Management of Chronic Toxin Accumulation

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Introduction

Modern medicine is quite successful in diagnosing and treating acute intoxications as medical emergencies (heavy metal accumulation, drug poisoning, etc.) as well as various sub-acute, symptomatic toxicities (chemicals, drugs, and/or other xenobiotics), but only if laboratory evidence of intoxication is found. In recent years, however, the burden of chronic toxin accumulation has become clearer and more disturbing as the effects of minute doses of toxins over time and effects on subsequent generations become evident.[1,2]

Individual tolerance of or susceptibility to specific toxins may vary. A biological system's tolerance of a toxin is partly genetic and partly acquired on the basis of enzymatic induction and/or inhibitions, the degree of functionality of the target organ, and functional reserve capacity of specific organ systems. The clinical manifestations of biological effects of toxins depend not only on the physical and chemical properties of the toxin itself but also on the duration and route of exposure, the toxin's mechanism of action, and (obviously) on individual susceptibility. Modern laboratories can now test for individual susceptibility.

Chemical compounds, which comprise the bulk of environmental toxins, have spread throughout the world via the ground water, rain, and winds, and are now present even in areas where the chemicals were never used. Bioaccumulation of these compounds causes disease in living beings. In humans, the immune, endocrine, and neurological systems are the most affected.[3]

Xenobiotics and/or individual inability to deal with them seem to be at the root of many modern diseases, including Parkinson's disease, chronic fatigue syndrome, and cancer.[4-6]

Managing chronic toxin accumulation

As is clear from the above, in assessing a patient with toxicity, multiple factors need to be taken into account, including not only the total toxin load but also the individual patient's response. Two patients exposed to the same amount of the same toxin may respond differently. Individual differences are apparent not only in how patients deal with toxins (primarily differences in metabolism or biotransformation) but also in how the toxins are stored and eliminated. Rather than assessing total exposure, therefore, it is more important to assess what each patient is doing with the toxin load. In homotoxicology, this is assessed indirectly on the Disease Evolution Table, where we measure the patient's regulatory ability in terms of disturbance in homeostasis.[7]

Biotransformation or metabolization of toxins

Substances may undergo processes that make them water-soluble and thus more readily excreted, or they may undergo bioinactivation, which reduces the toxicity of the end product. Biotransformation takes place primarily in the liver and the intestinal tract and to a lesser extent in the skin, kidneys, and other organs.

Phase I and II reactions

These have been described elsewhere and will not be discussed in depth here.[8] Suffice it to say that phase I involves oxygenation; in phase II, conjugation adds a water-soluble group to the reactive site formed in phase I. Thus detoxification is not a single process but a number of processes involved in the biotransfomation of xenobiotics. Every step depends on several cofactors such as vitamins and minerals. Because phase I enzymes are mixed-function oxidases, a number of free radicals are formed during the detoxification process, so it is important to provide adequate nutritional and antioxidant support for the patient.

Phase III –
The antiporter system

This system is active primarily in the intestines. Paradoxically, the intestinal mucosa functions both as a barrier and as a filter. As the first point of contact with drugs and food as well as environmental xenobiotics, the mucosa has developed a complex set of defense mechanisms, one of which is the so-called antiporter system. In this process, xenobiotics are actively pumped out of the cell to reduce their intracellular concentrations. This phenomenon was first observed in cancer cells, which actively eliminate chemotherapy agents. Antiporter activity in the intestinal wall seems to be co-regulated with the phase I CYP3A4 enzyme.[9] It is therefore important to use products such as Mucosa compositum to support the intestinal wall during any detoxification and drainage treatment.

Storage and elimination of toxins

Release of toxins from their reservoirs depends on toxicokinetics (toxins are cleared "upstream" first, i.e., out of the blood stream), on whether the reservoir is a rapid or slow exchange system, and on whether the chronobiology of the tissue (e.g., the matrix) is intact.[8] Adipose tissue, a major reservoir of fat-soluble toxins, is a slow exchange system, as is bone. Consequently, obese patients may have a higher toxic load. When one or more factors will affect the release of toxins, drainage should be stimulated long enough to ensure clearance of the tissue in question (see below). A patient's total toxic load thus depends on the exposure and storage on the one hand and on biotransformation and elimination on the other.

