# Amyotrophic Lateral Sclerosis (ALS): Lou Gerhig's Disease

## The Mercury Connection

Bernie Windham (Ed.)

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Amyotrophic Lateral Sclerosis (ALS): Lou Gerhig's Disease - The Mercury Connection.

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## 1.1 Introduction

ALS is a systemic motor neuron disease that affects the corticospinal and corticobulbar tracts, ventral horn motor neurons, and motor cranial nerve nuclei (405). Approximately 10 percent of ALS cases are of the familial type that has been linked to a mutation of the copper/zinc super oxide dismustase gene (Cu/Zn SOD). The majority of ALS cases are of the sporadic type. Based on studies of groups of monozygous twins, animal studies, and ALS patient case studies, the majority of ALS cases do not appear to be genetic but rather have primarily environmental related causes often affecting genetically susceptible individuals (405, 416, 423, 471, 520, 93, 94, 97, 200, 303, 580, 35, etc.).

ALS is not a unique disease with a single cause or factor, but instead is a result of damage to motorneurons and the support system that they depend on by a variety of factors. Spinal and bulbar-onset subtypes of the disease appear to be biochemically different and have differences in mechanisms of causality (416f). Some of the mechanisms of neural damage found in ALS include increased free radical generation/oxidative damage, impaired electron transport, disrupted calcium channel function, reactive astrogliosis and dysfunctional transporters for L-glutamate, neurotoxicity, oxidative damage to mitochondrial DNA/ inhibition of the mitochondrial respiratory chain, autoimmunity, and generalized disruption of metabolism of neuroexciotoxic amino acids like glutamate, aspartate, NAAG. The mechanisms by which exposure to mercury and other neurotoxic substances cause all of this will be documented.

The main factors determining whether chronic conditions are induced by metals appear to be exposure and genetic *susceptibility*[1], which determines individuals immune sensitivity and ability to excrete and detoxify metals (405, 342, 60, 181, 303, 314, 330, 464). Very low levels of exposure have been found to seriously affect relatively large groups of individuals who are immune sensitive to toxic metals, or have an inability to detoxify metals due to such as deficient sulfoxidation or metallothionein function or other inhibited enzymatic processes related to detoxification or excretion of metals. Those with the genetic allele ApoE4 protein in the blood have been found to detox metals

[1] **Informativo:** "Susceptibility Factors in Mercury Toxicity: Immune Reactivity, Detoxification System Function, Enzymatic Blockages, Synergistic Exposures".

poorly and to be much more susceptible to chronic neurological conditions than those with types ApoE2 or E3 (437, 577). There are also other similar factors.

Some of the toxic exposures which have been found to be a factor in ALS like symptoms other than mercury include lead (94a), pyretherins (93), agricultural chemicals (94b), Lyme disease (471, 580), monosodium glutamate (MSG, 580), *failed root canaled teeth*[2] (35, 200, 437), post-poliomyelitis (580), and smoking (94cd). All have been demonstrated to cause some of the mechanisms of damage listed above seen in ALS and since such exposures are common as is exposure to mercury, such exposures appear to synergistically cause the types of damage seen in ALS. This paper will demonstrate that mercury is the most common of toxic substances which are documented to accumulate through chronic exposure in the neurons affected by ALS and which have been documented to cause all of the conditions and symptoms seen in ALS. It will also be noted that chronic infections such as mycoplasma, echo-7 enterovirus, and candida albicans also usually affect those with chronic immune deficiencies such as ALS patients and need to be dealt with in treatment. Some studies have also found persons with chronic exposure to electromagnetic fields (*EMF*[3]) to have higher levels of mercury exposure and excretion (28) and higher likelihood of getting chronic conditions like ALS (526).

## 1.2 Documentation of High Common Exposures and Accumulation of Mercury in Motor Neurons

Amalgam dental fillings are the *largest source*[4] of mercury in most people with daily exposures documented to commonly be above government health guidelines (49, 79, 183, 506, 599, 600). This is due to continuous vaporization of mercury from amalgam in the mouth, along with galvanic currents from mixed metals in the mouth that deposit the mercury in the gums and oral cavity (600). Mercury has been found in autopsy studies to accumulate in the brain of those with chronic exposures, and levels are directly proportional to the number of amalgam filling surfaces (85, 270). Due to the high daily mercury exposure and excretion into home and business sewers of those with amalgam, dental amalgam is also the *largest source of the high levels of mercury found in all sewers and sewer sludge*[5], and thus according to government studies a significant source of mercury in rivers, lakes, bays, fish, and crops (603). People also get significant exposure from vaccinations, fish, and dental office vapor (600).

When amalgam was placed into teeth of monkeys and rats, within one year mercury was found to have accumulated in the brain, trigeminal ganglia, spinal ganglia, kidneys, liver, lungs, hormone glands, and lymph glands (20). People also commonly get exposures to mercury and other toxic metals such as lead, arsenic, nickel, and aluminum from food, water, and other sources (601). All of these are highly neurotoxic and are documented to cause neurological damage which can result in chronic neurological conditions over time.

Mercury has been found to accumulate preferentially in the primary motor function related areas involved in ALS- such as the brain stem, cerebellum, rhombencephalon, dorsal root ganglia, and anterior horn motor neurons, which enervate the skeletal muscles (20, 291, 327, 329, 442, 48).

Mercury, with exposure either to vapor or organic mercury tends to accumulate in the glial cells in a similar pattern, and the pattern of deposition is the same as that seen from morphological changes (327g, 287, 305). Though mercury vapor and organic mercury readily cross the blood-brain barrier, mercury has been found to be taken up into neurons of the brain and CNS without having to cross the blood-brain barrier, since mercury has been found to be taken up and transported along nerve axons as well through calcium and sodium channels and along the olfactory path (329,

[2]**Internet:** "http://www.flcv.com/RChealth.html".
[3]**Internet:** "http://www.flcv.com/emfeff.html".
[4]**Informativo:** "Dental Amalgam Mercury Solutions".
[5]**Internet:** "http://www.flcv.com/damspr2f.html".

288, 333, 34). Exposure to inorganic mercury has significant effects on blood parameters and liver function. Studies have found that in a dose dependent manner, mercury exposure causes reductions in oxygen consumption and availability, perfusion flow, biliary secretion, hepatic ATP concentration, and cytochrome P450 liver content (260), while increasing blood hemolysis products and tissue calcium content and inducing heme oxygenase, porphyria, platelet aggregation through interfering with the sodium pump.

## 1.3 Effects of Exposure to Mercury and Toxic Metals

A direct mechanism involving mercury's inhibition of cellular enzymatic processes by binding with the hydroxyl radical (SH) in amino acids appears to be a major part of the connection to allergic/immune reactive/ conditions such as eczema, psoriasis, rheumatoid arthritis, Lupus, Scleroderma, allergies, autism, schizophrenia, (114c, 181, 303, 330, 331, 411, 412, 152b, 439, 602, 601), as well as to autoimmune conditions such as ALS, *Alzheimer's*[6] (AD), *Chronic Fatigue*[7] (CFS), *Fibromyalgia*[8] (FM), etc. (405, 342, 60, 181, 303, 314b, 513, 580, etc.). For example mercury has been found to strongly inhibit the activity of dipeptyl peptidase (DPP IV) which is required in the digestion of the milk protein casein (411, 412) as well as of xanthine oxidase (439) Additional cellular level enzymatic effects of mercury's binding with proteins include blockage of sulfur oxidation processes (33, 114c, 194, 330, 331, 412), enzymatic processes involving vitamins B6 (417) and B12 (418), effects on the cytochrome-C energy processes (43, 84, 232, 338c, 35), along with mercury's adverse effects on cellular mineral levels of calcium, magnesium, copper, zinc, and lithium (43b, 96, 198, 333, 338, 386, 427, 430, 432, 461, 489, 507). And along with these blockages of cellular enzymatic processes, mercury has been found to cause additional neurological and immune system effects in many by causing immune/ autoimmune reactions (60, 152c, 181, 288c, 314, 342, 405, 513). Recent studies gives a comprehensive review of studies finding a connection between ALS, toxic metals, and autoimmunity (405, 580). Studies have found the presence of antibiodies in ALS patients that interact with motor neurons, inhibiting the sprouting of axons. Immune complexes have also been found in the spinal cords of ALS patients (580). T cells, activated microglia, and IgG within the spinal cord may be a primary event that leads to lesions and tissue destruction.

Oxidative stress and reactive oxygen species (ROS) have been implicated as major factors in neurological disorders including ALS, motor neuron disease (MND), CFS, FM, Parkinson's (PD), Multiple Sclerosis (MS), and Alzheimer's (AD) (13, 43, 56, 84, 145, 169, 207b, 424, 442-444, 453, 462, 496, 577). Mercury forms conjugates with thiol compounds such as glutathione and cysteine and causes depletion of glutathione (56), which is necessary to mitigate reactive damage. One study found that insertion of amalgam fillings or nickel dental materials causes a suppression of the number of T-lymphocytes (270), and impairs the T-4/T-8 ratio. Low T4/T8 ratio has been found to be a factor in autoimmune conditions. Mercury induced lipid peroxidation has been found to be a major factor in mercury's neurotoxicity, along with leading to decreased levels of glutathione peroxidation and superoxide dismustase (SOD) (13, 254, 490, 494-496). Only a few micrograms of mercury severely disturb cellular function and inhibits nerve growth (305, 147, 175, 226, 255). Metalloprotein (MT) have a major role in regulation of cellular copper and zinc metabolism, metals transport and detoxification, free radical scavenging, and protection against inflammation (114, 442, 464, 602). Mercury inhibits sulfur ligands in MT and in the case of intestinal cell membranes inactivates MT that normally bind cuprous ions (477, 114), thus allowing buildup of copper to toxic levels in many and malfunction of the Zn/Cu SOD function (495, 13a, 443). Mercury also causes displacement of

[6]**Informativo:** "Alzheimer's Disease and Other Autoimmune Degenerative Conditions: the Mercury Connection".

[7]**Informativo:** "Chronic Fatigue Syndrome, Fibromyalgia, Scleroderma, Lupus, Rheumatoid Arthritis, MCS: The Mercury Connection".

[8]**Informativo:** "Chronic Fatigue Syndrome, Fibromyalgia, Scleroderma, Lupus, Rheumatoid Arthritis, MCS: The Mercury Connection".

zinc in MT and SOD, which has been shown to be a factor in neurotoxicity and neuronal diseases (405, 495, 517). Exposure to mercury results in changes in metalloprotein compounds that have genetic effects, having both structural and catalytic effects on gene expression (114, 241, 296, 442, 464, 477, 495, 517). Some of the processes affected by such MT control of genes include cellular respiration, metabolism, enzymatic processes, metal-specific homeostasis, and adrenal stress response systems. Significant physiological changes occur when metal ion concentrations exceed threshold levels. Such MT formation also appears to have a relation to autoimmune reactions in significant numbers of people (114, 60, 342, 369, 442, 464). Of a population of over 3000 tested by the immune lymphocyte reactivity test (MELISA, 60, 342), 22% tested positive for inorganic mercury and 8% for methyl mercury, but much higher percentages tested positive among autoimmune condition patients. In the MELISA laboratory, 12 out of 13 ALS patients tested showed positive immune reactivity lymphocyte responses to metals in vitro [60c], indicating metals reactivity a likely major factor in their condition. A recent study assessed the possible causes of high ALS rates in Guam and similar areas and the recent decline in this condition. One of the studies conclusions was that a likely major factor for the high ALS rates in Guam and similar areas in the past was chronic dietary deficiency since reduced Ca, Mg and Zn induced excessive absorption of divalent metal cations such as mercury which accelerates oxidant-mediated neuronal degenerations in a genetically susceptible population (466). The Veterans Administration concluded that higher levels of veterans of Gulf War I than normal contracted ALS (580). These veterans were subjected to large exposures of toxic metals in vaccines and other toxic exposures and there is evidence that aluminum hydroxide in vaccines can cause symptoms seen in ALS (582).

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 inducement of the inflammatory cytokine Tumor Necrosis Factor-alpha (TNFa) (126), reactive oxygen species and oxidative stress (13, 43a, 56a, 296b, 495), reduced glutathione levels (56, 126a, 111a), liver enzyme effects and inhibition of protein kinase C and cytochrome P450 (43, 84, 260), nitric oxide and peroxynitrite toxicity (43a, 521, 524), excitotoxicity and lipid peroxidation (490, 496), excess free cysteine levels (56d, 111a, 33, 330), excess glutamate toxicity (416, 13b), excess dopamine toxicity (56d, 13a), beta-amyloid generation (462, 56a), increased calcium influx toxicity (296b, 333, 416, 432, 462c, 507) and DNA fragmentation (296, 42, 114, 142) and mitochondrial membrane dysfunction (56de, 416).

Chronic neurological conditions such as ALS appear to be primarily caused by chronic or acute brain inflammation. The brain is very sensitive to inflammation. Disturbances in metabolic networks: e.g., immuno-inflammatory processes, insulin-glucose homeostasis, adipokine synthesis and secretion, intra-cellular signaling cascades, and mitochondrial respiration have been shown to be major factors in chronic neurological conditions (592, 593, 598, 580, etc.). Inflammatory chemicals such as mercury, aluminum, and other toxic metals as well as other excitotoxins including MSG and aspartame cause high levels of free radicals, lipid peroxidation, inflammatory cytokines, and oxidative stress in the brain and cardiovascular systems (13, 582, 595-598, etc.)

In amyotrophic lateral sclerosis (ALS) non-neuronal cells play key roles in disease etiology and loss of motoneurons via noncell-autonomous mechanisms. Reactive astrogliosis and dysfunctional transporters for L-glutamate are common hallmarks of ALS pathology (416d). Oxidative and excitotoxic insults exert differential effects on spinal motoneurons and astrocytic glutamate transporters in the progression of ALS. Excitotoxicity in ALS affects both motor neurons and astrocytes, favouring their local interactive degeneration. Mercury and other toxic metals inhibit astrocyte function in the brain and CNS (119), causing increased glutamate and calcium related neurotoxicity (119, 333, 416, 496). Mercury and increased glutamate in the plasma activate free radical forming processes like xanthine oxidase which produce oxygen radicals and oxidative neurological damage (142, 416, 13). Nitric oxide related toxicty caused by peroxynitrite formed by the reaction of NO with superoxide anions, which results in nitration of tyrosine residues in neurofilaments and manganese

Superoxide Dimustase (SOD) has been found to cause inhibition of the mitochondrial respiratory chain, inhibition of the glutamate transporter, and glutamate-induced neurotoxicity involved in ALS (524, 521). A recent study has linked some cases of sporadic ALS with the failure to edit key residues in ionotropic glutamate receptors, resulting in excessive influx of calcium ions into motor neurones which in turn triggers cell death. The study suggests that edited AMPA glutamate (GluR2) receptor subunits serve as gatekeepers for motor neurone survival. (525)

These inflammatory processes damage cell structures including DNA, mitochondria, and cell membranes. They also activate microglia cells in the brain, which control brain inflammation and immunity. Once activated, the microglia secrete large amounts of neurotoxic substances such as glutamate, an excitotoxin, which adds to inflammation and stimulates the area of the brain associated with anxiety (598). Inflammation also disrupts brain neurotransmitters resulting in reduced levels of serotonin, dopamine, and norepinephrine. Some of the main causes of such disturbances that have been documented include vaccines, mercury, aluminum, other toxic metals, MSG, aspartame, etc. (582, 593, 598, 600, etc.) High levels of aluminum exposure along with low levels of other minerals such as calcium and magnesium have been documented to cause neurological degeneration and appear to be the cause of high ALS and Parkinson's in the past in Guam (518). There is evidence that aluminum hydroxide in vaccines can cause symptoms such as those seen in ALS (582). Aluminum has been found to be a factor in some *Alzheimer's*[9] and *Parkinson's*[10] cases.

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 (56bc, 416). Mitochondrial DNA mutations or dysfunction is fairly common, found in at least 1 in every 200 people (275), 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 ALS, Parkinson's disease, autism, etc. (33, 56, 416, 442).

Reduced levels of magnesium and zinc are related to metabolic syndrome, insulin resistance, and brain inflammation and are protective against these conditions (595, 43). Mercury and cadmium inhibiting magnesium and zinc levels as well as inhibiting glucose transfer are other mechanisms by which mercury and toxic metals are factors in metabolic syndrome and insulin resistance/diabetes (43, 196, 338, 580, 597).

