The Genetic Connection: Why Some Individuals Are More Affected By Toxins than Others

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The human body is exposed to a wide array of xenobiotics in one's lifetime, and complex enzymatic mechanisms are genetically available to detoxify these substances. A variety of mechanisms support or impair the body's natural ability to detoxify and scientific literature suggests an association between impaired detoxification and certain diseases.

Missing or nonfunctioning enzyme systems impair biotransformation systems, consequently increasing the need for lifestyle changes, including the avoidance of certain toxins.

An individual's ability to tolerate toxins depends on how quickly the body can eliminate the toxic burden, and this important biological detoxification mechanism depends on enzyme functions. Certainly, the human body contains multiple enzyme systems involved in the detoxification process, but when one or more important enzymes are missing or are functioning improperly, the body's ability to eliminate the excess burden is affected. Normal detoxification is impaired.

In the United States, case-control studies have reported that an important detoxification enzyme, Glutathion-S-Transferase M1 (GSTM1) is missing in 23%-41% of people of African descent; 32%-53% for those of Asian descent, 40%-53% for those of Hispanic descent, and 35%-62% for those of European descent. Several population studies have reported the deletion polymorphism among U.S. Caucasians as ranging from 48%-57%. Other countries have reported varying frequencies of the deletion polymorphism, and an Iranian study showed that in 31 percent to 38 percent of the population the GSTM1 enzyme was missing. Groups such as Pacific Islanders and Malaysians have a reported frequency of 62%-100%. Other Asian populations have high-reported frequencies of the deletion genotype ranging from 48%-50% for Japanese and 35%-63% for Chinese. A population-based study conducted among Chinese reported a frequency of 51% for the GSTM1 deletion genotype. Two Korean case-control studies found frequencies of 53% and 56% for the GSTM1 deletion genotype.

These statistics demonstrate that missing detoxification enzymes are playing a large role in most populations. Since the genetic make-up is inherited, it would make sense to have patients tested before detoxification programs are initiated. Since a person with an inadequately functioning enzyme system is particularly vulnerable to toxic exposure, lifestyle changes and detoxification programs are important throughout life.

The Detoxification Pathway Phase 1
While much is known about the role of Phase I enzymes in the metabolism of pharmaceuticals as well as their activation by environmental toxins, the role of Phase I detoxification in clinical practice has received less consideration than the Phase II enzyme systems.

Enzymes involved in the Phase I metabolism are Cytochrome P450, and the SOD Enzymes.

The Cytochrome P450, Specifically the CYT 450 1A1
These enzymes are involved in the metabolism of drugs or exogenous toxins such as chemical solvents or drugs, including steroids. The amount of the CYP enzymes present in the liver reflects their importance in the detoxification process.

The Superoxide Dismutase (SOD) Enzymes are present in practically all cells and in extracellular fluids. The SODs are considered free radical scavengers, preventing oxidative damage and thus are considered important to delay the aging process. Genetic polymorphism in SOD enzymes and their altered expressions and activities are associated with oxidative DNA damage and an increased cancer risk. (Khan MA, Tania M, Zhang D, Chen H. Antioxidant enzymes and cancer. Chin J Cancer Res 22(2);87-92. 2010)

SOD enzymes contain metal cofactors which can be copper, zinc, manganese or iron. While all people have an abundance of SOD enzymes, deficiency in any of these metals will lower certain SOD levels and function. In other words, a nutritional deficiency in any of these trace elements potentially impairs SOD enzyme function, leading to a disruption in the detoxification pathway.

Superoxide Dismutase 1 (SOD1)
SOD1 is also called the copper/zinc superoxide dismutase or CuZnSOD. It is present in the cytosol, the nucleus and the mitochondria. Its primary function is to act as an antioxidant enzyme, lowering the steady-state concentration of superoxide. High concentrations are found in liver, brain and testes, but also in red blood cells, pancreas and the lung. Inactivity of an SOD enzyme disturbs the cell metabolism.

A copper or zinc deficiency reduces the function and activity of the SOD1 enzyme.

Superoxide Dismutase 2 (SOD2)
This gene, also called MnSOD, is a member of the iron/manganese superoxide dismutase family. Mutations in this gene have been associated with idiopathic cardiomyopathy, premature aging, (IDC) sporadic motor neuron disease,

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and cancer. (NCBI Report. SOD2 superoxide dismutase 2. upd May 2011)

SOD-gene defects have been associated with diseases such as Amyotrophic lateral sclerosis (ALS) (Banzi et al. SOD1 und amyotrophic lateral sclerosis: mutation and oligomerization. PLoS 3/-/2008. NCBI; Furukawa Y et al. Complete loss of post-translational modifications triggers fibrillar aggregation of SOD1 in familial form of ALS. J. Biol. Chem.283/35/2008)

A reduced Phase I Metabolism reduces the detoxification ability of a variety of xenotoxins including the potentially toxic metals.

