unique phytochemicals have specific influences on activation of phase 1, 2, and 3 biotransformation processes. Cruciferous vegetables, including cabbage, Brussels sprouts, broccoli and cauliflower contain a family of phytochemicals termed glucosinolates. When digested, these compounds release a number of secondary metabolites into the gut, such as sulforaphane, indole-3-carbinol, and phenylethyl isothiocyanate. These secondary metabolites have been found to influence the genetic expression of both specific CYP450 and phase 2 enzyme systems. These phytochemicals are considered to be “bifunctional,” in that they simultaneously influence the function of both the phase 1 and phase 2 biotransformation/detoxification enzymes. It is very important to achieve proper regulation in modulating phase 1 and phase 2 enzyme systems to produce a substance that can be readily excreted. This process is known as “balanced detoxification.”

Other vegetable and fruit-derived phytochemicals, such as resveratrol from grapes, have also been found to have specific influences on phase 1, 2, and 3 biotransformation functions, as well as on the activation of the genomic antioxidant response element. It is interesting to note that the xenobiotic response element (XRE), antioxidant response element (ARE), and metal response element (MRE) are all co-localized in the human genome, indicating that they share promoter activities. The XRE, ARE, and MRE control the expression of the genes involved in detoxification of foreign chemicals, protection against oxidant stress, and detoxification of toxic heavy metals, respectively. One of the central transcription factors induced by consumption of specific phytochemicals is nuclear regulatory factor 2 (Nrf2), which activates the XRE, ARE and MRE. When activated by specific phytochemicals, Nrf2 regulates the genetic expression of phase 1, 2, and 3 biotransformation and antioxidant enzymes, such as glutathione peroxidase, peroxidase and catalase.

The mechanism of action of phytochemicals and their influence on detoxification
The discovery of the cellular mechanism by which phytochemicals influence detoxification has contributed to the understanding of the important role that diet and foods have on biotransformation. It is recognized that the relatively small amount of phytochemicals in a well-constructed food plan can have a much greater impact on cellular physiology than would be presumed from a traditional “dose-response” pharmacology perspective. This enhanced activity has been termed “hormesis,” which means that the physiological impact of exposure at relatively low levels of dietary intake is amplified due to a unique mechanism of action. The proposed mechanism of action of phytochemicals has been termed “xenohormesis” by Sinclair. The xenohormetic mechanism is built around the recognition that specific phytochemicals influence intercellular signal transduction and the induction of specific nuclear transcription factors. These nuclear transcription factors regulate the expression of unique families of genes, which in turn control critical cellular functions, such as xenobiotic detoxification, anti-oxidation, anti-inflammation, and metal detoxification. It is this influence of specific phytochemicals on important regulatory nodes within the genome of an individual that results in a unique metabolic response to exposures to foreign substances.

Cellular biology studies, animal model systems and human intervention trials have all demonstrated the important role of xenohormesis in modulating physiological function associated with biotransformation and detoxification. This development in our understanding of the role that diet and specific substances within foods play on intercellular signal transduction has been considered to be
the seminal nutritional discovery of the 21st century, potentially rivaling the 20th century discovery of vitamins in its importance for combating disease. The exciting developments in the field of nutrition related to metabolic biotransformation and detoxification have been reinforced by a number of published human clinical trials. These studies have been built upon a solid foundation of basic cellular and animal science. As an example, it was shown that animals that were pre-treated with a nutritional mixture of phytochemicals were able to prevent acetaminophen-induced cellular injury by a xenohormetic increase in biotransformation/detoxification and antioxidant response. Another example is the evaluation of the influence of the cruciferous vegetable-derived phytochemical indole-3-carbinol (I3C) and its companion diindolylmethane (DIM) on estrogen biotransformation/detoxification and reduction of breast cancer risk. Minich and Bland reviewed the history, safety and use of cruciferous vegetable phytochemicals in detoxification in 2007, concluding their therapeutic use to be both safe and efficacious based upon the studies.

The Department of Molecular and Cellular Biology at MetaProteomics and the Functional Medicine Clinical Research Center recently conducted a human clinical trial investigating the influence of a phytochemically-enriched diet on detoxification enzyme systems. Their results demonstrated the effectiveness of this intervention in both enhancing specific detoxification function through activation of genetic expression and reducing clinical symptoms associated with fibromyalgia. A recent series of published clinical trials studied the effects of phytochemical supplementation in patients with metabolic disturbances associated with insulin resistance. Both the control groups and the intervention groups consumed a low glycemic load Mediterranean diet high in phytochemically-dense foods. The treatment groups received phytochemical supplementation and had a statistically significant improvement in multiple physiological markers associated with biotransformation function. The phytochemical supplementation came in the form of a food concentrate containing specific rho-iso-alpha acids from the common hops plant (Humulus lupulus L.) and polyphenol-containing extract from Acacia nilotica, along with soy-derived phytoestrogens. It is important to note that the control groups consuming the low glycemic load Mediterranean diet achieved an excellent clinical response to the dietary intervention, but the inclusion of the specific phytochemical concentrate targeting intercellular signal transduction pathways, in conjunction with the diet, produced statistically superior outcomes. Lerman et al, in a 2011 clinical intervention study, found that the Mediterranean-style low glycemic load food plan improved the variables of metabolic syndrome in women, and the addition of a phytochemical-rich medical food enhanced the benefits on lipoprotein biotransformation.

Based on a series of clinical intervention trials, Schiltz et al developed and published a food plan focused on phytochemical support of biotransformation/ cellular signaling metabolic networks. In discussing the role of phytochemicals in this food plan, Minich and Bland reviewed the functions of specific dietary constituents in supporting proper metabolic biotransformation and the correction of metabolic disturbances and concluded that specific phytochemically-rich foods can improve cellular signaling related to detoxification processes, inflammatory response and insulin sensitivity.

Is there a “detoxification diet”?

The science that underlies clinical nutrition is undergoing a paradigm shift. The concept that specific phytochemicals can modulate intercellular signal transduction processes that regulate genetic expression of phase 1,2, and 3 enzymes involved in the control of biotransformation processes represents a very important advance in understanding the role that diet and specific foods play in detoxification. These scientific advances, coupled with advances in the field of nutrigenomics, provide for a better appreciation of how to develop personalized nutritional intervention programs. While there is not a specific detoxification diet, there are principles relating certain foods and phytochemicals to the detoxification process, which can be used to develop personalized dietary intervention programs for people with disturbed metabolism associated with impaired biotransformation/ detoxification. The take-away message emerging from the progress made in the fields of clinical nutrition, nutrigenomics and nutrioxidogenomics over the past ten years is that food, dietary quality and the specific nutrient and phytonutrient signature of the diet have an important impact on biotransformation/detoxification processes in humans.

Jeffrey S. Bland, Metagenics’ Chief Science Officer, and President of Metaproteomics, is an internationally recognized leader in the nutritional medicine field. Headquartered in Gig Harbor, WA, Dr. Bland founded HealthComm International, Inc. in 1985, and served as its Chief Executive Officer until the merger with its strategic partner, Metagenics, in 2000. A nutritional biochemist and registered clinical laboratory director, Dr. Bland is a former professor of biochemistry at the University of Puget Sound, and a previous Director of Nutritional Research at the Linus Pauling Institute of Science and Medicine. Dr. Bland has authored five books on nutritional medicine for the healthcare professional and five books on nutrition and health for the general public. He is the principal author of over 100 peer-reviewed research papers on nutritional biochemistry. Contact Dr. Bland at 253-851-3943 / 800-843-9660 or Fax: 253-851-9749.

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References continued on page 90

SAVE THE DATE!
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Cardiovascular disease and diabetes are twin epidemics with common roots in obesity, metabolic dysfunction, and toxic overload. Nutrition interventions and lifestyle strategies are the most powerful tools available to confront this healthcare challenge. This workshop will teach practitioners to apply an integrative and functional approach to cardio-metabolic syndrome including an overview of core imbalances, nutrition physical assessment, dietary supplements and functional laboratory testing. The concept of emotional brain training (EBT) to support behavior change, alleviate stress and promote well-being will be introduced. Case studies illustrating application in clinical practice will be reviewed along with resources for further exploration.

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What is a Detoxification Diet?

Objectives

After reading this CPE article, the nutrition professional will be able to:

1. Describe how genetic polymorphisms can influence xenobiotic metabolism.
2. Identify the role glucosinolates from cruciferous vegetables play in biotransformation.
3. Define “xenohormesis.”
4. Describe the mechanism of action of phytochemicals and their influence on detoxification.
5. Discuss the scientific evidence for the use of phytochemicals in enhancing biotransformation processes.
6. Differentiate between the concept of a specific “detoxification diet” versus using what is known about certain foods and phytonutrients to develop individualized diets to aid in the detoxification process.

What is a “Detoxification Diet”?

Circle the one best answer

1. Which of the following describes an example of how genetic polymorphism can affect xenobiotic metabolism?
   a. Can determine the detoxification genotypes.
   b. Can affect the speed of metabolism of specific substances.
   c. Can predict the metabolites of first pass metabolism.

2. What role do the glucosinolates from cruciferous vegetables play in biotransformation?
   a. Can modulate genetic expression of specific enzyme systems of both phase 1 and 2.
   b. Delay the excretion of phase 3 compounds allowing enhanced detoxification.
   c. Increase phase 1, first pass metabolism, while allowing phase 2 to remain constant.

3. Greater than expected cellular physiologic activity achieved at a low level of phytochemical intake is an example of which of the following?
   a. Balanced detoxification
   b. Xenohormesis
   c. Yellow canary syndrome

4. Which of the following describes the phytochemical mechanism of action and its influence on detoxification?
   a. Inhibition of specific nuclear transcription factors & de-activation of phases 2 & 3.
   b. Induction of specific nuclear transcription factors & activation of phases 1, 2, & 3.
   c. Deactivation of glucosinolate metabolites, which increases activation of phase 3.

5. Which of the following is an example of the scientific evidence for the use of phytochemicals in enhancing biotransformation processes?
   b. Reversal of acetaminophen poisoning by IV infusion of cruciferous vegetable extracts.
   c. In vivo studies demonstrating the prevention of HIV infection by stimulating CYP450.

Answer Key: 1. b; 2. a; 3. b; 4. b; 5. a
Hepatic Detoxification — An Overview

Shari Pollack, MPH, RD

Introduction

Among the liver’s many functions, detoxification has long been recognized as playing a vital role in maintaining good health and preventing disease. Whether the liver needs help to detoxify the onslaught of toxic compounds it faces or is capable of handling the job unassisted is an area of intense debate within the medical community. Some argue that the growing toxic burden we face from environmental pollutants, coupled with the nutrient-poor standard American diet, places too great a stress on the liver. Therefore, detoxification support in the form of diet and nutrient supplementation is needed to prevent the accumulation of toxins. Others argue that the body is well-equipped to handle the load and that attempting to assist in the detoxification process may cause more harm than good. A solid understanding of the hepatic detoxification system is necessary for one to appreciate the arguments on either side.

Biotransformation

The cell membrane is one of the body’s first lines of defense against foreign compounds, or xenobiotics. Its lipid bilayer blocks entry of polar, or hydrophilic, compounds. Lipid-soluble compounds, on the other hand, diffuse across cell membranes with little difficulty. When hydrophobic xenobiotics, such as pharmaceutical and recreational drugs, food toxins, pesticides, and other environmental pollutants find their way into the body, their non-polarity makes them difficult to excrete. The main task of hepatic detoxification is to convert these lipid-soluble compounds into water-soluble metabolites that can be more easily excreted in the urine or bile. This conversion process, called biotransformation, is accomplished in two phases—functionalization and conjugation—first identified by RT Williams in 1947.1

Phase 1

In phase 1, lipid-soluble compounds are converted into more polar compounds through chemical reactions that either add or expose a functional group, such as a hydroxyl group (–OH). Oxidation, reduction, and hydrolysis are the main reactions in phase 1.2 In some cases, the resulting metabolite may be excreted directly. More often, however, it requires further transformation by phase 2 enzymes.

The cytochrome P450 (CYP450) enzymes are responsible for catalyzing the majority of phase 1 reactions. This “superfamily of mixed function oxidases” is found throughout all biological kingdoms.2 Humans have 57 different CYP450 genes.3 The CYP enzymes are found in the endoplasmic reticulum (ER) and mitochondria, mainly in the liver, but also in the gastrointestinal tract, kidneys, lungs, brain, and other tissues. They are hemoproteins with broad substrate specificity that act not only on xenobiotics, but also on endogenous compounds such as fatty acids, cholesterol, steroid hormones, and eicosanoids. With NADPH as a cofactor, they catalyze reactions that introduce one atom of oxygen into a substrate; as such, they are sometimes referred to as monoxygenases.

