Susceptibility Factors in Mercury Toxicity:
Immune Reactivity, Detoxification System Function, Enzymatic Blockages, Synergistic Exposures

B. Windham (Ed.)

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It is well documented in the medical literature that the major factors in mercury toxicity effects, in addition to dose, are susceptibility factors like immune reactivity (1, 2), degree of other toxic exposures and *synergisms*[1] (3, 15, 27), systemic detoxification ability based on blood allele type (4, 15, 27) or metallothionein function (5), sulfur detoxification deficiencies (6), or other inhibited enzymatic processes related to detoxification (7-10, 27) or methylation (27, 28). It has been shown that such susceptibility factors can play a larger role in effects than dose among a population with significant exposure to mercury and at extremely low levels of exposure. Toxic metals such as aluminum and lead have been documented to have *synergistic*[2] effects with mercury, increasing mercury effects significantly. Aluminum has its own toxic effects plus increasing mercury effects by depleting glutathione.

Inherited defects or differences in the body's ability to detoxify can contribute to heavy metal accumulation (27, 4, 11, 15, etc.). Deficiencies of certain minerals, vitamins, and amino acids reduce the body's ability to excrete toxins following exposure (27). Those with the genetic allele ApoE4 protein in the blood have been found to detoxify metals poorly and to be much more genetically susceptible to chronic neurological conditions than those with types ApoE2 or E3 (4, 11, 15). Researchers have shown that genetic carriers of the brain protein APO E2 are protected against Alzheimer's disease (AD) whereas genetic carriers of the APO E4 genotype are at enhanced risk factor for developing AD and other degenerative neurological conditions. APO E proteins are synthesized in the brain with the assigned physiological task of carrying waste material from the brain to the cerebrospinal fluid, across the blood brain barrier into the plasma where the material is cleared by the liver. The biochemical difference between APO E2 and APO E4 is that APO E2 has two additional thiol groups, capable of binding and removing mercury (and ethyl mercury) that APO E4 does not have. The second highest concentration of APO E proteins is in the cerebrospinal fluid. Therefore, the protective effects of APO E2 is due to its ability to protect the brain from exposure to oxidants like mercury and ethyl mercury by binding these toxicants in the cerebrospinal fluid and keeping them from entering the brain.

Another study found that polymorphisms in glutamyl-cysteine ligase and glutathione S-tranferases genes modify mercury retention in humans exposed to elemental mercury vapor. Genotypes with decreased GSH availability for mercury conjugation affect the metabolism of inorganic mercury, increasing mercury retention (26). Similarly, many people lack a Metallothionene related glutathione-S-Transferase gene called GSTM1 or have a related polymorphism that appears to be key for proper

[1] **Internet:** "http://www.flcv.com/synergis.html".
[2] **Internet:** "http://www.flcv.com/synergis.html".

functioning of the body's own natural detoxification mechanisms. This may explain at least in part why some people develop the chronic health problems linked to heavy metals while others who are similarly exposed do not. (31)

Recent studies found that *prenatal mercury exposures*[3] from mother's amalgams and other sources along with susceptibility factors such as ability to excrete mercury appear to be major factors in those with chronic neurological conditions like autism and ADHD (11, 15, 20, 27). Infants whose mothers received prenatal Rho D immunoglobulin injections containing mercury thimerosal for RH factor or whose mother's had high levels of amalgam fillings had a much higher incidence of autism. While the hair test levels of mercury of infants without chronic health conditions like autism were positively correlated with the number of the mother's amalgam fillings, vaccination thimerosal exposure, and mercury from fish, the hair test levels of those with chronic neurological conditions such as autism were much lower than the levels of controls and those with the most severe effects had the lowest hair test levels, even though they had high body mercury levels. This is consistent with past experience of those treating children with autism and other chronic neurological conditions (12). Exposure to toxics such as mercury have been found to inhibit enzymes needed to digest wheat gluten and milk casein, resulting in symptoms of *autism, ADHD, diabetes*[4], etc. after chronic exposure to gluten or casein. These conditions commonly significantly improve after avoidance of gluten and casein. Some cases of *hypothyroidism*[5] are driven by immune reactions to gluten in celiac disease (27) Genetic or toxic exposure related impairments in methylation function, detoxification, clearance of catecholamines, or in the clearance of adrenalin may contribute to symptoms in autism or ADD/ADHD for those subjected to stress or inadequate nutrition to overcome impairments (27). Prenatal and neonatal toxic exposures also can cause leaky gut in infants; 'Leaky gut' in autism can promote toxic burden in the body, as well as the development of food allergies (27) which have been found to often be *factors in autism symptoms*[6].

