

NUTRI NEWS



**Douglas
Laboratories®**
Raising the Standard for Nutrition and Wellness™

Recent health and nutrition information from Douglas Laboratories

May/June 2002

DETOXIFICATION: STRATEGIES FOR WELLNESS AND LONGEVITY

DETOXIFICATION: A GENERAL OVERVIEW

James L. Wilson D.C., N.D., Ph.D.

From the late 1800s until recently, the value and use of detoxification have been championed mainly by the naturopathic profession and those interested in natural health. However, with the emergence of increasingly sophisticated laboratory tests and the growing influence of natural medicine, detoxification is gaining recognition as a valid method of removing obstacles to healing and producing greater levels of health.

Detoxification, of course, is the removal of toxins. The word toxin comes from the Greek *toxon*, meaning a type of poison, and poison is defined as any substance that may cause damage to structure or disturbance of function producing symptomatology, illness or death.¹ Health care practitioners tend to think of detoxification as limited to procedures such as colon cleansing or chelation of heavy metals. But toxicity occurs at every level of function and structure in the body from the psychological to the molecular. It may even be present at the energetic (structural vibration) level as evidenced by the value of homeopathic remedies such as lycopodium, nux vomica and sulphur in detoxification².

Toxicity can arise from a variety of internal and external sources including physical obstruction and an excess or deficiency of endogenous or exogenous substances. Some of the most obvious sources are chemical, petrochemical, biochemical, thermals, and irradiation contamination. Physical obstructions include partial or complete mechanical blockages of function such as impacted fecal matter in the colon, thick mucus restricting absorption of nutrients in the small intestine, gallstones preventing bile flow in the bile duct, or tumors or cysts blocking lymph or blood vessels. Detoxification in such instances involves physical removal of the obstruction by whatever means is most prudent.

continued on page 2

METABOLIC PATHWAYS OF LIVER DETOXIFICATION

*Lise Alschuler, N.D., Medical Director,
Bastyr Center for Natural Health*

The liver is our primary site of detoxification. Hepatic detoxification is comprised of two phases. Phase I refers to cytochrome P450 enzyme detoxification. Phase II refers to conjugation of the detoxified intermediates from Phase I. Detoxification begins within each hepatocyte. The mitochondrial membrane is home to a complex and intricate system of detoxification enzymes. These enzymes, known as the cytochrome P450 (a.k.a. mixed-function oxygenase [MFO] system) occur mainly in the liver and to a lesser extent in the intestines and lungs. The cP450 enzymes are a superfamily

continued on page 4

INSIDE THIS ISSUE

Detoxification: A General Overview . . .	page 1
Metabolic Pathways of Liver Detoxification	page 1
First Do No Harm: The Physiological Consequences of Mercury in the Body	page 6

Detoxification (continued from page 1)

Toxicity also occurs at the tissue and organ level, with each organ and tissue signaling its own need for detoxification. For example, toxic manifestations of the liver are expressed in the extreme as the various cirrheses, blocked detoxification pathways and necrotic degeneration of cell tissues. The heart shows its toxicity by manifesting non-specific reactions such as irregular beats and decreased ejection fractions. The brain reveals its toxicity clinically through “foggy” headedness, difficulty concentrating, impaired memory, poor coordination and other non-specific lapses in function. Brain toxins produce a variety of changes, from interruptions of normal synapse transmissions to altered brain biochemistry and even to malignancy.

The problems created by toxicity manifest at the cellular level in many ways. Both active and passive transport can be

interrupted or altered across the outer cell wall. Sodium/potassium pump activity can be affected leading to electrolyte and water imbalances within the cell. Toxicity can also produce aberrant changes in receptor site numbers, configuration and sensitivity to a variety of essential biochemical substances such as hormones. Fatty acid metabolism and protein metabolism are also adversely influenced by toxicity, resulting in leaky, inflexible or non-adaptive cell walls. Intracellularly, toxicity alters second messenger transmissions and responses, modifies cellular pH and interrupts the normal physiology in the cytosol. In the mitochondria, toxicity can interfere with cellular respiration. Metabolically, toxicity can impair energy production (ATP, NAD, FAD) by altering the citric acid cycle, pentose phosphate pathways, oxidative phosphorylation and electron transport chain reactions. Toxicity of the endoplasmic reticulum affects messenger and transfer RNA synthesis, protein translation and transcription, as well as other aspects of cellular expression and metabolism. Interference with these biochemical substrate reactions often occur through competitive and non-competitive inhibition.

NUTRI NEWS

Douglas Laboratories®
Being As Good As You Can Be™

Publisher Peter W. Hefele
Editor In Chief Andrew D. Halpner, Ph.D.
Assistant Editor Michael Traficante
Assistant Editor
& Research Natalie Shamitko
Technical Advisors/Contributors:

Nita Bishop, N.D.
Martin P. Gallagher, M.S., D.C.
Mitchell J. Ghen, D.O., Ph.D.
Vern S. Cherewatenko, M.D., MEd
Derek DeSilva Jr., M.D.
James Wilson, Ph.D.

Contact Us:
NutriNews Inquiries
600 Boyce Road • Pittsburgh, PA 15205
Phone: (412) 494-0122 • Fax: (412) 278-6804
Email: nutrinews@douglaslabs.com
Canadian Inquiries
Toll-Free: 866-856-9954
Email: douglaslaboratories@on.aibn.com

DOUGLAS LABORATORIES WOULD LIKE TO WELCOME NEW TECHNICAL ADVISOR – VERN S. CHEREWATENKO, M.D., MEd

Dr. Cherewatenko received his Doctor of Medicine degree from the University of Washington School of Medicine in 1986, is Board Certified by the American Board of Family Practice, and is Board Eligible by the American Board of Bariatric Medicine. Dr. Cherewatenko is one of three founders and current President and CEO of the American Association of Patients and Providers (AAPP). He is also a founding board member of the Puget Sound Physicians' Association in Washington State. Dr. Cherewatenko has authored *The Diabetes Cure*, numerous articles and essays, and the soon to be released book *The Female Stress Cure*.

