

Chemical Exposures and the Elimination of Toxic Metals from the Human Body



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Faculty Disclosure

Dr. Stephen J Genuis

- Relationship with commercial interests - None
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- Conflict of interest – None

Chemical Exposures & Elimination of Toxic Metals from the Human Body

I. Background – Chemical exposures in context

II. What can you do clinically?

- ❖ Elimination of Toxic Metals from the Body
- ❖ Case Reports

I. Background– Chemical exposure in context

- Unparalleled rates of chronic mental and physical illness
- Toxic chemical exposures and bioaccumulation: major determinant of the escalating prevalence of chronic disease

The Problem: *America* (2015 figures)

- Chronic diseases accounts for 86% of health care costs
- Half of all American adults have at least one chronic condition
- Almost one in three Americans has multiple chronic conditions
- Of the 2 Trillion dollars spent annually on healthcare, 75% of it goes to treating chronic disease
- Chronic disease accounts for 81% of hospital admissions

- Centers for Disease Control and Prevention. Saving Lives, Protecting People. <http://www.cdc.gov/chronicdisease/>
- US Department of Health & Human Services. Prevention makes common cents. <https://aspe.hhs.gov/pdf-report/prevention-makes-common-cents>
- <http://www.fightchronicdisease.org/sites/default/files/docs/GrowingCrisisofChronicDiseaseintheUSfactsheet81009.pdf>

Age Groups:

Alzheimer's

- "The number of people affected by Alzheimer's and dementia is growing at an epidemic pace, and the skyrocketing financial and personal costs will devastate the world's economies and healthcare systems, and far too many families."

William Thies, Ph.D.,
Chief Medical & Scientific Officer
Alzheimer's Association.

Inflammatory Bowel Disease in Children

- 10-fold increase over 10 years.

Gynecological Problems

- Every year, more than 670,000 women in the USA have a hysterectomy.
 - **24% increase between 1996-2002.**
- In USA: 30-40% of women <65 have had a hysterectomy (2009)

1. Brill AI. What is the role of hysteroscopy in the management of abnormal uterine bleeding. Clin Obstet Gynecol 1995;38:319-45.
2. Kupperman M et al. Sexual functioning after total compared with supracervical hysterectomy: a randomized trial. Obstetrics & Gynecology 2005; 105:1309-18.
3. Candiani M et al. Laparoscopic vs. vaginal hysterectomy for benign pathology. AJOG 2009: 368.e1-e7.

Prostate Cancer

75% increase in prostate
cancer between
1977 – 2006!



Canadian Cancer Society/National Cancer Institute of Canada (2006, April) Table 7.1 & Table 8.1

Assorted Types of Afflictions:

Chronic Pain

2008 Study: Increasing number of people living with chronic pain

- 70 Million Americans live with chronic pain
- Chronic pain affects ~ 4 / 10 seniors in institutions
- Waiting lists often >1 year for consultation at pain clinics
- 2009 Report – significant adverse effect on productivity and economy
- Escalating problem with adolescents living with chronic pain

Rates of Mental Illness

- An estimated 26.2 percent of Americans ages 18 and older — about one in four adults — suffer from a diagnosable mental disorder in a given year.
 - Leading cause of disability in the U.S.A. and Canada.
 - Recent talk...25% of reproductive aged woman in the USA are on antidepressants
-
- Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Archives of General Psychiatry*, 2005 Jun;62(6):617-27.
 - The World Health Organization. *The global burden of disease: 2004 update*, Table A2: Burden of disease in DALYs by cause, sex and income group in WHO regions, estimates for 2004. Geneva, Switzerland: WHO, 2008.

Tidal Wave of Cancer



U.S. Lifetime Cancer Rates:

1923 – 3% of the population

2010 – Women: 1 in 3
Men: 1 in 2

- *Significant increase in cancer in young as well as mature individuals*
- Rates will continue to increase
- Anticipate 50% increase in rates of cancer over the next 15 years

Medical Literature: The increase in chronic conditions

- “Health and social welfare systems are unprepared for the rapid growth in demands that will arise from these epidemics.”

Perrin JM, Bloom SR, Gortmaker SL JAMA 2007;297:2755-2759.
The increase in childhood chronic conditions in the United States.

Query:

- Does exposure to toxic chemicals including heavy metals have anything to do widespread erosion of personal and public health in adults and children?

Historical...

Ludwig van Beethoven

(1770-1827)

Lived in turmoil suffering from both acquired deafness and mania and depression

Crashed and banged his piano, dousing his head with copious amounts of water while scribbling his melodies and harmonies on walls and shutters

Oft thought to be related to syphilis

Recent study from hair and bone analysis: Lead poisoning

- received from doctor in treatment for health complaints



Vincent Van Gogh (1853-1890)

- The Starry Night – lead poisoning – causes swelling of retina causing light circles like halos around objects
- Nibbled at his paints – heavily contaminated with lead
- Had classic symptoms of lead poisoning
- Acute exposures upon painting
- Serious psychiatric illness



CIGARETTE SMOKING

- Dr. Norm Delarue , thoracic surgeon at TGH: in 1947 recognized the relationship between smoking and lung cancer.
- Info on smoking & mortality published in 1954 BMJ & still ignored
- Took the usual 30-40 years before widely accepted
- Recognized as a determinant of many illnesses
- Plethora of vocal programs to diminish rates of smoking

*Now we have a plethora of other chemical exposures
that people are routinely exposed to.
(some of which are at least as toxic as smoking)*

Chemical Revolution

- 75 years ago, synthetic chemicals were a futuristic idea
- Chemical Revolution: since then, more than 90,000 anthropogenic compounds have been created and many released into the environment
- Majority have not been tested for their impact on human health
- Exposure is now a routine part of daily life for most people – beauty, safety, convenience, efficiency, etc...

Chemical Pollutants

Toxic Elements

- Mercury
- Lead
- Cadmium
- Aluminum
- Arsenic
- etc

Organic Pollutants

- Synthetics
- Petrochemicals
- Biological agents
- Byproducts & metabolites

- Nanotoxicology: Nanoscale Pollutants (Organic & Inorganic)

People are routinely exposed...

- 1) Breathe
- 2) Smell
- 3) Absorb through skin or mucous membranes
- 4) Ingest
- 5) Vertical transmission
- 6) Implanted or injected

After exposure, what happens?

Depending on

- i) properties of the chemical
- ii) detoxification abilities of the individual

Some chemicals
are eliminated

Some chemicals persist – why?