Studies[7] have documented that prenatal mercury exposure causes lasting effects that causes increased susceptibility to future toxic exposures. The effects of chronic, low-dose fetal and lactational organic (MeHgCl) and inorganic (HgCl2) mercury intoxication on *epilepsy/seizures*[8] were investigated and compared in rats and were found to have significant correlations between seizure susceptibility and cortical mercury level (16) Inorganic mercury exposure facilitated the duration of seizure discharges in younger animals and appeared to be more permanent than methyl mercury exposure. Another researcher had similar findings for infants (17). A study of children of mothers consuming a marine diet which exposes them to mercury, found that there are significant cardiovascular effects as birth mercury blood level increases from 1 microgram per liter to 10 μg/L (a), as well as effects on ability to respond to sensory stimuli in exposed children later in life (18). Children with lower birth weights experienced blood pressure increases about 50% higher than normal birth weight children having similar mercury levels. At seven years of age, clear dose-response relationships were observed for deficits in attention, language, and memory (b). Thus a levels of exposure below current Government health safety limits, mercury is documented to have significant cardiovascular effects and the recommended limit for mercury has been decreased from the former limit of 10 μg/L in blood.

Large studies of U.S. dentists and dental assistants have found that mercury level in urine is significantly associated with neurological dysfunction using several different measures, but that among

[3]**Informativo:** "Infertility, Birth Defects, and Fetal Developmental Effects Related to Mercury from Amalgam Dental Fillings & Other Toxins".

[4]**Internet:** "http://www.flcv.com/autismgc.html".

[5]**Internet:** "http://www.flcv.com/ASDendo.html".

[6]**Informativo:** "Neurological and Immune Reactive Conditions Affecting Kids: The mercury connection to neurological pervasive developmental disorders (**autism, schizophrenia, dyslexia, ADD, childhood depression, learning disabilities, OCD, etc.**) and developmental immune conditions (**eczema, asthma, and allergies**)".

[7]**Informativo:** "Infertility, Birth Defects, and Fetal Developmental Effects Related to Mercury from Amalgam Dental Fillings & Other Toxins".

[8]**Informativo:** "Epilepsy/Seizures".

a population with low level mercury exposure those with a polymorphism in blood heme (CPOX4) or to a polymorphism in neurofactor (BDNF) or to a functional single nucleotide polymorphism (Val158Met) in the gene encoding the catecholamine catabolic enzyme catechol O-methyltransferase (COMT) were more susceptible to neurological effects or deficits (19). An association in a population with low level mercury exposure between such polymorphisms and mood disorders was found only for female dental assistants. The associations between a polymorphism of the serotonin transporter gene (5-HTTLPR), dental mercury exposure, and self-reported symptoms were evaluated among 157 male dentists and 84 female dental assistants. The findings suggest that within this restricted population of mercury exposed workers, increased symptoms of depression, anxiety, and memory are associated with the 5-HTTLPR polymorphism among both males and females (19d).

Inherited impairments in methylation or toxic related inhibition of functional methylation by toxics such as mercury can have a dramatic effect on mood regulation and *depression*[9] (27, 28). Genetic related or toxic exposure related hormone imbalances are documented to make people more susceptible to *depression and anxiety disorders*[10] (27). Many patients with depression suffer from thyroid hormone imbalances that may make them more treatment-resistant, or imbalances of DHEA or cortisol (27), which can be related to genetic susceptibility or *toxic exposures to toxics such as mercury.*[11] Thyroid imbalances can strain the adrenal glands; or adrenal imbalances can also disrupt normal thyroid function; either making an individual more susceptible to *depression or anxiety disorders*[12] (27).

