

Chronic Illness and Mercury Toxicity

Dietrich Klinghardt MD PhD

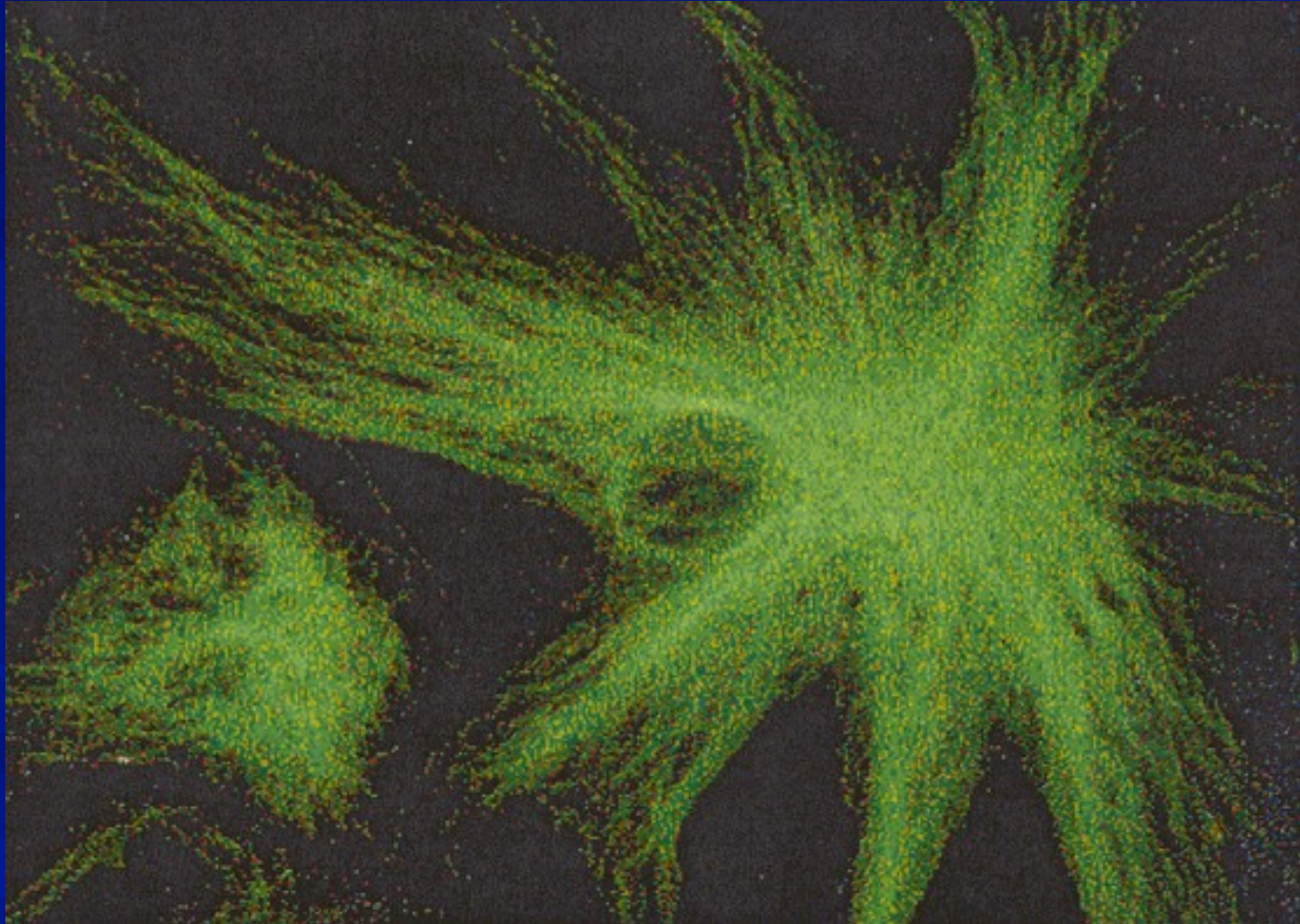
Institute of Neurobiology

www.neuraltherapy.com

Phone 425-637-9669

Fax 425-637-9339

Neuronal Tubulin, the Most Abundant Brain Protein, Is Especially Vulnerable to Mercury



Symptoms of Chronic Mercury Toxicity

Central Nervous System

- Irritability, anxiety/nervousness, often with difficulty in breathing
- Restlessness
- Exaggerated response to stimulation
- Fearfulness
- Emotional instability
 - Lack of self-control
 - Fits of anger, with violent, irrational behavior
- Loss of self-confidence, Indecision
- Shyness or timidity, being easily embarrassed
- Loss of memory, Inability to concentrate
- Lethargy/drowsiness
- Insomnia

Symptoms of Chronic Mercury Toxicity

Central Nervous System

- Mental depression, Manic depression, despondency
- Withdrawal, Suicidal tendencies
- Numbness and tingling of hands, feet, fingers, toes, or lips
- Muscle weakness progressing to paralysis
- Ataxia
- Tremors/trembling of hands, feet, lips, eyelids, or tongue
- Lack of coordination
- Myoneural transmission failure resembling Myasthenia Gravis
- Motor neuron disease (ALS), Multiple Sclerosis

Inorganic Mercury is Transported from Muscular Nerve Terminals to Spinal and Brainstem Motorneurons

Muscle and Nerve October 1992

Björn Arvidson, MD, PhD

"Evidence is presented that the mechanisms for accumulation of mercury in motorneurons of the spinal cord and brainstem is retrograde axonal transport from nerve terminals in muscle."

Oxidative damage to nucleic acids in motor neurons containing mercury

Journal of the Neurological Sciences 159 (1998) 121-126

Roger PAmphlett, Michael Slater, Siân Thomas

"...heavy metals have been implicated in the pathogenesis of sporadic motor neuron disease (MND). A method of examining oxidative damaged DNA in situ was used to examine individual motor neurons. Findings showed that environmental toxins such as mercury can enter and damage motor neurons..."

Evidence that mercury from silver dental fillings may be an etiological factor in smoking

Toxicity Letters 68 (1993) 307-310

The smoking habits of 119 subjects without silver/mercury dental fillings were compared to 115 subjects with amalgams. The amalgam group had 2.5 times more smokers per group than the non-amalgam group. Because mercury decreases dopamine, serotonin, norepinephrine, and acetylcholine in the brain and nicotine has just the opposite effects on these neurotransmitters, this may help explain why persons with amalgams smoke more than those without amalgams.

Symptoms of Chronic Mercury Toxicity Immune System

Amalgam/Mercury Detox as a Treatment for Chronic Viral, Bacterial, and Fungal Infections

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Editorial Note: The following article is a transcription of a lecture presented by Dr. Klinghardt at the Annual Meeting of the International and American Academy of Clinical Nutrition, San Diego, CA, September 1996.

On the Amalgam "Controversy"

From a scientific point of view there is no more "controversy" about the ill health effects of the metals contained in and released by the typical dental amalgam fillings. The sheep and monkey studies conducted at the University of Calgary, Canada—under the guidance of [i.e. Murray Vawr, DDS—showed that radioactively labeled mercury released from healthy and correctly placed amalgam fillings (in a monkey study) appeared quickly in the kidneys, brain and wall of the intestines. Through its affinity for sulphydryl-groups, mercury binds very firmly to structures in the nervous system. Other studies showed that mercury is taken up in the periphery by all nerve endings (i.e., the trigeminal nerve of the tongue,¹ the autonomic nerves of the lung or intestinal wall and coeliac plexus) and is, partially transported inside the axon of the nerves (axonal transport) to the spinal chord and brainstem.² On its way from the periphery to the brain, mercury immobilizes the cytoskeleton that is essential for "making" tubulin.³ Tubulin forms tubular structures within each nerve, along which the nerve-cell transports metabolic waste from the nerve cell into the periphery and along which the nutrients required by the nerve cell are transported from the periphery to the cell. Once mercury has traveled up the axon, the nerve cell is impaired in its ability to detoxify itself and in its ability to regenerate itself. The cell becomes toxic and dies—as lives in a state of chronic malnutrition. The mercury that has entered the nerve cell can no longer be excreted in the normal axonal transport routes (some can exit through the Ca²⁺ and Na⁺ channels) and begins to exert its more well-known ill-effects on the mitochondria, nucleus

and other organelles of the cell. A multitude of illnesses, usually associated with neurological symptoms, result.

Mercury and Chronic Infections

Practitioners have long observed that patients diagnosed with chronic viral illnesses (EBV, CMV, HIV, herpes zoster and genital herpes, CFIDS, etc.) chronic fungal illnesses (Candidiasis and others) and recurrent episodes of bacterial infections (chronic sinusitis, tonsillitis, bronchitis, bladder/prostate infections, HIV related infections) often have dramatic recoveries following an aggressive mercury/amalgam detoxification program.

The fact that the presence of mercury in the tissues impairs the immune system has long been known and is supported by the literature.^{4,5,6,7} This would explain a general immune enhancing effect of any solid mercury detoxification program. It has also been shown that the presence of amalgam fillings conveys immunity to antibiotics to various bacteria and also impairs the body's own defense system.⁸ Mercury is therefore the only substance ever shown that induces antibiotic resistance in bacteria, other than an antibiotic itself. It is known that periodontal disease is caused by bacteria and that the removal of amalgam fillings can often be curative.⁹ No studies have tested the mercury hypothesis in other infections, even though the clinical evidence is overwhelming.

In chronic fungal syndromes, the scientific literature gives only circumstantial evidence that mercury fosters these infections. The most valuable clinical pearls I found in a book written for the mining industry: "Absorption of Heavy Metals."¹⁰ To increase the yield of precious metals in old mines, so-called "blossoms" are sprayed into the mine shaft, washed out with water, and collected on ion exchange membranes. A blossom is a sludge of membranes from mostly mono-cellular organisms that have a tendency to accumulate metals in their outer cell wall that they are exposed to.

The list of organisms that have the highest affinity for toxic metals reads like a "who's who" of our typical infectious diseases fungi of the candida species, streptococci, staphylococci, amoebae, etc., etc. The list is topped by two algae: *Chlorella pyrenoidosa* and *Chlorella vulgaris* (not spirulina or super blue green algae). The list prompted me to state what in Germany is now referred to as the "Klinghardt Axiom": Most—if not all—chronic infectious diseases are not cured by a failure of the immune system, but are a conscious adaptation of the immune system to an otherwise lethal heavy metal environment. Mercury facilitates the intracellular respiratory mechanism and can cause cell death. So, the immune system makes a deal: it cultivates fungi and bacteria that can bind large amounts of toxic metals. The gain: the cells can breathe. The cost: the system has to provide nutrition for the microorganisms and has to deal with their metabolic products ("toxins"). That does not in any way mean that the cultured germ cannot grow out of control, as it sometimes clearly does. Therefore, there is still a limited place for antifungal/antibacterial treatment—but only for the acute phase of the disease. A so-called "die-off effect" (the sometimes severe crisis or even lethal reaction a patient can have in the initial stages of aggressive pharmacological antifungal or antibacterial treatment) is often nothing else but acute heavy metal toxicity—metals released from the cell walls of dying microorganisms as suggested by my own correlation of clinical symptoms and autopsies for metals. Collagran in Germany are working on a study at this time. Preliminary results show a dramatic improvement in clinical and scientific parameters in chronic Candidiasis using the Klinghardt protocol for heavy metal detoxification.

When it comes to chronic viral conditions, the evidence is even more circumstantial. There are several articles in the clinical literature showing remarkable

- Repeated infections
 - Viral and fungal
 - Mycobacterial
 - Candida and other yeast infections
- Cancer
- Autoimmune disorders
 - Arthritis
 - Lupus erythematosus (SLE)
 - Multiple sclerosis (MS)
 - Scleroderma
 - Amyolateral sclerosis (ALS)
 - Hypothyroidism

Symptoms of Chronic Mercury Toxicity

Cardiovascular Effects

- Abnormal heart rhythm/ tachycardia
- Characteristic findings on EKG
 - Abnormal changes in the S-T segment and/or lower
 - Broadened P wave
- Unexplained elevated serum triglycerides
- Unexplained elevated cholesterol
- Abnormal blood pressure, either high or low
- Cardiomyopathy
- Coronary heart disease
- Mitral valve prolapse

Symptoms of Chronic Mercury Toxicity

Systemic Effects

- Chronic headaches
- Allergies
- Severe dermatitis
- Unexplained reactivity (MCS)
- Thyroid disturbance
- Subnormal body temperature
- Cold, clammy skin, especially hands and feet
- Excessive perspiration, with frequent night sweats
- Unexplained sensory symptoms, including pain
- Unexplained numbness or burning sensations

Symptoms of Chronic Mercury Toxicity

Systemic Effects, cont.

- Unexplained anemia (G-6-PD deficiency)
- Chronic kidney disease
 - Nephritic syndrome
 - Receiving renal dialysis
 - Kidney infection
- Adrenal disease
- General fatigue
- Loss of appetite/with or without weight loss
- Loss of weight
- Hypoglycemia

From The IV-C Mercury Detox Program, A Guide for the Patient (S. and M.Ziff) and Chronic Mercury Toxicity, New Hope Against an Endemic Disease (H.L. and B. Queen).

Symptoms of Chronic Mercury Toxicity

Head, neck, oral cavity disorders

- Bleeding gums
- Alveolar bone loss
- Loosening of teeth
- Excessive salivation
- Foul breath
- Metallic taste
- Burning sensation, with tingling of lips, face

Symptoms of Chronic Mercury Toxicity

Head, neck, oral cavity disorders, cont.

- Tissue pigmentation (amalgam tattoo of gums)
- Leukoplakia
- Stomatitis
- Ulceration of gingival, palate, tongue
- Dizziness/acute, chronic vertigo
- Ringing in the ears
- Hearing difficulties
- Speech and visual impairment
 - Glaucoma
 - Restricted, dim vision

Symptoms of Chronic Mercury Toxicity

Gastrointestinal effects

- Food sensitivities, especially to milk and eggs
- Abdominal cramps, gas and bloating
- Colitis Crohn's disease, IBS
- Diverticulitis,
- Chronic diarrhea/constipation
- Dysbiosis
- Therapy resistant parasites
- Colon cancer

Chronic Illnesses

Examples are not generally known to be caused by mercury toxicity, but respond dramatically to systemic mercury elimination (personal observation)

- Alzheimer's disease
- Autism
- Lymphoma (non-Hodgkin)
- Most chronic pain syndromes
- Chronic intractable depression
- CFIDS and MCS
- Bowel Dysbiosis (yeast syndrome)
- Many Malignancies
- Behavioral disorders in children and teenagers
- Most addictions
- Premature aging
- Sexual disorders and infertility

Where does the mercury in our body come from?

