The impact, assessment, and treatment of heavy metals and radioactive elements on health

The impact, assessment, and treatment of heavy metals and radioactive elements on health

Objectives:

1. Understanding the increasing exposure and symptoms of heavy metals and radioactive elements

2.Evaluating for metals and radioactive elements through laboratory, environmental, and clinical testing

3. Basic understanding of treatment through detoxification, diet, targeted neuctraceutical and pharmaceutical therapy

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Integrated Functional Medicine

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Toxic Metals and RadioActive Elements - Summary points

Toxic Metals are UBIQUITOUS

Exposure is UNAVOIDABLE

Low Level Exposure - ACCUMULATION

METAL TOXICITY - subtle and non-specific

Effects of toxic metals - DEPLETING, INFLAMMATORY, DEGENERATIVE

MINIMIZING body burden = one of HIGHEST PRIORITIES of Preventive/Functional Med

OPTIMIZING nutrient levels is ESSENTIAL to protection / detoxification

Metal Detoxification with Pharmaceutical/Nutraceuticals - SCIENTIFIC, SAFE, EFFECTIVE

Heavy Metals and Radioactive Elements

Heavy Metals vs Toxic Metals vs Minerals vs Radioactive Elements

3/4 of known elements are METALS

- Metal Properties - hardness high melting point malleable density conductor of heat / electricity
- Chromium - hardest metal - used to strengthen materials
- Cesium - softest
- Gold, Silver, Copper malleable and ductile
- Alloy - mixture of metals
- Distinguished from non-metals
- Capacity to loose electrons = become oxidized (the receiving atom / molecule = reduced)
- Oxidized - increased electrical charge after loosing an electron - form positively charged ions
- Reduced - accepting or gaining an electron is reducing the total electrical charge
- Participating in an oxidation - reduction reaction
- Metalloids - elements on the border between metals and non-metals

  (Arsenic)

Metals / Minerals - Sources / Exposure

Metals - Estimated to make up for 1/4 of Earth's mass

Sea water

Volcanoes

Natural weathering

Mining and processing of metals

Use of Metals

1st metals used by humans found in elemental metallic state - copper, gold, silver

Most metals exist in ores - compounds or mixtures of the elements with oxygen or sulfur

Iron and tin - easiest to extract / separate - used earlier in human history

* Mining and processing of ore - leads to build up of " waste or metal materials " - distributed by water

* Released into air environment from burning of coal and fuels and trash incineration

Toxic Metals / Minerals

Metals - toxic elements

1. No known biological function
2. Capable of disrupting normal physiological processes
3. Capable of causing DISEASE

Ex. mercury, cadmium, lead, aluminum

4. Elements in the wrong form

Chromium 3+ essential

Chromium 6+ carcinogenic

Heavy metals vs Toxic metals

Heavy = weight

Toxic = effect " biological bully "

Cadmium, lead, mercury - heavy and toxic

Molybdenum - heavy and essential (beneficial)

Beryllium - light but toxic

Metal Exposure

Modern industrial use of metals

Increased redistribution (from the crust) into environment

More charged / toxic forms

Long lasting complexes within biological systems (fish, animals, humans)

Potential for increasing concentrations at higher levels on the food chain

Toxic Effect of Metals

Displacing an essential metal ion

- Cadmium - for zinc - in function and structure
- Lead - for calcium - in bone

Combing with sulfur based AAs

Metals - consuming / stealing electrons from

- Redox reactions - disrupt biological reactions
- DNA bases

Toxic Metals - Effecting / displacing essential minerals

- Zinc
- Essential trace element - cannot live with out
- **Activator factor in over 100 enzymes**
- Structural ion in RNA transcription
- Functions in all classes of enzymes in humans
- Body contains between 2000-4000 mg
- Brain, muscle, bone , kidney, and liver
- Highest - prostate, semen, and eye
- RNA/DNA metabolism, signal transduction, gene expression, apoptosis
- **10% human proteins bind / interact with zinc**
- Brain - synaptic plasticity - learning - dopamine metabolism

Heavy Metal Toxicity

3 Basic Concepts

Think:

- Exposure / accumulation
- Minerals / sulfur status
- Detoxification

Heavy Metals and Radioactive Elements

Summary Points:

Heavy metals / radioactive elements are **ubiquitous** in environment - man made

Exposure is **unavoidable**

Metals have a tendency to **accumulate** in the human body with **chronic exposure**

Toxic effect of metals is more pronounced in the context of **mineral / anti-oxidant deficiencies**

Genetic weakness in detoxification

Higher index of suspicion:

- Based on environmental factors - maternal history, vaccines, amalgams, older housing, occupation
- Neurological / kidney related conditions / cancer / chronic resistant infections / auto-immune

Detoxify or Die

- Chelation therapy for heavy metal toxicity is **well researched** and **utilized** - through out the world
- Heavy Metal detoxification - science of **Sulfur and Mineral** metabolism

Heavy Metal Toxicity

Slowly excreted and easily deposit / accumulate in the body

Slowly and subtly disruption normal processes / homeostasis

Disrupting repair and immune defense

Resulting in degenerative conditions in most tissues

Toxicity is in large part due to their accumulation in biological tissues - prolonged half lives

Lead - 15 - 27 years in bone tissue
Cadmium 10-30 years

Severity of adverse health effects is related to the **chemical form** of heavy metals, **duration** of exposure, **dose**

As well as the **ability** of the body to detoxify and nutrient status (**minerals/sulfer**)

Mechanism of Toxicity

Displacement of essential minerals

Enzymatic inhibition

Depletion of Sulfur groups

Impaired antioxidant metabolism

Oxidative stress - resulting in DNA damage, lipid peroxidation, and depletion of sulfur based molecules (glutathione)

Slowing / blocking cellular metabolism and function

Loss of normal regulation

Degeneration of cell and tissue function

Immune activation - hyperactive

Recognition of Toxic Substances

Top 10 List

Agency for Toxic Substances and Disease Registry Priority List of Hazardous Substances - HHS

The ATSDR 2015 Substance Priority List

2015 RANK	SUBSTANCE NAME	TOTAL POINTS	2013 RANK	CAS RN
1	ARSENIC	1671.6	1	007440-38-2
2	LEAD	1529.4	2	007439-92-1
3	MERCURY	1458.6	3	007439-97-6
4	VINYL CHLORIDE	1358.9	4	000075-01-4
5	POLYCHLORINATED BIPHENYLS	1345.1	5	001336-36-3
6	BENZENE	1327.6	6	000071-43-2
7	CADMIUM	1318.8	7	007440-43-9
8	BENZO(A)PYRENE	1304.4	8	000050-32-8
9	POLYCYCLIC AROMATIC HYDROCARBONS	1279.1	9	130498-29-2
10	BENZO(B)FLUORANTHENE	1249.7	10	000205-99-2

1. Arsenic 2. Lead 3. Mercury 7. Cadmium

Agency for Toxic Substances and Disease Registry (ATSDR)

Federal public health agency within HHS

Focus on minimizing human health risks from exposure to hazardous substances

Works with CDC

Budget $ 80 million

300 full time employees

Toxic Elements Exposure Profile

DOCTOR'S DATA INC

LAB #: H000000-0000-0
PATIENT: Sample Patient
ID: PATIENT-S-00041
SEX: Female
AGE: 51

CLIENT #: 12345
DOCTOR:
Doctor's Data, Inc.
3755 Illinois Ave.
St. Charles, IL 60174

Toxic Element Exposure Profile; Hair

TOXIC METALS		RESULT µg/g	REFERENCE INTERVAL	PERCENTILE 68th 95th
Arsenic	(As)	**0.021**	< 0.14	
Lead	(Pb)	**0.38**	< 3.0	
Mercury	(Hg)	**0.21**	< 3.0	
Cadmium	(Cd)	**0.032**	< 0.20	
Chromium	(Cr)	**0.52**	< 0.85	
Beryllium	(Be)	**< 0.01**	< 0.050	
Cobalt	(Co)	**0.010**	< 0.15	
Nickel	(Ni)	**0.54**	< 1.0	
Zinc	(Zn)	**170**	< 300	
Copper	(Cu)	**160**	< 70	
Thorium	(Th)	**< 0.001**	< 0.005	
Thallium	(Tl)	**< 0.001**	< 0.005	
Barium	(Ba)	**1.3**	< 8.0	
Cesium	(Cs)	**< 0.002**	< 0.010	
Manganese	(Mn)	**0.19**	< 1.5	
Selenium	(Se)	**0.70**	< 2.1	
Bismuth	(Bi)	**0.018**	< 5.0	
Vanadium	(V)	**0.049**	< 0.20	
Silver	(Ag)	**0.86**	< 1.6	
Antimony	(Sb)	**< 0.01**	< 0.12	
Palladium	(Pd)	**0.011**	< 0.015	
Aluminum	(Al)	**24**	< 19	
Platinum	(Pt)	**< 0.003**	< 0.010	
Tungsten	(W)	**< 0.001**	< 0.015	
Tin	(Sn)	**0.38**	< 1.0	
Uranium	(U)	**0.26**	< 0.20	
Gold	(Au)	**0.082**	< 0.50	
Tellurium	(Te)	**< 0.05**	< 0.050	
Germanium	(Ge)	**0.029**	< 0.045	
Titanium	(Ti)	**0.70**	< 2.0	
Gadolinium	(Gd)	**< 0.001**	< 0.008	

SPECIMEN DATA

Comments: **insufficient sample to recheck results**

Date Collected: **10/26/2011**
Date Received: **12/1/2011**
Date Completed: **12/3/2011**

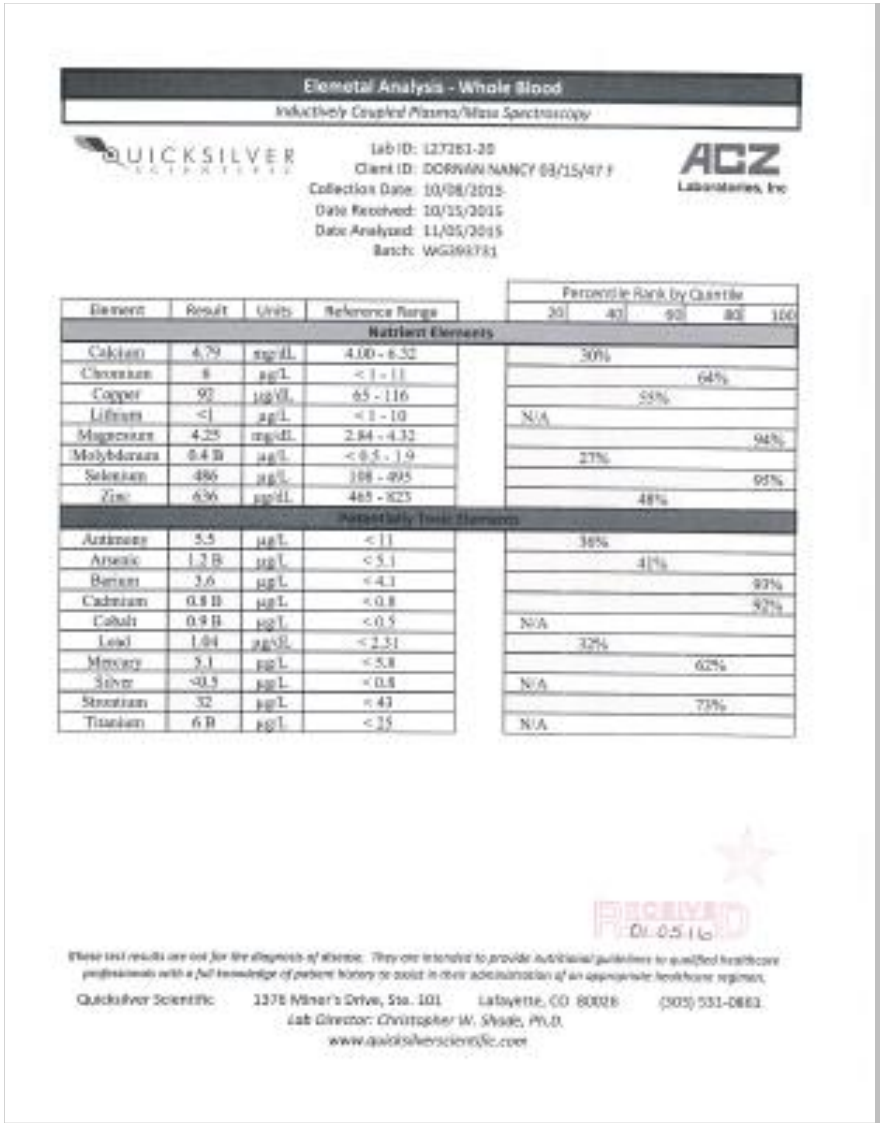
Method: **ICP-MS**
<dl: **less than detection limit**
µg/g = ppm

Sample Type: **Head**
Sample Size: **0.161 g**
Hair Color: **Brown**
Treatment:
Shampoo: **V05**

Metals are listed in descending priority order based upon data from the Agency for Toxic Substances and Disease Registry which considers not only the relative toxicity per gram metal, but also the frequency for occurrence of exposure.