Measurement of toxin accumulation and the ability to biotransform toxins

One of the major obstacles facing a physician is how to assess each patient's current toxic load and exposure risk. It is well known in biological medicine that individuals respond differently to the same exposure – a fact that makes the physician's task even more daunting. Since intoxication may produce no symptoms, researchers are now hunting for biomarkers to aid in assessing toxin accumulation and the effect of the toxin on individuals and especially in identifying individuals at risk for the effects of certain exposures.[10]

For practical purposes, testing methods can be divided into four groups:

1. Testing for the presence of toxins
2. Assessing the body's ability to biotransform toxins and to protect itself from their effects
3. Assessing individualized risk
4. Assessing toxicity indirectly, through symptoms

1. Testing for the presence of toxins

In recent years, more sophisticated biomarkers have supplanted the commonly used fat aspiration biopsy. Fat biopsy is an invasive procedure that ultimately provides information only on the accumulation of fat-soluble toxins; it says nothing about how the toxin interacts with and impacts the tissue. Biomarkers of toxin exposure may be either exogenous substances or their metabolites or products of the interaction of the xenobiotics with target molecules or cells within a compartment of the body, e.g., adducts with DNA or red blood cells. Many of the assays are highly sophisticated and beyond the scope of this article, since they are not routinely used in practice but rather for research purposes and epidemiological studies of exposures.[10]

Testing for toxic metals can also be done via hair analysis or urinary testing after provocation with DMSA, as these compounds are largely undetected by normal laboratory analyses. Serum testing, however, may be used for lead, mercury, aluminum, and cadmium.[9]

2. Assessing the body's ability to biotransform toxins and to protect itself from their effects

2.1 Urinary metabolic profile

Biomarkers commonly used in practice include the so-called urinary organic acids. Originally used to detect inborn errors of metabolism, these tests now are a useful tool in the assessment of chronic diseases. Organic profiling can be used not only to detect biomarkers of toxicity but also to assess central energy pathway intermediates, carbohydrate metabolism, specific vitamin deficiency indicators, neurotransmitter metabolism, and the products of the intestinal flora. Where available, it offers a comprehensive way to assess the patient's individual response from a genetic and environmental perspective and indicates which cofactors should be replaced to ensure optimum detoxification.[11]

Direct markers of toxicity include glucarate, a by-product of phase II detoxification. Decreased glucarate indicates reduced overall hepatic function, whereas elevated glucarate indicates enzyme induction. For example, glucarate is elevated in patients exposed to pesticides. Elevated orotate is a sensitive test of both ammonia build-up and arginine

availability. 2-methylhippurate, a metabolite of the common solvent xylene, is used to monitor xylene exposure; pyroglutamate measures glutathione metabolism and sulfate measures sulfatation pathways. When the sulfate-creatinine ratio is low, the sulfur containing phase II pathways need replenishment (glutathione, cysteine, taurine).

2.2 *Challenge testing*

Standard liver and kidney function tests reveal only pathologies, not metabolic integrity. In contrast, challenge tests may measure not merely liver integrity, for example, but the function of all organs involved in metabolizing the substance in question, such as the kidneys and P450 in the skin as well. The most common of these probe tests is the caffeine clearance test, which assesses the integrity of CYP1A2 activity. In this challenge test, a specified amount of caffeine is ingested, after which two or three saliva samples are measured at specific times. Because caffeine is almost completely absorbed in the intestine, its clearance rate reflects the metabolic activity of the P450 enzymes. Other probes are available for specific P450 enzymes, e.g., erythromycin (breath test) to measure CYP3A4 activity.

3. Measuring individual susceptibility

There is increasing interest in the role human genome variations play in modifying the effect of environmental health hazards, rendering some individuals or groups more susceptible to post-exposure development of disease.[12] More than 99 percent of human DNA is identical in all individuals, yet the less than one percent of DNA that differs from person to person ensures that no two humans (other than identical twins) are exactly alike. To create all the cells and tissues in the body, DNA must replicate itself billions and trillions of times, creating numerous opportunities for errors. The most common error is called a single nucleotide polymorphism or SNP (pronounced "snip"), in which a single nucleotide in a gene is changed. SNPs in a gene may increase – or more commonly, decrease – the activity of detoxifying enzymes, either of which can be harmful. For instance, CYP1B1 is responsible for 4-hydroxylation of estrogen and activation of polycyclic aromatic hydrocarbons (which occur, for example, in cigarette smoke, car exhaust, and charbroiled foods). Thus activation of this enzyme produces oxidative stress and 4-hydroxyestrogens, which cause DNA damage in breast tissue. Other SNPs have been associated with lower 2:16-hydroxyestrone ratios and increased risk of breast cancer, especially with concomitant xenobiotics exposure and accumulation.