- Corpse studies: in the brain 2-12 fold elevation of Hg level in people with amalgam fillings (does not account for people who had amalgam fillings in past but had them removed and none at time of death. The true number may be much higher)
- EPA (1991) over 90% of mercury body burden is from amalgam
- 70% of brain mercury from amalgam fillings (Aposhian et al. 1998).
- 77% of brain Hg from amalgam fillings (Weiner & Nylander)
- Even though fish contains significant and ever increasing amounts of methyl mercury, fish also contains mechanisms for detoxification (selenium etc.) that are effective within certain limits


Inorganic Mercury (Hg^{2+}) Transport through Lipid Bilayer Membranes

Membrane Biol. 61, 61-66 (1981)

John Gutknecht

This was a study of how various forms of inorganic mercury would diffuse through bilayer membranes. Different tissues varied in permeability and diffusion rates. However under all the different conditions it was shown that Chloride facilitated the diffusion of mercury through the lipid bilayer.

Visualization Of Mercury Emitting From A Dental Amalgam



This is Mercury
escaping from an
amalgam filling.
The filling is 50
years old. The
tooth was
extracted 15
years ago.

Source:
David Kennedy's IAOMT tape
www.uninformedconsent.com

Mercury Contamination from Amalgams

Swedish Dental Journal, Vol. 11, 1987. 179–187.

Nylander, et al.

Key Findings

- Study done on 34 human cadavers, of which 5 did not have amalgams
- Statistically significant higher concentration of Hg found in the kidneys and brains of the 29 cadavers with amalgams
- The concentration of inorganic Hg in the brains of the cadavers with amalgams was on average 80% higher than that in the brains of the cadavers without amalgams
- The researchers concluded that the primary reason for the high Hg concentration was due to the release of Hg vapor from the amalgams.

The Path Of Mercury From Tooth To Tissue

- Uptake by dental pulp
- Evaporation of vapor and absorption by tissue or lungs
- Abrasion and swallowing with:
 - Neuronal uptake, via axonal transport to the spinal chord (sympathetic neurons) or brainstem (parasympathetics) – and from here back to the brain
 - Venous uptake via the portal vein back to the liver
 - Lymphatic uptake via the thoracic duct to the subclavian vein
 - Uptake by bowel bacteria and tissues of the intestinal tract

Whole-body imaging of the distribution of mercury released from dental fillings into monkey tissue

FASEB Journal 4: 3256–3260. 1990 Leszek J. Hann, Reinhard Kloiber,
Ronald W. Leininger, Murray J. Vimy, and

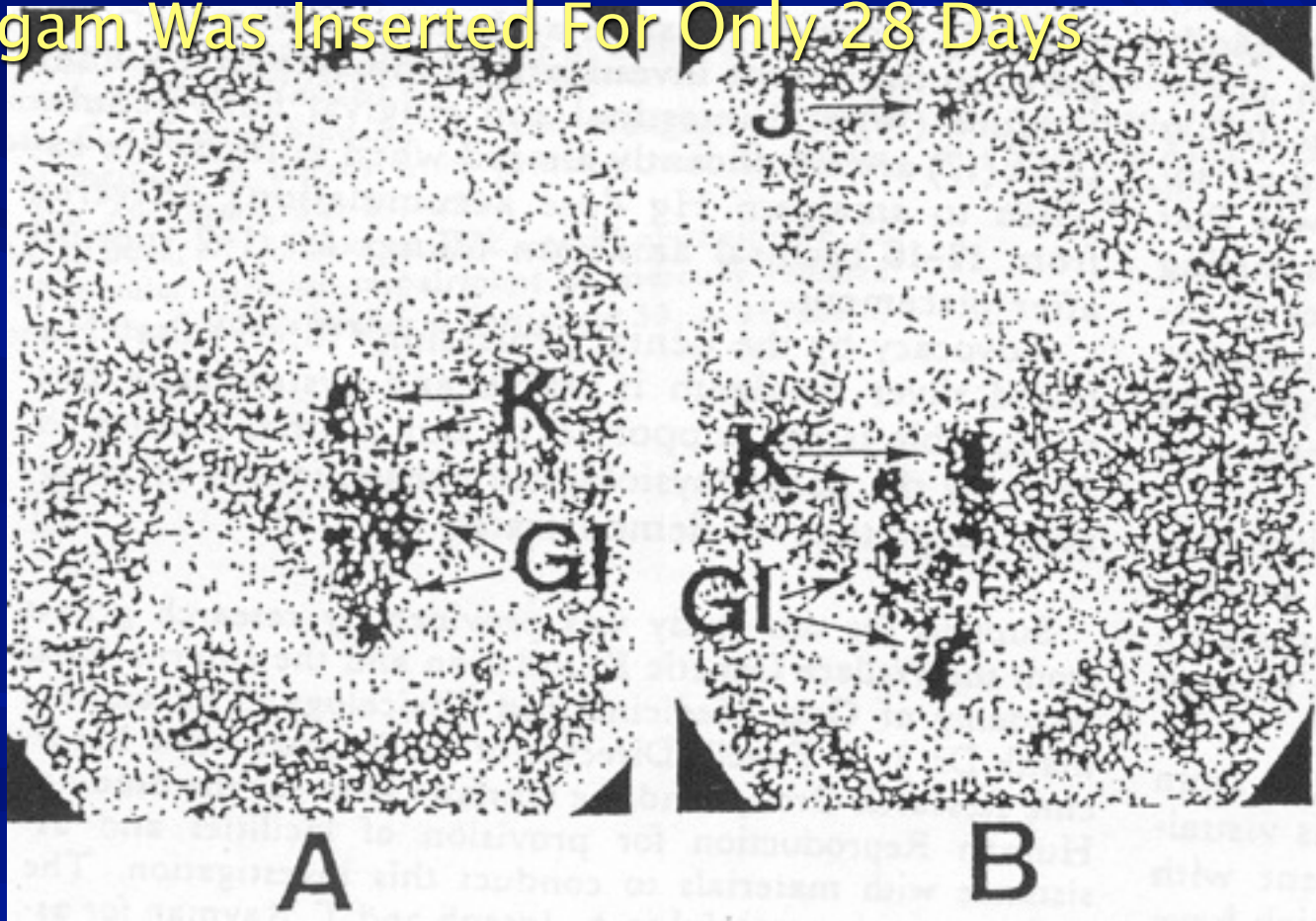
Whole body imaging of monkeys shows the delivery of tracer radioactive Hg placed in the mouth migrated within 4 weeks. The highest concentrations of Hg were found in the kidneys, gastrointestinal tract, and jaw. This means the advocacy of using amalgam as a stable tooth restorative was NOT supported by these findings.



Prof. Murray Vinny

Mercury in a 7 year old Monkey after removal of HG203 traced dental Amalgam

Amalgam Was Inserted For Only 28 Days



A: frontal image. B: dorsal image. J=Jaw, K=Kidney, GI= Gastro-Intestine

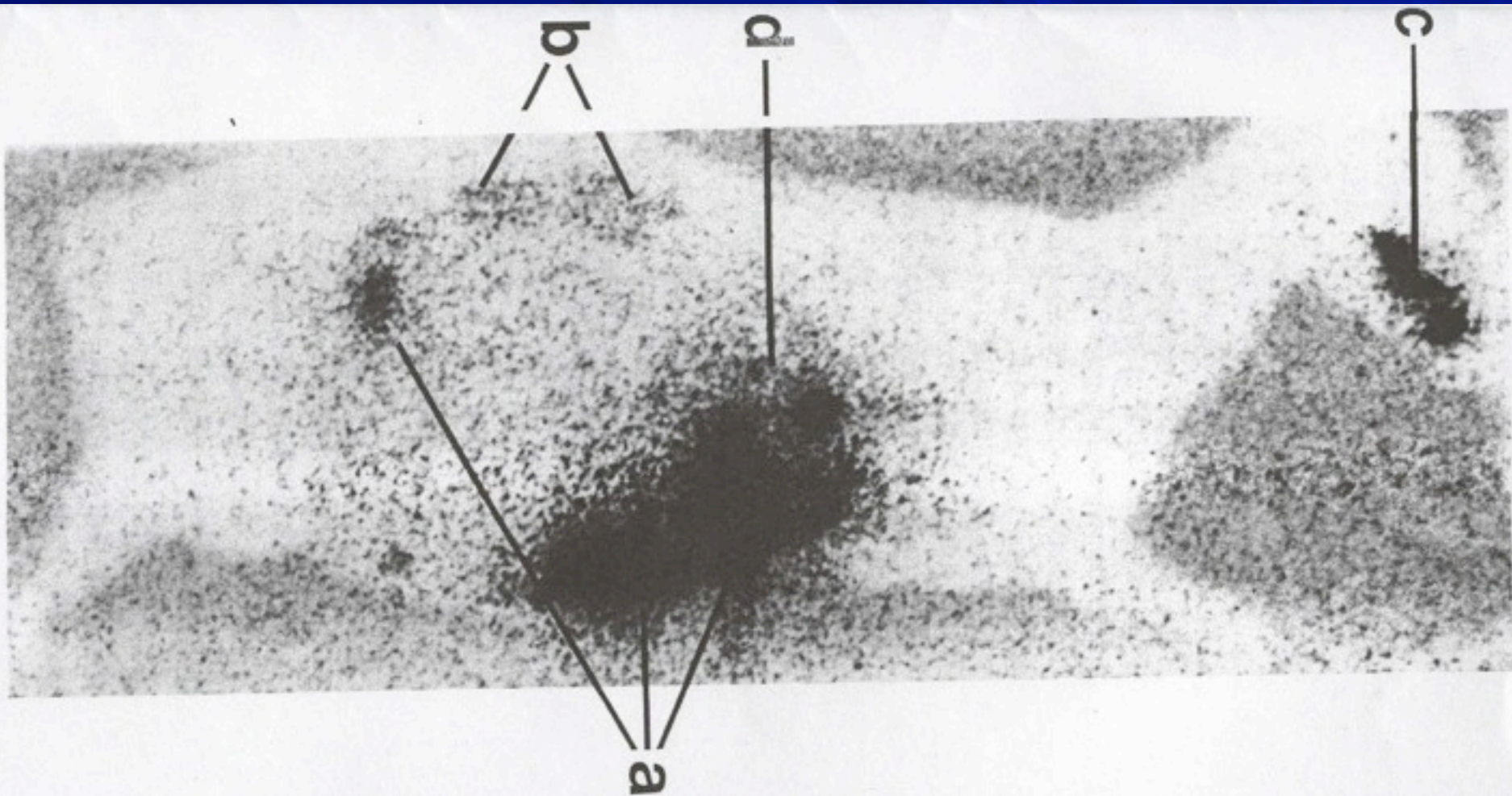


TABLE 1. Concentration of amalgam Hg in monkey tissues 28 days after placement of dental amalgam tooth fillings

Tissue	ng Hg/g
Whole blood	5.8
Urine	17.7
Synovial membrane (knee joint)	31.6
Skeletal muscle (gluteus)	1.9
Fat (mesentery)	0.0
Tooth alveolar bone	7756.1
Oral mucosa	86.6
Gingivae	4190.4
Tongue	253.3
Parotid gland	1.6
Stomach	18.4
Small intestine	68.9
Large intestine	983.1
Colon	482.7
Bile	243.1
Feces	3490.2
Heart (ventricle)	6.6
Lung	15.0
Trachea	12.6
Kidney	3053.5
Liver	133.1
Spleen	15.6
Frontal cortex	7.2
Occipital cortex	12.6
Thalamus	9.9
Sciatic nerve	0.0
Spinal cord	0.0
Cerebrospinal fluid	1.9
Pituitary	83.6
Thyroid	4.1
Adrenal	31.3
Pancreas	15.6
Testes	12.7

Abstract The fate of mercury (Hg) released from dental "silver" amalgam tooth fillings into human mouth air is uncertain. A previous report about sheep revealed uptake routes and distribution of amalgam Hg among body tissues. The present investigation demonstrates the bodily distribution of amalgam Hg in a monkey whose dentition, diet, feeding regimen, and chewing pattern closely resemble those of humans. When amalgam fillings, which normally contain 50% Hg, are made with a tracer of radioactive ^{203}Hg and then placed into monkey teeth, the isotope appears in high concentration in various organs and tissues within 4 wk. Whole-body images of the monkey revealed that the highest levels of Hg were located in the kidney, gastrointestinal tract, and jaw. The dental profession's advocacy of silver amalgam as a stable tooth restorative material is not supported by these findings. — HAHN, L. J.; KLOBER, R.; LEININGER, R. W.; VIMY, M. J.; LORSCHIEDER, F. L. Whole-body imaging of the distribution of mercury released from dental fillings into monkey tissues. *FASEB J.* 4: 3256-3260; 1990.

Key Words: dental amalgam • mercury • tooth fillings • mercury vapor • mercury exposure

Mercury (Effects) I

- evaporates at room temperature (odorless, colorless, invisible, tasteless)
- freezing point (becomes solid) at -39 degrees C
- dissolves other metals, including gold
- found in nature together with gold
- most toxic non-radioactive metal

Mercury (Effects) I Cont.

- Metallic form Hg^0 - poor GI absorption, good skin absorption. Evaporated Hg^0 : excellent mucous membrane absorption
- Recycling into human body from contaminated food, water and air
- Inorganic forms (salts): Hg^+ , Hg^{++}
- Organic compounds $\text{CH}_3\text{-Hg}^+$ (bacterial conversion from Hg^0 to methyl- Hg^+) – excellent GI and mucous membrane absorption. 50-100 times more toxic than Hg^0

Mercury (Effects) I Cont.

- Used as fungicide in seed and grain, in several diuretics, teething powders, homeopathics, in glues (Band-Aids, estrogen skin patches, etc.), dyes (pink dye in partials and dentures), amalgam fillings 50% , mercurochrome and other skin disinfectants, thermometers and industrial gauges, vaccines (ethyl mercury), eye drops
- By-product in chlorine manufacturing (100s of tons every year in US alone), coal burning power plants and crematoriums (in Switzerland amalgam fillings have to be removed from deceased person before allowing to cremate)

Mercury (Effects) I Cont.