- Enterohepatic circulation (EHC)
- Renal tubular reabsorption
- Affinity to tissues – e.g. lipophilic
- Impaired detoxification mechanisms
 - Organ dysfunction – e.g. liver, kidney
 - Deficient in nutrients for elimination
 - Polymorphisms
 - Toxicants interfering with elimination

- Jandacek RJ, Tso P. Enterohepatic circulation of organochlorine compounds: a site for nutritional intervention. *J Nutr Biochem* 2007;18:163–7.
- Andersen ME, et al. modeling of saturable, renal resorption of perfluoroalkylacids in monkeys – probing the determinants of long plasma half-lives. *Toxicology* 2006;227:156–64.

Toxic metals interfere with all stages of liver detoxification

Phase I – Activation of Xenobiotic

- via cytochrome P450 enzymes
- Impaired by Hg, Pb, As, Cd

Phase II – Conjugation of activated xenobiotic

- via mechanisms including GSH-S-Transferase
- Impaired by Hg, Pb, As, Cd

Phase III – Elimination of xenobiotic complex –

- Various toxic metals alter microbiome which is intimately involved in elimination

- Result facilitates bioaccumulation of all xenobiotics
- Breton C et al. Toxicology of metals and metalloids in the liver microbiome. BMC Microbiology 2013;14:62.
- Maier A et al. Disruption of dioxin-inducible phase I and phase II gene expression patterns by cadmium, chromium, and arsenic. Molec Carcinogenesis 2000. 28:225-35
- Moore M . A commentary on the impacts of metals and metalloids in the environment upon the metabolism of drugs and chemicals. *Toxicol Letters*, 148, 2004, 153-158
- Fatma M El-Demerdash, et al. Cadmium-induced changes in lipid peroxidation, blood hematolgy, biochemical parameters and semsn quality of male rats. Food and Chemical Toxicology, Volume 42, Issue 10, October 2004, 1563-1571
- Y.C. Awasthi (2006). *Toxicology of Glutathionine S-transfserases*. CRC Press Inc..
- Bozcaarmutlu A.et al.Effect of mercury, cadmium, nickel, chromium, and zinc on kinetic properties of NADPH cytochrome P450 reductase *in Vitro*,Toxicol 21: 2007, 408-416

Is chemical exposure & bio-accumulation a common problem?



Department of Health and Human Services

Centers for Disease Control and Prevention

National Report on
Human Exposure to
Environmental Chemicals

- Most American adults and children have bio-accumulated numerous potentially toxic chemicals

American Red Cross collected Cord Blood Samples:

Chemical stew found in umbilical blood

Study found 287 industrial pollutants in cord blood of 10 babies

COLLEEN DUSKIN
Knight Ridder Newspapers
BARRACKS, N.J.

Mothers pass on hundreds of chemicals — from pesticides to flame retardants — to their babies through their umbilical cords, according to a groundbreaking study.

The study, released Thursday, found 287 industrial chemicals and pollutants in umbilical cord blood from 10 babies born in U.S. hospitals. The blood harbored pesticides, chemicals from non-stick cooking pans and plastic wrap, long-banned PCBs and wastes from burning coal, gasoline and garbage. On average, each baby had been exposed to 200 chemicals.

Scientists have long cautioned expectant mothers to limit their exposure to chemicals, by avoiding mercury-tainted fish, for example, and staying out of the nursery until the paint is dry. But the study, paid for by the Washington-based Environmental Working Group, is the first to examine the sheer number of exposures infants can have, via the umbilical cord.

It's nearly impossible for their mothers to avoid, the researchers said.

It is the first to measure a baby's "body burden," the term used to describe the amount of pollutants buried in the blood stream, organs, tissues and fat cells.

Researchers and environmental advocates said the results are disconcerting.

"The numbers are startling when you hear them," said Dr. Alasy Greene, a Stanford University pediatrician who wrote a commentary on the study.

In the moments before the baby's birth, the umbilical cord pumps at least 300 quarts of blood each day back and forth from the placenta to the fetus, bringing the baby oxygen and nutrients. Scientists once believed that the placenta shielded cord blood and the baby from most chemicals and pollutants.

Greene described the placenta as a "true-life, living胎盘" that the blood vessels in the umbilical cord draw from.

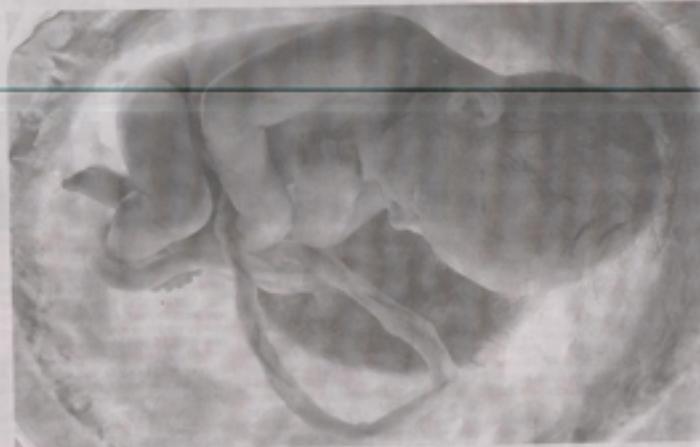
Today, this most primal of links has become polluted with industrial contaminants, Greene said. "And developing babies are nourished exclusively from this polluted pool. They maintain the

blood, injecting them into their veins more powerfully than any IV drug administration."

The study raises more questions than it answers, in particular what the cumulative effect of all these chemicals might be on a newborn, said Tim Kropp, a senior scientist with the Environmental Working Group.

"For some of the chemicals, we know some safe levels for a single chemical in adults," Kropp said. "In none of them, however, do we know what the safe level is in combination with each other and not what it is in babies."

The Environmental Working Group paid \$10,000 apiece to test the cord samples. (Source: <http://ewg.org/reports/bodyburden2/execsumm.php>)



This is a model of a fetus in the womb. Cumulative effect of chemical pollutants on babies is still unknown.

used by the Red Cross for possible use in transplant operations.

Kropp said no identifying information was provided, meaning it is impossible to know whether the pregnant mothers had lived near pollution hot spots. But a hot spot would account for just a few chemicals; these babies tested for exposure to far more, showing, Kropp said, just how pervasive chemicals are in our society.

The blood sample with the lowest readings contained 154 chemicals. The highest held 231.

Exposure to chemicals is a bigger concern with infants because the blood-brain barrier — the body's defense that keeps contaminants from reaching the

central nervous system — is not developed, meaning babies can suffer neurological harm, Greene said.

Greene and others utilized or study say it poses to the need for a publicly funded study of the long-term effects of chemical exposure to children.

Advocacy groups say there are consumers can reduce their exposure.

Suggestions include eating organic food farmed without pest control chemicals, buying organic cosmetics, fragrances and deodorants, avoiding Teflon-coated, and not microwaving to heat foods in plastic containers that might leach chemicals.