0001643

Toxic Elements Exposure Profile



Elemetal Analysis - Whole Blood

Inductively Coupled Plasma/Mass Spectroscopy

QUICKSILVER SCIENTIFIC

Lab ID: L27281-20
Client ID: DORMAN NANCY 08/15/47 F
Collection Date: 10/08/2015
Date Received: 10/15/2015
Date Analyzed: 11/05/2015
Batch: WG893781

ACZ Laboratories, Inc

Element	Result	Units	Reference Range	Percentile Rank by Quintile (20 / 40 / 60 / 80 / 100)
Nutrient Elements				
Calcium	4.79	mg/dL	4.00 - 6.32	30%
Chromium	8	µg/L	< 1 - 11	64%
Copper	92	µg/dL	65 - 116	59%
Lithium	<1	µg/L	< 1 - 10	N/A
Magnesium	4.25	mg/dL	2.84 - 4.32	94%
Molybdenum	0.4 B	µg/L	< 0.5 - 1.9	27%
Selenium	486	µg/L	108 - 895	95%
Zinc	636	µg/dL	465 - 925	48%
Potentially Toxic Elements				
Antimony	5.5	µg/L	< 11	36%
Arsenic	1.2 B	µg/L	< 5.1	42%
Barium	3.6	µg/L	< 4.1	93%
Cadmium	0.8 B	µg/L	< 0.8	92%
Cobalt	0.9 B	µg/L	< 0.5	N/A
Lead	1.04	µg/dL	< 2.31	32%
Mercury	5.1	µg/L	< 5.8	62%
Silver	<0.5	µg/L	< 0.8	N/A
Strontium	32	µg/L	< 43	73%
Titanium	6 B	µg/L	< 25	N/A

RECEIVED
DEC 05 2015

These test results are not for the diagnosis of disease. They are intended to provide nutritional guidelines to qualified healthcare professionals with a full knowledge of patient history to assist in their administration of an appropriate healthcare regimen.

Quicksilver Scientific 1378 Miner's Drive, Ste. 101 Lafayette, CO 80026 (303) 531-0883
Lab Director: Christopher W. Shade, Ph.D.
www.quicksilverscientific.com

Toxic Metals Prof

GENOVA DIAGNOSTICS
www.gdx.net • 800.522.4762

Accession #:
Order #:
Reference #:
Patient:
Date of Birth:
Age:
Sex:
Reprinted:
Comment:

Date Collected:
Date Received:
Date of Report:

Telephone:
Fax:

Elements Nutrient & Toxic Metals

0026 Toxic Metals Profile - Whole Blood

Methodology: Inductively Coupled Plasma/Mass Spectrometry

		Results ppb		Quintile Ranking 1st 2nd 3rd 4th 5th	95% Reference Range
1.	Aluminum	29		45	<= 140
2.	Arsenic	40.0	H	5.1	<= 13.7
3.	Cadmium	0.95		0.60	<= 1.50
4.	Lead	14		18	<= 36
5.	Mercury	2.7		4.3	<= 13.8

Toxic metals are flagged high when the result is above the 95% Reference Range. Results for whole blood toxic elements that are within normal limits do not rule out metal accumulation in other tissues. This can be evaluated by urinary porphyrin or 24-hour urine chelation challenge tests.

Metals - J Toxicology 2011

Most effected organ - CNS (Arsenic, Lead, Mercury)

1. Neurological disease – Mercury, Lead, Aluminum
2. Most common health effect - Cancer (Arsenic, Lead, Cadmium)

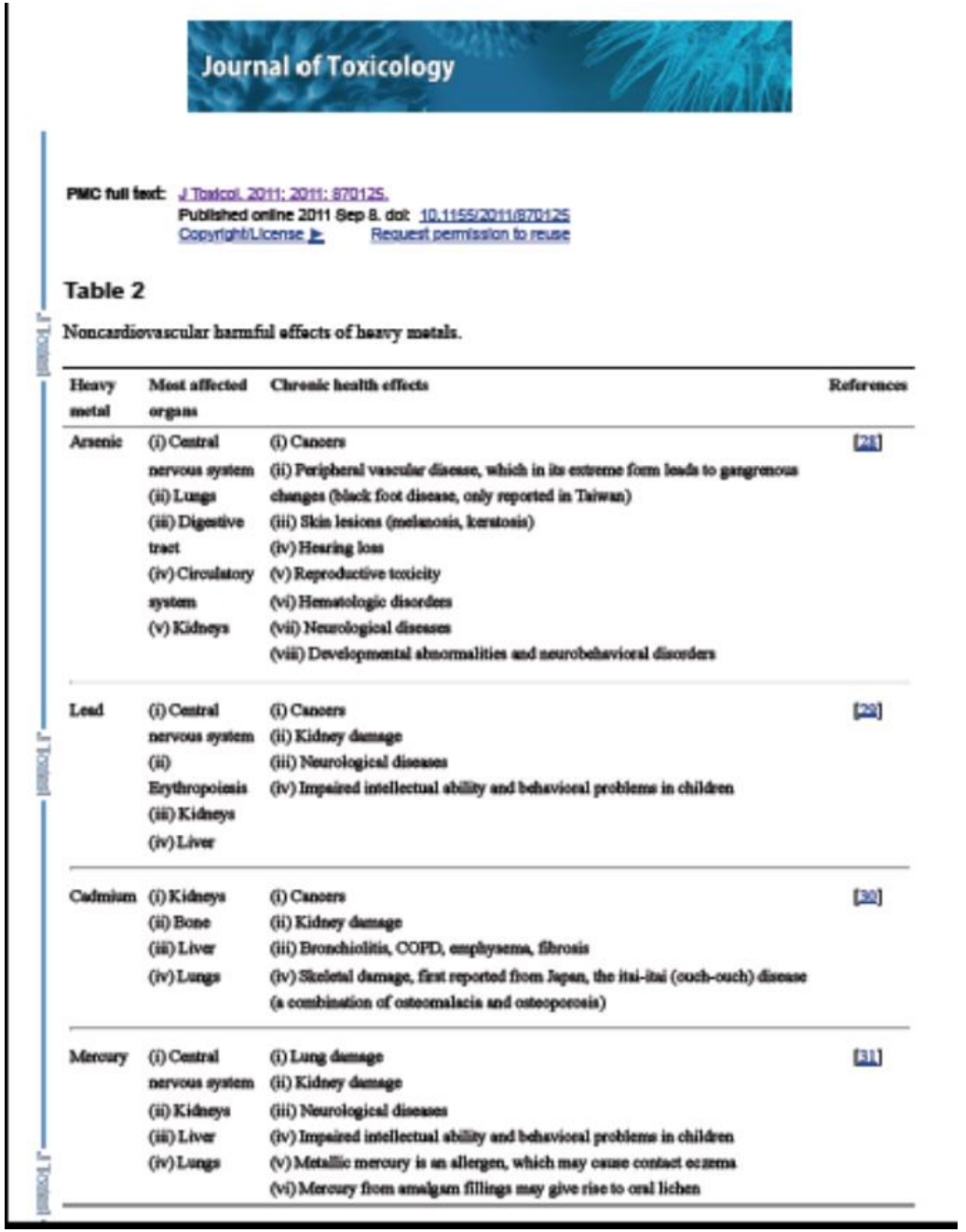
Metals - Most Affected Organs - Most Common Health Effects

J Toxicol. 2011; 2011: 870125.

Heavy metal

Most affected organs

Chronic health effects



Journal of Toxicology

PMC full text: J Toxicol. 2011; 2011: 870125.
Published online 2011 Sep 8. doi: 10.1155/2011/870125

Table 2

Noncardiovascular harmful effects of heavy metals.

Heavy metal	Most affected organs	Chronic health effects	References
Arsenic	(i) Central nervous system (ii) Lungs (iii) Digestive tract (iv) Circulatory system (v) Kidneys	(i) Cancers (ii) Peripheral vascular disease, which in its extreme form leads to gangrenous changes (black foot disease, only reported in Taiwan) (iii) Skin lesions (melanosis, keratosis) (iv) Hearing loss (v) Reproductive toxicity (vi) Hematologic disorders (vii) Neurological diseases (viii) Developmental abnormalities and neurobehavioral disorders	[28]
Lead	(i) Central nervous system (ii) Erythropoiesis (iii) Kidneys (iv) Liver	(i) Cancers (ii) Kidney damage (iii) Neurological diseases (iv) Impaired intellectual ability and behavioral problems in children	[29]
Cadmium	(i) Kidneys (ii) Bone (iii) Liver (iv) Lungs	(i) Cancers (ii) Kidney damage (iii) Bronchiolitis, COPD, emphysema, fibrosis (iv) Skeletal damage, first reported from Japan, the itai-itai (ouch-ouch) disease (a combination of osteomalacia and osteoporosis)	[30]
Mercury	(i) Central nervous system (ii) Kidneys (iii) Liver (iv) Lungs	(i) Lung damage (ii) Kidney damage (iii) Neurological diseases (iv) Impaired intellectual ability and behavioral problems in children (v) Metallic mercury is an allergen, which may cause contact eczema (vi) Mercury from amalgam fillings may give rise to oral lichen	[31]

Heavy Metals - Carcinogenic

The International Agency for Research on Cancer (IARC)

Classifies

Cadmium - known carcinogen

Inorganic lead - probable carcinogen

Methylmercury - possible carcinogen

Cobalt - possible

International Agency for Research on Cancer (IARC) Agents Classified by the IARC Monographs. 2012;1–106

Mercury

#3 on ATSDR 2011 Substance Priority List

Once mercury is absorbed / injected into the body:

W**ell distributed** through the body

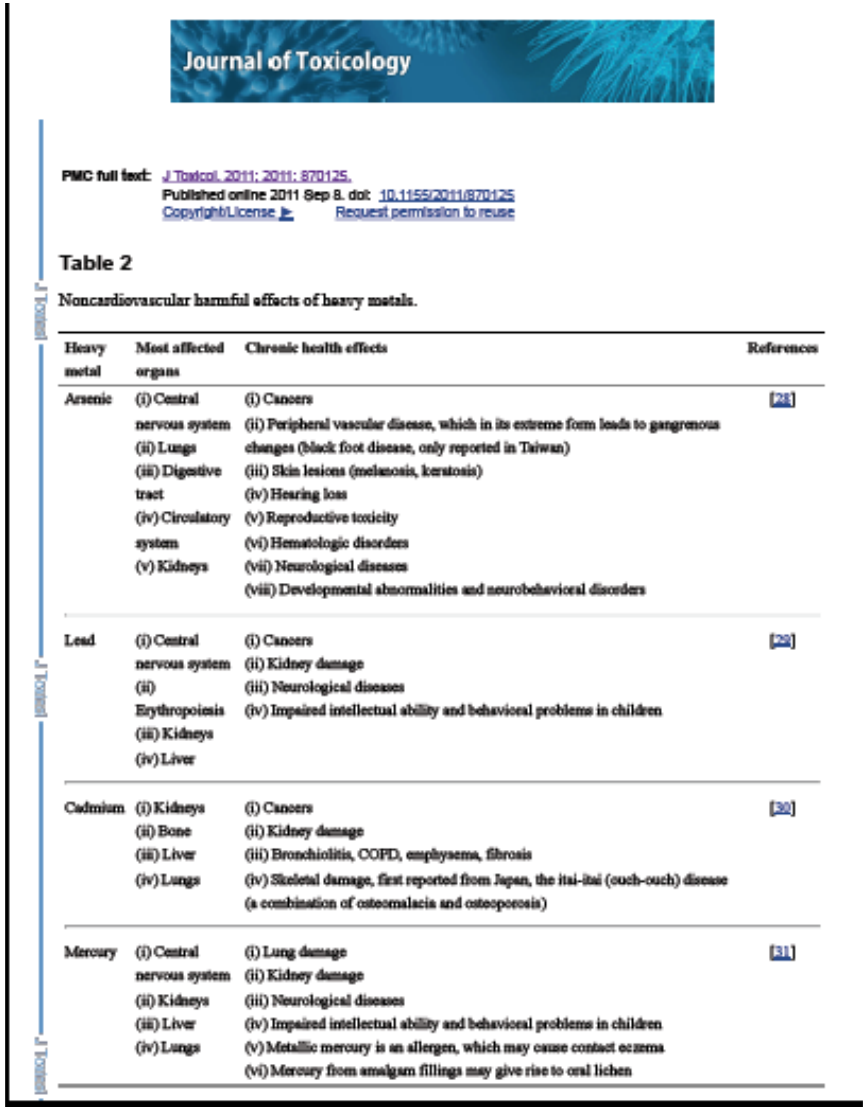
R**eacts with SH groups on molecules in all tissues**

or

** Potentially interfering with the function of any cellular sub cellular structure, protein, enzyme

** Mercury is primarily a **neurological poison**

Effects of Metals



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Mercury - International Awareness / Concern

13th International Conference on Mercury as a Global Pollutant

Providence, Rhode Island, USA

July 16-21, 2017

Mercury

The International Agency for Research on Cancer (IARC)

Classifies

Cadmium - known carcinogen

Inorganic lead - probable carcinogen

methylmercury - **possible carcinogen**

International Agency for Research on Cancer (IARC) *Agents Classified by the IARC Monographs*. 2012;1–106

Mercury

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Classifies

Cadmium - known carcinogen

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Methylmercury - possible carcinogen

International Agency for Research on Cancer (IARC) Agents Classified by the IARC Monographs. 2012;1–106

Mercury - Toxicity - Symptoms

Primary target organ is the brain and nervous system

Range of symptoms:

- Cognitive emotional
- Nerve function motor function

Mercury can effect any tissue and system of the body:

- Kidney Allergic
- Fatigue Endocrine
- Chronic infections Gastro-Intestinal

Unique symptoms:

- Burning sensations heaviness in muscles
- Electric shock sensations visual abnormalities

Mercury - Ancient Culture

Element of the ancients - power

Hg - Greek "hydrargyrum" - liquid silver

"Quicksilver" - reference to its mobility

Speed and mobility - Roman god, Mercury - messenger to all the other gods

Power - toxic

Mining - 1st mercury related human illness – tremors and cognitive

Public health disasters - Mercury

Minamata Bay, Japan (1956), Niigata, Japan (1960) and Iraq (1971)

Exposure to methyl mercury in Minamata Japan - 1956, 1960

Chemical factory - release of waste water with mercury 1950 - 1968 - accumulated in shellfish and fish

"Epidemic of the central nervous system"

Ataxia, paresthesias, muscle weakness, loss of peripheral vision, decreased hearing and speech

Paralysis, coma

Congenital

Mercury related neurological syndrome - Minamata Syndrome

2265 (2001 figure)

Deaths - 35% early on

Hair Hg

700 ppm - Minimato disease

200 ppm - non symptomatic

4 ppm - living outside of the area of exposure

Public health Disasters - Mercury

Iraq - Poison Grain - seeds treated with methymercury fungicide

neurological symptoms

> 650 deaths

> 6000 ill

1970 New Mexico

Family exposed to seed grain contaminated with mercury - fed to their family pigs - who became ill - butchered - fed to family

Children more effected

Youngest 2 children died after prolonged vegetative state

Older children - chronic neurological - visual defects

Mercury

Elemental Pure Liquid

Mercury - Public Health

200,000 and 400,000 children in the United States are born each year with

> Pre-natal exposure to methylmercury sufficient to put them at risk of neurologic impairment

1994 - United States Public Health Service declared that **mercury amalgam exposure was higher than their established minimal risk** level standard for the general population

100 million mercury fillings / year in the U.S.