TNFa (tumor necrosis factor-alpha) is a cytokine that controls a wide range of immune cell response in mammals, including cell death (apoptosis). This process is involved in inflammatory and degenerative neurological conditions like ALS, MS, Parkinson's, rheumatoid arthritis, etc. Cell signaling mechanisms like sphingolipids are part of the control mechanism for the TNFa apoptosis mechanism (126a). glutathione is an amino acid that is a normal cellular mechanism for controlling apoptosis. When glutathione is depleted in the brain, reactive oxidative species increased, and CNS and cell signaling mechanisms are disrupted by toxic exposures such as mercury, neuronal cell apoptosis results and neurological damage. Mercury has been shown to induce TNFa, deplete glutathione, and increase glutamate, dopamine, and calcium related toxicity, causing inflammatory effects and cellular apoptosis in neuronal and immune cells (126b, 126c). Mercury's biochemical damage at the cellular level include DNA damage, inhibition of DNA and RNA synthesis (42, 114, 142, 197, 296, 392); alteration of protein structure (33, 111, 114, 194, 252, 442); alteration of the transport and signaling functions of calcium (333, 43b, 254, 416d, 462, 507); inhibitation of glucose transport (338, 254, 580), and of enzyme function and transport of other essential nutrients (96, 198, 254, 263, 264, 33, 330, 331, 339, 347, 441, 442); induction of free radical formation (13a, 43b, 54, 405, 424), depletion of cellular glutathione (necessary for detoxification processes) (56, 111, 126, 424), inhibition of

[9]**Informativo:** "Alzheimer's Disease and Other Autoimmune Degenerative Conditions: the Mercury Connection".
[10]**Informativo:** "Toxic Exposures and Parkinsons: the Mercury Connection".

glutathione peroxidase enzyme (13a, 442), inhibits glutamate uptake (119, 416), induces peroxynitrite and lipid peroxidation damage (521b), causes abnormal migration of neurons in the cerebral cortex (149), immune system damage (111, 194, 226, 252, 272, 316, 325, 355); inhibits functional methylation (504), inducement of inflammatory cytokines (126, 152, 181) and autoimmunity (226, 272, 369, 405, etc.)

Exposure to mercury vapor and methyl mercury is well documented to commonly cause conditions involving tremor, with populations exposed to mercury experiencing tremor levels on average proportional to exposure level (250, 565). However bacteria, yeasts, and Vitamin B12 methylate inorganic mercury to methyl mercury in the mouth and intestines (599, 505) and mercury inhibits functional methylation in the body, a necessary process (504).

Mercury exposure causes high levels of oxidative stress/ reactive oxygen species (ROS) (13), which has been found to be a major factor in apoptosis and neurological disease (56, 250, 441, 442, 443, 13) including dopamine or glutamate related apoptosis (288c).

Mercury and quinones form conjugates with thiol compounds such as glutathione and cysteine and cause depletion of glutathione, which is necessary to mitigate reactive damage. Such conjugates are found to be highest in the brain substantia nigra with similar conjugates formed with L-Dopa and dopamine in Parkinson's disease (56). Mercury depletion of GSH and damage to cellular mitochondria and the increased lipid peroxidation in protein and DNA oxidation in the brain appear to be a major factor in Parkinson's disease (33, 56, 442) and a factor in other neurological conditions.

Mercury blocks the immune function of magnesium and zinc (198, 427, 38), whose deficiencies are known to cause significant neurological effects (461, 463, 430, 601). The low Zn levels result in deficient CuZnSuperoxide dismustase (CuZnSOD), which in turn leads to increased levels of superoxide due to toxic metal exposure. This is in addition to mercury's effect on metallothionein and copper homeostasis as previously discussed (477). Copper is an essential trace metal which plays a fundamental role in the biochemistry of the nervous system (477, 489, 495, 463, 464). Several chronic neurological conditions involving copper metabolic disorders are well documented like Wilson's Disease and Menkes Disease. Mutations in the copper/zinc enzyme superoxide dismustase (SOD) have been shown to be a major factor in the motor neuron degeneration in conditions like familial ALS (580). Exposures to toxic metals such as mercury and cadmium have been found to cause such effects (13a, 495, 517, etc.) and similar effects on Cu/Zn SOD have been found to be a factor in other conditions such as autism, Alzheimer's, Parkinson's, and non-familial ALS (489, 490, 495, 464, 469, 111). This condition can result in zinc deficient SOD and oxidative damage involving nitric oxide, peroxynitrite, and lipid peroxidation (490, 495, 496, 489, 521, 524), which have been found to affect glutamate mediated excitability and apoptosis of nerve cells and effects on mitochondria (119c, 412, 416, 495, 496, 502, 519, 524). These effects can be reduced by zinc supplementation (464, 495, 517, 430), as well as supplementation with antioxidants and nitric oxide-suppressing agents and peroxynitrite scavengers such as Vit C, Vit E, lipoic acid, Coenzyme Q10, carnosine, gingko biloba, N-acetyl cysteine, melatonin, etc. (444, 464, 494, 495, 469, 470, 521, 524, 572). Ceruloplasmin in plasma can be similarly affected by copper metabolism dysfunction, like SOD function, and is often a factor in neurodegeneration (489).

Motor neuron dysfunction and loss in amyotrophic lateral sclerosis (ALS) have been attributed to several different mechanisms, including increased intracellular calcium (333, 496, 507), glutamate dysregulation and excitotoxicity (119c, 412, 416, 496, 502), oxidative stress and free radical damage (13, 43, 56, 442, 490), nitric oxide related toxicity caused by peroxynitrite (524, 521), mitochondrial damage/dysfunction (519), neurofilament aggregation and dysfunction of transport mechanisms (507), and autoimmunity (313, 314, 369, 405, 513). These alterations and effects are not mutually exclusive but rather are synergistic, and increased calcium and altered calcium homeostasis appears to be a common denominator. Mercury forms strong bonds with the-SH groups of proteins causing alteration of the transport of calcium (333, 43, 96, 254, 329, 432, 496) and causes mitochondrial release

of calcium (21, 35, 43, 329, 333, 432, 496, 519). This results in a rapid and sustained elevation in intracellular levels of calcium (333, 496). Calcium plays a major role in the extreme neurotoxicity of mercury and methyl mercury. Both inhibit cellular calcium ATPase and calcium uptake by brain microsomes at very low levels of exposure (270, 288, 329, 333, 432, 56,). Protein Kinase C (PKC) regulates intracellular and extra cellular signals across neuronal membranes, and both forms of mercury inhibit PKC at micro molar levels, as well as inhibiting phorbal ester binding (43, 432). They also block or inhibit calcium L-channel currents in the brain in an irreversible and concentration dependent manner. Mercury vapor or inorganic mercury exposure affects the posterior cingulate cortex and causes major neurological effects with sufficient exposure (428, 453). Metallic mercury is much more potent than methyl mercury in such actions, with 50% inhibition in animal studies at 13 ppb (333, 329). Mercury is seen to be a factor in all of these known mechanisms of neural degeneration seen n ALS and other motor neuron conditions.

Spatial and temporal changes in intracellular calcium concentrations are critical for controlling gene expression and neurotransmitter release in neurons (432, 496, 43, 114). Mercury alters calcium homeostasis and calcium levels in the brain and affects gene expression and neurotransmitter release through its effects on calcium, etc. Mercury inhibits sodium and potassium (N, K) ATPase in dose dependent manner and inhibits dopamine and noreprenephrine uptake by synaptosomes and nerve impulse transfer (288, 270, 56, 43, 35). Mercury also interrupts the cytochrome oxidase system, blocking the ATP energy function (35, 43, 84), lowering immune growth factor IGF-I levels and impairing astrocyte function (119, 152, 416d, 497). Astrocytes are common cells in the CNS involved in the feeding and detox of nerve cells. Increases in inflammatory cytokines such as caused by toxic metals trigger increased free radical activity and damage to astrocyte and astrocyte function (152, 416d). IGF-I protects against brain and neuronal pathologies like ALS, MS, and Fibromyalgia by protecting the astrocytes from this destructive process.

Na (+), K (+)-ATPase is a transmembrane protein that transports sodium and potassium ions across cell membranes during an activity cycle that uses the energy released by ATP hydrolysis. Mercury is documented to inhibit Na (+), K (+)-ATPase function at very low levels of exposure (288ab). Studies have found that in ALS cases there was a reduction in serum magnesium and RBC membrane Na (+)-K+ ATPase activity and an elevation in plasma serum digoxin (263, 260d). The activity of all serum free-radical scavenging enzymes, concentration of glutathione, alpha tocopherol, iron binding capacity, and ceruloplasmin decreased significantly in ALS, while the concentration of serum lipid peroxidation products and nitric oxide increased. The inhibition of Na+-K+ ATPase can contribute to increase in intracellular calcium and decrease in magnesium, which can result in 1) defective neurotransmitter transport mechanism, 2) neuronal degeneration and apoptosis, 3) mitochondrial dysfunction, 4) defective golgi body function and protein processing dysfunction. It is documented in this paper that mercury is a cause of most of these conditions seen in ALS (13a, 111, 288, 442, 521b, 43, 56, 263, etc.)

Mercury exposure also degrades the immune system resulting in more susceptibility to viral, bacterial, or parasitic effects along with candida albicans which are often present in those with chronic conditions and require treatment (404, 468, 470, 485, 600). Four such commonly found in ALS patients are mycoplasma AND echo-7 enterovirus (468, 470), candida albicans (404), and parasites (485). One clinic found that over 85% of patients with ALS tested have mycoplasma infection, often M. Pneumoniae (470), but in Gulf War veterans mostly a manmade variety used in bioterrorism agents-M. fermentans. Mercury from amalgam interferes with production of cytokines that activate macrophage and neutrophils, disabling early control of viruses or other pathogens and leading to enhanced infection (131). While the others are also being commonly found, mycoplasma has been found in 85% of ALS patients by clinics treating such conditions (470). Mycoplasma appears to be a cofactor with mercury in the majority of cases and shifts the immune T cell balance toward inflammatory cytokines (470b). Treatment of these chronic infections are required and documented to cause improvement in such patients (470).

Mercury lymphocyte reactivity and effects on amino acids such as glutamate in the CNS induce CFS type symptoms including profound tiredness, musculoskeletal pain, sleep disturbances, gastrointestinal and neurological problems along with other *CFS symptoms and Fibromyalgia*[11] (346, 342, 369, 416, 496, 513, 119b, 152, 314). Mercury has been found to be a common cause of Fibromyalgia (293, 346, 369), which based on a Swedish survey occurs in about 12% of women over 35 and 5.5% of men (342). ALS patients have been found to have a generalized deficiency in metabolism of the neuroexcitotoxic amino acids like glutamate, aspartate, NAAG, etc.(416). Glutamate is the most abundant amino acid in the body and in the CNS acts as excitory neurotransmitter (346, 412, 416, 438, 496, 119c), which also causes inflow of calcium. Astrocytes, a type of cell in the brain and CNS with the task of keeping clean the area around nerve cells, have a function of neutralizing excess glutamate by transforming it to glutamic acid. If astrocytes are not able to rapidly neutralize excess glutamate, then a buildup of glutamate and calcium occurs, causing swelling and neurotoxic effects (119, 152, 333, 416, 496, 524). Mercury and other toxic metals inhibit astrocyte function in the brain and CNS (119, 152, 416), causing increased glutamate and calcium related neurotoxicity (119, 152, 333, 226a, 496) which are responsible for much of the Fibromyalgia symptoms and a factor in neural degeneration in MS and ALS. This is also a factor in conditions such as CFS, Parkinson's, and ALS (346, 416, 496, 524, 600). Animal studies have confirmed that increased levels of glutamate (or aspartate, another amino acid excitory neurotransmitter) cause increased sensitivity to pain, as well as higher body temperature-both found in CFS/Fibromyalgia. Mercury and increased glutamate activate free radicals forming processes like xanthine oxidase which produce oxygen radicals and oxidative neurological damage (346, 142, 13). Nitric oxide related toxicty caused by peroxynitrite formed by the reaction of NO with superoxide anions, which results in nitration of tyrosine residues in neurofilaments and manganese Superoxide Dimustase (SOD) has been found to cause inhibition of the mitochondrial respiratory chain, inhibition of the glutamate transporter, and glutamate-induced neurotoxicity involved in ALS (524, 521).

In addition to the documentation showing the mechanisms by which mercury causes the conditions and symptoms seen in ALS and other neurodegenerative diseases, many studies of patients with major neurological or degenerative diseases have found direct evidence mercury and amalgam fillings play a major role in development of conditions such as such as ALS (92, 97, 207, 229b, 305, 325, 327, 416, 423, 442, 468, 470, 520, 35). Such supplements including N-acetylcysteine (NAC), Vitamins E and C, zinc, and creatinine have been found to offer significant protection against cell apoptosis and neurodegeneration in neurological conditions such as ALS (13c, 56a, 517, 524, 564, 494).

Medical studies and doctors treating chronic conditions like Fibromyalgia have found that supplements which cause a decrease in glutamate or protect against its effects have a positive effect on Fibromyalgia and other chronic neurologic conditions. Some that have been found to be effective include CoQ10 (444), ginkgo biloba and pycnogenol (494a), NAC (54, 494a), Vit B6, methyl cobalamine (B12), L-carnitine, choline, ginseng, vitamins C and E, nicotine, and omega 3 fatty acids (fish and flaxseed oil) (417, 495e). A study demonstrated protective effects of methylcobalamin, a vitamin B12 analog, against glutamate-induced neurotoxicity (503), and similarly for iron in those who are iron deficient.

In a study of the brains of persons dying of ALS, spherical and crescent-shaped introneuronal inclusions (SCI) were distributed in association with each other among the parahippocampal gyrus, dentate gyrus of the hippocampus and amygdala, but not any non-motor-associated brain regions (522). The occurrence of SCI in both the second and third layers of the parahippocampal gyrus and amygdala was significantly correlated to the presence of dementia in ALS cases. Mercury has been found to accumulate in these areas of the brain and to cause adverse behavioral effects in animal studies and humans (66, 287, 305).

[11] **Informativo:** "Chronic Fatigue Syndrome, Fibromyalgia, Scleroderma, Lupus, Rheumatoid Arthritis, MCS: The Mercury Connection".

Another neurological effect of mercury that occurs at very low levels is inhibition of nerve growth factors, for which deficiencies result in nerve degeneration. Only a few micrograms of mercury severely disturb cellular function and inhibits nerve growth (175, 147, 226, 255, 305, 149). Prenatal or neonatal exposures have been found to have life long effects on nerve function and susceptibility to toxic effects. Prenatal mercury vapor exposure that results in levels of only 4 parts per billion in newborn rat brains was found to cause decreases in nerve growth factor and other effects (305). This is a level that is common in the population with several amalgam fillings or other exposures (600). There is also evidence that fetal or infant exposure causes delayed neurotoxicity evidenced in serious effect at middle age (255). Insulin-like-growth factor I (IGF-I) are positively correlated with growth hormone levels and have been found to be the best easily measured marker for levels of growth hormone, but males have been found more responsive to this factor than women (497). IGF-I controls the survival of spinal motor neurons affected in ALS during development as well as later in life (497, 498). IGF-I and insulin levels have been found to be reduced in ALS patients with evidence this is a factor in ALS (497, 498). Several clinical trials have found IGF-I treatment is effective at reducing the damage and slowing the progression of ALS and Alzheimer's with no medically important adverse effects (498). It has also been found that in chronically ill patients the levels of pituitary and thyroid hormones that control many bodily processes are low, and that supplementing both thyrotropin-releasing hormone and growth control hormone is more effective at increasing all of these hormone levels in the patient (499).

Extremely toxic anaerobic bacteria from root canals or cavitations formed at incompletely healed tooth extraction sites have also been found to be common factors in Fibromyalgia and other chronic neurological conditions such as Parkinson's and ALS, with condensing osteitis which must be removed with a surgical burr along with 1 mm of bone around it (35, 200, 437, 600). Cavitations have been found in 80% of sites from wisdom tooth extractions tested and 50% of molar extraction sites tested (35, 200, 437). The incidence is likely somewhat less in the general population. Medical studies and doctors treating Fibromyalgia have found that supplements which cause a decrease in glutamate or protect against its effects have a positive effect on Fibromyalgia and other chronic neurologic conditions like ALS. Some that have been found to be effective include Vit B6, methyl cobalamine (B12), L-carnitine, choline, ginseng, Ginkgo biloba, vitamins C and E, CoQ10, nicotine, and omega 3 fatty acids (fish and flaxseed oil) (417, 468).