Environmental Working Group. Body burden - the pollution in newborns A benchmark investigation of industrial chemicals, pollutants and pesticides in umbilical cord blood. (Executive Summary) July 14, 2005. [Accessed Sept 16, 2005] <http://ewg.org/reports/bodyburden2/execsumm.php>.

What is the impact of toxic chemical exposure?

No sustained
damage
evident

Irreversible
damage after
exposure

Persistent exposure
continually disrupting
physiology as a result of
bio-accumulated toxicants

Chronic illness

Chronic illness
(modifiable)

Impact of Some Persistent Chemicals

Chronic presence of toxicants



Chronic disruption of human biology



Chronic illness

Just as chemical pharmaceuticals alter physiology...

An internal dose of other biologically active foreign chemicals *may disrupt physiology*

Clinical Observation: Mounting Evidence

**Remove presence of toxicants
in many cases**



**No longer chronic metabolic
disruption of human biology**



**Clinical improvement or
resolution**

- Redgrave TG et al. Treatment with a dietary fat substitute decreased Arochlor 1254 contamination in an obese diabetic male. J Nutr Biochem. 2005 Jun;16(6):383-4
- Genuis SJ. Toxic causes of mental illness are overlooked. Neurotoxicology 2008;29:1147-9. [LOE-B]

Toxicants and Metabolism

- By various recognized pathophysiological mechanisms, chemical toxicant exposure and bioaccumulation cause harm

Etiology
Chemical
Toxicants

Pathophysiology or
Mechanism of Harm

Numerous
Mechanisms

Outcome

Clinical Illness

Chemical Toxicants



Pathophysiology Mechanism of illness



Clinical Manifestations

Direct

Cytotoxic Damage

Dys. GABA, Glutamate, Glutathione

Endocrine Disruption

Epigenetic

Enzyme dysregulation

Displacement

Oxidative Stress

Inflammatory

Plaque formation



Indirect (secondary impact)

Immune Dysfunction

- Suppression
- Autoimmunity
- Hypersensitivity

Nutritional compromise

Impair detoxification pathways

Microbiome damage

ANS dysregulation

➤ *Endocrine Disruption*

- Many toxicant compounds distort endocrine function
- May interfere with synthesis, transport, action, or excretion of hormones
- May mimic hormones, block hormone receptors, act synergistically with hormones, have anti-hormonal action, etc.

Endocrine disrupting chemicals (EDC)

- Many chemicals are endocrine disruptors, including several pesticides and various heavy metals (xenoestrogens)
- Can affect fertility, thyroid function, puberty, sexual development, and hormone sensitive organs such as prostate, breast, endometrium, etc. etc.

- Mnif et al. Effect of Endocrine Disruptor Pesticides: A Review. Int J Environ Res Public Health. 2011 June; 8(6): 2265–2303.
- Gioiosa et al. The effects of bisphenol A on emotional behavior depend upon the timing of exposure, age and gender in mice. Horm Behav. 2013 doi: 10.1016/j.yhbeh.2013.02.016. [LOE-B]

➤ *Microbiome damage*

What is germ ecosystem responsible for?

- Detoxification
- Involved in neurotransmitter release
- Breakdown of foods
- Absorption
- Production of required nutrients etc. etc – e.g. vitamin K2
- etc

Alteration of microbiome impairs its ability to carry out normal biology

➤ *Microbiome damage*

- Immune mediated health problems
- Toxicant related vs. Biome related???
- Recent talk – toxicants vs. biome
- Many wonderful talks on healing the gut

Toxicants and Metabolism

Etiology → Pathophysiology or Mechanism of Harm → Outcome

Chemical Toxicants → Biome Disruption → Clinical Illness

Toxicant Burden & Ongoing Exposures...

- Etiology of much biome disruption
- e.g. chlorine, heavy metals, pesticides, antibiotics, etc.
- Persistent toxicants cause persistent biome damage –
 - must address toxicant burden and exposure to restore biome
 - Addressing toxicant exposures & burden allow for 'healing the gut'

- Breton J, Massart S, Vandamme P, De Brandt E, Pot B, Foligne B. Ecotoxicology inside the gut: impact of heavy metals on the mouse microbiome. BMC Pharmacol Toxicol 2013;14:62.
- Microbiome/Environment Interactions. National Institute of Environmental Health Sciences Division of Extramural Research and Training Cellular, Organs and Systems Pathobiology Branch. NATIONAL ADVISORY ENVIRONMENTAL HEALTH SCIENCES COUNCIL <http://www.niehs.nih.gov/news/newsletter/2012/3/spotlight-council/file62863.pdf> [LOE-B]
- Samsel et al. Glyphosate's Suppression of Cytochrome P450 Enzymes and Amino Acid Biosynthesis by the Gut Microbiome: Pathways to Modern Diseases Entropy 2013, 15(4), 1416-1463

What kind of disease processes may result from chemical toxicant exposure?

Damaging human health in many ways:

- Carcinogenic
- Hepatotoxic
- Neurotoxic
- Immunotoxic
- Developmental toxicity
- etc. etc

Toxicity linked with all kinds of illness

- Dementia
- Widespread autism
- Infertility
- Cancer
- Mental health problems
- Autoimmune illness
- Allergies
- Skin Disorders
- Etc, etc, etc



Enormous attention in the literature exploring potential causal connections

- Many scientific and public health journals : *Environmental Health Perspectives; Environmental Research, Science of the Total Environment; J Environ & Public Health, myriad Toxicology journals, etc...*
- NIH recently begun funding studies exploring elimination of persistent toxicants
- Extensive research on persistent EDCs & Epigenetics
- etc...

- Centers for Disease Control, Department of Health and Human Services. Fourth National Report on Human Exposure to Environmental Chemicals. 2009. [Accessed Jan 18, 2009] Atlanta: Georgia. pp.1-529. <http://www.cdc.gov/exposurereport/pdf/FourthReport.pdf> 2009.
- National Institutes of Health (NIH) Grant Proposal (NIH K99/R00) on 'Biomonitoring for and detoxification of environmental chemicals in humans.' (2010)

Pronouncements from medical bodies

Pediatric Academic Societies 2001 Annual Meeting:

“Low level exposure to environmental toxicity may be impacting the functioning of the current generation”

World Health Organization:

“Acute and chronic, high and low-level exposures to chemicals in the environments of children may cause functional and organic damage.”

etc. etc...

- *Journal of Perinatal Medicine*: Volume 34(3) May 2006. 185–195
- World Health O. Children's Health and the Environment. WHO Training Package for the Health Sector. World Health Organization. [www.who.int/ceh accessed Jul 8, 2009].