Test panels for SNPs involved in detoxification are now available through selected laboratories. Genetic testing, once of only theoretical interest for the future, is increasingly becoming part of our quest to individualize patient treatment and to assess risk. Of course this gives new meaning to the famous words of Claude Bernard, who said that the bacterium is nothing, but the terrain is everything! Tests for SNPs related to detoxification enzymes assess the terrain the toxin will encounter, thus the predisposition of the patient to be affected by the toxin.

4. Indirect assessment through symptoms

This method, although the least specific, offers an inexpensive, practical means of following patients with toxicity. Here, the constellation and severity of symptoms play a role, so a simple questionnaire* is administered and then repeated every time the patient comes for a follow-up. In effect, the patient serves as his or her own control from baseline. Movement of symptoms can also be used as a diagnostic predictor, as symptoms tend to move from deeper to more superficial organs and from the deposition phase to the excretion phase as toxins are eliminated and the patient improves.


Detoxification and Drainage Questionnaire

Point count

Never or almost never have the symptom — Points 0
Occasionally have it — 1
Occasionally have it, effect is severe — 2
Frequently have it, effect is not severe — 3
Frequently have it, effect is severe — 4

Emotions — Points
Irritability
Nervousness
Mood swings
Frequent crying
Anger
Anxiety
Fear
Confusion
Depression
Suicidal thoughts
Total Emotions — 0

Skin — Points
Increased sweating, ear wax, oily skin
Dry / rashes
Brown spots on hands and face
Boils
Skin tags, small hanging warts
Acne
Eczema
Hives / allergy
Warts
Total Skin — 0

Ear, Nose and Throat — Points
Hormonal infection
Mouth ulcers
Common cold
Sinusitis
Sore throats
Ear infections
Hay fever
Loss of smell
Croup
Total Ear, Nose and Throat — 0

Mind and Brain — Points
Hyperactivity
Stammering when speaking or word finding problems
Inability to concentrate
Sleep disturbance
Difficulty in making decisions
Headache
Epilepsy / seizures
Dizziness / vertigo
Convulsions / fainting
Severe sleep disturbance
Memory loss
Total Mind and Brain — 0

The detoxification questionnaire is a self-administered test that includes questions about all the major toxicity symptoms.

Practical management of bioaccumulated toxins

After a careful history and a thorough medical examination, the patient should be classified according

** To obtain a copy of the Detox questionnaire, please contact your local Heel distributor.*

to the severity of his or her illness, using either the Disease Evolution Table or a questionnaire. If available, one or more specialized tests may be added. Patients with high toxic loads (either a point count of over 100 on the questionnaire or multiple markers in urinary metabolic testing) and patients with specific health problems (e.g., cancer, obesity, prior drug addiction, flare-ups of inflammatory disease, etc.) constitute a group that needs organotropic, supportive treatment of the organs of detoxification and elimination before drainage is implemented. After six weeks of supportive treatment, the regimen shifts to functiotropic support of tissue drainage (Detox-Kit). Patients with low toxic exposure and mild symptoms such as skin rashes and fatigue may begin immediately with the functiotropic/drainage approach (see Table 1 for summary).

As mentioned above, it is vitally important to allow slow exchange systems to release all accumulated toxins. In patients with high toxic loads, this may take several months. Lymphomyosot is thus added to the regimen for several weeks or months to ensure complete detoxification.

Conclusion

Treatment of chronic toxin accumulation is individualized according to the severity of the intoxication and the patient's regulatory status. Several tools are available to asses these factors, but simple questionnaires seem to be the most practical and inexpensive choice. Advanced organotropic organ support is employed first in severe cases, followed by the functiotropic Detox-Kit for drainage. Use of Lymphomyosot over weeks or months ensures drainage of slow exchange compartments such as adipose tissue.

References:

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	Liver	Urinary tract/ Kidney	Lymph	Gallbladder	Connective tissue
Advanced organ support for six weeks for patients with severe toxicity	Hepar comp.	Solidago comp.		Hepar comp.	Thyreoidea comp.
Alternative products (if above not available)	Hepeel	Reneel			Pulsatilla comp.
Basic detoxification and drainage for 12 weeks	Detox-Kit	Detox-Kit	Detox-Kit	Chelidonium-Homaccord	Detox-Kit
For cellular detoxification, add	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.	Coenzyme comp./ Ubichinon comp.
Note	Cellular detoxification is best added during the advanced organ support phase, although in some cases (e.g., inflammatory skin disease), it is not added until the basic detoxification phase. Continue with Lymphomyosot for 4-6 weeks for patients with mild toxicity and 12 weeks for patients with severe toxicity.				
Dosage	Ampoules: In general, 3-1 times weekly 1 ampoule i.m., s.c., i.d. Drops: In general, 10 drops 3 times daily				

Table 1:
Advanced and basic detox therapy