BIOTOXINS:

Supporting removal via intrinsic pathways

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I. Introduction

The human body has evolved intrinsic mechanisms for the removal of toxicants from the body. Where medical advances have not provided effective therapies for biotoxin related illness such as disease caused by typhoid toxins, mycotoxins, quinolinic acid from lyme disease, and gangrene caused by 3 known staphylococcal toxins, pathophysiologic research and clinical experience suggest that patient improvement can occur when the body's intrinsic detoxification pathways are therapeutically activated. Modern day exposures in the face of nutrient depletion and epigenetic changes caused by exposures to toxins and trauma in the parent's and grandparent's generation compromise one's ability to detoxify. This chapter premises how the body's natural detoxification mechanisms can be enhanced.

II. Epidemiology

What has changed at the population level regarding biotoxins that manifests what clinicians and their patients' experience?

On one hand advances in medicine, especially the use of some vaccines and antibiotics, have reduced morbidity. The fact that tetanus, typhoid and streptococcal exposures are now rare represents a public health success.

On the other hand some pathogens cause more disease on the population level. This can be from increased virulence factors adapted by the organism, spread to increasingly more populations, but can also be caused by increased population density and world travel, or increased vulnerability on the part of the host. Possible causes include micronutrient depletion, synergistic effects of environmental pollutants accumulated in the body and steadily increased exposure to electromagnetic radiation from cell phone broadcasting and other sources.

One organism increasingly attributed to disease in humans is *Borrelia burgdorferi*, the organism causing Lyme disease thought to have become a human pathogen more recently. However in 2011 epidemiologic evidence emerged from an unlikely source, "Oetzi" the iceman. Spirochetes were identified in 5,300-year-old cadaver whose body was preserved in the Alpine ice was recently determined to be infected with *Borrelia* [1]. Oetzi was estimated to have been a healthy 20-45 year old man at the time of his death

which has been attributed to trauma. *Borrelia* spirochetes have been around a long time and may have only recently developed their pathogenicity.

III. Pathophysiology

The overarching principle relevant to this chapter and the treatments presented is that chronic illness is not caused by the presence of pathogens themselves but by their metabolic activity and the creation of potent biotoxins. The return to health is determined by appropriate immune reactions and the body's own ability to remove biotoxins, which can be enhanced in two key ways:

1. Using integrative nutritional and other approaches to restore the detoxification capacity or/and upregulate the metabolic enzymes of the biotoxin pathway.

2. Reducing the easier-to-control harmful exposures which occupy the same detoxification pathways as those biotoxins which are less amenable to treatment and exposure reduction.

Genetic propensities play a major role in how well the toxin elimination pathways work to start with. This is demonstrated in the connection between apolipoprotein E (APO-E) subtypes and Alzheimer's disease[2]. The APO-E subtype 2 has two glycine molecules which enables this compound to bind and eliminate sulfhydryl affinitive toxic metals from inside the cell. The subtype E-4 has no glycine and is unable to participate in the constant clean up of the cell. The efficiency of the biotoxin pathway is also influenced by HLA system genotypes, which determines how the immune system responds to offending toxins and microbes. Several subtypes are significantly less able to eliminate toxins from the body, as illustrated in a case-control study of ciguatoxin fish poisoning [3].

Biotoxin exposures are diverse. They include tetanus toxin; botulinum toxin (botox); ascaridin from intestinal parasites;, streptolysin toxins from *Streptococci*; toxins from *Staphylococci*, Lyme disease, chlamydia, *Babesia microti,* and tuberculosis; fungal toxins also called mycotoxins; venom from brown recluse spiders; and toxins triggered by viral infections.

Biotoxins are minute molecules (200-1000 kilodaltons) containing nitrogen and sulfur. They belong to a group of chemical messengers which microorganisms use to control the host's immune system, host behavior and even the host's eating habits. Aggressive staphylococcus infections that cause tissue necrosis are caused by at least three potent biotoxins, not by the presence of the microbes themselves. The diversity of the biotoxins may be profound. For example *Candida albicans* produces 600 different known biotoxins.

Rationale for reducing neurotoxin exposure in patients with chronic Lyme disease

Biotoxins are neurotoxins as are heavy metals, xenobiotics (man-made environmental toxins such as dioxin, formaldehyde, insecticides, wood preservatives, polychlorinated

biphenyls), and food additives. Neurotoxins are a subgroup of biotoxins attracted to the mammalian nervous system.

Neurotoxins act with synergy, making the fact that human pathophysiology surrounding Lyme disease and several other potentially chronic infections comes from nerve-damaging biotoxins clinically relevant. For example, in a rat toxicology study combining mercury and lead, each at doses lethal to 1 in 100 animals (LD1), all the rats died (LD100). The exponential effect of the combined neurotoxins can be expressed as: LD1 of Hg +LD1 lead = LD100. Similar applications have been made in marine ecosystems where combined toxicities are greater than individual ones[4].