Clinical tests of patients with ALS, MND, Parkinson's, Alzheimer's, Lupus (SLE), and rheumatoid arthritis have found that the patients generally have elevated plasma cysteine to sulphate ratios, with the average being 500% higher than controls (330, 331, 56, 84), and in general being poor sulphur oxidizers. This means that these patients have blocked enzymatic processes for converting the basic cellular fuel cysteine to sulfates and glutathione, and thus insufficient sulfates available to carry out necessary bodily processes. Mercury has been shown to diminish and block sulphur oxidation and thus reducing glutathione levels which is the part of this process involved in detoxifying and excretion of toxics like mercury (33). Glutathione is produced through the sulphur oxidation side of this process. Low levels of available glutathione have been shown to increase mercury retention and increase toxic effects (111), while high levels of free cysteine have been demonstrated to make toxicity due to inorganic mercury more severe (333, 194, 56, 33b). The deficiency in conjugation and detoxification of sulfur based toxins in the liver results in toxic metabolites and progressive nerve damage over time (331). Mercury has also been found to play a part in inducing intolerance and neuronal problems through blockage of the P-450 enzymatic process (84, 33b). Patients with some of these conditions have found that bathing in Epsom Salts (magnesium sulfate) offers temporary relief for some of their symptoms by providing sulfates that avoid the blocked metabolic pathway. A test that some doctors treating conditions like ALS usually prescribe to measure the cysteine to sulfate ratio and other information useful in diagnosis and treatment is the Great Smokies Diagnostic Labs comprehensive liver detox test (386). The test results come with some recommendations for treatment. A hair test for toxic metals is also usually ordered to determine toxic exposures that

might be involved (386). A more definitive test such as MELISA for immune reactivity to toxics is available by sending blood to a European lab (87). Other labs also have other useful tests such as Immune Reactivity Biocompatability Tests (445), ELISA or organic acid panels or amino acid panels (386). Treatment using IV glutathione, vitaminC, and minerals has been found to be very effective in the stabilizing and amelioration of some of these chronic neurological conditions by neurologist such as Perlmutter in Florida (469).

In one subtype of ALS, damaged, blocked, or faulty enzymatic superoxide dimustase (SOD) processes appear to be a major factor in cell apoptosis involved in the condition (443, 495). Mercury is known to damage or inhibit SOD activity (13, 33, 111).

## 1.4 Prevention and Treatment of ALS

Tick-borne encephalitis, such as Lyme Disease, has been found to cause ALS symptoms in a significant portion of untreated acute cases (471). Lyme disease is widespread in the U.S. Large numbers of patients diagnosed with ALS and other neurological conditions have been found to have treatable tick-borne encephalitis, and many have recovered after treatment. Anyone diagnosed with degenerative neurological symptoms should investigate the possibility of lyme disease or post-polio encephalitis. Poliomyelitis also has a chronic state that resembles ALS (580).

Since elevated plasma cysteine has been reported in some ALS patients, sulfite and cysteine toxicity may be involved in other cases of ALS. Patients with ALS with nonmutant-SOD should be tested for sulfite toxicity, cysteine, glutamate and GSH levels, and whether they have low levels of GSH metabolism enzymes. During the time when strict dietary and supplement measures normalized a patient's whole blood GSH, blood cysteine, and urine sulfite, the patient did not experience additional physical decline (330b).

Total dental revision (TDR) which includes replacing amalgam fillings, extracting root canaled teeth, and treating cavitations has been found to offer significant health improvements to many with ALS and other autoimmune conditions (35, 200, 293, 437). Root canals and cavitations have been found to harbor anaerobic bacteria which give off toxins of extreme toxicity which block enzymatic processes at the cellular level causing degenerative processes according to the medical labs that do the tests (437, 200, 35), similar to mercury's effects but in some cases even more toxic. IGF-1 treatments have also been found to alleviate some of the symptoms of ALS (424). Medical studies and doctors treating Fibromyalgia have found that supplements which cause a decrease in glutamate or protect against its effects have a positive effect on Fibromyalgia. Some that have been found to be effective in treating metals related autoimmune conditions include Vit B6, CoenzymeQ10, methyl cobalamine (B12), SAMe, L-carnitine, choline, ginseng, Ginkgo biloba, vitamins C and E, nicotine, and omega 3 fatty acids (fish and flaxseed oil) (417, 444, 468, 580).

One dentist with severe symptoms similar to ALS improved after treatment for mercury poisoning (246), and others treated for mercury poisoning or using TDR have also recovered or significantly improved (97, 229, 405, 406, 437, 468-470, 485, 35).The Edelson Clinic in Atlanta which treats ALS patients reports similar experience (406), and the Perlmutter Clinic has also had some success with treatment of ALS and other degenerative neurological conditions (469).

While there are many studies documenting effectiveness of chemical chelators like DMSA and DMPS at reducing metals levels and alleviating adverse effects for most conditions, and many thousands of clinical case results (600, 601); there is also some evidence from animal studies that these chelators can result in higher levels of mercury in the motor neurons in the short term which might be a problem for ALS patients (600). Thus other detox options might be preferable for ALS patients until enough clinical evidence is available treating ALS patients with them with mercury toxicity. Another chelator used for clogged arteries, EDTA, forms toxic compounds with mercury and can

damage brain function (307). Use of EDTA may need to be restricted in those with high Hg levels. N-acetyl cysteine (NAC) has been found to be effective at increasing cellular glutathione levels and chelating mercury (54). Experienced doctors have also found additional zinc to be useful when chelating mercury (222) as well as counteracting mercury's oxidative damage (43). Zinc induces metallothionein which protects against oxidative damage and increases protective enzyme activities and glutathione which tend to inhibit lipid peroxidation and suppress mercury toxicity (430, 464). Also lipoic acid, LA, has been found to dramatically increase excretion of inorganic mercury (over 12 fold), but to cause decreased excretion of organic mercury (572d) and copper. Lipoic acid has a protective effect regarding lead or inorganic mercury toxicity through its antioxidant properties (572), but should not be used with high copper until copper levels are reduced. LA and NAC (N-acetyl cysteine) also increase glutathione levels and protect against superoxide radical/ peroxynitrite damage, so thus have an additional neuroprotective effect (494ab, 521, 572c, 54). Zinc is a mercury and copper antagonist and can be used to lower copper levels and protect against mercury damage. Lipoic acid has been found to have protective effects against cerebral ischemic-reperfusion, excitotoxic amino acid (glutamate) brain injury, mitochondrial dysfunction, diabetic neuropathy (494).

Antioxidants such as carnosine (495a), Coenzyme Q10, Vitamins B & C & E & D, gingko biloba, superoxide dismutase (SOD), N-acetyl-cysteine (NAC), Alpha Lipoic Acid, and pycnogenol have also been found protective against degenerative neurological conditions (494, 495e, 444, 580). Other supplements found to be protective against neuronal degenerative conditions include Acetyl-L-Carnitine, EFAs (DHA/EPA), DHEA, CoQ10, magnesium, Vit B1 & B5, hydergine, and octacosanol (580). Such supplements only offer limited protection and reductions in progression of ALS without other measures that deal with underlying mechanisms of causality.

Other supplements that appear useful in conditions involving neurotoxicity or muscle function degeneration include creatine (502, 580) and lithium (590). In the motor cortex of the ALS group the N-acetylaspartate (NAA)/creatine (Cr (t)) metabolite ratio was lower than in our control group, indicating NAA loss. Upon creatine supplementation we observed in the that creatine supplementation causes an increase in the diminished NAA levels in ALS motor cortex as well as an increase of choline levels in both ALS and control motor cortices. This indicates an improvement in function of the pathological ALS skeletal muscles related to changes of mitochondrial respiratory chain which appears to affect motor neuron survival. In another study by the NAS, lithium carbonate at 150 mg twice daily significantly reduced the degeneration of ALS patients (590). A recent study demonstrated that combined treatment with lithium and valproic acid elicits synergistic neuroprotective effects against glutamate excitotoxicity in cultured brain neurons. Combined lithium and valproate treatment delays disease onset, reduces neurological deficits and prolongs survival in an amyotrophic lateral sclerosis mouse model (590c). Methylcobalamin and SAMe have also been found to provide some protection against neurotoxicity (580).

Two experimental treatment for ALS that has shown some effectiveness at reducing disease progression is recombinant human insulin-like growth factor and Orap (Pimozide) (580).

## 1.5 References

(13) (a) S.Hussain et al, "Mercuric chloride-induced reactive oxygen species and its effect on antioxidant enzymes in different regions of rat brain", J Environ Sci Health B 1997 May;32 (3):395-409; & P.Bulat, "Activity of Gpx and SOD in workers occupationally exposed to mercury", Arch Occup Environ Health, 1998, Sept, 71 Suppl:S37-9; & Stohs SJ, Bagchi D. Oxidative mechanisms in the toxicity of metal ions. Free Radic Biol Med 1995; 18 (2): 321-36 ; & D.Jay, "Glutathione inhibits SOD activity of Hg", Arch Inst cardiol Mex, 1998, 68 (6): 457-61 & El-Demerdash FM. Effects of selenium and mercury on the enzymatic activities and lipid peroxidation in brain, liver, and blood of rats. J Environ Sci Health B. 2001 Jul;36 (4):489-99. &(b) S.Tan et al, "Oxidative stress induces

programmed cell death in neuronal cells", J Neurochem, 1998, 71 (1):95-105; & Matsuda T, Takuma K, Lee E, et al. Apoptosis of astroglial cells [Article in Japanese] Nippon Yakurigaku Zasshi. 1998 Oct;112 Suppl 1:24P-; & Lee YW, Ha MS, Kim YK.. Role of reactive oxygen species and glutathione in inorganic mercury-induced injury in human glioma cells. Neurochem Res. 2001 Nov;26 (11):1187-93. & (c) Ho PI, Ortiz D, Rogers E, Shea TB. Multiple aspects of homocysteine neurotoxicity: glutamate excitotoxicity, kinase hyperactivation and DNA damage. J Neurosci Res. 2002 Dec 1;70 (5):694-702; & (d) The role for oxidative stress in neurodegenerative diseases, [Article in Japanese], Shibata N, Kobayashi M. Brain Nerve. 2008 Feb;60 (2):157-70

(20) (a) Galic N, Ferencic Z et al, Dental amalgam mercury exposure in rats. Biometals. 1999 Sep;12 (3):227-31; & Arvidson B, Arvidsson J, Johansson K,. Mercury deposits in neurons of the trigeminal ganglia after insertion of dental amalgam in rats. Biometals. 1994 Jul;7 (3):261-3; & (b) Danscher G, Horsted-Bindslev P, Rungby J. Traces of mercury in organs from primates with amalgam fillings. Exp Mol Pathol. 1990 Jun;52 (3):291-9; & L.Hahn et al, Distribution of mercury released from amalgam fillings into monkey tissues", FASEB J., 1990, 4: 5536

(21) R.A.Goyer, "Toxic effects of metals"in: Caserett and Doull's Toxicology-TheBasic Science of Poisons, McGraw-Hill Inc., N.Y., 1993; & Goodman, Gillman, The Pharmacological Basis of Therapeutics, Mac Millan Publishing Company, N.Y. 1985.

(28) F.Schmidt et al, "Mercury in urine of employees exposed to magnetic fields", Tidsskr Nor Laegeforen, 1997, 117 (2): 199-202; & Sheppard AR and EisenbudM., Biological Effects of electric and magnetic fields of extremely low frequency. New York university press. 1977; & Ortendahl T W, Hogstedt P, Holland RP, "Mercury vapor release from dental amalgam in vitro caused by magnetic fields generated by CRT's", Swed Dent J 1991 p 31 Abstract 22.

(33) (a) Markovich et al, "Heavy metals (Hg, Cd) inhibit the activity of the liver and kidney sulfate transporter Sat-1", Toxicol Appl Pharmacol, 1999, 154 (2):181-7; & (b) S.A.McFadden, "Xenobiotic metabolism and adverse environmental response: sulfur-dependent detox pathways", Toxicology, 1996, 111 (1-3):43-65; &(c) S.C. Langley-Evans et al, "SO2: a potent glutathion depleting agent", Comp Biochem Physiol Pharmocol Toxicol Endocrinol, 114 (2):89-98; & (d) Alberti A, Pirrone P, Elia M, Waring RH, Romano C. Sulphation deficit in "low-functioning" autistic children. Biol Psychiatry 1999, 46 (3):420-4.

(34) Henriksson J, Tjalve H. Uptake of inorganic mercury in the olfactory bulbs via olfactory pathways in rats. Environ Res. 1998 May;77 (2):130-40.

(35) Huggins HA, Levy, TE, Uniformed Consent: the hidden dangers in dental care, 1999, Hampton Roads Publishing Company Inc; & Hal Huggins, Its All in Your Head, 1993; & Center for Progressive Medicine, 1999, ALS *http://www.hugginsappliedhealing.com/als.php*[12]

(42) Rodgers JS, Hocker JR, et al, Mercuric ion inhibition of eukaryotic transcription factor binding to DNA. Biochem Pharmacol. 2001 Jun 15;61 (12): 1543-50; & K.Hansen et al A survey of metal induced mutagenicity in vitro and in vivo, J Amer Coll Toxicol, 1984:3;381-430;

(43) (a) Knapp LT; Klann E. Superoxide-induced stimulation of protein kinase C via thiol modification and modulation of zinc content. J Biol Chem 2000 May 22; & P.Jenner, "Oxidative mechanisms in PD", Mov Disord, 1998; 13 (Supp1):24-34;& (b) Rajanna B et al, "Modulation of protein kinase C by heavy metals", Toxicol Lett, 1995, 81 (2-3):197-203: & Badou A et al, "HgCl2-induced IL-4 gene expression in T cells involves a protein kinase C-dependent calcium influx through L-type calcium channels"J Biol Chem. 1997 Dec 19;272 (51):32411-8, & D.B.Veprintsev, 1996, Institute for Biological Instrumentation, Russian Academy of Sciences, Pb2+ and Hg2+ binding to alpha-lactalbumin".Biochem Mol Biol Int 1996 ;39 (6): 1255-65; & M. J. McCabe, University of Rochester School of Medicine & Dentistry, 2002, Mechanisms of Immunomodulation by Metals, www.envmed.rochester.edu/envmed/TOX/faculty/mccabe.html; & Buzard GS, Kasprzak KS. Pos-

[12]**Internet:** "http://www.hugginsappliedhealing.com/als.php".

sible roles of nitric oxide and redox cell signaling in metal-induced toxicity and carcinogenesis: a review. Environ Pathol Toxicol Oncol. 2000;19 (3):179-99

(48) K.Arvidson, "Corrosion studies of dental gold alloy in contact with amalgam", Swed. Dent. J 68: 135-139, 1984; & Skinner, EW, The Science of Dental Materials, 4th Ed.revised, W.B.Saunders Co., Philadelphia, p284-285, 1957.

(49) Kingman A, Albertini T, Brown LJ. National Institute of Dental Research, "Mercury concentrations in urine and blood associated with amalgam exposure in the U.S. military population", J Dent Res. 1998 Mar;77 (3):461-71.

(54) M.E. Lund et al, "Treatment of acute MeHg poisoning by NAC", J Toxicol Clin Toxicol, 1984, 22 (1):31-49; & Livardjani F; Ledig M; Kopp P; Dahlet M; Leroy M; Jaeger A. Lung and blood superoxide dismustase activity in mercury vapor exposed rats: effect of N-acetylcysteine treatment. Toxicology 1991 Mar 11;66 (3):289-95. & G.Ferrari et al, Dept. Of Pathology, Columbia Univ., J Neurosci, 1995, 15 (4):2857-66; & RR. Ratan et al, Dept. of Neurology, Johns Hopkins Univ., J Neurosci, 1994, 14 (7): 4385-92;

(56) (a) A.Nicole et al, "Direct evidence for glutathione as mediator of apoptosis in neuronal cells", Biomed Pharmacother, 1998; 52 (9):349-55; & J.P.Spencer et al, "Cysteine & GSH in PD", mechanisms involving ROS", J Neurochem, 1998, 71 (5):2112-22: & & J.S. Bains et al, "Neurodegenerative disorders in humans and role of glutathione in oxidative stress mediated neuronal death", Brain Res Rev, 1997, 25 (3):335-58; & Medina S, Martinez M, Hernanz A, Antioxidants inhibit the human cortical neuron apoptosis induced by hydrogen peroxide, tumor necrosis factor alpha, dopamine and beta-amyloid peptide 1-42.. Free Radic Res. 2002 Nov;36 (11):1179-84. &(b) Pocernich CB, et al. Glutathione elevation and its protective role in acrolein-induced protein damage in synaptosomal membranes: relevance to brain lipid peroxidation in neurodegenerative disease. Neurochem Int 2001 Aug;39 (2):141-9; & D. Offen et al, "Use of thiols in treatment of PD", Exp Neurol, 1996, 141 (1):32-9; & (c) Pearce RK, Owen A, Daniel S, Jenner P, Marsden CD. Alterations in the distribution of glutathione in the substantia nigra in Parkinson's disease. J Neural Transm. 1997;104 (6-7):661-77; & A.D.Owen et al, Ann NY Acad Sci, 1996, 786:217-33; & JJ Heales et al, Neurochem Res, 1996, 21 (1):35-39; & & X.M.Shen et al, Neurobehavioral effects of NAC conjugates of dopamine: possible relevance for Parkinson'sDisease", Chem Res Toxicol, 1996, 9 (7):1117-26; & Chem Res Toxicol, 1998, 11 (7):824-37; & (d) Li H, Shen XM, Dryhurst G. Brain mitochondria catalyze the oxidation of 7-(2-aminoethyl)-3,4-dihydro-5-hydroxy-2H-1,4-benzothiazine-3-carboxyli c acid (DHBT-1) to intermediates that irreversibly inhibit complex I and scavenge glutathione: potential relevance to the pathogenesis of Parkinson's disease. J Neurochem. 1998 Nov;71 (5):2049-62; & (e) Araragi S, Sato M. et al, Mercuric chloride induces apoptosis via a mitochondrial-dependent pathway in human leukemia cells. Toxicology. 2003 Feb 14;184 (1):1-9.