Malabsorption in genetically or *toxic related celiac disease*[13] can interfere with mood regulating neurotransmitters and nutrients such as vitamin B12 (27).

Inherited defects in detoxification of environmental chemicals (as previously documented) may promote toxicity and *fatigue in CFS*[14], and inherited tendencies toward inflammation and methylation defects can exacerbate the chronic pain of fibromyalgia (27). Exposures to heavy metal toxins can impair energy production and further burden the detoxification system. Stress can over time cause hormonal imbalances and deficiencies and leaky gut and malabsorption of essential nutrients either genetic or related to toxic exposures can result in inability to detoxify harmful substances and waste products (27), enabling chronic conditions.

Chronic exposure to toxic substances such as mercury can facilitate overgrowths of pathogenic bacteria, viruses, and yeast (27), leading to chronic conditions. *Thyroid imbalances*[15] related to genetic susceptibility or toxic exposures can strain the adrenal glands; or adrenal imbalances in similar regards can disrupt normal thyroid function (27).

Genetic factors or toxic exposures that weaken the *immune system*[16] can result in increased susceptibility to allergies and biological pathogens.

Inherited impairments in detoxification function can also interact with environmental factors to promote multiple chemical sensitivity (*MCS*[17]) (27). Defects in the body's ability to neutralize environmental chemicals lead directly to the accumulation of toxins, and the body's ability to neutralize and excrete environmental toxins depends on the availability of key nutrients (27). Some cases of

[9]**Informativo:** "Depression and other Neurotransmitter Related Conditions - The Mercury Connection".
[10]**Informativo:** "Depression and other Neurotransmitter Related Conditions - The Mercury Connection".
[11]**Internet:** "http://www.flcv.com/endohg.html".
[12]**Informativo:** "Depression and other Neurotransmitter Related Conditions - The Mercury Connection".
[13]**Internet:** "http://www.flcv.com/inflamhg.html".
[14]**Informativo:** "Chronic Fatigue Syndrome, Fibromyalgia, Scleroderma, Lupus, Rheumatoid Arthritis, MCS: The Mercury Connection".
[15]**Internet:** "http://www.flcv.com/endohg.html".
[16]**Informativo:** "Immune Reactive Conditions: The Mercury Connection to Eczema, Psoriasis, Lupus, Asthma, Scleroderma, Rheumatoid Arthritis, and Allergies".
[17]**Informativo:** "Chronic Fatigue Syndrome, Fibromyalgia, Scleroderma, Lupus, Rheumatoid Arthritis, MCS: The Mercury Connection".

MCS may be secondary to *'leaky gut'*[18] and the passage of toxins or food particles into the system. *Arthritis*[19] is an inflammatory condition also often secondary to 'leaky gut', which can be caused by toxic exposures, and to the related passage of toxins or undigested food particles into the system (27). Individuals with asthma often have an inherited predisposition to produce excessive inflammatory mediators (27) or *increased inflammatory cytokines*[20] related to either *prenatal*[21] or later toxic exposures to toxics such as mercury.

Inherited defects in methylation or control of inflammation in the body or *similar toxic related effects*[22] can influence the course of heart disease (27)

Inherited risks associated with cardiovascular disease, obesity, or estrogen metabolism may exacerbate Metabolic Syndrome, for which *toxic exposures are also significant factors*[23]. Metabolic Syndrome *increases cardiovascular risk*[24] by promoting hyperlipidemia, clot formation, inflammation, and hypertension. Imbalances or deficiencies in key nutrients can exacerbate metabolic imbalances in Metabolic Syndrome and prevent healing (27). High insulin levels in Metabolic Syndrome contribute to oxidative stress by unstable free radicals in the body (27). As men age, declining testosterone may trigger metabolic imbalances that promote insulin resistance with significant differences depending on genetic factors and *cumulative toxic exposures*[25].