The primary reason for the adverse effects being more than additive is that the human body experiences toxins every day and has common metabolic pathways to dispose of them. However when several toxins are present at one time the pathways may become overwhelmed. Neurotoxins not promptly metabolized are absorbed by nerve endings and travel inside the neuron to the cell body. On their way they disrupt vital functions of the nerve cell, such as axonal transport of nutrients, mitochondrial respiration and proper DNA transcription.

The clinical corollary is that by reducing exposure to and facilitating the elimination of neurotoxins, the body can more effectively eliminate the biotoxins directly associated with medical illness.

Rationale for gastrointestinal support

The body is constantly trying to eliminate neurotoxins via the available exit routes: the liver, kidney, skin and exhaled air. Detoxification mechanisms include acetylation, sulphation, glucoronidation, oxidation and others. **Figure 1** depicts how enzymes, cofactors and toxicants interact in the metabolic pathways of detoxification. Detoxification occurs in 3 phases.

Phase 1 breaks the toxin into smaller particles some of which may be more toxic than the original substance.

Phase 2 binds these toxic substances to the body's own molecules which makes the toxin less toxic, soluble in bile as in the process of glucoronidation, or soluble in water so that it can be excreted by the kidney.

Phase 3 binds the substance to a transporter molecule shuttled out to kidney, skin or liver.

Approximately 90% of the molecules are removed through liver to the bile and then excreted in the stool. However, because of the lipophilic/neurotropic nature of the neurotoxins, most are reabsorbed by the abundant nerve endings of the enteric nervous system in the intestinal wall.

The exact mechanisms for the signaling from the gastrointestinal tract have not been determined, but the possible mechanisms are several since the re-uptake of neurotoxins occurs in many pathways. Toxins undergoing neuronal uptake are transported via axons to the spinal chord (autonomic nervous system neurons) or brainstem (parasympathetics) and from here back to the brain. Venous uptake and via the portal vein back to the liver occurs (enterohepatic circulation). Lymphatic uptake via the thoracic duct to the subclavian vein occurs. There is also uptake by bowel bacteria and tissues of the intestinal tract. The late Dr. Alfred Pischinger advanced the understanding of these mechanisms, which have been recently translated into English by those continuing his work[5].

In order to prevent the resorption of neurotoxins we give binding agents such as *Chlorella* species to act in the gut. That gives a feedback signal to the liver that more toxins can be eliminated. Binding toxins in the gut signals the liver and a successful phase 2 relays feedback to phase 1. To initiate a cascade of detoxification all the way from the interior of the cell to the inside of the bowel it is most often not necessary to use intracellularly-acting, sophisticated toxin elimination agents. It is most often sufficient to use binding agents in the gastrointestinal tract.

Facilitating peroxisomal activity

Detoxification occurs in every cell of the body, most prominently the liver followed by the kidney and skin. All are rich in these detoxification enzymes found in the peroxisomes. Peroxisomes are the "liver" of each cell and process neurotoxins. Detoxification can be facilitated when methods are used to increase peroxisomal function:

- Fever
- Hyperbaric oxygen
- Exercise
- Phosphatidyl choline
- Actos (acts as an agonist to the peroxisome proliferator activator receptor (PPAR) -gamma)
- *Chlorophyll* (PPAR-alpha and beta agonist)

In contrast, excessive amounts of antioxidants (such as certain types of high dose vitamins) can inhibit peroxisomal activity.

Restoring detoxification nutrients when they are depleted through bacterial and fungal virulence factors

What are the mechanisms that the microbes are using to establish themselves in the human host? With a highly evolved human immune system the mechanisms by which toxin-producing organisms evade the immune system are surprising in their complexity. One clinically significant, but less known, mechanism by which Lyme spirochetes evade host immune mechanisms is to deplete the host of nutrients integral to its defenses, by blocking one of the 8 enzymes needed in the heme pathway, leading to the formation of

hemopyrollactams [6] and inefficient heme molecules. The heme molecule is part of the hemoglobin system and also used in p450 liver detoxification system.

Hemopyrrollactamuria (HPU), formerly known as kryptopyroluria, was identified in 1958 by Abrahm Hoffer, a psychiatrist researcher focusing his healing work on people with schizophrenia. He observed high concentrations of this substance in the urine of his patients and not in the general population. The HPU compound binds strongly to vitamin B6, zinc and other micronutrients listed in **Table 1** and illustrated in **Figure 2**. As the nutrients chaperone the hemopyrrollactams to be eliminated via the urine, the nutrients are also eliminated in excess of usual physiologic amounts, usually in direct proportion to the amount of hemopyrrollactams[7].