(60) V.D.M.Stejskal, Dept. Of Clinical Chemistry, Karolinska Institute, Stockholm, Sweden LYMPHOCYTE IMMUNO-STIMULATION ASSAY -MELISA" & V.D.M.Stejskal et al, "Mercury-specific Lymphocytes: an indication of mercury allergy in man", J. Of Clinical Immunology, 1996, Vol 16 (1);31-40. VDM Stejskal et al, "MELISA: tool for the study of metal allergy", Toxicology in Vitro, 8 (5):991-1000, 1994; & Metal-specific lymphocytes: biomarkers of sensitivity in man.Stejskal VD, Danersund A, Lindvall A, Hudecek R, Nordman V, Yaqob A, Mayer W, Bieger W, Lindh U.Neuroendocrinology Letters 1998 *www.melisa.org*[13]

(79) L.Bjorkman et al, "Mercury in Saliva and Feces after Removal of Amalgam Fillings", Toxicology and Applied Pharmacology, 1997, 144 (1), p156-62

(84) J.C.Veltman et al, "Alterations of heme, cytochrome P-450, and steroid metabolism by mercury in rat adrenal gland", Arch Biochem Biophys, 1986, 248 (2):467-78; & A.G.Riedl et al, Neurodegenerative Disease Research Center, King's College, UK, "P450 and hemeoxygenase enzymes

[13]**Internet:** "http://www.melisa.org/".

in the basal ganglia and their role's in Parkinson's disease", Adv Neurol, 1999; 80:271-86; & Alfred V. Zamm. Dental Mercury: A Factor that Aggravates and Induces Xenobiotic Intolerance. J. Orthmol. Med. v6#2 pp67-77 (1991).

(85) J.A.Weiner et al, "The relationship between mercury concentration in human organs and predictor variables", Sci Tot Environ, 138 (1-3):101-115, 1993; & M.Nylander et al, "Mercury concentrations in the human brain and kidneys and exposure from amalgam fillings", Swed Dent J 1987; 11:179-187; & D.W.Eggleston et al, Correlation of dental amalgam with mercury in brain tissue. J Prosthet Dent, 1987, 58 (6), 704-7.

(92) L. Tandon et al, "Elemental imbalance studies by INAA on ALS patients", J Radioanal Nuclear Chem 195 (1):13-19, 1995; & Y.Mano et al, "Mercury in the hair of ALS patients", Rinsho Shinkeigaku, 1989, 29 (7): 844-848; & Mano et al, 1990, Rinsho Shinkeigaku 30: 1275-1277; & Khare et al, 1990, "Trace element imbalances in ALS", Neurotoxicology, 1990, 11:521-532; & Carpenter DO. Effects of metals on the nervous system of humans and animals. Int J Occup Med Environ Health 2001;14 (3):209-18.

(93) Vaccari A, Ruiu S, Mocci I, Saba P, Bernard B. Brodie. Selected pyrethroid insecticides stimulate glutamate uptake in brain synaptic vesicles. Neuroreport 1998 Oct 26;9 (15):3519-23; Gassner B, Wuthrich A, Scholtysik G, Solioz M; The pyrethroids permethrin and cyhalothrin are potent inhibitors of the mitochondrial complex I. J Pharmacol Exp Ther 1997 May;281 (2):855-60; Narahashi T. Nerve membrane Na+ channels as targets of insecticides. Trends Pharmacol Sci 1992 Jun;13 (6):236-41; Zhao X, Dai S, Chen G. Inhibition of glutamate uptake in rat brain synaptosome by pyrethroids. Chung Hua Yu Fang I Hsueh Tsa Chih 1995 Mar;29 (2):89-91; Eldefrawi AT, Eldefrawi ME. Receptors for gamma-aminobutyric acid and voltage-dependent chloride channels as targets for drugs and toxicants. FASEB J 1987 Oct;1 (4):262-71; D. Zuccari Bissacot and I. Vassilieff. HPLC Determination of Flumethrin, Deltamethrin, Cypermethrin, and Cyhalothrin Residues in the Milk and Blood or Lactating Dairy Cows. Journal of Analytical Toxicology, Volume 21, Number 5, September 1997, pp. 397 -402.; Gassner B, Wuthrich A, Lis J, Scholtysik G, Solioz M. Topical application of synthetic pyrethroids to cattle as a source of persistent environmental contamination.J Environ Sci Health B 1997 Sep;32 (5):729-39; Patient Information Network, Exposure Survey of patients with ALS, http://members.aol.com/alspinpoint/results.html; & & McGuire, Longstreth et al, Occupational exposures and amyotrophic lateral sclerosis; Am J Epidemiol 1997 Jun 15;145 (12):1076-88 & Baker, 1996.

(94) (a) Kamel F, Umbach DM, Hu H, Sandler DP; Lead Exposure and Amyotrophic Lateral Sclerosis. Epidemiology 2002 May;13 (3):311-319; & Conradi S, Ronnevi LO, Vesterberg O. Abnormal tissue distribution of lead in amyotrophic lateral sclerosis. J Neurol Sci 1976 Oct;29 (2-4):259-65:; Epidemiologic correlates of sporadic amyotrophic lateral sclerosis, Armon C, Kurland LT, Daube JR, O'Brien PC. Neurology. 1991 Jul;41 (7):1077-84, &(b) McGuire V, Longstreth WT Jr, van Belle G. Occupational exposures and amyotrophic lateral sclerosis. A population-based case-control study. Am J Epidemiol 1997 Jun 15;145 (12):1076-88.; & (c) Nelson LM, McGuire V, Longstreth WT Jr, Matkin C. Population-based case-control study of amyotrophic lateral sclerosis in western Washington State. I. Cigarette smoking and alcohol consumption. Am J Epidemiol 2000 Jan 15;151 (2):156-63 ; & (d) An evidence-based medicine approach to the evaluation of the role of exogenous risk factors in sporadic amyotrophic lateral sclerosis, Armon C. Neuroepidemiology. 2003 Jul-Aug;22 (4):217-28

(96) A.F.Goldberg et al, "Effect of Amalgam restorations on whole body potassium and bone mineral content in older men", Gen Dent, 1996, 44 (3): 246-8; & (b) K.Schirrmacher, 1998, "Effects of lead, mercury, and methyl mercury on gap junctions and [Ca2+]I in bone cells", Calcif Tissue Int 1998 Aug;63 (2): 134-9.

(97) Redhe O, Pleva J, "Recovery from ALS and from asthma after removal of dental amalgam fillings", Int J Risk & Safety in Med 1994; 4:229-236, & Adams CR, Ziegler DK, Lin JT., "Mercury

intoxication simulating ALS", JAMA, 1983, 250 (5):642-5; & ALS and mercury intoxication: A relationship?

References and further reading may be available for this article. To view references and further reading you must *purchase*[14] this article. Julien Praline et al, Clin Neurol Neurosurg. 2007 Dec;109 (10):880-3. Epub 2007 Aug 23

(98) A.Seidler et al, Possible environmental factors for Parkinson's disease", Neurology 46 (5): 1275- 1284, 1996; & Vroom FO, Greer M, "Mercury vapor intoxication", 95: 305-318, 1972; & Ohlson et al, "Parkinson's Disease and Occupational Exposure to Mercury", Scand J. Of Work Environment Health, Vol7, No.4: 252-256, 1981; L.G.

(111) (a) Quig D, Doctors Data Lab, "Cysteine metabolism and metal toxicity", Altern Med Rev, 1998;3:4, p262-270, & (b) J.de Ceaurriz et al, Role of gamma-glutamyltraspeptidase (GGC) and extracellular glutathione in dissipation of inorganic mercury", J Appl Toxicol, 1994, 14 (3): 201-; & W.O. Berndt et al, "Renal glutathione and mercury uptake", Fundam Appl Toxicol, 1985, 5 (5):832-9; & Zalups RK, Barfuss DW. Accumulation and handling of inorganic mercury in the kidney after coadministration with glutathione, J Toxicol Environ Health, 1995, 44 (4): 385-99; & T.W.Clarkson et al, "Billiary secretion of glutathione-metal complexes", Fundam Appl Toxicol, 1985, 5 (5):816-31;

(114) (a) M.Aschner et al, "Metallothionein induction in fetal rat brain by in utero exposure to elemental mercury vapor", Brain Research, 1997, dec 5, 778 (1):222-32; & Baauweegers HG, Troost D. Localization of metallothionein in the mammilian central nervous system.. Biol Signals 1994, 3:181-7. &(b) T.V. O'Halloran, "Transition metals in control Of gene expression", Science, 1993, 261 (5122):715-25; &(c) Matts RL, Schatz JR, Hurst R, Kagen R. Toxic heavy metal ions inhibit reduction of disulfide bonds. J Biol Chem 1991; 266 (19): 12695-702; Boot JH. Effects of SH-blocking compounds on the energy metabolism in isolated rat hepatocytes. Cell Struct Funct 1995; 20 (3): 233-8.;

(119) (a) L.Ronnback et al, "Chronic encephalopaties induced by low doses of mercury or lead", Br J Ind Med 49: 233-240, 1992; & H.Langauer-Lewowicka, " Changes in the nervous system due to occupational metallic mercury poisoning" Neurol Neurochir Pol 1997 Sep-Oct;31 (5):905-13; &(b) Kim P, Choi BH. "Selective inhibition of glutamate uptake by mercury in cultured mouse astrocytes", Yonsei Med J 1995; 36 (3): 299-305; &(b) Brookes N. In vitro evidence for the role of glutatmate in the CNS toxicity of mercury. Toxicology 1992, 76 (3):245-56; & (c) Albrecht J, Matyja E. Glutamate: a potential mediator of inorganic mercury toxicity. Metab Brain Dis 1996; 11:175-84; & (d) Heavy metals modulate glutamatergic system in human platelets; & (e) Borges VC, Santos FW, Rocha JB, Nogueira CW. Neurochem Res. 2007 Jun;32 (6):953-8; & (f) Exploration of the direct metabolic effects of mercury II chloride on the kidney of Sprague-Dawley rats using high-resolution magic angle spinning 1H NMR spectroscopy of intact tissue and pattern recognition; Wang Y, Bollard ME, Nicholson JK, Holmes E. J Pharm Biomed Anal. 2006 Feb 13;40 (2):375-81; & Mercury compounds disrupt neuronal glutamate transport in cultured mouse cerebellar granule cells; Fonfría E, Vilaró MT, Babot Z, Rodríguez-Farré E, SuÃ*pm*ol C. J Neurosci Res. 2005 Feb 15;79 (4):545-53

(126) (a) Singh I, Pahan K, Khan M, Singh AK. Cytokine-mediated induction of ceramide production is redox-sensitive. Implications to proinflammatory cytokine-mediated apoptosis in demyelinating diseases. J Biol Chem. 1998 Aug 7;273 (32):20354-62; & Pahan K, Raymond JR, Singh I. Inhibition of phosphatidylinositol 3-kinase induces nitric-oxide synthase in lipopolysaccharide-or cytokine-stimulated C6 glial cells. J. Biol. Chem. 274: 7528-7536, 1999; & Xu J, Yeh CH, et al, Involvement of de novo ceramide biosynthesis in tumor necrosis factor-alpha/cycloheximide-induced cerebral endothelial cell death. J Biol Chem. 1998 Jun 26;273 (26):16521-6; & Dbaibo GS, El-Assaad W, et al, Ceramide generation by two distinct pathways in tumor necrosis factor alpha-induced cell

[14] **Internet:** "http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6T5F-4PGPM2B-1&_user=10&_coverDate=12%2F31%2F2007&_rdoc=1&_fmt=full&_orig=browse&_cdi=5001&_sort=d&_docanchor=&view=c&

death. FEBS Lett. 2001 Aug 10;503 (1):7-12; & Liu B, Hannun YA.et al, Glutathione regulation of neutral sphingomyelinase in tumor necrosis factor-alpha-induced cell death.J Biol Chem. 1998 May 1;273 (18): 11313-20; & (b) Noda M, Wataha JC, et al, Sublethal, 2-week exposures of dental material components alter TNF-alpha secretion of THP-1 monocytes. Dent Mater. 2003 Mar;19 (2):101-5; & Kim SH, Johnson VJ, Sharma RP. Mercury inhibits nitric oxide production but activates proinflammatory cytokine expression in murine macrophage: differential modulation of NF-kappaB and p38 MAPK signaling pathways. Nitric Oxide. 2002 Aug;7 (1):67-74; & Dastych J, Metcalfe DD et al, Murine mast cells exposed to mercuric chloride release granule-associated N-acetyl-beta-D-hexosaminidase and secrete IL-4 and TNF-alpha. J Allergy Clin Immunol. 1999 Jun;103 (6):1108-14; & (c) Tortarolo M, Veglianese P, et al, Persistent activation of p38 mitogen-activated protein kinase in a mouse model of familial amyotrophic lateral sclerosis correlates with disease progression.. Mol Cell Neurosci. 2003 Jun;23 (2):180-92.

(131) Christensen MM, Ellermann-Eriksen S, Mogensen SC. Influence of mercury chloride on resistance to generalized infection with herpes simplex virus type 2 in mice. Toxicology 1996, 114 (1): 57-66;

(142) Ariza ME; Bijur GN; Williams MV. Lead and mercury mutagenesis: role of $H_2O_2$, superoxide dismutase, and xanthine oxidase. Environ Mol Mutagen 1998;31 (4):352-61; & M.E. Ariza et al, "Mercury mutagenisis", Biochem Mol Toxicol, 1999, 13 (2):107-12; & M.E.Ariza et al, "Mutagenic effect of mercury", InVivo 8 (4):559-63, 1994;

(145) J.M.Gorell et al, "Occupational exposure to mercury, manganese, copper, lead, and the risk of Parkinson's disease", Neurotoxicology, 1999, 20 (2-3): 239-47

(147) .M.Wood, "Mechanisms for the Neurotoxicity of Mercury", in Organotransitional Metal Chemistry, Plenum Publishing Corp, N.Y, N.Y, 1987. & R.P. Sharma et al, "Metals and Neurotoxic Effects", J of Comp Pathology, Vol 91, 1981.

(149) F. Monnet-Tschudi et al, "Comparison of the developmental effects of 2 mercury compounds on glial cells and neurons in the rat telencephalon", Brain Research, 1996, 741: 52-59

(152) Langworth et al, "Effects of low exposure to inorganic mercury on the human immune system", Scand J Work Environ Health, 19 (6): 405-413.1993; & Walum E et al, Use of primary cultures to sutdy astrocytic regulatory functions. Clin Exp Pharmoacol Physiol 1995, 22:284-7; & J Biol Chem 2000 Dec 8;275 (49):38620-5; & (b) Kerkhoff H, Troost D, Louwerse ES. Inflammatory cells in the peripheral nervous system in motor neuron disease. Acta Neuropathol 1993; 85:560-5; & (c) Appel Sh, Smith RG. Autoimmunity as an etiological factor in amyotrophic lateral sclerosis. Adv Neurol 1995; 68:47-57.

(169) C.H.Ngim et al, Neuroepidemiology, "Epidemiologic study on the association between body burden mercury level and idiopathic Parkinson's disease", 1989, 8 (3):128-41.

(175) L.Larkfors et al, "Methyl mercury induced alterations in the nerve growth factor level in the developing brain ", Res Dev Res, 62 (2), 1991, 287- ;

(181) Mathieson PW, "Mercury: god of TH2 cells", 1995, Clinical Exp Immunol., 102 (2):229-30; & (b) Heo Y, Parsons PJ, Lawrence DA, Lead differentially modifies cytokine production in vitro and in vivo. Toxicol Appl Pharmacol, 1996; 138:149-57; & (c) Murdoch RD, Pepys J; Enhancement of antibody and IgE production by mercury and platinum salts. Int Arch Allergy Appl Immunol 1986 80: 405-11;

(183) World Health Organization (WHO), 1991, Environmental Health criteria 118, Inorgtanic Mercury, WHO, Geneva; & Envir. H. Crit. 101, Methyl Mercury; 1990.