Common retort – No impact at low doses!

- Inherent physiology occurring as a result of biochemical reactions involving ppb & ppt
- Endocrine disruption with equally low doses of xenobiotics

“If we drained the blood of 250,000 pre-menopausal women, we’d get one teaspoon of the active estrogen – estradiol.”

Natalie Angier (Pulitzer Prize winning author of *Woman: An Intimate Geography*)

Welshons WV, Thayer KA, Judy BM, Taylor JA, Curran EM and Vom Saal

FS (2003) **Large effects from small exposures.** Environ Health Perspect 111,994–1006.[LOE-B]

Kenneth A. Cook, Environmental Working Group Subcommittee on Superfund, Toxics, and, Environmental Health.
Presentation to Senate Environment & Public Works Committee (Feb. 4, 2010))

Metabolic Impact at low doses

- Serum PFOS change of 5 ppbs made significant changes in SUA (source - stain resistance in clothes, furniture and carpets)

NHANES (CDC) 2004 average level	PFOS	20.7		
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- “Our results indicate that bisGMA at concentrations less than 0.1 micromolar cause an extreme depletion of intracellular glutathione as well as increasing apoptosis.” (bis-GMA – typically used in dental restorations)

- Steenland K. et al. Association of perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) with uric acid among adults with elevated community exposure to PFOA. Environ Health Perspect. 2010 Feb;118(2):229-33.
- Engelmann J. et al. Effects of BisGMA on glutathione metabolism and apoptosis in human gingival fibroblasts in vitro. Biomaterials. 2004 Aug;25(19): 4573-80 [LOE-B]

Another retort: NOAEL safety testing

No observed adverse effect level

- the level of exposure of an organism to a chemical or agent (e.g. radiation), at which no such adverse effect is found in exposed test organisms

i. Most compounds not tested

ii. Testing is one time exposure – real life is persistent ongoing exposure of bioaccumulated toxicants

iii. Only looking at short term outcomes

iv. Detoxification mechanisms different in rats -cannot extrapolate findings to people

*Mounting evidence that ubiquitous
chemical toxicant exposure
of the late 20th and early 21st century
is a major determinant of
the profound decline of individual and public health*

Exposure to
myriad
chemical
substances

The Chemical Erosion of Human Health

Persistence &
accumulation
of some

Individual
& synergistic
toxicity
recognized

Adverse
health
effects
documented

Individuals
& populations
affected

Managing
the Problem



II. What can you do clinically to address the chemical erosion of health?

- I. Prevent further exposure to individuals and population groups
- II. Get the stuff out of people already with an internal dose

Genuis SJ, Sears ME, Schwalenberg G, Hope J, Bernhoft R (2013) Clinical detoxification: elimination of persistent toxicants from the human body. *TheScientificWorldJournal* 2013: 238347

Detoxification - flourishing

Spectrum of therapies used:

- Medications – e.g. bile acid sequestrants
- Blood filtration – e.g. hemodialysis
- Plasma exchange or removal – e.g. therapeutic apheresis, phlebotomy
- Binding therapies – e.g. chelation
- Physical therapies – e.g. transdermal depuration, various types of baths, foot pads, constitutional hydrotherapy, etc
- Microbiome enhancement – selected probiotics
- Enterohepatic interruption – e.g. Olestra
- Colonic therapies – e.g. oil enemas, coffee enemas, etc
- Energy therapies
- Liver/Gallbladder flushes
- Food therapies – e.g. fibre, chlorella, broccoli sprouts (e.g. benzene)
- Etc, etc

Detoxification schools of thought

(editor of Journal edition on detoxification – researchers, clinicians, organizations, programs, etc)

- Panchakarma – Ayurvedic medicine
- Scientology approach
- Gerson technique
- ‘Experts’
- Energy-related detox strategies
- Etc.

Many claims

Lots of anecdotal reporting

Limited evidence-based research in the scientific literature

Some techniques based on science

Many lack scientific credibility

Focus on what has scientific evidence

Clinical Detoxification

- elimination of persistent toxic substances from the body

I. Avoidance

II. Intrinsic Detoxification

III. Extrinsic Detoxification

I. Precautionary Avoidance

Single Most Important: *Avoid, Avoid, Avoid!*

Personal Inventory

- Breathe
- Ingest
- Dermal Application
- Smell
- Implanted or injected
- Vertical Transmission

e.g. Some Unrecognized Common Sources

- Emissions from computers – Hg, Pb, As, Be, PBDEs, etc
- Airplane travel – compressed air in engine –metals, petro,
- Some candles – wicks to slow rate of burning – e.g. Pb, etc
- Vehicle emissions – engine compartment
- Some supplements – some sourced from polluted areas
- Plastics – in IVs and tubing
- etc. etc...

II. Intrinsic Detoxification

- Optimizing inherent function of the body to detoxify
- Raw materials required for biochemical processes (e.g. glutathione) – nutritional adequacy
- Minimize obstructing features (e.g. EtOH, meds, etc)
- Address impairments (e.g. PST sulfation problem – phenols – v. acidic, impact CNS)

Intrinsic Detoxification - Limitations

- Intrinsic detoxification cannot effectively remove all compounds
 - Enterohepatic circulation
 - Renal tubular reabsorption (pH dependent)

*** Need other mechanisms to remove some bioaccumulated agents*

III. Extrinsic Detoxification

Targeted Interventions to facilitate removal of accrued toxins

- 1) Endeavor to identify the burden of persistent toxicants – toxicological testing
- 2) Intervene with appropriate therapy

Identify what the total burden is

Chemical Pollutants

Toxic Elements

Organic Pollutants

Challenges of assessing and managing toxic element contamination

1. Toxic element chemistry is complex
2. Each toxic element has specific properties -they do not all behave the same
3. Synergy and interactions with other pollutants not completely understood
4. Testing is imprecise

Explore some fundamentals of toxic elements...

Multiple toxic elements

In addition to Hg, Pb, As, Cd, Al, also..

- **Gadolinium** - MRIs
- **Platinum** – post-chemo
- **Thallium** – electronics and glass industry – has seeped into kale and cruciferous veggies – cabbage, broccoli, cauliflower, collard, etc
 - found in regions of California lately
- **Nickel** – occupational, proximity to industrial sources, food processing industry
- **Antimony** - used in some materials as a flame retardant
- etc.