While the action of the CYPs 450 enzymes are generally thought of as detoxifying, phase 1 reactions can also produce intermediate compounds that are more toxic than the parent compounds; this is referred to as bioactivation.4 These reactive metabolites, if not modified by phase 2 enzymes, are capable of interacting with cellular components, such as proteins, RNA and DNA, causing damage that “can lead to carcinogenicity, immunotoxicity, [and] necrosis.”4

Phase 2

Biotransformation continues in phase 2. The phase 2 enzymes catalyze reactions that add a polar group to the reactive site of the intermediate compounds produced by phase 1 reactions (though some toxins bypass phase 1 and are metabolized by phase 2 enzymes directly). The resulting conjugates are water-soluble and can be excreted in the urine and bile. The six main reactions in phase 2 are glucuronidation, sulfation, acetylation, glutathione conjugation (with subsequent mercapturic acid formation), amino acid conjugation, and methylation.5 The co-factors, enzymes, and substrates associated with these reactions can be found in Table 1.

According to Jeffery (2007), some products of glucuronidation are excreted via the bile but are then reabsorbed due to the action of a beta-glucuronidase in the gut microflora, which “can break the conjugate, reversing the hydrophilicity gained from conjugation.”6

Phase 3 — Antiporter Activity

The efflux proteins, such as p-glycoprotein, multidrug resistance-associated proteins (MRPs), and breast cancer resistance protein (BCRP), along with solute carrier transporters, carry out phase 3 of detoxification.7 These ATP-binding cassette (ABC) transporters, or antiporters, are present in the apical membranes of enterocytes and hepatocytes and act as pumps, mediating both the uptake of toxins from the intestinal lumen and the excretion of metabolites into bile.10 As such, they play an important role, first in regulating the degree to which a given toxin is absorbed, and then in shutting out of the liver the hydrophilic compounds resulting from phase 2 reactions.

Balancing Act

Age, sex, genetics, smoking status, pregnancy, disease, environmental exposure, and diet can all impact the body’s ability to metabolize xenobiotics.1,7,11 The enzymes involved in both phase 1 and phase 2 reactions can be induced or inhibited by many factors. For example, some compounds will upregulate the production of particular enzymes required for their own biotransformation, thus increasing the rate of detoxification. Some may influence a single enzyme or phase (monofunctional inducers), while others may induce multiple enzyme activities (multifunctional inducers).11 According to Liska (2005):
Mono-functional inducers, such as poly-cyclic hydrocarbons from cigarette smoke and aryl amines from charbroiled meats, result in dramatic induction of the CY-P1A1 and CYP1A2 enzymes, leading to a substantial increase in Phase 1 activity, with little or no induction of phase 2 enzymes...Induction of these activities without co-induction of Phase 2 activities may lead to an uncoupling of the Phase 1 and Phase 2 balance of activity and, therefore, a higher level of reactive intermediates, which can cause damage to DNA, RNA, and proteins.17

Likewise, induction of phase 1 by supplementation with nutrients that increase CYP450 activity, such as ascorbic acid, selenium, and polyphenols, without concomitant support for phase 2 activity, could lead to cellular damage, as the high concentration of circulating reactive compounds exceeds the capacity of phase 2 pathways to detoxify them. Inhibition of xenobiotic metabolism can result from the action of a single compound (for example, the flavanone naringenin, found in grapefruit, which exerts an inhibitory effect on CYP1A2) or multiple compounds (as when two or more toxins compete for the same enzyme or enzymes). Insufficient intake of protein, fatty acids, phytonutrients, and micronutrients involved as enzymatic cofactors can also decrease detoxification. Furthermore, detoxification can be downregulated by the depletion of cofactors. For example, the generation of free radicals by phase 1 reactions can result in the depletion of glutathione, an important free radical scavenger/antioxidant, which in turn decreases phase 2 glutathione con-

### Table 1: The Major Phase 2 Reactions

<table>
<thead>
<tr>
<th>Reaction and Co-factor</th>
<th>Enzymes</th>
<th>Substrates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucuronidation</td>
<td>Glucuronosyltransferases</td>
<td>Most prescription drugs, Fat-soluble vitamins, Steroid hormones, Bilirubin, Food additives/dietary toxins</td>
</tr>
<tr>
<td>conjugation with glucuronic acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfation</td>
<td>Sulphotransferases</td>
<td>Certain drugs (acetaminophen, warfarin), Ethyl alcohol, Melatonin, Neurotransmitters, Steroid hormones, Thyroid hormones, Food additives, Intestinal bacterial toxins</td>
</tr>
<tr>
<td>conjugation with adenosine 3'-phosphate-5'-phosphosulfate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetylation</td>
<td>Acetyltransfersases</td>
<td>Dietary toxins, Caffeine, Histamine, Serotonin, B-complex vitamins</td>
</tr>
<tr>
<td>conjugation with acetyl-CoA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glutathione Conjugation</td>
<td>Glutathione S-transferases</td>
<td>Aflatoxin (mold from Aspergillus flavus on peanuts, for example), Bacterial toxins, Bilirubin, Ethyl alcohol metabolites, Lipid peroxides, Naphthalene (from plastics), Petrochemicals, Prostaglandins, Toxic metals</td>
</tr>
<tr>
<td>conjugation with reduced glutathione (GSH)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amino Acid Conjugation</td>
<td>Acyl-coenzyme A ligase, Acyl-CoA-amino-acid-N-acyltransferase</td>
<td>Food preservatives, Herbicides, Insecticides, NSAIDs (Ibuprofen)</td>
</tr>
<tr>
<td>conjugation with arginine, glutamine, glycine, ornithine, or taurine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylation</td>
<td>Methyltransferases</td>
<td>Drugs, Estrogens, Vitamin B-12, Pesticides, Mercury</td>
</tr>
<tr>
<td>donation of methyl groups from S-adenosylmethionine (SAM)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Salguero 2 Queen 3 Murray 4 Knights
jugation activity.

Take Home Message

With 3.93 billion pounds of toxic chemicals released into the US environment, by the latest estimates, there can be little doubt that properly functioning detoxification pathways are vital to defending the body against the associated health threats. Reducing one's exposure to environmental toxins, including food additives and pesticide residues, minimizing intake of processed foods, and optimizing nutrient intake through a whole foods diet is a conservative and prudent approach to handling the ever-increasing toxic burden with which we are faced. Due to individual variability in detoxification capacity related to factors such as genetics, lifestyle, drug intake, and other environmental exposures, this approach may not go far enough. Hepatic detoxification involves a highly complex array of enzymes, cofactors, and reactions. Maintaining the proper balance between phase 1 and phase 2 activity is essential, and attempts to support the detoxification process through diet or nutritional supplementation require a thorough understanding of the complicated pathways involved.

Shari Pollack, MPH, RD is the Education and Staff Development Dietitian at the Jesse Brown VA Medical Center in Chicago and is the CPE Editor for the DIFM newsletter. She can be contacted at sbethp@gmail.com or 312-569-6568.

References

Hepatic Detoxification—An Overview

Objectives

After reading this CPE article, the nutrition professional will be able to:

7. Describe the general process by which the liver detoxifies xenobiotics.
8. Differentiate between biotransformation and bioactivation.
9. Identify the main outcome of phase 1 reactions.
10. Identify the primary family of enzymes involved in phase 1 detoxification.
11. Identify at least 4 types of conjugation reactions involved in phase 2 detoxification.
12. Understand possible reasons for and consequences of an imbalance between phase 1 and phase 2 reactions.
13. Understand the role of the phase 3 efflux proteins.

Choose the one best answer.

1. Which of the following is the general process by which the liver detoxifies xenobiotics?
   a. Converting lipid-soluble compounds into excretable water-soluble metabolites.
   b. Converting water-soluble compounds into excretable lipid-soluble metabolites.
   c. Altering the lipid membrane creating tight junctions to prevent entry of foreign matter.

2. Which of the following describes bioactivation?
   a. Formation of a less reactive/toxic product after phase 1 reaction.
   b. Formation of a more reactive/toxic product after phase 1 reaction.
   c. Formation of a neutral compound after phase 2 reaction.

3. Which of the following best describes biotransformation?
   a. Conversion process relying largely on oxidases, glucosinolases and ligases.
   b. Conversion process that results in a hydrophobic metabolite post phase 2.
   c. Conversion process relying largely on CYP450 enzymes and conjugation OR Conversion process accomplished via functionalization and conjugation.

4. Which of the following is the main outcome of phase 1 reaction?
   a. Hydroxylated or more polar compound.
   b. Hydroxylated or more hydrophobic compound.
   c. Lipid peroxidation to a neutral compound.

5. Which is the primary family of enzymes involved in phase 1 detoxification?
   a. Mixed function oxidases; CYM 450.
   b. Mixed function oxidases; CYG 450.
   c. Mixed function oxidases; CYP 450.

6. Which four types of conjugation reactions are involved in phase 2 detoxification?
   a. Peroxidation, sulfation, acetylation and glutathione conjugation.
   b. Amino acid conjugation, methylation, glucuronidation and sulfation.
   c. Sulfation, hydroxylation, acetylation, and glucuronidation.

7. Which of the following is a role of the phase 3 efflux proteins?
   a. Mediating uptake of intestinal toxins & excretion of the conjugated compound.
   b. Inducing the activity of CYP1A1 enzymes and inhibiting CYP1A2 enzymes.
   c. Re-establishing the lipid bilayer of the cell membrane after phase 1 reactions.

Answer Key: 1. a; 2. b; 3. c; 4. a; 5. c; 6. b; 7. a
CPE Objectives and Questions

CPE answer sheet for questions for Spring 2012 CPE and reporting instructions: Detoxification

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What is a “Detoxification Diet”?

1. a; b; c
2. a; b; c
3. a; b; c

Hepatic Detoxification—an Overview

1. a; b; c
2. a; b; c
3. a; b; c
4. a; b; c
5. a; b; c
6. a; b; c
7. a; b; c

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Detoxification in Practice

By Kathie Madonna Swift MS, RD, LDN

Detox diets are born, bred and branded at breakneck speed. There is no doubt that “detox” is a hot topic for consumers searching for natural ways to ward off disease, manage body burden, achieve healthy weight, and treat inflammatory conditions. A dietician trained in integrative and functional medicine can guide an individual interested in “detoxing” and advance their client’s understanding of this sophisticated physiological process that is highly dependent on optimal nutrition.

Here are a few key steps that outline how to apply evidence-based research to support detoxification:

1. **Use the Integrative and Functional Medical Nutrition Therapy (IFMNT) Radial** as a “detox map.” This outlines the critical factors to consider in an integrative and functional nutrition “detox” care plan including:

   a. **Genetics.** There are certain genetic tendencies or “SNPs” (single nucleotide polymorphisms) that influence detoxification, such as GSTM, MTHFR, COMT, SOD, etc. If you do not have SNP data, investigate your client’s family history and consider the possibilities that may lie within the family DNA and the individual’s environment that could be interacting with their “book of life.”

   b. **Triggers.** P.A.I.N.T.S. is a heuristic that encompasses essential detox data to gather: P=pathogens, A=allergens, I=intolerances, N=neuro-endocrine (SNPs), T=toxins and S=Stress. Incorporate a thorough environmental history as a part of your nutrition assessment that investigates P.A.I.N.T.S.

   c. **Lifestyle.** Tune into clues in the patient’s story or medical history that are especially relevant to detoxification (e.g. mold exposure, toxic food load, sleep deprivation, emotional trauma, medications, supplements, etc.).

   d. **Core Imbalances.** A holistic approach to detoxification appreciates that it is not a stand-alone process but is highly integrated and influenced by cellular integrity, energy metabolism, digestive processes, neuro-endocrine-immune function, oxidative stress and nutritional status.

   e. **System, Signs & Symptoms.** A nutrition-focused physical can provide further evidence about detoxification function. A medical symptom questionnaire (MSQ) is a useful tool that provides information about physical symptoms relevant to detoxification, including fatigue, brain fog, fluid retention, elimination problems, etc.

   f. **Biomarkers.** Conventional labs should include basic biomarkers such as C-reactive protein, MTHFR, serum homocysteine, liver enzymes including GGT (marker of potential toxic burden), A1C, and nutrient levels including serum 25-OH vitamin D, B vitamins, magnesium and zinc. There are a number of functional diagnostics that expand the biochemical data, such as urine organic acids, urine toxic elements (heavy metals) and detoxigenomics profiles.

   g. **Metabolic Pathways/Networks.** An understanding of the liver detoxification pathways (Phase 1, 2 & 3) and their interconnectedness to other biological processes is essential. The liver, aptly dubbed the workhorse organ of detoxification, should be viewed in the context of a “whole systems” approach to health and healing. Connecting the dots of detox data together requires a comprehensive understanding of physiological networks beyond our working knowledge of the infamous Kreb’s cycle.