In HPU nutrient deficiencies can arise from excess urine losses even when nutrient intake and absorption are adequate. The symptoms of this illness are related to the resulting depletion of the nutrients listed in **Table 1.** Treating with high doses of zinc and B6 reverses many of the symptoms.

HPU lowers serum levels of reduced glutathione. Glutathione levels and a variant of the glutathione peroxidase enzyme are correlated with longevity [8]. We therefore felt it clinically significant that our patients with Lyme consistently have presented with low glutathione levels. Once we began treating HPU we saw a steady increase in glutathione to levels of age-adjusted healthy patients, in keeping with earlier research findings[7, 9].

Some patients with HPU experience reduction in their symptoms with antibiotics. Some Lyme patients convert from HPU positive to HPU negative as their condition improves with antimicrobial treatment [10]. It is not yet fully understood, but clinical observations suggest that HPU is reversible through different treatment mechanisms and once HPU resolves the nutrients losses abate, although without supplementation recovery of nutrient status is delayed.

IV. Patient evaluation

Antibiotics successfully treat the acute infection with Lyme disease and a subset of patients with chronic Lyme disease. However, patients in integrative medical practices around the country testing positive for Lyme disease tend to be the patients who did not sufficiently respond to antibiotic interventions. The fact that patients referred to my practice haven't responded to prior conventional medical treatment greatly increases the probability of clinically significant neurotoxin exposure.

History

Exposure history: A patient history in my clinic emphasizes neurotoxin exposures. These include but are by no means limited to:

- Current or prior amalgam fillings, because of evaporation of metallic mercury, leaching of tin

- Tick or other insect bites. Most so called "tick borne diseases" such as lyme disease can also be carried by stinging flies, spiders and insects other than ticks.
- Occupations such as working in machine shops with solvents; welding, which is associated with metal fume fever from aerosolized metal toxicants; veterinary clinic work; or working in a beauty salon, keeping in mind the paraben exposure. Sometimes a parent's occupational exposures are transferred to children, so a family exposure history may be appropriate here.
- Hobbies can point to exposures such a working with stained glass, autorepair, or exposure to munitions at a rifle range.
- Long hours of computer work can point to electromagnetic radiation and also possible off-gassing of heavy metals and other toxicants from the electronic equipment.

Symptoms: Of particular note are symptoms of fatigue, insomnia, lack of zest, short term memory loss, cognitive problems, and mood disorders. Symptoms can point to cranial nerve issues: Facial paralysis (CN VII), facial pain (CN V), deteriorating eye sight (CNs II, IV, and VI), tinnitus (CN VIII), vertigo (CN VIII), hearing loss (CN VIII), and difficulty swallowing or GERD (CN X). Some patients report neurological symptoms lacking a defined neurologic basis, but are temporally associated with their illness. Examples are crawling under the skin and vibration inside the skull.

Another aspect of assessing a patient's symptoms is to inquire about what actions they took which improved their symptoms. Such patient observations can be clinically relevant and point to feasible treatment options.

Physical exam

Upper motor neuron signs: Neurologic findings include evaluation for the abnormal reflexes of hyperreflexia, ankle clonus, and the Babinski sign, which is common with *Bartonella henselae*.

Cranial nerve symptoms: Facial nerve paralysis is strongly associated with (pathognomonic) *Borrelia burgdorferi* infection. Other signs of neurotoxic damage to the cranial nerves include deviation of the tongue due to effects on the hypoglossus nerve; decreased or complete loss of smell from cranial nerve 1 involvement; lazy eye from cranial nerve 6 involvement; tinnitus or vertigo from effects on cranial nerve 8; difficulties swallowing due to cranial nerves 9 and/or 10 involvement; intractable pain in the lower neck/upper shoulders which can be due to cranial nerve 12 involvement. Note that cardiac arrhythmias can involve cranial nerve 10 dysfunction.

Skin findings include pale translucent skin as commonly observed in HPU; cherry angiomata which are associated with Babesia; striae in unusual areas in young non-pregnant clients, and furthermore these striae tend to be blue with Babesia and red with Bartonella; and skin tags associated with insulin resistance, which can be induced by Lyme and Bartonella in patients without other risk factors. Often the skin ages

prematurely due to microbe-upregulated metallo-proteinases (MMP-9) from yet-elucidated mechanisms.

Nail findings include longitudinal ridges, which are a sign of a disturbed protein matrix of the nail often caused by underlying hypochlorhydria. Hypochlorhydria can be a sign of cranial nerve 10 dysfunction, and is common in many chronic infections. Brittle nails and hair are often a sign of functional hypothyroidism, which may be more often associated with excessive exposure or sensitivity to electromagnetic radiation, rather than a direct effect of the microbial pathogens.

