

Mercury and Environmental toxicity

Dietrich Klinghardt MD,PhD

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www.KlinghardtNeurobiology.com

In the News

- 45 States Have Issued Mercury Advisories: coal-fired power plants
 - Source: News-Leader.com – Quoted from the EPA and Department of Natural Resources
- Mercury and Fish Advisories Issued for Nine More Waterways
 - Source: De Ridder Beauregard Daily News –Quoted from The Louisiana Department of Health and Hospitals Environmental Quality
- Dangerous Lead Levels Found in More Homes
 - Source: Cincinnati Enquirer – Quoted from the EPA
- Lead Linked to Premature Deaths in Adults: Early Exposure = 46% Higher Mortality
 - Source: The Baltimore Sun – Quoted from the CDC

In the News

- California Sues Over Heavy-Metal Fish
 - Source: Business Report – Quoted from the California Attorney General
- Lead Poisoning Alert
 - Source: pediatrics.about.com – Quoted from the FDA
- Mercury Air Level is Worry for Ohio
 - Source: Akron Beacon Journal – Quoted from the EPA
- EPA Doubles Estimates of Children with Mercury in Blood
 - Source: Access North Georgia – Quoted from the EPA
- Mercury List Longer Each Year
 - Source: The News-Press – Quoted from Dept. of Environmental Protection

In the News

- CDC Vaccine Data Leads Scientists to Shocking Discovery: Possible Autism/Mercury/Neurological Link
 - Source: Yahoo News – Quoted from the CDC
- Chromated Copper Arsenate: CCA-Treated Lumber Poses Danger from Arsenic
 - Toxicol Sci. 2004 Jun;79(2):287-95
- EPA: Amount of Toxins in Air, Water and Land Increased at Record Rate...
 - Source: Axis of Logic – Quoted from the EPA
- FDA Warns Pregnant Women to Limit Tuna
 - Richard Simmons -Los Angeles Times 3/2004

Major Heavy Metal Toxins

- Mercury - #3 on the ASTDR's* list of the 20 most hazardous substances
- Lead - #2 on list
- Cadmium - #7 on list
- Aluminum – not a heavy metal, but is addressed by ASTDR due to a possible link to dementias, #194 on list
- Arsenic - #1 on list
- Nickel - #51 on list

*ASTDR – Agency for Toxic Substances and Disease Registry, Atlanta GA, an agency of the USDHHS.

Sources of Toxic Metals - Aluminum

- Eating small amounts of aluminum in food
- Breathing aluminum dust in air
- Drinking contaminated water near:
 - Waste Sites
 - Manufacturing plants
 - Areas naturally high in aluminum
- Antacids
- Cooking utensils
- Household drinking water (aluminum chlorine)



Source: Agency for Toxic Substances & Disease Registry

Sources of Toxic Metals - Arsenic

- Eating food, drinking water or breathing air containing arsenic
- Non-organic chicken (extremely high load)
- Treated wood
- Wood used in children's playgrounds
- Breathing contaminated air
- Breathing sawdust, burning smoke
- Living near hazardous waste sites
- Living near high levels of arsenic in rock



Source: Agency for Toxic Substances & Disease Registry

Sources of Toxic Metals - Cadmium

- Breathing contaminated air
 - Battery manufacturing
 - Car exhaust (especially in inner cities)
 - Cigarette smoke (from treated paper)
 - Metal soldering or welding
- Eating foods containing cadmium:
 - Shellfish, Liver, Kidney meats
- Breathing cigarette smoke
- Drinking contaminated water
- Breathing contaminated air
 - Burning of fossil fuels, municipal waste



Source: Agency for Toxic Substances & Disease Registry

Sources of Toxic Metals - Mercury

- Eating fish or shellfish
- Breathing vapors from:
 - Spills, incinerators, industry
- Dental work, medical treatments
- Breathing contaminated air or skin contact
 - Dental, health services, chemical, other industries using mercury



Source: Agency for Toxic Substances & Disease Registry

Sources of Toxic Metals - Lead

- Eating food, drinking water that contains lead
- Lead base paints
- Working where lead is used
- Health care products containing lead
- Hobbies which lead is used:
 - Glass staining
 - sautering



Source: Agency for Toxic Substances & Disease Registry

Global Chronic Low Level Metal Toxicity

- Recognized by:
 - US Environmental Protection Agency (EPA)
 - Food & Drug Administration (FDA)
 - Centers for Disease Control (CDC)
 - State Health Departments
- Treatment standards are needed
 - Preventative measures
 - Comprehensive medicine with proven results
 - Reduction of crisis management

Olive ReLeaf's study

- *The cohort included 67 uniformed service personnel and 33 residents of Lower Manhattan who had suffered consequences of 9/11.*
- *Lists the health issues and the outcomes as self-reported by the end of the project (two to four months per individual).*
- *Values represent, on a 1 to 5 scale, level of self-reported symptoms before and after treatment with 5 being the most severe.*

- **Kamau Kokayi, MD, et :” Findings of and Treatment for High Levels of Mercury and Lead Toxicity in Ground Zero Rescue and Recovery Workers and Lower Manhattan Residents**
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Self-Reported Health Issues and Health Outcomes

| <i>Symptoms</i> | <i>Rating Before</i> | <i>Rating After</i> |
|----------------------------------|----------------------|---------------------|
| <i>Sleep disorder</i> | 4 | 2 |
| <i>Depression</i> | 3 | 2 |
| <i>Anxiety</i> | 3 | 2 |
| <i>Fatigue/ stress</i> | 4 | 2 |
| <i>Back pain</i> | 3 | 1 |
| <i>Respiratory problems</i> | 3 | 2 |
| <i>Mucosal lining irritation</i> | 3 | 2 |
| <i>Allergies</i> | 2 | 2 |
| <i>Persistent cough</i> | 4 | 2 |
| <i>Skin rashes</i> | 4 | 1 |
| <i>Weight gain</i> | 5 | 1 |
| <i>Gastrointestinal problems</i> | 3 | 2 |
| <i>Elevated blood pressure</i> | 4 | 2 |

Olive ReLeaf's study

Treatment methods:

- DMSA
- Immune system function support
- Acupuncture
- Supplementation with NAC, glutathione, α -lipoic acid, and vitamin C, herbal formulas; glandulars; homeopathy
- Massage, sound healing, Reiki
- Infrared sauna
- Neurotransmitter supplementation

Olive ReLeaf's study

“...within two to three months of beginning the course of treatment... over 60% of the clients reported significant improvement in all of the major health complaints presented at the outset “

Kamau Kokayi, MD, et :” Findings of and Treatment for High Levels of Mercury and Lead Toxicity in Ground Zero Rescue and Recovery Workers and Lower Manhattan Residents

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

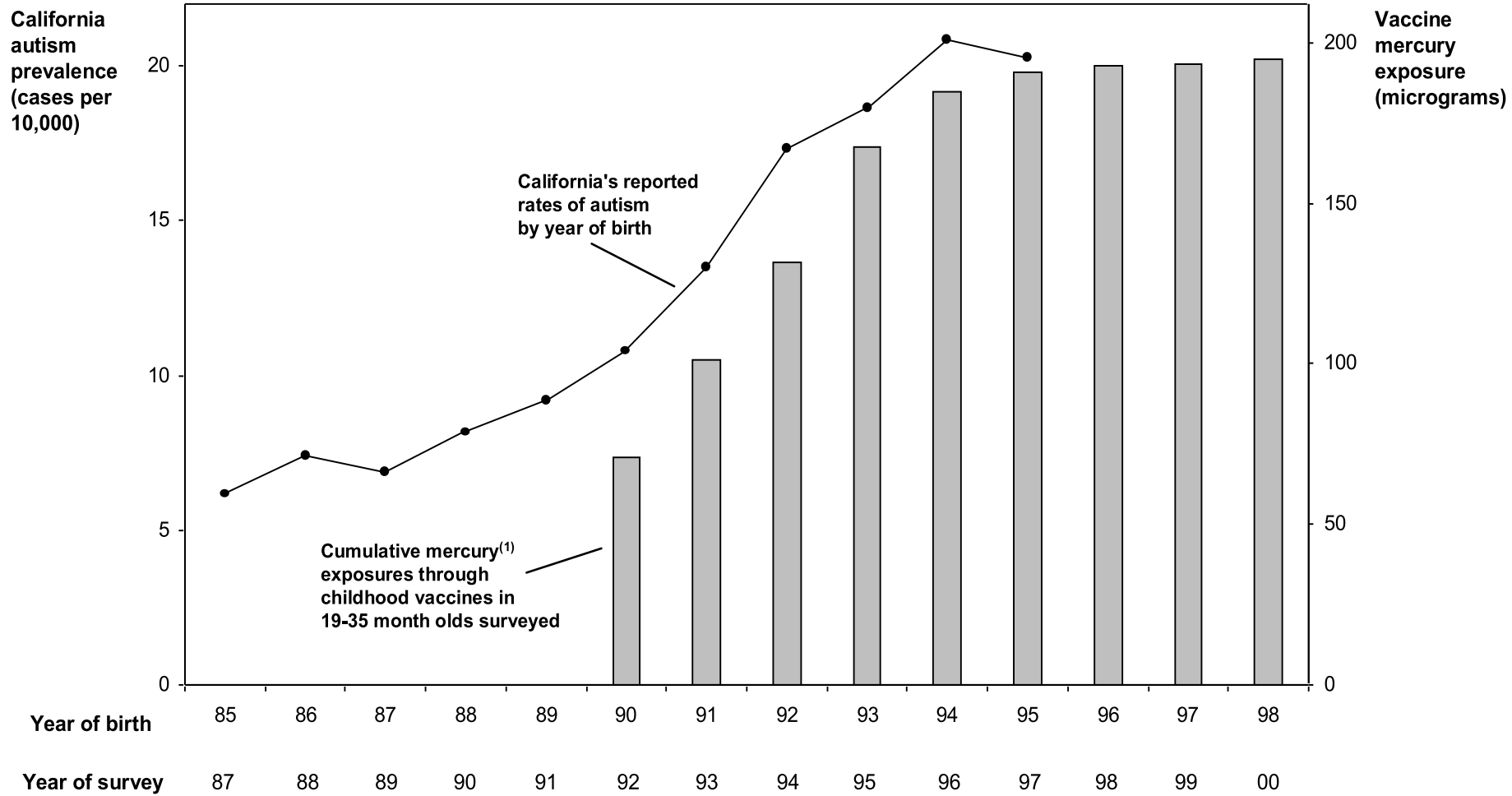
Geier DA, Sykes LK, Geier MR: J Toxicol Environ Health B Crit Rev. 2007 Dec;10(8):575-96

A review of Thimerosal (Merthiolate) and its ethylmercury breakdown product: specific historical considerations regarding safety and effectiveness

Thimerosal (ethyl-mercury thiosalicylate) from vaccines, Rh-prevention (Rhogam), other medications

Autism and ASD is absent in the Amish community where children are not vaccinated. As soon as they do, they also become ill

FIGURE 1: VACCINE MERCURY BURDEN AND AUTISM RISK: UNITED STATES



(1) Includes DPT, haemophilus influenza B and hepatitis B exposures weighted by survey year compliance

2. **Environmental** (Environmental mercury release, special education rates and autism disorder: an ecological study of Texas. F.Palmer et al., Health and Place, Vol 12, Issue 2, June 2006, pp 203-209) "on average, for each 1000 lb of environmentally released mercury, there was....a 61% increase in the rate of autism"

1977-2002 increase in environmental Hg 3–5 fold (UNEP,2002)

1790-1990 increase of environmental Hg 20 fold, in fish at least 1000 fold (Bender 2002 Mercury Policy Project,USA)

3. **Mother** (2/3rds of body burden passed on to child during gestation and breastfeeding) .

70-80 % of mother's Hg burden from amalgam fillings

Stoz et al 1995: Hg in umbilical chord vein 0.2-5ng/ml

Jedrychowski et al 2005: Neurodevelopmental problems in children, when Hg in chord blood over 0.8 ng/ml

Toxin transfer during gestation and lactation period can be significantly reduced by giving the mother regular doses of the algae chlorella (BioPure/sound cracked): 12 -30 tbl. 3 times /day

Algenpraeparat hilfreich bei Amalgamausleitung

D.Klinghardt Erfahrungsheilkunde 7/1999, 435-438

Maternal-fetal distribution and transfer of dioxins in pregnant women in Japan, and attempts to reduce maternal transfer with Chlorella pyrenoidosa supplements

S.Nakano et al, Chemosphere, 2005

Chlorella pyrenoidosa Supplementation decreases dioxin and increases IgA concentration in breast milk

S. Nakano et al, J Med Food 10 (1)2007, 134-142

Metal Toxicity Mechanisms

- Denaturing enzymes
- Displace minerals in cells and tissues
- Interfere with cell membranes functions, ie transport, uptake and release
- Create free radicals/oxidative stress
- Induction of Inflammatory Cytokines
- Mitochondrial damage
- DNA damage

Clarkson TW. The three modern faces of mercury. *Environ Health Perspect* 2002;110:11-23

National Research Council. *Toxicological Effects of Methylmercury*. Washington, DC: National Academy Press 2000:31-70

Yee S, Choi BH. Oxidative Stress in Neurotoxic effects of methymercury poisoning. *Neurotoxicology* 1996;17:17-26

Biological Effects of Heavy Metal Toxicity

- **Neurotoxic:** damage brain structures; lower IQ; down-regulates dopamine activity
- **Nephrotoxic**
- **Immune dysregulation**
- **Cardiovascular**
- **Blood/Circulatory:** Anemia, Raynaud's
- **Bone & tissue deposits**
- **Dysbiosis:** fungal mycotoxins
- **Endocrine disruption:** thyroid, adrenal, sex hormone
- **Cognitive problems:** ADHD, Alzheimer's
- **Mood disorders:** anxiety, depression, OCD
- **Metabolic dysregulation:** energy decline, Weight gain, type II diabetes, hypertension, elevated serum lipids, etc

Restoring Neuroendocrine Function

The Adrenals and Metal Toxicity

- Lead, mercury and cadmium inhibit adenyl cyclase
- Adenyl cyclase catalyzes synthesis of cAMP from ATP
- cAMP co-factor for enzymes in the adrenal cortex and the pituitary

Restoring Neuroendocrine Function

Pesticides and Thyroid Function

- A literature review of effects of synthetic chemicals (DDT, amitrole, thiocarbamates, ethylenethiourea, polyhalogenated hydrocarbons, phenol derivatives and phthalates) on thyroid. Results: 1. Mild thyroid disruption in adult humans with occupational or accidental exposures 2. Several studies linked compromised neurological function in infants and children with high background levels of exposure to PCB's, dioxins, and/or other contaminants. Effects could be due to thyroid disruption or direct neurotoxicity.

Brucker-Davis F. Effects of environmental synthetic chemicals on thyroid function. *Thyroid*. 1998 Sep; 8(9):827-56

Pesticides and Thyroid Function

- Potential effects of common persistent pollutants that contaminate food, water and air on hypothalamic-pituitary-thyroid (HPT) axis – a rat study: A mixture of 16 common organochlorines were administered at minimum risk levels or tolerable daily intakes. All examined endpoints were significantly altered, with TSH significantly increased, and hepatic outer ring deiodinase significantly decreased with a 1x dose and showed dose related increases in severity with increasing dose. Median thyroid follicle cross sectional area was significantly reduced relative to control. Wade MG, et al. Toxicol Sci 2002 Jun;67(2):207-18.
- Bottom Line – Low doses of ubiquitous environmental contaminants can alter HPT physiology in sexually mature males.

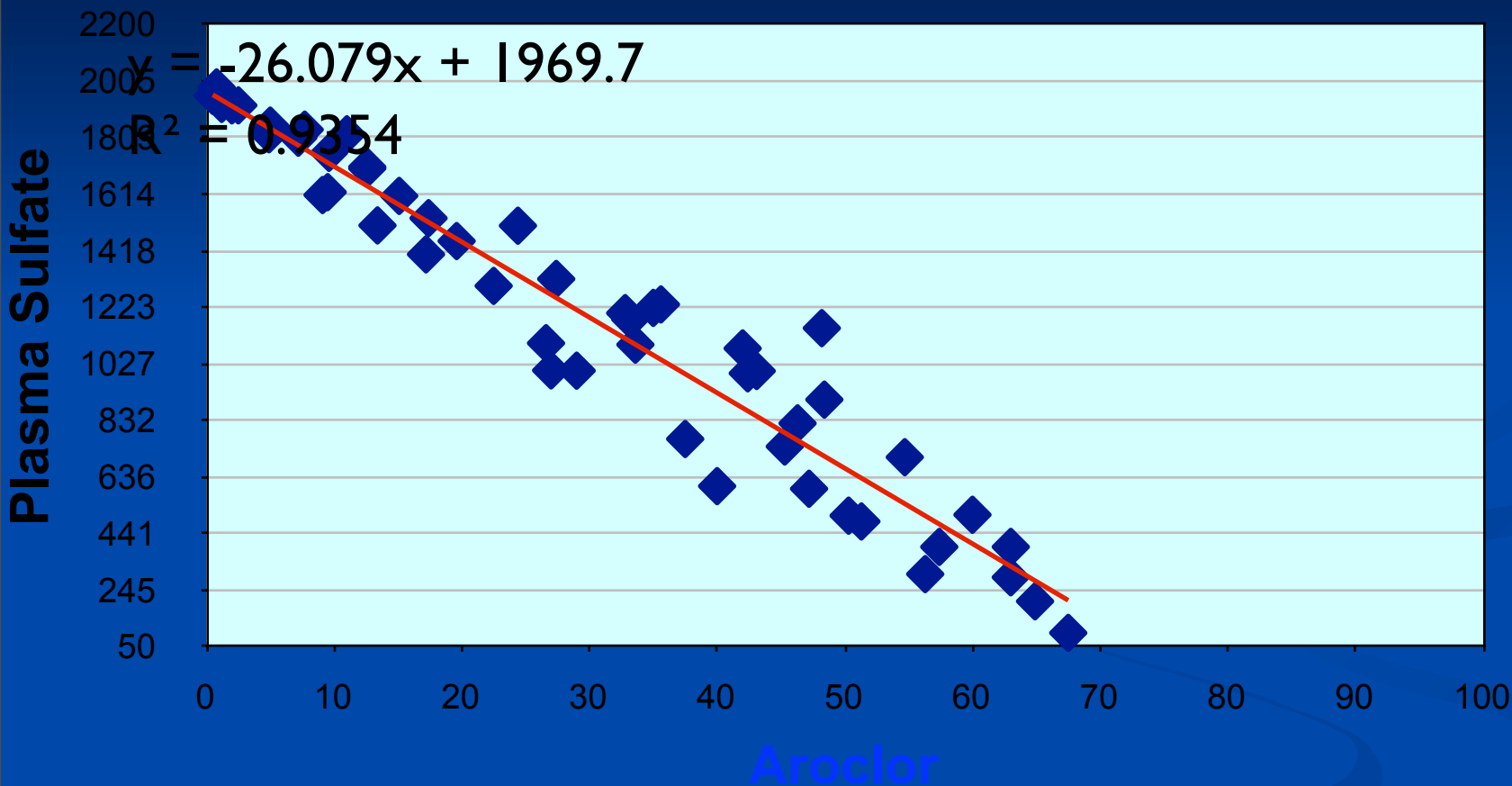
Thyroid Function: goiter causing synergistic effects between toxic metals and pesticides

- Effects of PCB's and organochlorinated pesticides on the thyroid in long term heavy exposure in adults: Results – all thyroid volumes were significantly higher than in the control area.