2. **Begin with food.** As simple as it sounds, a “foods first” approach is the ideal way to support detoxification including these key strategies:

   a. **Optimize calories and macronutrients to support detox.** The detoxification pathways are dependent on fuel in the form of high quality, nutrient dense whole foods. Short-changing the system of an optimal amount of calories, as often promoted in popularized fasts or cleanses, may impair both phase 1 & 2 detoxification. However, there is some research on water and juice fasting protocols that warrant our continued attention.

   b. **Eliminate toxic ingredients and harmful cooking methods.** There are numerous chemicals in the food supply (e.g. BPA, organochlorine compounds, parabens, etc.) that increase body burden and disrupt the endocrine system. Advise your clients of the sources of these toxins and identify cookware and cooking methods that are safe to use. A valuable resource for environmental
health information is www.ewg.org.

c. Remove food allergens and intolerances. Adverse food reactions, including both food allergens (e.g. egg, shellfish, etc.) and intolerances (gluten, dairy, fructose, etc.) contribute to a host of systemic disruptions. Compromised intestinal permeability, also known as “leaky gut,” impairs detoxification capacity.

d. Focus on fiber and fluids. Fiber is a matrix that has multiple functions and is essential for digestive health. Adequate fluids partnered with fiber aids in elimination, an important exit route for toxins. Fiber also nourishes the gut flora, resident bugs that communicate with the immune system and influence the second brain (gut brain).

e. Boost antioxidant and micronutrient defense. Endogenously derived metabolic toxins, such as advanced glycation end products (AGEs), lipid peroxides, and uric acid are often the result of a nutritionally challenged/Standard American diet (SAD). Cleaning up the diet by eliminating refined and processed foods, unhealthy fats, excess animal protein and other adulterations is one of the most significant changes that can promote healthy detoxification.

f. Include the Detoxicants. A squad of nutrients, dubbed “detoxicants,” provides the co-factors necessary to drive the detoxification process. A colorful, plant-centric plate should include: dark greens (dandelion, spinach, broccoli raab, etc.); yellow/orange (sweet potatoes, carrots, peaches, etc.); red/pink (grapefruit, radicchio, vine-ripened tomatoes, etc.); white/green (garlic, onions, fennel, etc.); blue/purple (blueberries, blackberries, eggplant, etc.), along with the phytonutrients found in herbs and spices (turmeric, ginger, rosemary, etc.). By diversifying plant foods in the diet, the messages found in the phytoDNA are transcribed to the benefit of the host.

3. Supplement strategically. A personalized supplement program may be designed based on the data analyzed and synthesized from a comprehensive nutrition assessment using the IFMNT Radial map. Medical foods, amino acids, B vitamins, omega-3 fatty acids, and digestive products are commonly used supplements in a detoxification program and, if used, must be tailored to the individual’s unique needs.

4. Integrate complementary healing modalities. Body, mind and spirit should be integrated in a natural detoxification program. Meditation, mindfulness, movement, tai chi, chi gong, guided imagery, prayer and other modalities can be transformative experiences in a healing journey.

5. Explore more about detox. There are a number of resources for the Integrative RD interested in detoxification. One of my favorite books is Detoxification and Healing: The Key to Optimal Health by functional medicine expert, Dr. Sydney Baker. The archived Integrative RD sample menu is included below:

**Detox Sample Menu**

**Breakfast Smoothie:** Dark greens, organic apple, fresh ginger, pumpkin seed protein powder, coconut milk

**Snack:** Pink grapefruit slices

**Lunch:** Wild salmon (grilled or canned) with parsley pesto, sweet potato, curried cauliflower

**Snack:** Avocado slices with a splash of lime

**Dinner:** White Bean Minestrone Soup, radicchio, fennel & arugula salad with extra-virgin olive oil and lemon vinaigrette

* Dairy, Grain, Soy, Nut, Shellfish free

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### White Bean Minestrone Soup

**Prep Time:** 20 min  **Cook Time:** 40 min  **Makes:** 6 (1 ½ cups) Servings

- 6 cups low-sodium, gluten-free vegetable broth (or The Inside Tract Vegetable Broth)
- 2 carrots, peeled and cut into 1/2”-thick rounds
- 2 ribs celery, cut into 1/2” pieces
- 1 cup baby portobello mushrooms, quartered
- 3 small zucchini, halved lengthwise, cut into 1/2” pieces
- 1 can (15 ounces) cannellini beans, drained
- 1 can (14 1/2 ounces) chopped tomatoes
- 1 teaspoon dried basil
- 1 teaspoon crushed dried rosemary
- Sea salt to taste
- Freshly ground black pepper to taste
- 2 cups chopped escarole
- Fresh basil

Add all the ingredients except the escarole to a 6- to 8-quart pot. Increase the heat to high and bring the soup to a boil. Reduce the heat to medium-low, partially cover the pot and simmer for 30 minutes. Stir in the escarole and simmer 5 minutes longer. Sprinkle with fresh basil and ladle the soup into 6 bowls.

*(Used with permission from The Inside Tract: Your Good Gut Guide to Great Digestive Health, Rodale 2011)*
Detoxification in Practice

tiveRD webinar on Persistent Organic Pollutants by Dr. Elizabeth Redmond is loaded with clinical pearls on detoxification. You can also purchase the Pre-FNCE CD, Achieving Hormone Balance: An Endocrine Dance of Environment, Genes, Diet and Detoxification from www.IntegrativeRD.org. And if you are up for a detox retreat, join me and my esteemed colleagues in the beautiful Berkshires in Massachusetts, for a five-day CPEU program on natural detoxification at Kripalu Center for Yoga and Health (www.kripalu.org).

Kathie Madonna Swift, MS, RD, LDN is the founder of SwiftNutrition (www.swiftnutrition.com) and author with Dr. Gerard Mullin of The Inside Tract: Your Good Gut Guide to Great Digestive Health (Rodale, 2011). Kathie leads Healthy Living Immersion programs at Kripalu Center for Yoga and Health, Stockbridge MA. Detoxification in Practice is an excerpt from Natural Detoxification in her upcoming “SwiftNutrition” ebook series.

References
2. Food As Medicine, Center for Mind Body Medicine, 2008.

New name, a new look is coming. The DIFM newsletter name has changed to THE INTEGRATIVE RD and the look will be changing soon.

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Ethan A. Bergman, PhD, RD, CD, FADA
Academy President • 2012-2013

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We generate and are exposed to compounds that are potentially harmful to our health. These compounds must be broken down and eliminated from the body to minimize negative health effects. Xenobiotics such as pesticides, herbicides, fungicides, plastic-based endocrine disruptors (phthalates, Bisphenol A, etc.), toxic heavy metals (cadmium, lead, mercury, arsenic, etc.), industrial chemicals (PCBs, PBBs, solvents, styrenes, etc.), and medications can disrupt metabolism and damage cells if not defused and removed. Even endogenously generated hormones, including estrogen and epinephrine, must be metabolized and eliminated properly. Even at low levels, chronic exposure to and bioaccumulation of toxins and metabolites can alter metabolism and disrupt homeostasis. Such disruptions can negatively affect endocrine, nervous, and immune systems and may contribute to Parkinson’s, Alzheimer’s and autoimmune diseases (e.g. systemic lupus erythematosus and scleroderma), allergies, cognitive deficits and mood changes, glucose dysregulation, and cancer.

We must detoxify or “biotransform” these harmful elements into compounds that can be more easily excreted. The process primarily involves conversion of a fat-soluble toxin into a less harmful, water-soluble compound that can be excreted via urine or sweat. There are two main phases of detoxification, with an intermediary phase during which molecules with greater toxicity can be generated. Balance between phase I and phase II, as well as ample antioxidant protection during the intermediary phase, is essential for safe and effective detoxification. Upregulation of phase I without adequate completion of phase II can ultimately increase toxic burden and disrupt metabolism. Excretion of biotransformed toxins—via urine, feces, and sweat—is also a crucial step in the process. Saunas may be instrumental in this process by facilitating the mobilization and excretion of stored toxins. Some toxins may require chelating or “binding” and can be excreted in the bile and feces. If toxins are not completely detoxified and excreted, they can accumulate in the liver or get packaged and shipped out for storage in adipose tissue—virtually a “toxic waste dump.” This vital task of detoxification depends on total exposure and body burden, nutritional status, and genetic competence. A system that is overloaded with toxins and undersupplied with nutrient cofactors may eventually reach TILT (Toxin Induced Loss of Tolerance) and detoxification is no longer adequate or effective. Functional deterioration quickly ensues and signs and symptoms of disease prevail. For a case-based overview of the many facets of detoxification, see Detoxify for Life: How Toxins Are Robbing You of Your Health and What You Can Do About It by Dr. John C. Cline, a physician specializing in the treatment of chronic and complex illnesses.

A person’s genetic makeup and degree of exposure also factor into the detoxification equation. Some individuals may have a SNP (single nucleotide polymorphism) that compromises detoxification capabilities because of altered or inadequate production of the enzymes and cofactors. Bioaccumulation and exposure during critical periods of development must also be taken into account. Toxins become concentrated at the top of the food chain and in areas of greater contamination. Prenatal exposure to toxins also must be taken into account considering that an average of 200 chemicals have been measured in the cord blood of newborns—indicative of what the mother was exposed to and stored herself. We may be able to reduce our exposure to toxins by increasing awareness of their sources, especially pesticides commonly used in food production. The Environmental Working Group has compiled a user-friendly list of “The Dirty Dozen” and “The Clean 15” (a downloadable PDF) that ranks fresh produce by its content and accumulation of pesticides. All phases of detoxification rely heavily on a host of nutrients and phytonutrients for completion. The process is energy-dependent as well. Phase I (via oxidation, reduction, hydrolysis, hydration, or dehalogenation) utilizes B-complex vitamins, glutathione, branched-chain amino acids, flavonoids, and phospholipids. Phase II (via sulfation, glucuronidation, glutathione conjugation, acetylation, amino acid conjugation, or methylation) employs glycine, taurine, glutamine, N-acetylcysteine, cysteine, methionine, and methyl donors. The volatile intermediary phase is tempered by ascorbic acid, tocopherols, selenium, copper, zinc, manganese, CoQ10, thiols (from garlic, onions, and cruciferous vegetables—broccoli, Brussels sprouts, cauliflower, watercress and cabbage), bioflavonoids, silymarin, and pycnogenol.

Functional Laboratory Assessment

Comprehensive laboratory assessment of detoxification should address current nutritional status, actual toxic load, genetic polymorphisms, and detoxification competence. A basic nutrition assessment should include review of an individual’s dietary intake, supplement plan, possible toxic exposures and triggers, physical evaluation of nutrient deficiencies, potential drug-induced nutrient depletions, complete metabolic panel (including RBC magnesium and 25-OH vitamin D) and a CBC with differential. Though the majority of detoxification activity takes place in the liver, traditional “liver function” tests measuring AST, ALT, and GGPT tell us about liver pathology, not actual metabolic function or detoxification capacity. The gastrointestinal tract plays a role in detoxification and elimination of toxins and byproducts as well.

Specific lab tests are needed to assess an individual’s actual detoxification activity, capacity, and genetic competence. Serum, urine, saliva, and hair tests help identify toxic load and detoxification capacity. Genetic tests are available to identify SNPs.
Functional Laboratory Assessment of Detoxification and Biotransformation

for the enzymes involved in detoxification, including N-Acetyltransferase and glutathione S-transferase M1 and T1. SNPs in folate metabolism and DNA repair are also important in assessing clinical picture and disease risk. A functional evaluation of micronutrient status is also recommended, which enables us to look beyond serum levels and assess what is available at the cellular level. Spectracell Laboratories, Inc. assesses micronutrient status by using depletion and repletion studies in white blood cells.

Assessment of Phase I

Phase I detoxification of xenobiotics is carried out primarily by the cytochrome P450 (CYP) enzymes, a family of mixed function oxidases active in gastrointestinal wall cells, kidneys, lung, brain and, most abundantly, in the liver. Several compounds can influence and regulate CYP enzymes, including transcriptional factors such as NF-kappaB and nutritional compounds such as vitamins and minerals. Table 1 lists nutritional influences on CYP enzymes. However, one need note that caution must be used in extrapolating these animal results to humans and that “many studies with individual nutrients were done several years ago and the indexes that were measured were often not very specific for particular P450 enzymes.” The CYP enzymes are believed to be “distinct gene products” and SNPs that affect their function now can be easily identified. Current CYP activity can be assessed through “challenge testing” using a “probe substance” with subsequent measurement of metabolites in urine, blood, or saliva.