Autonomic response testing (ART): Practitioners unfamiliar with ART may wish to read this book's chapter authored by Yoshiaki Omura, since he patented the bi-digital O-ring test on which ART is based. It is a method to assess whether a food, medication or biologic agent will be tolerated by the individual patient. When allergenic foods are placed on the patient's tongue or in proximity to the patient's skin the heart rate increases. The more rapid pulse indicates a withdrawal of parasympathetic activity and activation of the sympathetic nervous system. At the same time the muscle tone of skeletal muscles changes throughout the body, which can be monitored by a trained practitioner [11]. Many techniques are based on this phenomenon, including electrodermal screening, applied kinesiology and the bi-digital O-ring test. This author has developed a sensitive modification of the muscle testing named "autonomic response testing". ART incorporates a signal enhancer (SE), which is a plate of plastic with a special molecular structure. The SE amplifies the autonomic response and may be therefore an easier technique to learn. If a substance is placed on the SE near the client's body, the system will respond as if the person had ingested this substance. This allows the testing of many foods and substances in a short period of time. This system helps predict if a particular medication or biological agent will be tolerated.

Functional acuity contrast test, also called visual contrast sensitivity: In this test the ability of the client is tested to perceive different shades of contrast. Research has shown that the quality of contrast perception is directly related to intra-cranial arterial blood flow, sometimes diminished in chronic neurotoxicity from mold, Lyme or exposure to tetrachloroethylene [12].

Laboratory diagnostics for heavy metals

There is no direct way to assess the body burden of heavy metal neurotoxins. We start by establishing an experience-based general toxin metal elimination protocol. Six weeks into that we do a hair analysis of the proximal inch of hair which will reflect what was mobilized during those 4-6 weeks through the body's own activity. Over time we use the urine porphyrin testing, red cell mineral tests, and urine and stool challenge tests.

Hair analysis: The inch of hair proximal to the scalp reflects the last month of circulating metals in the blood. Metals get into the hair by circulating through the arterial supply of the hair root. Hair binds methyl mercury very well, but less so to metallic mercury or mercury salts. The major disadvantage is that toxic metals not only indicate high levels

of toxins in the body. They also reflect the increased ability of this body to excrete metals. The hair test will not show what was not mobilized [13]. The same is true for hair mineral analysis. High levels of zinc for example in the hair analysis may reflect high plasma levels or high levels of loss. Patients with HPU may be severely depleted of zinc for losses, yet in the early years may have very high levels of zinc in the hair analysis.

Porphyrin testing for HPU: The urine porphyrin test is available from a few diagnostic labs. It is a 24 hour urine collection with an approximately 3 week turn-around time. One gram of ascorbate is added to the urine as a preservative. The urine collection container is wrapped with aluminum foil to avoid the chemical reaction of the HPU compound to light.

There are some additional points about porphyrin testing. Toxic metals and also biotoxins damage many of our metabolic enzymes, including those of the porphyrin synthesis. These enzymes are most sensitive to metal damage and respond with upregulation and increased urinary enzyme excretion. Since the porphyrin related enzymes are intracellular, this test may reflect truly intracellular toxicity. However, since mercury, lead and zinc are compartmentalized, that means, they are present in some body compartments but not in others, it is never clear, if the test results reflect clearing or toxicity of one body compartment, while another is still extremely toxic, not reflected by the test since porphyrins are not equally created in each cell of the body.

The red cell toxic metal test: Erythrocytes actively absorb metals into their interior. The levels may reflect metal levels over the several month lifespan of the red blood cells. However, it is unclear, if red cells damaged by chronic illness or invaded by microbes as in chronic infections can absorb levels of toxic metals equivalent to the average blood level.

Urine challenge test: A complexing or chelating agent is injected or ingested prior to urine collection. 6 or 24 hr urine sample will accurately reflect what this particular agent mobilized via the kidneys, but not via the intestinal tract. Detoxification through the intestinal tract is preferred so reabsorption is avoided. The kidney epithelium can be damaged by pushing too much of a concentration of toxic metals via the kidneys. The gut epithelium is less vulnerable to injury due to its large surface area and the high turnover rate of gastrointestinal epithelial cells.

Stool analysis: This is the only test to reveal effectiveness of hepatic and biliary pathway of excretion of metals. However, it is difficult to interpret, since different areas of stool may contain very different amounts of sequestered metal.

Laboratory testing for biotoxin-producing pathogens and metabolic sequelae

Although there are few direct tests for pathogenic organisms and their associated biotoxins, many tests are available each with their respective shortcomings. Testing can

include yeast and other fungal infections, stool analysis for ova and parasites, bacterial infections including Lyme disease and mycoplasma.