- Aquatic plants (kelp, sea weed), all fish, ocean mammals are the end stage of mercury contaminated water (waste water).
- Each step in the food chain from one animal to the next higher one concentrates mercury 10 000 times. Fallout from the air has now contaminated even the most remote streams in the Himalayas

Mercury (Effects) II

- Inhibition of enzymes, ion channels and transport proteins
- ↑ Protein aggregation
- ↑ Free radicals and ↓ antioxidants enzymes
- Strong binding with Selenium (Hg-Selenide)→
 - ↓ Se-dependent enzymes (e.g. glutathione peroxidase)
 - Selenium depletion

Mercury (Effects) II Cont.

- Lipid peroxidation, leading to membrane damage
- DNA damage
- Nonspecific inhibition and specific activation of the immune system
- ↓ Nerve growth factors

Mercury (Effects) III

- ↓ Glutamate degradation and ↑ glutamate oxidation
- Irreversible inhibition of tubulin (the most important intracellular transport protein; it is especially sensitive to mercury)
 - Decreased endo- and exocytosis
 - ↓ Neurotransmitters
 - Profound effect on non-dividing cells (e.g. nerve cells)

Mercury (Effects) III Cont.

- ↓ Glutathione (the most important cell protective enzyme)
- ↓ Energy metabolism (glucose, mitochondria, ATP, NADH)
- Synergistic effect ($1+1=100$) with other toxins, for example LD1 (Hg) and LD1 (Pb) = LD100
- In vitro: ↑Tau + NFT↑ + A-Beta↑ via Hg in low concentration

Mercury and Alzheimer's Disease

Alzheimer's Disease (AD)

- It is the most common form of dementia; over 70% of all dementias are AD
- Documented for the first time in 1907 by Alois Alzheimer (Breslau)
- 3-5% of all cases are linked to genetics (amyloid metabolism)
- 95-97% of all cases: Cause? Therapy?
- Average length of time of onset of disease until death: 6-10 years
- Average age at onset of disease: early type: 30-65 yrs., later type: >65 yrs.
- First typical changes in the brain occur 50 years before onset of disease (neurofibrillary tangles; stages I and II). Symptoms are noticeable only in later years. AD is not a disease of old age.
- There is overwhelming evidence, that methyl mercury deposits in the brain are the initiating cause of AD. The damage opens the blood brain barrier. Chronic infections (mycoplasma, strep, herpes viruses, Borrelia B. etc.) settle in the affected areas and drive the progression of the illness

Increased Blood Mercury Levels in Patients with Alzheimer's Disease

C. Hock et al. Journal of Neural Transmission (1998) 105: 59–68

■ The dying brain releases mercury back into the blood stream

"...Alzheimer's Disease (AD) is a common neurodegenerative disease that leads to dementia and death.

Blood levels were more than two-fold higher in AD patients compared to control groups.

In early onset AD patients (n=13), blood mercury were almost three-fold higher than controls..."

Why Mercury and Alzheimer's disease (AD)? I

- **Cadaver studies**: indications of high Mercury levels in the brain
- **Studies of live AD patients**: indications of high blood Mercury levels (correlated with β -Amyloid in CSF)
- **Animal studies**: only with Mercury are similar biochemical changes elicited as are apparent in AD
- **Cell culture studies**: Only Mercury (not Pb, Cd, Al, Mn, Zn, Cu) in low concentrations can elicit all symptoms typical of AD (but Synergy $LD1(Hg)+LD1(Pb)=LD100$)
- There is a plausible correlation between **genetic risk factors** (Apolipoprotein E) and Mercury: various Mercury-clearing capabilities ($E2>E3>E4$)

Alzheimer's disease (Epidemiology) I

- 4th leading cause of death (USA)
- USA: > 4 million people with AD (263 million population in USA)
- Worldwide: 12 million affected (1997)
- Costs in the USA: \$90 billion per year (1997)
- 30-50% of all people > 85 yrs. are affected
- Projected rates of AD:
 - USA 2050: 16 million people
 - Worldwide 2050: 48 million people

Why Mercury and Alzheimer's disease (AD)? II

Mercury is the only toxin that can cause the typical changes in the AD brain at low doses

- Tubulin activation [Duhr et al. 1993; Pendergrass et al. 1995, 1996, 1997]
- Hyperphosphorylation of the Tau-protein [Olivieri et al. 2000, 2002]
- Formation of NFT [Olivieri et al. 2000, 2002; Leong et al. 2001]
- Secretion of β -amyloid [Olivieri et al. 2000, 2002]
- Degeneration of nerve cells [Leong et al. 2001]
- Heightened oxidative stress [Olivieri et al. 2000, 2002]

Why Mercury and Alzheimer's disease (AD)? II

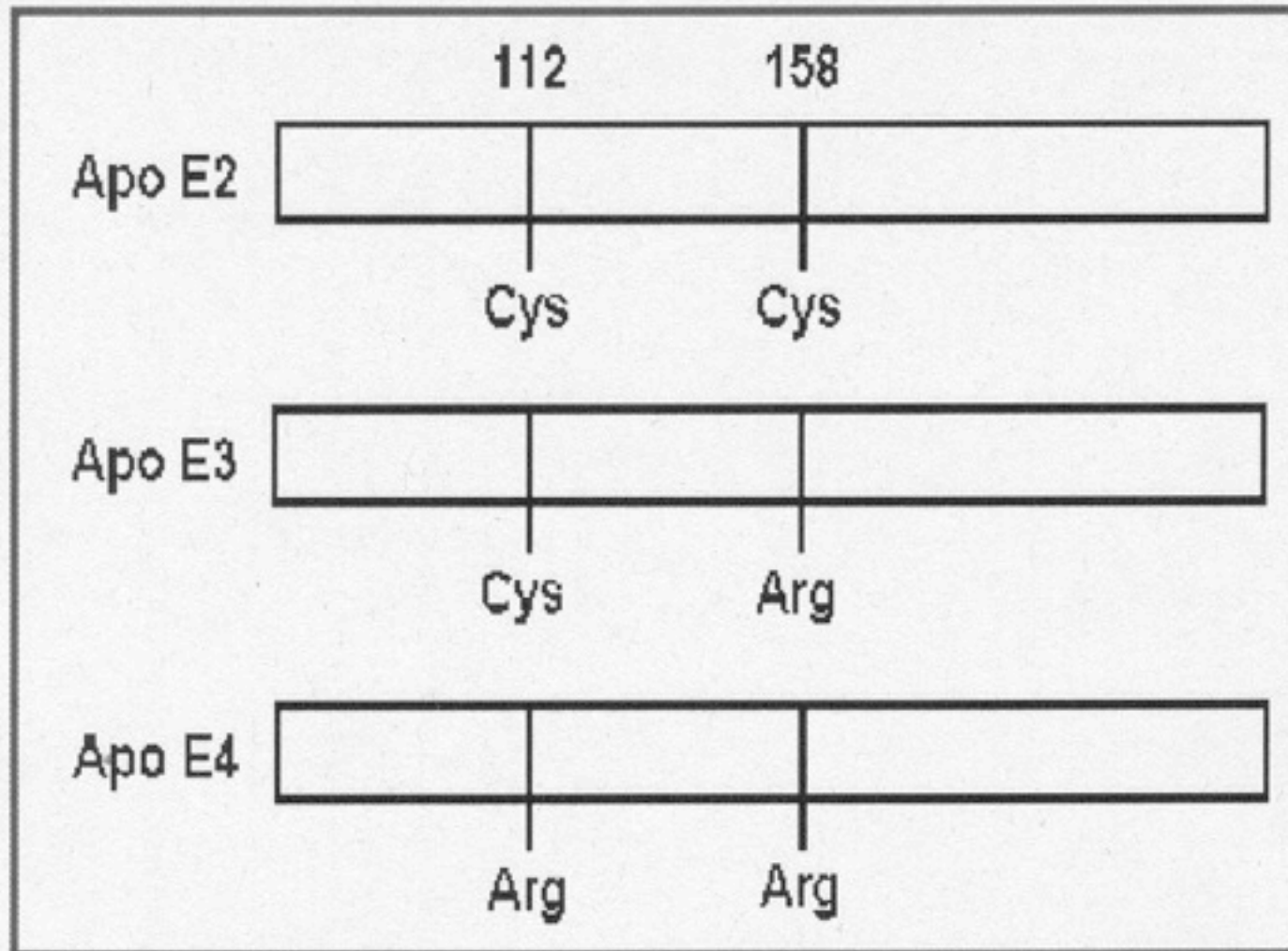
- Reduced glutathione concentration; inhibition of glutathione reductase and glutathione synthetase [Queiro et al. 1998; Zalups & Lasch 1996; Miller et al. 1991]
- Protein aggregation via formation of S-Hg-S bridges
- Inhibition of ion transport proteins (Na-K-ATPase, cellular channels)
- Augmentation of the neurotoxic effects of glutamate
- Reduced creatine kinase and glutamine synthetase
- Decreased energy production in mitochondria
- Induction of lipid peroxidation
- Reduction in nerve growth factors

Apolipoprotein E4 Genotype Increases the Susceptibility to the Development of AD

APOE Genotype	% U.S. Population	Age of AD Onset (yr.)
2/2	<1	?
2/3	11	>90
2/4	5	80-90
3/3	60	80-90
3/4	21	70-80
4/4	2	<70

Adapted from Roses, A.D. (1995) *Sci. Am. Science & Med.* 16-25.

Substitution of Arginine for Cysteine in Apo E3 and Apo E4 at Positions 112 and 158 Results in Loss of Potential Binding Sites for Sulfhydryl Reactive Heavy Metals such as Mercury





GENOVATIONS™

Patient: **ROBERT**
K

Age: 75

Sex: M

MRN: 0000225619

Order Number: **57210417**

Completed: September 30, 2004

Received: September 21, 2004

Collected: September 20, 2004

Security Code: 3654320

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Ste A100
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CardioGenomic™ Profile Results

This CardioGenomic™ Profile identifies genetic single nucleotide polymorphisms associated with increased risk of developing atherosclerosis, hypertension and coronary artery disease. Risk factors include cholesterol regulation and transport defects, methylation defects, hypercoagulation, chronic inflammation and cardio-protective markers.

Cholesterol Regulation and Atherosclerosis

APO E: Apolipoprotein E is involved in the clearance of chylomicron and VLDL remnants resulting from dietary fat intake. Accumulation of remnants can result in premature coronary disease and peripheral vascular disease. Three allelic variants exist, APO E2, APO E3 and APO E4, which are based on single nucleotide polymorphisms at two nucleotide sites. An individual's APO E combination can affect risk of hypercholesterolemia, coronary event and senile plaque formation.

CETP: Cholesteryl ester transfer protein is a critical step in the transfer of insoluble cholesteryl esters among lipoprotein particles and maintaining normal cholesterol homeostasis. Polymorphisms in CETP result in impaired ability to remove cholesterol from the system and lower HDL cholesterol levels, with consequent increased risk of developing atherosclerosis and coronary artery disease.

SELE: E-Selectin or endothelial leukocyte adhesion molecule-1, participates in the interaction between leukocytes and the endothelium of blood vessels and is involved in the pathophysiology of atherosclerotic processes. Individuals with SELE polymorphisms are at increased risk for early, severe atherosclerosis.

Methylation

MTHFR: Methylene tetrahydrofolate reductase is a critical enzyme in folate metabolism and polymorphisms in MTHFR lead to elevated homocysteine levels and defective methylation capacity. Diseases associated with this SNP include atherosclerosis, coronary artery disease, stroke, deep vein thrombosis, cervical dysplasia, cervical cancer, colon cancer, cognitive impairment, senility, Alzheimer's disease, neural tube defects and preeclampsia.

The Third Wave™ Invader DNA assay is used to detect polymorphisms in the patient's DNA sample. In this assay, a solution hybridization method is used in which two oligonucleotides hybridize in tandem with the specific DNA sequences. Subsequent Cleavase® and hybridization reactions result in generation of fluorescent signal. The biplex format of the assay enables simultaneous detection of all variants in a single reaction tube. The sensitivity and specificity of this assay is 99.7%.

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CardioGenomic™ summary - part 1

Cholesterol Regulation & Atherosclerosis

APO E



CETP



SELE



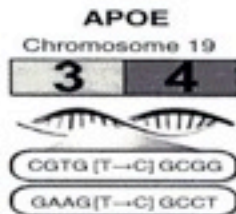
Methylation

MTHFR



63 Zillicoa St. Asheville, NC 28801-1074 - www.genovations.com

Cholesterol Regulation & Atherosclerosis



www.genovations.com/gcapoe

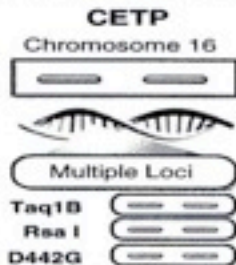
HEALTH IMPLICATIONS: APO E variations are one of the genetic determinants of serum cholesterol and triglyceride levels. APO E is involved in cholesterol and triglyceride transfer from chylomicrons and VLDL particles. The APO E3/4 genotype is the second most prevalent after 3/3 and accounts for >25% in most populations. Having an E4 allele is associated with higher cholesterol, Apo B, LP(a), and triglyceride levels as well as with lower HDL levels, all of which increase risk of atherosclerosis. The APO E3 allele is, however, moderately protective.

MINIMIZING RISKS: The effects of dietary fat and cholesterol on serum cholesterol levels is least with the E2 allele and greatest with the E4 allele. As the sum of the allele numbers increases, so too does the effect of dietary fats on serum cholesterol levels. Because of the presence of an APO E4 allele, a very low-fat and low-cholesterol diet (e.g., Pritikin or Ornish Diets) is warranted. High fiber has also been shown to lower cholesterol levels in 3/4 individuals. APO E3/4 women were able to lower cholesterol with moderate alcohol consumption. Individuals with an E3 allele respond well to regular aerobic exercise.