Activity of the phase I cytochrome P450 enzyme CYP1A2 can be assessed using a caffeine challenge. CYP1A2 is instrumental in detoxifying several substances including polyaromatic hydrocarbons and amines (found in pesticides and charbroiled meat, respectively), as well as a number of the carcinogens generated from cigarette smoke. Several factors can influence an individual’s CYP1A2 activity, including alcohol intake, toxin exposure, medication ingestion, nutritional status, and genetic factors. Following caffeine ingestion, two to three saliva samples are obtained. The amount of caffeine and timing of sample acquisition are determined prior to test administration. Caffeine clearance can then be measured in the saliva.

Assessment of Phase II

Phase II conjugation combines a toxin or activated metabolite with an endogenous substrate (glucuronic acid, sulfate, glutathione, a methyl or acetyl group, or an amino acid) to produce a water-soluble compound that is more easily excreted. Defects in any of these steps can lead to suboptimal detoxification and metabolic abnormalities.

Phase II detoxification can best be evaluated by assessing amino acid and glutathione conjugation, glucuronidation, and sulfation. Using acetylamphetamine as a probe substance, normal detoxification via phase II sulfation (to form acetylamphetamine sulfate), or glucuronidation (to form acetylamphetamine glucuronide) can be assessed. If metabolic cofactors are absent or inadequate, or if associated SNPs are present, acetylamphetamine will undergo a phase II biotransformation first, followed by glutathione conjugation, which will yield acetylamphetamine mercapturate. N-acetyl-p-benzoquinoneimine (NAPQI)—the highly reactive intermediary compound produced from this alternative metabolic pathway—is toxic to the liver and must be cleared quickly. NAPQI can easily accumulate if phase I activity is induced without a balance of phase II glutathione conjugation. It is for this reason that high doses of the glutathione precursor N-acetyl-cysteine (NAC) are used as a rescue treatment to detoxify NAPQI in the event of acetaminophen overdose.

Phase II amino acid conjugation may utilize a variety of amino acids including glycine, arginine, taurine, and ornithine. Because glycine conjugation is a major pathway in humans, its assessment can be useful in evaluating amino acid conjugation overall. Aspirin or sodium benzoate can be utilized as a probe substance for assessing this common pathway. Because aspirin is degraded to salicylic acid, measurement of salicylic acid (the major metabolite) in the urine can assess the competence of glycine conjugation. The minor metabolite salicylic glucuronide can be measured in the urine as well. If an individual is sensitive to salicylates, sodium benzoate can be used to assess phase II glycine conjugation. Evaluation of any of these detoxification pathways should be preceded by a 24 hour or more elimination of aspirin, acetaminophen, foods that contain salicylates and/or sodium benzoate.

Assessment of Antioxidant Status

Antioxidant intake and status can be assessed by a thorough nutrition intake evaluation, as well as cell-based assessment of antioxidant status. Spectracell Laboratories provides analysis of lipoic acid, CoQ10, cysteine, glutathione, selenium, vitamin E, and a SPECTROX™ evaluation of total antioxidant function as part of their micronutrient testing. Several other nutrients are evaluated as well.

Heavy Metal Burden

The most common toxic elements tested are mercury, lead, arsenic, cadmium, aluminum, and nickel. The CDC’s Agency of Toxic Substance and Disease Registry discusses individual toxins, http://www.atsdr.cdc.gov/toxfaqs/index.asp. Evaluation of a heavy metal burden can be accomplished by using a variety of tests, including blood, urine (both provocative and not), fecal, and hair analysis. Traditionally, urine levels of heavy metals are only measured following administration of a flushing agent such as DMSA (dimercaptosuccinic acid), which mobilizes toxins from storage. Clinicians are now recommending testing a random serum sample prior to administration of the flushing agent in order to measure cirulating toxins, especially cadmium. Pre-flush samples may also assist in determining which chelating agent is best for the individual. Samples taken after the flushing agent has been administered will reflect total body burden.

Laboratory Testing

The Institute of Functional Medicine (IFM) offers a plethora of user-friendly tools, as-
Functional Laboratory Assessment of Detoxification and Biotransformation

Assessment forms, and educational materials, many that address detoxification. Guidelines and questionnaires are provided for addressing toxic exposure, functional laboratory testing, toxic metal provocation testing (to be administered by a physician), and components of a nutrition physical exam. In-depth education tools, programs, and updates are readily available as well. The IFM recommends the tests included in the Laboratory Testing Handout following this article for assessing detoxification and biotransformation.

There are a number of laboratories that conduct the tests listed. Some can be ordered by the patients themselves through websites such as DirectLabs.com, while others must be ordered through a professional account with the specific lab. Some tests must be administered by a physician. Sample lab reports from several of these tests can be viewed online via their respective websites. The following are examples of laboratories and tests available at the time of this writing; information listed is directly from the respective websites and full descriptions are available online.

**Doctor’s Data** ([www.doctorsdata.com](http://www.doctorsdata.com))
**Direct Labs** ([www.directlabs.com](http://www.directlabs.com))
**Genova Diagnostics** ([www.gdx.net](http://www.gdx.net))
**Metametrix** ([www.metametrix.com](http://www.metametrix.com))
**Spectracell Laboratories Micronutrient Testing** ([www.spectracell.com](http://www.spectracell.com))

Author’s notes: I have had personal communication with functional medicine physicians and practitioners (MD, DO, ND, ARNP, RD, CCN, etc.) and have received and provided continuing education on the topic of laboratory assessment of detoxification, including recommendations to use the laboratories listed above. Once practitioners study and recognize the roles that xenobiotics, detoxification, nutrigenomics, and nutritional status play in both health and disease, evaluation of detoxification capacity will become mainstream.

**Disclosure:**

The author does maintain professional accounts with Directlabs, Metametrix, and Spectracell, but does not receive financial or other compensation.

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**TABLE 1** Effect of micronutrients on activities in animals linked to cytochrome P450 (CYP450)

<table>
<thead>
<tr>
<th>Nutritional status</th>
<th>Effect on index measured</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A deficiency</td>
<td>Decrease in P450 (total); decrease in oxidations of aminopyrine, ethylmorphine, aniline, benzo[a]pyrene, and 7-ethoxycoumarin</td>
</tr>
<tr>
<td>Vitamin A, high concentration</td>
<td>Increase in oxidations of aniline and 7-ethoxycoumarin</td>
</tr>
<tr>
<td>Niacin deficiency Mild</td>
<td>Decrease in metabolism of anesthetics</td>
</tr>
<tr>
<td>Niacin deficiency Severe</td>
<td>Decrease in NADPH-P450 reductase; increase in oxidations of N-nitrosodimethylamine, aniline, and aminopyrine</td>
</tr>
<tr>
<td>Pyridoxine deficiency</td>
<td>No effect in several mixed-function oxidases</td>
</tr>
<tr>
<td>Thiamine deficiency</td>
<td>Increase in P450 2E1, NADPH-P450 reductase, and cytochrome b5; decrease in oxidations of N-nitrosodimethylamine, acetaminophen, aniline, aminopyrine, ethylmorphine, zoxazolamine, and benzo[a]pyrene</td>
</tr>
<tr>
<td>Vitamin C deficiency</td>
<td>Decrease in P450, NADPH-P450 reductase, and several mono-oxygenation activities</td>
</tr>
<tr>
<td>Vitamin C, high concentration</td>
<td>Decrease in several monoxygenation activities</td>
</tr>
<tr>
<td>Vitamin E deficiency</td>
<td>Decrease in oxidations of codeine, ethylmorphine, and benzo[a]pyrene</td>
</tr>
<tr>
<td>Folic acid deficiency</td>
<td>Decrease in induction of P450 2B1 by barbiturates</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>Decrease in oxidations of hexobarbital and aminopyrine; increase in oxidation of anilin</td>
</tr>
<tr>
<td>Iron, high concentration</td>
<td>Increase in NADPH-dependent lipid peroxidation</td>
</tr>
<tr>
<td>Copper deficiency</td>
<td>Decrease in oxidations of aniline and hexobarbital; increase in oxidation of benzo[a]pyrene</td>
</tr>
<tr>
<td>Zinc deficiency</td>
<td>Decrease in oxidations of pentobarbital and aminopyrine</td>
</tr>
<tr>
<td>Calcium deficiency</td>
<td>Decrease in several monoxygenation activities</td>
</tr>
<tr>
<td>Magnesium deficiency</td>
<td>Decrease in several monoxygenation activities</td>
</tr>
<tr>
<td>Selenium deficiency</td>
<td>Decrease in induction of P450 by phenobarbital</td>
</tr>
<tr>
<td>Aluminum, high concentration</td>
<td>Decrease in hepatic P450 oxidations of p-nitrophenetole and ethylmorphine</td>
</tr>
<tr>
<td>Calcium, cobalt, other heavy metals, high concentration</td>
<td>Decrease in P450 and related activities Increase in several monoxygenation activities</td>
</tr>
</tbody>
</table>

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Functional Laboratory Assessment of Detoxification and Biotransformation

Beth Ellen DiLuglio is a Certified Clinical Nutritionist and Registered Dietitian. She has taught Elements of Nutrition at Palm Beach State College for over a decade, as well as a wide range of continuing education courses focused on nutrition for health professionals. Contact Beth at NutritionMission.org@gmail.com or 561.881.9999.

References:

Inflammatory Process
Blood Amino Acids
Blood Fatty Acids
Blood Nutrient/Toxic Elements
Blood Food Antibody
Blood ADMA
Blood Vitamin D
Blood Lymphocyte Growth Assays
Blood Lipid
Blood Antioxidant Capacity
Blood Oxidant Stress Markers (e.g., Glutathione)
Blood HS-CRP, Ferritin, and/or Fibrinogen
Blood SNP Genomic Tests
Urinary Toxic Metals (provoked and unprovoked)
Urinary Organic Acids
Urinary Oxidant Stress Markers
Fecal Lysozyme
Fecal Lactoferrin
Fecal Calprotectin

Hormone and Neurotransmitter
Regulation
Blood Amino Acids
Blood Fatty Acids
Blood Food Antibody
Blood Estrogen, Progesterone, Testosterone, DHEA, SHBG
Blood Estrogen Metabolites
Blood Vitamin D
Blood Lymphocyte Growth Assays
Blood Lipid
Blood Thyroid Function (T3, T4, TSH, RT3, antibody)
Blood Insulin/Glucose
Blood SNP Genomic Tests
Urinary Organic Acids
Urinary Toxic Metals (provoked and unprovoked)
Urinary Amino Acids
Urinary Estrogen Metabolites
Urinary Iodide
Urinary Neurotransmitter Metabolites

Salivary Estrogen, Progesterone, Testosterone
Salivary Cortisol, DHEA
Salivary Melatonin

Digestion, Absorption and Barrier Integrity
Blood Fatty Acids
Blood Food Antibody
Blood H. Pylori
Blood Candida Antibody/Antigen
Blood Celiac Profile
Blood Lymphocyte Growth Assays
Blood Lipid
Urinary Organic Acids
Urinary Lactulose/Mannitol
Fecal Lysozyme
Fecal Lactoferrin
Fecal Ova & Parasites
Fecal Bacteriology Culture
Fecal Short-Chain Fatty Acids
Fecal Digestive Elements
**Laboratory Testing Handout**

**Part I: Tests Grouped by the Functional Medicine Matrix**

<table>
<thead>
<tr>
<th>Fecal Absorptive Elements</th>
<th>Hair Toxic Metals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal Mycology Culture</td>
<td><strong>Oxidative/Reductive Homeodynamics</strong></td>
</tr>
<tr>
<td>Fecal H. Pylori Antigen</td>
<td>Blood Amino Acids</td>
</tr>
<tr>
<td>Fecal Clostridium Difficile Toxins A &amp; B</td>
<td>Blood Nutrient/Toxic Elements</td>
</tr>
<tr>
<td>Fecal Enterohemorrhagic E. Coli Cytotoxin</td>
<td>Blood ADMA</td>
</tr>
<tr>
<td>Fecal Elastase-1</td>
<td>Blood Estrogen Metabolites</td>
</tr>
<tr>
<td>Fecal Calprotectin</td>
<td>Blood Vitamin D</td>
</tr>
<tr>
<td>Breath Lactose Intolerance</td>
<td>Blood Oxidant Stress Markers (Glutathione)</td>
</tr>
<tr>
<td>Breath Small Intestine Bacterial Overgrowth</td>
<td>Blood Antioxidant Capacity</td>
</tr>
</tbody>
</table>

**Detoxification and Biotransformation**

| Blood Amino Acids | Blood Lymphocyte Growth Assays |
|-------------------| Blood Antioxidant Capacity |
| Blood Nutrient/Toxic Elements | Blood Oxidant Stress Markers |
| Blood Estrogen Metabolites | Urinary Organic Acids |
| Blood Oxidant Stress Markers (e.g., Glutathione) | Urinary Oxidant Stress Markers |
| Blood SNP Genomic Tests | Urinary Toxic Metals (provoked and unprovoked) |
| Urinary Organic Acids | Urinary Estrogen Metabolites |
| Urinary Amino Acids | Urinary Challenge Detox Profiles |
| Urinary Toxic Metals (provoked and unprovoked) | Urinary Amino Acids |
| Urinary Estrogen Metabolites | Urinary Bone Resorption |
| Urinary Challenge Detox Profiles | Urinary Amino Acids |
| Urinary Mercapturic and D-Glucaric Acids | Blood Fatty Acids |
| Urinary Oxidant Stress Markers | Urinary Organic Acids |
| Fecal Toxic Metals | Urinary Toxic Metals (provoked and unprovoked) |

**Part II: Brief Descriptions of Functional Laboratory Tests**

*(Tests are organized alphabetically using the names shown in Part I above.)*

**Blood ADMA**

Plasma asymmetric dimethylarginine (ADMA) is a primary endogenous inhibitor of nitric oxide synthase that inhibits nitric oxide production. Elevated levels are implicated in cardiovascular disease and are a cause of hypertension, hyperhomocysteinemia, diabetes mellitus types 1 & 2, and pre-eclampsia. ADMA becomes elevated due to loss of activity for the ADMA-degrading enzyme DDAH when antioxidant protection is lacking.