J Occup Environ Med 2003 May;45(9):526-32

Organophosphates and sulfur levels

Aroclor vs Plasma Sulfate





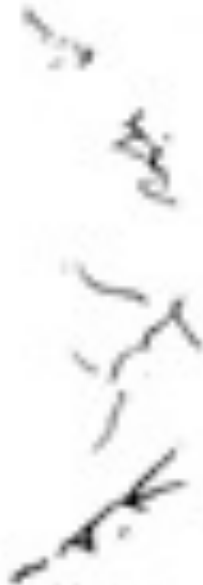
Drawings of a Person

4-year-old girls

5-year-old boys



Little
pesticide
exposure



Heavy
pesticide
exposure



Little
pesticide
exposure



Heavy
pesticide
exposure

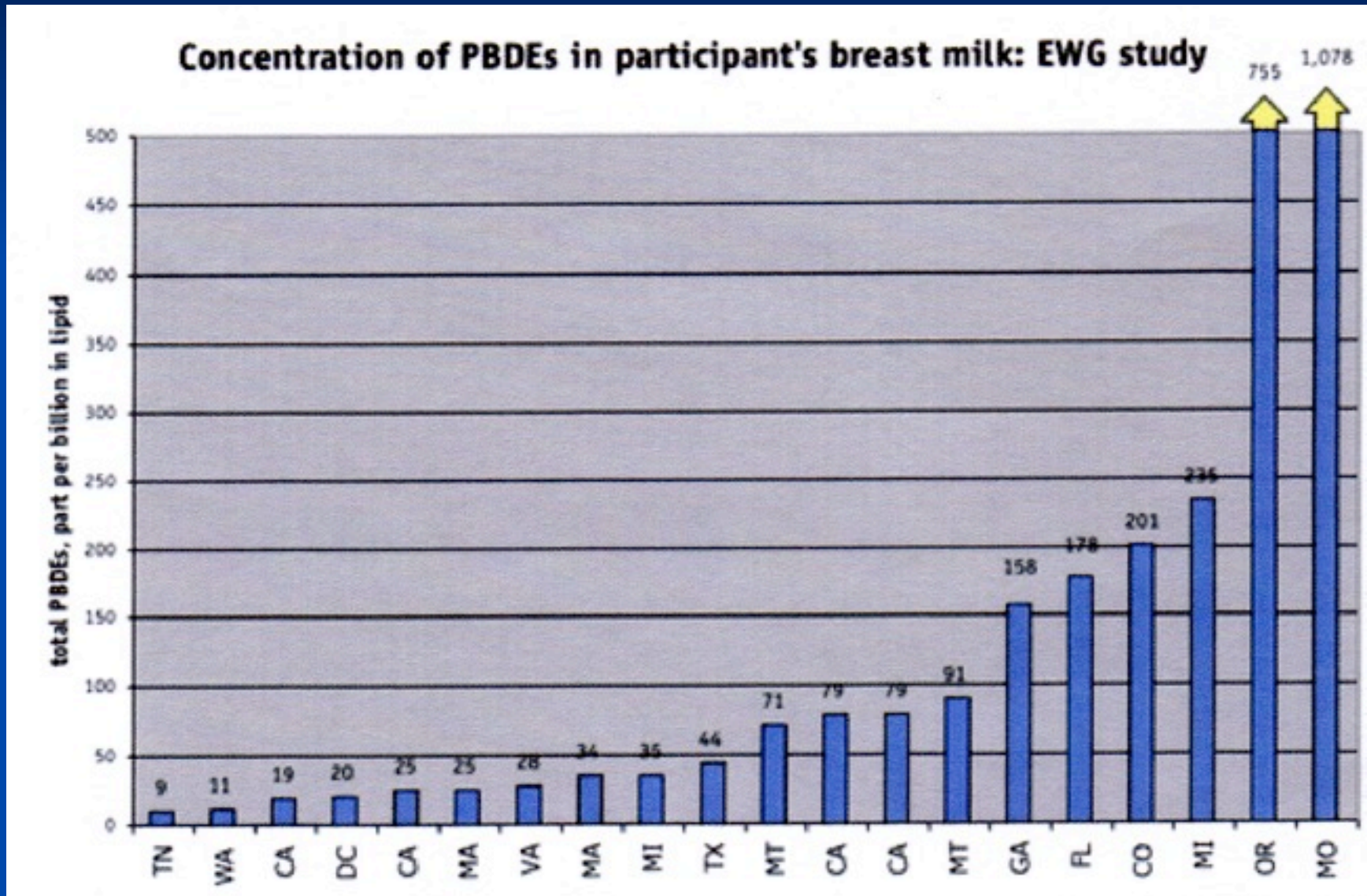
Sources of other toxins in the ASD child: It's all your mother's fault

www.EWG.org

Mothers' Milk: Findings: Levels in U.S. women highest in the world

- Between November 2002 and June 2003, EWG recruited 20 healthy, pregnant women from across the country, all of whom were expecting their first child, to participate in a study of fire retardants in breast milk. Participants collected a breast milk sample within several months of the birth of their child and completed an exposure assessment questionnaire that provided information about their lifestyle and home and work environments. Samples were analyzed by a certified laboratory.
- The lab found PBDEs in every breast milk sample tested — 35 different PBDEs in all. More significantly, our tests found levels higher than those reported previously for U.S. women, including two of the highest levels of PBDEs ever reported in human beings in the world. Levels ranged from 9.5 to 1,078 parts per billion (ppb) in milk fat (lipid), with an average level of 159 ppb, and a median value of 58 ppb. Six of 20 participants had PBDE levels above 100 ppb, with two participants exceeding 700 ppb. The highest PBDE level previously reported in the United States was 580 ppb in maternal blood lipid for a woman in Central Indiana. [45]
- The good news: when we put nursing moms on high doses of BioPure chlorella, most toxins disappeared from the breast milk. All were greatly reduced

Mother-to-child toxin transfer in breast milk



Mercury in the Intestines

- Ingested or inhaled mercury inhibits neutrophils and their subsequent TH1 and TH2 cytokine effects which control Candida. Lowered neutrophil activity allows proliferation of candida.
- Candida organisms methylate mercury vapor from the mouth in the intestines and the mouth.
- Also candida albicans may trap mercury.
- Candida albicans and its mycotoxins are associated with chronic fatigue and autoimmune disorders.

Symptoms of Chronic Mercury Toxicity

Immune System

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

©Copyright 1997 by David Klinghardt, MD, Ph.D., Seattle, Washington, USA

Editorial Note: The following article is a transcription of a lecture presented by the author 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, usually transported inside the axon of the nerve (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 maintain 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 suppresses the immune system has long been known and is supported by the literature.^{4,5,6,7,8,9} This would explain a general immune suppressing 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.¹ 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.¹⁰ 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."¹¹ To increase the yield of precious metals in old mines, so-called "blowmen" are strapped into the mine shaft, washed out with water, and collected on ion exchange membranes. A blowman is a sludge of microorganisms from usually 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 suffocates the intracellular respiratory mechanism and can cause cell death. So, the immune system makes a deal: it outwits fungi and bacteria that bind large amounts of toxic metals. The game the cells can handle. 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 immune system grows 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 syndromes and autolysis for metals. Colleagues 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.

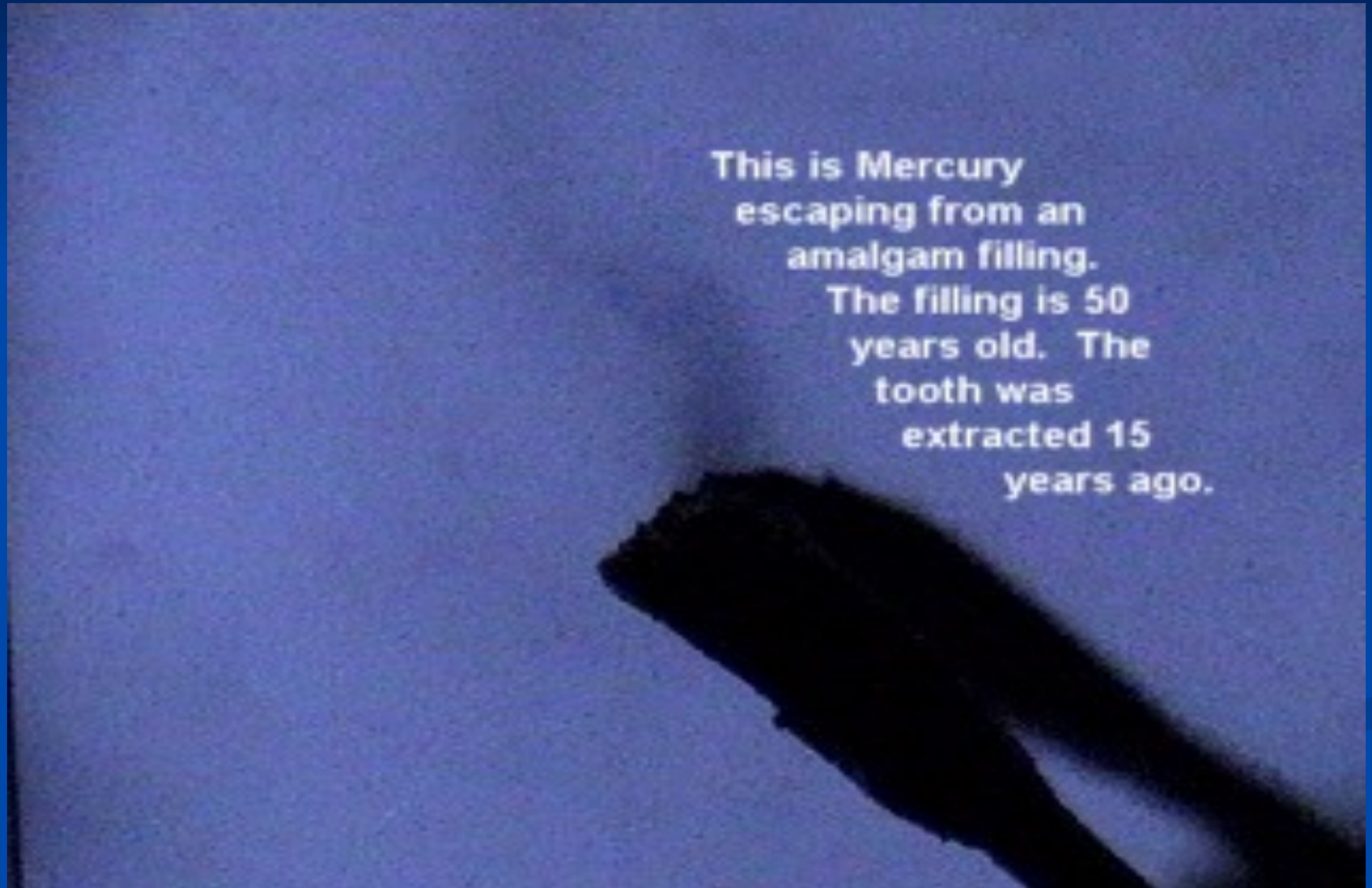
When it comes to chronic viral conditions, the evidence is even more circumstantial. There are several articles in the clinical literature showing remarkable

- 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

Mercury and Candida References

- M.L.S. Queiroz et al, "Immunoglobulin Levels in Workers Exposed to Inorganic Mercury", *Pharmacol Toxicol* 74:72-75, 1994; & "Presence of Micronuclei in lymphocytes of mercury exposed workers", *Immunopharmacol Immunotoxicol*, 1999, 21(1):141-50; & D.C.Santos, "Immunoglobuline E in mercury exposed workers", 1997, 19(3):383-92..
- S. Yannai et al, "Transformationss of inorganic mercury by candida albicans and saccharomyces cerevisiae", *Applied Envir Microbiology*, 1991, 7:245-247
- B.J. Shenker et al, Dept. Of Pathology, Univ. Of Penn. School of Dental Med., "Immunotoxic effects of mercuric compounds on human lymphocytes and monocytes: Alterations in cell viability" and "Immune suppression of human T-cell activation", *Immunopharmacological Immunotoxicol*, 1992, 14 (3):555-77
- P.E. Bigazzi, "Autoimmunity and Heavy Metals", *Lupus*, 1994; 3: 449-453.
- (235) H.J.Hamre, "Mercury from Dental Amalgam and Chronic Fatigue Syndrome", *The CFIDS Chronicle*, Fall 1994, p44-47.
- M. E. Godfrey, "Candida, Dysbiosis and Amalgam", *J. Adv. Med.* vol 9 no 2 (1996); & Romani L, "Immunity to Candida Albicans: Th1, Th2 cells and beyond", *Curr Opin Microbiol* 1999, 2(4):363-7

**Mercury outgases from amalgam fillings for a long, long time.
Up to 80% end up in the CNS**



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

Mercury concentrations in the human brain and kidneys in relation to exposure from dental amalgam fillings



Nylander, M; Friberg, L; Lind, B
Swedish Dental Journal [SWED. DENT. J.]. Vol. 11, pp. 179-187. 1987.

Samples from the central nervous system (occipital lobe cortex, cerebellar cortex and ganglia semilunare) and kidney cortex were collected from autopsies and analysed for total mercury content using neutron activation analyses. Results from 34 individuals showed a statistically significant regression between the number of tooth surfaces containing amalgam and concentration of mercury in the occipital lobe cortex (mean 10.9, range 2.4-28.7 ng Hg/g wet weight). The regression equation $y = 7.2 + 0.24x$ has a 95% confidence interval for the regression coefficient of 0.11-0.37. In 9 cases with suspected alcohol abuse mercury levels in the occipital lobe were, in most cases, somewhat lower than expected based on the regression line. It is concluded that the cause of the association between amalgam load and accumulation of mercury in tissues is the release of mercury vapour from amalgam fillings.

Mercury compartmentalizes in a sheep after placement of several amalgam fillings (Vimy, Lorscheider et al)

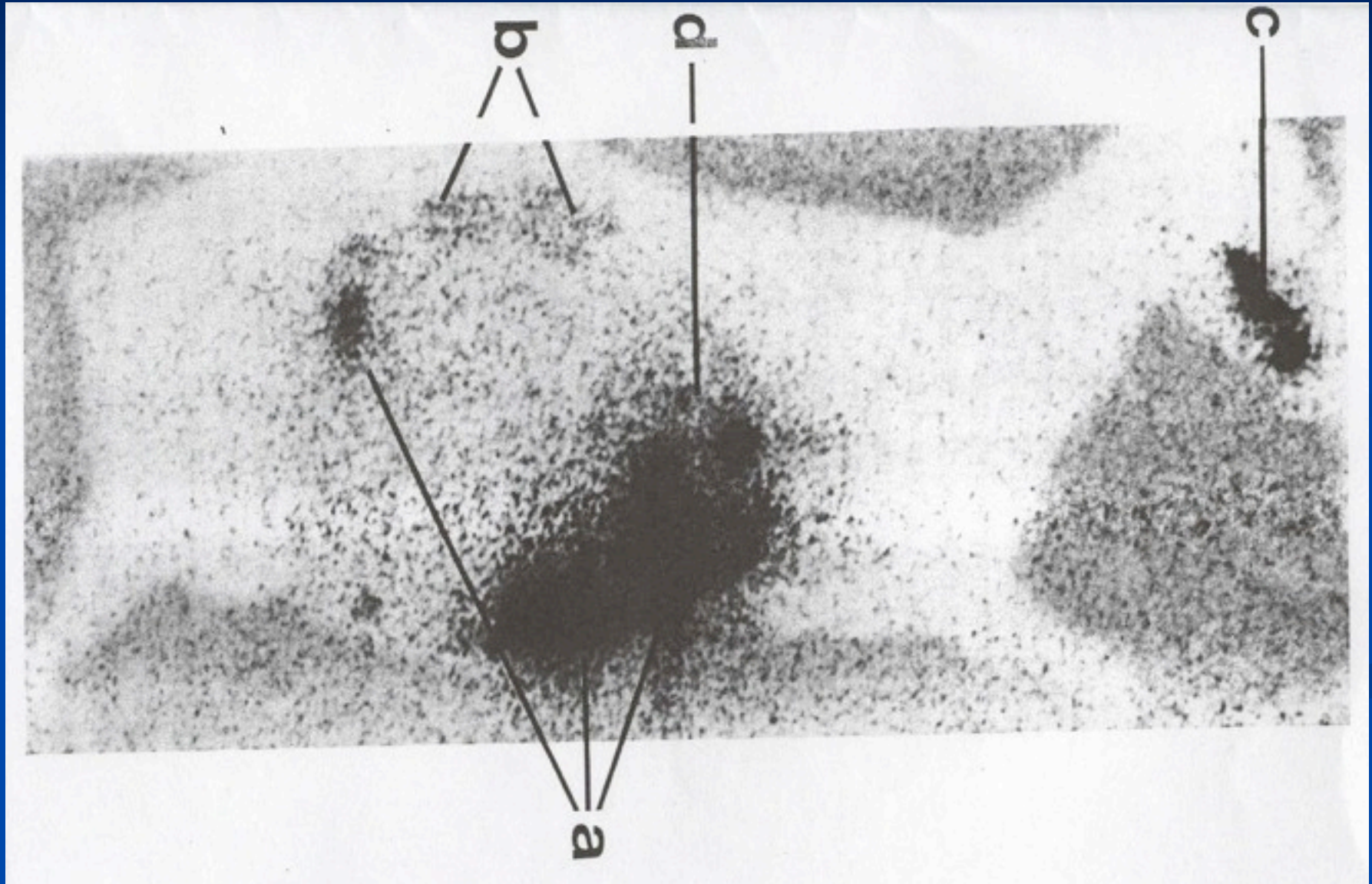


TABLE 1. Concentration of amalgam Hg in monkey tissues 28 days after placement of dental amalgam tooth fillings

| 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 |

Mercury distribution in the rat brain after mercury vapor exposure

- Brown Norwegian rats were exposed to mercury vapor at a concentration of approximately 1 mg/m³ for 5 weeks 24 hr/day 7 days a week and 6 hr/day 3 days a week, respectively. The total mercury absorption was calculated to 264 and 35 µg per week and 100 g body weight. The mean blood mercury concentration was 0.25±0.03 and 0.09±0.01 µg/g, and the total concentration in the brain was 5.03±0.73 and 0.71±0.10 µg/g tissue, respectively. The mercury distribution in the brains was examined using a method based on chemographic principles.
- **Mercury was found primarily in the neocortex, in the basal nuclei, and in the cerebellar Purkinje cells**
- Toxicology and Applied Pharmacology (Toxicol. appl. pharmacol.)
1992, vol. 117, no1, pp. 46-52 (24 ref.)
WARFVINGE K. ; JIANYI HUA ; BERLIN M. ;

Mercury induces inflammatory mediator release from human mast cells

Kempuraj D, Asadi S, Zhang B, Manola A, Hogan J, Peterson E, Theoharides TC.

J Neuroinflammation. 2010 Mar 11;7(1):20.

- Mercury is known to be neurotoxic, but its effects on the immune system are less well known. Mast cells are involved in allergic reactions, but also in innate and acquired immunity, as well as in inflammation. Many patients with Autism Spectrum Disorders (ASD) have "allergic" symptoms; moreover, the prevalence of ASD in patients with mastocytosis, characterized by numerous hyperactive mast cells in most tissues, is 10-fold higher than the general population suggesting mast cell involvement. We, therefore, investigated the effect of mercuric chloride (HgCl₂) on human mast cell activation.

METHODS:

Human leukemic cultured LAD2 mast cells and normal human umbilical cord blood-derived cultured mast cells (hCBMCs) were stimulated by HgCl₂ (0.1-10 microM) for either 10 min for beta-hexosaminidase release or 24 h for measuring vascular endothelial growth factor (VEGF) and IL-6 release by ELISA.

■ RESULTS:

HgCl₂ induced a 2-fold increase in beta-hexosaminidase release, and also significant VEGF release at 0.1 and 1 microM (311+/-32 pg/10*6 cells and 443+/-143 pg/10*6 cells, respectively) from LAD2 mast cells compared to control cells (227+/-17 pg/10*6 cells, n=5, p<0.05). Addition of HgCl₂ (0.1 microM) to the proinflammatory neuropeptide substance P (SP, 0.1 microM) had synergistic action in inducing VEGF from LAD2 mast cells. HgCl₂ also stimulated significant VEGF release (360 +/- 100 pg/10*6 cells at 1 microM, n=5, p<0.05) from hCBMCs compared to control cells (182 +/-57 pg/10*6 cells), and IL-6 release (466+/-57 pg/10*6 cells at 0.1 microM) compared to untreated cells (13+/-25 pg/10*6 cells, n=5, p<0.05). Addition of HgCl₂ (0.1 microM) to SP (5 microM) further increased IL-6 release.

CONCLUSIONS:

HgCl₂ stimulates VEGF and IL-6 release from human mast cells. This phenomenon could disrupt the blood-brain-barrier and permit brain inflammation. **As a result, the findings of the present study provide a biological mechanism for how even low levels of mercury may contribute to ASD pathogenesis.**

<http://www.ncbi.nlm.nih.gov/pubmed/20222982>

Public Health and Economic Consequences of Methyl Mercury Toxicity to the Developing Brain *Environ Health Perspect.* 2005 May; 113(5): 590–596.