Because toxicity can occur at any level, and sometimes at several simultaneously, detoxification must also take place at the appropriate levels to be fully effective. Multilevel detoxification is complicated by the fact that toxin elimination from the body has a limited number of exit pathways - the bowel, respiratory tract, skin, and urinary tract. Therefore any detoxification must first include the preparation of the organs of elimination by making certain they are functioning at full capacity or at least able to handle the toxic load. Water-soluble toxins exit through all four pathways. Some oil soluble toxins can also exit through the skin. But more commonly they enter the liver where they are either degraded into water-soluble substances and eliminated through the kidney/urinary pathway or they remain fat soluble and are carried in the bile through the intestinal tract and eliminated with ingested fiber. A lack of fiber in the diet often leads to re-absorption of these toxins via the entero-hepatic pathway. Substances that are neither oil nor water-soluble or that bind strongly or non-competitively to tissues or biochemical substrates are more difficult to rid from the body. Mercury, being one such difficult toxin, is given special consideration later in this publication.

There are many ways to detoxify. Some methods are simple and broad spectrum while others are very precise and focused. Fasting, breathing techniques, aerobic exercise, and exposing the skin to fresh, clean air and sun are just some of the more common general detoxification methods. Because water is the great catalyst, it has been used in many forms for detoxification. Steam baths, hot and cold baths, mineral baths (hot and cold), Epsom salt baths, herbal baths, oxygen saturated baths and oatmeal baths have all been used with success. In addition sweat tents, wet and dry saunas, sweat baths and scrub baths by themselves and in combination with other remedies and detoxification regimens have increased the

health and healing ability of many.

Detoxification through the skin is facilitated by promoting sweating. This can be accomplished by ingesting sudorific (diaphoretic) herbs like ginger, mustard and cayenne, either by themselves or in conjunction with fasting, saunas, baths and sweats. Packs of clay, mud, salt, charcoal, seaweed, volcanic ash and castor oil have also proven useful in increasing the elimination of toxins through the skin.

Detoxification through the intestinal tract is enhanced by fasting, mono, high fiber and mucusless diets, ingestion of substances such as charcoal, mud and grasses, and in some cases by the use of cathartics that either lubricate, increase fluidity, add bulk or stimulate peristaltic motion. More is given on intestinal detoxification later in this publication.

This introductory section has touched on the importance and the depth of this crucial topic. Detoxification is in its infancy in this new wave of health and healing. It is important that you, the health practitioner, understand its many uses and avoid its misuses to reap the wonderful benefits. In my clinical experience, detoxification is often the key to bringing patients to a level of health they could not otherwise achieve. What is needed are more accurate laboratory and clinical methods for identifying the specific toxic substances, their prevalence and the body burden created by them. Although we may never be completely free of toxins, our goal should be to reduce them to a level at which the body can function optimally.

¹ Dorland's Medical Dictionary Edition 28, WB Saunders Philadelphia 1988. p 1322.

² Boericke, William Pocket Manual of Homeopathic Materia Medica 9th Ed. Jain Publishers, New Delhi 110016, India 1978, p 409, 475 & 520 respectively.

Metabolic Pathways (continued from page 1)

of enzymes. Each enzyme is designated by the letters "CYP" followed by another Arabic numeral (e.g. CYP2D6). There is significant individual variability since 71 genes code for these enzymes. This variability may explain differences in individual susceptibility to various toxins and individual reactivity to medications and endogenous compounds, such as hormones. The main function of the cP450 system is to convert fat-soluble toxins into water-soluble, polarized compounds, which can then be conjugated and excreted in the bile or urine. These compounds are normally conjugated through one of the following pathways: sulfation, glucuronidation, glutathione conjugation, acetylation, methylation, or other amino acid conjugation.

Upon exposure to toxic substances, the activity of the involved cP450 enzymes increase as a consequence of up-regulation. Also up-regulated are other hepatic detoxification enzymes involved in conjugation, namely sulfur transferase, acetylation and sulfation. Chronic toxic exposure with resultant increase in cP450 system enzymes can cause hepatic and other tissue damage. The detoxified intermediates produced by cP450 enzyme activity can be more reactive than the original toxin. While these intermediates are normally conjugated into non-reactive compounds and excreted, in a state of chronic toxic exposure, the conjugating nutrients (i.e. SOD, Vit. E, Vit. C, carotenes, glutathione peroxidase, glutathione reductase, etc.) may become depleted leading to tissue damage (peroxidation and fibrosis). Conversely, some people have under-active cP450 enzymes, which makes it more difficult to clear hormones and inflammatory compounds (such as histamine). This, in turn, leads to metabolic toxicity and inflammation. Additionally, people with under-active cP450 enzymes are more susceptible to the development of cancer, caffeine intolerance, and environmental sensitivities.

In supporting hepatic detoxification, there are several considerations that must be taken into account. It must be under-

stood that the primary source of toxicity to the liver is the leakage of gut-derived toxic compounds into the blood. The majority of these are endotoxins. Given this influx of toxic compounds from the gut, the first step in a detoxification support program must be to assess and restore optimal intestinal permeability. Many individuals suffer from hyperpermeable intestines as a consequence of dietary allergens, intestinal exposure to inflammatory compounds, impaired gut associated lymphoid tissue function, and/or intestinal exposure to certain medications (such as certain chemotherapeutic agents). In these individuals, intestinal permeability testing may be considered (lactulose/mannitol loading test is considered the most reliable test). If increased intestinal permeability exists, a treatment program for restoration of the intestinal barrier is the crucial first step in a detoxification program. This treatment may involve dietary manipulation, L-glutamine, demulcent herbs (*Ulmus fulva*, *Althea officinalis*, etc.), etc.

Once the intestinal reparative therapy is well underway, the next step in supporting hepatic detoxification is to directly support Phase I and Phase II detoxification. Some clinicians find that measuring aspects of Phase I and Phase II detoxification is a helpful way to provide specific detoxification support. Liver detoxification profiles are available from a number of independent laboratories. These tests usually include a caffeine clearance test to measure Phase I and several conjugation tests to determine the activity of Phase II. Based upon these test results or one's clinical assessment, a comprehensive program of hepatic detoxification support should be initiated.