In individuals with elevated cholesterol, those with an E3 allele typically respond better to statin drugs and likely would respond to statin mimetics like inositol hexaniacinate, red rice yeast or polycoanol. However, those with an E4 allele respond better to probucol than to gemfibrozil or cholestyramine to lower cholesterol. The E4 allele should probably dictate first-line cholesterol-lowering therapy. Since probucol acts as a potent anti-oxidant, higher doses of mixed natural anti-oxidants including alpha- and gamma-tocopherol may be an alternative long-term therapeutic approach.

FURTHER EVALUATION: Since APO E polymorphisms affect cholesterol and triglyceride values, regular monitoring of LDL, HDL and total cholesterol and triglycerides is recommended. Since other metabolic factors are also known to affect cardiovascular disease risk (e.g., lipoprotein (a), homocysteine, C-reactive protein, and fibrinogen), a comprehensive cardiovascular assessment is recommended for baseline functional assessment.

Cholesterol Regulation & Atherosclerosis



www.genovations.com/gccetp

HEALTH IMPLICATIONS: Cholesteryl ester transfer protein is responsible for the transfer of insoluble cholesteryl esters from HDL to other lipoproteins. Thus, CETP is responsible for maintaining normal serum cholesterol levels, including total, LDL and HDL cholesterol. This wild type variant of CETP is associated with decreased CETP levels and with higher HDL cholesterol levels, and consequently with decreased risk of developing atherosclerosis and coronary artery disease.

MINIMIZING RISKS: While individuals with normal CETP gene activity are at reduced risk for developing atherosclerosis and heart disease, these genetic advantages are completely nullified in individuals who smoke or are overweight. Individuals who have high serum cholesterol levels respond favorably to a high polyunsaturated fat, low cholesterol diet.

FURTHER EVALUATION: A comprehensive cardiovascular assessment is indicated to measure baseline levels of total, LDL and HDL cholesterol levels, as well as to monitor therapeutic effectiveness.

Cholesterol Regulation & Atherosclerosis



www.genovations.com/gcsele

HEALTH IMPLICATIONS: E-selectin is a glycoprotein molecule that modulates the adhesion of circulating neutrophils to the endothelial lining of blood vessels. E-selectin is expressed on the surface of endothelial cells following stimulation by inflammatory mediators (NFκB-mediated). Polymorphisms in SELE increase the production and expression of E-selectin, dramatically increasing the risk of atherosclerosis and premature coronary artery disease. Having a homozygous negative genotype means that you have a reduced risk of developing E-selectin-induced atherosclerosis.

MINIMIZING RISKS: Even though you have a favorable genotype, high levels of oxidative stress and free radicals can induce the production of E-selectin. Thus, higher levels of anti-oxidants are indicated. A diet rich in colorful vegetables and fruits contains anti-oxidants. Effective supplements may include vitamin E, vitamin C, n-acetyl-cysteine, milk thistle, green tea polyphenols, etc. Pro-inflammatory cytokines TNF-α and IL-1 also increase NFκB activation and E-selectin production. Anti-oxidants, fish oil and milk thistle (silymarin) supplementation have each been shown to suppress IL-1 and TNF-α production directly.

FURTHER EVALUATION: An oxidative stress profile evaluates the functional state of reduction-oxidation balance in the body and may be warranted for all individuals concerned about oxidative stress levels.

GENOVATIONS

Optimizing your Genomic Potential

Hypertension

GNB3: The Guanine Nucleotide-binding Protein β -3 (GNB3) is pivotal in many cell-to-cell signal transduction pathways, including that by which angiotensin II acts to stimulate vasoconstriction and elevate blood pressure. This polymorphism in GNB3 is associated with both essential hypertension and obesity.

AGT: Angiotensin is a polypeptide hormone that stimulates smooth muscle contraction as well as sodium and water retention, resulting in elevated blood pressure. An AGT polymorphism is associated with increased AGT production and consequently with essential hypertension and coronary artery disease.

AGTR1: The angiotensin II receptor-1 is an important effector controlling blood pressure and volume in the cardiovascular system. Angiotensin II stimulates vasoconstriction as well as sodium and water retention. AGT polymorphisms may be associated with increased binding affinity between angiotensin II and AGTR1 and consequently with increased risk for essential hypertension and coronary artery disease.

Coagulation

Factor 2: Coagulation Factor II, prothrombin, is a plasma protein that plays a critical role in blood coagulation and clotting. Individuals with this polymorphism have elevated plasma prothrombin levels and, therefore, an increased risk of venous thrombosis, myocardial infarction and stroke.


Factor 5: Factor V, Leiden, is an important component of the extrinsic pathway for blood clotting combining with Factor X to form prothrombin activator which accelerates the conversion of prothrombin into thrombin. Individuals with this polymorphism are at increased risk for venous thromboembolism. Risk of thromboembolism increases dramatically with a concurrent Factor II SNP or with oral contraceptive use.

Reduction-Oxidation Balance


CYBA*8: Cytochrome b-245-a codes for the p22phox subunit of NADH/NADPH Oxidase, which plays a critical role in maintaining the redox balance in the smooth muscle cells surrounding blood vessels. This polymorphism is associated with reduced NAD(P)H activity and lower superoxide production. The net effect of this variant however is to accelerate atherosclerosis progression.

CardioGenomic™ summary - part 2

Hypertension

GNB3 

AGT 


AGTR1 

Coagulation

Factor 2 

Factor 5 

Reduction-Oxidation Balance

CYBA*8 

Methylation

MTHFR

Chromosome 1

677C-T



GAAG[C→T]CGAT

HEALTH IMPLICATIONS: Methylene tetrahydrofolate reductase is a critical enzyme in folate metabolism and polymorphisms in MTHFR lead to defective methylation capacity and elevated homocysteine levels. Homocysteine levels rise as the body cannot re-methylate the homocysteine into methionine. Diseases associated with elevated homocysteine levels include atherosclerosis, coronary artery disease, stroke, deep vein thrombosis, cervical dysplasia, cervical cancer, polyps and colon cancer, cognitive impairment, senility, Alzheimer's disease, neural tube defects and preclampsia. Homozygote negative individuals (677CC) are generally not at increased genomic risk for developing these conditions. However, inadequate dietary folic acid, B2, B6, or B12 can still result in homocysteinemia, even though the MTHFR enzyme is functioning optimally.

MINIMIZING RISKS: Folic acid (folate) supplementation of ~400 mcg/d may be indicated. The biochemical pathways that control methylation are supported by a number of other vitamins, including B2, B6 and B12.

Foods high in folic acid: greens, lettuce, spinach, common beans, baker's yeast, etc. should also be emphasized in the diet.

FURTHER EVALUATION: Methylation capacity and folic acid status can be determined through one of two metabolic markers in either the plasma or the urine: homocysteine and methylmalonic acid. If either of these markers is elevated the functional risk of developing the conditions listed above is substantially increased. The detection of borderline homocysteinemia may be improved with methionine loading. One protocol uses 25 mg/kg of methionine given 4-6 hours before a fasting blood draw to measure serum homocysteine levels.

www.genovations.com/gcmthfr

Hypertension

GNB3

Chromosome 12

825C-T



CGTC[C→T]GTGG

HEALTH IMPLICATIONS: Guanine nucleotide-binding protein, beta-3 (GNB3), or G protein, is pivotal to many cell-to-cell signal transduction pathways including the actions of angiotensin to raise blood pressure. The substitution of a thymine for a cytosine at nucleotide 825 results in a deletion of 41 amino acids in the final G protein. The CC wild type variant produces less biologically active G protein than a T allele. Consequently, this polymorphism is associated with decreased risk of essential hypertension and decreased risk for depression and bipolar disorder.

MINIMIZING RISKS: Individuals with hypertension who do not have a polymorphism in GNB3, should look at the other possible polymorphic variants that may adversely affect blood pressure control, namely, AGT and AGTR1. Follow therapeutic suggestions if a polymorphism exists in either of these genes.

While CC homozygotes were less susceptible to depression and bipolar disorder, they were also less responsive to antidepressant therapy - regardless of the class of anti-depressant used (TCA, SSRIs, NASSAs, or StRIs).

FURTHER EVALUATION: Hypertension should be evaluated and therapeutic progress monitored by regular measurement of blood pressure.

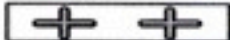
www.genovations.com/gcgnb3

Hypertension

AGT

Chromosome 1

M235T



CAAG[A→C]GCCG

HEALTH IMPLICATIONS: Angiotensin I is produced when its precursor protein angiotensinogen is cleaved by renin. Angiotensin I is rapidly converted to Angiotensin II by angiotensin converting enzyme (ACE). Angiotensin II is a potent vasoconstrictor and also stimulates the reabsorption of sodium and water from the kidney, raising blood pressure. The 235T polymorphism has been associated with increased production of angiotensin and an increased risk of developing hypertension. TT homozygotes have significantly higher blood pressure. Hypertension is an independent risk factor for heart disease. Several studies have shown that TT homozygotes have an increased risk of developing coronary artery disease of 1.5-1.8 times. Women carriers of the 235T allele tended to have a greater fat mass.

MINIMIZING RISKS: The 235T variant identifies individuals with a salt-sensitive form of essential hypertension. Accordingly, one primary therapeutic focus for these individuals should be dietary sodium restriction. Such a diet should emphasize fresh fruits and vegetables while eliminating fast foods, prepared foods, luncheon meats, etc., and completely avoid the addition of table salt to any foods. The DASH diet that emphasizes low fat in addition to lots of fruits and vegetables also demonstrated substantial reduction in blood pressure.

While aerobic exercise produces many diverse physiologic benefits in almost all individuals, TT homozygotes did not significantly lower their blood pressure through exercise.

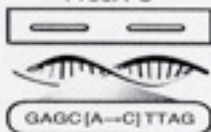
ACE inhibitors produced more dramatic reductions in 235T allele carriers than in the MM genotype.

FURTHER EVALUATION: Hypertension should be evaluated and therapeutic progress monitored by regular measurement of blood pressure. Compounding the effects of the 235T allele, both estrogens and androgens have been shown to increase transcription of angiotensinogen; care should be taken to monitor blood pressure closely during pregnancy, while taking oral contraceptives or hormone replacement therapy.

www.genovations.com/gcagt

Hypertension

AGTR1
Chromosome 3
1166A-C



www.genovations.com/gcagtr1

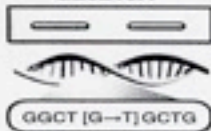
HEALTH IMPLICATIONS: The angiotensin receptor mediates the cellular actions of angiotensin, including vasoconstriction and increased sodium resorption in the kidneys, both of which act to increase blood pressure. As an AA homozygote, you have less risk of developing hypertension than those carrying a C allele.

MINIMIZING RISKS: Individuals with hypertension who do not have a polymorphism in AGTR1, should look at the other possible polymorphic variants that may adversely affect blood pressure control, namely, AGT and GNB3. Follow therapeutic suggestions if a polymorphism exists in either of these genes. If no polymorphisms exist, consider nutritional supplements that have been shown in animal models to affect the actions of angiotensin on its receptor, including fish oils, borage seed oil, magnesium, potassium, arginine and taurine. These may prove a useful nutritional therapeutic approach.

FURTHER EVALUATION: Hypertension should be evaluated and therapeutic progress monitored by regular measurement of blood pressure.

Coagulation

Factor 2
Chromosome 11
G20210A



www.genovations.com/gcfact2

HEALTH IMPLICATIONS: Coagulation Factor II, prothrombin, is a plasma protein that plays a critical role in blood coagulation and clot formation. Individuals with the wild type 20210GG genotype have normal plasma prothrombin levels and, therefore, no increased risk of venous thrombosis. However, it should be cautioned that venous thrombosis is a multifactorial process with risk increased by numerous genetic polymorphisms and environmental factors acting synergistically. The vast majority of individuals experiencing deep vein thrombosis or pulmonary embolism do not carry the mutant 20210A allele.

MINIMIZING RISKS: None indicated for the wild type genotype.

FURTHER EVALUATION: Since venous thrombosis is a multifactorial process, a comprehensive cardiovascular assessment may be the best indicator of overall functional risk of cardiovascular disease.

Coagulation

Factor 5 (Leiden)
Chromosome 1
R506Q



www.genovations.com/gcfact5

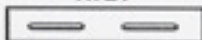
HEALTH IMPLICATIONS: Factor V, Leiden, is an important component of the extrinsic pathway for blood clotting. Factor V combines with Factor X to form prothrombin activator that, in turn, accelerates the conversion of prothrombin into thrombin. Individuals with a polymorphism in Factor V have a decreased rate of fibrinolysis by activated protein C and are subsequently at increased risk for venous blood clots that can lead to deep vein thrombosis or pulmonary embolism. Your genotype indicates that you are NOT at any increased risk for a venous clot formation.

MINIMIZING RISKS: None indicated.

FURTHER EVALUATION: Many factors contribute to cardiovascular health. Functional risk for venous thrombosis may be more fully evaluated by running a comprehensive cardiovascular and an essential fatty acid profile since both fibrinogen and essential fatty acid imbalances can increase the risk of blood clot formation.

Reduction- Oxidation Balance

CYBA*8
Chromosome 16
H72Y



GAAG[C→T]ACAT

www.genovations.com/gcyb8

HEALTH IMPLICATIONS: Cytochrome b-245 is the terminal, heme-binding component of NADPH oxidase, an enzyme that produces superoxide free radicals in vascular smooth muscle cells and controls vasoconstriction. There are two variants of CYBA: one improves protection against oxidative stress (640A-G, or CYBA*11) and one impairs protection (H72Y, or CYBA*8). The 640AA and 72YY genotypes were found to be in linkage disequilibrium (having one means you are likely to have the other) and this genotype combination had the highest risk of heart disease. The 72HH genotype is associated with increased NADPH oxidase activity, possibly due to improved heme-binding, but with a significant decreased risk of atherosclerosis and heart disease.

MINIMIZING RISKS: While risk of heart disease is less in people with your genotype, heart disease is a multi-factorial process and many elements have an additive effect on overall risk. Elevated cholesterol and triglycerides, smoking, central obesity, lack of exercise, and insulin resistance all increase cardiovascular disease risk in all genotypes.

FURTHER EVALUATION: Because of the multifactorial nature of heart disease a comprehensive cardiovascular profile that includes lipids as well as independent risk factors like Lp(a), homocysteine, fibrinogen and C-reactive protein is indicated.

This test has been developed and its performance characteristics determined by Genova Diagnostics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or treatment recommendations. Diagnosis and treatment decisions are the responsibility of the practitioner.