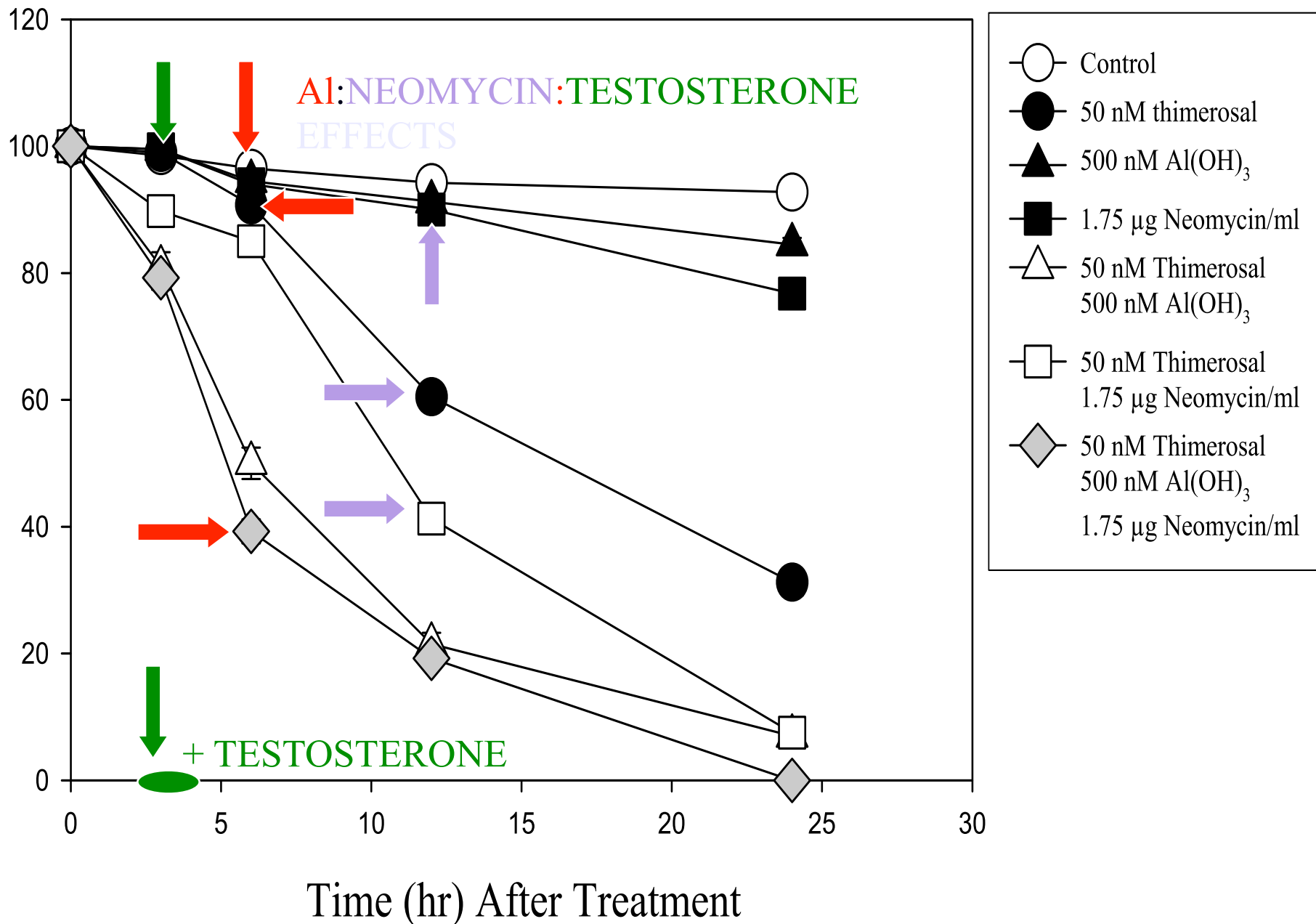
Leonardo Trasande,^{1,2,3,4} Philip J. Landrigan,^{1,2} and Clyde Schechter⁵

1Center for Children's Health and the Environment, Department of Community and Preventive Medicine, and 2Department of Pediatrics, Mount Sinai School of Medicine, New York, New York, USA;

Abstract

Methyl mercury is a developmental neurotoxicant. Exposure results principally from consumption by pregnant women of seafood contaminated by mercury from anthropogenic (70%) and natural (30%) sources. Throughout the 1990s, the U.S. Environmental Protection Agency (EPA) made steady progress in reducing mercury emissions from anthropogenic sources, especially from power plants, which account for 41% of anthropogenic emissions. However, the U.S. EPA recently proposed to slow this progress, citing high costs of pollution abatement. To put into perspective the costs of controlling emissions from American power plants, we have estimated the economic costs of methyl mercury toxicity attributable to mercury from these plants. We used an environmentally attributable fraction model and limited our analysis to the neurodevelopmental impacts—specifically loss of intelligence. Using national blood mercury prevalence data from the Centers for Disease Control and Prevention, we found that between 316,588 and 637,233 children each year have cord blood mercury levels $> 5.8 \mu\text{g/L}$, a level associated with loss of IQ. **The resulting loss of intelligence causes diminished economic productivity that persists over the entire lifetime of these children.** This lost productivity is the major cost of methyl mercury toxicity, and it amounts to \$8.7 billion annually (range, \$2.2–43.8 billion; all costs are in 2000 US\$). Of this total, \$1.3 billion (range, \$0.1–6.5 billion) each year is attributable to mercury emissions from American power plants. This significant toll threatens the economic health and security of the United States and should be considered in the debate on mercury pollution controls.

SYNERGISTIC TOXICITIES



Mercury

Increased blood mercury levels in patients with Alzheimer's disease

Journal of Neural Transmission

1998, vol. 105, no1, pp. 59-68 (1 p.1/4)

HOCK C. (1) ; DRASCH G. (2) ; GOLOMBOWSKI S. (1) ; MÜLLER-SPAHN F. (1) ;
WILLERSHAUSEN-ZÖNNCHEN B. (3) ; SCHWARZ P. (3) ; HOCK U. (1) ; GROWDON J.
H. (4) ; NITSCH R. M. (5) ;

Alzheimer's disease (AD) is a common neurodegenerative disorder that leads to dementia and death. In addition to several genetic parameters, various environmental factors may influence the risk of getting AD. In order to test whether blood levels of the heavy metal mercury are increased in AD, we measured blood mercury concentrations in AD patients (n = 33), and compared them to age-matched control patients with major depression (MD) (n = 45), as well as to an additional control group of patients with various non-psychiatric disorders (n = 65).

Blood mercury levels were more than two-fold higher in AD patients as compared to both control groups ($p = 0.0005$, and $p = 0.000$, respectively). In early onset AD patients (n = 13), blood mercury levels were almost three-fold higher as compared to controls ($p = 0.0002$, and $p = 0.0000$, respectively). These increases were unrelated to the patients' dental status. Linear regression analysis of blood mercury concentrations and CSF levels of amyloid β -peptide ($A\beta$) revealed a significant correlation of these measures in AD patients (n = 15, $r = 0.7440$, $p = 0.0015$, Pearson type of correlation). These results demonstrate elevated blood levels of mercury in AD, and they suggest that this increase of mercury levels is associated with high CSF levels of $A\beta$, whereas tau levels were unrelated. Possible explanations of increased blood mercury levels in AD include yet unidentified environmental sources or release from brain tissue with the advance in neuronal death.

The beneficial effect of amalgam replacement on health in patients with autoimmunity

MELISA[®] testing was done on 35 patients with autoimmune diseases such as MS who responded to Hg *in vitro*

- Amalgams were replaced in some of patients
- Majority of patients who removed amalgams **improved** and their **response to Hg *in vitro* decreased**.
- In contrast, there was no change in health and in laboratory parameters in patients who did not replace amalgams.

The beneficial effect of amalgam replacement on health in patients with autoimmunity

Prochazkova J, Sterzl I, Kucerova H, Bartova J, Stejskal V. Neuroendocrinology Letters 2004;25(3): 211-218

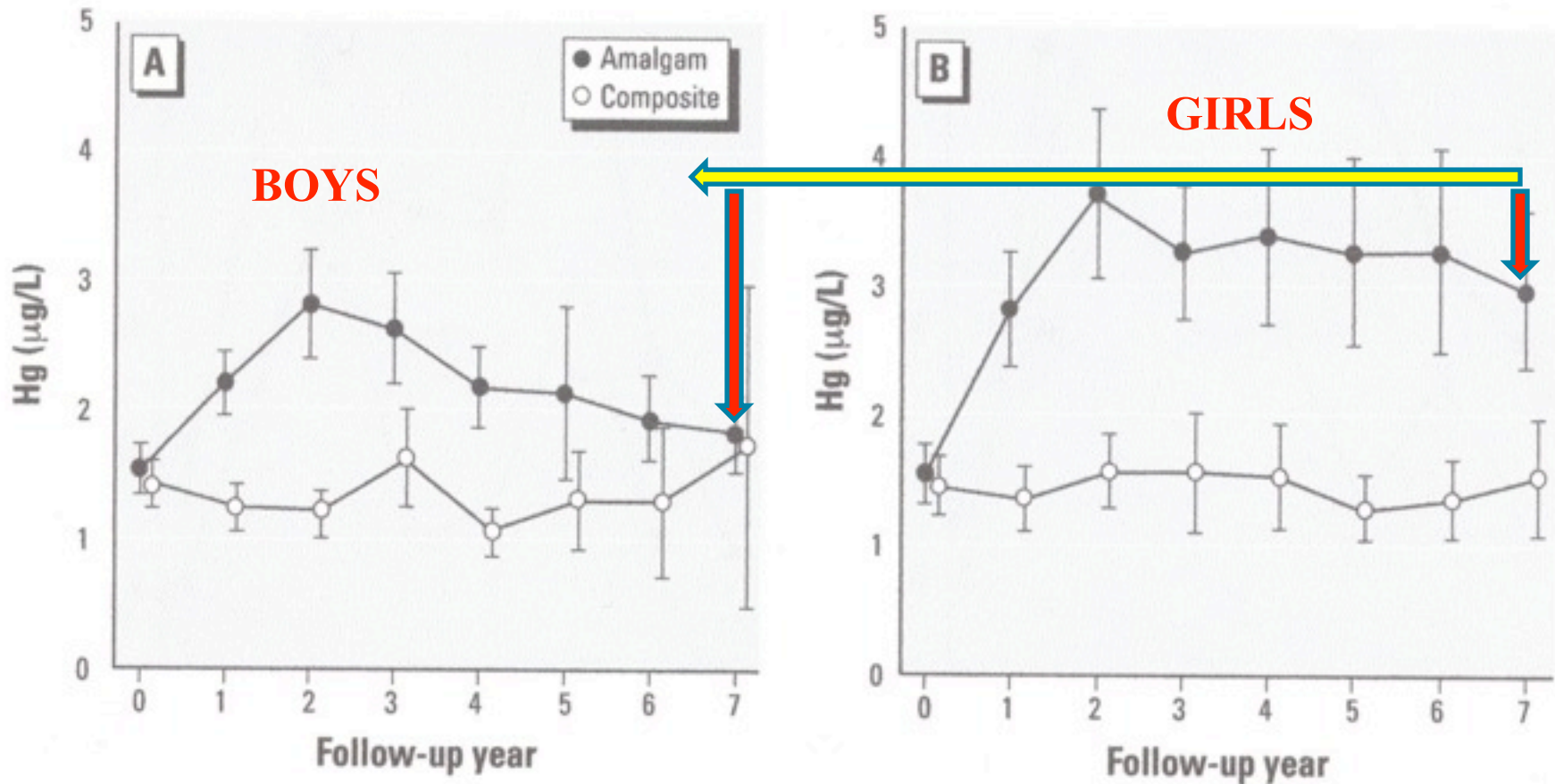
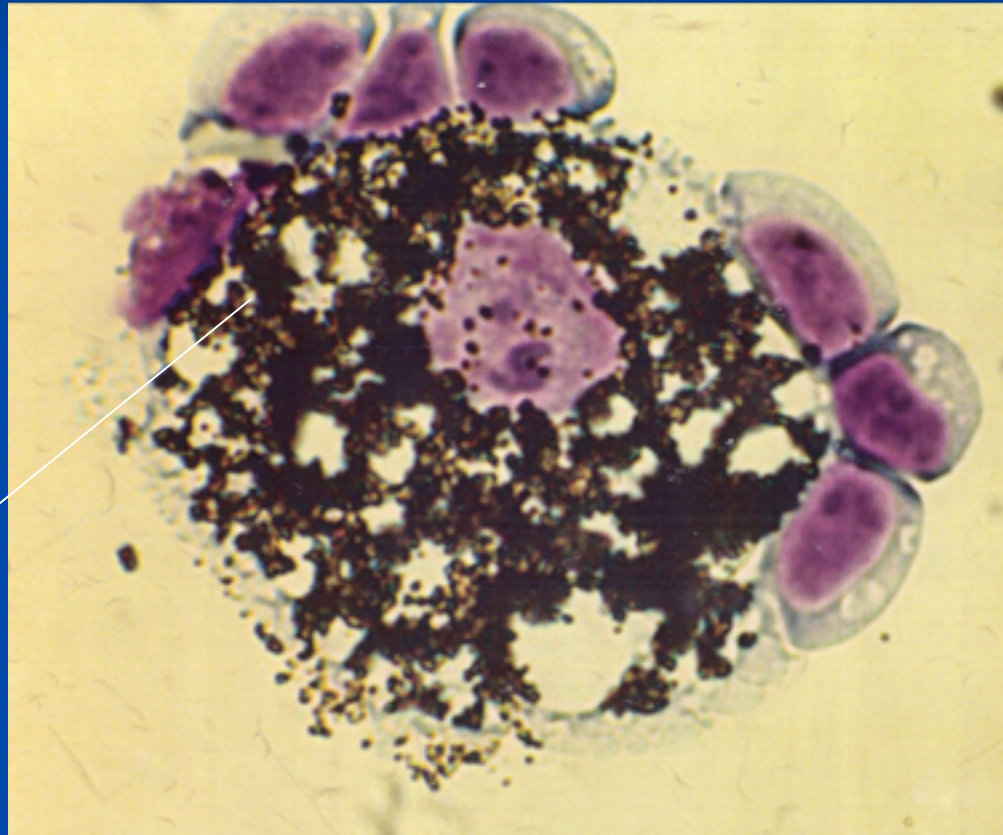


Figure 3. Mean urinary mercury concentrations for the amalgam group and composite group separately for male (A) and female (B) participants. Error bars show 95% confidence intervals for the group means. Differences between males and females in the amalgam group were statistically significant ($p < 0.05$) at all follow-up years except follow-up year 3. The sex comparisons were not altered significantly by adjustment for creatinine (results not shown).

J. Woods, et al., *Environmental Health Perspectives* (2007) 115;10, 1527-1531.

Macrophages cannot handle metals and act as transporters of metal ions



Titanium

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

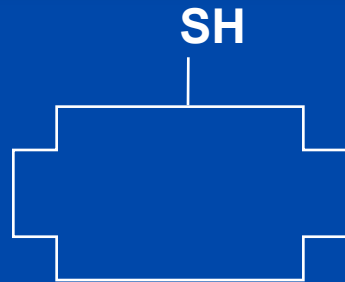
ARMILA PROCHÁZKOVÁ M.D, PH.D., IVAN ŠTERZL M.D., PH.D.*, HANA KUČEROVÁ M.D., JIŘINA BÁRTOVÁ PH.D., VERA D.M. STEJSKAL PH.D.**

From The Institute of Dental Research 1st Medical Faculty and General University Hospital, Prague, Czech Republic (J.P., H.K., J.B.), The Institute of Endocrinology, Prague, Czech Republic (I.Š.) and MELISA MEDICA Foundation, Stockholm, Sweden (V.D.M.S.).

- This article is the first to show clearly that **most if not all autoimmune 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.
- MELISA.org

Metals bind to sulfur (SH) groups and change their configuration. Such cells are recognized

Own cells

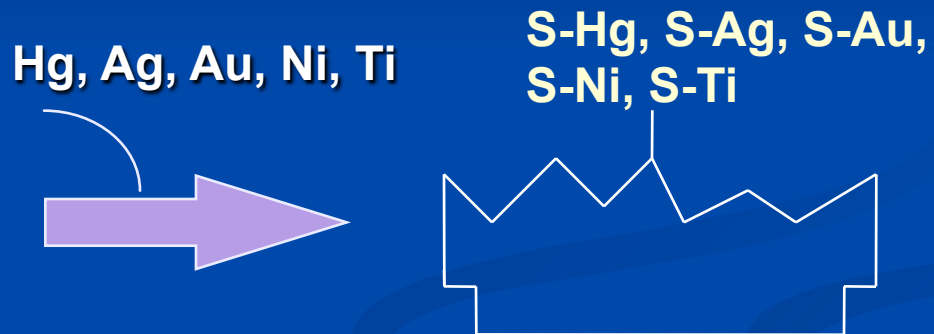


Does not stimulate the immune system



Zzz...

Changed cells



Stimulates the immune system

→ Allergy

→ **Autoimmunity**



007... With license to kill!

Removal of dental amalgam decreases anti-TPO and anti-Tg autoantibodies in patients with autoimmune thyroiditis

The impact of dental amalgam removal on the levels of anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-Tg) antibodies was studied in patients with autoimmune thyroiditis (AT) with and without mercury allergy.

Removal of dental amalgam decreases anti-TPO and anti-Tg autoantibodies in patients with autoimmune thyroiditis. Sterzl I, et al. *Neuro Endocrinol Lett* 2006; 27(1-2):25–30.

Multiple sclerosis study

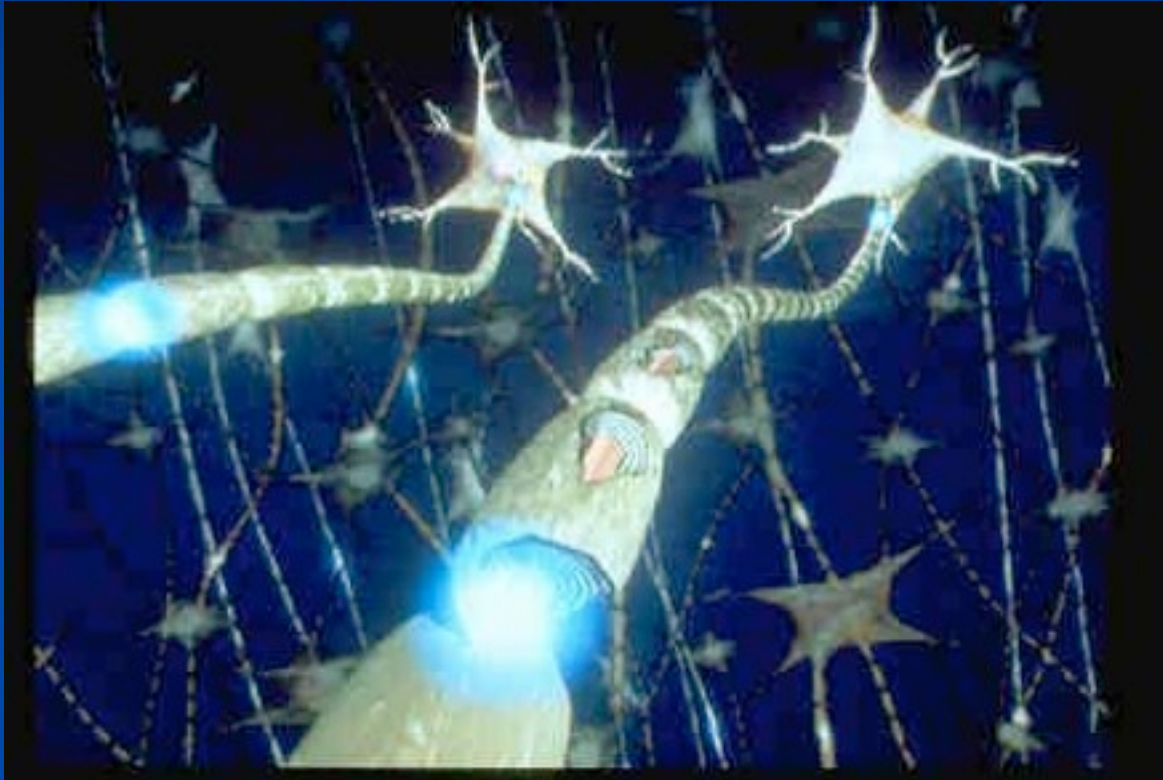
- 106 patients with multiple sclerosis
 - 82 females and 24 males
- 144 healthy controls
 - 80 females and 64 males
- Results
 - MS patients' reactions to metals was significantly increased to following metals: inorganic Hg, phenyl Hg, methyl Hg, gold, palladium, lead, titanium and nickel as compared to healthy subjects
 - In some patients, replacement of allergenic dental materials drastically reduced the symptoms (long term health follow-up until 15 yrs)

Diagnosis and treatment of metal-induced side-effects, Stejskal V, Hudecek R, Stejskal J, Sterzl I. Neuro Endocrinol Lett 2006; 27(Suppl 1): 7-16

Patient EV, F, 52 yrs old

- Thyroiditis with auto-antibodies, fatigue, endocrine problems
- Dental status: 9 amalgam fillings
- Patch test: Nickel +, mercury -
- MELISA: Nickel strongly positive (SI 43), mercury ++ (SI 19), Tin +, MeHg+, PhHg+
- Treatment: Removal of amalgams and anti-oxidant therapy
- Outcome: Improved health, disappearance of auto-antibodies, down-regulation of metal-specific lymphocyte reactivity
- Follow up 9 yrs later, good health!