1999 - U.S. Public Health Service and American Academy of Pediatrics recommendation.

1. Remove mercury in the vaccines administered in the U.S.
2. Recognition of mercury as a toxic agent

Mercury Symptoms / Health Effects

- Chronic fatigue depression anxiety
- Poor memory and cognitive function emotional instability
- Peripheral numbness or tingling
- Decreased senses of touch, hearing or vision
- Slurred speech
- Hypersensitivity and allergies
- Persistent / recurrent infections
- Chronic yeast / fungal overgrowth
- Compromised immune function
- Cardiovascular disease
- Dementia / tremor
- Headaches, joint pain, metallic taste in mouth

Mercury - Environment / Pollution

- Atmospheric exposures - outgassing from rock or through volcanic activity
- Human sources - coal burning and mining (mercury and gold), industrial waste in water
- Atmospheric elemental mercury - settles in water - converted by microorganisms into organic (methyl or ethyl)
- Ingested by smaller creatures which are eventually consumed by larger fish.
- Bio-accumulation - by larger fish - tuna, swordfish, or shark
- **Greatest source of mercury in biosphere - human origin**
- 1/3 emitted naturally
- **Global pollutant - arctic fish and whales have high mercury**

Mercury - Exposure

Most human exposure to mercury is caused by

1) Outgassing of mercury from dental amalgam
2) Ingestion of contaminated fish
3) Occupational exposure

World Health Organization, "Inorganic mercury: environ- mental health criteria 118," in International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, **1991**

Additional significant exposure:

Vaccines past - childhood vaccines

Current - flu vaccines - 160 million (2016-2017)

Mercury - Exposure

EPA (1995) - safe daily mercury intake level = 0.1 ug / kg BW

Intake amounts that can be consumed every day over the course of an entire lifetime without significant risk of harm

150 pounds (68 kilograms) - 7 micrograms of daily mercury

5 - 10 ug daily

Low mercury fish - Pacific salmon 1 ug / oz - 4 - 8 oz

Higher mercury - canned Atlantic albacore tuna 13 ug/ oz 2 - 4 oz 10x

Mercury - Exposure

EPA (1995) - safe daily mercury intake level = 0.1 ug / kg BW = **5-10 ug / day**

Vaccines **25 ug** (multi-dose flu and meningococcal) 15# / 7 kg = 0.7 ug = **35x**

Amalgams **15 ug per amalgam** per day / 4 amalgams = 60 ug daily **(6 - 12 x)**

Mercury - Exposure

Occupational:

- Battery manufacturing ink manufacturing chlor-alkali processing
- Fish canning mining electrical component manufacturing
- Fluorescent lighting bronzing photo engraving

Home location - Living near fertilizer, paint, or chlor-alkali manufacturing plants

Medications:

- Nasal sprays and decongestants antibiotic eye solutions
- Skin lightening creams waterproof mascara
- Hemorrhoidal ointments

Home care products: Fungicides, pesticides, drain cleaners

Mercury Exposure: Amalgams - WHO

Most human metallic mercury exposure comes from mercury vapor outgassing from amalgam fillings

At a rate of 2 to 28 micrograms per facet surface per day, of which about 80% is absorbed - World Health Organization and Berglund et al.

15 mcg / amalgam per day - mercury vapor / 80% absorbed

M. Richardson, The Safety of Dental Amalgam, ISBN 0-662- 24873-2, Minister of Health, Canada, 1996.

A. Berglund, L. Pohl, S. Olsson, and M. Bergman, "Determination of the rate of release of intra-oral mercury vapor from amalgam," Journal of Dental Research, vol. 67, no. 9, pp. 1235–1242, 1988.

Mercury - Exposure

Amalgams are NOT stabile in the mouth

Release mercury vapor - widely distributed - accumulates - toxic effects

Amalgams

- 300 tons of mercury in U.S.
- Dental office # 2 user

Removal - disposal - environmental contamination – **mercury does not biodegrade** - water soluble

Intake by animals and fish - converted to **methyl mercury - fat soluble - stored / accumulates**

FDA advisory: 2010

Amalgams should not be used in vulnerable populations

Amalgam risk should be disclosed to consumers and parents

Mercury Exposure – Lakes

50,000 U.S. lakes - warnings regarding eating fish

(20% of U.S. lakes)

(50% of Florida lakes)

3000 lakes are closed due to mercury contamination

Biological toxin

- Primarily a neurotoxin
- Susceptible populations:
- Children fetus kidney disease

Mercury exposure - Reality, history, legal

Dupont chemical company - $50 M settlement with state of Virginia to clean up mercury pollution

Rayon production factory - leaked mercury into the South River - 1929 to 1950

Mercury - tested / discovered in 1970s

High levels of mercury remain 60 years after exposure

U.S. National Academy of Science

(NAS) / Institute of Medicine (IOM)

Position paper - October 2006 - risks and benefits of fish consumption (Om 3 and mercury)

3 general recommendations:

- Children, pregnancy - limit fish to 2x weekly
- Restrict total weekly consumption
- Select fish that are lower in mercury

Mercury - Exists in three forms

Elemental / metallic and vaporized mercury –
thermometers and vapor out-gasing from amalgams

Inorganic mercury compounds - amalgams

Organic mercury - fish (methyl), vaccines (ethyl - thimerosal)

Mercury - Elemental and Gasous Vapor

Pure - uncombined form - not a natural state - not found significantly in nature

Silver liquid metal (Quicksilver) at room temperature - thermometer

Poorly absorbed through skin and GI tract

Vapor form - **highly absorbed — 80%** - through mucous membranes of mouth

Distributed widely in body

Primary target - CNS

Binds tightly to SH groups

Accumulates throughout life

Half-life of mercury in the brain -

estimated to be as long as **approximately 20 years**

Mercury - Inorganic

Inorganic - combining with elements other than Carbon

Mercury ions - found in salts - HgS, HgO, $HgCl_2$

Commonly found - white powders / red - $HgCl_2$ - turns black after exposure to light

More toxic - more reactive - more difficult to eliminate - accumulates

Used in amalgams - to capture gold / to harden

Chewing releases mercury as a vapor

More water soluble / do not readily cross BBB or BPB

Less absorption - 10%

Tends to effect GI tract

Greatest concentration - kidney = major target organ for inorganic

excreted in urine and feces

Mercury - Organic

- Mercury combined with carbon - methlymercury, dimethylmercury, phenyl mercury
- Dietary - methylmercury (fish, seafood)
- Relatively well absorbed - gastrointestinal tract
- Distributed to all tissues
- In the body - methylmercury - mainly bound to the sulfur atom
- In brain, liver, kidney - organic Hg converted to inorganic Hg - stored as divalent mercury cation - reactive
- LOW excretion / Accumulation is significant and life long
- Biliary / fecal elimination - inorganic mercury
- Reviews of Environmental Contamination and Toxicology, 2009
- S. Díez, "Human health effects of methylmercury exposure,"

Elemental and Vaporized Mercury

Massive acute exposure - mercury vapor

Erosive bronchitis and bronchiolitis

Respiratory failure

Tremor

Erethism (mad hatter disease) - severe behavior and personality changes, emotional excitability, loss of memory, insomnia, depression, fatigue, and in severe cases delirium and hallucination

Mercury Vapor - Mad Hatter Disease

Occupational disease among hatmakers - causes by chronic mercury poisoning

Felting exposured to **mercury vapors from dyes**

Neurotoxic effects - tremor and pathological shyness and irritability

" Danbury shakes" - haymaking industry in Danbury, CT

Elemental and Vaporized Mercury

- Chronic exposure - **Neurological dysfunction**
- Mood swings, nervousness, irritability, and other emotional changes
- Insomnia
- Headache
- Abnormal sensations
- Muscle twitching
- Tremors
- Weakness
- Muscle atrophy
- Decreased cognitive function
- High exposures - kidney malfunction, respiratory failure, and death

Inorganic Mercury Salts Poisoning Symptoms

ACUTE:

Oral mercury salts - **greater acute health effects**

Mercury salts are more corrosive than elemental mercury

Acute high dose exposure of mercuric salts

- Burning chest pain
- Darkened discoloration of the oral mucous membrane
- Severe gastrointestinal symptoms (corrosive damage)
- Stomatitis
- Impaired kidney function.
- 1 to 4 g of mercuric chloride is fatal in adults

Skin - dermatitis

Metal fume fever - acute phase of mercury vapor exposure

fever	chills
headache	abdominal cramping
dyspnea	dysuria
ejaculatory pain	dizziness

Inorganic Mercury Salts Poisoning Symptoms

Chronic:

Inorganic mercury poisoning

Target organ - kidney

Clinical - polyuria, proteinuria, edema, BP

Erethism - excessive sensitivity and reaction

Constellation of irritability, excitability, anxiety, insomnia, and social withdrawal

Chronic inorganic mercury toxicity

Classic Mercury Triad - chronic toxicity - tremors, gingivitis, and erethism

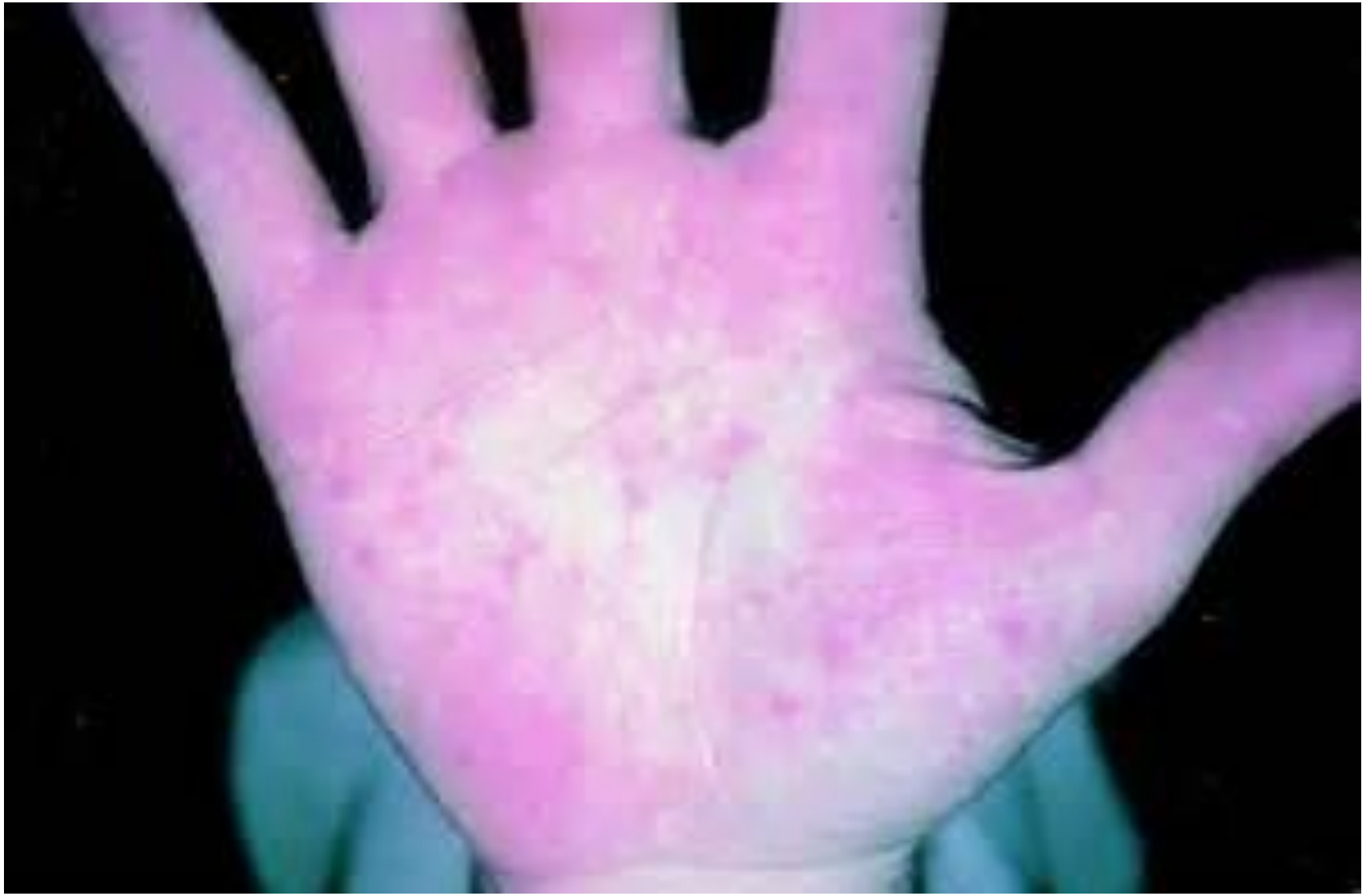
Additional - headache, visual disturbance (eg, tunnel vision), peripheral neuropathy, salivation, insomnia, and ataxia

Inorganic Mercury SALTS Poisoning Symptoms

- Acrodynia - pink disease - mercury toxicity and allergy in children
- Children - teething powders containing mercury compound (i.e., calomel)
    - Sweating
    - Erythematous rash of the palms and soles
    - Painful sensitivity to touch
    - Anorexia
    - Fatigue
    - Irritability
    - Photophobia
- Type of hypersensitivity reaction
- Caused by the deposit of mercuric chloride in the tissues
- Exposure to elemental mercury vapor can produce pink disease in children - paint and lacquer