The accuracy of genetic testing is not 100%. Results of genetic tests should be taken in the context of clinical representation and familial risk. The prevalence and significance of some allelic variations may be population specific.

Any positive findings in your patient's test indicate genetic predisposition that could affect physiologic function and risk of disease. We do not measure every possible genetic variation. Your patient may have additional risk that is not measured by this test. Negative findings do not imply that your patient is risk-free.

Dr. Amy Peace-Brewer
Laboratory Director

Dr. Patrick Hanaway
Chief Medical Officer



GENOVATIONS™

DetoxiGenomic™ Profile Physician's Copy

Patient: **ROBERT**
K
Age: 75
Sex: M
MRN: 0000144671

Order Number: 57210418
Completed: October 12, 2004
Received: September 21, 2004
Collected: September 20, 2004

COMPREHENSIVE MEDICAL CENTER
DIETRICH KLINGHARDT MD
1200 112th Ave NE
Ste A100
Bellevue, WA 98804

Security Code: 6854324

PHASE I Detoxification: The First Line of Defense

In Phase I detoxification, enzymes, known collectively as the cytochrome P-450 system, use oxygen to modify toxic compounds, drugs, or steroid hormones. Many toxins must undergo Phase II detoxification after a reactive site has been formed. Because there are many different toxic compounds the body might encounter, there are many variants of Phase I enzymes.

(CYP1A1) detoxifies polycyclic aromatic hydrocarbons (PAHs) produced from the combustion of organic materials (exhaust/fumes, charbroiled meats, etc.).

(CYP1B1) is involved in the ω -hydroxylation of estrogen.

(CYP2A6) detoxifies nitrosamines and nicotine

(CYP2C9) detoxifies coumarin and sulfonamides.

(CYP2C19) detoxifies proton-pump inhibitors (e.g., prilosec®) and many anticonvulsants (e.g., valium®).

(CYP2D6) detoxifies ~20% of all prescription drugs including tricyclics, MAOIs, SSRIs, opiates, anti-arrhythmics, beta-blockers, Cimetidine, etc.

(CYP2E1) detoxifies nitrosamines and ethanol (acetaldehyde).

(CYP3A4) detoxifies over 50% of all prescription medications and most steroid hormones.

Cytochrome P-450

Result	Gene	Internet information
✓	CYP1A1 *	www.genovations.com/gdgen01
●	CYP1B1 *	www.genovations.com/gdgen02
✓	CYP2A6	www.genovations.com/gdgen10
✓	CYP2C9 *	www.genovations.com/gdgen05
✓	CYP2C19 *	www.genovations.com/gdgen06
✓	CYP2D6	www.genovations.com/gdgen03
✓	CYP2E1	www.genovations.com/gdgen04
✓	CYP3A4 *	www.genovations.com/gdgen07

Your Results: Polymorphisms (SNPs) in the genes coding for a particular enzyme can increase or, more commonly, decrease the activity of that enzyme. Both increased and decreased activity may be harmful. Increased phase I clearance without increased clearance in Phase II can lead to the formation of toxic intermediates that may be more toxic than the original toxin. Decreased Phase I clearance will cause toxic accumulation in the body. Adverse reactions to drugs are often due to a decreased capacity for clearing them from the system.

Use of H2 blockers (e.g. Cimetidine) should be avoided as these bind to the heme-containing reactive site of all CYPs inhibiting binding to toxins.

General Therapies to Improve Detoxification:

Foods that generally improve Phase I detoxification and as well improve the efficiency of Phase II conjugation are generally recommended for individuals with CYP SNPs. These include most vegetables and fruits, but especially cruciferous vegetables (broccoli, Brussels sprouts, cauliflower, watercress, and cabbage), garlic, onions, soy, grapes, berries, green and black tea, and many herbs and spices like rosemary, basil, turmeric, cumin, poppy seeds, and black pepper. Indeed, improving Phase I and Phase II detoxification helps explain why vegetables and fruits protect against many cancers.

Key

- ✓ Optimal genomic potential - no polymorphism detected
- Polymorphism detected in this enzyme, increasing your susceptibility to toxins, if exposed
- * Multiple SNP locations were evaluated for these genes
- NR See commentary if applicable.



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PHASE II Detoxification: Conjugation of Toxins and Elimination

In Phase II detoxification, large water-soluble molecules are added to toxins, usually at the reactive site formed by Phase I reactions. After Phase II modifications, the body is able to eliminate the transformed toxins in the urine or the feces (through the bile).

(COMT SNP) higher risk for depression, bipolar disorder, ADHD and alcoholism.

Methylation				
Result	Gene	SNP Location	Internet Information	Affects
--	COMT	V158M	www.genovations.com/gdv158m	Liver/Gut

Your Results: Catechol-O-methyl transferase is the enzyme primarily responsible for breaking down the neurotransmitters dopamine, epinephrine, and norepinephrine.

(NAT SNP) both slow and rapid acetylators are at increased risk for developing lung, colon, bladder, or head & neck cancer.

Acetylation (N-acetyl transferase)				
SLOW METABOLIZER POLYMORPHISM				
Result	Gene	SNP Location	Internet Information	Affects
--	NAT1	R64W	www.genovations.com/gdr64w	All Cells
--	NAT1	R187Q	www.genovations.com/gdr187q	Liver/Gut
--	NAT2	I114T	www.genovations.com/gdi114t	Liver/Gut
+/-	NAT2	R197Q	www.genovations.com/gdr197q	Liver/Gut
--	NAT2	G286E	www.genovations.com/gdg286e	Liver/Gut
--	NAT2	R64Q	www.genovations.com/gdr64q	Liver/Gut
FAST METABOLIZER POLYMORPHISM				
--	NAT2	K268R	www.genovations.com/gdk268r	Liver/Gut

Your Results: N-acetyl Transferase detoxifies many environmental toxins, including tobacco smoke and exhaust fumes. Polymorphisms can result in slower than normal or faster than normal addition of an acetyl group to these toxins. Slow acetylators have a build up of toxins in the system and rapid acetylators add acetyl groups so rapidly that they make mistakes in the process. Both slow and rapid acetylators are at increased risk for toxic overload if they are exposed to environmental toxins. If the toxin exposure is reduced, the risk is reduced.

(GST SNP) The GST isoforms (M1, P1, and T1) are more or less prevalent in various tissues; all catalyze the conjugation of electrophilic compounds with glutathione. Defects in GST activity can contribute to fatigue syndromes, and to various cancers throughout the body.

Glutathione Conjugation (Glutathione s-transferase)				
Result	Gene	SNP Location	Internet Information	Affects
NULL	GSTM1	1p13.3	www.genovations.com/gdgstm1	Liver/Kidney
+/-	GSTP1	I104V	www.genovations.com/gdgstp1	Brain/Skin
--	GSTP1	A113V	www.genovations.com/gda113v	Brain/Skin

Your Results: Glutathione-S-transferase detoxifies many water-soluble environmental toxins, including many solvents, herbicides, fungicides, lipid peroxides, and heavy metals (e.g., mercury, cadmium, and lead). The various forms of GST work together to eliminate toxins. Decreased glutathione conjugation capacity may increase toxic burden and increase oxidative stress.

(SOD SNP) SOD1 is present in the cytosol; SOD2 is present in the mitochondria. Changes in the SOD enzyme are associated with changes in risk for neurodegenerative disorders like ALS.

Oxidative Protection				
Result	Gene	SNP Location	Internet Information	Affects
--	SOD1	G93A	www.genovations.com/gdg93a	Cytosol
--	SOD1	A4V	www.genovations.com/gda4v	Cytosol
+/-	SOD2	A16V	www.genovations.com/gda16v	Mitochondria

Your Results: Superoxide Dismutase is an enzyme that protects cells from increased oxidative stress and free radical damage to cell structures like membranes, mitochondria, DNA, and proteins.

Key

- Neither chromosome carries the genetic variation.
 - +/- One chromosome (of two) carries the genetic variation.
 - ++ Both chromosomes carry the genetic variation.
 - NR / NULL / IND See commentary
(You inherit one chromosome from each parent)
- Homozygous negative or wild type
Heterozygous positive
Homozygous positive

Phase I Detoxification commentary is provided only for polymorphisms for which impaired activity is indicated with a red dot, ●

Note: In the following charts, substrates, inhibitors, and inducers are listed for each cytochrome P450 enzyme (Phase I) included in the DetoxiGenomic Profile.

Substrates are compounds that are metabolized by that enzyme. The metabolism of some of these compounds is shared by other P450 enzymes (refer to chart).

Inhibitors may or may not be substrates of that enzyme, but will reliably reduce that enzyme's activity if present.

Inducers also may or may not be substrates, but will tend to increase the enzyme's activity.

Drug Interaction Resources

<http://medicine.lupui.edu/flockhart/table.htm>

● **CYP1B1**

www.genovations.com/gdgen02

Health Implications: Cytochrome P450 1B1 converts estrogen into 4-hydroxy estrogen that may contribute to estrogen-sensitive carcinogenicity. CYP1B1 is also partially responsible for detoxifying polycyclic aromatic hydrocarbons (PAHs), products of the burning of organic materials, like car exhaust, cigarette smoke and charbroiled foods.

Minimizing Risk: Regular aerobic exercise is important. You should make soy foods (tofu, tempeh and soy beans) and cold water fish (salmon, mackerel, etc.) a regular part of your diet. Moderate consumption of red wine (i.e., 1-2 glasses per day) may be beneficial. Do not smoke. Avoid charbroiled and well-done meats. Minimize exposure to car and diesel exhaust. Avoid contact with industrial solvents.

Increase the 2-hydroxylation of estrogens:

- > Indol-3-carbinol (I3C) or diindolylmethane (DIM)
- > Fish oil (EPA/DHA)

Down-regulate CYP1B1 induction and expression:

- > DHEA
- > Hesperetin (a flavonoid)
- > A daily glass of red wine may be beneficial

Substrate	Inhibitor	Inducers
Antidepressants: Amitriptyline (Elavil) Clomipramine (Anafranil) Imipramine (Tofranil) Acetaminophen (NAPQI) Caffeine Clozapine (Clozaril) Coumarin activation Estradiol, Estrone (4-hydroxylation) Heterocyclic amines Naproxen Propranolol (Inderal) Tacrine (Cognex) Testosterone Theophylline	Cimetidine Ciprofloxacin (Cipro) Erythromycin Fluvoxamine (Luvox) Pyrene Ticlopidine Grapefruit juice (naringenin) Ginseng (possible)	Omeprazole (Prilosec) Phenytoin (Dilantin) Phenobarbital Rifampin Polycyclic Aromatic Hydrocarbons: Cigarette smoke Charbroiled foods
CYP1B1: Up regulator - is involved in the 4-hydroxylation of estrogen.		

Physician Recommendations:

Phase II Detoxification commentary is provided only for polymorphisms with known health implications.

← - NAT2 R197Q

www.genovations.com/gdr197q

Health Implications: N-acetyltransferase 1 is found in extra-hepatic tissues, while NAT2 is found predominantly in the liver and the gut. Both are used in the Phase II acetylation of numerous environmental toxins, including heterocyclic aromatic amines. Slow acetylators do not clear toxins well and the resulting increased total toxic burden can increase the risk of lung, colon, breast, bladder, and head and neck cancers, though results have not been consistent in all studies. Urinary bladder cancer appears to have the most consistent association with slow acetylation.

Minimizing Risk: If you smoke, stop. Your risk of lung cancer is substantially higher than someone with normal NAT activity. Even occasional smoking or exposure to second hand smoke is harmful. Liberal consumption of most vegetables and fruits but especially cruciferous vegetables (broccoli, Brussels sprouts, cauliflower, watercress, and cabbage), garlic, onions, soy, grapes and berries will increase Phase II efficiency, including acetylation.

Physician Recommendations:

NULL	GSTM1	1p13.3	www.genovations.com/gdgstm1
+	GSTP1	1104V	www.genovations.com/gdgstp1

Health Implications: When there is no gene present on the chromosome it is called a null allele. In this case, there is no GSTM1 gene present on either chromosome.

Glutathione-S-transferase affords protection against oxidative stress (especially by reducing hydrogen peroxide and by regenerating oxidized vitamins C and E). GST also detoxifies electrophilic compounds including solvents, herbicides, fungicides, polycyclic aromatic hydrocarbons and heavy metals (Hg, Pb, Cd). Decreased glutathione conjugation capacity may increase toxic burden and increase oxidative stress resulting in a greater risk for various cancers and fatigue syndromes, especially if exposed to toxic compounds.

GST is critical for removing the cellular debris from free radical attacks: lipid peroxides, damaged DNA, proteins, etc. All GST isozymes act similarly but predominate in various tissues of the body.

GST polymorphisms should be seen as disease-modifying rather than disease-causing, likely via their role in cellular protection against cellular oxidative stress - a risk that appears to be additive with increasing numbers of polymorphisms to various isozymes. Thus, cancer susceptibility will be dependent not only on GST polymorphisms increase risk of lung, prostate, head and neck cancers, and malignant melanoma, as well as Hodgkin's and non-Hodgkins lymphomas.

GST polymorphisms generally indicate a poorer prognosis in cancer and chronic diseases. Ovarian cancer and malignant melanoma do not respond well to chemotherapy. Multiple sclerosis and cystic fibrosis have poorer prognoses with GST polymorphisms.

Minimizing Risk: Liberally consume brassica vegetables (broccoli, cauliflower, kale, cabbage, bok choy, etc.) and allium vegetables (onions, garlic, shallots, etc.). Regardless of genotype, increasing the body's production of glutathione will reduce oxidative stress and afford greater protection against a wide array of toxins. Numerous supplements can help raise glutathione levels including liberal consumption of colorful vegetables and fruits, vitamin C, n-acetylcysteine and milk thistle. Vitamin E supplementation may also be helpful. Consult your health care provider to find the supplement regimen that best fits your overall health needs. If you smoke, stop. Avoid exposure to herbicides, fungicides, insect sprays and industrial solvents.

Physician Recommendations:

+/- SOD2 A16V

www.genovations.com/gda16v

Health Implications: Superoxide dismutase is an anti-oxidant enzyme found inside the mitochondria of cells (where most of our energy is made). SOD2 converts reactive oxygen species into less reactive hydrogen peroxide. Polymorphisms in SOD2 (+ - and + +) are protective and are associated with a decreased risk of Parkinson's disease, breast cancer and motor neuron disease, including sporadic amyotrophic lateral sclerosis (ALS). These polymorphisms are associated with decreased oxidative stress.