Myelin sheets bind heavy metals



Patient: Dr BB, F, MD, 40 yrs old

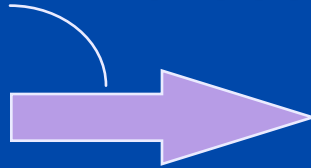
- Optical neuritis at the age of 27, diagnosed with multiple sclerosis year later.
- Dental status: amalgam fillings only
- Patch test + to mercury but negative to nickel, despite well known clinical metal allergy
- MELISA: Mercury + (SI 5,5), Nickel + (SI 6,6)
- Treatment: removal of amalgam under strict protection, replaced with non-metallic ceramic
- On-going anti-oxidant therapy
- Outcome: Symptom-free for last 15 yrs, MRI normalized, neurologist evaluates the patient as healthy

Metal-myelin synergy

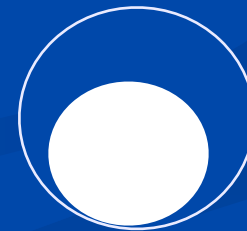
Myelin

Myelin-metal epitope

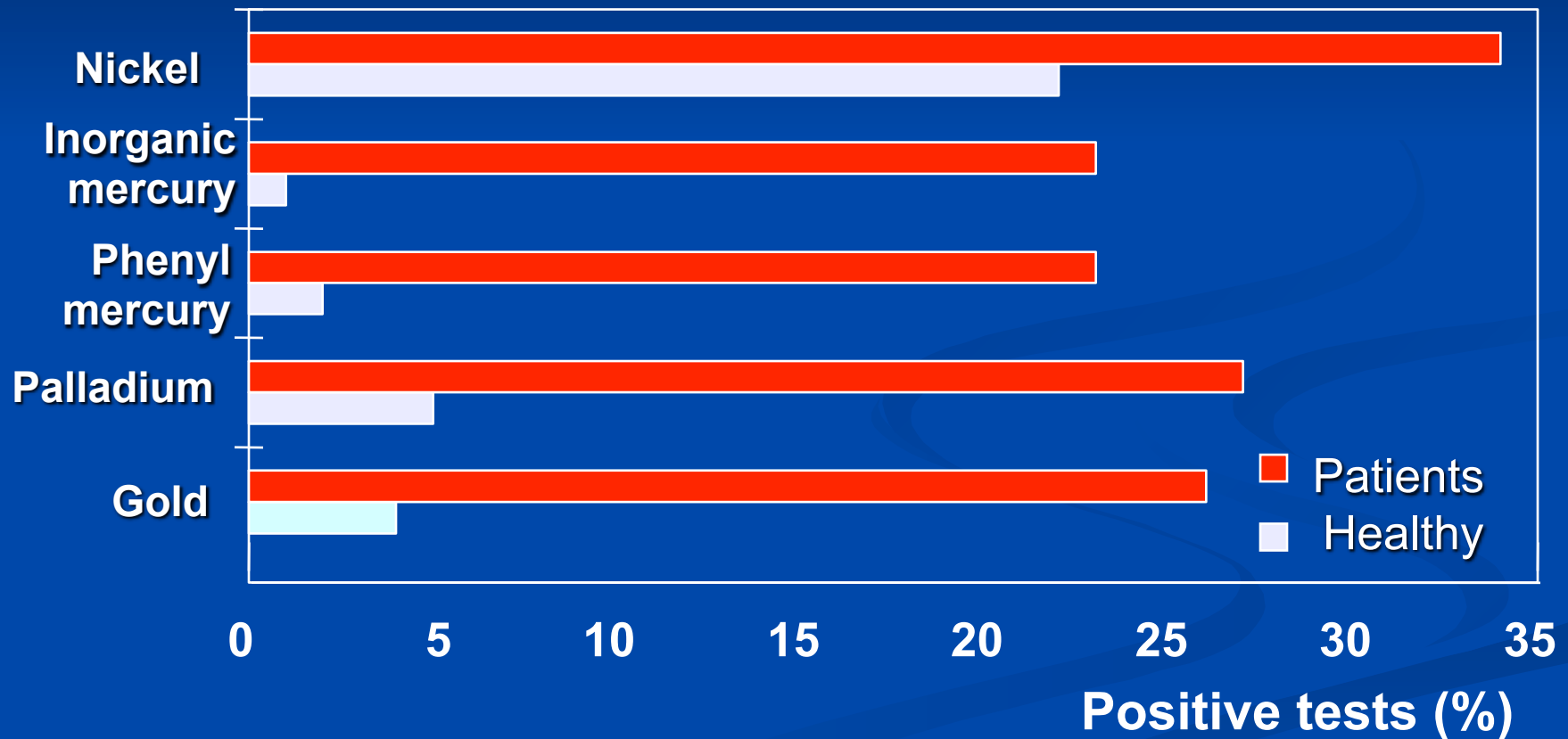
Hg, Thimerosal



Autoimmunity

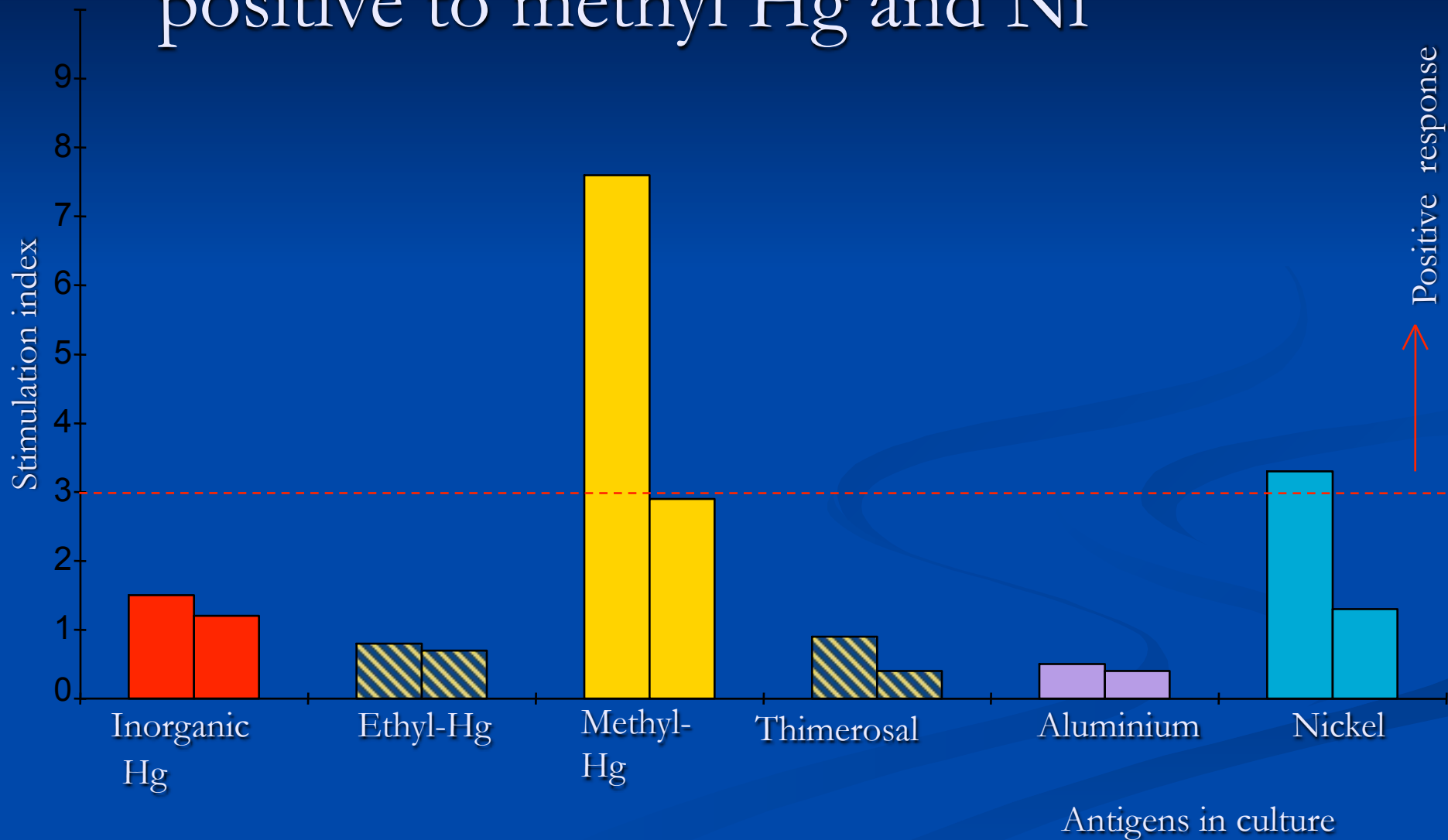


Most frequent metal allergens in 3,162 patients with chronic fatigue-syndrome and in 116 healthy subjects

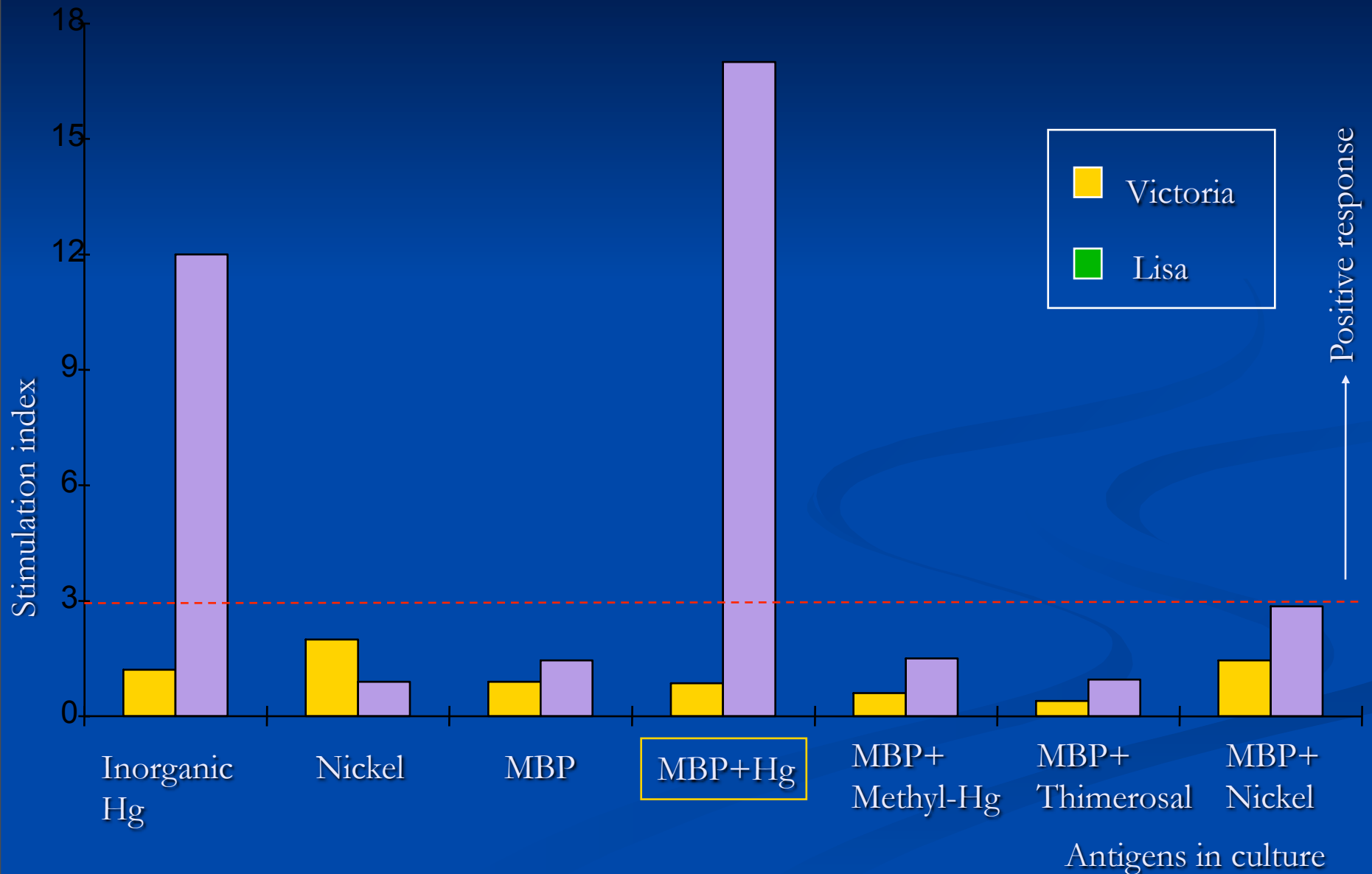


Metal-specific lymphocytes: biomarkers of sensitivity in man
Stejskal, V, et al. Neuroendocrinology Letters 1999; 20:289-298

Kevin D, autistic boy positive to methyl Hg and Ni



Victoria and Lisa P, anti-MBP response



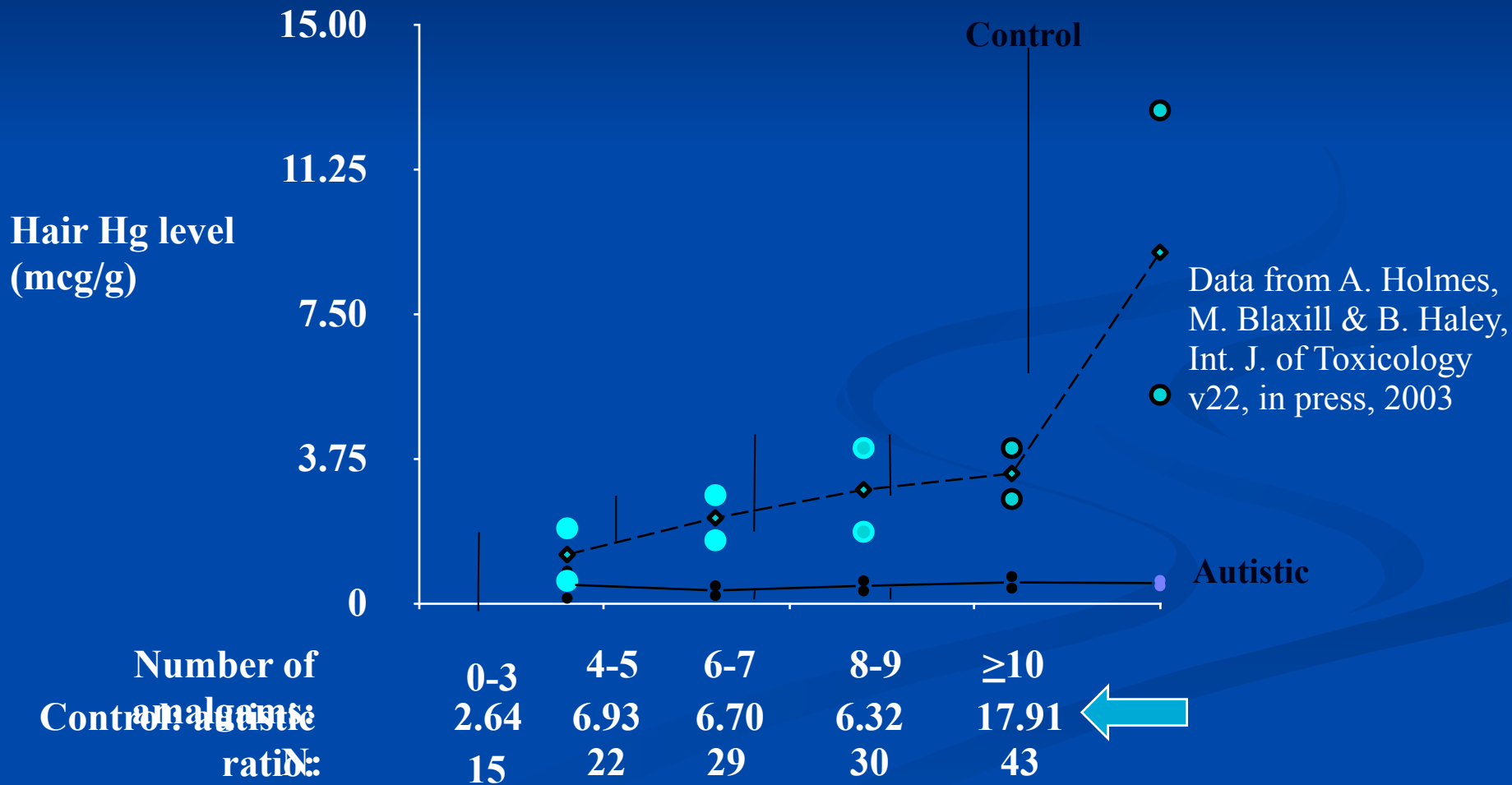
Monitoring methylmercury during pregnancy: maternal hair predicts fetal brain exposure.

Neurotoxicology. 1995 Winter;16(4):705-10

Cernichiari E, Brewer R, Myers GJ, Marsh DO, Lapham LW,
Cox C, Shamlaye CF, Berlin M, Davidson PW, Clarkson TW.

Autistic children fail to excrete Mercury

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



Chlorella in pregnant and breastfeeding mothers

- Effect of chlorella pyrenoidosa on fecal excretion and liver accumulastion of polychlorinated dibenzo-p-dioxin in mice
Chemosphere 2005;59 297-304
- Maternal-fetal distribution and transfer of dioxins in pregnant women in Japan, and attempts to reduce maternal transfer with Chlorella (Chlorella pyrenoidosa) supplements
S.Nakano et al Chemosphere, April 2005
- Chlorella Pyrenoidosa supplementation decreases Dioxin and increases Immunoglobulin A concentrations in breast milk
Shiro Nakano et al J Med Food 10 (1) 2007, 134-142).

Neurotoxic Effects of Postnatal thimerosal are mouse strain dependent

Mol Psychiatry 2004 Sep.;9(9): 833-45

Horning M, Chian D, Lipkin WI., Jerome L. and Dawn - 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

Synergistic factors (factors that increase toxic effects of mercury)

Synergistic factors

(factors that increase toxic effects of mercury)

■ Testosterone

- Recent testing of male and female ASD clients has revealed abnormally high serum testosterone levels in some children. The recommended use of Lupron to lower the levels has worsened symptoms in some children (this suggests that high testosterone is an adaptive mechanism rather than causative). The Lupron treatment is published by Mark and David Geier. Once every 28 days im injection with depot Lupron. Additional daily injection with small doses to achieve 100 microgram/kg bodyweight/day
- I use a special preparation of a homeopathic high dilution homaccord of testosterone (BioPure), which lowers testosterone naturally and corrects the unknown underlying reason for the elevation as demonstrated by the frequent improvement in clinical symptoms
- PC-SPES (several Chinese herbs) has been used successfully to lower testosterone in older male ASD patients.
- Ground flax seeds (1-2 tbsp/day) in yogurt or cottage cheese are binding hormone metabolites in the gut (including man-made hormone mimics such as some insecticides) preventing re-absorption and should be added to the diet where appropriate
- Lavender Oil and Tea tree oil have strong anti-androgenic effects and can be used to lower androgens and elevate estrogens. I recommend using a soap and shampoo containing the 2 oils (Henley et al: Prepubertal gynecomastia linked to lavender and tea tree oils N Engl J Md 2007;356:479-85)

Fluoride

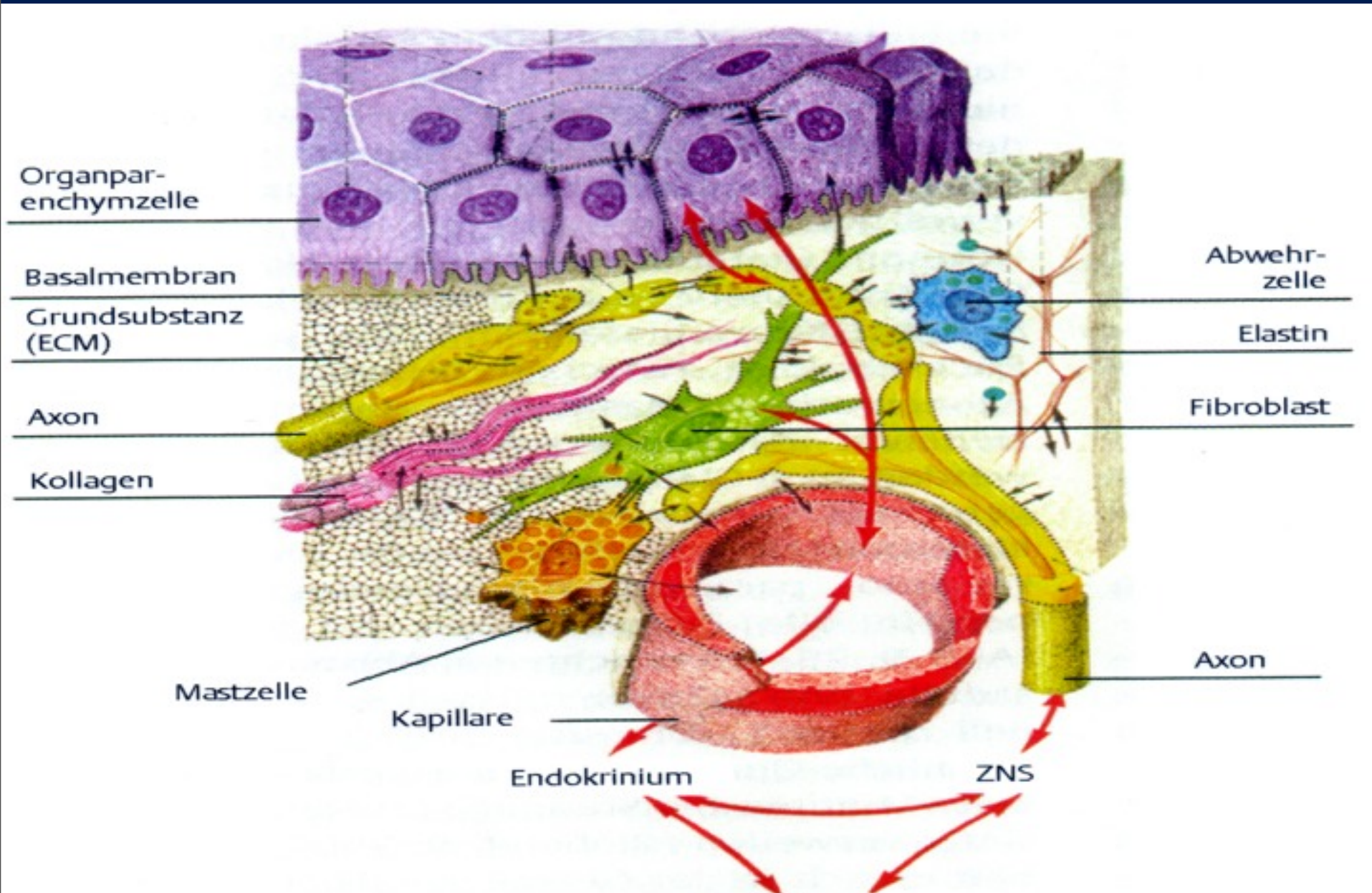
- Avoid or minimize fluoride exposure. Fluoride calcifies the pineal gland (J.Luke) and depletes the most important neuroprotective substance in the body: melatonin