If Phase I is determined to be overactive, several interventions may be helpful. Removal of environmental and lifestyle factors which up-regulate cP450 enzyme activity is the first step. These include: chronic toxic exposure, alcohol, smoking (nicotine), polycyclic aromatic hydrocarbons (formed during charcoal broiling and found in cigarette smoke), acetaminophen (Tylenol), Phenobarbital, indoles (found in Cruciferous vegetables), iron deficiency, and a high protein

diet. On the other hand, if cP450 is determined to be under-active, it is necessary to address factors that cause this down-regulation. Factors which down-regulate cP450 include: under-nutrition, fasting, protein deficiency, phosphatidylcholine deficiency (PUFA deficiency), benzodiazepines (Halcion, Librium, Valium, etc.), Antihistamines, Cimetidine (Tagamet), Ketoconazole, Sulfaphenazole, naringenin from grapefruit juice, vitamin C and A deficiencies, and bacterial endotoxins.

Once Phase I activity is proportional to the toxic load, additional support may be required for Phase II conjugation activities. Based upon liver detoxification test results, or clinical judgement, specific or generic Phase II support is often indicated. One type of phase II conjugation is adding an acetyl group to a cP450-produced metabolite. There is great individual variability of acetylation rates. Acetylation detoxifies sulfonamides and mescaline. Acetylation is inhibited by deficiencies of vitamin B2, B5, or Vit. C. There are no known inducers.

Glutathione is an important conjugating molecule. Glutathione is a tripeptide composed of glutamic acid, cysteine and glycine. The conjugation of glutathione with intermediary biotransformed xenobiotics from Phase I results in the excretion of mercapturic acids. Glutathione has two major functions in the body: conjugation to form mercapturic acid and quenching oxygen free radicals. Therefore, if the glutathione is used up in its conjugating role, there will be less available to quench free radicals. This sets the body up for free-radical induced damage and the further release of toxic compounds. These compounds are processed through cP450, kicking off more free radicals. Additionally, the new intermediate metabolites may not then be adequately conjugated due to diminished supplies of glutathione. A vicious circle of organ toxic damage is created. Glutathione conjugation detoxifies: acetaminophen, nicotine, organophosphates, and epoxides. Glutathione conjugation is inhibited by: deficiency of B2, glutathione, selenium, or zinc. Glutathione conjugation is

induced by: vitamin B6, Brassica family, limonene-containing foods (citrus peel, dill, caraway), NAC, vitamin E, carotenes, exercise (upregulates glutathione-S-transferase).

Glycine conjugates intermediary metabolites to form hippuric acid. Glycine conjugation detoxifies: amino acid conjugation, benzoate, and aspirin. Glycine conjugation is inhibited by: low protein diet. Glycine conjugation is induced by glycine.

Sulfation is the major conjugation pathway for amine neurotransmitter and steroid hormones, but also for drugs and other xenobiotics (esp. phenolic compounds). Individuals with intestinal permeability leak through xenobiotics that will deplete sulfur in liver conjugation pathways. It has been shown that the use of sulfur for hepatic conjugation takes precedence over the use of sulfur for amino acid formation (hence growth in children, tissue repair in adults and children is delayed when the conjugation demands for sulfur are chronically high). Sulfation detoxifies: aniline dyes, coumarin, acetaminophen, methyl-dopa, estrogen, testosterone, and thyroid hormone. Sulfation is inhibited by: tartrazine dye, NSAIDs, or molybdenum deficiency. Sulfation is induced by: cysteine, methionine, taurine, molybdenum.

Methylation is a Phase II pathway which adds methyl groups to toxic compounds. The methyl groups come from S-adenosylmethionine, which is synthesized from methionine. This synthesis requires choline, vitamin B12, and folic acid. This pathway is not directly assessed in a liver detoxification laboratory test, but may be inferred from serum homocysteine, vitamin B12 and folic acid levels. High homocysteine, low B12 and low folic acid all indicate a decrease in methylation. Methylation detoxifies: dopamine, epinephrine, histamine, thiouracil, and estrogen. Methylation is inhibited by folic acid or B12 deficiency. Methylation is induced by lipotropic nutrients (choline, methionine, betaine, folic acid, vitamin B12).

Glucuronidation is a Phase II pathway which adds glucuronic acid to toxic compounds. The presence of Gilbert's disease, yellow sclera or jaundice (non-Hep.) indicate a decrease in glucuronidation. Glucuronidation detoxifies: acetaminophen, morphine, diazepam, digitalis, aspirin, vanillin, and benzoates. Glucuronidation is inhibited by: aspirin and probenecid. Glucuronidation is induced by: fish oils, limonene-containing foods (citrus inner peels), birth control pills, cigarette smoking, and phenobarbital.

Imbalances in Phase I and Phase II detoxification is implicated in a variety of disorders such as chronic fatigue syndrome, Parkinson's disease, Alzheimer's disease, autoimmune disease, endocrine disorders, osteoporosis in smokers, migraine headache, and cancer. When supporting hepatic detoxification, it may be helpful to utilize the general treatment considerations of hepatic elimination and hepatic support. Elimination involves the identification and removal of anything which taxes the liver (increases the work of hepatocytes or other liver cells): OCP, toxic substances, exogenous estrogens, alcohol, other drugs, medications (if appropriate), excess protein, caffeine, unresolved anger/frustration, and immunological loads on the liver (Candida and yeast antigens, food allergies). Support of hepatic detoxification may involve the use of: phospholipids (lecithin), flavonoids, retinol, folate, pyridoxine, riboflavin, niacin, iron, oligosaccharides, zinc, glutathione, cysteine, vitamin E, methionine, selenium, vitamin C, Cu, N-acetyl-cysteine, L-cysteine, glycine, and pantothenate. Also, botanicals such as: *Silybum marianum*, *Glycyrrhiza glabra* and *G. uralensis*, *Taraxacum officinalis*, *Camellia sinensis*, Aromatic herbs (caraway, dill, fennel) may be useful. Foods such as: beets, carrots, artichokes, cabbage, dandelion, garlic, onion and liver support hepatic detoxification. Physical medicine such as hydrotherapy, diathermy, and spinal adjustments will support hepatic detoxification. The result of this approach should be more efficient hepatic detoxification and greater overall vitality and well-being.