(194) Lu SC, FASEB J, 1999, 13 (10):1169-83, "Regulation of hepatic glutathione synthesis: current concepts and controversies"; & R.B. Parsons, J Hepatol, 1998, 29 (4):595-602; & R.K.Zalups et al, "Nephrotoxicity of inorganic mercury co-administered with L-cysteine", Toxicology, 1996, 109

(1): 15-29.

(198) Cd2+ and Hg2+ affect glucose release and cAMP-dependent transduction pathway in isolated eel hepatocytes. Aquat Toxicol. 2003 Jan 10;62 (1):55-65, Fabbri E, Caselli F, Piano A, Sartor G, Capuzzo A. & Fluctuation of trace elements during methylmercury toxication and chelation therapy. Hum Exp Toxicol. 1994 Dec;13 (12):815-23, Bapu C, Purohit RC, Sood PP; & E.S. West et al, Textbook of Biochemistry, MacMillan Co, 1957, p853;& B.R.G.Danielsson et al, "Ferotoxicity of inorganic mercury: distribution and effects of nutrient uptake by placenta and fetus", Biol Res Preg Perinatal. 5 (3):102-109, 1984; & Danielsson et al, Neurotoxicol. Teratol., 18:129-134;

(200) Kulacz & Levy, "The Roots of Disease". Xlibris Corporation at 1-888-795-4274 www.xlibris.com; & B.E. Haley, www.altcorp.com; & G. Mienig, Root Canal Coverup, 1997.; & Dr. T. Rau, Paracelsus Allergy Clinic, Lustmuhle, Switzerland, 1996 *www.flcv.com/damspr11.html*[15]

(207) Boyd Haley, Univ. Of Kentucky, "The Toxic Effects of Mercury on CNS Proteins: Similarity to Observations in Alzheimer's Disease", IAOMT Symposium paper, March 1997 & (b)"Mercury Vapor Inhaltion Inhibits Binding of GTP ...-Similarity to Lesions in Alzheimers Diseased Brains", Neurotoxicology, 18: 315- June 1997; & (c) Met Ions Biol Syst, 1997, 34:461-78 (* web page & dental lab:cavitations, root canals-www.altcorp.com/) &(d) Palkiewicz P, Zwiers H, Lorscheider FL; ADP-Ribosylation of Brain Neuronal Proteins Is Altered by In Vitro and In Vivo Exposure to Inorganic Mercury, Journal of Neurochemistry. 62 (5):2049-2052, 1994 May

(222) M. Daunderer, Handbuch der Amalgamvergiftung, Ecomed Verlag, Landsberg 1998, ISBN 3-609-71750-5 (in German); & "Improvement of Nerve and Immunological Damages after Amalgam Removal", Amer. J. Of Probiotic Dentistry and Medicine, Jan 1991 (amalgam replacement & DMPS, over 5,000 cases)

(226) B.J. Shenker et al, Dept. Of Pathology, Univ. Of Penn. School of Dental Med., "Immunotoxic effects of mercuric compounds on human lymphocytes and monocytes:Alterations in cell viability" Immunopharmacologicol Immunotoxical, 1992, 14 (3):555-77; & M.A.Miller et al, "Mercuric chloride induces apoptosis in human T lymphocytes", Toxicol Appl Pharmacol, 153 (2):250-7 1998; &(b) Rossi AD, Viviani B, Vahter M. Inorganic mercury modifies Ca2+ signals, triggers apoptosis, and potentiates NMDA toxicity in cerebral granule neurons. Cell Death and Differentiation 1997; 4 (4):317-24. & Goering PL, Thomas D, Rojko JL, Lucas AD. Mercuric chloride-induced apoptosis is dependent on protein synthesis. Toxicol Lett 1999; 105 (3): 183-95;

(229) M.Davis, editor, "Defense Against Mystery Syndromes", Chek Printing Co., & March, 1994 (case histories documented); & Kantarjian A, "A syndrome clininically resembling amyotrophic lateral sclerosis following chronic mercurialism", Neurology 11:639-644 (1961)

(241) R. Schoeny, U.S. EPA, "Use of genetic toxicology data in U.S. EPA risk assessment: the mercury study", Environ Health Perspect, 1996, 104, Supp 3: 663-73

(246) K.Iyer et al, "Mercury Poisoning in a dentist", Arch Neurol, 1976, 33: 788-790.

(250) Sorensen FW, Larsen JO, Eide R, Schionning JD. Neuron loss in cerebellar cortex of rats exposed to mercury vapor: a stereological study. Acta Neuropathol (Berl). 2000 Jul;100 (1):95-100; & Shikata E, Mochizuki Y, Oishi M, Takasu T. [A case of chronic inorganic mercury poisoning with progressive intentional tremor and remarkably prolonged latency of P300] Rinsho Shinkeigaku. 1998 Dec;38 (12):1064-6. & Yamanaga H, "Quantitative analysis of tremor in Minamata disease", Tokhoku J Exp Med, 1983 Sep, 141:1, 13-22

(252) B.J. Shenker et al, Dept. of Pathology, Univ. of Pennsylvania, "Immunotoxic effects of mercuric compounds on human lymphoctes and monocytes: Alterations in cellular glutathione content", Immunopharmacol Immunotoxicol 1993, 15 (2-3):273-90.

[15]**Informativo:** "Dental Amalgam Mercury Syndrome - DAMS".

(254) al-Saleh I, Shinwari N. Urinary mercury levels in females: influence of dental amalgam fillings. Biometals 1997; 10 (4): 315-23; & Zabinski Z; Dabrowski Z; Moszczynski P; Rutowski J. The activity of erythrocyte enzymes and basic indices of peripheral blood erythrocytes from workers chronically exposed to mercury vapors. Toxicol Ind Health 2000 Feb;16 (2):58-64.

(255) D.C. Rice, "Evidence of delayed neurotoxicity produced by methyl mercury developmental exposure", Neurotoxicology, Fall 1996, 17 (3-4), p583-96; & Weiss B, Clarkson TW, Simon W. Silent latency periods in methylmercury poisoning and in neurodegenerative disease. Environ Health Perspect. 2002 Oct;110 Suppl 5: 851-4.

(260) Woods JS et al, Altered porphyrin metabolites as a biomarker of mercury exposure and toxicity", Physiol Pharmocol, 1996, 74 (2):210-15, & Strubelt O, Kremer J, et al, Comparative studies on the toxicity of mercury, cadmium, and copper toward the isolated perfused rat liver. J Toxicol Environ Health. 1996 Feb 23;47 (3):267-83; & Kaliman PA, Nikitchenko IV, Sokol OA, Strel'chenko EV. Regulation of heme oxygenase activity in rat liver during oxidative stress induced by cobalt chloride and mercury chloride. Biochemistry (Mosc). 2001 Jan;66 (1):77-82.; & (d) Kumar SV, Maitra S, Bhattacharya S. In vitro binding of inorganic mercury to the plasma membrane of rat platelet affects Na+-K+-Atpase activity and platelet aggregation. Biometals. 2002 Mar;15 (1):51-7.

(263) Kumar AR, Kurup PA. Inhibition of membrane Na+-K+ ATPase activity: a common pathway in central nervous system disorders. J Assoc Physicians India. 2002 Mar;50:400-6

(264) B.R. Danielsson et al, "Behavioral effects of prenatal metallic mercury inhalation exposure in rats", Neurotoxicol Teratol, 1993, 15 (6): 391-6;& A. Fredriksson et al, Prenatal exposure to metallic mercury vapour and methylmercury produce interactive behavioral changes in adult rats", Neurotoxicol Teratol, 1996, 18 (2): 129-34

(270) D.W. Eggleston, "Effect of dental amalgam and nickel alloys on T-lympocytes", J Prosthet Dent. 51 (5):617-623, 1984; & D.W.Eggleston et al, Correlation of dental amalgam with mercury in brain tissue, J Prosthet Dent, 1987, 58 (6), 704-7;

(272) BJ Shenker, "Low-level MeHg exposure causes human T-cells to undergo apoptosis: evidence of mitochondrial disfunction", Environ Res, 1998, 77 (2): 149-159; & O.Insug et al, "Mercuric compounds inhibit human monocyte function by inducing apoptosis: evidence for formation of reactive oxygen species (ROS), development of mitochondrial membrane permeability, and loss of reductive reserve", Toxicology, 1997, 124 (3):211-24;

(275) American Journal of Human Genetics, *www.tinyurl.com/68s7j2*[16], Aug 2008

(287) Warfvinge K, Mercury distribution in the neonatal and adult cerebellum after mercury vapor exposure of pregnant squirrel monkeys, Environ Res 2000, 83 (2): 93-101;

(288) (a) Hisatome I, Kurata Y, et al; Block of sodium channels by divalent mercury: role of specific cysteinyl residues in the P-loop region. Biophys J. 2000 Sep;79 (3):1336-45; & Bhattacharya S, Sen S et al, Specific binding of inorganic mercury to Na (+)-K (+)-ATPase in rat liver plasma membrane and signal transduction. Biometals. 1997 Jul;10 (3):157-62; & Anner BM, Moosmayer M, Imesch E. Mercury blocks Na-K-ATPase by a ligand-dependent and reversible mechanism. Am J Physiol. 1992 May;262 (5 Pt 2):F830-6. & Anner BM, Moosmayer M. Mercury inhibits Na-K-ATPase primarily at the cytoplasmic side. Am J Physiol 1992; 262 (5 Pt2):F84308; & Wagner CA, Waldegger S, et al; Heavy metals inhibit Pi-induced currents through human brush-border NaPi-3 cotransporter in Xenopus oocytes.. Am J Physiol. 1996 Oct;271 (4 Pt 2):F926-30; & Lewis RN; Bowler K. Rat brain (Na+-K+) ATPase: modulation of its ouabain-sensitive K+-PNPPase activity by thimerosal. Int J Biochem 1983;15 (1):5-7 & (b) Rajanna B, Hobson M, Harris L, Ware L, Chetty CS. Effects of cadmium and mercury on Na (+)-K (+) ATPase and uptake of 3H-dopamine in rat brain synaptosomes. Arch Int Physiol Biochem 1990, 98 (5):291-6; & M.Hobson,

[16]**Internet:** "http://www.tinyurl.com/68s7j2".

B.Rajanna, "Influence of mercury on uptake of dopamine and norepinephrine", Toxicol Letters, Dep 1985, 27:2-3:7-14; & & McKay SJ, Reynolds JN, Racz WJ. Effects of mercury compounds on the spontaneous and potassium-evoked release of [3H]dopamine from mouse striatial slices. Can J Physiol Pharmacol 1986, 64 (12): 1507-14; & Scheuhammer AM; Cherian MG. Effects of heavy metal cations, sulfhydryl reagents and other chemical agents on striatal D2 dopamine receptors. Biochem Pharmacol 1985 Oct 1;34 (19):3405-13 ;& K.R.Hoyt et al, "Mechanisms of dopamine-induced cell death and differences from glutamate Induced cell death", Exp Neurol 1997, 143 (2):269-81; & & (c) Offen D, et al, Antibodies from ALS patients inhibit dopamine release mediated by L-type calcium channels. Neurology 1998 Oct;51 (4):1100-3.

(291) H.A. Huggins, Solving the MS Mystery, 2002, & *http://www.hugginsappliedhealing.com/ms.php*[17] ; & H.A. Huggins & TE Levy, "cerebrospinal fluid protein changes in MS after Dental amalgam removal", Alternative Med Rev, Aug 1998, 3 (4):295-300.

(293) H.Huggins, Burton Goldberg, & Editors of Alternative Medicine Digest, Chronic Fatigue Fibromyalgia & Environmental Illness, Future Medicine Publishing, Inc, 1998, p197-; & CFS, *www.hugginsappliedhealing.com/fatigue.php*[18] & Depression, *www.hugginsappliedhealing.com/emotional.php*[19]

(296) L.Bucio et al, Uptake, cellular distribution and DNA damage produced by mercuric chloride in a human fetal hepatic cell line. Mutat Res 1999 Jan 25;423 (1-2):65-72; & & (b) Ho PI, Ortiz D, Rogers E, Shea TB. Multiple aspects of homocysteine neurotoxicity: glutamate excitotoxicity, kinase hyperactivation and DNA damage. J Neurosci Res. 2002 Dec 1;70 (5):694-702; &(c) & Snyder RD; Lachmann PJ; Thiol involvement in the inhibition of DNA repair by metals in mammalian cells. Source Mol Toxicol, 1989 Apr-Jun, 2:2, 117-28 L.Verschaeve et al, "Comparative in vitro cytogenetic studies in mercury-exposed human lymphocytes", Muta Res, 1985, 157 (2-3):221-6; & L.Verschaeve, "Genetic damage induced by low level mercury exposure", Envir Res, 12:306-10, 1976.

(303) Heavy Metals and Chronic Diseases, Dr. Dietrich Klinghardt, M.D., PhD, *http://www.neuraltherapy.*

(305) Soderstrom S, Fredriksson A, Dencker L, Ebendal T, "The effect of mercury vapor on cholinergic neurons in the fetal brain, Brain Research & Developmental Brain Res, 1995, 85:96-108; & Toxicol Lett 1995; 75 (1-3): 133-44.; & (b) E.M. Abdulla et al, "Comparison of neurite outgrowth with neurofilament protein levels In neuroblastoma cells following mercuric oxide exposure", Clin Exp Pharmocol Physiol, 1995, 22 (5): 362-3: &(c) Leong CC, Syed NI, Lorscheider FL. Retrograde degeneration of neurite membrane structural integrity of nerve growth cones following in vitro exposure to mercury. Neuroreport 2001 Mar 26;12 (4):733-7

(307) Duhr EF, Pendergrass JC, Slevin JT, Haley BE: HgEDTA complex inhibits GTP interactions with the E-site of brain beta-tubulin. Toxicology & Applied Pharmacology 1993; 122 (2): 273-80.

(313) Alexianu ME, Kozovska M, Appel SH. Immune reactivity in a mouse model of familial ALS correlates with disease progression. Neurology 2001 Oct 9;57 (7): 1282-9

(314) M.Kubicka-Muranyi et al, "Systemic autoimmune disease induced by mercuric chloride", Int Arch Allergy Immunol;1996, 109 (1):11-20 & M.Goldman et al, 1991, "Chemically induced autoimmunity ...", Immunology Today, 12:223-; & K. Warfyinge et al, "Systemic autoimmunity due to mercury vapor exposure in genetically susceptible mice", Toxicol Appl Pharmacol, 1995, 132 (2):299-309;& (b) L.M. Bagenstose et al, "Mercury induced autoimmunity in humans", Immunol Res, 1999, 20 (1): 67-78; &"Mercury-induced autoimmunity", Clin Exp Immunol, 1998, 114 (1):9-12;

(315) B.Engin-Deniz et al, "Die queckssilberkonzentration im spichel zehnjariger kinder in korrelation zur anzahl und Grobe iher amalgamfullungen", Zeitschrift fur Stomatologie, 1992, 89:471-179;

[17] **Internet:** "http://www.hugginsappliedhealing.com/ms.php".
[18] **Internet:** "http://www.hugginsappliedhealing.com/fatigue.php".
[19] **Internet:** "http://www.hugginsappliedhealing.com/emotional.php".
[20] **Internet:** "http://www.neuraltherapy.com/a_metals_disease.asp".