Minimizing Risk: Even so, liberal consumption of dietary antioxidants in colorful vegetables and fruits is recommended. Therapies that raise glutathione levels may also be helpful since glutathione works with SOD2 to prevent oxidative damage. Numerous supplements can help raise glutathione levels including vitamin C, n-acetylcysteine and milk thistle. Vitamin E supplementation may also be helpful. Consult your health care provider to find the supplement regimen that best fits your overall health anti-oxidant needs.

Physician Recommendations:

Mercury and Autism

Supporting literature review:

Mercury and Autism: Accelerating Evidence

Joachim Mutter. Neuroendocrinol Lett 2005; 26 (5): 439-446, Institute for Environmental Medicine and Hospital Epidemiology, University Hospital Freiburg, Germany.

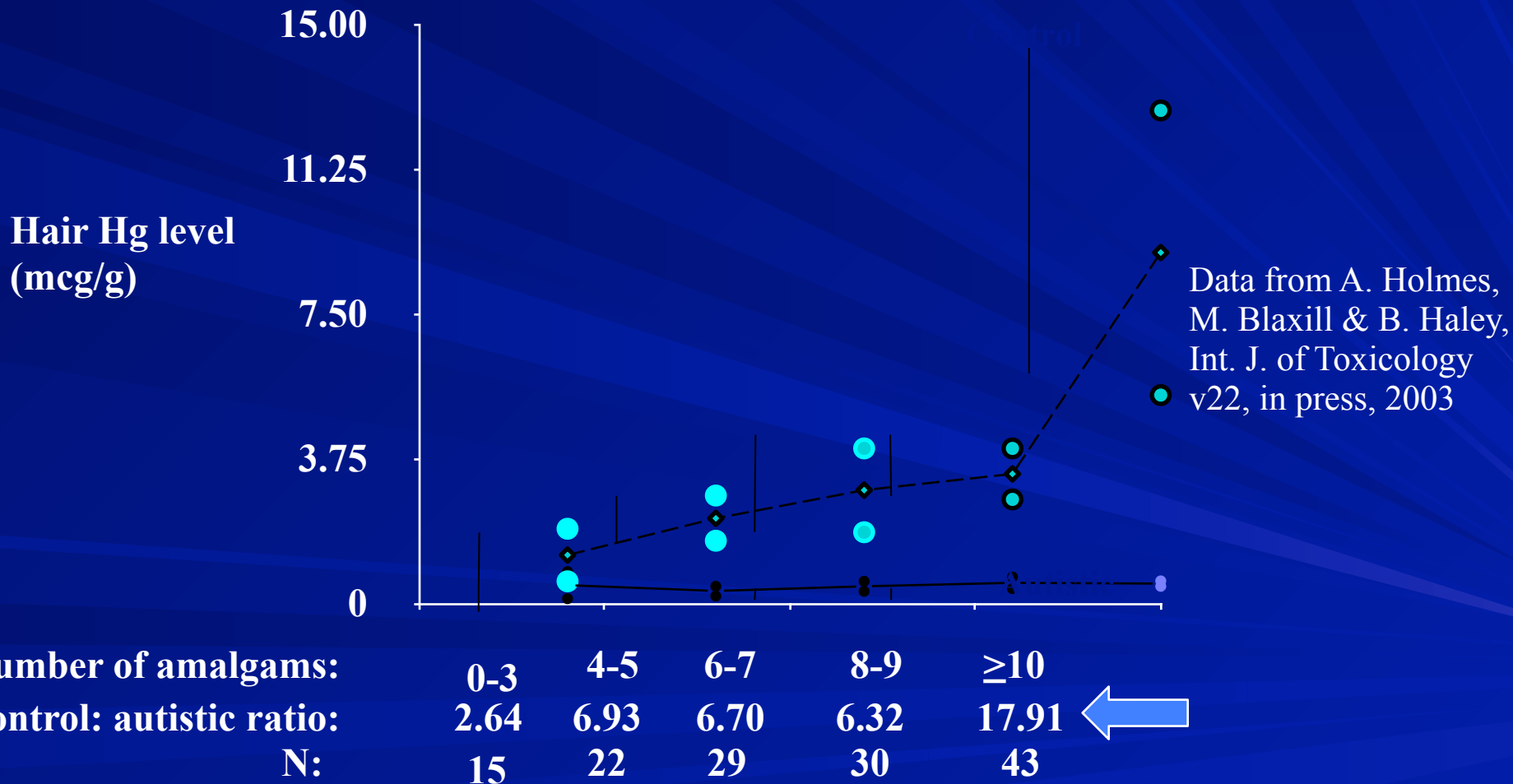
Collaborated with me for many years and works at my Alma Mater in Freiburg, Germany.

E-mail: joachim.mutter@uniklinik-freiburg.de

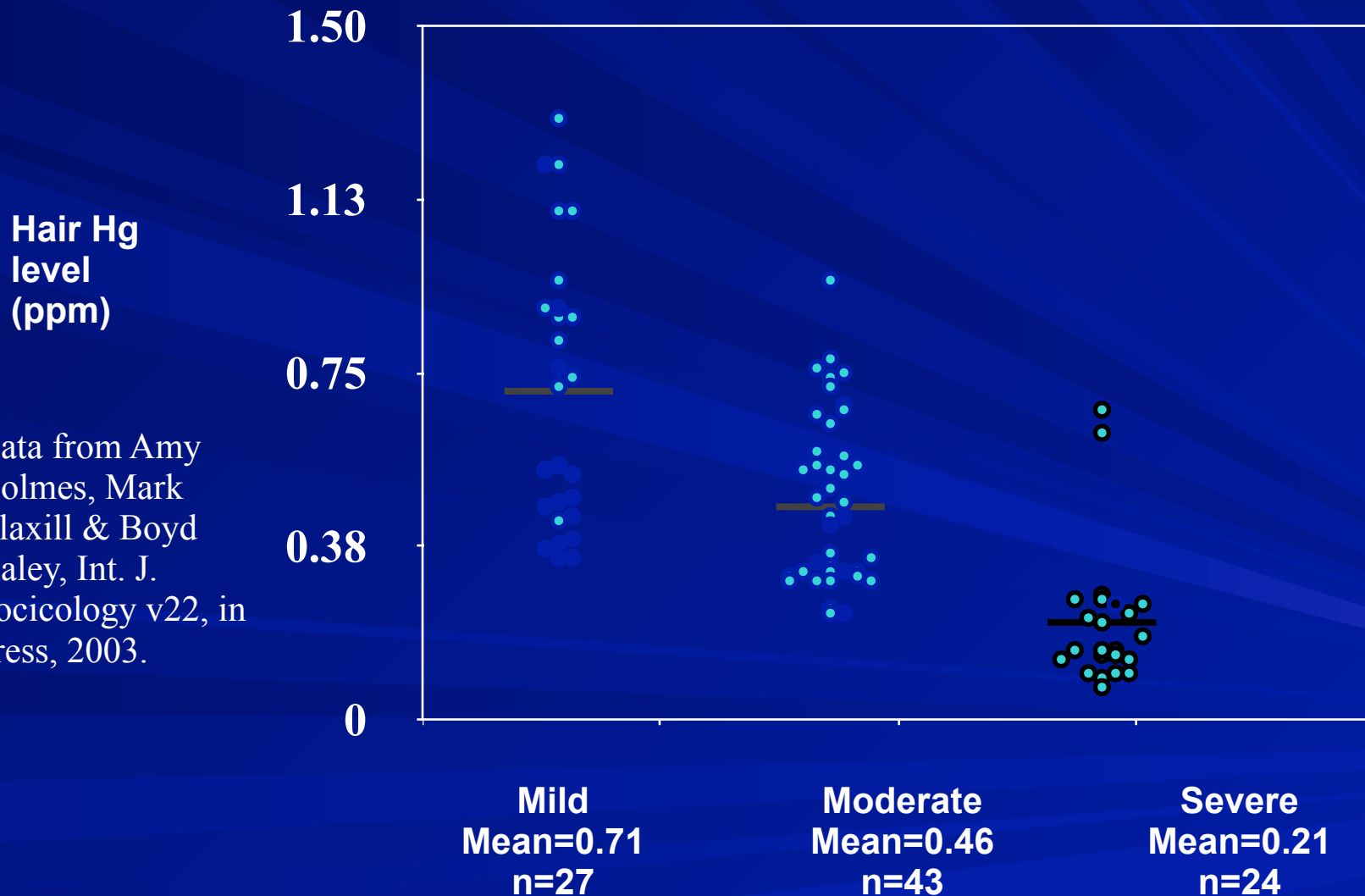
Epidemiological Studies

- Geier & Geier, Thimerosal in Childhood Vaccines, Neurodevelopment Disorders, and Heart Disease in the United States. J. Amer. Physicians & Surgeons v8, #1, p6-11, 2003.
- This study used the VAERS (vaccine adverse event reporting system) data base of the Center for Diseases Control to show that prevalence of autism goes up linearly with increased Hg exposure from vaccines.
- This study provides strong epidemiological evidence for a link between mercury exposure from vaccines and neurodevelopment disorders such as autism, speech disorders and heart disease.

Mercury Birth Hair Levels Vs. Amalgam Fillings In Autistic And Control Groups



Birth Hair Mercury By Severity Of Autism



Data from Amy Holmes, Mark Blaxill & Boyd Haley, Int. J. Toxicology v22, in press, 2003.

Contrast Between Birth Hair Hg Levels and body Hg Levels

- Autistic children have much lower Hg levels in their birth hair, yet numerous physicians have reported that autistic children carry a higher mercury body burden than control children.
- The obvious explanation is micro-mercurialism & genetic susceptibility to retention toxicity.
- There is an obvious gender difference. This is explained by testosterone effects on T-toxicity.

Neurotoxic Effects of Postnatal thimerosal are mouse strain dependent,
Horning M, Chian D, Lipkin WI., Jerome L. and Dawn Greene Infectious
Disease Laboratory, Dep. Of Epidemiology, Mailman School of Public Health,
Columbia University, New York

- Autoimmune propensity influences outcomes in Mice following thimerosal challenges that mimic routine childhood immunizations
- Mice show growth delay
- Reduced locomotion
- Exaggerated response to novelty
- Densely packed hippocampal neurons with altered glutamate receptors and transporters

Other recent findings:

- After the Am. College of Pediatrics recommended a vaccine schedule in 1989 considered by many insane, a sharp raise in new autism cases resulted across the US, not in other western countries that did not follow the US lead. After the college recommended to reduce the amount of thimerosal in the vaccines in 1999, a sharp drop in new autism cases was observed
- There is no autism in the Amish population. There are no vaccinations in the Amish. The only rare cases of autism in the Amish were found in members of the few families that did vaccinate

Mercury and MS/ALS

Cerebrospinal Fluid Protein Changes in Multiple Sclerosis After Dental Amalgam Removal

Alternative Medicine Review Volume 3 Number 4
1998;3(4) 295-300

Hal Huggins, DDS, MS, and Thomas E Levy, MD, JD,
FACC

“....dramatic changes in the photolabeling of cerebrospinal fluid proteins following the removal of amalgam fillings and other dental materials. Suggesting this may be a helpful manner to monitor MS...”

Recovery From Amyotrophic Lateral Sclerosis And From Allergy After Removal Of Dental Amalgam Fillings

International Journal of Risk and Safety in
Medicine, 4 (1994) 229–238

Elsevier Science BV
Olle Redhe and Jaro Pleva

Diagnosis of Mercury Toxicity

Diagnosing Mercury Toxicity

- History of Exposure: (Did you ever have any amalgam fillings? How much fish do you eat and what kind? A tick bite? Etc)
- Symptoms: (How is your short term memory? Do you have areas of numbness, strange sensations, etc)-
- Laboratory Testing:
Direct tests for metals: hair, stool, serum, whole blood, urine analysis, and breath analysis
Xenobiotics: fatty tissue biopsy, urine, breath analysis

Diagnosing Mercury Toxicity

- Indirect tests: cholesterol (**increased while body is dealing with Hg**), increased insulin sensitivity, creatinine clearance, serum mineral levels (**distorted, while Hg is an unresolved issue**), Apolipoprotein E 2/4, urine dip stick test: low specific gravity (**reflects inability of kidneys to concentrate urine**), persistently low urine ph (**metals only go into solution in acidic environments - which supports detoxing**), urine porphyrins
- Autonomic Response Testing: (Dr. Dietrich Klinghardt M.D., Ph.D.)

Diagnosing Mercury Toxicity

- BioEnergetic Testing (EAV, Kinesiology etc.)
- Response to Therapeutic Trial
- Functional Acuity Contrast Test (measure of Retinal Blood Flow)
- Non-specific neurological tests: upper motor neuron signs (clonus, Babinski, hyperreflexia), abnormal nerve conduction studies, EMG etc . Non-specific MRI/CT findings: brain atrophy as in AD, demyelination

Mercury-Specific Lymphocytes: An Indication of Mercury Allergy in Man

Journal of Clinical Immunology Vol. 16, No. 1, 1996
Vera Stejskal, Margit Forsbeck, Karin E. Cederbrandt,
and

“...Oral lichen planus (OLP) adjacent to amalgam fillings were tested in vitro with an optimized lymphocyte proliferation test, MELISA and with patch test. Patients OLP have significantly higher lymphocyte reactivity than the amalgam free control group. Concluding low grade exposure to mercury may induce systemic sensitization as verified by Hg-specific lymphocyte reactivity in vitro..”

Mercury allergy in patients with autoimmune diseases: diagnosis and treatment possibility.

ARMILA PROCHÁZKOVÁ M.D, PH.D., IVAN ŠTERZL M.D., PH.D.*, HANA KUČEROVÁ M.D., JIŘINA BÁRTOVÁ PH.D., VERA D.M. STEJSKAL PH.D.**

From The Institute of Dental Research 1st Medical Faculty and General

- This article is the first to show clearly that most if not all auto-immune diseases are caused by metal exposure and allergy. It also shows a clear relationship: the more amalgam fillings, the more allergy to mercury as shown in the MELISA test (especially or even if skin testing is negative). The more allergy to mercury, the more likely the development of an autoimmune disease.