FIRST DO NO HARM: THE PHYSIOLOGICAL CONSEQUENCES OF MERCURY IN THE BODY

Nita Bishop, N.D.

In 1978 a classic paper written by Theron Randolph, M.D. elucidated what may have been the precursor to our current understanding of environmental toxins and how they affect the body over a long period of time. Randolph refers to the overall dynamic interplay between specific environmental exposures and the chronic and acute responses of reacting individuals. He comments on stages that an organism goes through in order to adjust to gradually changing circumstances which he calls "adaptation," and provides us with a working blueprint of what may be occurring in the body as a result of mercury toxicity.

The human body functions as an intricate grid work of biochemical reactions which power metabolic functions leading to overall physiological functions. Negative effects on health often only become apparent after a number of years. Rather than a sudden onset, disease is caused by a certain number of cumulative biochemical processes that become aberrant over years, causing a slow progression from health to disease. By thoroughly studying this process, one may be able to identify a wide range of interrelated physical and mental illnesses. Mercury intoxication may reside somewhere in this gray area. Randolph states that environmental exposures have been blurred by the general tendency to treat most illnesses symptomatically by means of drugs. Unfortunately, these gray areas may often lead to misdiagnosis resulting in patients being treated ineffectively and often incorrectly. These symptoms may in some part be the culmination of many years of malfunctioning biochemical processes leading first to immune dysfunction then progressing to astrocyte destruction within the brain, neuronal swelling, inhibition of dopamine uptake, and alterations in serotonin and norepinephrine metabolism, all of which can have a negative affect on mood.

Neither the recognition nor the treatment of heavy metal toxicity is an isolated event. A patient may have periods of weeks to years where they are highly functional and productive, interspersed with periods of being nonproductive and having a difficult time completing tasks. These patients may be diagnosed with psychological problems including: borderline personality disorders, anxiety, schizophrenia spectrum disorders, attention deficit hyperactivity disorder, learning disabilities, depression, obsessive-compulsive disorder, manic depressive disorder, and panic attacks. All of these conditions may in some way be correlated to mercury intoxication. Additionally, some studies have investigated possible relationships of mercury levels to emotional disturbances in children. Subtoxic metal levels previously thought to be harmless are now being associated with hyperactivity, impulsiveness and decreased attention span.

In the Handbook of Toxicology of Metals, it is noted that "...at present, there is no suitable biological index of the mercury concentration in critical organs such as the brain..." Mercury is ubiquitous in our environment. Today the average person's body contains about 10-15 mg of mercury. Mercury is employed by medical and dental practitioners, found in drugs, used by agriculture in fungicides and pesticides and by the cosmetics industry as an antibacterial. Mercury in industrial waste has also polluted our waters and contaminated our fresh and salt water plants and fish.

Methylmercury and elemental mercury are the two forms most likely to be involved in human exposures in our environment. Elemental mercury is converted by bacteria to the more toxic methylmercury. Ingested methylmercury is absorbed through the GI tract while inhaled mercury vapor is retained by the pulmonary system. Skin absorption of mercury may also occur.

1. Methylmercury (recent exposure to organic mercury within last 90 days): This form is from industrial pollution and

gold mining. It accumulates mainly in the aquatic food chain. Greater than 95% is found in food, particularly fish (higher levels in shark, swordfish, tuna (canned, fresh/frozen), salmon, halibut. It tends to concentrate in the brain where it acts as a potent neurotoxin and teratogen.

Testing for Acute Exposure — utilizing hair, urine, blood and feces

2. Elemental (all other chronic exposures): Silver amalgam fillings are 50% Hg content. While the American Dental Association says it is stable, its release is increased by chewing food, chewing gum, tooth grinding, drilling or polishing teeth as well as consuming hot drinks.

Testing for Chronic Exposure — utilizing hair, fractioned urine porphyrin

Biochemical effects: Mercury binds covalently with sulfhydryl groups, especially those contained in hemoglobin, glutathione (GSH), and cysteine. It reduces glutathione synthase/reductase, selenium and vitamin E, and forms insoluble complexes with selenium, therefore decreasing selenium levels. It promotes formation of prooxidants such as hydrogen peroxide, lipid peroxides and hydroxyl radicals. Most importantly, it affects the Phase II detoxification pathway in the liver. After entry into the body, the liver is the main organ that neutralizes toxic compounds where they undergo metabolic changes whereby lipid soluble compounds are converted into polar, water-soluble products for purposes of excretion from the body. Phase I detoxification is where foreign compounds are converted to more potent or less potent compounds, readying them for the next phase of processing, which is Phase II detoxification. In Phase II detoxification metabolites produced in Phase I are combined with endogenous molecules and become less toxic and harmful, more water-soluble and therefore readily available for excretion.

What Mercury poisoning does to your body

Mercury has a number of mechanisms leading to toxicity in biological systems:

- Breaking of hydrogen bonds
- Displacement of other metallic ions from a ligand site
- Change in tertiary protein structure, leading to inhibition or acceleration of membrane permeability
- Attachments of ligands to cell membranes leading to inhibition or acceleration of membrane permeability
- Alteration of translational processes, leading to potential carcinogenic activity. Inhibition of DNA repair enzymes.

Cellular effects of mercury toxicity

The mitochondria are specialized compartments inside all cells (except red blood cells) that convert sugar and fats into energy. Within the mitochondria, mercury can disrupt critical processes resulting in decreased mitochondrial transmembrane potential. This can contribute to chronic fatigue, disruption of the cell growth and reproduction mechanisms, dissolution of microtubules in the cells affecting cell mitosis, decreasing phagocytosis and eliminating important immune cells such as monocytes and lymphocytes through apoptosis further decreasing cellular immune function.