Parasite tests are a deficient area in modern laboratory practice. Many species of worms autolyze and become undetectable 15-20 minutes after defecation. Typically the time from bowel movement to laboratory is several days. The PCR based stool and saliva tests have a notoriously low detection rate. The most reliable test in our practice is the establishment of a reasonable diagnosis, including history (foreign travel, prior seeing of worms in stool, etc.), abdominal palpation and indirect lab markers as elevated eosinophils and macrophages. Improvement following a short medical trial with appropriate medication and dosages can also allow for a presumed diagnosis. The client is instructed to examine every bowel movement for signs of worms, larvae or eggs. We had many patients send their delivered worms to our local laboratories, worms which were clearly still moving at the time of "delivery," only to come back with the diagnosis "taxonomy unavailable", or the lab expressing doubts that the moving creature was really there.

Given the inadequate tools for detecting pathogenic organisms and metal toxins, metabolic tests are useful. Tests altered during neurotoxin exposures are several. Not only can they serve as a "smoking guns" for the presence of neurotoxins, they can also guide nutrient therapy and serve as biomarkers for patient recovery:

The inflammatory markers C4A, TGF beta 1, and matrix metalloproteinases (MMP9) are commonly upregulated in chronic illness. In that case we use anti-inflammatory strategies such as the use of curcumin, ginger and a variety of common medical drugs such as Actos, nonsteroidal anti-inflammatories, cholestyramine, and steroids.

The regulatory neuropeptides melanocyte stimulating hormone (MSH), oxytocin, antidiuretic hormone (ADH), and vasoactive intestinal polypeptide (VIP) can be evaluated and guide treatment. Diabetes insipidus from biotoxin-related reduction of antidiuretic hormone production in the pituitary gland may be underlying the electrolytes and minerals imbalances. The neuropeptide imbalances may also be the basis for the observation that hormonal deficiencies are common, especially progesterone in women and testosterone and growth hormone in men. When MSH is low, sinus and nasal treatments may be beneficial[14]. We also use water that has been imprinted with the physical structure of the neuropeptides in question[15]. This has been very effective and inexpensive to the patient.

The nagalase enzyme is upregulated by the intelligent activity of microbes in the client's system. Nagalase blocks the vitamin D receptors on the cell wall of macrophages, which effectively paralyzes the macrophages and therefore a significant portion of our immune system. An elevated (positive) nagalase enzyme test can be followed by the injection of Gc-MAF (vitamin D_3-binding protein or Gc protein-derived macrophage activating factor) for several months. Initially the client often would observe a cytokine storm or other mild to severe immune reaction, which will be later followed by partial or complete recovery from their respective illness. Several sources of GcMAF are available[16].

Imaging and other diagnostic studies

Many chronically ill patients have narrowed anterior neck veins, restricting the venous return of blood from head and face, this in turn leading to significant hypoperfusion of the central nervous system. Cerebral magnetic resonance venography (MRV) can effectively evaluate for chronic cerebrospinal venous insufficiency. Single photon emission computed tomography (SPECT) and positron emission tomography (PET) imaging can be used to localize brain areas of increased or decreased metabolic activity. Results can inform decisions to either use drugs and nutrients which act for example on the monamine pathways, or to use mechanical means to open stenosed veins via a balloon catheter. For example, a child with autism and language delay with a SPECT that reveals that the frontal lobe has decreased uptake may benefit from low dose L-dopa. A patient with multiple sclerosis-like symptoms, cognitive deficits, and motor dysfunction may be treated with diagnosing and treating stenosed anterior neck veins.

Environment assessment for electrosmog

Microwave radiation from cell phone broadcasting, wireless set ups in homes, alarm systems and the use of the cell phone itself have increasingly been shown to have adverse biological effects that have not been considered as a source of chronic illness and uncontrolled growth of microbes in our system. Microwave exposure can and should be measured in the home and workplace using a handheld device. Electrosensitivity is in part genetically determined, leaving some people more vulnerable than others. Astute practitioners have noticed significant illness causing effects in some of their chronically ill patients. Initial studies in this area drew heavily on comparative biology, with sharks hunting with electromagnetic fields.

Electromagnetic radiation exposure has dramatically increased over the last few years. Electrosmog is likely to act directly on the host through a variety of mechanisms. It has been shown that microwave radiation form cell phones directly impairs intracellular signaling pathways. It is also likely to act indirectly by increasing biotoxin production. Fungi, when stressed by electrosmog employ their own defense mechanisms to a greater extent. This has been demonstrated with fungal organisms which produce more potent mycotoxins when exposed to electrosmog [10].

Therapeutic Trials

To the extent that treatment is an iterative process, diligently recording patients' subjective improvement to short single therapeutic trials can guide future interventions. This has become the most used and most successful strategy in biotoxin medicine.