**Blood Amino Acids**

Amino acid analyses aid in the assessment of: dietary protein adequacy and balance, gastrointestinal dysfunctions, forms of protein intolerance, nutritional deficiencies (vitamins, minerals), renal and hepatic dysfunction, psychiatric abnormalities, susceptibility to inflammatory response and oxidative stress, reduced detoxification capacity, susceptibility to occlusive arterial disease, and many inherent disorders of amino acid metabolism. Many free amino acids such as histidine, lysine, threonine and serine in plasma provide toxic element ligands for transport and renal excretion. Amino acid hepatic flux stimulates carcinogenic toxicant conjugation reactions. Amino acid analysis also shows phase II biotransformation substrates (glucose and sulfur amino acids) and status of glutathione precursor amino acids methionine and glycine. Fasting plasma and whole blood (bloodspot) levels provide a reliable assessment of dietary adequacy. Plasma hydroxylysine and hydroxyproline become elevated due to increased rates of bone resorption.

**Blood Antioxidant Capacity**

T-lymphocytes are cultured under optimal growth conditions and, following mitogenic stimulation, are exposed to increasing concentrations of free radicals to measure the cell's ability to resist oxidative stress. Specific antioxidants (i.e., selenium, tocopherols, glutathione, Coq10, etc.) are available to identify specific intracellular functional deficiencies that may limit anti-
Part II: Brief Descriptions of Functional Laboratory Tests

oxidant capacity within a highly interactive system of antioxidants.

**Blood Candida Antibody/Antigen**
Serum IgM, IgG, IgA antibodies for Candida albicans are used to indirectly assess current, past, and mucosal exposure to this yeast, respectively. Serum Candida albicans (antigen) is measured to identify its presence in circulation. Candida is associated with both acute and chronic conditions.

**Blood Celiac Profile**
Total immunoglobulins A, tissue transglutaminase IgA, and anti-gliadin IgA are measured. An elevated tissue transglutaminase IgA is highly sensitive and specific for gastrointestinal villous atrophy associated with Celiac. An elevated anti-gliadin IgA indicates specific gluten-activated immune response.

**Blood Estrogen Metabolites**
Blood estrogen metabolites include 2-hydroxyestrone and 16-alpha-hydroxyestrone, and reflect how estrogen is being processed in the body. Blood sampling provides a direct assessment of circulating estrogen metabolites that act directly on target tissues. Imbalances of these metabolites are associated with cardiovascular disease, depression, osteoporosis, lupus, and breast cancer.

**Blood Estrogen, Progesterone, Testosterone, DHEA, SHBG**
Serum assays provide an accurate and time-tested assessment of estrogen, progesterone, testosterone, and DHEA at a point in time. Sex hormone binding globulin (SHBG) is also measured in serum to provide an estimate of free testosterone and estradiol, which are primarily bound by this protein. These hormones are assessed to evaluate ovarian and adrenal dysfunction, and to determine need and dose of related hormone replacement therapy.

**Blood Fatty Acids (plasma, RBC, blood spot)**
Fatty acid (FA) profiles show quantitative results for individual fatty acids, including polyunsaturated omega-3 (including ALA, EPA, DHA), omega-6 (including GLA, DGLA, AA), omega-9 (including oleic, nervonic), saturates (including capric, palmitic, stearic, hexacosanoic), and trans-fatty acids. Fatty acid ratios such as LA/DGLA and AA/EPA are calculated to help identify imbalances. Essential FA deficiencies and metabolic effects manifest as imbalances within and between families of fatty acids.

**Blood Food Antibody**
Semi-quantitative levels of serum IgE or IgG subclass responses to 30-90 common foods are used to identify food allergy or sensitivity due to leaky gut and to customize elimination/rotation diets.

**Blood H. pylori**
*Helicobacter pylori* is the bacterium that causes peptic ulcer disease and is associated with increased risk of gastric cancer. Blood assays indirectly identify the presence of H. pylori by measuring antibody levels in circulation.

**Blood Hs-CRP, Ferritin, Fibrinogen**
Testing for these acute phase protein markers in serum provides insight relevant to the inflammatory cascade, free iron modulation, and the clotting cascade, respectively.

**Blood Insulin/Glucose**
Elevated fasting serum insulin indicates insulin insensitivity that produces increased serum triglycerides and LDL cholesterol. Euglycemia in this scenario is characteristic of the metabolic syndrome, which is associated with increased risk of cardiovascular disease and diabetes.

**Blood Lipids**
Cardiovascular disease is a multifactorial process whose etiology encompasses both size and number of various lipoproteins. These include HDL and LDL subclasses, remnant lipoprotein, VLDL, and lipoprotein (a). Homocysteine, although not a lipoprotein, is recognized as a contributing factor to hemostasis, neurological function, and cardiovascular disease, and is easily measured in blood lipid studies.

**Blood Lymphocyte Growth Assays**
T-lymphocytes are grown in tissue culture by mitogenic stimulation of proliferation. By culturing the cells under a variety of conditions, functional deficiencies of vitamins, minerals, amino acids, antioxidants and other micronutrients can be assessed. The assays are a long-term indicator of nutritional status and are useful not only in the identification of functional deficiency states, but also in monitoring the effectiveness of repletion to achieve optimal intracellular function of the cofactors within cellular metabolism.

**Blood Mold and Yeast**
Mold and yeast blood antibody testing is used to assess for the immunologic reaction to these potential toxins. Mold and yeast exposures are associated with various acute and chronic conditions.

**Blood Nutrient and/or Toxic Elements**
Whole blood element analysis is a diagnostic method that assists in determining deficiencies, excesses, and imbalances of essential elements, as well as recent or ongoing exposure to specific toxic elements. Whole blood analysis measures total element levels that circulate extracellularly (serum/plasma) as well as intracellularly (function within blood cells). RBC element levels are very useful for assessing: cardionic influences (magnesium, potassium); anti-inflammatory processes (selenium, copper, zinc); anemia (copper, iron); immunological function (zinc, copper, magnesium); and glucose tolerance (chromium, manganese, and possibly vanadium). Accurate assessment of essential element status aids in determination of appropriate supplementation.

**Blood Oxidant Stress Markers**
Plasma amino acid testing reveals ability to maintain fasting blood levels of glutathione precursors methionine, homocysteine and glycine (taurine adds a further assessment of sulfur metabolism). Total body oxidant stress is evaluated with serum lipid peroxides. Erythrocyte elemental analysis is used to assess essential elemental cofactors, selenium, zinc, copper and manganese for redox-balancing enzymes like superoxide dismutase, and elevation of toxic elements that contribute to oxidant stress.

**Blood SNP Genomic Tests**
Genomic testing identifies specific variations in nucleic acid sequencing called single nucleotide polymorphisms (SNPs).
SNPs can influence many different functions:

**Detoxification:** SNPs can alter the kinetics of enzyme activity, affecting phase I and phase II detoxification and folic acid activation. Identification of these SNPs may indicate the need for lifestyle adjustments and nutritional supplementation that support normal enzyme activity, and highlight environmental exposures that possess increased toxicity.

**Hormone and neurotransmitters:** SNPs that affect induction and activity of enzymes that metabolize hormones and neurotransmitters may increase risk for related cancers and mood disorders. Identification of these SNPs may indicate the need for lifestyle adjustments and nutritional supplementation that support normal enzyme activity.

**Immune:** SNPs that affect the levels and activity of cytokines can modulate immune and inflammatory activity. These variations can affect balance between cell (Th-1) and humoral (Th-2) immunity and reveal potential defects in immune system defense.

**Inflammatory:** SNPs that affect the levels and activity of cytokines can modulate immune and inflammatory activity. These variations can affect balance between cell (Th-1) and humoral (Th-2) immunity, reveal potential defects in immune system defense, and stimulate mechanisms leading to chronic, overactive inflammatory responses. Identification of these SNPs may indicate the need for lifestyle adjustments and nutritional supplementation that support normal cytokine activity.

**Oxidative stress:** SNPs that affect the production or management of oxidative stress are associated with chronic illness. SNPs can alter protein induction and activities that elevate oxidative stress, including phase I and II detoxification enzymes, superoxide dismutase, and cytokines.

**Blood Thyroid function (T3, T4, TSH, RT3, and antibody)**
A comprehensive thyroid function analysis includes free T3, free T4, TSH, reverse T3, as well as thyroid peroxidase and thyroglobulin antibodies. These tests are used to diagnose thyroid disease, and to determine need for thyroid support, including need and dose of related thyroid hormone therapy.

**Blood Vitamin D**
Serum 25-hydroxyvitamin D is the major circulating precursor to active 1, 25-dihydroxy vitamin D. Low values show vitamin D deficiency and repeat testing allows monitoring of repletion in patients with osteoporosis or chronic inflammatory disorders.

**Blood Vitamin Profile**
Measurement of serum concentrations of fat-soluble vitamins including A, E, CoQ10, beta-carotene, and lycopene allow direct assessment of dietary sufficiency for these key antioxidants, essential or conditionally essential nutrients.

**Breath Lactose Intolerance**
This breath test identifies bacterial fermentation of lactose in the GI and indicates presence and severity of lactose intolerance.

**Breath Small Intestine Bacterial Overgrowth**
This breath test identifies overgrowth of bacteria in the small intestine.

**Fecal Absorptive Elements**
Long-chain fatty acids, phospholipids, cholesterol, triglycerides, and total fecal fat are measured in the stool to assess malabsorption. When poorly absorbed, these fecal fats will be elevated in the stool.

**Fecal Bacteriology Culture**
Measurement of these specific E. coli cyto-toxins in the feces is a reliable tool for the diagnosis of EHEC infections.

**Fecal Calprotectin**
Calprotectin is a neutrophil-derived protein that is released in the GI tract in the presence of infectious, inflammatory, or malignant disease. This quantitative assay can identify mild, moderate and severe levels of inflammation, and is FDA approved to differentiate irritable bowel syndrome (IBS) from inflammatory bowel disease (IBD). It can also be used to assess the effectiveness of treatment and to predict relapse in IBD cases.
and serves as an important diagnostic tool for chronic GI symptoms. Fecal lactoferrin assessment is a noninvasive screening for IBD (Crohn’s disease and ulcerative colitis).

**Fecal Lysozyme**
Lysozyme is secreted at sites of inflammation in the colonic mucosa. Lysozyme is a general marker for inflammation that is commonly elevated in the presence of dysbiosis. High fecal lysozyme levels may also accompany elevated fecal lactoferrin in IBD.

**Fecal Mycology Culture**
Identification of abnormal levels of specific yeast species in the stool is an important diagnostic step in therapeutic planning for the patient with chronic gastrointestinal and extra-gastrointestinal symptoms. Yeast sensitivities to a variety of prescriptive and natural agents are provided when yeast is cultured at any level. This provides the clinician with useful clinical information to help plan an appropriate treatment protocol.

**Fecal Ova & Parasites**
Chronic gastrointestinal complaints are among the most common reasons that patients seek medical care. Fecal ova and parasite identification can identify a common underlying cause of chronic or acute GI symptoms.

**Fecal Secretory IgA**
The humoral immune status of the GI tract can be assessed by determining the fecal concentration of sIgA. The sIgA secreted by mucosal-associated lymphoid tissue (MALT) represents a pivotal and specific line of defense in the GI mucosa. As the principal immunoglobulin isotype present in mucosal secretions, sIgA plays an important role in controlling the intestinal milieu.