It is most important to recognize that Phase 1 enzyme test results are affected by trace element deficiencies. If the deficiency no longer exists, the Phase 1 enzyme system will improve and thus, a Phase 1 enzyme test result can change with treatment.

Phase 2 Enzymes
Phase II reactions follow Phase I reactions. Also known as conjugation reactions (e.g. with gluthation or amino acids or sulfonates), the Phase II system is an important defense mechanism against intake of toxins. If any of the Phase 2 enzymes is missing, it will always be missing. The Gluthation Transferases and N-Acetyltransferase 2 (NAT2) belong to the group of Phase II Enzymes.

A reduced phase II detoxification leads to the accumulation of toxins. Gene variants in the glutathione S-transferases (GST) may lead to poor management of the extremely radical intermediates from the Phase 1 responses and thereby transmit a predisposition for diseases associated with oxidative stress.

The glutathione S-transferases (GSTM1, GSTT1, etc) are one family of enzymes responsible for the detoxification process, particularly mercury and other toxic metal compounds. These enzymes are also known to play a role in the detoxification of polycyclic aromatic hydrocarbons found in tobacco smoke.

Glutathion-S-Transferase M1 (GSTM1)
GSTM1 is produced in the liver. Through conjugation with glutathion, it functions in the detoxification of environmental toxins and products of oxidative stress, electrophilic compounds, including carcinogens and therapeutic drugs. Individuals with the GSTM1 */0 Genotype do not have this functioning enzymes and are at greater risk to develop carcinomas.

Glutathion-S-Transferase T1 (GSTT1)
GSTT1 is found in lymphocytes and the liver, and is involved in the detoxification process of a variety of environmental chemicals, such as the ones used in polymer productions. Like all GST Enzymes, GSTT1 detoxifies cancer-causing chemicals as found in cigarette smoke. Approximately 38% of Kaukasions show a complete lack of GTT1 activity. This group with the GSTT1 */0 Genotype shows a high risk for carcinoma of the lung, breast and larynx.

Glutathion-S-Transferase (GSTP1)
GSTP1 is build in blood lymphozytes and tissues such as prostate, lung, breast and brain. It plays an important role in detoxification by catalyzing the conjugation of many drophobic and electrophilic compounds with reduced glutathion.

About 50% of the caucasion population shows complete loss of function, which aids the accumulation of reactive products and thus increases the risk of cancer and neurological diseases.

N-AcetylTransferase 2 (NAT2)
The NAT2 functions to both activate and deactivate arylamine and hydrazine drugs and carcinogens. Polymorphisms in this gene are responsible for the N-acetylation process in which humans are segregated into rapid, intermediate or slow acetylator phenotypes.

Lack of NAT2 function is associated with higher incidences of cancer and drug toxicity. Rapid acetylators have a higher risk for colorectal cancer. (Osian G., Procopciuc L, Vlad L. Nat2 gene polymorphism and sporadic colorectal cancer. Prevalence, tumor stage and prognosis. J. Gastrointestin Liver Dis. 2006; 15(4):357-53)

Summary: Why Genetic Testing
- When we know genetic 'disabilities', we are in a better position to prevent toxic overexposure.
- Since we have numerous enzyme systems involved in the detoxification process, we can strengthen our detoxification ability by supporting and strengthening other enzyme systems.
- Zinc and manganese deficiencies are not uncommon. Blood or hair analyses are an option. While blood tests reveal acute and immediate deficiencies, hair detects if the body has been chronically undersupplied. If test results indicate a need for supplementation, it would be logical to supplement for a few weeks before SOD testing is repeated.
- Even in the presence of metabolic or digestive disorders, sufficient nutrients are absorbed to restore SOD enzyme function to near normal.
- Phase 2 Enzymes are either present or not. When we know that Phase 2 Enzyme systems are missing or non-functional, we need to support the body's detoxification potential.

How To Test?
Genetic testing for detoxification enzymes is simple and inexpensive. The material needed for testing is 1ml of whole blood drawn into an EDTA tube, or 10 drops of whole blood on filter paper as used for newborn genetic tests. Test kits are available on request.

For more information: www.microtraceminerals.com
Excerpt from Blaurock-Busch: Autism & the Genetic Connection Booklet 1: Beat Autism Now - Logically, Effectively and Inexpensively.

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