The impaired neutrophil

Three different studies (Lindh, Perlingeiro, Worth, and Hrycek) appear to confirm that mercury affects T-cell populations and immune function. Heavy metals (mercury, zinc, copper, manganese, nickel and cobalt) have been shown to reduce immune housekeeping activities (i.e. respiratory burst and chemotactic functions). Interestingly, Omura and Beckman have reported continuous recurrence patterns of strongly resistant viruses such as chlamydia trachomatis, herpes simplex types I and II, CMV retreated to areas in the body which also held abnormal mercury, lead and other heavy

metal deposits. They used Chinese parsley (cilantro) to increase the excretion of mercury, lead and aluminum via urine and noted that both the heavy metals and the infections disappeared.

Chronic mercury intoxication affects the hypothalamus and the cascade effect continues throughout the endocrine system. Based on the viable data over the last 20 years, it is not unreasonable to propose a possible connection between mercury amalgam fillings and many mental disturbances and neurological deficits in mercury toxic patients. In the American Journal of Psychotherapy, Robert Siblingud's discussion of "The relationship between mercury from dental amalgam and mental health" suggested that mercury poisoning from dental amalgam³ may play a role in the etiology of mental illness. He states "evidence linking mercury exposure to psychological disorders has been accumulating over the past 60 years... as a result of mercury's strong affinity for brain tissue, it disrupts the emotional sphere and produces psychological disorders". In another paper Siblingud cites the well known MMPI-2 (Minnesota Multiphasic Personality Inventory-2) test which was used to evaluate patient symptom improvement after removal of mercury amalgam fillings. There were significant improvement in test scores in 41 of 61 component cases and 12 of the 20 subscales including schizophrenia, hysteria, paranoia and anger.

How Does Mercury toxicity present?

Acute symptoms: Metallic taste, thirst, discoloration and edema of oral mucosa, burning mouth pain, salivation, abdominal pain, vomiting, bloody diarrhea, severe gastroenteritis, colitis, nephrosis, anuria, uremia, shock, skin burns from alkyl and phenyl mercurials.

Chronic symptoms: gingivitis, weakness, ataxia, intention tremors, speech and hearing impairment, sensory disturbances, restlessness, irritability, excitability, fearfulness/anxi-

ety, temper outburst, insomnia, difficulty in concentration, impaired memory, depression, delirium and toxic psychosis (severe).

Chronic disease patterns will appear in a more multifactorial pattern. A classic cumulative constellation of symptoms include insomnia, the “domino effect” of endocrine dysfunction causing autoimmune diseases such as SLE (systemic lupus erythematosus), myelinopathies such as multiple sclerosis and myasthenia gravis, rheumatoid arthritis, multiple chemical sensitivity (MCS) from environmental illness, and chronic candidiasis. Many medical models, including Chinese, Ayurvedic, and Western, reference the gastrointestinal system as “the seat of disease.” We know that many chronic health problems can be traced to compromised digestive function. The digestive system breaks down food, absorbs nutrients and sends what it can’t handle on to the liver through the bloodstream for further breakdown. At some point during this process, the colon may become involved with symptoms such as colitis, severe gastroenteritis, burning pain in the mouth, salivation, abdominal pain, vomiting, irritable bowel syndrome, Crohn’s disease as well as many corresponding dermatological problems.

Lab diagnosis: No one test can show total body burden of heavy metals. Standard screening panels consist of hair, blood and urine, with conflicting evidence on which is the most accurate. One way heavy metals work is to displace other critical elements. Some studies point out that you can accurately detect Hg in the hair by recognizing signs of disordered mineral transport in the other essential elemental levels. In 27 subjects with health problems associated with dental amalgam there were significant increases of copper, iron, zinc, and strontium in patient plasma. Mercury was significantly increased in patient plasma, although there was overlap between the groups. There was a significant increase in calcium and a significant decrease in magnesium, copper, manganese and zinc. Cutler states that the hair analysis is most

accurate for mercury interpretation only by correlating it to the disordered mineral transport. Mercury levels in this application often show up low vs: the minerals/elements which are abnormally scattered (i.e. more highs and lows than expected).

Treatment: First Do No Harm

What happens when a large amount of mercury is dumped into hepatic and renal pathways? The Phase I and Phase II pathways are limited as to how many toxins they can handle at any one time. Sulfur and glutathione are major nutrients necessary in the detoxification pathways. Sulfur is also needed for thyroid hormone production and collagen physiology. Mercury can cause fatigue by several mechanisms: inhibiting conversion of T4 to T3, interfering with hormone metabolism, and by depleting glutathione and lipoic acid. Mercury has a strong affinity for sulfur-based (sulfhydryl) bonds. These sites include sulfhydryl groups, disulfide bridges, lipoproteins, glycoproteins and half-cysteine residues. It stands to reason that there would be an increased need for nutrients to fuel proper detoxification pathways in these patients.

Dietary sources of sulfur include garlic, onions, eggs, cruciferous vegetables (broccoli, brussels sprouts, cauliflower), green leafy vegetables (kale, spinach, dandelion, endive) work well. Amino acids and amino acid complexes such as cysteine, methionine, seleno-methionine, SAM (S-adenosyl methionine) and alpha lipoic acid all contain sulfhydryl groups which can assist in chelating heavy metals out of the body. It is the clinical experience of several physicians that plasma cysteine is a relevant marker. Clinical observations show patients with elevated plasma cysteine would be better served to exclude all of the above foods. Patients with low plasma cysteine need to eat all of the above. Patients with normal plasma cysteine need to eat these foods in moderation. Cysteine is the reduced monomer; cystine is the oxidized dimer. There is always the “canary in the coal mine” patient to

consider. Chemically reactive people tend to be genetically different. If a patient was compromised through either a dysbiotic gut or altered genetics, this could manifest as functional limitations in detoxification pathways.