V. Treatment

Allopathic and biological agents

Opportunistic infections and infestations (i.e. roundworms, strongyloides, streptococcus, staphylococcus, chlostridiae, etc.) are often best treated in the early phase of treatment of the chronic illness with conventional medical drugs such as ivermectin, nitazoxanide, or Praziquantel even though there are a variety of biological options. Parasites respond well to liposomal artemisinin, a wormwood extract and bacterial infections to a plethora of plant substances such as allicin from garlic, curcumin from turmeric, and cilantro for salmonella.

In Lyme disease coinfections can be acquired with the same insect bite as the primary *Borrelia* infection, most commonly *Babesia microti* and *Bartonella henselae*. Others respond well to herbal treatment with Japanese knowtweed, Smilax, freeze dried garlic and others, but also may be treated with conventional antibiotics such as intramuscularpenicillin and oral Mepron.

HPU is effectively managed with a simple commercial mix of minerals and vitamins [17], containing high dosages of pyridoxal 5 phosphate (B6) and zinc. HPU treatment re-arms the immune system which then is more capable of dealing with the chronic infections such as Lyme.

Neurotransmitter imbalances are typically addressed with a cocktail of oral amino acids and diet changes (whey drink, chlorella, and non-dairy natural amino acid sources) but can also be treated conventionally with appropriate psychotropic medication.

Vitamin D3 deficiency disables many aspects of immunity and is addressed with medical doses of D3 (depending on 25-OH cholecalciferol blood levels), until the system has regained normal levels. The often present circadian rhythm disturbance may have to be addressed with high doses of liposomal melatonin or psychotropic medication, but may also respond to propolis tincture. Direct sunlight can raise both vitamin D and melotonin levels.

Heavy metal burden may be addressed initially with medical drugs such as Sodium EDTA, DMSA, DMPS and others but may also respond to biological agents such as curcumin, chlorella, cilantro, and garlic.

There are both biological detoxification protocols as well as pharmaceutical protocols. The most common medical agents used for intravenous therapy are as follows:

A vitamin C drip mobilizes the heavy metals from the matrix and leads to excretion via the stool.

DMPS (oral, i.v., i.m., s.c.) clears the vascular endothelium of the kidney. It often takes weeks before DMPS can “work” again after the initial dosing. It is used mostly used for arsenic, lead, copper and mercury.

Desferal (s.c) is used for iron and aluminum excretion both via the stool and kidney.

Alpha Lipoic acid (usually 600 mg/iv.) is a weak complexing agent for sulfhydryl affinitive metals such as mercury and lead.

Glutahione (i.v., liposomal oral delivery) is a weak complexing agent. Together both a-lipoic and glutathione given at the same time are an excellent tool to eliminate mycotoxins stored or trapped in the liver. The most natural source of the precursor amino acids is goat and cow whey.

Penicillamin (oral) might be the only effective medical detoxification agent working at the intracellular level.

Protein intake

Proteins provide the important precursors to the endogenous metal detox and toxin-shuttle agents, such as coeruloplasmin, metallothioneine, glutathione and others. The branched-chain amino acids in cow and goat whey have valuable independent detoxification effects. The algae chlorella contains 50% aminoacids and peptides, with a profile similar to human breast milk. Chlorella can be a significant dietary source of protein and a vegan-source of vitamin B12 [18, 19].

Adequate minerals

Metals attach themselves in our tissues only in places that are programmed for attachment of metal ions. Mineral deficiency provides the opportunity for toxic metals to attach themselves to vacant binding sites. Repleted minerals including magnesium, selenium, zinc, manganese, germanium, and molybdenum is requisite for all metal detoxification attempts. Substituting minerals can detoxify the body by itself. We have observed, that by giving supplemental zinc the body immediately starts pushing out lead from the storage sites in the bone marrow. Just as important are electrolytes sodium, potassium, calcium, and magnesium which regulate the physiological parameters of the body fluids and help to transport toxic waste across the extracellular space towards the lymphatic and venous vessels and across the filtrating membranes of the kidney.

Improving lipid intake

Lipids made from fatty acids make up 60-80 % of the central nervous system and need to be constantly replenished. Deficiency makes the nervous system vulnerabe to the fat soluble metals, such as metallic mercury constantly escaping as odorless and invisible vapour evaporating from the amalgam fillings. Chlorella is 12% lipid. Its alpha-and gamma-linoleic acid help to balance the increased intake of fish oil during detoxification. Chlorella can normalize serum cholesterol and lipid- composition and levels [20, 21].

Hydration with electrolyte repletion

Without enough fluid intake the kidneys may become contaminated with metals. The basal membranes swell up and the kidneys can no longer efficiently filter toxins[10].

Adding a balanced electrolyte solution in small amounts to water helps to restore intra- and extracellular fluid balance.