R. Reiter PhD, J of Pineal Res : has most important references

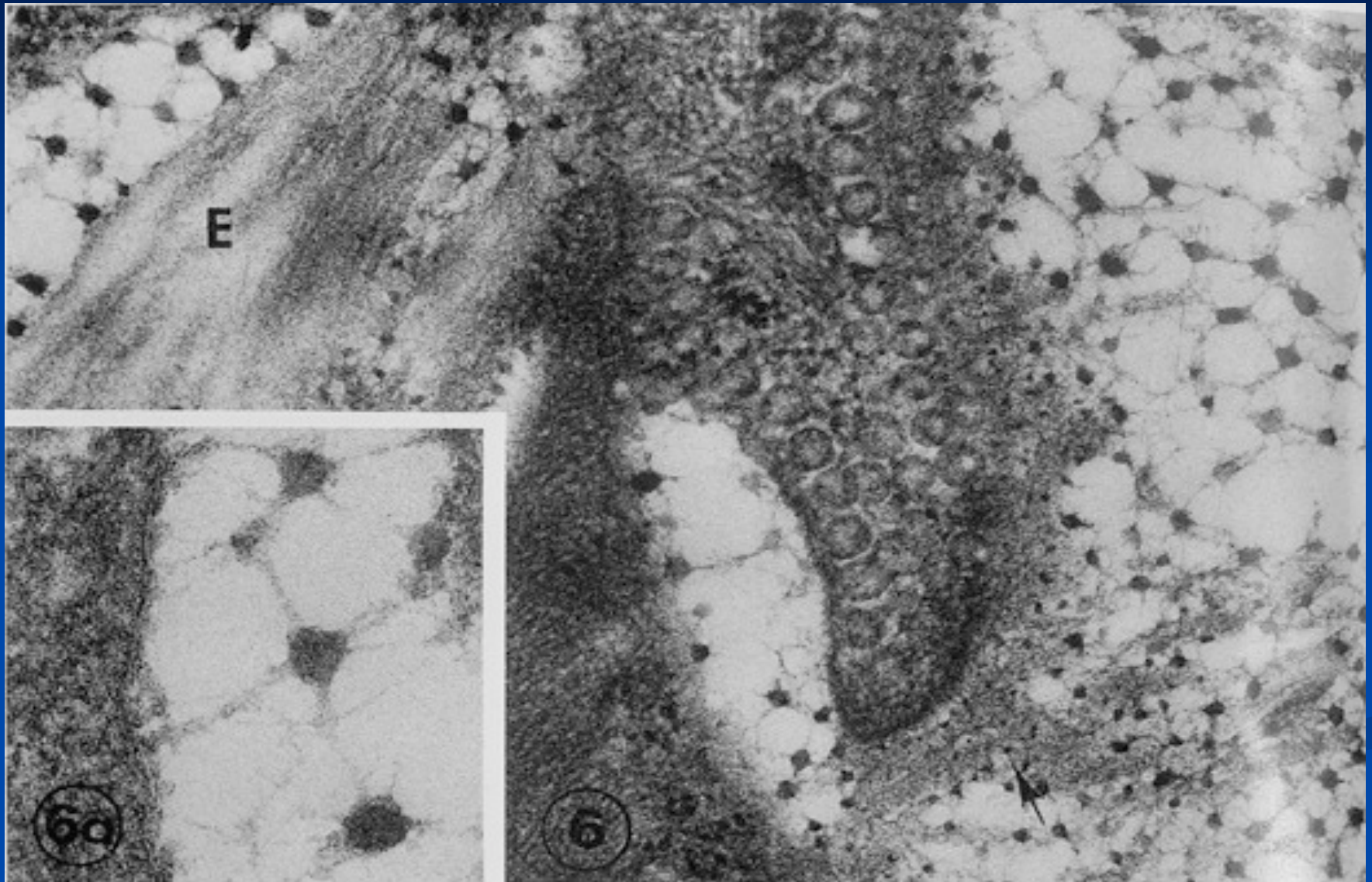
Sener, G.et al: "Melatonin protects against mercury induced oxidative tissue damage". Basic and Clinical Pharmacology & Toxicology Vol 93, Dec 2003, pp 290-296

- Fluoride has a massive synergistic effect with mercury
- Do not use fluoridated toothpaste
- If you live in a fluoridated area: move! If you cant: Get the only fluoride removing water filter for drinking water/cooking currently available: reverse osmosis
- Try to move to non -fluoridated area

Mercury and most other toxins are deposited in the matrix of the extracellular space when liver and kidneys are overwhelmed. Only when the matrix is overwhelmed, toxins enter the cell



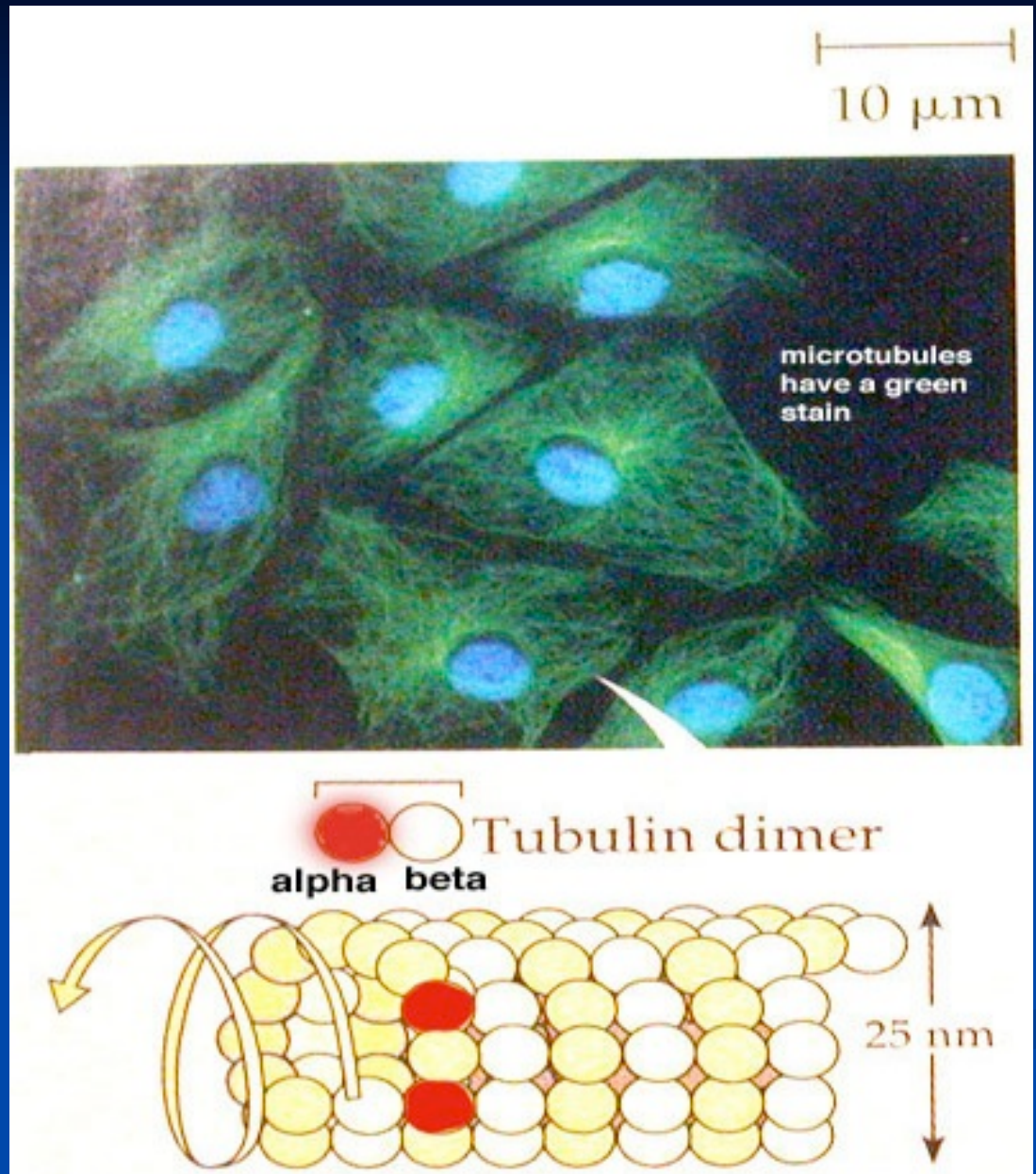
- The main volume of mercury is trapped in the connective tissue of the muscles, bones, ligaments outside the CNS



Magnified 100,000 times

Magnified 50,000 times

■ Later the Hg is taken up by all protein molecules inside the brain and brain-cells: GAGs in matrix, receptors on cell walls, enzymes, structural molecules, GTP, the enzyme which creates tubulin (see article by Joachim Mutter), enzymes of the citric acid cycle inside the mitochondria, etc.



www.lbl.gov

Man-made environmental toxins implicated in Parkinson's disease:

Industrial Solvents

- Carbon Sulfides

Miscellaneous Toxins

- MPTP and pyridyl analogues
- Isoquinolones
- Carbon Monoxide

Pesticides

- Rotenoids(Rotenone)
- Carbamates
(dithiocarbamate)
- Bipyridyls(paraquat)
- Organophosphates
(heptachlor,dieldrin)
- Pyrethroids

Environmental Toxins implicated in PD

Heavy Metals

- Lead
- Mercury
- Aluminum
- Manganese

Medical Drugs

- Dopamine drugs
- Amphetamines (ie, methamphetamine, Amphetamine)
- Haloperidol
- Thiazolines

Drugs that Precipitate Parkinsonian Symptoms

- **Antihypertensives, diuretics:** Diupres, Enduronyl,Hydropres, Regroton, Demi-Regroton, Salutensin, Se-Ap-Es
- **Antihypertensives:** Aldomet
- **Antidepressant:** Asendin, Aventyl/Pamelor, Elvil, Limbritrol, Ludiomil, Luvox, Norpramin, Paxil, Prozac, Sinequan, Tofranil, Triavil, Wellbutrin, Zoloft.
- **Antipsychotic:** Compazine, Haldol, Mellaril, Navane, Prolixin, Risperdal, Stelazine, Thorazine, Zyprexa
- **Other:** Reglan, Zyban

Source: Alternative medicine Review Volume 5 number 6 2000

Nutrient Deficiencies in PD

- CoQ10: electron acceptor in mitochondria
- Supplementation with CoQ10 nearly doubled complex I to healthy levels in PD patients
- NADH electron energy carrier within the mitochondrion oral supplementation 20% improvement of disability.
- L-Tyrosine (competes with Levadopa absorption)
- D-Phenylalanine (competes with L-dopa for absorption)
- Helps reduce rigidity, walking speech, depression but not tremor.
- Tryptophan, B3, B5: given together mood drive and functional improvement
- Tryptophan ameliorated motor dysfunction due to Levadopa

Metal Detoxification Agents and Common Dosages

Intravenous options

- 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: 600-1200 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)

Neural Therapy with detox agents: subcutaneous use, 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 (dilute 1 ml DMPS per 5-9 ml of 1% preservative free procaine)
- **Alpha Lipoic acid** is light sensitive and has to be handled quickly when used in neural therapy. Same dilution as DMPS. Use especially when mold toxins are suspected – best together with glutathion
- **Not suited: Vit. C, EDTA**

Sodium 2,3-dimercapto-1-propanesulfonate (DMPS) treatment does not redistribute lead or mercury to the brain of rats

Sodium 2,3-dimercapto-1-propanesulfonate
(DMPS) treatment does not redistribute lead or
mercury to the brain of rats

Mary M. Aposhian, Richard M. Maiorino,
Zhaofa Xua and H. Vasken Aposhiana

Toxicology

Volume 109, Issue 1, 3 May 1996, Pages 49-55

Detox agents: comparison ALA, DMPS, DMSA and EDTA

- DMPS – removed 86% of mercury in rabbit renal tissue (controversial in U.S.)
- DMSA – removed 65 % of mercury
- Penicillamine – removed 60%
- Glutathione – removed 50%
- ALA – removed 35%
- EDTA – removed 26%

Keith RL, et al. Toxicology 1997;116:67-75

Alpha Lipoic Acid

- Extends life of other free radical scavengers in the body by replenishing their missing electrons, which were lost by previous radical scavenging activity
- Alpha lipoic acid neutralizes both hydroxyl and singlet oxygen radicals. It can be converted in the body to dihydrolipoic acid, as it is effective in neutralizing peroxy and peroxynitrite
- Aids in detoxification of heavy metals

Alpha Lipoic Acid

- Builds and regenerates glutathione levels in cells
- A potent free radical scavenger that regenerates other antioxidants, such as vitamins C and E, and coenzyme Q10.
- Is protective for cells against neurotoxicity and hepatotoxicity of other agents
- Weak heavy metal detoxifier and may mobilize mercury stores in body only to relocate them in other tissues
- Should be used only as an adjunct to other chelators. Limit dosage to antioxidant and insulin receptor enhancing functions. 600mg/day

Alpha Lipoic Acid

- Modulates insulin sensitivity in Type 2 DM
- Reduces inflammatory markers in metabolic syndrome
- Stimulates uptake of glucose via stimulation of GLUT 4 protein (primary glucose transporter in muscle, cardiac, and fat cells)

ALA references

- Jacob S, et al. Free Radical Biology and Medicine 1999;27(3/4): 309-14.
- Sola S, et al. The ISLAND study. Circulation 2005 Jan 25;111(3):343-8.
- Estrada E, et al. 1996; Diabetes 45:1798-1804.
- Muller et al. 1990; Biochem Biophys Acta 1052:386-91.
- Mullet et al. 1995 J. Cereb. Blood Flow Metab. Jul; 15(4): 624-30.
- Gregus Z. et al. Toxicol Appl Pharmacol 1992;39:67-80.

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...”

Lipoic acid as a potential first agent for protection from mycotoxins and treatment of mycotoxicosis.

S. A. Rogers; Arch Environ Health, 58(8):528-532, August 2003

Mycotoxins - toxic substances produced by fungi or molds - are ubiquitous in the environment and are capable of damaging multiple biochemical mechanisms, resulting in a variety of human symptoms referred to collectively as “mycotoxicosis.” In fact, mycotoxins mimic multiple xenobiotics, not only with respect to their ultimate damage, but also in their routes of detoxification. This suggests potential therapeutic options for the challenging treatment of mycotoxicosis. In this brief review, the author examines the use of lipoic acid as an example of an inexpensive and available nutrient that has been shown to protect against, or reverse, the adverse effects of mycotoxins.

Our findings: DMPS, DMSA, DL-Methionine, PC-M, inhaled or i.v. glutathione and other agents used for metal detox also are potent mycotoxin elimination agents

The Mycotoxin Patulin Alters the Barrier Function of the Intestinal Epithelium: Mechanism of Action of the Toxin and Protective Effects of **Glutathione**

R. Manfoud et al.; *Toxicology and Applied Pharmacology*, 181:209-218 (2002)

The active site of PTP contains a cysteine residue (Cys215) that is essential for phosphatase activity. Sulfhydryl-reacting compounds such as acetaldehyde decrease TER through covalent modification of Cys215 of PTP. We propose that the toxicity of patulin for intestinal cells involves, among other potential mechanisms, an inactivation of the active site of PTP.

“Vitamin C, Glutathione, Or Lipoic Acid Did Not Decrease Brain Or Kidney Mercury In Rats Exposed To Mercury Vapor”

Authors: H. Vasken Aposhian ; Daniel L. Morgan ; H. L. Sam Queen ; Richard M. Maiorino ; Mary M. Aposhian

Clinical Toxicology, Volume 41, Issue 4 July 2003 , pages 339 - 347

On oral glutathion:

“The systemic availability of oral glutathione”

Witschi A, *et al*; *European Journal of Clinical Pharmacology* 1992;43(6):667-669.

Am J Physiol 1990; 259:G524-529.

Biochem Biophys Acta 1992;1113:13-23.

- Not thought to increase blood levels with oral administration though some studies have shown that it does
- Not cost effective
- New oral form recently available (acetyl-glutathion)but no data to show effectiveness in metal elimination.

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..”

Oral options

- *Chlorella vulgaris* (sound-cracked/BioPure): 4-16 grams/day
- Cilantro (energized/BioPure): 10-15 drops in hot water 4 times a day (before meals and at bedtime), or topical as segmental therapy treatment
- MicroSilica: silica spheres spiked with sulfhydryl groups
- Matrix Metals (nanonized cilantro and chlorella from BioPure): 1-10 sprays twice daily
- Disulfiram: 250 mg h.s for copper/zinc chelation if indicated
- DMEP: N,N'-bis(2-mercaptoethyl)isophthalamide – fat soluble DMPS related oral compound developed at the University of Kentucky, to increase intra-cellular glutathione and bind/eliminate mercury and its related compounds (ethyl-, methyl Hg, HgCl). Has to be dissolved in 1 tsp “Phospholipid Exchange” for full absorption
- Malic acid (aluminum)
- Intestinal binding: food fiber, clay (green and red from BioPure– 1 tsp twice daily),
- Green clay, beta sitosterol, charcoal, chlorella, apple pectin, zeolites
- DMSA: 10 mg/kg/day in divided doses q3-4 h (3 days on, 11 days off)
or: 250 mg bid q every other day, 3 weeks on, 1 week off
or 100 mg twice weekly at bedtime in treatment of Lyme disease

Chlorella increases metallothionein

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..”

Chlorella and Metal Binding

Cadmium

Hagino et al.: Effect of chlorella on fecal and urinary cadmium excretion in Itai-itai. *Jap. J. Hyg.* 30: 77, 4/1975

Nagano, T./Suketa, Y., et al.: Absorption and excretion of chlorella ellipsoidea cadmium-binding protein and inorganic cadmium in rats. *Jpn. J. Hyg.*, 38: 741-747, 1983

Carr, H.P., Carino, F.A., et al.: Characterization of the cadmium-binding capacity of chlorella vulgaris. *Bull. Environ. Contam. Toxicol.*, 60: 433-440, 1998

Uranium

Horikoshi, T./ Nakajima, A., et al.: Uptake of uranium by various cell fractions of chlorella vulgaris. *Radioisotopes* 28: 485-488, 1979

Nakajima, A; Horikoshi, T; Sakagushi, T.: Recovery of uranium by immobilised micro-organisms. *Evr. J. Appl. Microbiol. Biotech*, 16: 88-91, 1982.