(316) B.J.Shenker et al, Dept. Of Pathology, Univ. Of Pennsylvania School of Dental Medicine, "Immunotoxic effects of mercuric compounds on human lymphocytes and monocytes: Alterations in B-cell function and viability" Immunopharmacol Immunotoxicol, 1993, 15 (1):87-112; & J.R.Daum, "Immunotoxicology of mercury and cadmium on B-lymphocytes", Int J Immunopharmacol, 1993, 15 (3):383-94; & Johansson U, et al, "The genotype determines the B cell response in mercury-treated mice", Int Arch Allergy Immunol, 116 (4):295-305, (Aug 1998)

(325) B. Arvidson (Sweden), Inorganic mercury is transported from muscular nerve terminals to spinal and brainstem motorneurons. Muscle Nerve, 1992, 15 (10);1089-94, & Mitchell JD. Heavy metals and trace elements in amyotrophic lateral sclerosis. Neurol Clin 1987 Feb;5 (1):43-60; & M. Su et al, Selective involvement of large motor neurons in the spinal cord of rats treated with methylmercury. J Neurol Sci, 1998, 156 (1):12-7;

(327) (a) G. Danscher et al, Environ Res, "Localization of mercury in the CNS", 1986, 41:29-43; &(b) Danscher G; Horsted-Bindslev P; Rungby J. Traces of mercury in organs from primates with amalgam fillings. Exp Mol Pathol 1990;52 (3):291-9; & (c) "Ultrastructural localization of mercury after exposure to mercury vapor", Prog Histochem Cytochem, 1991, 23:249-255; &(d) Pamphlett R, Coote P, "Entry of low doses of mercury vapor into the nervous system", Neurotoxicology, 1998, 19 (1):39-47; & (e) Pamphlett et al, "Oxidative damage to nucleic acids in motor neurons containing Hg", J Neurol Sci, 1998, 159 (2): 121-6. (rats & primates); & (f) Pamphlett R, Waley P, "Motor Neuron Uptake of Low Dose Inorganic Mercury", J. Neurological Sciences 135: 63-67 (1996); & (g) Schionning JD, Danscher G, "Autometallographic inorganic mercury correlates with degenerative changes in dorsal root ganglia of rats intoxicated with organic mercury", APMIS 1999 Mar;107 (3):303-10

(329) Arvidson B; Arvidsson J; Johansson K, "Mercury Deposits in Neurons of the Trigeminal Ganglia After Insertion of Dental Amalgam in Rats", Biometals; 7 (3) p261-263 1994; &(b) Arvidson B. Inorganic mercury is transported from muscular nerve terminasl to spinal and brainstem motorneurons. Muscle Nerve 1992, 15: 1089-94; & Arvidson B, et al, Acta Neurol Scand, "Retograde axonal transport of mercury in primary sensory neurons" 1990, 82:324-237 & Neurosci Letters, 1990, 115:29-32; & (c) S.M. Candura et al, "Effects of mercuryic chloride and methyly mercury on cholinergic neuromusular transmission", Pharmacol Toxicol 1997; 80 (5): 218-24; & (d) Castoldi AF et al, "Interaction of mercury compounds with muscarinic receptor subtypes in the rat brain", Neurotoxicology 1996; 17 (3-4): 735-41;

(330) Wilkinson LJ, Waring RH. Cysteine dioxygenase: modulation of expression in human cell lines by cytokines and control of sulphate production. Toxicol In Vitro. 2002 Aug;16 (4):481-3; & (b) M.T.Heafield et al, "Plasma cysteine and sulphate levels in patients with Motor neurone disease, Parkinson's Disease, and Alzheimer's Disease", Neurosci Lett, 1990, 110 (1-2), 216, 20; & A.Pean et al, "Pathways of cysteine metabolism in MND/ALS", J neurol Sci, 1994, 124, Suppl:59-61; & Steventon GB, et al; Xenobiotic metabolism in motor neuron disease, The Lancet, Sept 17 1988, p 644-47; & Neurology 1990, 40:1095-98; & Cysteine, sulfite, and glutamate toxicity: a cause of ALS? Woolsey PB. J Altern Complement Med. 2008 Nov;14 (9):1159-64

(331) C.Gordon et al, "Abnormal sulphur oxidation in systemic lupus erythrmatosus (SLE) ", Lancet, 1992, 339:8784, 25-6; & P.Emory et al, "Poor sulphoxidation in patients with rheumatoid arthitis", Ann Rheum Dis, 1992, 51: 3, 318-20; & Bradley H, et al, Sulfate metabolism is abnormal in patients with rheumatoid arthritis. Confirmation by in vivo biochemical findings. J Rheumatol. 1994 Jul;21 (7):1192-6; & T.L. Perry et al, "Hallevorden-Spatz Disease: cysteine accumulation and cysteine dioxygenase defieciency", Ann Neural, 1985, 18 (4):482-489.

(333) A.J. Freitas et al, "Effects of Hg2+ and CH3Hg+ on Ca2+ fluxes in the rat brain", Brain Research, 1996, 738 (2): 257-64; & P.R.Yallapragoda et al, "Inhibition of calcium transport by Hg salts" in rat cerebellum and cerebral cortex", J Appl toxicol, 1996, 164 (4): 325-30; & E.Chavez et al, "Mitochondrial calcium release by Hg+2", J Biol Chem, 1988, 263:8, 3582-; A. Szucs et al, Effects

of inorganic mercury and methylmercury on the ionic currents of cultured rat hippocampal neurons. Cell Mol Neurobiol, 1997, 17 (3): 273-8; & D.Busselberg, 1995, "Calcium channels as target sites of heavy metals", Toxicol Lett, Dec;82-83:255-61; & Cell Mol Neurobiol 1994 Dec;14 (6): 675-87; & Rossi AD, et al, Modifications of Ca2+ signaling by inorganic mercury in PC12 cells. FASEB J 1993, 7:1507-14.

(338) (a) W.Y.Boadi et al, Dept. Of Food Engineering and Biotechnology, T-I Inst of Tech., Haifa, Israel, "In vitro effect of mercury on enzyme activities and its accumulation in the first-trimester human placenta", Environ Res, 1992, 57 (1):96-106;& "In vitro exposure to mercury and cadmium alters term human placental membrane fluidity", Pharmacol, 1992, 116 (1): 17-23; & (b) J.Urbach et al, Dept. of Obstetrics & Gynecology, Rambam Medical Center, Haifa, Israel, "Effect of inorganic mercury on in vitro placental nutrient transfer and oxygen consumption", Reprod Toxicol, 1992, 6 (1):69-75;& (c) Karp W, Gale TF et al, Effect of mercuric acetate on selected enzymes of maternal and fetal hamsters" Environmental Research, 36:351-358; & W.B. Karp et al, "Correlation of human placental enzymatic activity with tracemetal concentration in placenta", Environ Res. 13:470- 477, 1977; & (d) Boot JH. Effects of SH-blocking compounds on the energy metabolism and glucose uptake in isolated rat hepatocytes. Cell Struct Funct 1995 Jun;20 (3):233-8.

(346) Clauw DJ, "The pathogenesis of chronic pain and fatigue syndroms: fibromyalgia" Med Hypothesis, 1995, 44:369-78; & Hanson S, Fibromyalgia, glutamate, and mercury. Heavy Metal Bulletin, Issue 4, 1999, p5, 6.

(342) Metal-specific lymphocyte reactivity is downregulated after dental metal replacement. Yaqob A, Danersund A, Stejskal VD, Lindvall A, Hudecek R, Lindh U., Neuro Endocrinol Lett. 2006 Feb-Apr;27 (1-2):189-97; & Stejskal VDM, Danersund A, Lindvall A. Metal-specific memory lympocytes: biomarkers of sensitivity in man. Neuroendocrinology Letters 1999; & Stejskal V, Hudecek R, Mayer W, "Metal-specific lymphocytes: risk factors in CFS and other related diseases", Neuroendocrinology Letters, 20: 289-298, 1999; (patients with fatigue)

(369) Sterzl I, Prochazkova J, Stejskal VDM et al, Mercury and nickel allergy: risk factors in fatigue and autoimmunity. Neuroendocrinology Letters 1999; 20: 221-228; & Prochazkova J, Sterzl I, Kucerova H, Bartova J, Stejskal VD; The beneficial effect of amalgam replacement on health in patients with autoimmunity. Neuro Endocrinol Lett. 2004 Jun;25 (3):211-8. *http://www.melisa.org/pdf/Mercur and-autoimmunity.pdf*[21]

(386) Doctors Data Lab, http://www.doctorsdata.com, inquiries@doctors data.com, & Great Smokies Diagnostic Lab, http://www.gsdl.com; & MetaMatrix Lab, http://www.metamatrix.com & Biospectron/LMI, Lennart Mansson International ABlmi.analyslab@swipnet.se.

(404) M. E. Godfrey, Candida, Dysbiosis and Amalgam. J. Adv. Med. vol 9 no 2 (1996); & Romani L, Immunity to Candida Albicans: Th1, Th2 cells and beyond. Curr Opin Microbiol 1999, 2 (4):363-7

(405) J Stejskal, V Stejskal. The role of metals in autoimmune diseases and the link to neuroendocrinology Neuroendocrinology Letters, 20:345-358, 1999. http://www.melisa.org

(406) The Edelson Clinic, Atlanta, Ga. (www.edelsoncenter.com/ALS/als_an.htm)

(411) Puschel G, Mentlein R, Heymann E, 'Isolation and characterization of dipeptyl peptidase IV from human placenta', Eur J Biochem 1982 Aug;126 (2):359-65; & Kar NC, Pearson CM. Dipeptyl Peptidases in human muscle disease. Clin Chim Acta 1978; 82 (1-2): 185-92; & Seroussi K, Autism and Pervasive Developmental Disorders, 1998, p174, etc.; & Shibuya-Saruta H, Kasahara Y, Hashimoto Y. Human serum dipeptidyl peptidase IV (DPPIV) and its unique properties. J Clin Lab Anal. 1996;10 (6):435-40; & Blais A, Morvan-Baleynaud J, Friedlander G, Le Grimellec C. Primary culture of rabbit proximal tubules as a cellular model to study nephrotoxicity of xenobiotics. Kidney

[21] **Internet:** "http://www.melisa.org/pdf/Mercury-and-autoimmunity.pdf".

Int. 1993 Jul;44 (1):13-8

(412) Moreno-Fuenmayor H, Borjas L, Arrieta A, Valera V, Plasma excitatory amino acids in autism. Invest Clin 1996, 37 (2):113-28;& Carlsson ML. Is infantile autsim a hypoglutamatergic disorer? J Neural Transm 1998, 105 (4-5): 525-35. & (b) Rolf LH, Haarman FY, Grotemeyer KH, Kehrer H. Serotonin and amino acid content in platelets of autistic children. Acta Psychiatr Scand 1993, 87 (5): 312-6; & (c) Naruse H, Hayashi T, Takesada M, Yamazaki K. Metabolic changes in aromatic amino acids and monoamines in infantile autism and a new related treatment, No To Hattatsu, 1989, 21 (2):181-9;

(416) (a) Plaitakis A, Constantakakis E. Altered metabolism of excitatory amino acids, N-acetyl-aspartate and - acetyl-aspartyl-glutamate in amyotrophic lateral sclerosis. Brain Res Bull 1993;30 (3-4):381-6 &(b) Rothstein JD, Martin LJ, Kuncl RW. Decreased glutamate transport by the brain and spinal cord in ALS. New Engl J Med 1992, 326: 1464-8:& (c) Leigh Pn. Pathologic mechanisms in ALS and other motor neuron diseases. In: Calne DB (Ed.), Neurodegenerative Diseases, WB Saunder Co., 1997, p473-88; & P.Froissard et al, Universite de Caen, "Role of glutathione metabolism in the glutamate-induced programmed cell death of neuronal cells" Eur J Pharmacol, 1997, 236 (1): 93-99; & (d) Oxidative and excitotoxic insults exert differential effects on spinal motoneurons and astrocytic glutamate transporters: Implications for the role of astrogliosis in amyotrophic lateral sclerosis. Zagami CJ, Beart PM, Wallis N, Nagley P, O'Shea RD. Glia. 2009 Jan 15;57 (2):119-35; & Focal degeneration of astrocytes resulting from excitotoxicity in amyotrophic lateral sclerosis; Rossi D, Brambilla L, *Valori CF*[22], Roncoroni C, Crugnola A, Yokota T, Bredesen DE, Volterra A. Cell Death Differ. 2008 Nov;15 (11):1691-700. Epub 2008 Jul 11 ;& Kim P, Choi BH. "Selective inhibition of glutamate uptake by mercury in cultured mouse astrocytes", Yonsei Med J 1995; 36 (3): 299-305; & Brookes N. In vitro evidence for the role of glutatmate in the CNS toxicity of mercury. Toxicology 1992, 76 (3):245-56; & Albrecht J, Matyja E. Glutamate: a potential mediator of inorganic mercury toxicity. Metab Brain Dis 1996; 11:175-84; &(e) Tirosh O, Sen CK, Roy S, Packer L. Cellular and mitochondrial changes in glutamate-induced HT4 neuronal cell death Neuroscience. 2000;97 (3):531-41; &(f) Plasma glutamate and glycine levels in patients with amyotrophic lateral sclerosis; Andreadou E, Vassilopoulos D et al. In Vivo. 2008 Jan-Feb;22 (1):137-41

(417) Folkers K et al, Biochemical evidence for a deficiency of vitamin B6 in subjects reacting to MSL-Glutamate. Biochem Biophys Res Comm 1981, 100: 972; & Felipo V et al, L-carnatine increases the affinity of glutamate for quisqualate receptors and prevents glutamate neurotoxicity. Neurochemical Research 1994, 19 (3): 373-377; & Akaike A et al, Protective effects of a vitamin-B12 analog (methylcobalamin, against glutamate cytotoxicity in cultured cortical neurons. European J of Pharmacology 1993, 241 (1):1-6.

(418) Srikantaiah MV; Radhakrishnan AN. Studies on the metabolism of vitamin B6 in the small intestine. Purification and properties of monkey intestinal pyridoxal kinase. Indian J Biochem 1970 Sep;7 (3):151-6.

(423) T.Barber, "Inorganic mercury intoxification similar to ALS", J of Occup Med, 1978, 20:667-9; & Brown IA. Chronic mercurialism-a cause of the clinical syndrome of ALS. Arch Neurol Psychiatry 1954, 72:674-9; & Schwarz S, Husstedt I. ALS after accidental injection of mercury. J Neurol Neurosurg Psychiatry 1996, 60:698; & Felmus MT, Patten BM, Swanke L; Antecedent events in amyotrophic lateral sclerosis Neurology 1976 Feb;26 (2):167-72; & Patten BM, Mallette LE. Motor neuron disease: retrospective study of associated abnormalities. Dis Nerv Syst 1976 Jun;37 (6):318-21.

(424) Cephalon, Inc., http://www.cephalon.com/

(427) Chetty CS, McBride V, Sands S, Rajanna B. Effects in vitro on rat brain Mg (++)-ATPase. Arch Int Physiol Biochem 1990, 98 (5):261-7; & (b) Bara M, Guiet-Bara A, Durlach J. Comparison of the effects of taurine and magnesium on electrical characteristics of artificial and natural membranes.

[22]**Internet:** "http://www.ncbi.nlm.nih.gov/sites/entrez?Db=pubmed&Cmd=Search&Term=%22Valori%20CF%22%5BAut

V. Study on the human amnion of the antagonism between magnesium, taurine and polluting metals. [ French] Magnesium. 1985;4 (5-6):325-32.

(428) O'Carroll RE, Masterton G, Goodwin GM. The neuropsychiatric sequelae of mercury poisoning. The Mad Hatter's disease revisited. Br J Psychiatry 1995, 167 (1): 95-8; & PUBLIC HEALTH REPORTS, PUBLIC HEALTH BULLETIN #263. March 28, 1941. Mercurialism and its control in the felt hat industry.

(430) Fukino H, Hirai M, Hsueh YM, Yamane Y. Effect of zinc pretreatment on mercuric chloride-induced lipid peroxidation in the rat kidney. Toxicol Appl Pharmacol 1984, 73 (3): 395-401; Estevez AG, Beckman JS et al, Induction of nitric oxide-dependent apoptosis in motor neurons by zinc-deficient superoxide dismustase. Science 1999 Dec 24;286 (5449):2498-500.

(432) Sutton KG, McRory JE, Guthrie H, Snutch TP. P/Q-type calcium channels mediate the activity-dependent feedback of syntaxin-1A. Nature 1999, 401 (6755): 800-4;

(437) Affinity Labeling Technology, Inc.(Dental Lab), oral toxicity testing technology and tests, see research web pages on amalgam toxicity, root canals, cavitaions. http://www.altcorp.com ; &(b) Amer. Colleg of Medical Genetics Working Group on ApoE and Alzheimer's Disease, JAMA, 1995, 274: 1627-29; & Godfrey ME, Wojcik DP, Krone CA. Apolipoprotein E genotyping as a potential biomarker for mercury neurotoxicity. J Alzheimers Dis. 2003 Jun;5 (3):189-95; & Mercury toxicity presenting as chronic fatigue, memory impairment and depression: diagnosis, treatment, susceptibility, and outcomes in a New Zealand general practice setting (1994-2006), Wojcik DP, Godfrey ME, Christie D, Haley BE. Northland Environmental Health Clinic, Neuro Endocrinol Lett. 2006 Aug;27 (4):415-23.

(439) Part 1, mercuric chloride intoxication. Bull Environ Contam Toxicol 1978; 20 (6): 729-35 Mondal MS, Mitra S. Inhibition of bovine xanthine oxidase activity by Hg2+ and other metal ions. J Inorg Biochem 1996; 62 (4): 271-9; & Sastry KV, Gupta PK. In vitro inhibition of digestive enzymes by heavy metals and their reversal by chelating agents: Bull Environ Contam Toxicol. 1978 Dec;20 (6):729-35. : & Gupta PK, Sastry KV. Effect of mercuric chloride on enzyme activities in the digestive system and chemical composition of liver and muscles of the catfish. Ecotoxicol Environ Saf. 1981 Dec;5 (4):389-400.