Just like many good elements are required; an array of toxic elements must be avoided

Speciation – Chemistry (family)

- Exposure and accrual of toxic agents such as metals and metalloids can occur in different forms
 - e.g. Hg: Organic – methylmercury, ethyl Hg, dimethyl Hg, Hg-oxalate, etc
Inorganic – elemental mercury, mercuric chloride, divalent Hg,etc.
 - e.g. Pb – Organic – tetra-ethyl Pb, tetra-methyl Pb
Inorganic - lead oxide, lead sulphate (most cases)
 - Can exist in different forms in the body

Marked variability in toxicity and behavior of different species of same element:

- Different forms metabolized by the body in different ways
- Can interact with body biochemistry and change speciation state
- Assessing speciation state – can be complicated and expensive

Arsenic – Organic vs. Inorganic

Arsenic:

- Can exist in several ways: elemental, organic, inorganic, and gaseous
- Inorganic – very serious acute and chronic toxicity
- Organic – much less toxic – founds in many foods

Organic Arsenobetaine is a common constituent of seafood and is considered nontoxic.

Organic arsenic compounds in most seaweed are arsenosugars, mildly toxic

Inorganic arsenic was > 600 times more toxic than the arsenosugar typically found in seafood.

Organic vs inorganic metabolized totally differently

Organic As can be trivalent or pentavalent.

- Rose M, Lewis J, Langford N, Baxter M, Origgi S, Barber M, et al. Arsenic in seaweed: forms, concentration and dietary exposure. *Food Chem Toxicol.* 2007;45:1263–1267
- Andrewes P, Demarini DM, Funasaka K, Wallace K, Lai VWM, Sun H, et al. Do arsenosugars pose a risk to human health? The comparative toxicities of a trivalent and pentavalent arsenosugar. *Environ Sci Technol.* 2004;38:4140–4148.
- ATSDR (Agency for Toxic Substances and Disease Registry) Toxicological Profile for Arsenic (Update) (Draft for Public Comment) 2007b.
- Lewis AS Organic versus Inorganic Arsenic in Herbal Kelp Supplements. *Environ Health Perspect.* 2007 Dec; 115(12): A575
- Rusyniak D. Heavy metal poisoning: management of intoxication and antidotes. *Molecular, Clinical and Experimental Toxicology* 2010;2:365-395.
-

Properties of each element varies

(between and within families)

How each toxic element behaves

- > storage
- > distribution
- > toxicology & mechanisms of damage
- > elimination
- > etc.

varies between toxic elements and
different species of one element

e.g. **Storage varies** (where we live varies)

- Cadmium – widely distributed - mainly kidney then liver
- Lead – stores primarily in bones, teeth and brain
- Mercury – stores in brain and kidneys
- Aluminum – mainly in brain; some in bones
- Etc

- Storage also depends on speciation for some elements
 - e.g. Organic methy-Hg targets brain
Elemental Hg targets lungs, brain and kidney

e.g. Rate of spontaneous elimination

- Clearance is different in blood than in tissues...and between different tissues
- Can shift between compartments
- Individual variation - nutritional status, genetics, total load, detoxification status, etc

Lead

- Half-life of about 30 days in blood
- Half-life of 25-30 years in bone

Huge implications for testing

e.g. Mode of Excretion varies

- Between elements
- Between species of element
 - Cadmium and many toxic element species – excretion primarily through renal mechanisms
 - Thallium – primarily fecal with EHC recycling

What we do know

- Exposure and bioaccumulation of toxic heavy metals in some forms is very harmful to the body
- Can cause profound damage in many different ways (EDC, enzyme dysregulation, mitochondrial damage, epigenetic change, etc) resulting in myriad and serious clinical problems
- Elimination of these toxic agents can result in remarkable clinical improvement

Clinical Approach

1. Secure Avoidance*
2. Facilitate intrinsic decorporation*
3. Test
4. Treat

Testing for toxic element body burden -challenging

- Hair testing
 - DN show very recent exposure
 - DN show bioaccumulated burden
 - Subject to external contamination – hair dyes, etc
- Blood testing – recent exposure – depending on half-life
 - May vary with caloric state
- Sweat testing
 - some metals show that are not present in blood
 - some metals not excreted well in sweat
- Biopsy
 - Metals deposit differently
 - Differential findings at sites of same tissue
- Fingernail testing
- Energy Testing, etc – no published evidence seen
- etc...

No perfect means for assessing body burden

Porphyrin Profiles – shows outcomes

- Some toxic metals affect metabolic pathway of porphyrin production
- Porphyrins in the urine, can be an indicator of heavy metal poisoning - e.g. Pb, Hg
- *Porphyrins* are naturally occurring proteins essential for the production and function of heme – a component of hemoglobin
- Benefits: Can show extent of damage at cellular level and improvement with treatment

Drawbacks:

- Non-specific: potentially the result of other toxicants or other processes
- Does not give quantitative assessment of body burden

Many approaches – will discuss my approach

- No perfect approach – otherwise all would be using same
 - Use least invasive & least potential for toxicity
 - Respect and recognize that other approaches can work very well
1. Consider overall plan to assess & manage patient
 - toxic element approach one part of whole picture
 2. Know what toxic elements you are dealing with
 3. Look for source - avoidance of exposure is crucial
 4. Facilitate natural mechanisms of detoxification as much as possible to allow the body to do what it was designed to do – heal and protect itself.
 5. Use selected interventions to remove

Testing: My preference – minimally invasive and safe as out-pt

1. Whole blood toxic elements as part of nutritional screen – post L-GSH – indication of Cd, As, Al
2. Provoked DMSA urine (oral) – reflection of body burden of selected agents – Pb, Hg
 - mobilize and bind – L-GSH (up to 500mg) & Glycine higher dose (6 g)
 - cautious trial of components
3. Develop plan for removal

Drawbacks – Provoked DMSA does not adequately show Cd, As, Al

Better response to DMPS – more expensive and potentially more reactions

IV single or combined – e.g. EDTA & DMPS – more invasive

Extrinsic Detoxification of toxic elements: Strategies



Strategy #1: Transdermal Depuration

- Induced perspiration with excretion of toxicants through the skin



History of Therapeutic Sweating

Various cultures have used sweating techniques

- Aboriginal sweat lodges
- Finnish cultural practice
- Japanese Onsen
- Steam rooms
- etc



Sauna/hot yoga/steam bath/exercise/ etc

- Increases the thermal load to the body
- Body temperature rises ($39\text{ C} = 102+\text{ F}$), hypothalamus detects rise and initiates an ANS thermoregulatory heat-loss response
- Body responds by directing cardiac output to skin.
- Enhanced circulation to the skin from a baseline of 5–10% to a maximum of 60–70% of cardiac output.
- Perspiration ensues, with an excreted volume of up to 2 litres/h in some individuals.

Evidence for elimination of toxicants??

Sauna associated with

Short- and long-term amelioration of various cardiovascular, rheumatologic, and respiratory afflictions.