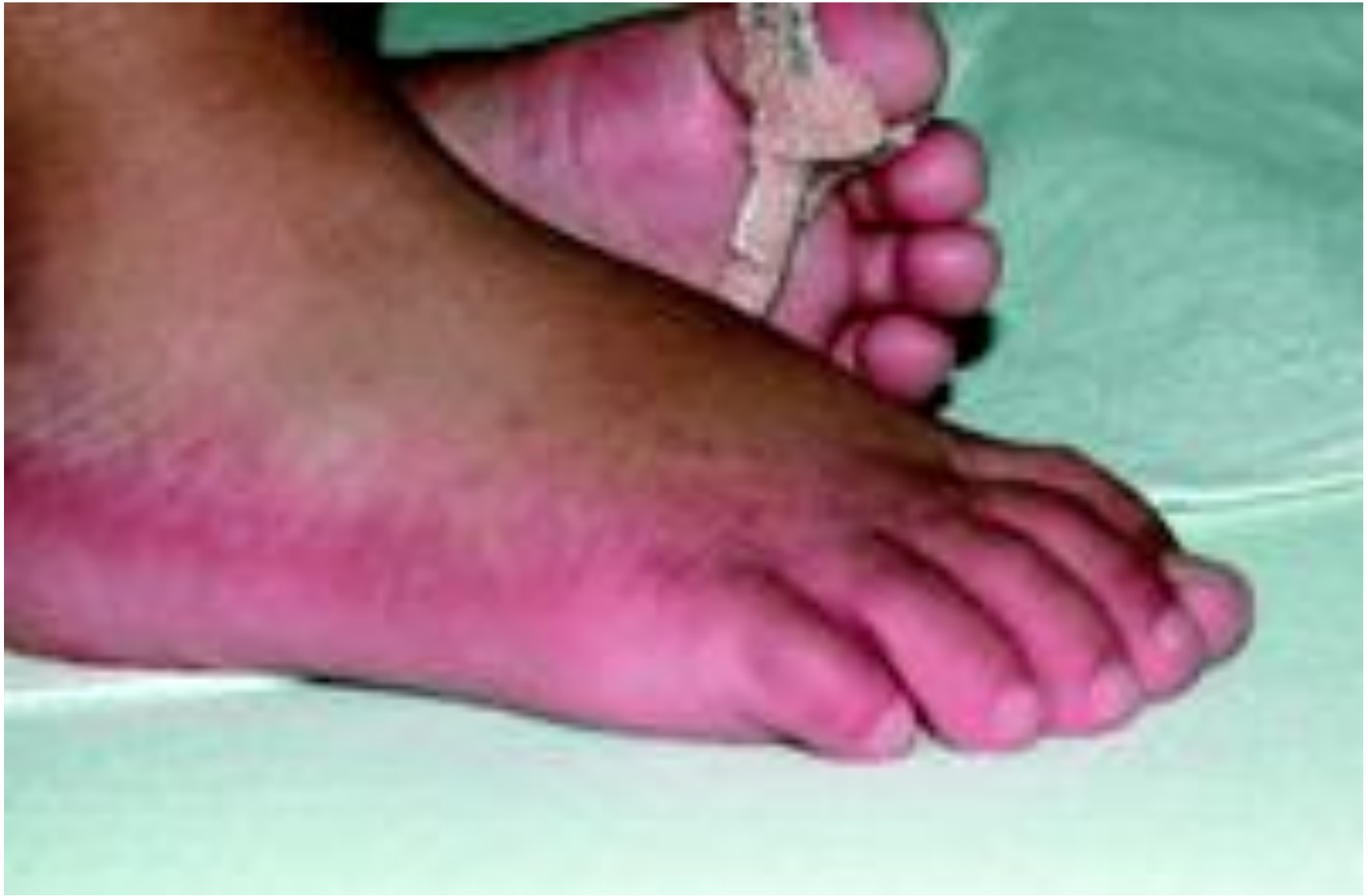
Mercury Poisioning

Pink Disease



Mercury Poisioning

Pink Disease



Organic Mercury Poisoning Symptoms

- Methylmercury - from ingestion of fish
- Ethyl mercury from vaccines
- Causes neurological dysfunction
- **Impaired neurological development - fetal / children**

ANY neurological symptom:

- Peripheral vision impairment
- Stinging or needle-like sensations in the extremities and mouth
- Loss of coordination
- Muscle weakness
- Impairments of speech and hearing
- Developmental delay
- Burning and electric shock

University of Calgary, Canada - Dr. Murray Vimy

Sheep and monkey studies

Radioactively labeled mercury released from correctly placed amalgam fillings

Appears quickly in the kidneys, brain and wall of the intestines

Hahn LJ, Kloiber R, Leininzer RW, Vimy MJ, Lorscheider FI; Whole-body imagine of the distribution of mercury released from dental fillings into monkey tissues. FASEB J 4:3256-3260. 1990.

Eggleston DW, Nylander M; Correlation of dental amalgam with mercury in the brain. J Prost Dent. 58:704-707. 1987.

Mercury - Toxicity

Mercury IM - within 24 hours - mercury is found in the spinal cord and brain

As well as other tissues - kidneys, lungs, connective tissue, and endocrine glands

Mercury does not appear to have a "half-life" in the central nervous system

Mercury - accumulates in nervous system

Pink Ladies: Mercury poisoning in twin girls

CMAJ 2003 Jan 21; 168(2): 201.

20-month-old twin girls presented with

Weakness, anorexia, papular rash, increasingly swollen, red and painful hands and feet * 1 month's duration.

Irritable and unwell and were diaphoretic

Tachycardia, one had an elevated blood pressure of 130/90 mm Hg

Reduced muscle power and diminished reflexes.

Palms and soles were erythematous and indurated

"Teething powder" from India once or twice a week over the 4 preceding months.

Blood mercury levels were 176 and 209 (normally < 18) µmol/L.

Teething powder still used in other parts of the world (Southeast Asia)

Calomel - alternative medicine products

Mercury - Related health conditions

High mercury content in hair was associated with an **increased progression of atherosclerosis and risk of CVD**

Atherosclerosis, vol. 148, no. 2, pp. 265–273, 2000.

"Mercury accumulation and accelerated progression of carotid atherosclerosis: a population-based prospective 4-year follow-up study in men in eastern Finland,"

Adverse effects on CVD have been observed at methylmercury levels much lower than those associated with neurotoxicity.

In vivo and in vitro studies: Mercury exposure promotes atherosclerosis

B. O. Lund, D. M. Miller, and J. S. Woods, "Studies on Hg(II)-induced H2O2 formation and oxidative stress in vivo and in vitro in rat kidney mitochondria," Biochemical Pharmacology, vol. 45, no. 10, pp. 2017–2024, 1993.

Y. L. Huang, S. L. Cheng, and T. H. Lin, "Lipid peroxidation in rats administrated with mercuric chloride," Biological Trace Element Research, vol. 52, no. 2, pp. 193–206, 1996.

Mercury - Related Health Conditions

Kuopio Ischemic Heart Disease Risk Factor (KIHD) study

Circulation, 1995

"Intake of mercury from fish, lipid peroxidation, and the risk of myocardial infarction and coronary, cardiovascular, and any death in Eastern Finnish men,"

Studies have correlated higher fish intake with lower CHD mortality

Men in Eastern Finland who ate fish had high CHD mortality

Concern was high content of mercury in fish of Eastern Finland

1833 men

No PMHx of CHD, stroke, claudication, and cancer

Dietary intake of fish and mercury

Hair and Urinary mercury

73 AMI

Highest levels of mercury in hair - 2x increase in AMI / 3x increase in cardiovascular death

Correlation - 24-hour urinary mercury excretion and the risk of AMI

Hair and urinary mercury associated significantly with titers **of immune complexes containing oxidized LDL.**

Increased risk may be due to the promotion of lipid peroxidation by mercury

Mercury - Related Health Conditions

Circulation, vol. 102, 2000.

Kuopio Ischaemic Heart Disease Risk Factor Study,"

"Fish oil-derived fatty acids, DHA, DPA, EPA and the risk of acute coronary events

Purpose: investigate the association between the serum om-3 fatty acids DHA, DPA, and EPA and the risk of acute coronary events in middle-aged men.

1871 men

Highest om-3 levels 44% less risk of AMI compared to lowest om-3 levels

Highest om-3 level and low hair Hg 67% less risk of AMI compared to lowest om-3 / high hair Hg

DHA+DPA were the protective oils

Conclusions: fish oil–derived fatty acids reduce the risk of acute coronary events

High mercury could reduce this protective effect

Mercury - Related Health Conditions

European Multicenter Case-Control Study on Antioxidants, Myocardial Infarction, and Cancer of the Breast

(EURAMIC) study

The New England Journal of Medicine, vol. 347, 2002

"Mercury, fish oils, and the risk of myocardial infarction,"

High mercury content may diminish the beneficial effects of fish consumption on cardiovascular health

Health Professionals Follow-up Study (HPFS)

Increased cardiovascular risk following mercury exposure among dentists

Mercury –

Toxicity - Mechanism of Action

- Methyl mercury reacts with **sulfhydryl groups** throughout the body
- **Potentially interfering with the function of any cellular or subcellular structure**
- Interfere with DNA transcription and protein synthesis
- - Destruction of endoplasmic reticulum and disappearance of ribosomes
- Cell membrane integrity
- Reduction in Natural Killer cell activity
- imbalance in Th2:Th1 ratios favoring autoimmunity
- Disruption of DNA repair

Mercury - Toxicity - Mechanism of Action

Induces oxidative stress

Depletes sulfhydryl - effects detoxification and antioxidant systems

Alters mitochondrial function

Induces apoptosis

Excessive immune activation

Imbalance in redox :

Increased reactive oxygen species generation

Reduced antioxidants defense capacity

Annual Review of Pharmacology, vol. 12, pp. 375–406, 1972

"The pharmacology of mercury compounds,"

Life Sciences, vol. 32, no. 13, pp. 1507–1514, 1983

"Stimulation of lipid peroxidation by methyl mercury in rats,"

Toxicology, vol. 124, no. 3, pp. 211–224, 1997

"Mercuric compounds inhibit human monocyte function by inducing apoptosis: evidence for formation of reactive oxygen species, development of mitochondrial membrane permeability transition and loss of reductive reserve,"

Biochemical Pharmacology, vol. 45, 1993

"Studies on Hg(II)-induced H_2O_2 formation and oxidative stress in vivo and in vitro in rat kidney mitochondria,"

Mercury - Toxicity - Mechanism of Action

Inhibit anti-oxidant systems

Strong binding for GSH - lowering and depleting levels

Inhibits the activities of two key enzymes involved in GSH metabolism: GSH synthetase and GSH reductase.14

Zalups RK, Lash LH. Interactions between glutathione and mercury in the kidney, liver and blood. In: Chang LW, ed. Toxicology of Metals. Boca Raton: CRC Press; 1996:145- 163.

Inhibits enzymes catalase, superoxide dismutase, and GSH peroxidase.

Altered mitochondrial function

Mercury alters the structural integrity of the mitochondrial inner membrane / loss of normal cation selectivity

"Studies on Hg(II)-induced H_2O_2 formation and oxidative stress in vivo and in vitro in rat kidney mitochondria,"

Biochemical Pharmacology, 1993.

Mercury - Toxicity - Mechanism of Action

- Inhibiting the activation of NF-κB (through SH binding)
  - Promote lipid peroxidation
  - Suppress NO production - inactivating the expression of iNOS gene

- Methyl mercury reacts with sulfhydryl groups throughout the body potentially interfering with the function of any cellular or subcellular structure.

Mercury - Toxicity - Mechanism of Action

Binding to Selenium - depletion

Mercury - high affinity for selenium - forms insoluble mercury selenide complexes

Reduce the bioavailability of selenium

Impair the activity of glutathione peroxidase

Promoting lipid peroxidation - atherosclerosis

"Mercury: selenium interactions and health implications," Seychelles Medical and Dental Journal, vol. 7, 2004

** selenium - potential protector against methylmercury toxicity in populations consuming seafood

Selenium: relation to decreased toxicity of methylmercury added to diets containing tuna," Science, vol. 175,1972

Mercury - Toxicity - Mechanism of Action

Displaces Minerals:

g and Cd displace Zn and Cu from metallothiene

- can cause functional deficiency of these minerals

Mercury - Toxicity - Additional

Auto-immune

Hypothyroidism

Hypoglycemia

Fibromyalgia

Immune suppression - chronic infections

Induces antibiotic resistance in bacteria,

Mercury

1. Distributed throughout the body
2. Reacts with sulfhydryl groups throughout the body,

Potentially interfering with the function of any cellular or subcellular structure

Mercury - Resources

TOXICOLOGICAL PROFILE FOR MERCURY

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Agency for Toxic Substances and Disease Registry

March 1999

Human Health Effects of Methylmercury Exposure

Reviews of Environmental Contamination and Toxicology - 2009

LEAD

2 on ATSDR 2015 Substance Priority List

EPA "probable human carcinogen"

1. Arsenic
2. Lead
3. Mercury
4. Cadmium

Agency for Toxic Substances and Disease Registry Priority List of Hazardous Substances - HHS

2015 RANK	SUBSTANCE NAME	TOTAL POINTS	2013 RANK	CAS RN
1	ARSENIC	1671.6	1	007440-38-2
2	LEAD	1529.4	2	007439-92-1
3	MERCURY	1458.6	3	007439-97-6
4	VINYL CHLORIDE	1358.9	4	000075-01-4
5	POLYCHLORINATED BIPHENYLS	1345.1	5	001336-36-3
6	BENZENE	1327.6	6	000071-43-2
7	CADMIUM	1318.8	7	007440-43-9
8	BENZO(A)PYRENE	1304.4	8	000050-32-8
9	POLYCYCLIC AROMATIC HYDROCARBONS	1279.1	9	130498-29-2
10	BENZO(B)FLUORANTHENE	1249.7	10	000205-99-2

LEAD

NOT essential or needed for normal human metabolism

- Serves NO useful purpose in the human
- Can affect every organ system
- Mechanisms for toxicity

    Inhibit or mimic the actions of calcium
    Interact / disrupt with proteins (sulfhydryl, amine, phosphate and carboxyl groups)

Nervous system - most sensitive target

No lower threshold for some of the adverse neurological effects of lead in children

Neurological effects in children - documented at exposure levels once thought to cause no harmful effects (<10 µg/dL)

No safe level

Increased susceptibility based mineral / nutrient levels, genetics, environmental exposure(Chemical, Vaccine)

LEAD

Primary Organ Sites for Noticeable Toxic Effects

Neurological / Kidney / Bone

Wide range of neurological effects - some irreversible

#1 Storage Tissue Site for Lead

Bone

Lead

2 forms - organic and inorganic

Inorganic lead - old paint, soil - more common exposure

Organic Lead - lead based gasoline / occupational / industrial uses)

- more toxic - more readily absorbed

Lead Exposure

Most lead exposure is inorganic - lead in old paint / soil / pipes

Public health concern - **children - more sensitive and greater long term impact on health**

Landrigan (2002) estimate - U.S. incurs **$43.4 billion** annually in **the costs of all pediatric environmental disease**

- Childhood lead poisoning accounting for the vast majority
- Medical costs, disability, education and parental lost work time.