Antioxidant support: NAC precursor to GSH

One way to effect change is targeting the mitochondria to eliminate destructive free radicals with alpha lipoic acid (ALA). Boosting the activity of carnitine acetyltransferase (which plays a key role in burning fuel in the mitochondria) with acetyl-L-carnitine, a substrate that the enzyme acts on may achieve positive results. The combination of both alpha lipoic acid and acetyl-L-carnitine improve mitochondrial activity and thus cellular metabolism, increasing the levels of vitamin C, another necessary antioxidant.

Zinc, and other minerals

Another supportive therapy would be to increase the levels of minerals and other nutrients before detoxification. Huggins, in his work with multiple sclerosis has noted that changes in the tertiary structure of a protein can lead to the inhibition of enzymatic activity. Therefore, minerals such as magnesium, (which tends to be low in mercury toxic patients) zinc, calcium, selenium and manganese which function as co-factors in various enzyme systems of the body should be supplemented. Zinc has several crucial functions in brain development and maintenance, including expression of several paramount genes. It is required for the production of superoxide dismutase, an antioxidant essential to prevent oxidative damage. Zinc is also required for the synthesis of serotonin and since serotonin is necessary for melatonin synthesis, a zinc deficiency may result in low levels of both hormones. Kelp, dulse and other sea vegetables are among the richest sources of minerals. Trace minerals are also concentrated in the germ layer of grains.

Both sides of alpha lipoic acid (ALA) controversy

It has been reported that ALA may enhance biliary excretion of mercury. (Revsvik, 1982/Grunert 1960/Anuradha 1999/ Leskova 1979). It is well known that ALA crosses the blood brain barrier. In two studies ALA was shown to prevent the pathological changes in the brain from mercury poisoning. Chapman and Chan's review, as well as references from Crinnion state that ALA is helpful and protective in patients with mercury overload. The root of this controversy is that ALA is a powerful chelating agent. As with any powerful substance improper prescribing often harms the patient. It could further be hypothesized that lipoic acid would facilitate biliary excretion of metals whose hepatobiliary transport is GSH-dependent. One study discussed by Gregus et al. points out that biliary elimination of methylmercury is completely and totally dependent on the presence of GSH. However, Gregus also states that ALA can complex with GSH, making it unavailable for metal elimination. He also found that a low dose of ALA enhances excretion versus a high dose which inhibits excretion. After analyzing the studies, one may conclude that ALA is an excellent therapeutic tool for inorganic mercury toxicity most often due to occupational exposures. Due to the sparse data, questions are still remaining regarding its use in methylmercury detoxification.

Support Nutrients

B12 – Some studies demonstrate that a relationship between vitamin B12, folic acid, ascorbic acid, mercury uptake and methylation exists. A study conducted by the Department of Nutrition and Food sciences, University of Tennessee suggested that megadoses of certain vitamins¹ appear to influence the in vivo methylation of mercuric chloride in guinea pigs. Though the mechanism is not clear, the actual data show that supplementation of an assorted spectrum of vitamins was dramatically more effective in reducing tissue deposition of mercury than single vitamins.

Cilantro, Chlorella and Algae and Psyllium² – Any green products, especially chlorella, can help absorb mercury and other metals as they pass thru the colon. Chlorella is a single cell algae, high in antioxidants (particularly carotenoids) which coat the intestine and binds mercury in the gut. Cilantro is known to be an herb with an affinity for mercury.

Skin and Digestion for binding and eliminating toxins: The primary portals of excretion (skin, intestine, lungs and kidneys) should be optimized before, during and after detoxification. The skin is good way to excrete toxins. Finnish saunas increase peripheral circulation, metabolic rate, oxygen consumption. The loss of water and electrolytes in a sauna is compensated by hormonal regulation of the kidneys via aldosterone. Intestinal agents such as psyllium, pectin and bran increase stool bulk, decrease transit time in the bowel, thereby absorbing and removing metals. The results from a study on mice fed with bran suggest that dietary bran may reduce the levels of mercury in the brain after methylmercury exposure and may therefore reduce the neurotoxic effects. Wheat bran works via modification of the metabolic activity of the gut microflora.

EDTA/DMSA/DMPS

Chelating agents can form bonds to metal ions and carry them out of the body. DMPS (Dimercaptopropanesulfonate) was found to be the most efficient chelation method for mercury removal from the kidneys. One study using EDTA (Ethylene Diamine Tetraacetic Acid) and DMSA (Dimercaptosuccinic Acid) showed a decrease in tissue burden and an increase in urinary output of lead. No increased burden of tissue metal toxicity was observed in the brain. DMSA can be started one to three weeks prior to amalgam removal.

Liver support: *Peumus boldo* (Amazonian herb), milk thistle, castor oil packs applied to the liver, epsom salt/baking soda baths. Use liver herbs the night before you do colonic irrigations or hydrotherapy.

Kidney support: Herbs: *Uva ursi* (bearberry), *Urtica dioica* (nettles) and colonic irrigations. Lecithin can protect the liver and kidneys in the detoxification process. Foods high in lecithin content are bee pollen and egg yolks.

Endocrine glands should be supported. Adrenals specifically need more B5 (pantothenic acid) and vitamin C.

The body burden of mercury and other environmental toxins and resulting tissue damage tends to accumulate with time leading to a cascade of chronic events and illness. However, there is a wide choice of detoxification methods that can be used to enhance the excretion systems in the body. Supporting increased digestion, improving liver function, supplementing with nutrients and supporting adequate antioxidant stores all address our objectives to reduce environmental exposures of mercury. Since foods and water represent the most common sources of mercury exposure, give your liver some assistance by consuming organically grown foods, filtered water and limiting your fish consumption to a monthly basis, especially if pregnant.

¹ Note: Most of the studies concur that vitamin C is not a good chelator and selenium actually raises levels of mercury.

² Note: An important caveat concerns supplements normalizing lab values that could make diagnosis of toxicity more difficult. Taking Milk thistle or lecithin before diagnosis, for example may normalize AST and ALT.