Urine Toxic Elements Post DMPS Challenge

C.N.: 35 year old male

Dx: CFIDS, FMS

Date	mcg Hg/24 hrs	ppb (post DMPS 3 mg/kg i.v push)
4/23/93	27.8	27.8
6/24/93	99.0	99.0
9/21/93	49.4	49.4
12/23/93	2.1	2.1
4/94-8/94	four treatments with neuraltherapy	
8/24/94	1514.4	1954.0

A.H.: 46 year old Dx: severe depression, multiple neurological symptoms (muscle weakness, numbness, whole body pain)

Date	mcg Hg /24 hrs	mcg Hg/g creatinine (post DMPS)
11/97-4/98	treatment with APN/MFT	
1/24/1998	2100	2700
2/3/1998		2900
4/3/1998	1500	930
4/18/1998		370

Treatments

The Klinghardt Method Of Toxin And Heavy Metal Detoxification

A system based on clinical observation: Tissue-bound toxic metals can only be removed by simultaneously using biochemical, electrochemical and psychobiological approaches

- To remove metals from the intra-cellular environment, psychobiological approaches (Applied Psycho-Neurobiology, Klinghardt) and electrochemical approaches (Toxaway foot bath, KMT microcurrent, homeopathy) are absolutely needed. It cannot be done by swallowing pills or injecting biochemical compounds alone!
- The body is constantly attempting to remove heavy metals, using biochemicals (glutathione and alpha lipoic acid, apolipoprotein E and metallothioneine), specific membrane carriers, macrophages, modulations of pH (metals go into solution in acid environments) and electrochemical interventions (by adding an electron to Hg it is made significantly less toxic) via the ANS
- The primary channels of elimination involve the liver and gallbladder (**R. Shoemaker, www.neurotoxins.com**), and secondary channels include the kidneys, skin, and lungs
- In the large intestine all neurotoxins reabsorbed into the enteric nervous system and transported in a retrograde fashion back into the CNS

Therapeutic goal: to interrupt the enterohepatic circulation of toxins and heavy metals

- Mobilization of toxins from their bound state (APN, coriander, photomobilization, freeze dried goat whey, microcurrent, minerals, etc.)
- Unidirectional transport of toxins through the extracellular tissue to the liver (APN, allium ursinum, goat whey, DMPS, DMSA, alpha-lipoic acid, glutathione, lymph drainage)
- Support the removal of toxins via the gall bladder (APN, coriander, taraxacum officinale, allium ursinum)
- Strong binding of the toxins to substances that can carry them out of the large intestine naturally and completely (activated charcoal, chlorella vulgaris, chlorella pyrenoidosa, chitin, chitosan, beta-sitosterol, apple pectin)

Challenge tests

They generally involve measuring the urine metal content, then administering an oral or i.v. mobilizing agent and re-measuring the metal content in the urine after a few hours.

- Most well known is the DMPS challenge test: **However, there is agreement amongst most researchers, that the urine Hg content does not reflect total body burden – only the currently mobilizable portion of Hg in the endothelium and kidneys.** If nothing comes out, there can still be detrimental but non-responsive amounts of Hg in the CNS, connective tissue and elsewhere
- DMPS mobilizes primarily metals in the kidney and vascular system
- DMSA mobilizes in the liver and gallbladder, less in the kidneys
- Neither agent is well suited to mobilize metals in the CNS. DMPS has also been shown to mobilize mycotoxins, Lyme toxins and other bacterial/fungal endo- and exotoxins. DMSA is known to redistribute metals back into the CNS in individuals with damaged blood-brain barrier

Metal Detoxification Agents and Common Dosages Intravenous

- DMPS: 3 mg/kg once per month i.m or slow i.v.
- IV Vitamin C: 37-50 grams in 500 ml distilled water with 10 ml Ca gluconate
- Glutathione: 1200 mg 1-3x weekly, IV push
- Alpha-lipoic acid: 600 mg in normal saline (250 cc) over 1 hr
- Phospholipids (Lipostabil – German product): 2 ampoules diluted with client's blood (50:50) given slow IV over 3 minutes
- Calcium EDTA: 4-10 ml slow IV push once weekly
- Zinc DTPA (not available in the US)

Subcutaneously, Nerve Blocks, Ganglion Blocks, Segmental Therapy

- Desferal: 500 mg in 4 divided doses over 4 days, 500 mg/week or up to 1x monthly (Kruck protocol for Alzheimer's disease)
- DMPS and glutathione: very effective in neural therapy and ganglion blocks

Vitamin C, glutathione, or lipoic acid did not decrease brain or kidney mercury in rats exposed to mercury vapor

J Toxicology: 2003; 41 (4): 339-47

Aposhian HV, Morgan DL, Queen HL, Maiorina RM, Aposhian MM

“...Young rats were exposed to Hg for 2 hours for a total of 7 days and then after a 7 day equilibrium period DMPS, DMSA, GSH, vitamin C, lipoic acid alone or in combinations were given for 7 days. None of these regiments reduced the Hg contents of the brain. DMPS and DMSA did help reduce Hg concentrations in the kidney..”

Methylmercury Efflux from Brain Capillary Endothelial Cells Is Modulated by Intracellular Glutathione but Not ATP

Toxicology and Applied Pharmacology 141, 526–531
(1996) Article NO. 0318 Laura E. Kerper, Elaine M. Mokrzan, Thomas W. Clarkson, and Nazzareno Ballatori

“..study preformed on bovine brains to show the efflux of methylmercury in relationship to the presence of glutathione (GSH) complex and ATP. There is evidence for transport for glutathione-metal complexes out of cells on specific membrane carriers..”

The Influence of Nutrition on Methyl Mercury Intoxication

Environmental Health Perspectives Vol 108, Supplement 1
1 March 2000 Laurie Chapman and Hing Man Chan

"..this study focus is on the research of methyl mercury, effects on kinetics, toxicity, and possible mechanisms. Children especially in vitro are the most sensitive to the adverse affects of mercury exposure. Foods such as fish, milk, meat, and wheat bran; minerals such as Se, zinc (Zn), copper (Cu), and magnesium (Mg); and vitamins such as vitamin C, vitamin E, and vitamin B complex have been implicated in the alteration of Hg metabolism. Nutritional deficiencies aggravated toxicity levels of mercury. A wide variety of foods and nutrients alter MeHg metabolism, but the mechanisms of interaction often remain speculative. More studies designed specifically to address the role of nutrition in the metabolism and detoxification of MeHg are needed.."

Food as a therapeutic intervention

FoodPharmacy™ Diet Therapy Software



Phone 866-411-1122
www.foodpharmacy.com

Oral administration

- Chlorella: 4-16 grams/day
- Cilantro: 10-15 drops in hot water at night, or topical as segmental therapy treatment
- NDF and NDF Plus (nanonized cilantro and chlorella): 1-10 drops twice daily
- Malic acid (aluminum)
- Intestinal binding: beta sitosterol, charcoal, chlorella, apple pectin
- DMSA: 10 mg/kg/day in divided doses q3-4 h (3 days on, 11 days off)

Oral administration, cont.

- D-Penicillamine (Russell Jaffe protocol)
- D-Alpha Lipoic: 100 mg q 3-4 hours (600 mg/day)- helps glutathione bound toxins to make it through the cell wall
- Organic freeze dried garlic (energetically enhanced from BioPure) : 2-3 caps after each meal 3-4 times/day
- Phospholipid Exchange (from BioPure: energized phospholipids, alpha-Lipoic acid, magnesium and Na-EDTA)- enhances acetylcholine in the brain
- cold processed whey (branched chain amino acids)

Oral administration, cont.

- Forceful electrolyte supplementation (Matrix Electrolyte from BioPure is the most balanced and best tolerated formula for metal detox)
- Forceful trace mineral supplementation, including copper (only Albion chelated minerals are absorbed in sufficient quantity, from Design for Health)
- Carnosine: 1000 mg 3x daily (prevents collagen breakdown)
- Branched chain amino acids: valine, leucine and iso-leucine (high in all whey products)
- Correct neurotransmitter imbalances (use Braverman test from “The Edge Effect”)
- Dopamine is most depleted when chronic infections are present. Use Mucuna powder as precursor

Effect of Lipoic Acid on Biliary Excretion of Glutathione and Metals

Toxicology and Applied Pharmacology 114, 88–96
(1992) Zoltán Gregus, Aron F. Stein, Ferenc Varga,
and Curtis D. Klaassen

“...alpha Lipoic acid increases the biliary excretion of glutathione-bound toxic metals...”

Chlorella

- Antiviral (especially effective against the cytomegaly virus from the herpes family)
- Toxin binding (mucopolysaccharide membrane) all known toxic metals, environmental toxins such as dioxin and others
- Repairs and activates the body's detoxification functions
- Dramatically increases reduced glutathione
- Sporopollenin is as effective as cholestyramin in binding neurotoxins and more effective in binding toxic metals than any other natural substances found
- Various peptides restore ceruloplasmin and metallothionine
- Lipids (12.4%) alpha- and gamma-linoleic acid help to balance the increased intake of fish oil during our detoxification program and are necessary for a multitude of functions, including the formation of their peroxisomes

Chlorella, cont.

- Methyl-cobalamine is food for the nervous system, restores damaged neurons and has its own detoxifying effect
- Chlorella Growth Factor helps the body detoxify itself in a profound way (this is not yet fully understood). It appears that over millions of years chlorella has developed specific detoxifying proteins and peptides for every existing toxic metal
- The porphyrins in chlorophyll have their own strong metal binding effect. Chlorophyll also activates the PPAR-receptor on the nucleus of the cell which is responsible for the transcription of DNA, coding the formation of the peroxisomes (see fish oil), opening of the cell wall which is necessary for all detoxification procedures, normalized insulin

The Standard Maintenance Dosage For Adults For The 6-24 Month Period

- Start with 1 gram (4 tablets) 3 to 4 times a day.
- When moving to the more active phase of the detoxification program the dosage should increase to 3 grams (12 tablets) 3-4 times per day whenever cilantro is given (one week on, 2-4 weeks off and back on the maintenance dosage – see above).
- Take 30 minutes before the main meals and at bedtime. This way chlorella is exactly in that portion of the small intestine where the bile squirts into the gut at the beginning of the meal, carrying with it toxic metals and other toxic waste. These are bound by the chlorella cell wall and carried out via the digestive tract.

The Standard Maintenance Dosage For Adults For The 6-24 Month Period, cont.

- When amalgam fillings are removed, the higher dose (3 grams 3-4 times a day) should be given for 2 days before and 2-5 days after the procedure (the more fillings are removed, the longer this dose should be given).
- If you take Vitamin C during your detoxification program, it must be taken as far away from Chlorella as possible and is best taken after meals.

The Side Effects

- Most side effects reflect the toxic effect of the mobilized metals that are shuttled through the body. This problem is instantly avoided by significantly increasing the chlorella dosage (NB – not by reducing the chlorella dosage, which would worsen the problem. Small chlorella doses mobilize more metals than are bound in the gut, large chlorella doses bind more toxins than are mobilized).
- Some people have problems digesting the cell membrane of chlorella. The enzyme cellulase resolves this problem. Cellulase is available in many health food stores in digestive enzyme products.
- Taking chlorella together with food also helps in some cases, even though it is less effective this way.
- Chlorella Vulgaris has a thinner cell wall and is better tolerated by people with digestive problems.
- Cell wall free chlorella extracts (NDF, PCA) are very expensive, less effective, but easily absorbed.

Protective effects of Chlorella vulgaris extract (CVE[®]) in lead-exposed mice infected with Listeria monocytogenes

Queiroz ML, Rodrigues AP, Bincoletto C, Figueiredo CA, Malacrida S.
Departamento de Farmacologia/Hemocentro, Faculdade de Ciências Médicas,
Universidade Estadual de Campinas (UNICAMP), C.P. 6111, CEP 13083-970, SP,
Campinas, Brazil. mlsq@fcm.unicamp.br *Int Immunopharmacol.* 2003 Jun;3(6):889-900

Chlorella vulgaris extract (CVE) was examined for its chelating effects on the myelosuppression induced by lead in Listeria monocytogenes-infected mice. The reduction in the number of bone marrow granulocyte-macrophage progenitors (CFU-GM) observed after the infection was more severe in the groups previously exposed to lead. Extramedullar hematopoiesis, which was drastically increased after the infection, was not altered by the presence of lead. Treatment with CVE, given simultaneously or following lead exposure, restored to control values the myelosuppression observed in infected/lead-exposed mice and produced a significant increase in serum colony-stimulating activity. The benefits of the CVE treatment were also evident in the recovery of thymus weight, since the reduction produced by the infection was further potentiated by lead exposure. The efficacy of CVE was evident when infected and infected/lead-exposed mice were challenged with a lethal dose of L. monocytogenes after a 10-day treatment with 50 mg/kg CVE/day, given simultaneously to the exposure to 1300 ppm lead acetate in drinking water. Survival rates of 30% for the infected group and of 20% for the infected/lead-exposed groups were observed. Evidence that these protective effects of CVE are partly due to its chelating effect was given by the changes observed in blood lead levels. We have observed in the group receiving the CVE/lead simultaneous exposure a dramatic reduction of 66.03% in blood lead levels, when compared to lead-exposed nontreated control. On the other hand, CVE treatment following lead exposure produced a much less effective chelating effect. CVE treatments for 3 or 10 days, starting 24 h following lead exposure, produced a reduction in blood lead levels of 13.5% and 17%, respectively, compared to lead-exposed nontreated controls. The significantly better response observed with the simultaneous CVE/lead administration indicates that the immunomodulation effect of CVE plays an important role in the ability of this algae to reduce blood lead levels. In this regard, additional experiments with gene knockout C57BL/6 mice lacking a functional IFN-gamma gene demonstrated that this cytokine is of paramount importance in the protection afforded by CVE. The antibacterial evaluation measured by the rate of survival demonstrated that, in face of a 100% survival in the control group composed of normal C57BL/6 mice, which are resistant to L. monocytogenes, we observed no protection whatsoever in the IFN-gamma knockout C57BL/6 mice treated with CVE and inoculated with L. monocytogenes.