Lead

Protective effects of chlorella vulgaris in lead exposed mice infected with *Listeria monocytogenes*
M.Queiroz et al *International Immunopharmacology* 3 (2003) 889-900

Mercury

Shieh, Y.J.; Barger, J: Uptake of mercury by chlorella and its effect on potassium regulation. *Planta*, 109: 49-60, 1973

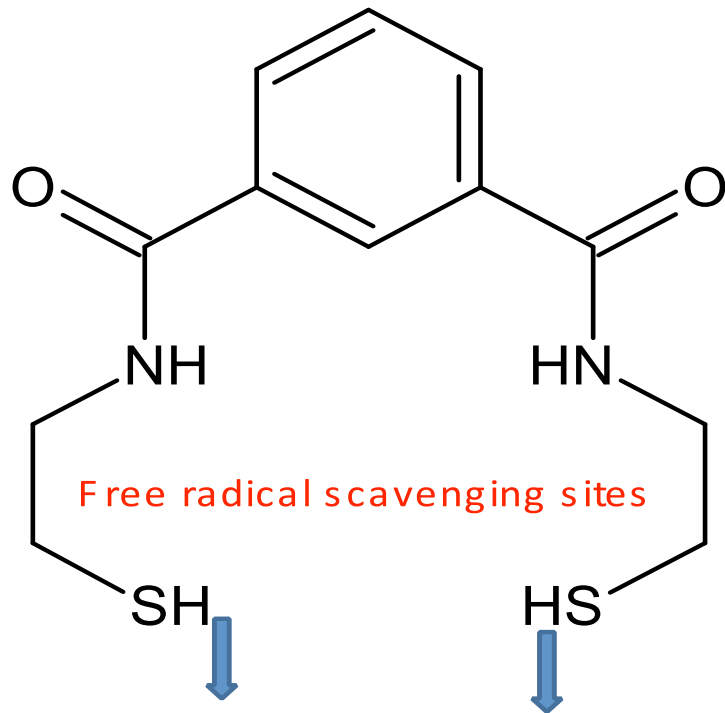
Klinghardt, D. :Algenpraeparat hilfreich bei der Amalgamausleitung
Erfahrungsheilkunde Band 48, Heft 7, Juli 1999

D.Klinghardt and J. Mercola: Mercury toxicity and systemic elimination agents D.Klinghardt and J. Mercola, *J of Nutritional and environmental Medicine* (2001) 11, 53-62

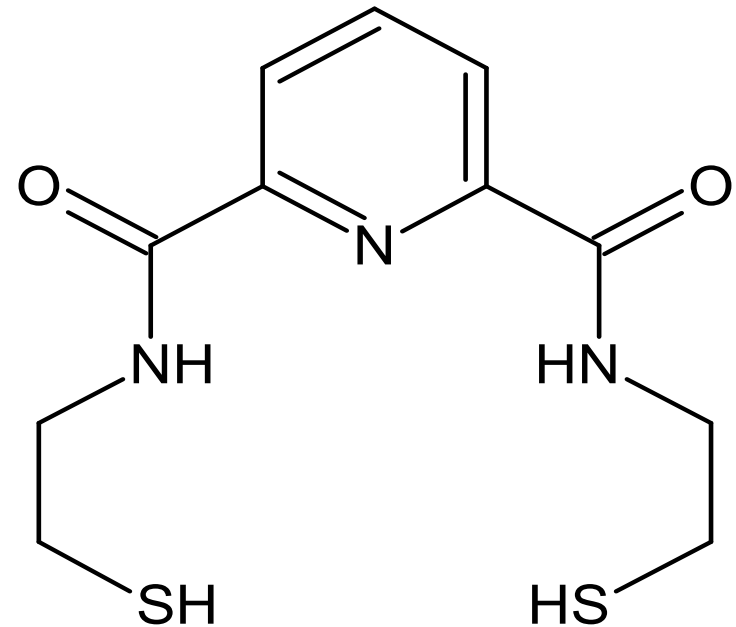
Parachlorella beyerinckii CK-5 is found to accelerate excretion of methyl-mercury both into feces and urine: "Japan Society for Bioscience, Biotechnology and Agro-chemistry"(JSBBA: <http://www.jsbba.or.jp>) Meeting in Nagoya City, Japan, March 29~30, 2008 .

DMEP/OSR (Dimercapto-ethyl-iso-phthalamine)

New Hydrophobic Antioxidant Agents



Benzene bis-amido bis-thiol



Pyridine bis-amido bis-thiol

Potent scavengers of hydroxyl radicals in lipophilic areas. Protect against oxidative stress caused by many toxins.

Water insoluble, but lipid soluble, coupling with glutathione makes this compound water soluble (next slide).

DMEP/OSR

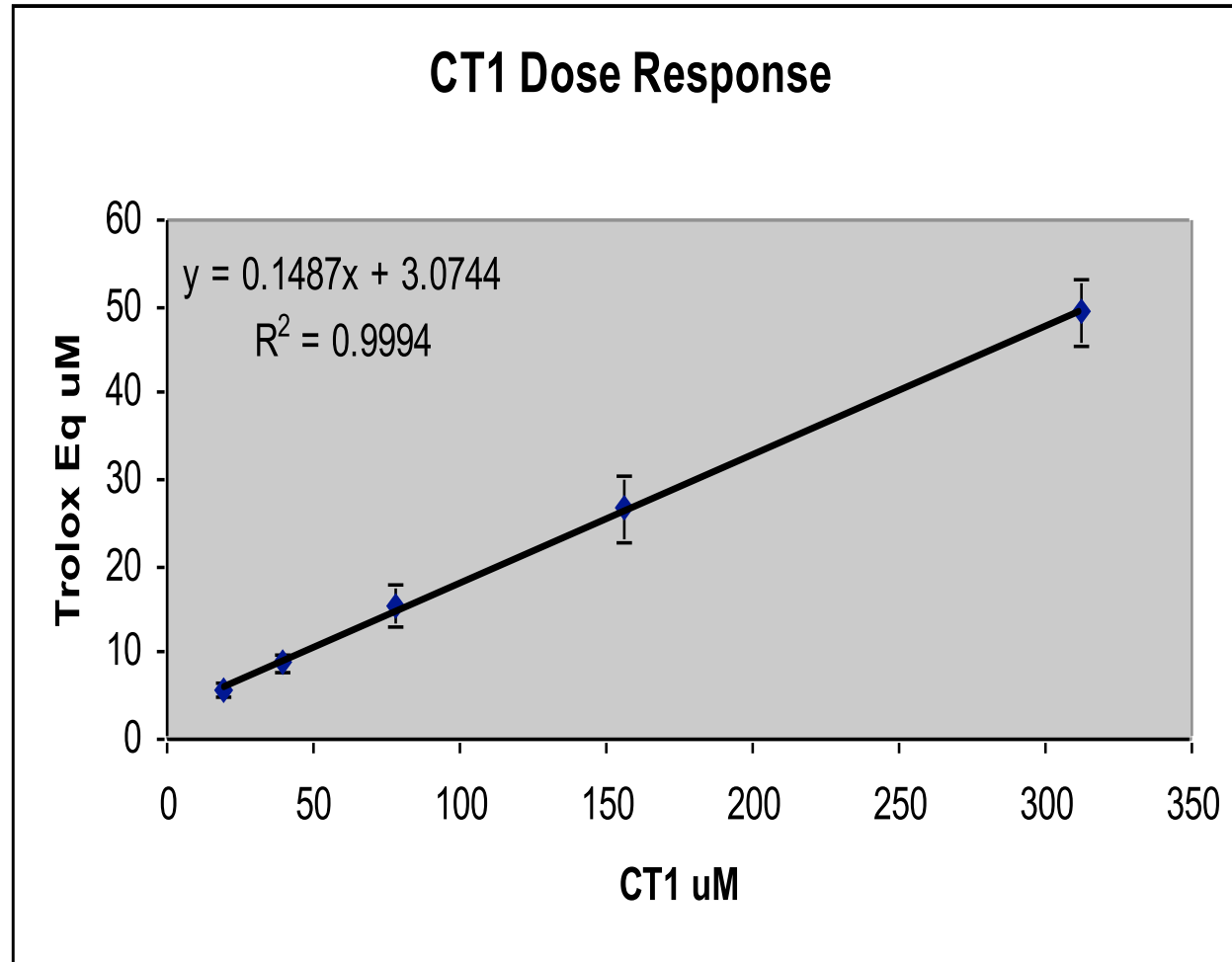
EFFECT OF OSR ON REDOX STATUS OF PATIENTS

| Time (months) | tGSH/GSSG | | | GSSG | | |
|---------------|-----------|------|------|-------|-------|-------|
| | 0 | 1 | 2 | 0 | 1 | 2 |
| Patent # | | | | | | |
| 1 | 40.3 | 53.6 | 87.1 | 0.133 | 0.129 | 0.065 |
| 2 | 42.9 | 37.5 | 87.7 | 0.159 | 0.209 | 0.117 |
| 3 | 24.8 | 32.3 | 64.5 | 0.167 | 0.154 | 0.083 |
| 4 | 14.8 | 22.1 | 28.6 | 0.482 | 0.282 | 0.189 |
| 5 | 66.9 | 73.7 | 93.7 | 0.108 | 0.103 | 0.067 |
| 6 | 14.1 | 33.4 | 38.5 | 0.308 | 0.154 | 0.137 |
| 7 | 36.9 | 40.3 | 44.9 | 0.127 | 0.113 | 0.081 |
| 8 | 17.3 | 36.2 | 28.7 | 0.236 | 0.146 | 0.195 |
| 9 | 11.4 | 16.9 | 48.9 | 0.521 | 0.396 | 0.139 |
| 10 | 15.8 | 42.8 | 69.6 | 0.283 | 0.165 | 0.119 |
| Average | 28.5 | 38.9 | 59.2 | 0.252 | 0.185 | 0.119 |

This data was collected from a single clinic where the subjects varied in age from 8 to 73 years old and were 5 and 5 male and female. All were in reasonable health with no obvious bacterial infections. GSH/GSSG ratios increased in all primarily due to the drop in GSSG levels in all subjects. GSH levels remained relatively constant and increased slightly in 7 of 10. The average tGSH/GSSG ratio almost doubled caused by a near average halving of the GSSG levels.

OSR

AN OXYGEN RADICAL ABSORBANCE STUDY OF ONE OF THE NEW ANTIOXIDANTS DONE IN AQUEOUS SOLUTION.



Common Biochemical Findings in ASD

James et al. 2005

| Table 1 | Control Children n=33 | Autistic Children n=20 | p value |
|-----------------------------------------|--------------------------|---------------------------|---------|
| Methionine ($\mu\text{mol/L}$) | 30.6 ± 6.5 | 19.3 ± 9.7 | 0.001 |
| SAM (nmol/L) | 90.0 ± 16.2 | 75.8 ± 16.2 | 0.01 |
| SAH (nmol/L) | 20.1 ± 4.3 | 26.1 ± 5.4 | 0.001 |
| Homocysteine ($\mu\text{mol/L}$) | 6.3 ± 1.2 | 5.4 ± 0.9 | 0.01 |
| Adenosine ($\mu\text{mol/L}$) | 0.28 ± 0.16 | 0.39 ± 0.19 | 0.05 |
| Cysteine ($\mu\text{mol/L}$) | 210 ± 18.5 | 163 ± 14.6 | 0.001 |
| Total glutathione ($\mu\text{mol/L}$) | 7.9 ± 1.8 | 4.1 ± 0.5 | 0.001 |
| Oxidized Glutathione (nmol/L) | 0.3 ± 0.1 | 0.55 ± 0.2 | 0.001 |
| GSH/GSSG Ratio | 25.5 ± 8.9 | 8.6 ± 3.5 | 0.001 |

Sulfate and glutathione levels in autistic children



Control Autistic

(n = 24)

(n= 41)

| | | | |
|----------------------------------|-----------|---------|---------|
| Sulphate (free) ¹ | 1.8-10 | 0.4-1.9 | 25% low |
| Sulphate (total) ¹ | 1400-3000 | 94-310 | 43% low |
| Glutathione (total) ² | 3.8-5.5 | 1.2-4.1 | 46% low |

¹ (nmole/mg protein)

² (µmole/ml)

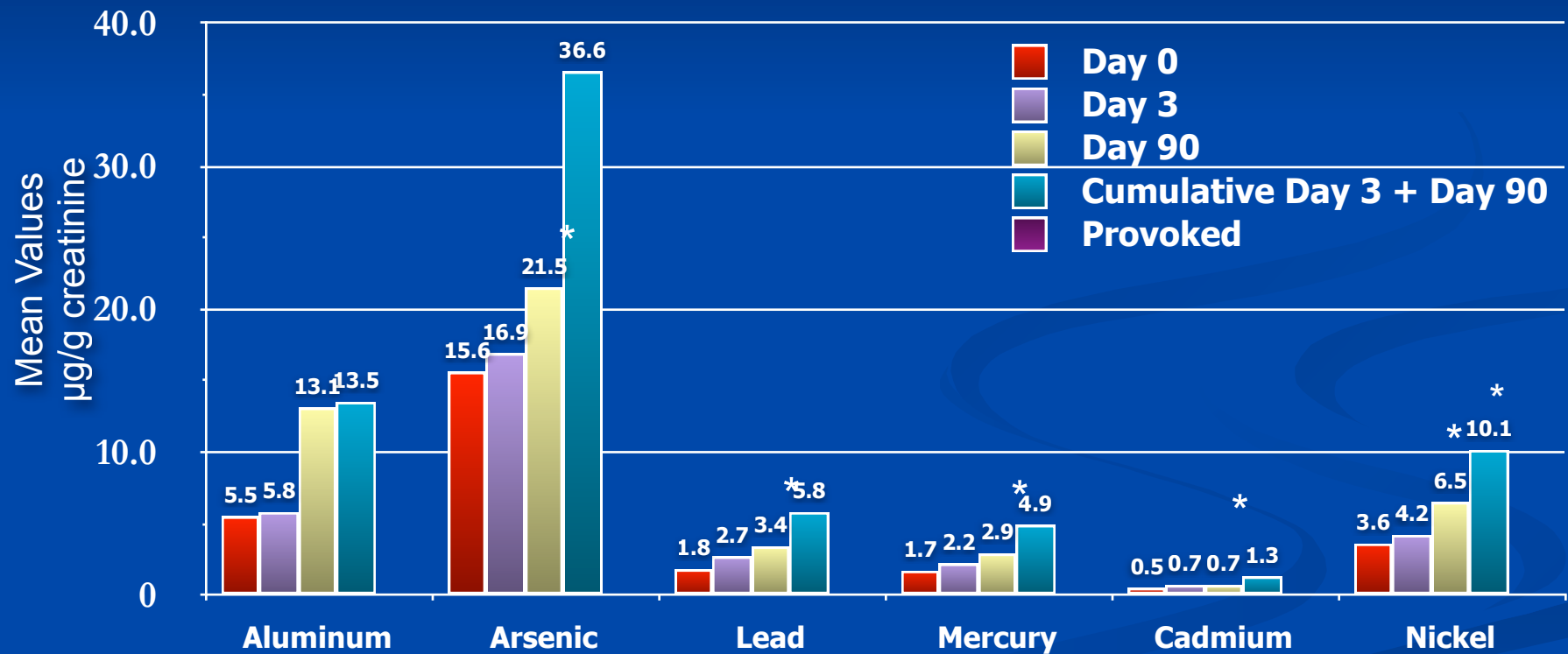
DMSA

- Approved by FDA
- Chelates both inorganic and organic mercury
- Has been tested in children and found to be safe and effective
- Though approved only for lead, it does remove mercury and other metals
- Must drink adequate amounts of water with DMSA for best results
- Triggers TNF alpha – imp. to address inflammation
- Dosage: Per individual tolerance, 100mg. at bedtime q.o.d. at night. Replete minerals on off nights. Child's dosing: $1/8 - 1/2$ mg./lb.

EDTA: Clinical Pilot Study Summary

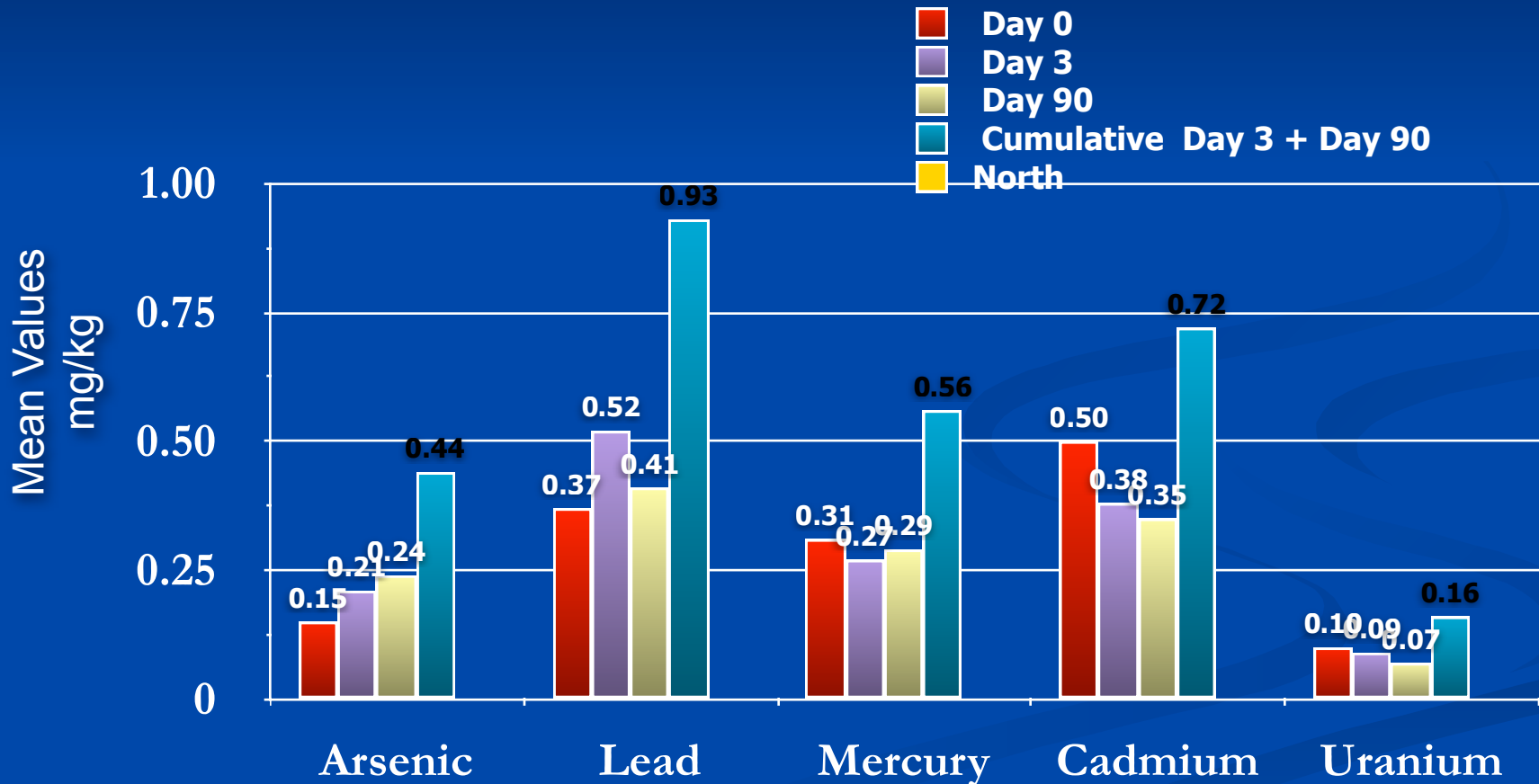
- Significant excretions observed
 - Fecal
 - Ar, Pb, Cd, Ni
 - Urine
 - Ar, Pb, Hg, Cd, Ni
- Average change in pre and post DMSA
 - Fifty percent for Al, Ar, Pb, Hg, Ni
 - No difference with Cd

EDTA: Excretion of Toxic Metals in Urine



*Significantly different from Day 0 (p<0.05)

EDTA: Excretion of Toxic Metals in Feces



* Significantly different from Day 0 ($p < 0.05$)

EDTA Safety

■ Comprehensive Metabolic Panel

- Albumin - Total Protein
- Total Bilirubin - Sodium
- Calcium - AST (SGOT)
- Chloride - Urea Nitrogen (BUN)
- Creatinine, Serum - Bicarbonate (CO₂)
- Glucose - ALT (SGPT)
- Alkaline Phosphatase - C-Reactive Protein
- Potassium

No statistical difference in above lab parameters between pre and post treatment with EDTA in all subjects

Cilantro-Coriandrum sativum (BioPure energized tincture)

- A European herb in the parsley family
- Accelerates the elimination of **mercury, lead, and aluminum** through the urine
- Improves effectiveness of anti-viral and antibiotics in subjects with localized deposits of Hg and Pb which often co-exist with chlamydia, herpes, and cytomegalovirus organisms.
- Dosage: 1-3 dropperfull in hot water daily in divided doses (If digestion is a problem, give cellulase.)

Omura, Y. et al. :

Acupunct. Electrother. Res. 1995; 20(3-4): 195-229.