**Fecal Short-Chain Fatty Acids (SCFAs)**
SCFAs are the end product of the bacterial fermentation process of dietary soluble fiber by beneficial bacteria in the GI. SCFAs decrease inflammation, stimulate healing, and contribute to normal cell metabolism and differentiation.

**Fecal Toxic Metals**
Fecal toxic metal analysis provides important information about the potential for toxic metal burden. For many toxic metals, fecal (biliary) excretion is the primary natural route of elimination from the body. Fecal elemental analysis also provides a direct indication of dietary/oral exposure to toxic metals, and can be used to gauge mercury exposure from dental amalgams.

**Hair Toxic Metals**
Toxic metals may be 200-300 times more highly concentrated in hair than in blood or urine. Hair is the tissue of choice for detection of recent or ongoing exposure to elements such as arsenic, aluminum, cadmium, lead, antimony, and mercury.

**Salivary Cortisol, DHEA**
When cortisol is measured in four serial specimens (spanning from morning to bedtime on a day of typical stressor exposure), abnormalities of cortisol circadian release in response to pituitary ACTH may be assessed. The average of the two mid-day salivary dehydroepiandrosterone (DHEA) levels allows inspection for depressed formation from cholesterol in protracted adrenal dysfunction. Measurement of total sIgA allows detection of suppressed levels due to chronic elevated cortisol impact on the gut-associated immune tissue. Further evaluation of this impact is provided by inspection for elevated anti-gliadin IgA.

**Salivary Estrogen, Progesterone, Testosterone**
Salivary estrogen, progesterone, and testosterone are convenient, noninvasive assays, measuring the free, bio-available form of these hormones. Salivary samples are collected at home, providing the opportunity to evaluate ovarian and adrenal function throughout their respective cycles, or to help account for mild fluctuations that occur in early menopause.

**Salivary Melatonin**
Salivary melatonin is a convenient, noninvasive assay that is commonly used to assess the circadian secretion patterns over a complete light-dark cycle. This testing can reveal abnormal levels of melatonin that relate to various physical and psychological symptoms as well as premature acceleration of the body’s aging process.

**Urinary Lactulose/Mannitol**
Oral challenge with a lactulose/mannitol sugar solution and measurement of urinary excretion identifies increased intestinal permeability and malabsorption.

**Urinary Amino Acids**
Amino acid analyses aid in the diagnosis of: dietary protein adequacy and balance, gastrointestinal dysfunctions, forms of protein intolerance, nutritional deficiencies (vitamins, minerals), renal and hepatic dysfunction, psychiatric abnormalities, susceptibility to inflammatory response and oxidative stress, reduced detoxification capacity, susceptibility to occlusive arterial disease, and many inherent disorders of amino acid metabolism. Amino acid hepatic flux stimulates carcinogenic toxicant conjugation reactions. Amino acid analysis also shows phase II biotransformation substrates (glycine and sulfur amino acids) and status of glutathione precursor amino acids methionine and glycine. Neurotransmitter and neurotransmitter precursor assessment is provided by measurement of phenylalanine, tyrosine, tryptophan, glycine, taurine and aspartic and glutamic acids. Urinary hydroxylysine and hydroxyproline become elevated due to increased rates of bone resorption. Both specimens also show 3-methylhistadine rise in states of muscle catabolism.

**Urinary Bone Resorption**
Urinary deoxypyridinoline (uDPD) assessment shows excretion of type I collagen peptide that is elevated when bone resorption increases to supply ionic calcium for critical cardiac and brain functions. Treatment efficacy can be monitored by repeat testing.

**Urinary Challenge Detox Profiles**
Challenge with caffeine, acetaminophen, and salicylic acid, with timed collection of urine and saliva, allows assessment of capacities for hepatic biotransformation phase I and II pathways, including CYP450 1A2, sulfation, glucuronidation, and glycination to meet toxin load demands. Measured compounds show the rate of Phase I caffeine clearance and percentage conversion of challenge compounds to oxidized,
sulfated, glucuronidated, and glycinated products.

**Urinary Estrogen Metabolites**

Urinary 2-hydroxyestrone, 2-hydroxyestradiol and 16-hydroxyestrone and the calculated 2/16 ratio are measured to assess the function of the primary (hepatic CYP1A1) and secondary CYP1B1 estrogen clearance pathways. A 2/16 ratio less than 2 is associated with increased risk of developing estrogen sensitive cancers. Extensively studied diet and food supplement regimens can be used to increase CYP1A1 activity to raise the ratio.

**Urinary Iodide**

Iodine/iodide is an essential element that is pivotal to normal function of the thyroid gland and the health and integrity of breast tissue. Iodine/iodide intake has decreased significantly over the past thirty years and clinical symptoms have become more apparent. Iodine/iodide sufficiency can be assessed by analysis of urinary iodide excretion with or without a loading protocol.

**Urinary Mercapturic and D-glucaric Acids**

Urinary D-glucaric acid, a byproduct of phase I detoxification, is a valuable indicator of chemical exposure or liver damage. Urinary mercapturic acids are direct end-product metabolites of conjugated xenobiotics. Combined assessment of the urinary levels of the two analytes provides valuable information about exposure to xenobiotics and liver disease, and the capability of the liver to eliminate toxins.

**Urinary Neurotransmitter Metabolites**

Urinary organic acid profiles show low or high levels of principal catabolites of nor-epinephrine and epinephrine (homovanillic acid and dopamine (vanilmandelate). These catecholamine metabolites reveal total body turnover that is depressed when the precursor amino acids phenylalanine and tyrosine are insufficient. Elevated levels found in patients with chronic stress response are a sign of accelerated utilization of the precursors that is antecedent to development of insufficiency. Similarly, the serotonin catabolite 5-hydroxyindolacetic acid reveals serotonin turnover and risk of tryptophan depletion. Simultaneous reporting of quinolinic acid and kynurenic acids allows inspection for inflammatory cytokine stimulation of glutamatergic neuronal activity.

**Urinary Organic Acids**

The full profile of organic acids in urine provides information on functional nutrient deficiencies, mitochondrial efficiency, methylation pathway cofactor sufficiency, neurotransmitter metabolites, oxidant stress, detoxification and dysbiosis markers. A primary biochemical communication from the immune system to the CNS is assessed by measuring urinary interferon gamma-stimulated quinolnic acid (NMDA agonist) and kynurenic acid (NMDA antagonist).

**Urinary Oxidant Stress Markers**

Urinary 8-hydroxy-2-deoxyguanosine reveals oxidative damage to DNA. Urinary organic acid profiles include p-hydroxyphenylaceta (elevated in conditions of increased cell proliferation such as cancer or chronic organ stress); alpha-hydroxybutyrate (elevation shows increased glutathione demand); pyroglutamate (elevation reveals glutathione wasting); and sulfate (low levels indicate total body glutathione depletion).

**Urinary Toxic Metals (provoked and unprovoked)**

Urinary metal analysis is an invaluable tool for the diagnosis or confirmation of toxic element burden and monitoring of detoxification therapy. A challenge consisting of pre and post provocation testing is recommended for diagnosing the presence of toxic element burdens.

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**Part II: Brief Descriptions of Functional Laboratory Tests**

34. T Rogan EG. The natural chemopreventive compound indole-3-carbinol: state of the science. In Vivo. 2006;20:221-228.
Adult Toxin Exposure Questionnaire

If you have been exposed to any of these in the LAST 12 MONTHS please check:

- (Y) Yes
- (N) No
- (?) Unknown
- (P) for exposure more than 12 months ago

### Community

<table>
<thead>
<tr>
<th>Do you have regular exposure to:</th>
<th>Y</th>
<th>N</th>
<th>?</th>
<th>P</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Automobile exhaust</td>
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<td>Farm/Industrial/Power plant or lines</td>
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<td>Radio tower</td>
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<td>Landfill/Dump</td>
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<td>Hydro tower</td>
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### Home and/or Work Environment

<table>
<thead>
<tr>
<th>Do you live in a: (Circle one)</th>
<th>House</th>
<th>Apartment Building</th>
<th>Mobile Home</th>
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<tr>
<td>Do you work in a: (Circle one)</td>
<td>House</td>
<td>Office Building</td>
<td>Factory</td>
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<tr>
<td>Bathing/Showering water source: (Circle one)</td>
<td>Well</td>
<td>Public Works</td>
<td>Bottled</td>
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</table>

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<thead>
<tr>
<th>Do you have regular exposure at home or work to:</th>
<th>Y</th>
<th>N</th>
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<tr>
<td>Forced air heat</td>
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<td>Renovations (new carpets; add ons; etc...)</td>
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<td>Basement cracks or dirt floor</td>
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<td>Damp basement or crawl space</td>
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<td>Wet windows or outside closet walls</td>
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<td>Water leaks (ceilings, walls, floors)</td>
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<td>Visible mold</td>
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<td>Old or cracking ceiling tiles</td>
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<td>Old or cracking vinyl linoleum flooring</td>
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<td>Crumbling pipe insulation</td>
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<td>Crumbling wall or ceiling insulation</td>
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<td>Old or cracking paint</td>
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<td>Carpets or rugs</td>
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<td>Stagnant or stuffy air</td>
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<td>Gas or propane stove</td>
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<td>Coal or wood stove</td>
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<td>Other gas appliance (water heater, furnace)</td>
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<tr>
<td>Regular contact with smokers</td>
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Adult Toxin Exposure Questionnaire

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<th>Do you have regular exposure to:</th>
<th>Y</th>
<th>N</th>
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<th>P</th>
<th>Notes</th>
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<tr>
<td>Pesticides or herbicides</td>
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<td>Harsh chemicals (varnish, glue, gas, acid...)</td>
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<td>Welding or soldering</td>
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<td>Metals (Lead, Mercury, etc)</td>
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<td>Paints</td>
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<td>Photo developing / Dark room</td>
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<td>Airplane travel</td>
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<tr>
<td>Cleaning chemicals</td>
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Personal - Diet

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<tr>
<th>Drinking/Cooking water source:</th>
<th>Well</th>
<th>Public Works</th>
<th>Bottled</th>
<th>Filtered</th>
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<tbody>
<tr>
<td>Caffeine?</td>
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<td>What kind:</td>
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<td>How Much:</td>
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<td>Do you regularly eat:</td>
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<td>Fish (fresh, frozen, canned, etc.)</td>
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<tr>
<td>Artificial sweeteners (Circle one): NutraSweet, Equal, Aspartame, Splenda</td>
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<tr>
<td>Alcohol</td>
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<td>Animal products</td>
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<td>How often?</td>
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<td>What percentage of your animal product is organic?</td>
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<td>Do you wash your produce</td>
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<td>What percentage of your produce is organic?</td>
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<td>Deep fat fried foods</td>
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<td>Sodas, juices, drinks containing High Fructose Corn Syrup – how many per day?</td>
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<tr>
<td>Do you have:</td>
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<tr>
<td>Allergies</td>
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<td>Sensitivity to smells (gas, perfume, paint, etc...)</td>
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<td>Artificial materials in the body (implants, pins, joints, etc...)</td>
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<td>Immunizations</td>
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<td>Have you ever:</td>
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<tr>
<td>Used tobacco</td>
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<td>Experimented with recreational drugs</td>
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<td>Led a high stress lifestyle</td>
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<td>Experienced a stressful or traumatic event</td>
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<td>Been under anaesthesia</td>
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<td>Had an illness during foreign travel</td>
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<td>Had an illness while camping or hiking</td>
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<tr>
<td>Had food poisoning</td>
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**Dental**

<table>
<thead>
<tr>
<th>Notes</th>
<th>Y</th>
<th>N</th>
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</table>

Do you currently have amalgam fillings or caps?
- How many amalgam fillings do you have now?

Have you removed or lost dental fillings or caps?
- How many fillings did you have?

Did you have fillings as a child?
- At what age?
- Any complications such as dry socket or abscesses?

Did you have your Wisdom teeth removed?
- How many and when were they placed?

Do you have any root canal treated teeth?
- How many and when were they placed?

Did your mother have dental fillings prior to giving birth to you?
- During her pregnancy with you?

Other:

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Please list all **PRESCRIPTION** or **OVER THE COUNTER** medications you currently take on a regular basis, including birth control pills and allergy injections:

<table>
<thead>
<tr>
<th>Name of medication</th>
<th>Dose (mg, ML, IU)</th>
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<th>How long have you taken it?</th>
<th>If you have side effects, please specify</th>
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Please list all **VITAMINS/MINERALS, HERBS, or OTHER SUPPLEMENTS** you currently take on a regular basis:

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<th>Name of supplement</th>
<th>Dose (mg, ML, IU)</th>
<th>How often do you take it?</th>
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**Drug Adverse Reactions:** Please list ANY medication / anesthetics / immunizations you have had to stop taking because of side effects or allergic reactions:

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<th>Name of medication/ immunization</th>
<th>Type of side effects or allergic reaction that caused you to stop it</th>
<th>Age</th>
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Therapeutic Fasting: The Buchinger Amplius Method
Francoise Wilhelmi de Toledo, MD, and Robert Hohler
Thieme (New York) 2012: 156 pp
Softcover, $34.99
ISBN 978-3-13-160361-6

For professionals wanting to educate themselves on detoxification diets, it is refreshing to find a comprehensive book written by an experienced medical expert. In Therapeutic Fasting: The Buchinger Amplius Method, Francoise Wilhelmi de Toledo, MD, writes with passion and conviction about her life’s work. The book is translated from the original German.