(442) Olanow CW, Arendash GW. Metals and free radicals in neurodegeneration. Curr Opin Neurol 1994, 7 (6):548-58; & Kasarskis EJ (MD), Metallothionein in ALS Motor Neurons (IRB #91-22026), FEDRIP DATABASE, National Technical Information Service (NTIS), ID: FEDRIP/1999/07802766.

(443) Troy CM, Shelanski ML. Down-regulation of copper/zinc superoxide dismutase causes apotic death in PC12 neuronal cells. Proc. National Acad Sci, USA, 1994, 91 (14):6384-7; & Rothstein JD, Dristol LA, Hosier B, Brown RH, Kunci RW. Chronic inhibition of superoxide dismutase produces apoptotic death of spinal neurons. Proc Nat Acad Sci, USA, 1994, 91 (10):4155-9.

(444) (a) Beal MF. Coenzyme Q10 administration and its potential for treatment of neurodegenerative diseases. Biofactors 1999, 9 (2-4):262-6; & DiMauro S, Moses LG; CoQ10 Use Leads To Dramatic Improvements In Patients With Muscular Disorder, Neurology, April 2001; & Matthews RT, Yang L, Browne S, Baik M, Beal MF. Coenzyme Q10 administration increases brain mitochondrial concentrations and exerts neuroprotective effects. Proc Natl Acad Sci U S A 1998 Jul 21;95 (15):8892-7; & Schulz JB, Matthews RT, Henshaw DR, Beal MF. Neuroprotective strategies for treatment of lesions produced by mitochondrial toxins: implications for neurodegenerative diseases. Neuroscience 1996 Apr;71 (4):1043-8; & Idebenone - Monograph. A potent antioxidant and stimulator of nerve growth factor. Altern Med Rev 2001 Feb;6 (1):83-86; & (b) Nagano S, Ogawa Y, Yanaghara T, Sakoda S. Benefit of a combined treatment with trientine and ascorbate in familial amyotrophic lateral sclerosis model mice. Neurosci Lett 1999, 265 (3): 159-62; & (c) C. Gooch et al, Eleanor & Lou Gehrig MDA/ALS Center at Columbia-Presbyterian Medical Center in New York; ALS Newsletter Vol. 6, No. 3 June 2001

(445) Clifford Lab, Dental Materials Biocompatability Testing, Colorada Springs, Colo.; & Peak Energuy Performance, inc., Dental Materials Biocompatibility Testing, http://www.peakenergy.com

(453) Blumer W, "Mercury toxicity and dental amalgam fillings", Journal of Advancement in Medicine, v.11, n.3, Fall 1998, p.219

(461) Rasmussen HH, Mortensen PB, Jensen IW. Depression and magnesium deficiency. Int J Psychiatry Med 1989;19 (1):57-63: & Bekaroglu M, Aslan Y, Gedik Y, Karahan C. Relationships between serum free fatty acids and zinc with ADHD. J Child Psychol Psychiatry 1996; 37 (2):225-7; & Maes M, Vandoolaeghe E, Neels H, Demedts P, Wauters, A, Meltzer HY, Altamura C, Desnyder R. Lower serum zinc in major depression is a sensitive marker of treatment resistance and of the immune/inflammatory response in that illness. Biol Psychiatry 1997;42 (5):349-358.

(462) Olivieri G; Brack C; Muller-Spahn F; Stahelin HB; Herrmann M; Renard P; Brockhaus M; Hock C. Mercury induces cell cytotoxicity and oxidative stress and increases beta-amyloid secretion and tau phosphorylation in SHSY5Y neuroblastoma cells. J Neurochem 2000 Jan;74 (1):231-6; & (b) Tabner BJ, Turnbull S, El-Agnaf OM, Allsop D. Formation of hydrogen peroxide and hydroxyl radicals from A (beta) and alpha-synuclein as a possible mechanism of cell death in Alzheimer's disease and Parkinson's disease. Free Radic Biol Med. 2002 Jun 1;32 (11):1076-83; &(c) Ho PI, Collins SC, et al; Homocysteine potentiates beta-amyloid neurotoxicity: role of oxidative stress. J Neurochem. 2001 Jul;78 (2): 249-53.

(463) Johnson S. The possible role of gradual accumulation of copper, cadmium, lead and iron and depletion of zinc, magnesium, selenium, vitamins B2, B6, D, and E and essential fatty acids in multiple sclerosis. Med Hypotheses 2000 Sep;55 (3):239-41; & White AR, Cappai R, Neurotoxicity from glutathione depletion is dependent on extracellular trace copper. J Neurosci Res. 2003 Mar 15;71 (6):889-97.

(464) Walsh, WJ, Health Research Institute, Autism and Metal Metabolism, http://www.hriptc.org/autism Oct 20, 2000; & Walsh WJ, Pfeiffer Treatment Center, Metal-Metabolism and Human Functioning, 2000, http://www.hriptc.org/mhfres.htm

(466) Chen KM, Department of Neurology, Guam Memorial Hospital; Disappearance of ALS from Guam: implications for exogenous causes, 2000.

(468) M.M. van Benschoten, "Acupoint Energetics of Mercury Toxicity and Amalgam Removal with Case Studies, " American Journal of Acupuncture, Vol. 22, No. 3, 1994, pp. 251-262; & M.M. Van Benschoten and Associates, Reseda, Calif. Clinic; http://www.mmvbs.com/

(469) BrainRecovery.com, the book, by David Perlmutter MD; Perlmutter Health Center, Naples, Florida, http://www.perlhealth.com/about.htm

(470) Dr. Garth Nicholson, Institute for Molecular Medicine, Huntington Beach, Calif., www.immed.org & Michael Guthrie, R.Ph. ImmuneSupport.com 07-18-2001 Mycoplasmas - The Missing Link in Fatiguing Illnesses, www.immunesupport.com/library/showarticle.cfm?ID=3066; & D. Cooper, ImmuneSupport.com, Professor Garth Nicolson's Studies and Treatments Explained, www.immed.org/reports/t & Dr. G. Nicholson, Institute for Molecular Medicine, New Treatments for Chronic Infections Found in Fibromyalgia Syndrome, Chronic Fatigue Syndrome, Rheumatoid Arthritis, Multiple Sclerosis, Amyotrophic Lateral Sclerosis, and Gulf War Illnesses, www.immed.org/reports/autoimmune_illness/rep1.htn & Nicolson G, Nasralla M, Haier J, Pomfret J. High frequency of systemic mycoplasmal infections in Gulf War veterans and civilians with Amyotrophic Lateral Sclerosis (ALS). J Clin Neurosci 2002 Sep;9 (5):525; & (b) Immunosciences Lab, www.immuno-sci-lab.com/index2.html

(471) Umanekii KG, Dekonenko EP. Structure of progressive forms of tick-borne encephalitis. Zh Nevropatol Psikhiatr Im S S Korsakova 1983;83 (8):1173-9. [article in Russian]; & B Hemmer, F X Glocker, R Kaiser. Generalised motor neuron disease as an unusual manifestation of Borrelia burgdorferi infection. J Neurol Neurosurg Psychiatry 1997;63:257-258;& Fredrikson S, Link H. CNS-

borreliosis selectively affecting central motor neurons. Acta Neurol Scand 1988;78:181-184[Medline]; & Halperin JJ, Kaplan GP, Brazinsky S, et al. Immunologic reactivity against Borrelia burgdorferi in patients with motor neuron disease. Arch Neurol 1990;47:586-594; & www.lymelink.com/chronic.htm

(477) Lars Landner and Lennart Lindestrom. Swedish Environmental Research Group (MFG), Copper in society and the Environment, 2nd revised edition. 1999; & White AR, Cappai R, Neurotoxicity from glutathione depletion is dependent on extracellular trace copper. J Neurosci Res. 2003 Mar 15;71 (6):889-97.

(485) Hulda Clark, The Cure for all Diseases, 2000, www.drclark.net (amalgam replacement, dental infection revision, detoxification, and treatment for parasites) (U.S. CDC confirms parasites common in those with chronic immune conditions) *http://www.drclark.net/en/testimonials/dental/index.php*[23] *http://www.drclark.net/en/testimonials/neuro/index.php*[24]

(489) Waggoner DJ, Bartnikas TB, Gitlin JD. The role of copper in neurodegenerative disease. Neurobiol Dis 1999 Aug;6 (4):221-30; & (b) Torsdottir G, Kristinsson J, Gudmundsson G, Snaedal J, Johannesson T. Copper, ceruloplasmin and superoxide dismustase (SOD) in amyotrophic lateral sclerosis. Pharmacol Toxicol 2000 Sep;87 (3):126-30; & (c) Estevez AG, Beckman JS et al, Induction of nitric oxide-dependent apoptosis in motor neurons by zinc-deficient superoxide dismustase. Science 1999 Dec 24;286 (5449): 2498-500; & (d) Cookson MR, Shaw PJ. Oxidative stress and motor neurons disease. Brain Pathol 1999 Jan;9 (1):165-86.

(490) Shibata N, Nagai R, Kobayashi M. Morphological evidence for lipid peroxidation and protein glycoxidation in spinal cords from sporadic amyotrophic lateral sclerosis patients. Brain Res 2001 Oct 26;917 (1):97-104 & Cookson MR, Shaw PJ. Oxidative stress and motor neurons disease. Brain Pathol 1999 Jan;9 (1):165-86.

(494) (a) Kobayashi MS, Han D, Packer L. Antioxidants and herbal extracts protect HT-4 neuronal cells against glutamate-induced cytotoxicity. Free Radic Res 2000 Feb;32 (2):115-24 (PMID: 10653482); & Ferrante RJ, Klein AM, Dedeoglu A, Beal MF. Therapeutic efficacy of EGb761 (Gingko biloba extract) in a transgenic mouse model of amyotrophic lateral sclerosis. J Mol Neurosci 2001 Aug;17 (1):89-96 & Packer L, Tritschler HJ, Wessel K. Neuroprotection by the metabolic antioxidant alpha-lipoic acid. Free Radic Biol Med 1997;22 (1-2):359- 78 (PMID: 8958163); &(e) Li Y, Liu L, et al. Vitamin E suppression of microglial activation is neuroprotective. J Neurosci Res 2001 Oct 15;66 (2):163-70

(495) Kang JH, Eum WS. Enhanced oxidative damage by the familial amyotrophic lateral sclerosis-associated Cu, Zn-superoxide dismustase mutants. Biochem Biophys Acta 2000 Dec 15;1524 (2-3):162-70; & (b) JH, Eum WS. Enhanced oxidative damage by the familial amyotrophic lateral sclerosis-associated Cu, Zn-superoxide dismustase mutants. Biochem Biophys Acta 2000 Dec 15; 1524 (2-3): 162-70; & (c) Liu H, Zhu H, Eggers DK, Nersissian AM, Faull KF, Goto JJ, Ai J, Sanders-Loehr J, Gralla EB, Valentine JS. Copper (2+) binding to the surface residue cysteine 111 of His46Arg human copper-zinc superoxide dismustase, a familial amyotrophic lateral sclerosis mutant. Biochemistry 2000 Jul 18;39 (28):8125-32; &(d) Wong PC, Gitlin JD; et al, Copper chaperone for superoxide dismustase is essential to activate mammalian Cu/Zn superoxide dismustase. Proc Natl Acad Sci U S A 2000 Mar 14;97 (6):2886-91; & (e) Kruman II, Pedersen WA, Springer JE, Mattson MP. ALS-linked Cu/Zn-SOD mutation increases vulnerability of motor neurons to excitotoxicity by a mechanism involving increased oxidative stress and perturbed calcium homeostasis. Exp Neurol 1999 Nov;160 (1):28-39

(496) Doble A. The role of excitotoxicity in neurodegenerative disease: implications for therapy. Pharmacol Ther 1999 Mar;81 (3):163-221; & Urushitani M, Shimohama S. N-methyl-D-aspartate receptor-mediated mitochondrial Ca (2+) overload in acute excitotoxic motor neuron death: a mech-

[23] **Internet:** "http://www.drclark.net/en/testimonials/dental/index.php".
[24] **Internet:** "http://www.drclark.net/en/testimonials/neuro/index.php".

anism distinct from chronic neurotoxicity after Ca (2+) influx. J Neurosci Res 2001 Mar 1;63 (5): 377-87; & Cookson MR, Shaw PJ. Oxidative stress and motor neurons disease. Brain Pathol 1999 Jan;9 (1):165-86

(497) Torres-Aleman I, Barrios V, Berciano J. The peripheral insulin-like growth factor system in amyotrophic lateral sclerosis and in multiple sclerosis. Neurology 1998 Mar;50 (3):772-6 ; & Dall R, Sonksen PH et al; The effect of four weeks of supraphysiological growth hormone administration on the insulin-like growth factor axis In women and men. GH-2000 Study Group. J Clin Endocrinol Metab 2000 Nov;85 (11):4193-200: & Pons S, Torres-Aleman I. Insulin-like growth factor-I stimulates dephosphorylation of ikappa B through the serine phosphatase calcineurin. J Biol Chem 2000 Dec 8;275 (49):38620-5;

(498) Lai EC, Rudnicki SA. Effect of recombinant human insulin-like growth factor-I on progression of ALS. A placebo-controlled study. Neurology 1997 Dec;49 (6):1621-30; & Yuen EC, Mobley WC. Therapeutic applications of neurotrophic factors in disorders of motor neurons and peripheral nerves. Mol Med Today 1995 Sep;1 (6):278-86; & Dore S, Kar S, Quirion R. Rediscovering an old friend, IGF-I: potential use in the treatment of neurodegenerative diseases. Trends Neurosci 1997 Aug;20 (8):326-31; & Couratier P, Vallat JM. Therapeutic effects of neurotrophic factors in ALS; Rev Neurol (Paris). 2000 Dec;156 (12):1075-7. French.

(499) Van den Berghe G, Bowers C et al, Neuroendocrinology of prolonged critical illness: effects of exogenous thyrotropin-releasing hormone and its combination with growth hormone secretagogues. J Clin Endocrinol Metab 1998 Feb; 83 (2):309-19.

(502) Vielhaber S, Kaufmann J, Kunz WS. Effect of Creatine Supplementation on Metabolite Levels in ALS Motor Cortices. Exp Neurol 2001 Dec;172 (2):377-82; & Andreassen OA, Jenkins BG, Dedeoglu A, Ferrante KL, Beal MF. Increases in cortical glutamate concentrations in transgenic amyotrophic lateral sclerosis mice are attenuated by creatine supplementation. J Neurochem 2001 Apr;77 (2): 383-90; & Friedlander, R et al, Combination of Creatine and Minocycline increase survival rate synergistically, Annals of Neurology, Jan 2003

(503) Protective effects of methylcobalamin, a vitamin B12 analog, against glutamate-induced neurotoxicity in retinal cell culture. Kikuchi M, Kashii S, Honda Y, Tamura Y, Kaneda K, Akaike A. Invest Ophthalmol Vis Sci. 1997 Apr;38 (5):848-54; van Rensburg SJ, Kotze MJ, Hon D, Haug P, Kuyler J, Hendricks M, Botha J, Potocnik FC, Matsha T, Erasmus RT. Metab Brain Dis. 2006 Sep;21 (2-3): 121-37. Epub 2006 May 26; & van Rensburg SJ, Kotze MJ, Hon D, Haug P, Kuyler J, Hendricks M, Botha J, Potocnik FC, Matsha T, Erasmus RT. Metab Brain Dis. 2006 Sep;21 (2-3):121-37. Epub 2006 May 26

(504) Activation of methionine synthase by insulin-like growth factor-1 and dopamine: a target for neurodevelopmental toxins and thimerosal, Waly M, Olteanu H, Deth RC et al, Mol Psychiatry. 2004 Apr;9 (4):358-70; & Mercury and multiple sclerosis, Clausen J. Acta Neurol Scand. 1993 Jun;87 (6):461-4

(505) **Chemical methylation of inorganic mercury with methylcobalamin, a vitamin B12 analog. Imura N**, Pan SK, Ukita T et al. Science. 1971 Jun 18; 172 (989): 1248-9; & Cobalamin-mediated mercury methylation by Desulfovibrio desulfuricans LS, Choi SC, Bartha R. Appl Environ Microbiol. 1993 Jan;59 (1):290-5, & Isolation of the provisionally named Desulfovibrio fairfieldensis from human periodontal pockets, Loubinoux J.; Bisson-Boutelliez C.; Miller N.; Le Faou A.E. Oral Microbiology and Immunology, Volume 17, Number 5, October 2002, pp. 321-323 (3)

(506) Leistevuo J, Pyy L, Osterblad M, Dental amalgam fillings and the amount of organic mercury in human saliva. Caries Res 2001 May-Jun; 35 (3):163-6

(507) Appel SH, Beers D, Siklos L, Engelhardt JI, Mosier DR. Calcium: the Darth Vader of ALS. Amyotroph Lateral Scler Other Motor Neuron Disord 2001 Mar;2 Suppl 1:S47-54;

(513) Niebroj-Dobosz I, Jamrozik Z, Janik P, Hausmanowa-Petrusewicz I, Kwiecinski H. Anti-neural antibodies in serum and cerebrospinal fluid of amyotrophic lateral sclerosis (ALS) patients. Acta Neurol Scand 1999 Oct;100 (4):238-43; & Appel SH, Stockton-Appel V, Stewart SS, Kerman RH. Amyotrophic lateral sclerosis. Associated clinical disorders and immunological evaluations. Arch Neurol 1986 Mar;43 (3):234-8: Pestronk A, Choksi R. Multifocal motor neuropathy. Serum IgM anti-GM1 ganglioside antibodies in most patients detected using covalent linkage of GM1 to ELISA plates. Neurology 1997 Nov;49 (5):1289-92; & Pestronk A, Adams RN, Cornblath D, Kuncl RW, Drachman DB, Clawson L. Patterns of serum IgM antibodies to GM1 and GD1a gangliosides in amyotrophic lateral sclerosis. Ann Neurol 1989 Jan;25 (1):98-102

(517) (a) Earl C, Chantry A, Mohammad N. Zinc ions stabilize the association of basic protein with brain myelin membranes. J Neurochem 1988; 51:718-24; & Riccio P, Giovanneli S, Bobba A. Specificity of zinc binding to myelin basic protein. Neurochem Res 1995; 20: 1107-13; & (b) Sanders B. The role of general and metal-specific cellular responses in protection and repair of metal-induced damage: stress proteins and metallothioneins. In: Chang L (Ed.), Toxicology of Metals. Lewis Publishers, CRC Press Inc, 1996, p835-52; & (c) Mendez-Alvarez E, Soto-Otero R, et al, Effects of aluminum and zinc on the oxidative stress caused by 6-hydroxydopamine autoxidation: relevance for the pathogenesis of Parkinson's disease. Biochim Biophys Acta. 2002 Mar 16;1586 (2):155-68.