Contraindications to sauna use:

- high-risk pregnancy
- severe aortic stenosis
- recent cardiovascular events
- unstable angina

Hannuksela ML, Ellahham S (2001) Benefits and risks of sauna bathing. Am J Med 110(2):118–126

Kukkonen-Harjula K, Kauppinen K (2006) Health effects and risks of sauna bathing. Int J Circumpolar Health 65(3):195–205

Extrinsic Detoxification through Induced Sweating

- Numerous studies have confirmed clinical benefit and release of selected toxicants into sweat



Published Sauna Research to Date

Actual analysis of perspiration:

- Methadone
- Cocaine
- Amphetamines
- Crystal meth
- Morphine

- Fucci N, De Giovanni N, Scarlata S. Sweat testing in addicts under methadone treatment: an Italian experience. *Forensic Sci Int.* Jan 30 2008;174(2-3):107-110.
- Henderson GL, Wilson BK. Excretion of methadone and metabolites in human sweat. *Res Commun Chem Pathol Pharmacol.* Jan 1973;5(1):1-8.
- Vree TB, Muskens AT, van Rossum JM. Excretion of amphetamines in human sweat. *Arch Int Pharmacodyn Ther.* Oct 1972;199(2):311-317.
- Ishiyama I, et al. The significance of drug analysis of sweat in respect to rapid screening for drug abuse. *Z Rechtsmed.* Mar 8 1979;82(4):251-256.

Sweat therapy & Body Burden (not sweat testing)

Sauna therapy can diminish the body burden of assorted bioaccumulated toxicants:

Polychlorinated biphenyls (PCBs)

Polybrominated biphenyls

Chlorinated pesticides

Hexachlorobenzene

- Schnare DW, Ben M, Shields MG. Body burden reduction of PCBs, PBBs and chlorinated pesticides in human subjects. *Ambio*. 1984;13:378-380.
- Dahlgren J, Cecchini M, Takhar H, Paepke O. Persistent organic pollutants in 9/11 world trade center rescue workers: reduction following detoxification. *Chemosphere*. Oct 2007;69(8):1320-1325.
- Roehm DC. Effects of a program of sauna baths and metavitamins on adipose DDE and PCBs and on clearing os symptoms of agnet orange (Dioxin) toxicity. *Clin Research*. 1983;31:243.
- Schnare DW, Robinson PC. Reduction of human body burdens of hexachlorobenzene and polychlorinated biphenyls. In Hexachlorobenzene: Proceedings of an International Symposium, CR Morris and JRP Cabral, eds., International Agency for Research on Cancer, Lyon, France, pp 597-603. 1986.
- Tretjak Z, Root DE, Tretjal A, et al. Xenobiotic reduction and clinical improvement in capacitor workers: a feasible method. *J Env Sci Health*. 1990;A25:731-751.
- Tretjak Z, Shields M, Beckman SL. PCB reduction and clinical improvement by detoxification: an unexploited approach. *Hum Exp Toxicol*. 1990;9:235-244.
- Schnare DW, Denk G, Shields M, Brunton S. Evaluation of a detoxification regimen for fat stored xenobiotics. *Medical Hypothesis*. 1982;9:265-282.

Toxic Element Excretion

Lead & nickel appear in analytical studies on sweat.

But lack of evidence for other toxic elements...

- Hohnadel DC, Sunderman FW, Jr., Nechay MW, McNeely MD. Atomic absorption spectrometry of nickel, copper, zinc, and lead in sweat collected from healthy subjects during sauna bathing. *Clin Chem.* Nov 1973;19(11):1288-1292.

BUS Study – (Blood, Urine, Sweat): 2007-2016

- Principal Investigator – Stephen Genuis MD
- Associates
 - Deib Birkholz PhD
(toxicological advice & testing)
 - Sanjay Beesoon PhD candidate
(stats and analysis)

Approval from Health & Ethics Research Board, University of Alberta

BUS Study Protocol

- Collected Blood, Urine & Sweat from 20 participants
- Tested for the presence of various (120) chemicals
- Compared the **Blood : Urine : Sweat** ratios for each compound
- Looked for differences in excretion rates based on
 - age
 - gender
 - health status
 - type of sauna used

BUS Study: Induced Sweating

- tested for 120 chemicals

Chemical groups studied:

1. **Toxic Elements** – heavy metals & metalloids
2. **Plasticizers** – phthalates & bisphenol A
3. **Solvents** – benzene, xylene, etc
4. **OC Pesticides** – DDT, DDE, etc
5. **PCBs** – many congeners
6. **PFCs** – PFHxS, PFOS, PFOA, etc
7. **PBDEs**