The autonomic nervous system in most toxic patients is dysfunctional. Electric messages in the organism are not received, are misunderstood or are misinterpreted. Toxins cannot be shuttled through the extracellular space. Increased intake of natural ocean salt such as celtic sea salt and avoidance of regular table salt has been found to be very effective in resolving some of these problems. Most common is the i.v use of Ringer's Lactate. An oral solution pioneered by the American chemist Ketkovsky is effective and one I recommend to my patients[22]. In patients who are sodium or chloride sensitive, caution must be taken to monitor the blood pressure and dosing of the electrolyte solution may need to be adjusted downward, however, in these patients the detoxification process takes longer and is more difficult.

Dosage: Use 1-3 tbsp in a quart of water and titrate to slightly salty taste. During times of greater stress the dosage can be temporarily increased.

Cilantro (Chinese parsley) in supplemental form

This kitchen herb is capable of mobilizing mercury, cadmium, lead and aluminum in both bones and the central nervous system[23]. It is probably the only effective biological agent in mobilizing mercury stored in the intracellular space which is attached to mitochondria, tubulin, and liposomes, and in the nucleus of the cell where it can potentially reverse the DNA damage of mercury[24]. Because cilantro mobilizes more toxins than it can carry out of the body, it should be used with supplemental *Chlorella*, algae species which are effective binding agents.

Cilantro in an alcohol solution (elixir) can be initiated at an oral dose of 5 drops twice daily taken just before a meal. Gradually the dose may be increased to 15 drops 3 times a day for full benefit. During the initial phase of the detoxification cilantro should be given 1 week on, followed by 2 -3 weeks off.

Cilantro can be incorporated into the diet. The cilantro solution described above can be consumed as a tea, by using 10 to 20 drops in cup of hot water and sipped slowly. Another way of taking cilantro is to rub 5 drops twice a day into ankles for mobilization of metals in all organs, joints and structures below the diaphragm, and into the wrists for organs, joints and structures above the diaphragm. The wrists have dense autonomic innervation which enables axonal uptake, and the wrists are crossed by the main lymphatic channels, allowing for lymphatic uptake.

Chlorella

The algae Chlorella has a long history in the Chinese and Japanese medical literature for cleaning up the body after environmental disasters and offers a sustainable approach with well-studied safety data due to its extensive use. Chlorella is effective at biotoxin uptake, especially in the gastrointestional tract.

Metal binding and elimination is facilitated by *Chlorella* and *Parpachlorella* species, because the polysaccharide, sporopollenin, in the cell wall has unique toxic metal binding properties [23]. Many studies have identified specific metal binding: Cadmium [25-27], uranium [28], lead [29], and mercury and methyl mercury[30, 31].

- *Chlorella* species also facilitate the elimination of neuro- and immunotoxic chemicals [32-36]. Sporopollenin is as effective as cholestyramin in binding neurotoxins and more effective in binding toxic metals then any other natural substance found.
- Along similar lines, *Chlorella* supplementation protects the fetus and newborn from maternal toxin transfer[37].
- There is support in the medical literature for an immune-system strengthening role [38-40] . Consistant with the immune-strengthening properties our personal observation is that *Chlorella* supplementation increases reduced glutathione[10].
- Presumably mediated by the binding of neurotoxins, Chlorella has been shown to delay cognitive decline [41].

Dosing is initiated with 1 gram (4 tablets) 3-4 times a day. This is the standard maintenance dosage for adults for a 6 to 24 month detoxification program. During the more active phase of the detoxification (1 week every 2-4 weeks), whenever cilantro is given, the dose can be increased to 3 grams 3-4 times per day (1 week on, 2-4 weeks back down to the maintenance dosage). Take 30 minutes before the main meals and at bedtime. The timing of 30 minutes before meals is to facilitate Chlorella's presence in the small intestine when bile is released, since bile carries with it toxic metals and other toxic waste. These are bound by the chlorella cell wall and carried out via the digestive tract.

Some people have problems digesting the cell membrane of chlorella. The enzyme cellulase resolves this problem. Cellulase is available in many health food stores in digestive enzyme products. Taking chlorella together with food also helps in some cases, even though it is less effective that way. *C. pyreneidosa* has better absorption of toxins, but is harder to digest. *C. vulgaris* is easier to digest, but with less metal absorbing capability. Some manufacturers have created cell wall free chlorella extracts which are more expensive - but more easily absorbed.

Chlorella growth factor

Chlorella growth factor (CGF) is a heat extract from chlorella that concentrates certain peptides, proteins and other ingredients. CGF has been administered in various settings with salutary effects[42, 43].In our experience, CGF makes the detoxification process easier, shorter and more effective. The recommended dosage is 1 capsule of CGF for each 10-20 tablets of Chlorella.

Garlic (allium sativum)

Garlic has been shown to protect the white and red blood cells from the oxidative damage caused by metals in the blood stream. It also has its own valid detoxification functions.