(518) (a) Aluminum deposition in the central nervous system of patients with amyotrophic lateral sclerosis from the Kii Peninsula of Japan; Yasui M, Yase Y, Ota K, Garruto RM. Neurotoxicology. 1991 Fall;12 (3):615-20; & Intraneuronal deposition of calcium and aluminium in amyotropic lateral sclerosis of Guam; Garruto RM, Swyt C, Fiori CE, Yanagihara R, Gajdusek DC. Lancet. 1985 Dec 14;2 (8468):1353, & (b) Low-calcium, high-aluminum diet-induced motor neuron pathology in cynomolgus monkeys; Garruto RM, Shankar SK, Yanagihara R, Salazar AM, Amyx HL, Gajdusek DC. Acta Neuropathol. 1989;78 (2): 210-9; & Magnesium deficiency over generations in rats with special references to the pathogenesis of the Parkinsonism-dementia complex and amyotrophic lateral sclerosis of Guam; Oyanagi K, Kawakami E, Yasui M. et al; Neuropathology. 2006 Apr;26 (2):115-28; & [Similarities in calcium and magnesium metabolism between amyotrophic lateral sclerosis and calcification of the spinal cord in the Kii Peninsula ALS focus ] [Article in Japanese] ; Yasui M, Yoshida M, Tamaki T, Taniguchi Y, Ota K. No To Shinkei. 1997 Aug;49 (8):745-51; & Comparative study of chronic aluminum-induced neurofilamentous aggregates with intracytoplasmic inclusions of amyotrophic lateral sclerosis; Wakayama I, Nerurkar VR, Strong MJ, Garruto RM. Acta Neuropathol. 1996 Dec;92 (6):545-54

(519) Kong J, Xu Z. Mitochondrial degeneration in motor neurons triggers the onset of ALS in mice expressing a mutant SOD1 gene. J Neurosci 1998; 18:3241-50; & (b) Cassarino DS, Bennett JPJ, Mitochrondrial mutations and oxidative pathology, protective nuclear responses, and cell death in neurodegeneration. Brain Res Brain Res Rev 1999; 29:1-25.

(520) Mitchell JD. Heavy metals and trace elements in amyotrophic lateral sclerosis. Neurol Clin 1987 Feb;5 (1):43-60; & Sienko DG, Davis JP, Taylor JA. ALS: A case-control study following detection of a cluster in a small Wisconsin community. Arch Neurol 1990, 9:255-62; & Provinciali L, Giovagnoli A. Antecedent events in ALS: do they influence clinical onset and progression? Neuroepidemiology 1990, 9:255-62; Roelofs-Iverson RA, Elveback LR. ALS and heavy metals, Neurology 1984, 34:393-5; & ArmonC, O'Brien PC, Epidemiologic correlates of sporadic ALS. Neurology 1991, 41:1077-84; & Vanacore N, Corsi L, Fabrizio E, Bonifati V, Meco G, "Relationship between exposure to environmental toxins and motor neuron disease: a case report", Med Lav 1995 Nov-Dec; 86 (6): 522-33; & Yase Y. Environmental contribution to the ALS process. In: Serratrice Gea (Ed.), Neuromuscular Diseases, New York, Raven Press, 1984. P335-9.

(521) Guermonprez L, Ducrocq C, Gaudry-Talarmain YM. Inhibition of acetylcholine synthesis and tyrosine nitration induced by peroxynitrite are differentially prevented by antioxidants. Mol Pharmacol 2001 Oct;60 (4):838-46; & & (b) Mahboob M, Shireen KF, Atkinson A, Khan AT. Lipid

peroxidation and antioxidant enzyme activity in different organs of mice exposed to low level of mercury. J Environ Sci Health B. 2001 Sep;36 (5):687-97. & Miyamoto K, Nakanishi H, et al, Involvement of enhanced sensitivity of N-methyl-D-aspartate receptors in vulnerability of developing cortical neurons to methylmercury neurotoxicity. Brain Res. 2001 May 18;901 (1-2):252-8; & (c) Anuradha B, Varalakshmi P. Protective role of DL-alpha-lipoic acid against mercury-induced neural lipid peroxidation. Pharmacol Res. 1999 Jan;39 (1):67-80.

(522) Kawashima T, Doh-ura K, Iwaki T. Cognitive dysfunction in patients with amyotrophic lateral sclerosis is associated with spherical or crescent-shaped ubiquitinated intraneuronal inclusions in the parahippocampal gyrus and amygdala, but not in the neostriatum. Acta Neuropathol (Berl) 2001 Nov;102 (5): 467-72

(524) Urushitani M, Shimohama S. The role of nitric oxide in amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord 2001 Jun;2 (2):71-81; & Torreilles F, Salman-Tabcheh S, Guerin M, Torreilles J. Neurodegenerative disorders: the role of peroxynitrite.Brain Res Brain Res Rev 1999 Aug;30 (2):153-63; & Aoyama K, Matsubara K, Kobayashi S. Nitration of manganese superoxide dismutase in cerebrospinal fluids is a marker for peroxynitrite-mediated oxidative stress in neurodegenerative diseases. Ann Neurol 2000 Apr;47 (4):524-7; & Guermonprez L, Ducrocq C, Gaudry-Talarmain YM. Inhibition of acetylcholine synthesis and tyrosine nitration induced by peroxynitrite are differentially prevented by antioxidants. Mol Pharmacol 2001 Oct;60 (4):838-46

(525) Edited GluR2 (glutamate receptors), a gatekeeper for motor neurone survival? ; Buckingham SD, Kwak S, Jones AK, Blackshaw SE, Sattelle DB. Bioessays. 2008 Nov;30 (11-12):1185-92

(526) Ahlbom II, Cardis E, Green A, Linet M, Savitz D, Swerdlow A. Review of the Epidemiologic Literature on EMF and Health. Environ Health Perspect 2001 Dec;109 Suppl 6:911-933.

(565) Beuter A, de Geoffroy A, Edwards R. Quantitative analysis of rapid pointing movements in Cree subjects exposed to mercury and in subjects with neurological deficits. Environ Res. 1999 Jan;80 (1):50-63.

(572) (b) "Decreased phagocytosis of myelin by macrophages with ALA. Journal of Neuroimmunology 1998, 92:67-75; & (c) Packer L, Tritschler HJ, Wessel K. Neuroprotection by the metabolic antioxidant alpha-lipoic acid. Free Radic Biol Med 1997;22 (1-2):359-78 (PMID: 8958163); & McCarty MF. Versatile cytoprotective activity of lipoic acid may reflect its ability to activate signalling intermediates that trigger the heat-shock and phase II responses. Med Hypotheses 2001 Sep;57 (3):313-7 & Whiteman M, Tritschler H, Halliwell B. Protection against peroxynitrite-dependent tyrosine nitration and alpha 1-antiproteinase inactivation by oxidized and reduced lipoic acid. FEBS Lett 1996 Jan 22;379 (1):74-6 (PMID: 8566234); & Patrick L. Mercury toxicity and antioxidants: Part 1: role of glutathione and alpha-lipoic acid in the treatment of mercury toxicity. Altern Med Rev. 2002 Dec;7 (6):456-71. (d) & Z.Gregus et al, "Effect of lipoic acid on biliary excretion of glutathione and metals", Toxicol APPl Pharmacol, 1992, 114 (1):88-96;

(577) Joachim Mutter et al, Alzheimer Disease: Mercury as pathogenetic factor and apolipoprotein E as a moderator, Neuroendocrinol Lett 2004; 25 (5):331-339

(580) Life Enhancement Foundation (MDs), Disease Prevention and Treatment, Expanded 4th Edition, 2003. *www.life-enhancement.com*[25]

(582) Aluminum Hydroxide: Another Poison Pediatricians Inject in Babies; IMVA, *http://imva.info/index.hydroxide/*[26] ; & (b) "Vaccines Show Sinister Side" March 23, 2006, underlineit www.straight.com/content.cfm?id=16717[27] ; (c) Blaylock, Russell. The Blaylock Wellness Report Vol 1, Issue 1; & (d) Cave, Stephanie, Mitchell, Deborah "What Your Doctor May Not

[25] **Internet:** "http://www.life-enhancement.com/".
[26] **Internet:** "http://imva.info/index.php/vaccines/aluminum-hydroxide/".
[27] **Internet:** "http://www.straight.com/content.cfm?id=16717".

Tell You About Children's Vaccinations", Warner Books, 01 September, 2001; & (e) Waly, M. et al Activation of methionine synthase by insulin-like growth factor-1 and dopamine: a target for neurodevelopmental toxins and thimerosal. Department of Pharmaceutical Sciences, Northeastern University. Molecular Psychiatry (2004) 1-13; & (f) Haley, Boyd. Mercury and Thimerosal Toxicity: A Factor in Autism; & (g) Dr. Fudenberg's comments above were from his speech at the NVIC International Vaccine Conference, Arlington VA September, 1997; & (h) *http://www.chinadaily.com.cn/china/2006-03/25/content_552145.htm*[28]

(590) Proc Natl Acad Sci USA, 08; 105:2052-2057 & Dr. D G Williams, Alternatives, Vol 12, No. 13, July 2008; & Neuroscience, 03; 117:55-61 & Neuropsychopharmcology 00;23 (S2):S39 & Lancet 00; 356:1241-42; & Combined lithium and valproate treatment delays disease onset, reduces neurological deficits and prolongs survival in an amyotrophic lateral sclerosis mouse model; Feng HL, Leng Y, Ma CH, Zhang J, Ren M, Chuang DM. Neuroscience. 2008 Aug 26;155 (3):567-72. Epub 2008 Jun 21.

(592) Should Depressive Syndromes Be Reclassified as "Metabolic Syndrome Type II"? Ann Clin Psychiatry. 2007 Oct-Dec ;19 (4):257-64. McIntyre RS, Soczynska JK, Kennedy SH et al ;& Inflammation, depression and dementia: are they connected? Neurochem Res. 2007 Oct ;32 (10):1749-56. Epub 2007 Aug 20 Leonard BE.

(593) Vaccines, Depression and Neurodegeneration After Age 50, By Russell L. Blaylock, *www.flcv.com/vax*

(595) High fructose consumption combined with low dietary magnesium intake may increase the incidence of the metabolic syndrome by inducing inflammation. Magnes Res. 2006 Dec ;19 (4):237-43. Rayssiguier Y, Gueux E, et al; & (b) Dietary magnesium and fiber intakes and inflammatory and metabolic indicators in middle-aged subjects from a population-based cohort. Am J Clin Nutr. 2006 Nov;84 (5):1062-9 Bo S, Durazzo M, Pagano G. et al; & (c) Hypomagnesemia, oxidative stress, inflammation, and metabolic syndrome. Diabetes Metab Res Rev. 2006 Nov-Dec ;22 (6):471-6. Guerrero-Romero F, Rodríguez-Morán

(596) Effects of antidiabetic and antihyperlipidemic agents on C-reactive protein. Mayo Clin Proc. 2008 Mar ;83 (3):333-42, Dandona P; & Role of advanced glycation end products in hypertension and atherosclerosis: therapeutic implications. Cell Biochem Biophys. 2007 ;49 (1):48-63, Vasdev S, Gill V, Singal P.

(597) Effects of mercuric chloride on glucose transport in 3T3-L1 adipocytes. Toxicol In Vitro. 2005 Mar ;19 (2):207-14. Barnes DM, Kircher EA; & Effects of inorganic HgCl2 on adipogenesis. Toxicol Sci. 2003 Oct ;75 (2):368-77. Epub 2003 Jul 25, Barnes DM, Hanlon PR, Kircher EA; & (b) Heavy metal-induced inhibition of active transport in the rat small intestine in vitro. Interaction with other ions. Comp Biochem Physiol C. 1986 ;84 (2):363-8, Iturri SJ, PeÃpma A; & Interaction of the sugar carrier of intestinal brush-border membranes with HgCl2. Biochim Biophys Acta. 1980 May 8 ;598 (1):100-14, Klip A, Grinstein S, Biber J, Semenza G. *****

(598) Overcoming Depression, Dr. Russell Blaylock, The Blaylock Wellness Report, Vol 5, No. 3, March 2008, & Food Additives, What you eat can kill you, Vol 4, No. 10, *www.blaylockreport.com/*[30]

(599) Documentation of mercury exposure levels from dental amalgam fillings, B. Windham (ED), *www.flcv.com/damspr1.html*[31]

(600) B. Windham, Annotated bibliography: Exposure levels and health effects related to mercury/dental amalgam and results of amalgam replacement, 2002; (over 3000 medical study references

[28] **Internet:** "http://www.chinadaily.com.cn/china/2006-03/25/content_552145.htm".

[29] **Internet:** "http://translate.googleusercontent.com/translate_c?hl=pt-BR&sl=en&u=http://www.flcv.com/vaxinfla.html&prev=/search%3Fq%3Ddental%2Bamalgam%26hl%3Dpt-BR%26biw%3D1024%26bih%3D566%26prmd%3Divnsb&rurl=translate.google.com.br&usg=ALkJrhgtr54OtoDaiNqhXihoIk0l

[30] **Internet:** "http://www.blaylockreport.com/".

[31] **Informativo:** "Dental Amalgam Mercury Solutions".

documenting mechanism of causality of 40 chronic conditions and over 60,000 clinical cases of recovery or significant improvement of these conditions after amalgam replacement-documented by doctors) *www.flcv.com/amalg6.html*[32] & *www.flcv.com/hgremove.html*[33]

(601) B. Windham, Cognitive and Behavioral Effects of Toxic Metal Exposures, 2002; (over 150 medical study references) *www.flcv.com/tmlbn.html*[34]

(602) The mechanisms by which mercury causes chronic immune and inflamatory condtions, B.Windham (Ed.), 2002, *www.flcv.com/immunere.html*[35]

(603) The environmental effects of mercury from amalgam affect everyone. B. Windham (Ed.) (Gov't studies)

[32]**Informativo:** "Mercury Exposure Levels from Amalgam Dental Fillings; Documentation of Mechanisms by Which Mercury Causes over 30 Chronic Health Conditions; Results of Replacement of Amalgam Fillings; and Occupational Effects on Dental Staff".

[33]**Internet:** "http://www.flcv.com/hgremove.html".

[34]**Informativo:** "Effects of Toxic Metals on Learning Ability and Behavior".

[35]**Informativo:** "Immune Reactive Conditions: The Mercury Connection to Eczema, Psoriasis, Lupus, Asthma, Scleroderma, Rheumatoid Arthritis, and Allergies".