The most widespread source of lead for U.S. children - lead paint that remains in older building and homes

Children - increased significant risk of lead poisoning

- Due to their **hand to mouth activity** - house dust and soil
- Due **to higher oral absorption and neurological distribution** duet to incomplete BBB
- Due to physiology and **greater impact on developing neurological tissue**

Lead - Exposure

Banned from consumer use paint and as an gasoline additive in the U.S. - 1970s

Released into the home environment by peeling, chipping, chalking, friction, or impact, home renovation

85% of all homes built before 1978 in the U.S. have lead-based paint in them (CDC 1997a)

Lead may be tracked into homes in significant quantities from **exterior soil** - contaminated by historical use of lead in paint, gasoline, or industries.

Concentrations in soil, air, and water can be especially high near historic or ongoing mining operations or smelters

Soil concentrations can be high on farms lands with past use of leaded gasoline and in yards of older homes

Occurs in drinking water through leaching from lead-containing pipes, faucets

Lead - Exposure

Industrial and commercial products

- Bright red and yellow paints on bread bags and candy may contain lead (ATSDR 2005; Mushak et al. 1989 as cited in AAP 1993).

- Imported cans may still contain lead

Food or beverages may be stored in lead-containing vessels

- “Safe" pottery and ceramic-ware can become harmful if the protective glaze wears off and exposes people to lead-containing pigments.

- Lead-glazed pottery - imported

Lead - Exposure

- Major exposure - industrial : inhalation and ingestion of lead-bearing dust and fumes
- Smelting, refining, and manufacturing industries experience the highest and most prolonged occupational exposures
- Increased risk for occupational lead:
  - Battery manufacturing plants construction workers - renovation/rehabilitation
  - Rubber products and plastics industries soldering
  - Steel welding/cutting operations bridge maintenance and repair workers
  - Municipal waste incinerator workers
  - Radiator repair mechanics pottery/ceramics industry employees

Lead - Exposure

Exposure - Common - Ubiquitous

Lead exposure is a **global issue** - Lead mining and lead smelting in many countries - children and adults

Inhalation, ingestion > dermal contact.

-Inhalation - workers in lead- related occupations - >90 absorption

-Ingestion - Lead exposure in the general population (including children) - > 50% absorption

Lead - Exposure

Lead paint is the major source of lead exposure for children

Lead paint deteriorates or pulverizes due to friction (e.g., in windowsills, steps and doors)

House dust and surrounding soil may become contaminated

Enters the body through normal hand-to-mouth activity.

(Sayre et al. 1974 as cited in AAP 1993)

Children are still at significant risk of lead poisoning

-Due to their hand to mouth activity - house dust and soil
-Due to higher oral absorption and greater neurological distribution (incomplete BBB)
-Due to greater sensitivity of developing neurological tissue

Children who live in older housing are more likely to have elevated BLLs

Lead - Exposure

Most adult exposures are occupational

Between **0.5 and 1.5 million workers** are exposed to lead in the workplace (ATSDR, 1999)

Lead dust can be transferred to homes

Lead - Exposure

Additional exposure:

Home renovation

Lead related hobbies and activities:

- Car repair
- Electronics soldering
- Glass or metal soldering
- Glazed pottery making
- Stained-glass making
- Target shooting
- Molding of bullets, slugs, or fishing sinkers
- Cosmetics - Imported

Supplements - Herbal (China, India)

Artificial turf

Toys and toy jewelry

Tattoos, hair dyes

Lead - Exposure

Blood Lead Levels

Toxic effects of lead - Neurological have been observed at low lead levels

NO SAFE level

2012 - CDC 5 µg/dL upper reference range value for BLLs in children

Advisory level **for environmental and educational intervention**

2015 - NIOSH <5 µg/dL the reference blood lead level for adults

National Institute for Occupational Safety and Health (NIOSH) –

Conducts research and making recommendations to HHS

For prevention of work-related injury and illness

Under HHS / CDC

Sister agency for enforcement is OSHA

Lead – Exposure

Contaminated Food

Main sources of lead contamination of food:

- Soil
- Industrial pollution
- Agricultural technology
- Food processing

Sources - account for most cases of lead exposure:

- Gasoline additives
- Food-can soldering
- Lead-based paints
- Ceramic glazes
- Lead pipe water systems
- Folk remedies

M. Markowitz, "Lead poisoning," Pediatrics in Review, vol. 21, no. 10, pp. 327–335, 2000.

LEAD – Exposure

Blood Lead Levels

Decreasing Blood Lead Levels (BLL) in U.S.

Average BLL - adults 18-74 years of age - (CDC 1997b)

1976-70 14.2 µg/dL from

1988-1991 3.0 µg/dL

Overall prevalence of elevated BLLs (> 10 µg/dL) - U.S. population - 0.7%. = 3 million (CDC 2005)

WHO-OSHA safe BLL in workers < 40 µg/dL

No safe level of lead exposure has yet been defined - by studies

Lead – Toxicity

Kidney

Lead exposure can lead to kidney dysfunction / conditions

Fanconi-like syndromes - impaired absorption at proximal renal tubule

- bicarbonate - renal acidosis
- phosphorous - bone disorders - osteomalacia, Ricket's

Chronic nephropathy

Gout

Most lead-associated renal effects or disease are a result of

- Ongoing chronic exposure
- Latent effect of chronic past lead exposure

Lead - Exposure / Storage in Tissues

95 % Body Burden - Bones and teeth - adults (children 75%)

Accumulates in the most metabolically active bone

Trabecular bone (inward, spongy) and growth plates during childhood

Cortical (outer hardened) and trabecular bone in adulthood

Two physiological STORAGE compartments exist for lead

- Relatively inactive bone can store lead for decades
- More active bone component readily exchanges bone lead with the blood

Bone-to-blood lead mobilization:

- Pregnancy lactation menopause physiologic stress
- Chronic disease hyperthyroidism kidney disease broken bones advanced age
- Vit D / Calcium deficiency

Lead – Nervous System

The nervous system = Most sensitive target of lead exposure

Neurological effects of lead in children have been documented at exposure levels once thought to cause no harmful effects (<10 µg/dL)

Otherwise asymptomatic individuals may experience neurological effects from lead exposure

Contribute significantly to socio-behavioral problems such as juvenile delinquency and violent crime (Needleman 2002, Nevino

Correlation between of higher BLL

The lower IQ

Higher hyperactivity / attention

Hearing impairment

Lead – Toxicity in Adults

Adults generally require higher exposure to be effected

Neuro-Cognitive -Psychiatric symptoms - lead-exposed workers - BLLs ranging from 40 to 120 µg/dL

Decreased libido
Diminished cognitive performance
Diminished reaction time
Dizziness
Fatigue
Impaired concentration
Increased nervousness
Lethargy
Paresthesia
Weakness
Peripheral nerve dysfunction
Depression/mood changes, headache
Diminished hand dexterity
Diminished visual motor performance
Dullness
Forgetfulness
Impotence
Irritability
Malaise
Reduced IQ scores
Postural balance

Slowed nerve conduction and forearm extensor weakness (wrist drop)

Lead - Toxicity

Bone Marrow

Inhibition of hemoglobin production

>50 µg/dL for occupationally exposed adults

>25 µg/dL for children

2 types of anemia - Basophilic stippling of the RBC

Acute high-level lead exposure - Hemolytic anemia

Chronic lead exposure - Frank anemia

Hypochromic
Normo- or microcytic
Reticulocytosis

Basophilic stippling of RBC - 1899 - Classic laboratory sign

Aggregations of ribosomes - Only found in RBCs

Lead Toxicity- Anemia

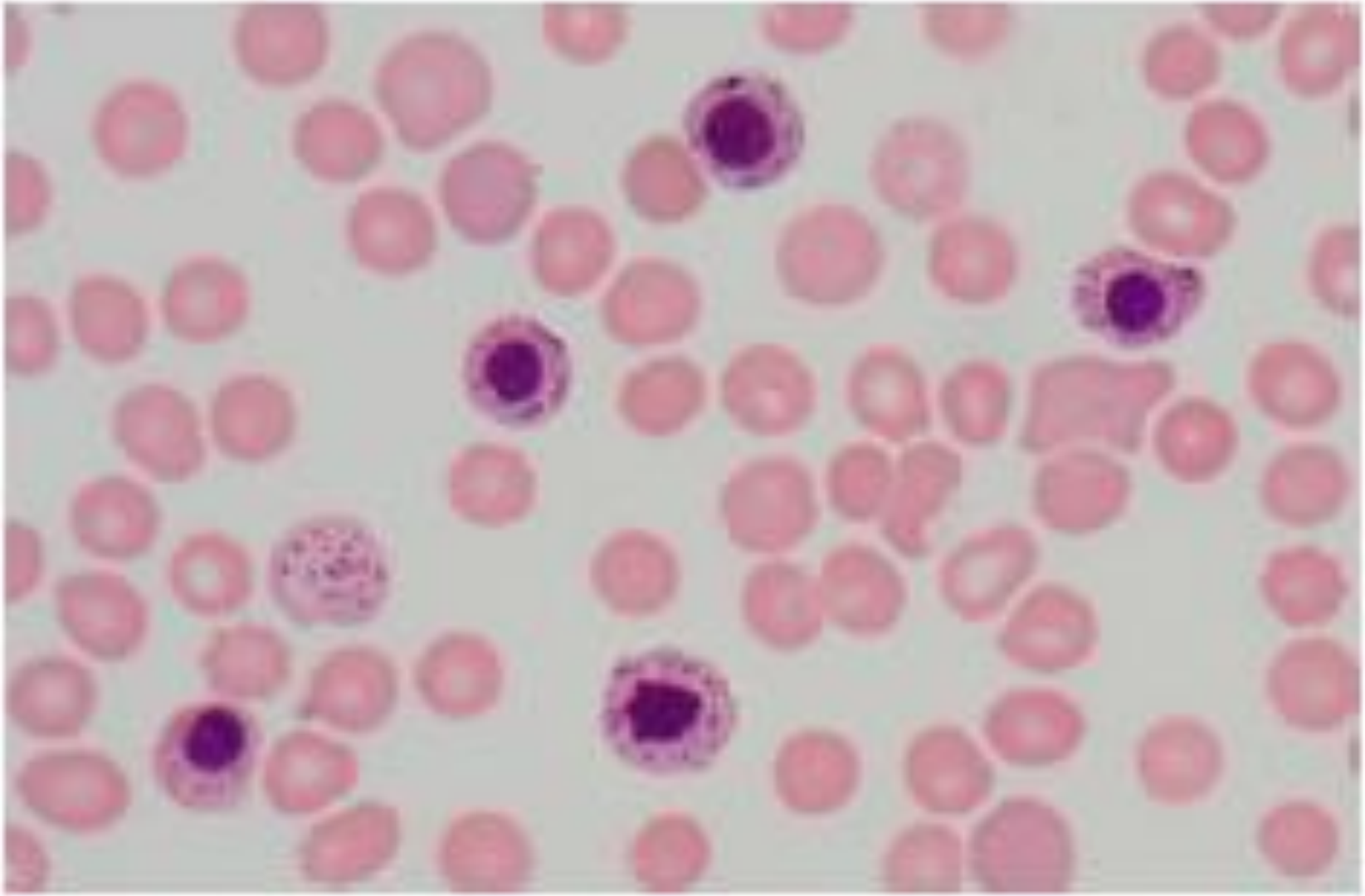
Basophilic strippling os RBC

1899

Classic Laboratory sign

Aggregations of ribosomes – only found in RBC's

Lead and Arsenic Metal Toxicity



Lead Toxicity - Anemia

Basophilic stippling of RBC

1899

Classic laboratory sign

Aggregations of ribosomes - only found in RBCs

Lead and Arsenic metal toxicity

Lead – Vascular / Hypertension

BLLs > 30

Hypertension

Hypertensive Heart Disease

Cerebrovascular Disease

A. Bhatnagar, "Environmental cardiology: studying mechanistic links between pollution and heart disease," Circulation Research, vol. 99, no. 7, pp. 692–705, 2006

J. A. Staessen, C. J. Bulpitt, R. Fagard et al., "Hypertension caused by low-level lead exposure: myth or fact?" Journal of Cardiovascular Risk, vol. 1, no. 1, pp. 87–97, 1994

T. S. Nawrot, L. Thijs, E. M. Den Hond, H. A. Roels, and J. A. Staessen, "An epidemiological re-appraisal of the association between blood pressure and blood lead: a meta-analysis," Journal of Human Hypertension, vol. 16, no. 2, pp. 123–131, 2002.

Arch Intern Med. 2005 Oct 10;165(18):2155-61.