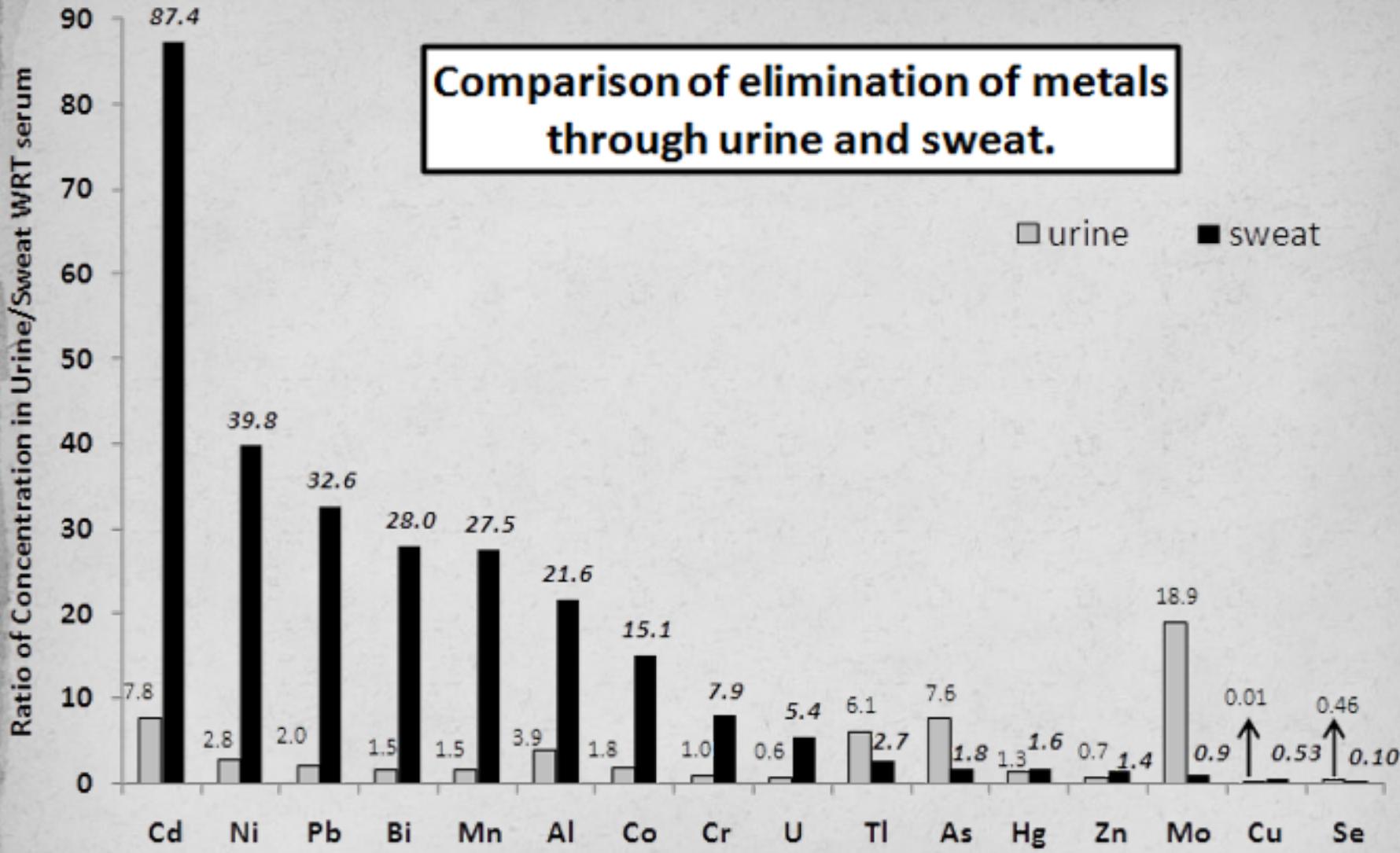
Variables in BUS Study

- 10 chronically ill vs. 10 healthy controls
- Varied ages – youth to senior
- Both genders
- 10 with infra-red sauna ; 7 regular sauna; 3 exercise sweat

Results: Toxic Elements

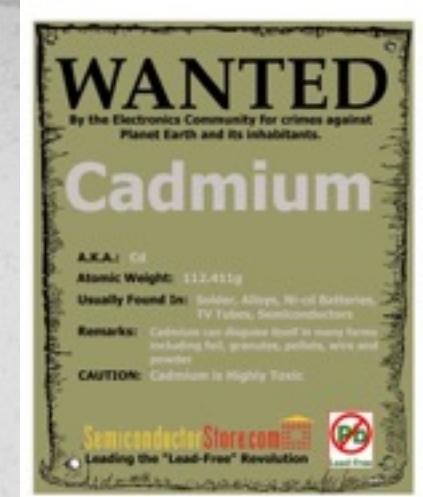
Toxic elements come out to varying degrees in sweat

Required minerals also come out to varying degrees in sweat



Cadmium

- 50% of participants had no detectable cadmium in their blood or urine.



- Of these, 80% had notable levels in sweat

- Cadmium can be stored in tissues with no evidence in blood or urine
- Sweat can release stored cadmium
- *Sweating is a mechanism for eliminating some toxic elements that may not be readily evident in testing*

Sauna Use – also removes various POPs

- Facilitation of perspiration
 - Preheat, exercise, hot fluids, clothing, etc
- Frequency
- Preparation
- Length
- Controversies – e.g. best type for efficacy, safety, etc
- Cautions
 - Mineral depletion
 - Type of sauna
 - Offgassing
 - EMFs
 - Toxicant mobilization – S & S

Strategy #2: Fasting

- Uncertain - Insufficient study
- Evidence:
 - Mobilizes lipophilic toxicants
 - Facilitates elimination of some lipophilic toxicants
 - Preliminary – not convinced based on testing

Strategy #3: Exercise

- Uncertain - Insufficient study
- Evidence:
 - Facilitates elimination of some solvents

Strategy #4:

Foods and nutrients that may help eliminate toxic elements

- Garlic
 - Chlorella
 - Apple/Citrus Pectin – dietary fiber esp in peel of citrus
 - Fermented foods and probiotics
-

- Folate - Rx As
 - Selenium (e.g. Brazil nuts) –Rx Hg
 - Malic acid (e.g. apples) – Rx Al
-

Comparison of therapeutic effects of garlic and d-Penicillamine in patients with chronic occupational lead poisoning.

Kianoush S et al. Basci Clin Pharm Toxicol. 2012 May;110(5):476-81.

Blood lead concentrations were reduced significantly in the garlic and d-penicillamine groups, respectively, with **no significant difference between the two groups.**

Insufficient testing regarding allicin from garlic & other toxic elements

Chlorella

- Numerous papers in the literature confirming ability of certain chlorella species to facilitate binding and elimination of heavy metals
- Caution vs. contamination

Pectin from fruit – citrus/apple

- Emerging evidence of inorganic element removal
- Success with radioactive elements in Chernobyl

Zhao ZY et al. The role of modified citrus pectin as an effective chelator of lead in children hospitalized with toxic lead levels. *Alt Ther Health Med.* 2008 Jul-Aug;14(4):34-8.

Nesterenko VB. et al. Reducing the (Cesium) 137Cs-load in the organism of "Chernobyl" children with apple-pectin. 2004 Jan 10;134(1-2):24-7.

Fermented foods & Probiotics

- Emerging evidence of organisms involved in elimination of toxic elements
- Pb – *L. rhamnosus GG*
- Cd – *L. plantarum*
- As (V) – *L. casei*

Folate and As

Am J Clin Nutr. 2007 Oct;86(4):1202-9.

- **Folic acid supplementation lowers blood arsenic.**

Gamble et al.

Selenium

Biometals. 2015 Aug;28(4):605-14

- **Selenium as an antidote in the treatment of mercury intoxication.**
- Bjorklund G.
- Secure adequacy

Malic acid and Aluminum

- Human Toxicology. 1988 May;7(3):259-62.
- **Comparative effects of several chelating agents on the toxicity, distribution and excretion of aluminium.**
- Domingo JL et al.