Omura, Y. et al:

Acupunct. Electrother. Res. 1996; 1(2): 133-60

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

Journal of Hazardous Materials B118 (2005) 133-139

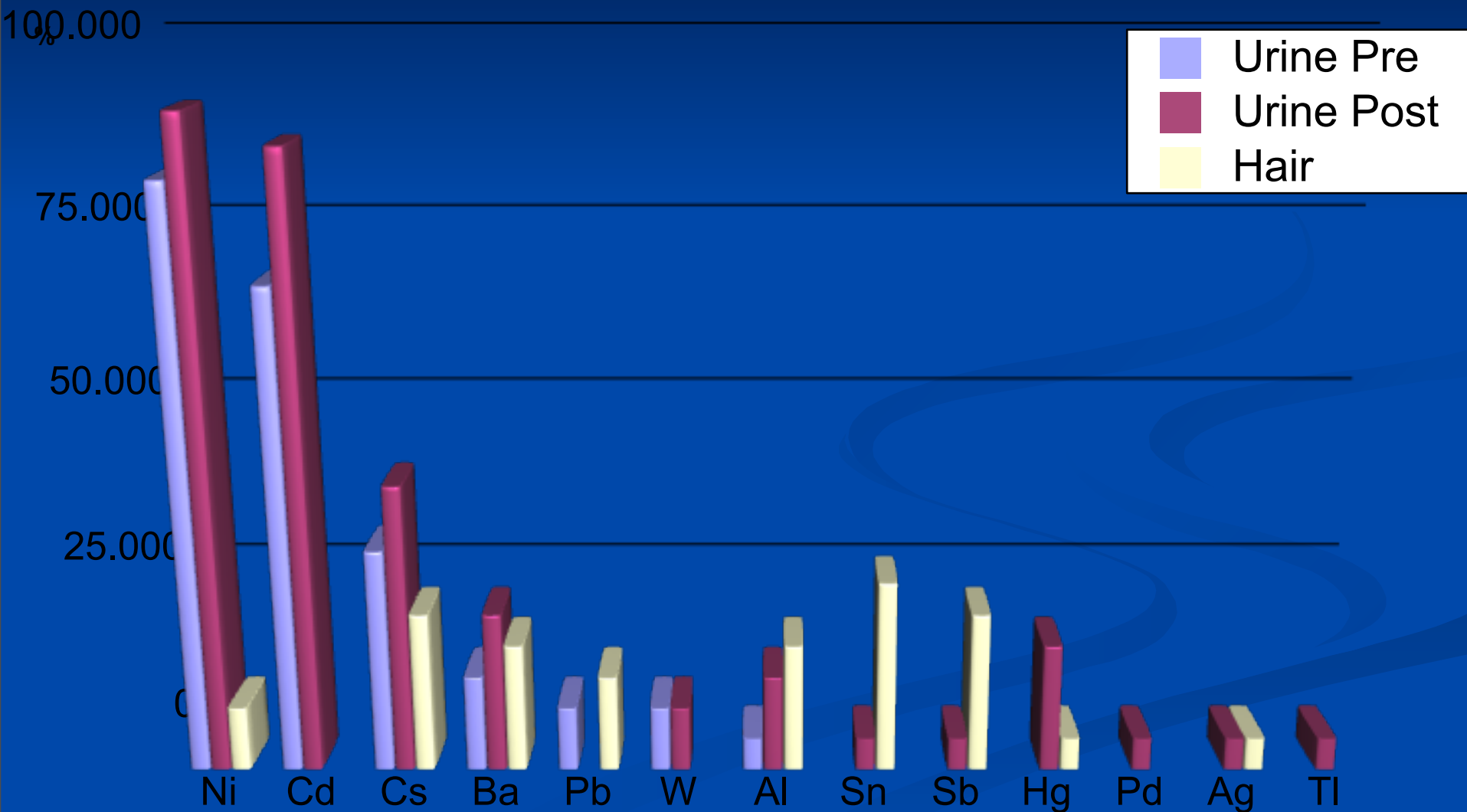
(National Center for Compositional Characterization of Materials (CCCM), Bhabha Atomic Research Centre)

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

Metal ions in urine and hair before and after cilantro provokation

| Hair | Urine pre- | Urine post |
|------------------------------------|----------------------------------------------|-------------------------------------------------------------------------------------|
| Zn-, Ca+, Mg+, Sr+, Sb+, Ba+, Ni+, | Se-, Ca+, Pb+, Cd+, Ni+, | Ca+, Cu+, Mn+, Zn+, Al+, Ba+, Cd+, Pd+, Hg+, Li+, Sr+ |
| | Se-, Cu+, Mn+, Zn+, Ba+, Pb+, Cd+, Ni+, Li+ | Se-, Fe-, Cr+, Cu+, Mn+, Cs+, Cd+, Ni+, Li+ |
| Zn-, Mg+, Al+, Ag+ | Mg+, Cs+, Cd+, Ni+ | Ca+, Mg+, Cr+, Cu+, Mn+, Mo+, Al+, Sb+, Ba+, Cs+, Cd+, Ni+, Hg+, Ti+, W+, Li+, Sr+, |
| Se-, Zn+, | Zn-, Ni+, | Ca+, Mg+, Mn+, Mo+, Cd+, Ni+, |
| Ni+, Sn+ | Se-, Cr+, Mn+, Ni+, W+ | Se-, Cu+, Zn+, Cd+, Ni+, |
| Co-, Mn-, Zn-, Al+, | Ca+, Cd+, Ni+, | Ca+, Cd+, Ni+, |
| Co-, Mo-, Sr-, Sb+ | Se-, | Cu-, Se-, |
| Mg-, Co-, Sr-, Al+, Sb+, | Ca+, Ba+, Cd+, Ni+, | Ca+, Cu+, Mo+, Cs+, Cd+, Ni+, Ag+, |
| Co-, Mn-, Zn-, | Se-, Cd+, | Cd+, Ni+, |
| Co-, Mn-, Zn-, Sn+ | Se-, Cs+, Cd+, Ni+, | Ba+, Cs+, Cd+, Ni+, |
| Co-, Zn-, Cu+ | Cs+, Ni+, | Ca+, Cs+, Ni+, |
| Mg-, Fe-, Co-, Zn- Sr-, | Mo-, Ca+, Mg+, Cr+, Al+, Ba+, Cs+, Cd+, Ni+, | Ca+, Mg+, Cr+, Mn-, Zn+, Ba+, Cs+, Cd+, Ni+, |
| Co-, Mn-, Zn-, Sb+, Pb+, Sn+ | Se-, Cd+, Ni+, | Cr+, Cu+, Mn+, Se-, Cd+, Ni+, Hg+, |
| Co-, Cu-, | Cd+, | Fe+, Cu+, Mn+, Al+, Cd+, Ni+, Zn+ |
| Co-, Mg+, Sn+ | Se-, Ca+, Mo+, Cs+, Cd+, Ni+ W+, | Ca+, Cr+, Ba+, Cs+, Cd+, Ni+, W+, |
| Se-, Sr+, Al+, Sn+, | Se-, Mg+, Cd+, Ni+, | Se-, Cr+, Mn+, Cd+, Ni+, Hg+ |
| Mo-, Se-, Zn-, Ca+, Mg+ | Se-, Cd+, Ni+, | Se-, Ca+, Cr+, Mn+, Ba+, Cd+, Ni+, |
| Hg+ | Fe-, Se-, Ca+, Cd+, Ni+, | Fe-, Se-, Cd+, Ni+, |
| - | Fe-, Se-, Ni+ | Fe-, Se-, Cs+, Cd+, Ni+ |
| Mg-, Co-, Zn-, Al+, Sn+ | Se-, Ni+, | Se-, Ca+, Ni+, |
| Co-, Cu-, Mn-, Mo-, Ba+ Sb+ | Se-, Li+ | Cu+, Ba+, Cs+, Cd+, Ni+, Li+ |
| Mo-, Zn-, | Co+, Cs+, Cd+, Ni+ | Co+, Mn+, Cs+, Cd+, Ni+ |

Toxic metal ions in urine and hair after provocation with a single dose of 15 drops energized cilantro tincture (30 patients)



Oral administration, cont.

- D-Penicillamine (Russell Jaffe protocol)
- D-Alpha Lipoic or R-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/BioPure) : 2-3 caps after each meal 3-4 times/day
- **Phospholipid Exchange** (from BioPure: energized phospholipids, alpha-Lipoic acid, magnesium and Na-EDTA)- only detox agent that reliably crosses the blood brain barrier. Also enhances acetylcholine in the brain
- cold processed whey (branched chain amino acids)

The blood brain barrier

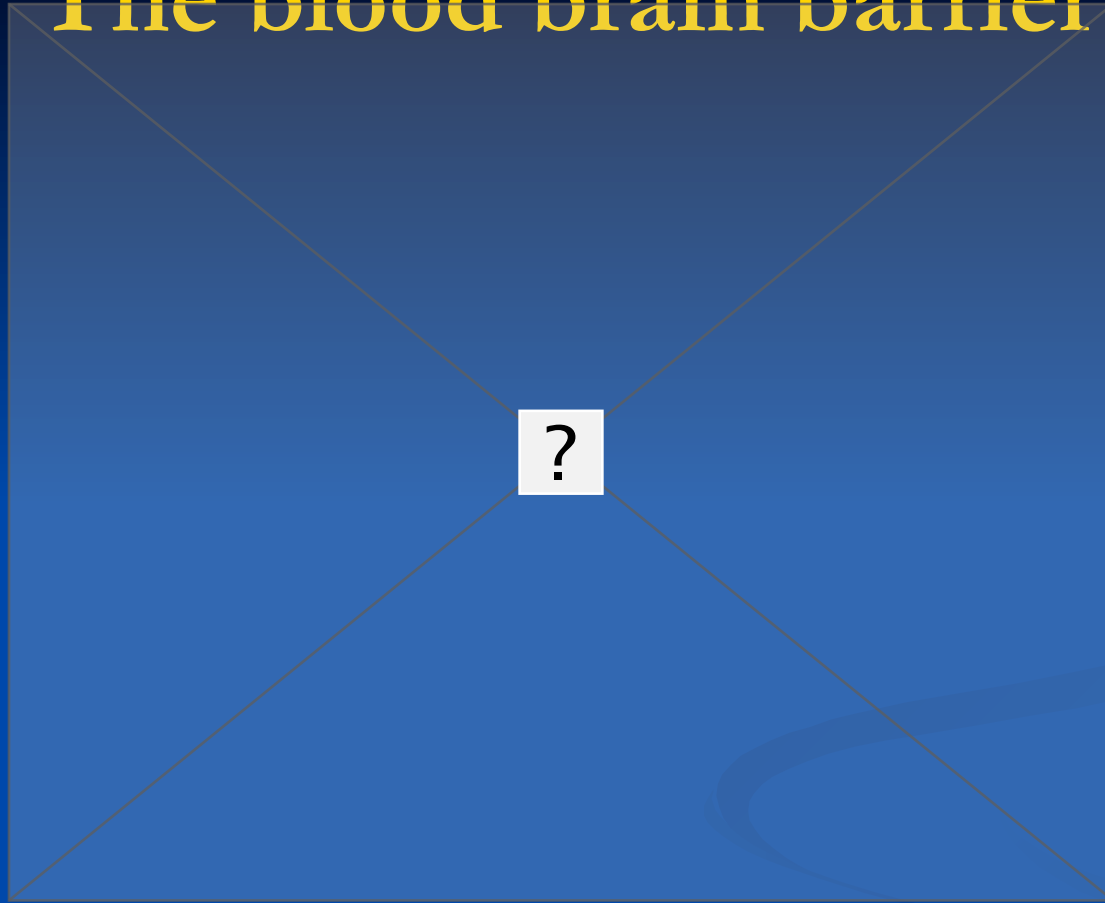


Diagram of a cerebral capillary enclosed in astrocyte end-feet. Characteristics of the blood-brain barrier are indicated: (1) tight junctions that seal the pathway between the capillary (endothelial) cells; (2) the lipid nature of the cell membranes of the capillary wall which makes it a barrier to water-soluble molecules; (3), (4), and (5) represent some of the carriers and ion channels; (6) the 'enzymatic barrier' that removes molecules from the blood; (7) the efflux pumps which extrude fat-soluble molecules that have crossed into the cells

High Alliin Freeze dried Garlic (BioPure)

One of the most widely studied natural compounds

- ↑ Glutathione
- ↑ Metal chelation abilities
- Protects Brain from oxidative stress
- Anti-viral properties –(some metals harbored within underlying viral and bacterial infections)
- ↑ antioxidant/anti-inflammatory actions
- ↓ homocysteine, cholesterol, LDL ox-LDL
- Anti-cancer properties
- Modulates Epinephrine & Norepinephrine
- Dosage – 600-2000mg twice daily
- ↓ Fibrinogen
- No known interactions with Coumadin

Literature: Li, G. et al. 1995. *Oncol. Rep.* 2: 787-791.

- Tiwari, R. et al. 1993. *Breast Cancer Res. Treat.* 27(1-2):80.
- Liu, J. et al. 1992. *FASEB J.* 6(4): 3230.
- Tadi, P. et al. 1991. *Nutr. Cancer* 15: 87-95.
- Sumiyoshi, H. et al. 1990. *Cancer Res.* 50: 5084-5087.
- Sumiyoshi, H. et al. 1989. *Proc. Am. Assoc. Cancer Res.* 30: 181.
- Lau, B. 1989. *Int. Clin. Nutr. Rev.* 9(1): 27-31.
- Yamasaki, T. et al. 1994. *Phytother. Res.* 8: 408-412.

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
- Carnosine: 1000 mg 3x daily (prevents collagen breakdown)
- Branched chain amino acids: valine, leucine and isoleucine (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 (BioPure) as precursor

Glutathione

- Not thought to increase blood levels with oral administration though some studies have shown that it does
- Not cost effective
- New oral form recently available but no data to show effectiveness in metal elimination.

Witschi A, *et al*: The systemic availability of oral glutathione, *European Journal of Clinical Pharmacology* 1992;43(6): 667-669.

Am J Physiol 1990; 259:G524-529.

Biochem Biophys Acta 1992;1113:13-23.

The role of thiols, dithiols, nutritional factors and interacting ligands in the toxicology of mercury

Abstract

Mercury has been known as a toxic substance for centuries. Whilst the clinical features of acute mercury poisoning have been well described, chronic low dose exposure to mercury remains poorly characterised and its potential role in various chronic disease states remains controversial. Low molecular weight thiols, i.e. sulfhydryl containing molecules such as cysteine, are emerging as important factors in the transport and distribution of mercury throughout the body due to the phenomenon of “Molecular Mimicry” and its role in the molecular transport of mercury. Chelation agents such as the dithiols sodium 2,3-dimercaptopropanesulfate (DMPS) and *meso*-2,3-dimercaptosuccinic acid (DMSA) are the treatments of choice for mercury toxicity. Alpha-lipoic acid (ALA), a disulfide, and its metabolite dihydrolipoic acid (DHLA), a dithiol, have also been shown to have chelation properties when used in an appropriate manner.

Whilst *N*-acetyl-cysteine (NAC) and glutathione (GSH) have been recommended in the treatment of mercury toxicity in the past, an examination of available evidence suggests these agents may in fact be counterproductive.

Zinc and selenium have also been shown to exert protective effects against mercury toxicity, most likely mediated by induction of the metal binding proteins metallothionein and selenoprotein-P. Evidence suggests however that the co-administration of selenium and dithiol chelation agents during treatment may also be counter-productive. Finally, the issue of diagnostic testing for chronic, historical or low dose mercury poisoning is considered including an analysis of the influence of ligand interactions and nutritional factors upon the accuracy of “chelation challenge” tests.

SAMe (s-adenosyl-methionine)

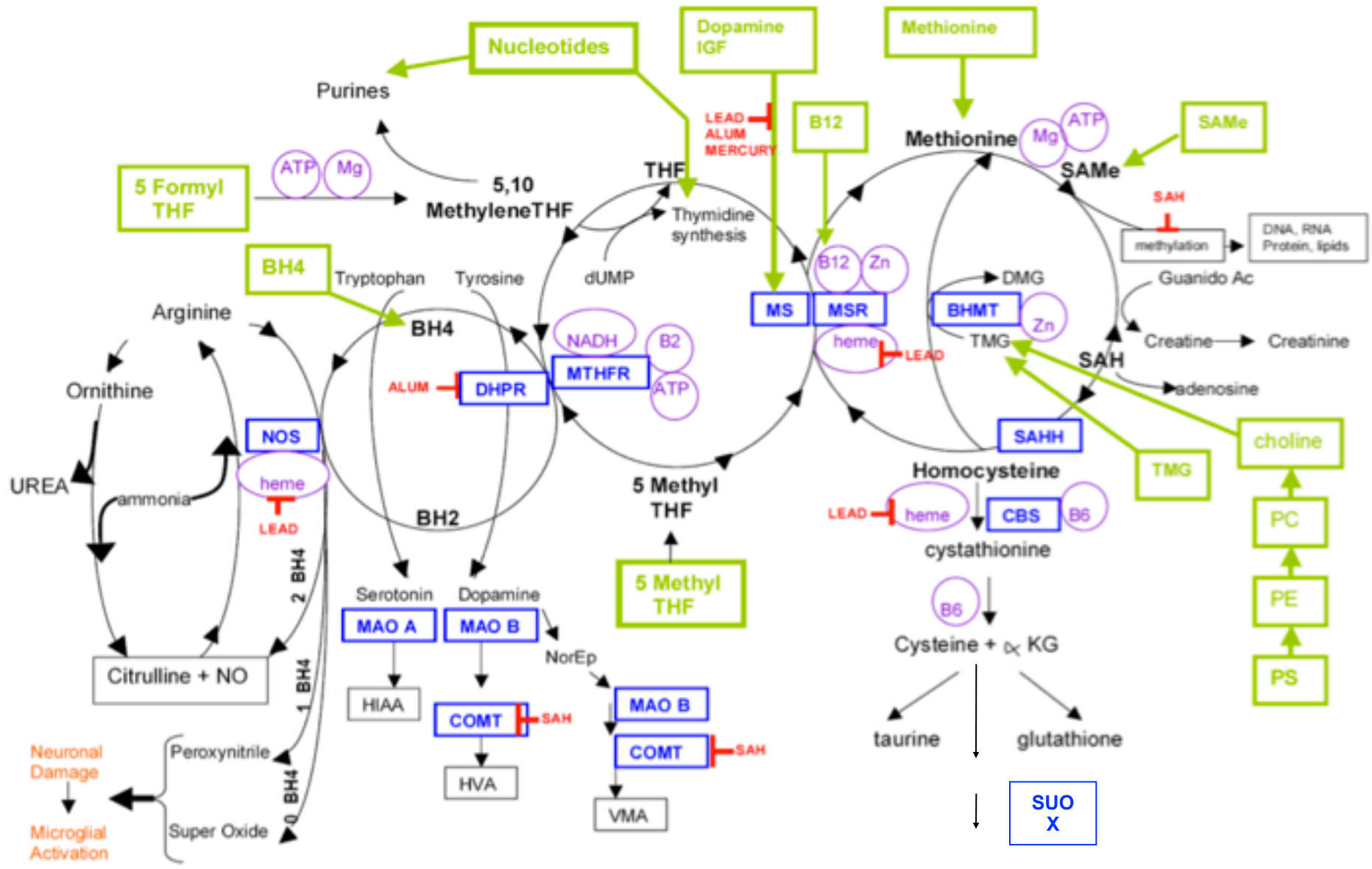
- SAMe has been called "the liver's super-nutrient." The liver contains the third highest amount of SAMe after the adrenals and the pineal glands.
- Reverses destructive effects of chemicals and alcohol as they occur.
- Performs methylation and trans-sulfuration reactions to increase glutathione.
- Plays a leading role in liver regeneration.
- SAMe protects against arsenic toxicity (Goering et al. 1999).
- Detoxifies Lead and Cadmium. Also effective in correcting zinc and glutathione concentrations. (Gubrelay et al. (2001) (Paredes et al. 1985).
- Dosage – 600 mg./day (methylation dose)

Vitamins/Minerals

Full range of vitamins/minerals to support pathways activated during detox, especially:

- Glycine, DMG, TMG
- B12 – hydroxy- and/or methylcobalamin
- B6 – P5P or pyridoxine HCL
- B2
- Folate – options folate, folic acid, MTHF

Pathways With Enzymes, Cofactors, Supplements & Blocking Metals/SAH



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

Security Code: 6854324

COMPREHENSIVE MEDICAL CENTER
DIETRICH KLINGHARDT MD
1200 112th Ave NE
Ste A100
Bellevue, WA 98004

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 4-hydroxylation of estrone.
(CYP2A6) detoxifies nitrosamines and nicotine
(CYP2C9) detoxifies cocaine and salicylates.
(CYP2C19) detoxifies proton-pump inhibitors (e.g., prilosec®) and many anticonvulsants (e.g., valium®).
(CYP2D6) detoxifies ~30% 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. |



GENOVATIONS™**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/gdgm1 | 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. Homozygous negative or wild type
- + - One chromosome (of two) carries the genetic variation. Heterozygous positive
- ++ Both chromosomes carry the genetic variation. Homozygous positive
- NIR / NULL / IND See commentary
- (You inherit one chromosome from each parent)

Parental assessment on behavioral improvement of autistic children

46% responded to vit. B6, Mg & Zn

36% responded to Sulphate

68% responded to Essential Fatty Acid (statistics from Tapan Audhya PhD)

Vitamin B-6

- ◇ Gastro-intestinal Symptoms
- ◇ Sociability
- ◇ Sleeping Pattern

Sulphate

- ◇ Repetitive Behavior Pattern
- ◇ Hyperactivity
- ◇ Expressive Language
- ◇ Gastrointestinal Symptoms