There is no given relationship between heavy metal content in the soil and heavy metal uptake by plants.

³ Note: Removing amalgam fillings can be an exhaustive and costly procedure. The benefit/risk ratio should be carefully evaluated before taking this step.

References

- Adachi T., Influence of dietary levels of protein and sulfur amino acids on the fate of methylmercury in mice, *Toxicology* Nov 1994;93(2-3):225-234.
- Adzet T, Camarasa J, Laguna JC. Hepatoprotective activity of polyphenolic compounds from *Cynara scolymus* against CCl₄ toxicity in isolated rat hepatocytes. *J Nat Prod.* 1987 Jul-Aug;50(4):612-7. PMID: 3430163 [PubMed - indexed for MEDLINE]
- Bland JS, Barrager E, Reedy RG, Bland K. A Medical Food-Supplemented Detoxification Program in the Management of Chronic Health Problems. *Altern Ther Health Med.* 1995 Nov 1;1(5):62-71. PMID: 9359760 [PubMed - as supplied by publisher]
- Bottiglieri T, Laundry M, Crellin R, Toone BK, Carney MW, Reynolds EH. Homocysteine, folate, methylation, and monoamine metabolism in depression. *J Neurol Neurosurg Psychiatry.* 2000 Aug;69(2):228-32. PMID: 10896698 [PubMed - indexed for MEDLINE]
- Chuang SE, Cheng AL, Lin JK, Kuo ML. Inhibition by curcumin of diethylnitrosamine-induced hepatic hyperplasia, inflammation, cellular gene products and cell-cycle-related proteins in rats. *Food Chem Toxicol.* 2000 Nov;38(11):991-5. PMID: 11038236 [PubMed - indexed for MEDLINE]

References (continued)