Continued decline in blood lead levels among adults in the United States: the National Health and Nutrition Examination Surveys

2 Nationally representative cross-sectional surveys

Third National Health and Nutrition Examination Survey

1988-1994 (n = 16,609)

1999-2002 (n = 9961)

1. Declining BLLs

2. Higher blood lead levels - associated - hypertension among non-Hispanic blacks and Mexican Americans.

3. Greater risk - chronic kidney and peripheral arterial diseases among the overall population

Lead –

Male Reproductive Effects

Current occupational exposures / BLL > 40 ug / dL

- Decrease sperm count totals and motility
- Increase abnormal sperm frequencies

(Alexander et al. 1996; Gennart et al. 1992; Lerda 1992; and Lin et al. 1996 as cited in ATSDR 2000)

Lead – Pregnancy Outcomes

At higher occupational / environmental exposure levels - adverse pregnancy outcomes

Increased frequency of spontaneous abortions (Nordstrom et al. 1979)

Miscarriages and stillbirths (Baghurst et al. 1987; McMichael et al. 1986)

Women with BLL 5-9 µg/dL 2-3x more likely to have a spontaneous abortion than were women with BLL lesser than 5 µg/dL. (Borja-Aburto et al. 1999).

Lead - Developmental Effects

Prenatal exposure to low lead levels (BLLs of 14 µg/dL) may increase the risk of reduced birth weight and premature birth

Increased risk for minor congenital abnormalities (minor skin abnormalities and undescended testicles)

Lead - bone development / growth

Lead can result in delayed growth in children

Increased likelihood of osteoporosis (weakened bones later in life) in animals exposed to lead

Suspected factor in human osteoporosis

Lead - Carcinogenicity / Cancer

EPA - classified lead and inorganic lead as Group 2B: **probable human carcinogens.** (ATSDR 1999)

National Toxicology Program classifies lead and lead compounds as "reasonably anticipated to be a carcinogen" (NTP 2004)

Lead – Signs and symptoms

Lead - clinical presentation / symptoms

Most patients who suffer from lead poisoning are asymptomatic

THUS - importance of exposure assessment and screening

1st Signs in children:

- Subtle neurobehavioral problems
- Changes in classroom behavior and social interaction
- Developmental, speech, and hearing impairments

Most people with lead toxicity are not overtly symptomatic

Some of the health effects of lead exposure on the various organ systems (see "Physiological Effects" section) are permanent or latent and may appear after exposure has ceased.

Lead Exposure -

Continuum of signs / symptoms

Lowest Exposure Dose Signs and Symptoms:

Impaired Abilities /often appears asymptomatic

Decreased learning and memory

Lowered IQ

Decreased verbal ability

Impaired speech and hearing functions

Early signs of hyperactivity or ADHD

Low Exposure Dose Signs and Symptoms:

Myalgia or paresthesia

Mild fatigue

Irritability

Lethargy

Occasional abdominal discomfort

Moderate Exposure Dose Signs and Symptoms

- Arthralgia
- General fatigue
- Difficulty concentrating/Muscular exhaustibility
- Tremor
- Headache
- Diffuse abdominal pain
- Vomiting
- Weight loss
- Constipation

High Exposure Dose Signs and Symptoms

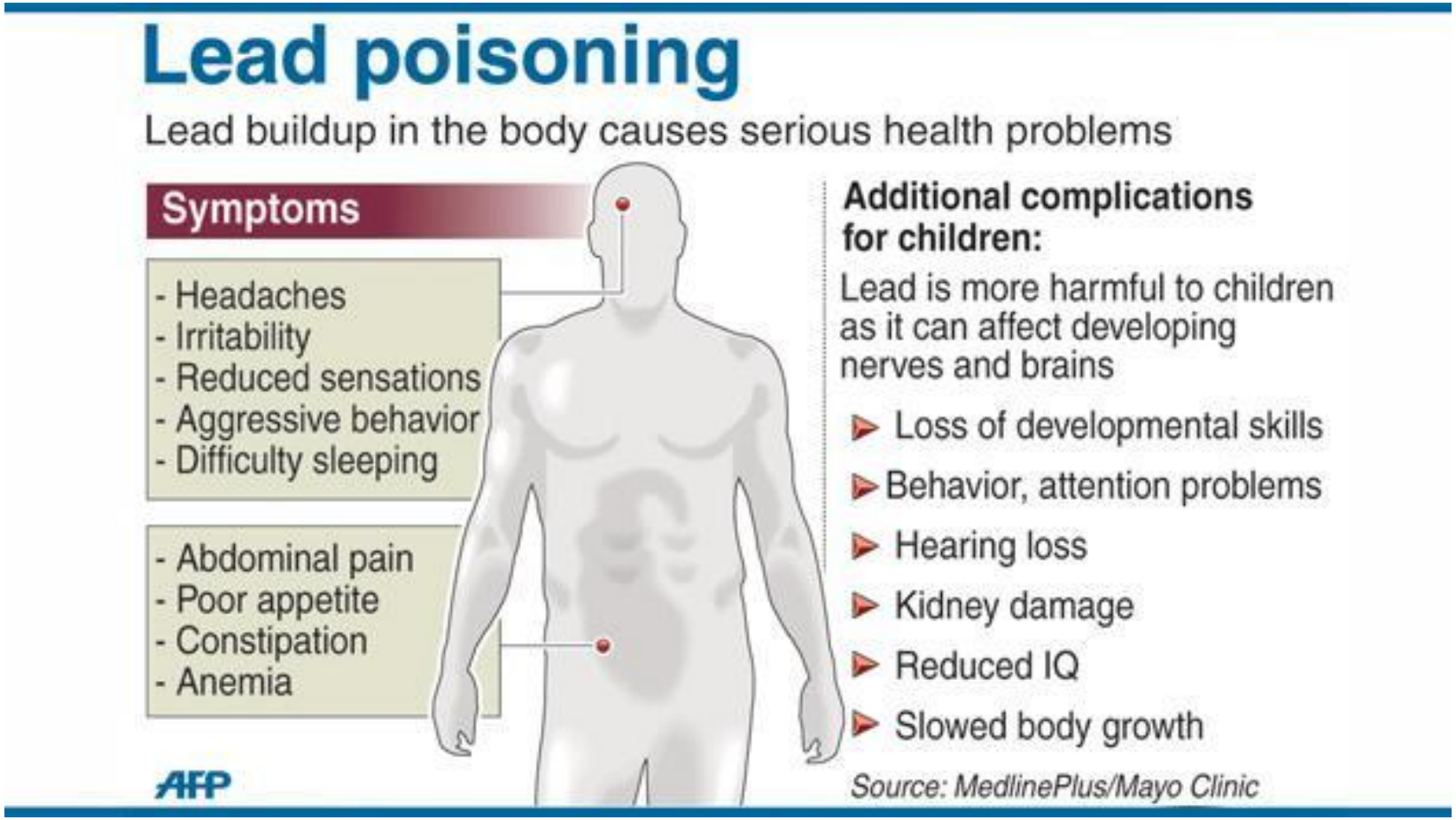
Paresis or paralysis

Encephalopathy—may abruptly lead to seizures, changes in consciousness, coma, and death

Lead line (blue-black) on gingival tissue

Colic (intermittent, severe abdominal cramps)

Lead Poisoning



Lead - Screening

Every child with:

- Behavioral disorder
- Speech impairment
- Who may have been exposed to lead
- Siblings, housemates, and playmates of children with suspected lead toxicity

Any person living:

- Older houses
- Certain occupations and farming conditions
- Degenerative neurological, kidney, and bone diseases

Lead Testing

Usual 1st test in suspected on-going exposure - blood lead level

Capillary blood draws (fingersticks) - not reliable for diagnosis - used for screening

Urine chelation challenge - for estimating body burden

Hair - screening test - of recent exposure

Greater risk of contamination using the finger-stick method, an elevated BLL obtained through finger-sticking should always be confirmed through venipuncture. (AAP 1993 and CDC, 1997a)

Most blood is stored in bone - BLL often under-represent the total body burden

Longbone radiographs - "lead lines" - increased density on growth platesof the bone - finding of chronic exposure.

Lead Lines

Longbone Radiograph of knees - "lead lines"

3 yo girl - blood lead level of 10.6 µg/dL

Lead - Detoxification / Treatment

Chelation - EDTA, DMPS, DMSA - effective / safe

Essential elements - calcium, zinc, iron, selenium, and antioxidant vitamins - counteract the toxic effects of lead

"Interaction of lead with some essential trace metals in the blood of anemic children from Lucknow, India,"

Clinica Chimica Acta, vol. 377, no. 1-2, pp. 92–97, 2007.

Cadmium - Toxicity

Chronic cadmium exposure - associated with hypertension and diabetes

Studies - cadmium may exert effects on the cardiovascular system at extremely low exposure levels

In-vitro studies data - initiation of pathophysiological changes in the vessel wall

Potentiates some diabetic complications related to renal tubular and glomerular function

National Health and Nutrition Examination Surveys (NHANES)

Significant association between high urinary Cd levels and elevated fasting blood glucose levels

- Arterial dysfunction
- Promoting atherosclerosis

Blood **cadmium level was independently associated with myocardial infarction**

"The vascular endothelium as a target of cadmium toxicity," Life Sciences, vol. 79, no. 16, pp. 1493–1506, 2006

"Cadmium-induced oxidative stress and histological damage in the myocardium," Toxicology and Applied Pharmacology, vol. 265, no. 3, pp. 380–389, 2012.

"Hypoproduction of erythropoietin contributes to anemia in chronic cadmium intoxication: clinical study on Itai-itai disease in Japan," Archives of Toxicology, vol. 68, no. 10, pp. 632–636, 1994

Cadmium - Toxicity - CVD

May contribute to the pathogenesis of CVD

- Increased oxidative stress - in vivo
- Depletion of glutathione and alteration of sulfhydryl homeostasis
- Indirectly increasing oxidative stress and lipid peroxidation

Vascular lining - allow for a increased transport of cadmium across the endothelium

Retaining high amounts of cadmium in smooth muscle cells disruption of endothelial integrity

Cadmium - Toxicity - Mechanism of Action

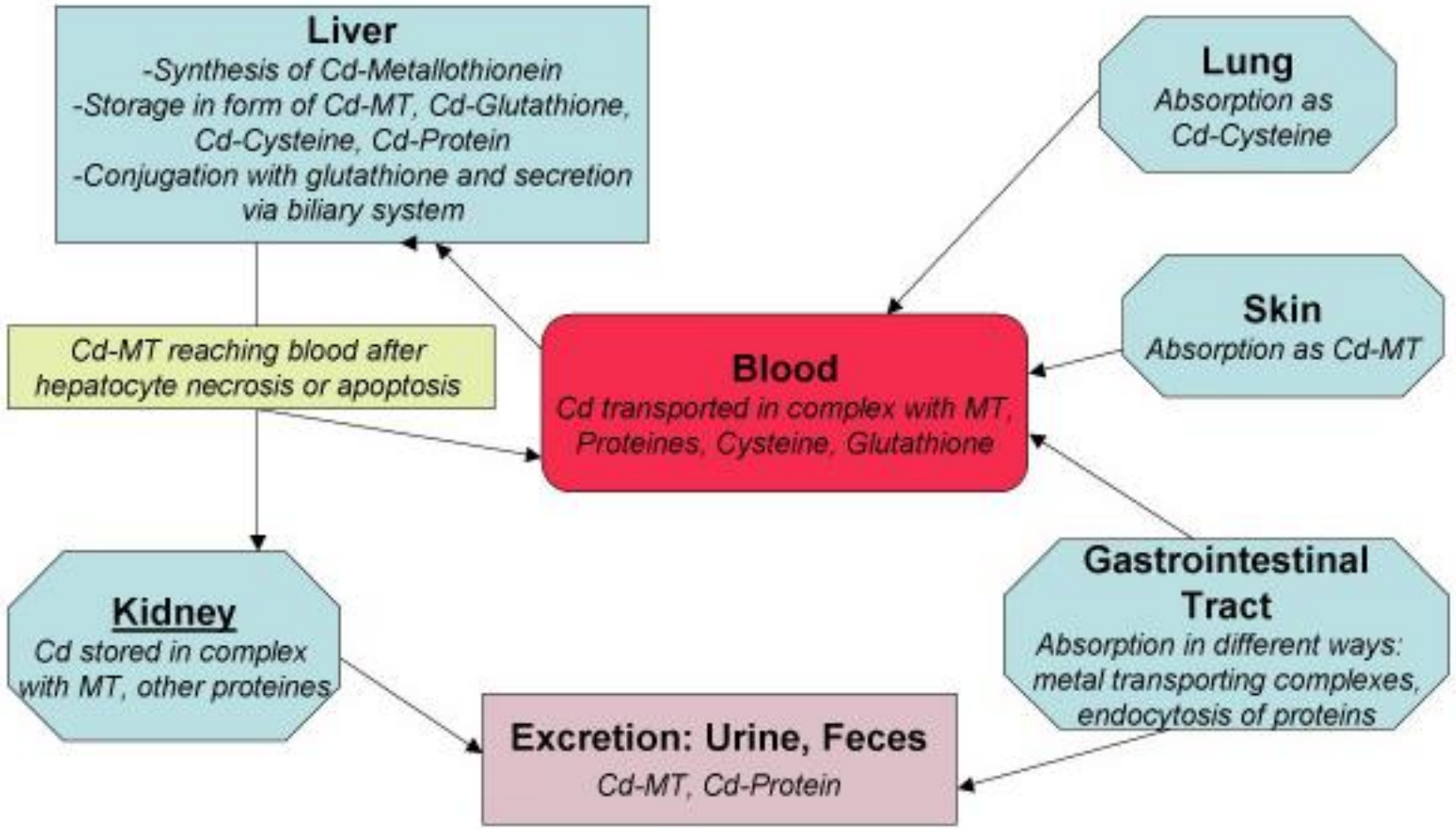
Interferes with the homeostasis and function of other minerals

Disruption of transport mechanisms - zinc (Zn^{2+}), iron (Fe^{2+}), manganese (Mn^{2+}), calcium , (Ca^{2+})

Replacement of other metals in cellular proteins (metallothionein)

** **Higher zinc levels protective against Cd toxicity** - probably through metallothionein induction

Cadmium – Toxicity



Cadmium - Toxic Effects

Itai-itai disease - severe anemia - suppression of erythropoietin production

Increased rates of autoimmunity

Increased production of nonspecific antibodies

Decreased production of antigen-specific antibodies

Suppressed Lymphocyte proliferation and natural killer cell activity

"Effects of physiological concentrations of heavy metals both individually and in mixtures on the viability and function of peripheral blood human leukocytes in vitro," Journal of Toxicology and Environmental Health A, vol. 71, no. 19, pp. 1327–1337, 2008

Cadmium - Endocrine

Disruption endocrine capacity - disregulating pituitary hormones

2007-8 NHANES survey

Increased blood Cd levels were associated with **suppressed TSH production**

"Cadmium as an endocrine disruptor: correlation with anterior pituitary redox and circadian clock mechanisms and prevention by melatonin," Free Radical Biology and Medicine, vol. 53, no. 12, pp. 2287–2297, 2012.