Garlic contains sulphur components, including the most valuable sulfhydryl groups which oxidize mercury, cadmium and lead and make these metals water soluble. This makes it easy for the organism to excrete these substances. Garlic also contains alliin which is enzymatically transformed into allicin, a potent antimicrobial agent. Metal toxic patients almost always suffer from secondary infections, which are often responsible for part of the symptoms. Garlic also contains bioactive selenium which blocks mercury absorption and mercury's adverse neurologic effects. Industrial selenium products are often less absorbable than garlic and do not seem to reach those body compartments in need for it. Garlic is also protective against heart disease and cancer, as mentioned in the related chapters of this text. The half-life of allicin, after crushing garlic, is less then 14 days. Therefore most commercial garlic products contain little allicin unless they have been freeze-dried.

The dosage is 1-3 capsules freeze dried garlic dissolved and stirred into water after each meal. Start with 1 capsule after the main meal per day, and slowly increase to the higher dosage. Initially the patient may experience bloating or nausea as part of the pathogenic organism response.

Psychologic approaches

In the 1980s amidst the genomics focus on medical research, Bruce Lipton instead focused his research on applying quantum physics to the inner workings of the cell. He theorized how cells, especially through their bilipid membranes, process and transmit information throughout the organism. In so doing he laid the groundwork for several areas of research including the interface between the mind – thoughts, beliefs, memories – and the body's metabolic functioning.

In keeping with the reasoning laid out by Dr. Lipton, we leverage psychologic therapies to facilitate innate detoxification. We use a variety of approaches to resolve past traumata and unresolved conflicts, such as eye movement desensitization and reprocessing (EMDR), mental field therapy, and family constellation work. Chronically ill clients, who have not responded to reasonable prior therapies, may start responding to treatment only after significant progress has been made in the psychological area. A client who never produced significant amounts of toxic metals in the urine after a challenge test, may start pouring out toxic metals in both stool and urine in large quantities after psychological treatment. We therefore conclude, that successful psychological resolution alters the epigenetic controls of the genome, deeply affecting metabolic enzymes (proteome) and their activity (metabolome), resulting in improved recovery and health.

Healing occurs on many levels. Patients with chronic illness may feel they are at an impasse and want to have their treatment options presented to them in a way that allows them to prioritize and better understand their own approach. Figure 3 presents the model of healing we use to guide patients about underlying causes of illness and available treatment options. These options are detailed in Table 2. The model may help arrive at

suggestions for appropriate referrals, prompt patients on paths of self exploration, or broaden a practitioner's approach in a systematic way.

VI. Clinical summary

The human body eliminates biotoxins such as those associated with Lyme disease, Streptococcal infections, foodborne illness, and associated immune reactions through a common detoxification pathway. This series of enzymatic steps is needed to eliminate all environmental toxins such as lead, benzene, mold toxins, food additives and most other neurotoxins. When these pathways are already fully occupied by a silent chronic load of lead, mercury, PBDEs and others, the client's system can not successfully deal with a new, biotoxin producing illness, such as Lyme disease or mold exposures from water damaged buildings. The system is on overload and shuts down. When the toxic burden is large and the elimination pathways are overloaded or constitutionally weak, healing will be impaired on all levels (**Figure 3**). Optimizing epigenetic, metabolic and nutritional support should be an essential part of a biotoxin-centered medical approach to chronic illness.

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Tables

Table 1. Alphabetical listing of nutrients known to be excreted in patients with hemopyrrollactamuria

Depleted nutrient	**Clinical and/or metabolic manifestations**
Biotin	Cognitive processing difficulties such as short term memory loss; Skin aging; Lowered immunity; Impaired detoxification
Chromium	Glycemic instability; Muscle loss
Glutathione	Antioxidant associated with longevity
Manganese	Needed for the antioxidant manganese superoxide dismutase, and when lacking it is associated with inflammation
Molybdenum	Difficulty processing sulfur
Vitamin B6	Difficulty with sleep; Peripheral neuropathies
Zinc	Immune problems, impaired detoxification

Table 2. The five levels of healing as a guide to diagnosis and treatment. Reproduced with permission from the work of Dietrich Klinghardt, M.D., Ph.D.

Figure Legend

Figure 1. Metabolic pathways reflect the interference of neurotoxins in detoxification. Reproduced with permission from Amy Yasko, PhD

Figure 2a-e. Correlation between hemopyrrollactams in urine and nutrient status Reproduced with permission from Dr. Tapan Audhya [7].

Figure 3. The 5 Levels of Healing. In this guide to diagnosis and treatment, the "Emotional Body" is a composite of Levels 1 through 3 and the "Soul" is a composite of Levels 2 through 4. Reproduced with permission from the work of Dietrich Klinghardt, M.D., Ph.D.

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