- Crinnion, WJ Environmental medicine, part three: Long-term effects of chronic low-dose mercury exposure, *Alt Med Rev*, 2000; 5(3):p.209-233.
- Crinnion, WJ Results of a decade of naturopathic treatment for environmental illnesses: A review of clinical records. *JMN*;7(2):21-27.
- Cutler, A Amalgam Illness: Diagnosis and Treatment, 1999. URL www.noamalgam.com
- Cyong JC, Ki SM, Iijima K, Kobayashi T, Furuya M. Clinical and pharmacological studies on liver diseases treated with Kampo herbal medicine. *Am J Chin Med*. 2000;28(3-4):351-60. PMID: 11154048 [PubMed - indexed for MEDLINE]
- de Morais SM, Uetrecht JP, Wells PG. Decreased glucuronidation and increased bioactivation of acetaminophen in Gilbert's syndrome. *Gastroenterology*. 1992 Feb;102(2):577-86. PMID: 1732127 [PubMed - indexed for MEDLINE]
- De Palma G, Manini P, Mozzoni P, Andreoli R, Bergamaschi E, Cavazzini S, Franchini I, Mutti A. Polymorphism of xenobiotic-metabolizing enzymes and excretion of styrene-specific mercapturic acids. *Chem Res Toxicol*. 2001 Oct;14(10):1393-400. PMID: 11599931 [PubMed - indexed for MEDLINE]
- Dill, DB, et al: Handbook of Physiology, Section 4: Adaptation to the Environment, Washington, D.C., 1964; Am Physiol Soc.
- Dirks, MJ Mercury excretion and intravenous ascorbic acid, *Arch Environ Health*, Jan-Feb 1994;49(1):49-52.
- Domingo J.L. Developmental and reproductive effects of metal chelators in Toxicology of Metals, Chang L.W. Editor, 1996; CRC Press: Boca Raton, 1153-1167.
- Flora K, Hahn M, Rosen H, Benner K. Milk thistle (*Silybum marianum*) for the therapy of liver disease. *Am J Gastroenterol*. 1998 Feb;93(2):139-43. Review. PMID: 9468229 [PubMed - indexed for MEDLINE]
- Forman, J. et al, A cluster of pediatric metallic mercury exposure cases treated with meso-2,3-dimercaptosuccinic acid (DMSA). *Environ Health Perspectives*, 2000; 108(6):575-577.
- Fryer AA, Jones PW. Chapter 22. Interactions between detoxifying enzyme polymorphisms and susceptibility to cancer. *IARC Sci Publ*. 1999;148:303-22. Review. PMID: 10493264 [PubMed - indexed for MEDLINE]
- Gregus, Z et al Effect of Lipoic Acid on Biliary Excretion of Glutathione and Metals, Department of Pharmacology, University Medical school of Pecs, Hungary and Department of Pharmacology, Toxicology and Therapeutics, University of Kansas Medical Center, Kansas City, Kansas; January 3, 1992.
- Grunert, R.R. The effect of DL- α -Lipoic acid on heavy metal intoxication in mice and dogs, *Archives of Biochemistry and Biophysics*, 1960; Vol. 86:190-4.
- Hrycek A, et al The effect of heavy metals on neutrophils, *Wiad Lek* (Polish translated to English) 1996;49(7-12):107-111.
- Huggins, H. Cerebrospinal fluid protein changes in multiple sclerosis after dental amalgam removal, *Alt Med Review*, 1998; Vol 3, No.4:295-300.
- Kabelitz, L Heavy metals in herbal drugs, *European Journal of Herbal Medicine*, Vol 4; Issue 1.
- Kennedy JA, Clements WD, Kirk SJ, McCaigue MD, Campbell GR, Erwin PJ, Halliday MI, Rowlands BJ. Characterization of the Kupffer cell response to exogenous endotoxin in a rodent model of obstructive jaundice. *Br J Surg*. 1999 May;86(5):628-33. PMID: 10361183 [PubMed - indexed for MEDLINE]
- Kuchel O, Buu NT, Racz K, De Lean A, Serri O, Kyncl J. Role of sulfate conjugation of catecholamines in blood pressure regulation. *Fed Proc*. 1986 Jul;45(8):2254-9. PMID: 3720964 [PubMed - indexed for MEDLINE]
- Leskova, Protective effect of lipoic acid amide in experimental mercurialism, *Gig Tr Prof Zabol.*, Jun 1979;6(2):27-30.
- Lindh, U et al, Department of Oncology, Uppsala University, Sweden, *Journal of Clinical Chem Lab Med*, Feb 2001; 39(2):134-42.
- Macklon AF, Savage RL, Rawlins MD. Gilbert's syndrome and drug metabolism. *Clin Pharmacokinet*. 1979 May-Jun;4(3):223-32. Review. PMID: 383356 [PubMed - indexed for MEDLINE]
- Magos L, et al Comparison of the protection given by selenite, selenomethionine and biological selenium against renotoxicity of mercury, *Arch Toxicol* Aug 1987;60(6):422-6
- Manini P, Andreoli R, Bergamaschi E, De Palma G, Mutti A, Niessen WM. A new method for the analysis of styrene mercapturic acids by liquid chromatography/electrospray tandem mass spectrometry. *Rapid Commun Mass Spectrom*. 2000;14(21):2055-60. PMID: 11085418 [PubMed - indexed for MEDLINE]
- Marlowe, Lead and mercury levels in emotionally disturbed children, *Area of Special Education*, University of Wyoming, *Journal of Orthomolecular Psychiatry*, 1983;12:260-220.
- Miller, AL Dimercaptosuccinic acid (DMSA), a non-toxic water-soluble treatment for heavy metal toxicity, *Alt Med Rev*, Jun 1998;3(3):199-207
- Minchin RF, McManus ME, Boobis AR, Davies DS, Thorgeirsson SS. Polymorphic metabolism of the carcinogen 2-acetylaminofluorene in human liver microsomes. *Carcinogenesis*. 1985 Dec;6(12):1721-4. PMID: 4064248 [PubMed - indexed for MEDLINE]
- Moss, J A viewpoint on mercury: Methods and controversies concerning treatment. Part V, *Nutritional Perspectives*, 2002 Vol. 25, No.2.
- Neilsen JB The toxicokinetics of mercury in mice offspring after maternal exposure to methylmercury?effect of selenomethionine, *Toxicology* Sept 1992;74(2-3):233-241.
- Perlingeiro RC, et al Measurement of the respiratory burst and chemotaxis in polymorphonuclear leukocytes from mercury-exposed workers, *Mar* 1995;14(3):281-286.
- Polonen IJ, Partanen KH, Jalava TK, Toivonen VF. Effect of dietary glycine and benzoate level on benzoate metabolism in mink (*Mustela vison*), blue fox (*Alopex lagopus*), and raccoon dog (*Nyctereutes procyonoides*). *J Anim Sci*. 2000 Apr;78(4):976-86. PMID: 10784188 [PubMed - indexed for MEDLINE]
- Randolph, TG: Human Ecology and Susceptibility to the Chemical Environment, Springfield, Illinois: C.C. Thomas, 1962.
- Randolph, TG; Historical development of clinical ecology, *Clinical Ecology*, Dickey LD (Ed.) Springfield, Illinois: C.C. Thomas, 1976.
- Rowland, IR et al The effect of various dietary fibres on tissue concentration and chemical form of mercury after methyl mercury exposure in mice, *Arch Toxicol* Jul 1986;59(2):94-98.
- Rutherford PP, Deacon AC. The mode of action of dandelion root -fructofuranosidases on inulin. *Biochem J*. 1972 Sep;129(2):511-2. No abstract available. PMID: 4643338 [PubMed - indexed for MEDLINE]
- Siblerud, R The relationship between mercury from dental amalgam and mental health, *American Journal of Psychotherapy*, October 1989;Vol. XLIII, No. 4.
- Siblerud, R. et al A comparison of mental health of multiple sclerosis patients with silver/mercury dental fillings and those with fillings removed, *Psychol Rep* 1992;70:1139-1151.
- Soleo L, Strzelczyk R. [Xenobiotics and glutathione] *G Ital Med Lav Ergon*. 1999 Oct-Dec;21(4):302-8. Review. Italian. PMID: 10771744 [PubMed - indexed for MEDLINE]
- Sonne J. Factors and conditions affecting the glucuronidation of oxazepam. *Pharmacol Toxicol*. 1993;73 Suppl 1:1-23. Review. PMID: 8415417 [PubMed - indexed for MEDLINE]
- Suda, et al Degradation of methyl and ethyl mercury into inorganic mercury by oxygen free radical-producing systems: involvement of hydroxyl radicals, *Arch Toxicol* 1991;65(2):129-134.
- Tajmir-Riahi HA Coordination chemistry of vitamin C. Part II Interaction of L-ascorbic acid with Zn(II), Cd(II), Hg(II), and Mn(II) ions in the solid state and in aqueous solution, *J Inorg Biochem* Apr 1991;42(1):47-55.
- Wittayalerpanya S, Mahachai V. Caffeine clearance in patients with chronic viral hepatitis: before and after interferon therapy. *J Med Assoc Thai*. 2001 Jun;84 Suppl 1:S189-96. PMID: 11529334 [PubMed - indexed for MEDLINE]
- Worth, RG et al, Mercury inhibition of neutrophil activity: evidence of aberrant cellular signaling and incoherent cellular metabolism, *Jan* 2001;53(1):49-55.
- Zalups RK, et al Relationships between alterations in glutathione metabolism and the disposition of inorganic mercury in rats: effects of biliary ligation and chemically induced modulation of glutathione status, *Chem Biol Interact*, Dec 1999;123(3):171-195.
- Zhao B, Seow A, Lee EJ, Lee HP. Correlation between acetylation phenotype and genotype in Chinese women. *Eur J Clin Pharmacol*. 2000 Dec;56(9-10):689-92. PMID: 11214777 [PubMed - indexed for MEDLINE]
- Zorn, NE, et al ?A relationship between vitamin B12, folic acid, ascorbic acid, and mercury uptake and methylation?, University of Tennessee, Department of Nutrition and Food Sciences, 1990;47(2):167-73.