"Metals in blood and urine, and thyroid function among adults in the United States 2007-2008," International Journal of Hygiene and Environmental Health, 2012

Cadmium - Metalloestrogen

In vitro and in vivo animal studies

Binding of Cd to breast cancer estrogen receptors

"Cadmium a metalloestrogen: are we convinced?" Journal of Applied Toxicology, vol. 35, no. 2, pp. 318–332, 2012

"Cadmium mimics the in vivo effects of estrogen in the uterus and mammary gland," Nature Medicine, vol. 9, no. 8, pp. 1081–1084, 2003.

Cadmium - Toxicity - Infertility / Gonadal dysfunction

Rat Studies

Male infertility - damage to the blood-testis barrier, decreasing germ cell adhesion leading to germ cell loss, reduced sperm count and subfertility or infertility

Increased prostaglandin F2alpha

Male - cavernosal vasoconstriction - **suppressed testosterone synthesis** and secretion

Female - **destruction of corpus luteum** and fetus in the female.

Human epidemiological studies have not associated Cd as a cause of male infertility or erectile dysfunction

"The blood-testis barrier and its implications for male contraception," Pharmacological Reviews, vol. 64, no. 1, pp. 16–64, 2012

Cadmium - Toxicity

Insulin resistance / Diabetes

Y. W. Chen, C. Y. Yang, C. F. Huang, D. Z. Hung, Y. M. Leung, and S. H. Liu, "Heavy metals, islet function and diabetes development," Islets, vol. 1, no. 3, pp. 169–176, 2009.

Metabolic syndrome .

B. K. Lee and Y. Kim, "Blood cadmium, mercury, and lead and metabolic syndrome in South Korea: 2005–2010 Korean National Health and Nutrition Examination Survey," American Journal of Industrial Medicine, 2012.

Cadmium - Toxicity

Nerve cells

- **Oxidative stress and membrane disturbances in the central nervous system**
- Reduction in acetylcholinesterase activity
- Increase in oxidative stress markers
- **Depletion of glutathione, superoxide dismutase 2, and other antioxidants**
- Depletion of catalase, glutathione peroxidase, and glutathione-S-transferase
- **Apoptosis of cortical cells in the central nervous system**
- Decreased attention level and memory decreased learning ability.
- **Decreased low-frequency hearing**

"Could cadmium be responsible for some of the neurological signs and symptoms of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome," Medical Hypotheses, vol. 79, no. 3, pp. 403–407, 2012

"Heavy metals exposure and hearing loss in US adolescents," Archives of Otolaryngology-Head and Neck Surgery, vol. 137, no. 12, pp. 1183–1189, 2011

Cadmium Toxicity - Detoxification Treatment

Zinc 25 - 100 mg

MIT - Metallothionein Induction Therapy

Minerals - selenium, manganese

Vit C - 5000 mg

Dietary - meat, seeds

Chelation DMPS, EDTA, DMSA

SH - GSH, Methionine

Sauna - odor or taste sensation, fatigue, moody, pain in kidneys and bones, facial and skin burning rash

"Metallothionein protection of cadmium toxicity," Toxicology and Applied Pharmacology, vol. 238, no. 3, pp. 215–220, 2009.

Cadmium - Detoxification - Chelation

EDTA > DMSA, DMPS

EDTA - mobilizes intracellular / tissue cadmium

Enhanced excretion - GSH, Methionine, Zinc

Dose: EDTA 1 gram / hour - not sooner than 5 days apart

I one gram per hour nor in dosage greater than three grams per session.

Replacement of essential minerals between sessions.

Chelation Protocols - by national physician associations

International College of Integrative Medicine, "Diagnostic and treatment protocols for safer, effective mercury human biohazard management," Tech. Rep., Consensus Development Working Group of the International College of Integrative Medicine, Bluffton, Ohio, USA, 2003.

American College for Advancement in Medicine, Chelation Module, American College for Advancement in Medicine, Irvine, Calif, USA, 2010.

Advanced Medical Education and Services Physician Associatio, Introduction To Clinical Metal Toxicology, Advanced Medical Education and Services Physician Association, San Antonio, Tex, USA, 2007.

Autism Research Institute, Clinician Seminar Level 1, Autism Research Institute, San Diego, Calif, USA, 2010.

Cadmium - Detoxification - Sauna

Significantly increased during sauna

S. J. Genuis, D. Birkholz, I. Rodushkin, et al., "Blood, urine, and sweat (BUS) study: monitoring and elimination of bioaccumulated toxic elements," Archives of Environmental Contamination and Toxicology, vol. 61, no. 2, pp. 344–357, 2010

Cadmium - Basic considerations

Average absorption - 5%

Younger population - higher cadmium absorption rates - 20–40% - reuptake via enterohepatic circulation

Zinc, Calcium, and Iron deficiency: INCREASE Cd absorption

Prevention of Cadmium Toxicity - # 1 Zinc / #2 Minerals

Cd - generally higher in women - lower iron levels

Smokers - 2x cadmium body burden vs. Nonsmokers

Binds tightly to metallothionein - not efficiently excreted from body

Poor excretion = accumulation

Irreversibly accumulates in the human body - kidneys and liver and testes (metallothionein production)

Kidney - most effected organ - accumulation and toxicity

Aluminum

Aluminum

#3 abundant element (8 percent) in the Earth's crust (oxygen - 47% and silicon - 28 percent)

Not essential / vital to human metabolism and health

Tendency to accumulate - with continued exposure

Less toxic than mercury, arsenic, lead or cadmium / **more persistent / more insidious**

Aluminum = neurotoxin / excitotoxin

Brain - most sensitive organ to Al - even more true for a developing nervous system

Impossible to avoid - but awareness / prevention - proactive - remediation - limiting

Aluminum - Toxicity

MSDS (Material Safety Data Sheet)

Aluminum is a poison that accumulates in the brain and tissues of the body

TOXICOLOGICAL PROFILE FOR ALUMINUM

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Agency for Toxic Substances and Disease Registry

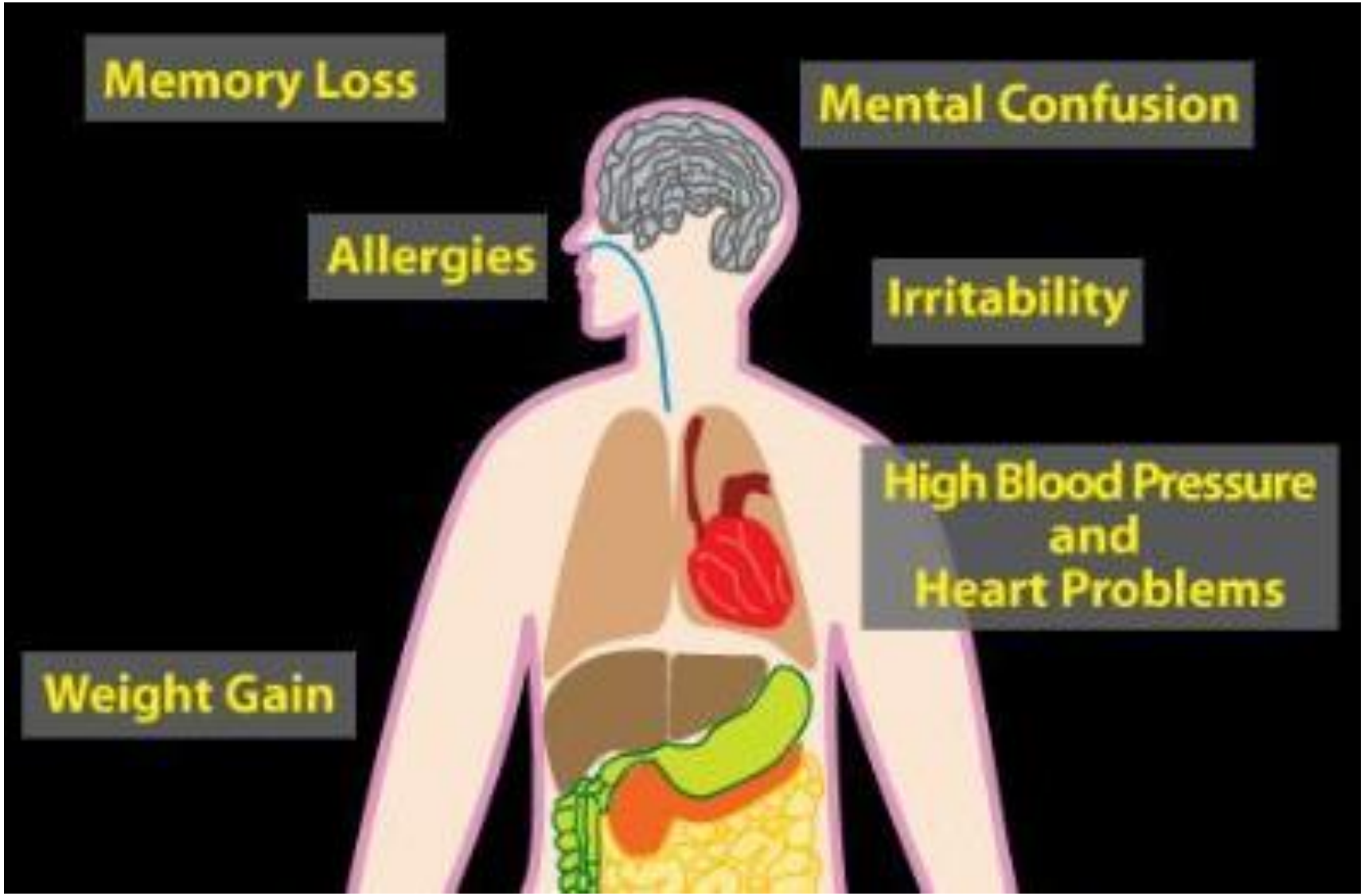
400 page

September 2008

Aluminum – Toxicity Clinical

- Personality changes, altered mood, depression
- Fatigue, lethargy
- Diminished alertness, brain fog
- Microcytic anemia, weakness, fatigue
- Visual and auditory hallucinations
- Epileptic seizures
- Memory loss
- Dementia
- Bone Disease / Osteomalacia / Osteodystrophy
- Speech and language impairment
- Motor disturbances (tremors, myoclonic jerks, ataxia, convulsions, asterixis, motor apraxia, muscle fatigue)

Aluminum Toxicity



Aluminum - Toxicity

Notable symptoms of aluminum toxicity:

Diminishing **intellectual** function

Forgetfulness

Inability to **concentrate**

In high doses:

Dementia and large enough doses - **cardiac arrest**

Aluminum - Exposure

Steady increase of aluminum in our environment and diet

U.S. production of aluminum

1986 1.4 million tons.

2006 2.37 million tons

Total amount of Al in adult: 50 to 150 mg

Estimated amount ingested through food and water: 10 - 100 mg DAILY

2007 JECFA (Joint Expert Committee on Food Additives)
provisional tolerable weekly intake (PTWI) for aluminium from all sources
1 mg/kg of body weight (FAO/WHO, 2007)
70 mg / week
10 mg / day

Aluminum - Exposure

Leading Edge Research Group

Half of the water utilities use aluminum sulphate to clarify drinking water

Most of the utilities in Europe and the United States exceed the maximum safe amount of aluminum (100 mcg. per liter)

Some of these by as much as 60 times the amount considered "safe."

Aluminum - Exposure

Aluminum in OTC:

Maalox® extra strength 306 mg. of aluminum hydroxide for each dose

Mylanta®contains 500 mg

Aluminum - Sources

Cooking utensils—aluminum pots, teflon pans and foil-wrapped foods

Beverages in aluminum cans – phosphoric acid leaches

Anti-caking agent to salt and sugar

Baking powder

Bleaching agent in white flour

Emulsifier in processed cheeses

Cake mixes, self-rising flour and frozen dough

Commercial teas

Antiperspirants

Toothpaste

Sunscreen lotions

Cosmetics

Cigarette filters

Infant formulas – soy formulas 10x

Vaccines

OTC medications: anti-acids , buffered aspirin, vaginal douches, anti-diarrheal

Occupational—welding and smelting

Aluminum - Effects in body

Primary - brain and bones

Less toxic, more insidious, more persistent

Aluminum / Essential Nutrients

A deficiency in essential mineral - accumulation / deposition
aluminum - bones, lungs and brain

50 % skeleton,

25 % lung tissue

25 % brain

Ascorbates, sulfur and magnesium contribute to body's ability to excrete aluminum efficiently

Aluminum Toxicity -

International Journal of Alzheimer's Disease

Effects of aluminum on the central nervous system

(1) Nucleus and gene expression

Binding to DNA

Binds to histone-DNA complex and induces conformational changes of chromatin.

Induces topological changes of DNA.

Altered gene expression

Induces decreased expression of neurofilament and tubulin.

Induces altered expression of genes of neurofilament, APP, and neuron specific enolase.