Fatty Acids

- ◇ Sociability
- ◇ Eye Contact
- ◇ Sleeping Pattern
- ◇ Cognition/Thinking

Supportive Modalities

- Exercise – avoiding post exercise fatigue
- Body Vibration
- Sauna
- Electro-mobilization (KMT 24, Toxaway foot bath)
- Mercury vapor lamp
- Photo-mobilization (light shield, health light, photon wave and green laser photopheresis, Valkion singlet oxygen energy (water and inhalation)
- Colon hydrotherapy
- Lymphatic drainage massage
- Applied Psychoneurobiology (APN)

Activating the detoxification systems with inhaled singlet oxygen

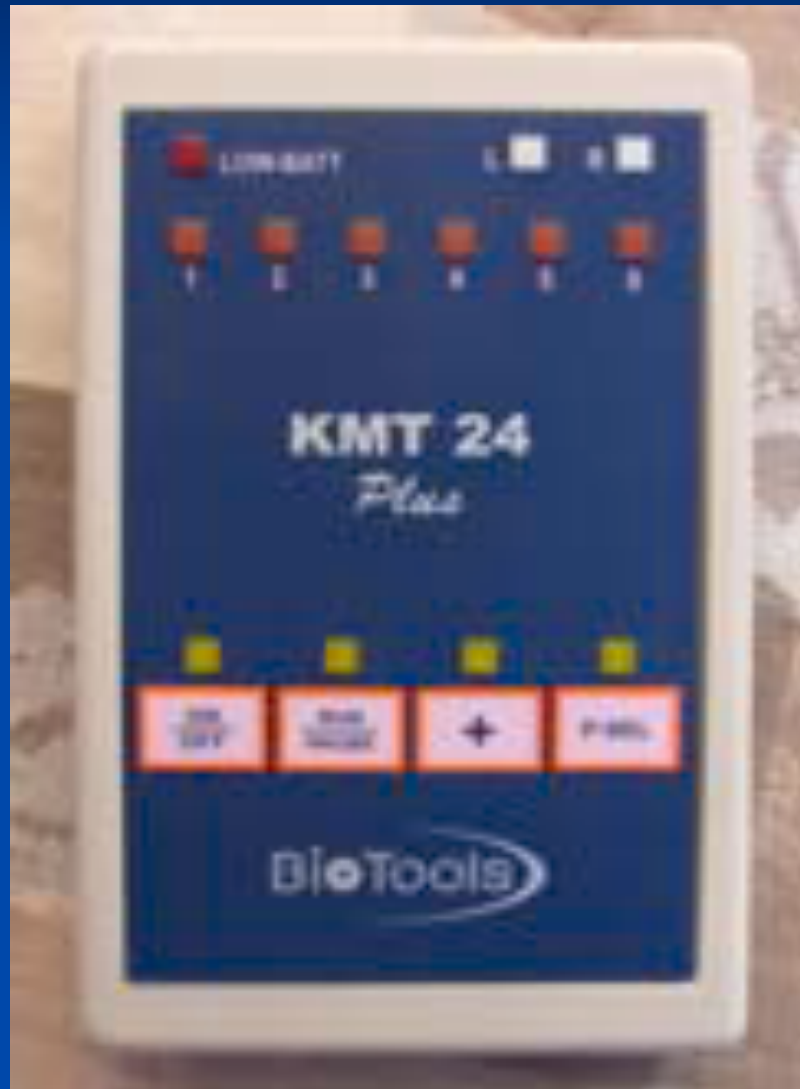


Health Light: LED diodes with unique properties: pain relief, anti-inflammatory, unblocking of energy cysts. Many other uses: to enhance phase I liver detox and metabolic activity, kidney drainage and kidney health, to eliminate seizure focus, medication uptake enhancement, constipation relief, detoxification of tissues



Jae Laser: self-moving low level green laser scanner. Can be used for biophoton field restructuring, elimination of specific toxins, nutrient delivery and uptake enhancement, food allergy desensitization and with anti-inflammatory effects on the brain and CNS

KMT 24 microbial inhibition frequencies: can be used like a TENS unit or wireless photoelectric converter, to be used as “electronic antibiotic therapy”, for lymphatic drainage, pain relief, brain anti-inflammatory, immune system entrainment and metal-detoxification



Diagnosis of metal toxicity

- Options
- 1. Porphyrin test – may indicate body burden
- 2. Urine challenge – indicates those metals that are easily mobilized with the agent used
- 3. stool test – major route of detox but test seems inaccurate (split sampling unsatisfying). Shows value of i.v. Vit C
- 4. Hair analysis: excellent to monitor effectiveness of detox agent (if hair levels of toxin go up for a while), best for methyl-mercury
- 5. red cell test: depends on active transport (vulnerable to lack of ATP) – may or may not represent true levels



Urinary Porphyrin Chromatogram

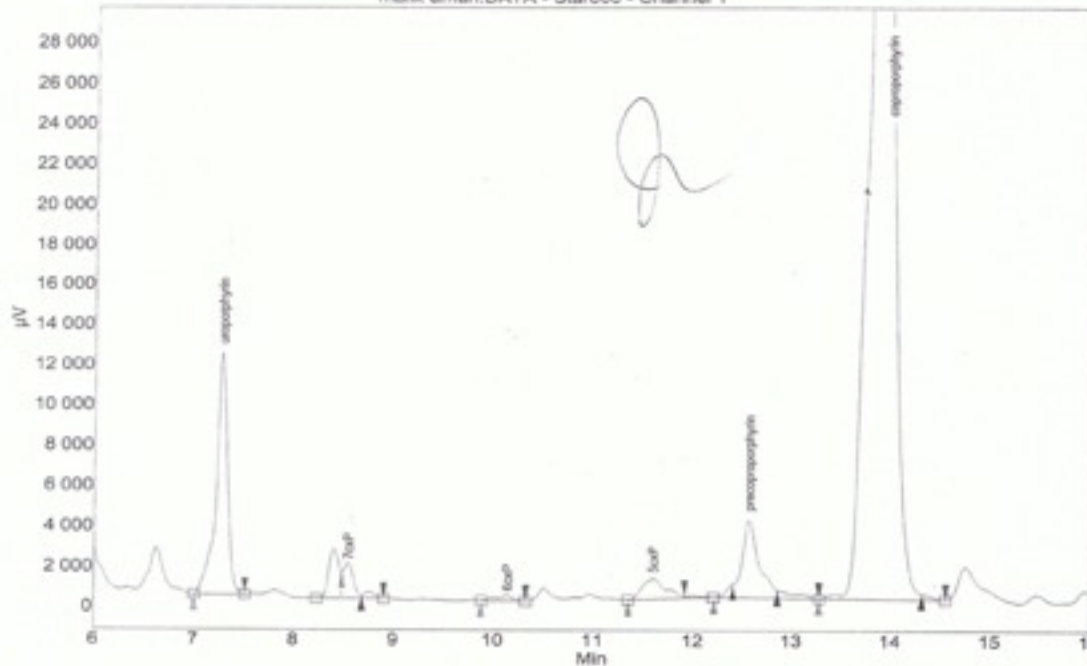
(nmol/l urine)

4 years

COPY FOR YOUR INFORMATION

System : HPLC_FLUO
 Method : porphyrines 071108 Varian 8
 Sample set : por 071113
 Acquired : 14/11/2007 22:36:42
 Processed : 16/11/2007 08:46:42

malik aman.DATA - Star800 - Channel 1



| Name | Quantity [nmol/l] | Quantity /gr Cr [nmol/gr] | Area % [%] | Time [Min] |
|-------------------|-------------------|---------------------------|--------------|------------|
| uroporphyrin | 37,04 | 33,07 | 8,2 | 7,28 |
| 7cxP | 4,24 | 3,78 | 1,1 | 8,54 |
| 6cxP | 1,26 | 1,13 | 0,3 | 10,14 |
| 5cxP | 5,78 | 5,16 | 1,5 | 11,60 |
| precoproporphyrin | 17,95 | 16,03 | 4,1 | 12,56 |
| coproporphyrin | 405,40 | 361,96 | 83,8 | 13,91 |
| Total | 471,67 | 421,13 | 100,0 | |

| Reference (nmol/gr Cr) |
|------------------------|
| UP : 8 - 20 |
| 7cxP : 2.5 - 4.5 |
| 6cxP : 0.5 - 1.5 |
| 5 cxP : 2 - 4 |
| PrCP : 5 - 9 |
| CP : 100 - 200 (child) |
| CP : 70 - 140 (adult) |

Ratios :

| | |
|---------------------|------|
| PrCP / UP | 0,48 |
| 5cxP+PrCP / UP+7cxP | 0,58 |
| PrCP / 5cxP | 3,11 |
| PrCP / CP | 4,4 |
| 5cxP/7cxP | 1,36 |
| CP / UP | 10,9 |

Reference Range :

| |
|-----------|
| 0,2 - 0,5 |
| 0,2 - 0,6 |
| 1,5 - 3,0 |
| 2 - 6 % |
| < 1,0 |
| 5 - 9 |

urinary creatinin
1120 mg/l



LABORATOIRE PHILIPPE AUGUSTE
 119 Ave Philippe Auguste 75011 Paris France
 Tel (33) 1 43 67 57 00 fax (33) 1 43 79 00 27
 Email : contact@labbio.net

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Urinary porphyrins

HPLC-UV+Fluorescence

| | nmol/l | nmol/gCr | % | reference nmol/gCr | Interpretation |
|-------------------------------|------------------|----------|-------|-----------------------|-------------------------|
| Uroporphyrins I & III (UP) | 37 | 33 | 7,9% | 8-20 | Increased rate |
| Heptacarboxy porphyrin (7cxP) | 4,2 | 3,8 | 0,9% | 2,5-4,5 | Average Rate |
| Hexacarboxy porphyrin (6cxP) | 1,3 | 1,1 | 0,3% | 0,5-1,5 | Average Rate |
| Pentacarboxy porphyrin (5cxP) | 5,8 | 5,2 | 1,2% | 2-4 | Slightly increased rate |
| Precoproporphyrin (PrCP) | 18,0 | 16,0 | 3,8% | 5-9 | Increased rate |
| Coproporphyrins I & III (CP) | 405 | 362 | 89,3% | 100-200 | Increased rate |
| PrCP/UP | PrecoP/Uro ratio | | 0,48 | 0,2-0,5 | |
| (5cxP+PrCP)/(UP+7cxP) | ratio | | 0,6 | 0,3-0,6 | |
| PrCP/5cxP | ratio | | 3,1 | 1,5-3 | |
| PrCP/CP | PrecoP/COP ratio | | 4,4 % | 2-6 | |
| CP / UP | copro/uro ratio | | 10,90 | 5-9 | |

Interpretation

Urinary Porphyrin Profile suggestive a moderate mercury toxic effect on bodily physiology high in coproporphyrin

Urinary porphyrin profile is a powerful biochemical tool in diagnosis of intoxication associating sensitivity, specificity and quantificity

* sensitivity- because heme biosynthesis is highly sensitive to inhibition by many inorganic toxicants such as Mercury, Lead, Arsenic, Aluminium as well as organic agents: chlorinated benzene, biphenyls (PCB), dioxins (TCDD) and also alcohol.

* Specificity-because nearly each toxic generates a specific urinary porphyrine excretion pattern for example: Biphenyls, Dioxins, Aluminium inhibit an early enzyme on porphyrin biosynthesis pathway Uro-Decarboxylase, Mercury inhibits Copro-oxidase and L.

*Quantificity or quantitative relationship between increase of specific porphyrins species and toxic or heavy metal body burden with a high degree of correlation designating it as a reliable biomarker for chelation therapy

urinary creatinine 1120 mg/l

Urine Toxic Elements Post DMPS Challenge

C.N.: 35 year old male

Dx: CFIDS, FMS

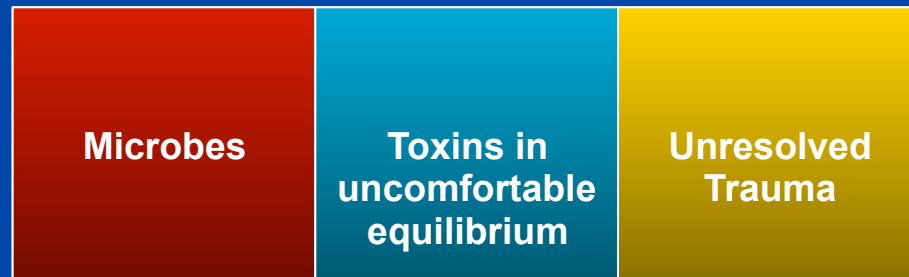
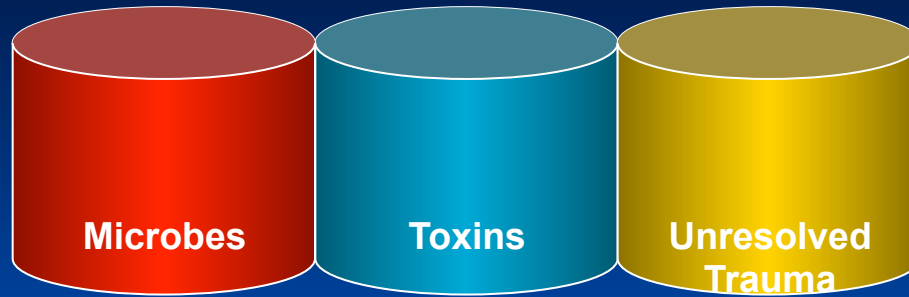
| <u>Date</u> | <u>mcg Hg/24 hrs</u> | <u>ppb (post DMPS 3 mg/kg i.v push)</u> |
|-------------|-------------------------------------------|-----------------------------------------|
| 4/23/93 | 27.8 | 27.8 |
| 6/24/93 | 99.0 | 99.0 |
| 9/21/93 | 49.4 | 49.4 |
| 12/23/93 | 2.1 | 2.1 |
| 4/94-8/94 | four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

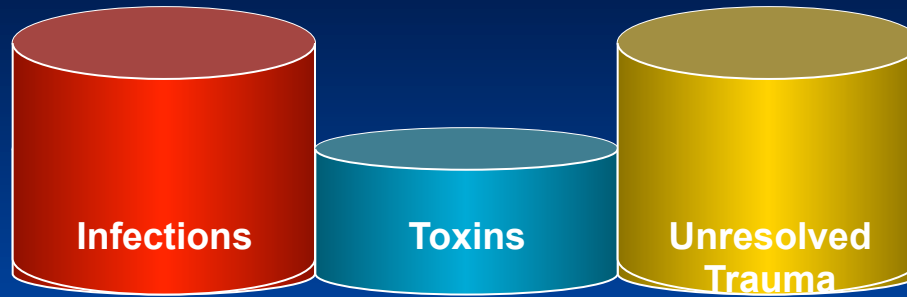
A.H.: 46 year old woman Dx: severe depression, multiple neurological symptoms (muscle weakness, numbness, whole body pain)

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

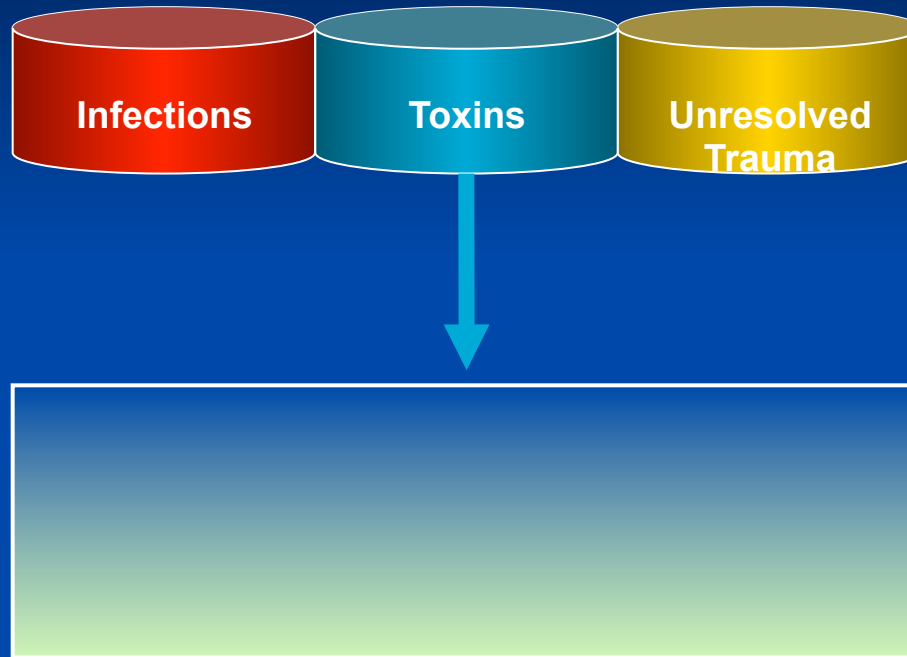
The Klinghardt Axiom II

- *The body always strives to achieve an equilibrium between stored unresolved emotional issues, toxin storage and the presence of pathogenic microbes*
- The reverse axiom:
a patient cannot be “detoxed” beyond the degree to which also emotional issues are released
The body burden of stored toxins predicts the presence of pathogenic microbes: the immune system cannot achieve dominion in contaminated body compartments
Microbes grow and prosper proportional to the amount of toxins stored



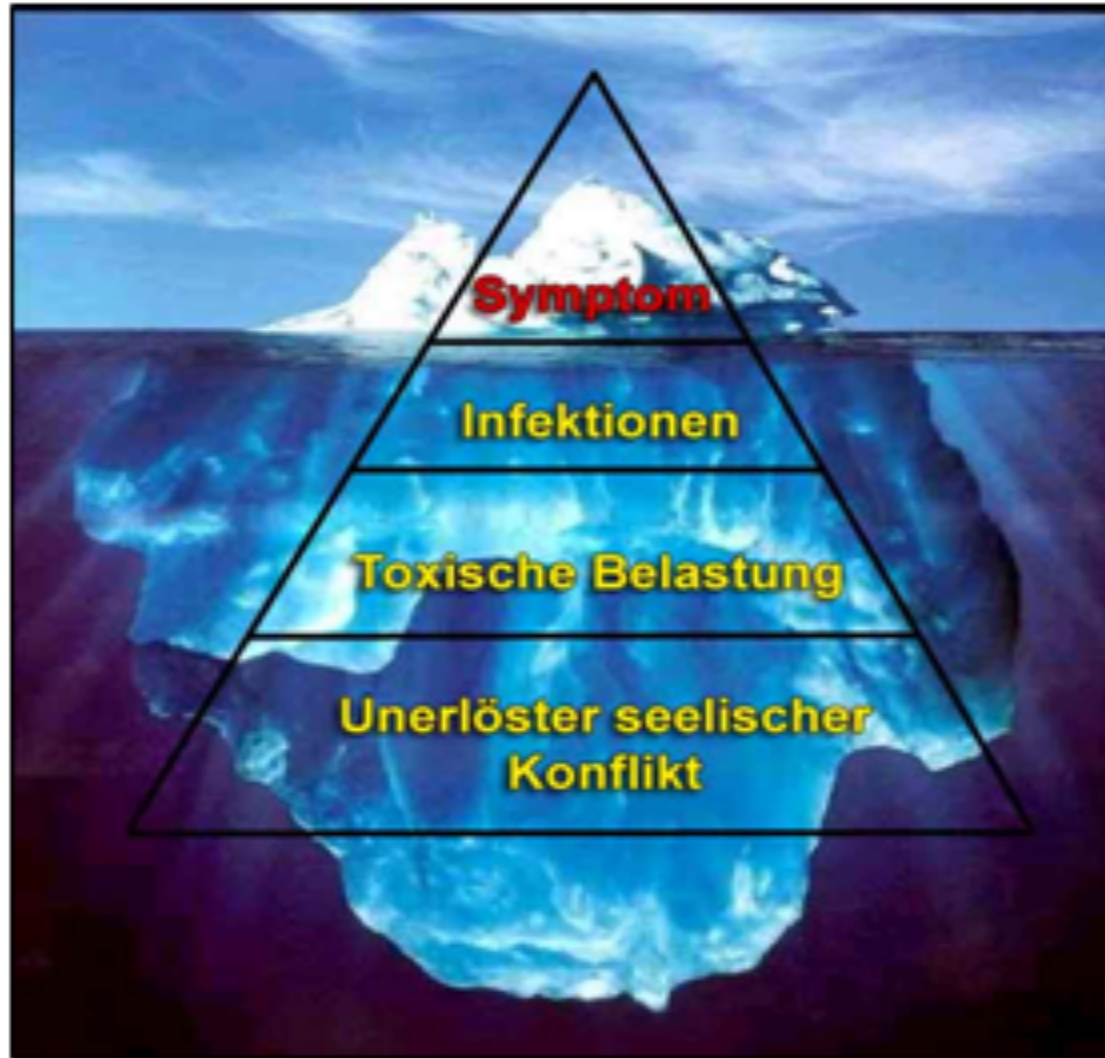


Dysequilibrium:
this patients is entering into a “healing crisis” (if the detox treatment is not paused)
The symptoms will predictably be both infection/immune response related
and psychological



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this patients is entering into a “healing crisis” (if the detox treatment is not paused)
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and psychological

Klinghardt axiom III: the iceberg principle





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