Wilhelmi de Toledo has published numerous scientific papers on therapeutic fasting and is the medical director of the Buchinger Fasting clinics. The Buchinger Amplius Fasting Method was originally developed by the author’s father-in-law, German Physician Otto Buchinger (1878-1966). The Maria Buchinger foundation website is a great source of scientific information on therapeutic fasting and can be found at: http://maria-buchinger-foundation.com/en/fasten/scientific-publications.

The book opens with an intriguing explanation of fasting as an “evolutionary adaptation to the climatic conditions on our planet,” when the availability of food changed with the seasons and before the conveniences of modern agriculture and food preservation. According to the fasting principles, when you “temporarily and voluntarily abstain from eating,” your metabolism switches automatically from “external nutrition to nutrition taken from fat reserves.” After the first three days of a therapeutic fast, fat metabolism increases (as ketones are formed) and amino acid transformation to glucose (gluconeogenesis) is minimized. The therapeutic explanation of the benefits of protein breakdown were a little surprising and quite interesting. On page 33, the author writes “from a naturopathic point of view, fasting offers the opportunity to metabolize old, pathological, and dispensable protein structures or molecules,” such as “proteins damaged by free-radicals, antigen-antibody immune complexes, and AGEs (advanced glycation end products); for example, carcinogen acrylamides contained in potato chips and French fries.”

The Buchinger Amplius Method is a modified fast that includes fresh vegetable broth, fruit and vegetable juices, water and herbal teas (for a total of about 250 calories per day). The fasting method is presented in great detail and intended to be carried out under medical supervision by a physician and/or a well-trained fasting counselor. A table on page 35 lists absolute contraindications to fasting, including cachexia, and relative contraindications such as cancer, that require experienced medical care. The approach is holistic and includes spiritual-religious, socio-humane, and medical-physical dimensions. Techniques and detailed instructions provided for enhancing the fast include breathing, yoga, massage, hot liver packs, and daily colonic irrigation, to name a few. Although the therapeutic fast is a 10 day fast that includes 5 transitional days and 5 days of fasting, the case is made for occasional transitional “detox” days for the anti-aging and rejuvenating effects of temporary calorie restriction.

The book concludes with low calorie whole food recipes and menus to be used during and after the fast. Some of the recipes are quite interesting, such as the nutrient dense Budwig cream, but knowledge of European ingredients would be helpful and be sure to have your metric conversions handy. Other practical information includes an interesting discussion with Chef Hubert Hohler from the Buchinger Fasting Clinics about cooking with cold pressed oils and whole grains.

Barbara Goldman MS, RD, CDE, Associate Professor of Nutrition, Palm Beach State College Contact Barbara at: goldmanb@palmbeachstate.edu.

The Happiness Diet: A Nutritional Prescription for a Sharp Brain, Balanced Mood, and Lean, Energized Body
Tyler Graham and Drew Ramsey, MD
www.thehappinessdietbook.com
ISBN 978-60529-327-1

The Happiness Diet is a why-to and how-to guide for anyone interested in exploring how diet impacts overall health, particularly mood, mental health and brain function, and taking a “foods first” approach to healing. The overall sensible advice offered in the book takes a specific stance when it comes to dietary fats, defending dietary cholesterol and wholefood sources of organic, pasture-raised animal fats and criticizing highly processed vegetable fats, like trans fats.

The book is organized into two major parts: part one focuses on the effects of foods on the brain, providing a brief history of the Modern American Diet (MAD), describing “Bad Mood” foods and “Good Mood” foods. The book describes and implicates MAD as a major contributor of obesity and diabetes, as well as all too common mental diseases, ranging from depression and anxiety to Parkinson’s and Alzheimer’s Diseases. MAD is notably high in sugar and overly processed vegetable fats, both relatively new to the human diet, and the authors detail the historical timeline.
A Nutritional Prescription for a Sharp Brain, Balanced Mood, and Lean, Energized Body

The Happiness DIET

Tyler Graham & Drew Ramsey, MD

Resource Review: The Happiness Diet

that has led to these components’ prominence in the modern world. Also discussed were the studies that demonized dietary fats and cholesterol, as well as the inherent weaknesses and flaws in those studies. Bad Mood foods include sugar and refined carbohydrates, industrially manufactured vegetable fats, conventionally raised animal foods and vegetables imported from far-flung places, bred for transport and storage rather than flavor. Good Mood foods are minimally refined or processed foods that provide 12 key nutrients referred to as the “Essential Elements of Happiness,” like vitamin B12, iodine, magnesium and others, which are described by their actions in the body and what happens when the body is depleted of those nutrients. Best food sources are provided for each nutrient.

Part two delves into which foods to eat, divided into foods for focus, energy and mood. Free range eggs, grass-fed beef and milk are praised for their brain supporting fats, and a strong case is made for diets high in phytochemical-rich fruits and vegetables, nutrient-dense nuts, low contaminant fish, leafy greens, legumes, and even coffee and cocoa. The stance on produce is resoundingly pro-organic and local, and the authors include information on the effects of pesticides on the body as well as in the environment, which may appeal to many readers. This section also offers tips on food shopping, storage and preparation, as well as recipes and meal plans.

Sprinkled throughout the book are “Top 100 Reasons to Avoid Processed Foods” factoids, which address a wide variety of reasons to shun processed foods, from potential cancer-causing effects of blue dye No. 2 (used in textiles and found in blue M&Ms) to the specific effects of various preservatives, pesticides and other additives found in highly processed foods. Also included are gross-out details of common junk foods, like rot allowances in potato chips and allowable maggot content of maraschino cherries.

The authors boldly name names, as they discuss the origins of Crisco by then-soap makers Procter & Gamble and Coca Cola, point out the ill effects of Pringles’ Oles-tra, and the chemicals created by Monsanto that are found in Old El Paso Taco Dinners. Also mentioned by name are Mountain Dew, Fruit Roll Ups, Dannon, McDonalds and Wonder Bread. Perhaps reading the specific criticisms of such recognizable brands may strengthen the message among consumers.

Overall, this book would be a good read for patients and clients interested in improving their eating habits, but who may need a little convincing as to why they should stop fearing minimally processed fats from a variety of minimally processed foods, cut industrially manufactured foods and move to a more locally grown, whole foods diet. It would also be helpful for the many people who struggle with mild mood disorders, like depression, who would like to use a foods-first approach to improve mood and overall health.

Robin Foroutan, MS, RD, HHC is an Integrative Nutritionist in private practice and the DIFM Communications Chair for 2012-2013. Contact Robin at rforoutan@mac.com.

Resource Review

Commentary

ALOX5 Gene Variants Affect Eicosanoid Production and Response to Fish Oil Supplementation


Abstract

The objective of this study was to determine whether 5-lipoxygenase (ALOX5) gene variants associated with cardiovascular disease affect eicosanoid production by monocytes. The study was a randomized, double-masked, parallel intervention trial with fish oil (5.0 g of fish oil daily, containing 2.0 g of eicosapentaenoic acid [EPA] and 1.0 g of docosahexaenoic acid [DHA]) or placebo oil (5.0 g of corn/soy mixture). A total of 116 subjects (68% female, 20-59 years old) of African American ancestry enrolled, and 98 subjects completed the study. Neither ALOX5 protein nor arachidonic acid-derived LTB4, LTD4, and LTE4 varied by genotype, but 5-hydroxyeicosatetraenoate (5-HETE), 6-trans-LTB4, 5-oxo-ETE, 15-HETE, and 5,15-diHETE levels were higher in subjects homozygous for the ALOX5 promoter allele containing five Sp1 element tandem repeats (“55” genotype) than in subjects with one deletion (d) (three or four repeats) and one common (“d5” genotype) allele or with two deletion (“dd”) alleles. The EPA-derived metabolites 5-HEPE and 15-HEPE and the DHA-derived metabolite 17-HDoHE had similar associations with genotype and increased with supplementation; 5-HETE and 15-HEPE increased, and 5-oxo-ETE decreased to a greater degree in the 55 than in the other genotypes. This differential eicosanoid response is consistent with the previously observed interaction of these variants with dietary intake of omega-3 fatty acids in predicting cardiovascular disease risk.1

The following is a commentary on the above abstracted article
Eicosanoids are lipid mediators of inflammation, and include a variety of compounds (prostaglandins, thromboxanes, leukotrienes (LT), hydroxy- and epoxy-fatty acids, lipoxins and isoprostanes) derived from the ubiquitous 20 (in Greek: eicosa)-carbon atom arachidonate and a few similar polyunsaturated fatty acids. Esterified in phospholipids of biological membranes, these fatty acids are released upon a variety of stimuli, becoming substrates for metabolizing enzymes. More than 20 years ago, Samuelsson and coworkers identified LT as a class of eicosanoids derived through the action of 5-lipoxygenase (5-LO). This enzyme, selectively expressed in bone marrow-derived cells such as neutrophils, monocytes, macrophages, dendritic cells and mast cells, catalyzes the transformation of arachidonic acid (AA) into LTA4. In turn, LTA4 is either converted by enzymatic hydrolysis into LTB4, or is conjugated with glutathione to form LTC4. LTB4 and its metabolites LTD4 and LTE4 are together referred to as “cysteinyl”(cys)-LT. LTB4 is a potent chemoattractant for neutrophils, macrophages and other inflammatory cells, and induces the chemokinesis and adhesion of these cells to the vascular endothelium. On the other hand, cys-LT increase vascular permeability and contract smooth muscle cells, causing bronchoconstriction and vasoconstriction. LT have been identified as mediators of a variety of inflammatory and allergic conditions including rheumatoid arthritis, inflammatory bowel disease, psoriasis and allergic rhinitis, but their most relevant pathophysiological implication has so far been bronchial asthma. Blockers of the cys-LT1 receptor or of 5-LO have been marketed worldwide as effective anti-asthmatic medications.

The transcription rate of the 5-LO gene (located in humans on chromosome 10, and conventionally termed ALOX5) is controlled by its promoter, and particularly by a region, termed core promoter, containing a sequence of GC-rich tandem repeats, which are binding sites for two transcription factors, Sp-1 and Egr-1. Genetic variants in the core promoter region may change the binding of these transcription factors and the rate of 5-LO transcriptional activation under inflammatory conditions. Indeed, a family of mutations in the GC-rich region, consisting of the deletion of one, deletion of two, or addition of one such binding sites, was associated with altered (reduced) transcription of the 5-LO gene compared to the common allele. It was then found that carriers of these genetic variants had diminished clinical responses to treatment with anti-LT drugs, indicating a pharmacogenetic effect of the promoter sequences on treatment responses.

Originally confined to the area of asthma, these findings more recently expanded their implications to atherosclerosis.

In search for candidate genes contributing to atherosclerosis susceptibility in two widely used mouse models of atherosclerosis, the apo-E -/- mice, and the LDL-receptor -/- mice, a locus on mouse chromosome 6 was found to confer almost total resistance to atherogenesis. The ALOX5 gene, located in this locus in the mouse, turned out to totally account for this effect, since LDL receptor -/- mice missing even one of the two allelic copies of the 5-LO gene had a dramatic decrease (about 26-fold) in lesion development. Also, when bone marrow (supplying circulating blood cells) from 5-LO -/- mice was transplanted into LDLR -/- there was a significant protection from atherosclerosis, suggesting that 5-LO from white blood cells (likely monocyte-macrophages) was necessary for atherogenesis. The important contribution of 5-LO to atherosclerosis may occur because the products of 5-LO, LT, mostly produced by monocyte-macrophages or dendritic cells in the arterial intima, would foster the chemotraction of monocytes, T-cells or other circulating cell types within the vessel wall and/or increase vascular permeability. This creates a vicious cycle in which inflammatory cells, by producing these lipid mediators, beget local vascular inflammation perpetuating the recruitment of inflammatory cells and the further production of mediators. 5-LO might also contribute by oxidizing LDL or producing natural ligands for nuclear receptors, such as peroxisome proliferator-activated receptor α (PPARα).