Insufficient study to provide solid evidence

- Cilantro (Coriander) – mobilizes some elements from CNS
insufficient direct evidence on toxic element removal
- Alfalfa (high fiber – able to bind some chemicals in colon)
insufficient direct evidence on toxic element removal
- Rutin – phytoextract from buckwheat, black tea,
insufficient direct evidence on toxic element removal
- etc, etc

Strategy #5: 'Natural Agents for eliminating toxic elements'

Natural Occurring Zeolites – from volcanic ash & seawater

- Through cation exchange, toxins are allegedly absorbed into the zeolite cage and then excreted - prevent reabsorption in the EHC
- Confirmed to work in wastewater – insufficient human evidence
- Unpublished data from colleagues – unsuccessful work in humans
- May have some toxicity – with contamination

Bentonite Clay & Charcoal

- Toxicant uptake -Works in environmental and industrial settings e.g. water purification - lacks human evidence
- Interrupt EHC e.g. thallium absorbed by activated charcoal in vitro

Saponins - Originating from soy or the yucca plant

- Alleged to bind some toxicants in bile to prevent reabsorption in the EHC – lack of evidence in human work for toxic elements
- etc

•

Strategy #6: Medications

Agents that bind or 'chelate' metals

i) Dimercaprol (BAL – British anti-Lewisite).

- Previously used for metal poisoning – As, Hg, Pb, Antimony, Ni, Cobalt, etc
- Effective vs. inorganic Hg, not against phenyl- or alkyl Hg.
- Potentially toxic with multiple side effects

ii) d- Penicillamine – was used for Pb, As, Hg, Cd

- Lot of side effects, potentially toxic

Flora, SJ; Pachauri, V (2010), "Chelation in metal intoxication", Int J Research & Public health 7 (7): 2745–2788,
Goldman M, Dacre JC. (1989) Lewisite: its chemistry, toxicology, and biological effects. Rev Environ Contam Toxicol 110: 75-11
Proc R Soc Med. 1977; 70(Suppl 3): 43–45. The use of D-penicillamine for lead poisoning.
Beattie et al. WHJ Rheumatol Suppl. 1981 Jan-Feb;7:96-9Penicillamine in metal poisoning

Many Rx approaches – workshops available

- DMSA – (oral, transdermal, p.r.) effective against many toxic elements – but not all
Hg, Pd, Gd, Tl, Ni, etc
- DMPS – (oral or IV) much better vs. As, Cd (prohibitively expensive \$900/month; less well tolerated; more potentially toxic; concern re nephrotoxicity of rapid Cd release)
- calcium EDTA (oral, sublingual, transdermal, and rectal, IV) – better vs. As, Cd, Al; Poor affinity for Hg
Oral EDTA is only about 5% absorbed. Rectal EDTA might be absorbed as much as 35% to 37%

Toxic element consideration

- DMSA nor DMPS do not generally cross the blood brain barrier on their own in humans
- EDTA does cross blood brain barrier
- We do not completely understand redistribution of toxicants

Efficacy with brain mercury

- Animal work: DMSA and DMPS diminish brain and kidney concentrations of Hg

Aposhian H et al. Vitamin C, glutathione, or lipoic acid did not decrease brain or kidney mercury in rats exposed to mercury vapor. J Toxicol Clin Toxicol. 2003;41(4):339-47.

DMSA in children with ASD

Evidence for sustained improvement with interventions to diminish the load of toxic elements

-oral DMSA in children with autism

- Patel et al. 2007. A comprehensive approach to treating autism and attention-deficit hyperactivity disorder: a pre pilot study. J Alternative and complementary medicine 13(10):1091-1097.
- Adams JB et al. 2009. Safety and efficacy of oral DMSA therapy for children with autism spectrum disorders: part A--medical results. BMC Clin Pharmacol 9:16.
- Adams JB, et al. 2009 Safety and efficacy of oral DMSA therapy for children with autism spectrum disorders: part B - behavioral results. BMC Clin Pharmacol 9:17.
- Kidd PM. Autism, an extreme challenge to integrative medicine. Part II: Medical management. Alternative Medicine Review 2002;7:472-99
- Genuis SJ (2009) Toxicant exposure and mental health--individual, social, and public health considerations. Journal of forensic sciences 54: 474-477.

Medications to eliminate toxic elements: Maintain Mineral Status

Propensity to lose minerals

Must replete minerals on ongoing basis

Nutrient flooding

Juicing

Smoothies

Bone broth

Supplements

Strategy 7 – Colonic therapies

Colon Hydrotherapy

Enemas

Panchakarma (multi-therapy program) – Pb exposure (Anecdotal)

No scientific evidence for removal of toxic elements found in scientific literature via colonic therapy

Strategy #8: Physical Interventions & Energy Rx

- Massage – anecdotal
- Epsom salt baths
- Energy - Qi Gong
- Energy machines
- Etc.

Insufficient direct evidence on toxic element removal

Have seen many people who have had these treatments



Extrinsic Detoxification

Ionic Foot Baths: Sends a current into the body to generate positively charged ions which allegedly attach to negatively charged toxins and discards bound toxicants through foot pores.

- Kennedy DA et al. Objective assessment of an ionic footbath (IonCleanse): testing its ability to remove potentially toxic elements from the body. J Env Public Health 2012;2012:258968.

Energy treatments: Techniques which purport to enhance the biophysical energy of the body (e.g. Qi Gong) to stimulate detoxification pathways.

Review: My Approach – well tolerated and effective

- i) Take history
- ii) Testing
- iii) Avoidance***
- iv) Rx:
 - Thermal Depuration
 - Detox Foods and supplements – chlorella, garlic, pectin, etc
 - DMSA 1-2 /week po
 - EDTA 1 /week p.r.
 - Probiotics and fermented foods
- v) f/u testing Q 6 months

Clinical Outcomes

- *Case Histories...*

Case: Man with Bipolar Disease & Progressive Dementia

- 62 year old with 33 year history of bipolar illness. Recent development of progressive dementia.
- Memory, comprehension, communication and reasoning - rapidly declining.
- “Irreversible, degenerative condition.”
- Recommendation: chronic care placement.

Case 2 cont: **Heavy Metal Exposure**

- Assessment: History of work with stained glass in confined space – lead exposure
- Massive amounts of lead on challenge test;
minimal levels on blood testing
- Pb detoxification: use over 9 months, astonishing recovery in
mentation & mood
- Good sense of humor
- “Great to have the man I married back in my life.”

Case: Young man with depression & intrusive thoughts

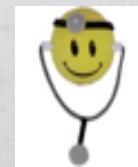
- Teacher with escalating thoughts of hurting young children
- Increasing depressed with inclination toward self-harm
- Marked elevation of Hg – blood and provoked urine
- Likely source – daily consumption of tuna fish
- Pursuing health and consumption of omega-3 fatty acids
- Avoidance
- Sauna / chlorella / probiotics / DMSA
- Complete resolution in few months

Concluding Message

Bio-accumulated chemical toxicants, often from repeated low-level exposures, are the cause of many chronic mental and physical health problems.

Eliminating the underlying burden of chemical toxicants including toxic elements may prevent adverse health outcomes and restore health in those with chronic afflictions

References and papers: Researchgate



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