Although a study of mercury in children showed that females given the same exposure as males excrete more mercury (30) and males are more likely to have autism, another study found that females are two to three times more likely to develop local (e.g., lichenoid contact stomatitis) or systemic adverse health outcomes (e.g., skin disorders) compared with males from prolonged exposure to mercury vapor from dental amalgams (29). Moreover, given that inorganic mercury [Hg2+] binds mainly to thiol ligands [-SH] as homocysteine (Bridges and Zalups 2004), the authors suggest that future clinical trials addressing the role of sex in mercury excretion should include an evaluation of serum homocysteine, which is higher in males than in females and might account for an increased tissue retention of mercury (29b). Toxic exposures can facilitate dysbiosis (digestive problems) related to *leaky gut*[26], chronic maldigestion, exposure to gut pathogens, and/or suppression of protective microorganisms by toxic exposures (27). Chronic imbalances in the intestinal flora can irritate the mucosa due to poor diet or toxic exposures, allow the passage of toxins into the system, weaken the immune system, etc (27). Many of the same underlying environmental factors promoting dysbiosis in the colon can encourage bacterial overgrowth in the delicate small bowel. Parasite infestation occurs more easily with dysbiosis and deficiencies of protective bacteria (27). 'Leaky gut' from intestinal irritants can allow bacterial toxins to enter the system and promote skin inflammation such as *eczema*[27] (27). Identifying high levels of various *gluten-associated*[28] antibodies is an important first step in the diagnosis and correction of either genetic or toxic related *celiac disease*[29] (27).

Programmed cell death (apoptosis) is documented to be a major factor in degenerative neurological conditions like ALS, Alzheimer's, MS, Parkinson's, etc. Some of the factors documented to be involved in apoptosis of neurons and immune cells include mitochondrial membrane dysfunction

[18]**Internet:** "http://www.flcv.com/leakyghg.html".
[19]**Internet:** "http://www.flcv.com/inflamhg.html".
[20]**Internet:** "http://www.flcv.com/inflamhg.html".
[21]**Informativo:** "Neurological and Immune Reactive Conditions Affecting Kids: The mercury connection to neurological pervasive developmental disorders (**autism, schizophrenia, dyslexia, ADD, childhood depression, learning disabilities, OCD, etc.**) and developmental immune conditions (**eczema, asthma, and allergies**)".
[22]**Informativo:** "Documentation of Common Cardiovascular Health Effects from Mercury from Amalgam".
[23]**Internet:** "http://www.flcv.com/endohg.html".
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(22bc, 24). Mitochondrial DNA mutations or dysfunction is fairly common, found in at least 1 in every 200 people (23), and toxicity effects affect this population more than those with less susceptibility to mitochondrial dysfunction. Mercury depletion of GSH and damage to cellular mitochrondria and the increased lipid peroxidation in protein and DNA oxidation in the brain appear to be a major factor in conditions such as autism, Parkinson's disease, etc. (21-25).

The mechanisms by which low level chronic mercury exposure causes over *30 chronic health conditions*[30] such as those looked at in this review are well documented in the literature and differences in susceptibilities are documented in all of these; and the fact that those treated for mercury toxicity *usually recover after treatment*[31] is also well documented by many dozens of medical studies in the literature and thousands of clinical cases (13). Some of the autoimmune conditions commonly caused by immune reactivity to mercury include chronic fatigue syndrome (*CFS*[32]), *fibromyalgia*[33], *lupus*[34], rheumatoid arthritis, *Parkinson's*[35], multiple sclerosis (*MS*[36]), amyotropic lateral sclerosis (*ALS*[37]), *depression*[38], *autism*[39], *ADHD*[40], *eczema*[41], *asthma*[42], etc. (14, 1, 2, hyperlinks). People are documented to vary significantly in immune reactivity to toxic substances and susceptibility to these conditions (see hyperlinks).

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note: underlined or shaded statements have hyperlinks to additional documentation that can be reached by clicking on the link.