Genetic variants of the 5-LO promoter, previously described as associated with variable sensitivity to anti-asthmatic medications, also influence atherosclerosis. A few years ago, Dwyer and coworkers reported that this is apparently the case. ALOX5 gene variants were found in 6% of a cohort of 470 healthy middle aged women and men. Frequent variations occur especially in the promoter region of the ALOX5 gene, which has from 3 to 8 tandem repeats of a consensus binding site for the transcription factors Sp1 and Egr1. The most frequent allele has 5 such repeats. Variant alleles with 3 or 4 sites (or, rarely, >5 sites) are associated with greater intima-media thickness of the carotid artery in healthy adults from Los Angeles and with occurrence of a first myocardial infarction (MI) in a case-control study in Costa-Ricans. In both studies, the observed diet-gene interactions were more pronounced in subjects with high dietary AA intake and carrying the deletion variants (i.e., “3” or “4” repeats, referred to jointly as “deletion” (“d”) alleles) relative to subjects with two common alleles (i.e., the “SS” genotype). Conversely, in the Los Angeles study, this atherogenic effect was reversed in the subjects with the “d” alleles having high eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) intake. Since EPA and DHA may decrease the formation of LT by competing with arachidonic acid as substrates for 5-LO and also generate the weaker LT of the 5-series, those findings suggested that the antiatherogenic effect...
Resource Review: ALOX5 Gene Variants Affect Eicosanoid Production and Response to Fish Oil Supplementation

Effects of fish-derived EPA and DHA might be more prominent in (or perhaps limited to) genotype variants favoring increased 5-LO activity.

The direction of the change in IMT in the “d” variant group was however contrary to what one would have expected on the basis of previous findings in vitro, and rather consistent with increased, rather than decreased, 5-LO promoter activity associated with the mutant alleles. This issue clearly deserved further investigation through measurements of 5-LO expression and of LT and other eicosanoids in these genetic variants, and evaluation of the interaction with recently identified mutations in other genes related to LT production, such as that of 5-lipoxygenase activating protein (FLAP).

In this latest report by Stephensen et al., from the same group initially reporting the nutrigenetic effects of fish oil across ALOX5 variants, the authors now aimed at determining if ALOX5 variants associated with cardiovascular disease affect eicosanoid production by monocytes. The study was a randomized, double-masked, parallel intervention trial with fish oil (5.0 g fish oil daily containing 2.0 g eicosapentaenoic acid [EPA] and 1.0 g docosahexaenoic acid [DHA]) or placebo oil (5.0 g of a corn/soy mix). 116 subjects (68% female, 20 - 59 yr) of African American ancestry enrolled and 98 completed the study. Contrary to the most obvious hypothesis, neither ALOX5 protein nor arachidonic acid (AA)-derived LTB4, LTD4 and LTE4 varied by genotype. However 5-hydroxyeicosatetraenoate (5-HETE), 6-trans-LTB4, 5-oxo-ETE, 15-HETE and 5,15-DiHETE were higher in subjects homozygous for the ALOX5 promoter allele containing 5 Sp1 element tandem repeats (“55” genotype, the “protective” genotype) than in subjects with one “deletion” (3 or 4 repeats) and one common allele (“d5”) or with two deletion alleles (“dd”). The EPA-derived metabolites 5-HEPE and 15-HEPE and the DHA-derived metabolite 17-HDoHE had similar associations with genotype and increased with supplementation; 5-HEPE and 15-HEPE increased and 5-oxo-ETE decreased to a greater degree in the “55” than in the other genotypes. This differential eicosanoid response is consistent with the previously observed interaction of these variants with dietary intake of omega-3 fatty acids in predicting cardiovascular disease risk and suggests that products different from the originally postulated leukotrienes, but rather hydroxyl and peroxo-fatty acids produced through 5-LO may mediate the pharmacogenetic effects reported previously. Research in anti-inflammatory, anti-atherogenic properties of the various eicosanoids increased in the “55” protective genotype, and increased further by fish oil, are now warranted. PMID: 20950718


Resource Review

HOT Nutritional Genomics Research Publications


Variants in the CYP27B1 gene such as Arg389His result in lower levels of calcitriol (1,25-dihydroxyvitamin D3). This may explain a gene-environment relationship which has been seen between lower levels of UV light and higher risk of multiple sclerosis. The authors conclude by suggesting that vitamin D supplementations studies for prevention are “strongly warranted.”

Metabolic syndrome: Evidences for a personalized nutrition. Mol Nutr Food Res. 2012 Jan;56(1):67-76. doi: 10.1002/mnr.201100531. Epub 2011 Nov 17. New research is beginning to reveal important gene-environment interactions that may be useful for prevention of metabolic syndrome by use of personalized nutrition. Variants of the following genes are discussed: ADIPOQ, ADIPOR1, ADIPOR2, CAPN10, GCKR, TCF7L2, and LEPR.

Dietary flavonoids are neuroprotective through Nrf2-coordinated induction of endogenous cytoprotective proteins. Nutr Neurosci. 2011 Sep;14(5):226-36. Nrf2 (NFE2L2 gene) is emerging as an important regulator of neuroprotective gene expression resulting from dietary flavonoids. This may lead to novel complementary and alternative therapies for various neurological disorders, including strokes.

Black tea extract prevents lipopolysaccharide-induced NF-κB signaling and attenuates dextran sulfate sodium-induced experimental colitis. BMC Complement Altern Med. 2011 Oct 11;11:91. Black tea extract was found to reduce colon inflammation by blocking NF-kappaB signaling and apoptosis.


Genetic and nutritional interactions in cardiovascular disease. World Rev Nutr Diet. 2011;102:150-5. Epub 2011 Aug 5. Nutrition plays a large role in modulating gene expression, and in influencing many of the modifiable risk factors associated with a first myocardial infarction. Variants in genes like ALOX5 and in APOA1 are mentioned as examples. The APOA5 -1131T-C variant is also described in some detail.
NOS3 Glu298Asp polymorphism interacts with virgin olive oil phenols to determine the postprandial endothelial function in patients with the metabolic syndrome. J Clin Endocrinol Metab. 2011 Oct;96(10):E1694-702. Epub 2011 Aug 3. The Glu298Asp (or 894G-T) variant of NOS3 is considered a risk factor for hypertension and cardiovascular disease associated with endothelial dysfunction. In this study, subjects with metabolic syndrome who carry two copies of this variant were found to have lower postprandial levels of endothelial NOS. Most of this difference was reduced when high-phenol olive oil was used instead of low-phenol olive oil.


The anti-inflammatory action of lycopene in cells exposed to cigarette smoke is explored, with evidence of a mechanism involving the inactivation of NF-kappaB.

The impact of common gene variants on the response of biomarkers of cardiovascular disease (CVD) risk to increased fish oil fatty acids intakes. Ann Rev Nutr. 2011 Aug 21;31:203-34. This review article describes inconsistencies in response to dietary omega-3 fatty acids, and provides an extensive listing and discussion of genes and gene variants which may be responsible. More research is warranted in light of its “wide public health relevance.”

For inquiries about above references, contact Ron L Martin, MS, President, Nutrigenetics Unlimited, Inc.; ron@nutrigenetics.net. Check out www.isnn.info/ and choose the “ISSN Application” button to learn more about the Dietitians in Integrative and Functional Medicine membership discount.

ISNN will be hosting a Pre-Congress, Introductory Workshop for Dietitians, November 18, 2012 in Sao Paulo, Brazil. More information can be obtained from the ISNN website noted above.

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Chair’s Corner: Kathy Moore, RD, CCN

Kathy Moore, RD, CCN
DIFM Chair 2011-2012

“Things may come to those who wait, but only the things left by those who hustle.”

---Abraham Lincoln, Sixteenth President of the United States

As this fiscal year for DIFM draws to a close, and my term as Chair ends, I have been reading a very inspiring book, The Success Principles™️, How to Get from Where You Are to Where You Want to Be, by Jack Canfield and Janet Switzer. The quote above is in this book, in the Chapter called “Take Action”. I believe that this charge is so appropriate for our DIFM practice group and for our members. We have a lot at stake as we work to carve out the niche in the nutrition and healthcare world, establishing Integrative RDs as a valued and trusted resource for guidance in integrative and functional nutrition. One of our first achievements was the publishing of our Standards of Practice and Standards of Professional Performance in June of 2011. Our application to the Council on Future Practice for Certified Specialist Integrative and Functional Nutrition is now being refined for resubmission. It is critical for us to take action—now, and each and every day—to become well educated and highly experienced in our field, so that we earn the credibility and reputation that makes us the “go-to” professionals. This means that every member, and every RD who sees integrative nutrition as a key requirement in the holistic picture of health and healthcare, must “own” their desire to participate.

We really must hustle so that we have a position at the table. We can’t sit around and wait! Consumers are demanding this information and this care. Integrative RDs are uniquely poised to blend the art of whole foods and their nutrient components with the science of discovering one’s biochemical needs based on the individuality of nutritional genomics, lifestyle, and environment. Learning needs to be continual, as this fascinating approach to health continues to unfold like the layers of an onion. So we must take action as a DPG and as individuals to make the education accessible, make it happen, and then apply the principles in practice to achieve the experience. Will you participate with us?

Your Executive Committee is working on the “big picture plans”. We have offered many valuable webinars this year. Other online training will be coming, as will a valuable pre-FNCE conference in Philadelphia. We welcome your input and suggestions; please send them by email to info@integrativerd.org.

Thank you to the over 30 members who have worked diligently throughout this year to move DIFM to action, to help us get “where we want to be”. It has been an honor to serve as your Chair this year.

In closing, consider this quote from John Ruskin, English author, art critic, and social commentator:

“What we think or what we know or what we believe is, in the end, of little consequence. The only consequence is what we do.” Let’s commit to TAKE ACTION!

Kathy Moore, RD, CCN
DIFM Chair, 2011-2012
The first day of spring has come and gone, but the season is in full bloom. Like the New Year, many people look at spring as a time to start fresh or renew. Magazines on the racks beckon us to clean our house, our closets, and our lives of clutter and debris. This issue is not about cleansing our house but about cleansing or detoxing our bodies of the environmental and physiological clutter and debris that we have gathered over the winter or over a lifetime. This issue of the DIFM newsletter will take you from basic liver physiology, to what a detox diet is and why it can be beneficial, to how to test for harmful compounds, to the correct and healthful way to detox. This will be one issue that members will want to keep as a reference for years to come.

Thinking of Spring and renewal, don’t forget to renew your dues for this valuable practice group if you have not already. Additionally, some of you have unsubscribed to the DIFM eblasts which are our means of communicating with our membership and the vehicle we use to send the DIFM newsletters. Please resubscribe to the DIFM mailing list, so you don’t miss out! To resubscribe, click this link http://visitor.r20.constantcontact.com/manage/optin ea?v=001zyOLoEKyAZZbJk_JleM2Q%3D%3D and add your email address. If you have questions, contact Amy Jarck at info@IntegrativeRD.org.

As Editor, I always welcome your input and suggestions and encourage you to contact me at peaknut@centurylink.net. Comments, suggestions, and yes, criticisms are shared with our fantastic, diligent Executive Committee who are hard at work on credentialing for the Integrative RD.

I write this as I am listening to the birds, whom I have not heard for so long, sing and converse in the trees outside my office window. After ten years of desert living, Colorado beckoned once again and I returned to a place of seasons—and a healthier environment. Moving was the first step in my own process of detoxing and now I am ready to proceed on to the next by using the key steps and information from this issue to enhance my physiological health. This issue has been much like planting the garden I am planning. The seeds are here to be sown and if they are not planted, they will not grow. So as I put the finishing touches on this issue, I am looking forward to planting the seeds of knowledge gained in this issue as well as the seeds in my first real garden in years!

**SAVE THE DATE:**

**NUTRITIONAL GENOMICS INTRODUCTORY WORKSHOP 1PM-6PM**

*Sunday, November 18, 2012 (São Paulo, Brazil)*

Promoted by:
- International Society of Nutrigenetics/Nutrigenomics (ISNN)
- Brazilian Food and Nutrition Society (SBAN)
- Dietitians in Integrative and Functional Medicine DPG (Dietetic Practice Group) of the American Academy of Nutrition and Dietetics

**6th ISNN Nutrigenetics and Nutrigenomics Congress November 18-21, 2012**

(São Paulo, Brazil)

Please note, the Introductory Workshop has been designed specifically for dietitians and precedes the ISNN Congress, offering a wonderful opportunity to get updated on the latest developments in nutritional genomics. Specific information can be found at [http://www.isnnbrazil.org.br/](http://www.isnnbrazil.org.br/).

The ISNN and Congress organizers are pleased to offer a **30% discount** in registration fee for the VI ISNN Congress to the members of American Academy of Nutrition and Dietetics!
THANK YOU TO OUR SPONSORS
Without your generous contributions, many of the opportunities and member benefits would not be possible.

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