PMID: 12781705 [PubMed - in process]

Algenpraeparat hilfreich bei Amalamausleitung

- 25 healthy subjects, 13 weeks
- In this study regular urine and stool tests were performed while clients were put on chlorella regime.
- Results: increased Hg excretion in the stool, decreased Hg excretion in the urine. Significant improvement of subjective health parameters

Dietrich Klinghardt, MD, PhD

Erfahrungsheilkunde, Acta medica empirica, Heidelberg, July 1999 pg 435-438



REVIEW

Mercury Toxicity and Systemic Elimination Agents

JOSEPH MERCOLA DO¹ AND DIETRICH KLINGHARDT MD PhD²

¹Optimal Wellness Center, 1443 W. Schaumburg, Schaumburg, IL 60194, USA;

²American Academy of Neural Therapy, 2802 E. Madison#147, Seattle, WA 98112, USA

Abstract

This paper reviews the published evidence supporting amalgam toxicity and clinical techniques that facilitate mercury elimination. A literature review is provided which documents effective mercury elimination strategies to improve mercury toxicity syndromes. Considering the weight of evidence supporting mercury toxicity, it would seem prudent to select alternative dental restoration materials and consider effective mercury elimination strategies if mercury toxicity is present.

Keywords: amalgam and mercury toxicity, DMPS, DMSA, chlorella, cilantro.

MERCURY EXPOSURE AND TOXICITY IS A PREVALENT AND SIGNIFICANT PUBLIC HEALTH THREAT

Chronic mercury exposure from occupational, environmental, dental amalgam and contaminated food exposure is a significant threat to public health [1]. Those with amalgam fillings exceed all occupational exposure allowances of mercury exposure of all European and North American countries. Adults with four or more amalgams run a significant risk from them, while in children as few as two amalgams will contribute to health problems [2]. In most children, the largest source of mercury is that received from immunizations [3-6] or that transferred to them *in utero* from their mothers [7, 8].

DENTAL AMALGAMS ARE A MAJOR SOURCE OF MERCURY TOXICITY

A single dental amalgam filling with a surface area of only 0.4 cm^{-2} is estimated to release as much as $15 \mu\text{g Hg day}^{-1}$ primarily through mechanical wear and evaporation [1, 9-11]. The average individual has eight amalgam fillings and could absorb up to $120 \mu\text{g Hg day}^{-1}$ from their amalgams. These levels are consistent with reports of $60 \mu\text{g Hg day}^{-1}$ collected in human feces [12]. By way of contrast, estimates of the daily absorption of all forms of mercury from fish and seafood is $2.3 \mu\text{g}$ and from all other foods, air and water is $0.3 \mu\text{g}$ per day [13]. Currently, Germany, Sweden and Denmark severely restrict the use of amalgams [1].

A "silver" filling, or dental amalgam, is not a true alloy. Amalgams are made up of 50% mercury. The amalgam also consists of 35% silver, 9% tin, 6% copper and a trace of zinc [6]. More than 100 million mercury fillings are placed each year in the US as over 90% of dentists use them for restoring posterior teeth [14]. The mercury vapor from the amalgams is lipid soluble and passes readily through cell membranes and across the blood-brain

'Chlorella Accelerates Dioxin Excretion in Rats'

Morita, K; Matsueda T; Iida, T; Hasegawa, T:

Journal of Nutrition. 1999 Sept; 129 (9): pps 1731-6

Abstract:

We investigated the effects of *Chlorella* on the fecal excretion of polychlorinated dibenzo-p-dioxin (PCDD) congeners and polychlorinated dibenzofuran (PCDF) congeners in Wistar rats administered the rice oil that caused Yusho disease, as a substitute for purified dioxin. The rats were fed 4g of a control diet or a 10% *Chlorella* diet containing 0.2 mL of the rice oil once during the 5-d experimental period. The amounts of PCDD and PCDF congeners excreted in feces from d 1 to 5 in the group fed 10% *Chlorella* were 0.2-11.3 and 0.3-12.8 times greater ($P < 0.05$), respectively, than those of the control group. We then investigated the fecal excretion of PCDD and PCDF congeners from d 8 to 35 in rats administered 0.5 ml of the rice oil. Rats consumed the basal diet for 1 wk. After 1 wk, they consumed either the basal diet or the 10% *Chlorella* diet. The fecal excretions of PCDD and PCDF congeners in the group fed 10% *Chlorella* were 0.3-3.4 and 0.5-2.5 times greater (most, $P < 0.05$), respectively, than those of the control group. Thus the fecal excretions of PCDD and PCDF congeners were greater in rats fed *Chlorella*. **These findings suggest that the administration of *Chlorella* may be useful in preventing gastrointestinal absorption and for promoting the excretion of dioxin already absorbed into tissues. Moreover, these findings suggest that *Chlorella* might be useful in the treatment of humans exposed to dioxin.**

This report unfortunately does not reveal which strain of *chlorella* was used in the study (*vulgaris* and *pyrenoidosa* are the two most frequently used for medical research purposes). It is safe to assume, however, that if the *vulgaris* strain was used, then the researchers might well have obtained **higher** dioxin excretion rates by testing with the *pyrenoidosa* strain.

Some of the early research into *chlorella*'s ability to remove chemical toxins was conducted here in the US at The University of West Virginia School of Medicine.

That study showed that rats fed a diet containing chlordecone (a chlorinated hydrocarbon insecticide), that were subsequently given *chlorella pyrenoidosa*, effectively decreased the half-life of the circulating toxin from **40 days to 19 days**. When the experiment was repeated with *chlorella vulgaris*, the reduction in half-life was not nearly so pronounced (40 days to almost 33 days.)

This difference between *chlorellas* has been attributed to the presence of a carotene-like substance known as 'sporopollenin' that is unique to the *pyrenoidosa* strain. ⁽¹⁾

If you and your family fall into any of the 'high-risk for dioxin exposure' groups, - **including consuming a diet containing foods that potentially harbor high levels of dioxin**, two of the smartest things you can do are obviously to reduce your intake of the foods that are on the high-risk list, and ensure that **Nature's Balance Pure Premium Grade *Chlorella pyrenoidosa*** features in your daily supplement regimen!

1. Pore, R.S.: Detoxification of chlordecone poisoned rats with *chlorella* and *chlorella*-derived sporopollenin. *Drug-Chem-Toxicol.* 1984, 7(1), 57-71

Recent studies on metallothionein: protection against toxicity of heavy metals and oxygen free radicals.

Tohoku J Exp Med 2002 Jan: 196(1):9-22
Sato M, Kondoh M.

“..metallothionein (MT) is a cysteine rich, metal binding protein. Rat studies have shown MT is capable of scavenging oxygen free radicals, protects tissues against oxidative injury including radiation, lipid peroxidation, anti-cancer drug stress, and conditions of hyperoxia..”

Heavy metal Detoxification Supportive Modalities

- Sauna
- Electro-mobilization (Toxaway foot bath, KMT 24, KMT 300)
- Mercury vapor lamp
- Photo-mobilization (IR- light shield, Photon Wave, Dinshah color therapy, Mandel color puncture, BioPure eye glasses)
- Colon hydrotherapy
- Lymphatic drainage (KMT or Vodder technique)
- Foot pads (Segiun, Kinotakara)
- Applied Psychoneurobiology / MFT

Mercury exposure evaluations and their correlation with urine mercury excretion : Elimination of mercury by sweating.

J. Occup Med 15;590-591 (1973)

Lovejoy HB, Bell ZG, Vizona TR

The elimination of mercury via sweat has been shown to constitute a significant route for removal of mercury from the body (blood stream)

...

Heavy Metal Detoxification Accessory Agents

- Alpha tocopherol: 1200-2400 IU/day during acute reverse toxicity
- Methylcobalamin: IV with procaine (McGuff: (800) 854-7220)
- Selenium: locks Hg into inert complex, which can be removed via sauna tx
- Hyaluronic acid: enhances IV therapy

Cilantro (Chinese Parsley)

- Mobilizing mercury, cadmium, lead and aluminum in both bones and the central nervous system
- It is probably the only effective agent in mobilizing mercury stored in the intracellular space (attached to mitochondria, tubulin, liposomes etc.) and in the nucleus of the cell (reversing DNA damage of mercury)
- Bile stimulant

Cilantro (Chinese Parsley), cont.

Recommended dosage and application of cilantro tincture:

- Cilantro contains a moderately toxic compound just as parsley does. It is completely inactivated by exposure to hot water
- I recommend to take 10 drops in hot water at bedtime. The effect is potentiated by using the Toxaway foot bath 2-3 times/week. Sip this cilantro tea slowly. This clears the brain quickly of many neurotoxins and is excellent for headaches and other acute symptoms (joint pains, angina, headache etc. Alternatively, rub 10-15 drops into the painful area. This can achieve instant pain relief). This recipe was established by famous nun, medical intuitive and composer Hildegard von Bingen in the year 1040 AC.
- To increase bile neurotoxin excretion (and to stimulate digestive juices) it is best to take 10 drops cilantro in a little hot water 10 minutes before each meal as an herbal bitter. Best if mixed with a small amount of dandelion tincture

Other ways to take cilantro

- Transdermal application:
rub 5 drops twice a day into your ankles for mobilization of metals (and mycotoxins) in all organs, joints and structures below the diaphragm, and into the wrists for the organs, joints and structures above the diaphragm. Ankles and wrists have dense autonomic innervation (axonal uptake of cilantro) and are crossed by the main lymphatic channels (lymphatic uptake).
- The mobilized mercury appears in the exhaled air minutes after application. Therefore not recommended to do in the office

Preventative Effects of Chinese Parsley on Aluminum Deposits in ICR Mice

Acupuncture & Electro-Therapeutics Research 28 (1/2) 1-44 (2003)

82 ABSTRACTS: 18TH ANNUAL INTL. SYMPOSIUM ON ACUPUNCTURE & ELECTRO-THERAPEUTICS

Preventive Effect of Chinese Parsley (*Coriandrum sativum*, Cilantro) on Aluminum Deposition in ICR Mice

Shigeharu FUKUDA Ph.D., Shingo USHIO Ph.D. and Masashi KURIMOTO Ph.D.
Amase Institute and Fujisaki Institute, Hayashihara Biochemical Laboratories Inc.,
Okayama, Japan

Yoshihiro SHIMOTSUURA, M.D., F.J.C.A.E., Cert. ORT-MID (5 Dan)
O-Ring Test Life Science Research Institute & Shimotsuura Clinic,
Kurume, Fukuoka, Japan

Yoshiaki OMURA, M.D., Sc.D., F.A.C.A., F.J.C.A.E., F.A.A.I.M., F.A.S.M.
Director of Medical Research, Heart Disease Research Foundation; President, International College of
Acupuncture & Electro-Therapeutics; Professor, Dept. of Non-Orthodox Medicine, Ukrainian
National Medical University, Kiev, Ukraine; Adjunct Professor, Dept. of Community and Preventive
Medicine, New York Medical College

ABSTRACT

[Purpose] Environmental exposure to Al may present a serious risk to human because it is the most abundant metal in the Earth's crust. It induces disturbances in the functions of the nervous, osseous and erythropoietic systems (1).

Dr. Omura discovered that the accumulation of mercury in tissues, particularly in cell nucleus, may be one of the main causes of cancer and he found that these metal deposits can be removed by using Chinese parsley and Omura's Selective Drug Uptake Enhancement Method (2-5). We previously reported about the scavenging effect of Chinese parsley on localized lead deposition in animal model (6). In this report, the preventive effect of Chinese parsley on aluminum (Al) deposition in male ICR mice exposed to Al is described.

[Materials and Methods] Seven weeks old ICR male mice were exposed to 1000 ppm Al as Al chloride in drinking water for 39 days. Administration of Chinese parsley to mice by gastric intubation was performed for 25 days from 14 days after beginning of Al exposure to the end of experiment. After 39 days, the mice were sacrificed for the comparison of Al distribution. The localized Al in various tissues was analyzed by kinetic differentiation mode of HPLC.

[Results] The total dose of Al given to each experimental group of mice was approximately 200mg. During the experimental period, all the animals gained weight and no differences were found. There were no symptoms of neurotoxicity or other abnormalities. After Al exposure, Al was found to accumulate in the brain, kidney and femur. The highest concentration of Al was observed in the femur. Localized Al deposition in brain was significantly decreased by the administration of

ABSTRACTS: 18TH ANNUAL INTL. SYMPOSIUM ON ACUPUNCTURE & ELECTRO-THERAPEUTICS 83

2.4mg/body of Chinese parsley as shown in Fig.1. The similar results were obtained in femur (Fig.2). Surprisingly, Al levels in femur on Chinese parsley administered group were lower than that on control. It was supposed that the metal deposition may be removed by the administration of Chinese parsley.

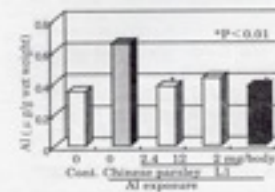


Fig.1 Effect of Chinese parsley on Al concentration in the brain



Fig.2 Effect of Chinese parsley on Al concentration in the femur

1,3-(1,2-diaminohyl-3-hydroxy)pyrid-4-one): a chelating agent used for positive control

[Conclusion] Orally administered Chinese parsley is effective at reducing the deposition of Al in the tissues. These findings suggest the possibility that Chinese parsley may be useful as a natural antidote for Al intoxication.

[References]

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Removal and preconcentration of inorganic and methyl mercury from aqueous media using a sorbent prepared from the plant *Coriandrum sativum*

D. Karunasagar*, M.V. Balarama Krishna, S.V. Rao, J. Arunachalam

National Center for Compositional Characterization of Materials (CCCM), Bhabha Atomic Research Centre, Department of Atomic Energy, ECIL Post, Hyderabad 500062, India

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Abstract

Asorbent prepared from the plant *Coriandrum sativum*, commonly known as coriander or Chinese parsley, was observed to remove inorganic (Hg^{2+}) and methyl mercury (CH_3Hg^+) from aqueous solutions with good efficiency. Batch experiments were carried out to determine the pH dependency in the range 1–10 and the time profiles of sorption for both the species. Removal of both the forms of mercury from spiked ground water samples was found to be efficient and not influenced by other ions. Column experiments with silica-immobilized coriander demonstrated that the sorbent is capable of removing considerable amounts of both forms of mercury from water. The sorption behaviour indicates the major role of carboxylic acid groups in binding the mercury. The studies suggest that the sorbent can be used for the decontamination of inorganic and methyl mercury from contaminated waters.