Induces decreased expression of transferrin receptor.

Induces altered expression of RNA polymerase I.

Induces downregulation of mitochondrial cytochrome c oxidase.

Induces altered expression of calbindin-D28k.

Induces decrease in the expression of nerve growth factor (NGF) and brain derived neurotrophic factor (BDNF).

Induces expression of pro-inflammatory genes and pro-apoptotic genes.

Induces elevated expression of APP.

Induces altered expression of oxidative stress marker genes (SOD1, glutathione reductase, etc.).

Induces decreased expression of neprilysin.

Induces altered expression of β-APP secretase (BACE1 and BACE2).

International Journal of Alzheimer's Disease

Table 1: Effects of aluminum on the central nervous system.

(2a) Cellular functions

Energy metabolism

Inhibits Krebs cycle enzymes

Inhibits the activity of hexokinase

Inhibits the activity of phosphofructokinase

Inhibits the activity of glucose-6-phosphate dehydrogenase

Causes mitochondrial dysfunction and depletion of ATP

Decreases in activity and expression of TCA-cycle related enzymes (succinate dehydrogenase (SDH), alpha-ketoglutarate dehydrogenase (KGDH), isocitrate dehydrogenase-NAD+ (IDH), fumarase (FUM), aconitase (ACN), and cytochrome c oxidase (Cyt C Ox)).

Phosphorylation and dephosphorylation

Inhibits the activity of protein phosphatase.

Increases the activity of protein kinase C and cytoskeleton proteins.

Accelerates phosphorylation and accumulation of neurofilament.

Enhances Ca2+/Calmodulin dependent protein kinase activity.

Accelerates phosphorylation of MAP 2 and neurofilament.

Inhibits dephosphorylation of tau.

Induces nonenzymatic phosphorylation of tau.

International Journal of Alzheimer's Disease

Table 1: Effects of aluminum on the central nervous system.

(2b) Cellular functions

Abnormal accumulation of proteins

Causes the conformational change and the accumulation of neurofilament and MAP1A, MAP1B

Accelerates the phosphorylation of tau and its accumulation

Causes the accumulation of tau protein in neuroblastoma cells or in primary cultured neurons

Causes the accumulation of tau protein in experimental animals

Causes neurofibrillary degeneration in vivo

Causes the accumulation of AβP in cultured neurons or in neuroblastoma cells

Causes the accumulation of AβP in vivo

Neurotransmitter release / receptor inhibition

Inhibits glutamate release

Impairs synaptic transmission

Inactivates glutamate dehydrogenase

Inhibits NMDA-type glutamate receptor

Inhibits choline acetyl transferase and tyrosine hydroxylase, glutamate decarboxylase.

Aluminum - Toxicity

TOXIC to cells and central nervous system

Exposure - **ubiquitous / unavoidable**

Accumulation - **gradual**

Subtle and non-specific changes

Difficult to detect

Greater risk - with nutrient / anti-oxidant deficiencies and oxidative stress / inflammation

Activates immune system to the Th2, or antibody driven immune system - allergic responses and auto-immune

Aluminum in Vaccines - Purpose and Safety

Purpose: vaccine adjuvant - when mixed with the antigen of virus / bacteria - greater immune response

Higher Abs

Helps overcome the anti inflammatory effect of breast milk

Safety: studies to support claims of safety - LACKING

Aluminum - Exposure - Vaccines

Which vaccines typically contain aluminum?

Live vaccines do not contain aluminum

Killed/inactivated viruses / "toxoid" vaccines DO contain aluminum

17 aluminum based vaccines in U.S.

ex. DTaP and hepatitis B vaccines

How Much Aluminum ? Vaccine Exposure

1970s 4 vaccines - **1200 mcg**

2010 17vaccines

In 18 months = **4,92**5 micrograms (mcg) of aluminum

100 % absorbed —— transported - distributed

2016 6150 mcg

Aluminum - Exposure - Vaccines

- 5000 mcg 4,925 micrograms (mcg) of aluminum within the first 18 months of life (plus formula, water)
- 200 - 600 additional 170 to 625 mcg **by the age of 6**
- **6000 mcg once completed all vaccines**
- **6 mg**
- **100 % absorbed** vs. orally ingestion - 1%

Inactivated Vaccines (Aluminum containing) - higher risk of reactions / toxicity)

African study - 2014

Mortality during 12 months of follow-up after vaccination with live versus inactivated vaccines.

Some children received multiple injections of live vaccines

Others received both live and inactivated vaccines

Death rate - over the following six months:

8x - live and inactivated vaccines

64 percent higher mortality rate

- Vaccine. 2014 Jan 23;32(5):598-605
- Co-administration of live measles and yellow fever vaccines and inactivated pentavalent vaccines is associated with increased mortality compared with measles and yellow fever vaccines only. An observational study from Guinea-Bissau.
- Studies from low-income countries indicate - co-administration of inactivated DTP and live attenuated MV = increased mortality compared with receiving MV only.
- Pentavalent (DTP-H. Influenza type B-Hepatitis B) vaccine is replacing DTP in many low-income countries
- 2007-2011 randomised placebo-controlled trial
- 2331 children

- Placebo - live vaccines only (MV or MV+YF)
- Combination - live and inactivated vaccines (MV+DTP or MV+YF+pentavalent)
- 6 month follow up - mortality rate ratio
- 3.2 live and inactivated vaccines vs live only
- 7.3 MV+YF+pentavalent - live and inactivated vs live only

- CONCLUSION:
  - In line with previous studies of DTP, the present results indicate that pentavalent vaccine co-administered with MV and YF is associated with increased mortality
  - 2X INCREASED MORTALITY WHEN PENTAVALENT VACCINE + LIVE VIRUS VACCINES

Aluminum Toxicity –

Vaccine Auto-Immune Reaction

Autoimmune - Inflammatory Syndrome Induced by Adjuvants (ASIA)

Shoenfeld's syndrome - autoimmune - proposed by Israeli immunologist Yehuda Shoenfeld in 2011

J Autoimmun. 2011

'ASIA' - autoimmune/inflammatory syndrome induced by adjuvants.

In recent years, four conditions LINKED to adjuvants:

Siliconosis

Gulf war syndrome (GWS)

Macrophagic myofasciitis syndrome (MMF)

Post-vaccination phenomena

Aluminum Toxicity

BMC Med. 2013

Translocation of bio-persistent particles (aluminum) from muscle to brain

252 patient reports of alum-associated ASIA

Mouse experiments - assess bio-distribution of vaccine-derived aluminum and of alum-particle fluorescent surrogates injected in muscle

Intramuscular injection of alum-containing vaccine was associated with the appearance of aluminum deposits in distant organs, such as spleen and brain where they were still detected one year after injection

Particles linearly accumulated in the brain up to the six-month endpoint

Occurs at a very low rate in normal conditions explaining good overall tolerance of alum despite its strong neurotoxic potential.

However, continuously escalating doses of this poorly biodegradable adjuvant in the population may become insidiously unsafe, especially in the case of over immunization or immature/altered blood brain barrier

Aluminum Exposure –

Accumulation - Toxicity

Front Neurol. 2015

Bio-persistence and brain translocation of aluminum adjuvants of vaccines.

Concerns - causative role in the so-called macrophagic myo-fasciitis (MMF) lesion - patients with myalgic encephalomyelitis/chronic fatigue/syndrome.

MMF revealed - l**ong-lasting bio-persistence of alum within immune cells**

Promptly phagocytosed in muscle and the draining lymph nodes - disseminate within phagocytic cells throughout the body and slowly accumulate in brain

Strongly suggests that long-term **bio-persistence** within phagocytic cells is a **prerequisite for slow brain translocation and delayed** neurotoxicity

ADMISSION: The understanding of basic mechanisms of particle bio-persistence and brain translocation represents a major health challenge…

**** Unknown**

**** The toxicity of aluminum in vaccines—may even exceed the toxicity of mercury in the human body**

Aluminum Exposure - Breast milk vs Formula

Breast milk - 21 mcg of aluminum / day

Conventional formula - 114 mcg / day

5x fold increase exposure

Aluminum Exposure - Accumulation

Rabbit studies: **80 to 94 percent - retained 28 days after IM**

Autopsy examinations: accumulated - **kidneys, spleen, liver, heart, lymph nodes, and brain.**

Long-term - bones

Aluminum Exposure - accumulation

Studies on human infants - **aluminum is not excreted**

Blood and urine levels of aluminum over 12 hours

No increase in blood levels of aluminum following vaccination

No significant increase in urinary excretion

" stays at the site of injection" "not a risk to nervous system "

- Excretion of aluminum is not as efficient in infants and young children

- Non excretion = accumulation

Aluminum Exposure –

Accumulation - Toxicity

J Med Case Rep. 2014

Elevated brain aluminium and early onset Alzheimer's disease in an individual occupationally exposed to aluminium: a case report.

Aluminium - neurotoxin and occupational exposure to aluminium has been implicated in neurological disease including Alzheimer's disease

The first comprehensive and unequivocal data demonstrating significantly elevated brain aluminium content in an individual occupationally exposed to aluminium

CASE PRESENTATION: 66-year-old Caucasian man who died with Alzheimer's disease

Significantly elevated brain aluminium content, 2.98 (2.73) µg/g dry weight

Following occupational exposure to aluminium over a period of 8 years

Aluminum - “normal levels and safety “

2013 Children's Hospital of Philadelphia's (CHOP) vaccine education center website :

"Aluminum is considered to be an **essential** metal with quantities fluctuating naturally during normal cellular activity.

It is found in all tissues and is also **believed to play an important role** in the development of a healthy fetus."

International Journal of Alzheimer's Disease Volume 2011

Review Article

Link between Aluminum and the Pathogenesis of Alzheimer's Disease: The Integration of the Aluminum and Amyloid Cascade Hypotheses

Aluminum - widely recognized neurotoxin

Inhibits more than 200 biologically important functions

Causes various adverse effects in plants, animals, and humans

Aluminum may play crucial roles as a cross-linker in β-amyloid oligomerization

Heavy Metals - Tattoos

Known toxins and carcinogens:

Heavy metals - mercury, cadmium, aluminum, arsenic, nickel, cobalt, chromium, titanium

Benzopyrene

Phthalate

Heavy Metals - Tattoo Pigments

Quantification of Sensitizing Metals in Tattooing Pigments by SF-ICP-MS Technique

Istituto Superiore di Sanità, Rome, Italy

Allergic reactions to metals and metal salts used in pigments for tattoos are surprisingly frequent

Mass spectrometry analysis of tattoo dyes:

Highest elements

Chromium, Nickel , Cadmium

Lower elements

Cobalt , Mercury, Beryllium

Color - Metal Relationships :

Red	Hg, Cd
Blue	Co, Al
Yellow	CD
White	Ni, Cd
Green	Chr

Heavy Metals - Tattoo

American Environmental Safety Institute (AESI)

index card (3 by 5 inch) sized tattoo - average of 1.23 ug lead

>2x amount permitted per day (0.5 ug) - California's Proposition 65

Tattoo Takeover

Prevalence of Tattoos - Exposure to Heavy Metal

Pew Research Center - 2013 - **45 million Americans**

Harris Poll - 2015 - `2,225

U.S. adults - online survey

30% tattoos vs. 20% (2010) - 70% have more 2 or more

47% of Millennials

$ 1.6 Billion annually in U.S.

Heavy Metals - Tattoos

2007 lawsuit - American Environmental Safety Institute (AESI)

Two tattoo ink manufacturers must now place warning labels on their product containers, catalogs and websites

"Inks contain many heavy metals, including lead, arsenic and others" and that the ingredients have been linked to cancer and birth defects.

FDA does not regulate or approve tattoo pigments does have the authority and ability to investigate should health concerns warrant

Tattoos - Heavy Metals - Reactions

Common reactions to tattoo ink and tattooing process:

Allergic rashes

Infection

Inflammation from sun exposure

Chronic skin reactions

Cutaneous tuberculosis and non-tuberculous mycobacterial infections -

(contaminated ink or diluting water)

Red ink is associated more frequently with long-term reactions

Granulomatous and pseudo lymphomatous phenomena

Morphea-like lesions

Vasculitis - Hg, Cd

J Cutan Aesthet Surg. 2015 Jan-Mar;8(1):30-6

Complications of Tattoos and Tattoo Removal: Stop and Think Before you ink.

Eur Ann Allergy Clin Immunol. 2016 Mar;48(2):46-8.

Chemical research on red pigments after adverse reactions to tattoo

20% of tattooed patients - adverse reactions

Allergic contact dermatitis psoriasis with Koebner's phenomena and granulomatous reactions (red)

Tattoos - Heavy Metals - Risks ?

Lancet. 2016 Jan 23;387(10016):395-402.

A medical-toxicological view of tattooing.

little is known about the toxicological risks of the ingredients used

Tattoos - Heavy Metals - Risks of Cancer

Lancet Oncol. 2012 Apr;13(4)

Tattoos, inks, and cancer.

A large amount of metallic salts and organic dyes remain in the skin for lifetime

Potential local and systemic carcinogenic effects of tattoos and tattoo inks

Reviewed the literature and found **50 cases of skin cancer on tattoos:**

- 23 cases of squamous-cell carcinoma and keratoacanthoma
- 16 cases of melanoma
- 11 cases of basal-cell carcinoma

The number of skin cancers arising in tattoos is low - considered as coincidental.

Cadmium - Toxic Metal

Periodic table of chemistry: cadmium below zinc

"Zinc blocking metal" - 200 enzymes effected

Toxic heavy metal - one of the more toxic - # 7 on ATSDR 2015 Substance Priority List

Disrupts biological systems at much lower level than most toxic metals

Cigarette smoking - most significant source of human cadmium exposure

Primary organ of toxic impact in the human - kidney

Other organ: cardiovascular, bone, skin

Human studies - estimated 7% of the general population have renal tubule dysfunction from Cd exposure

Health effects of cadmium exposure, a review of the literature and a risk estimate

Scand. J. Work Environ. Health 24(Suppl.):1–51

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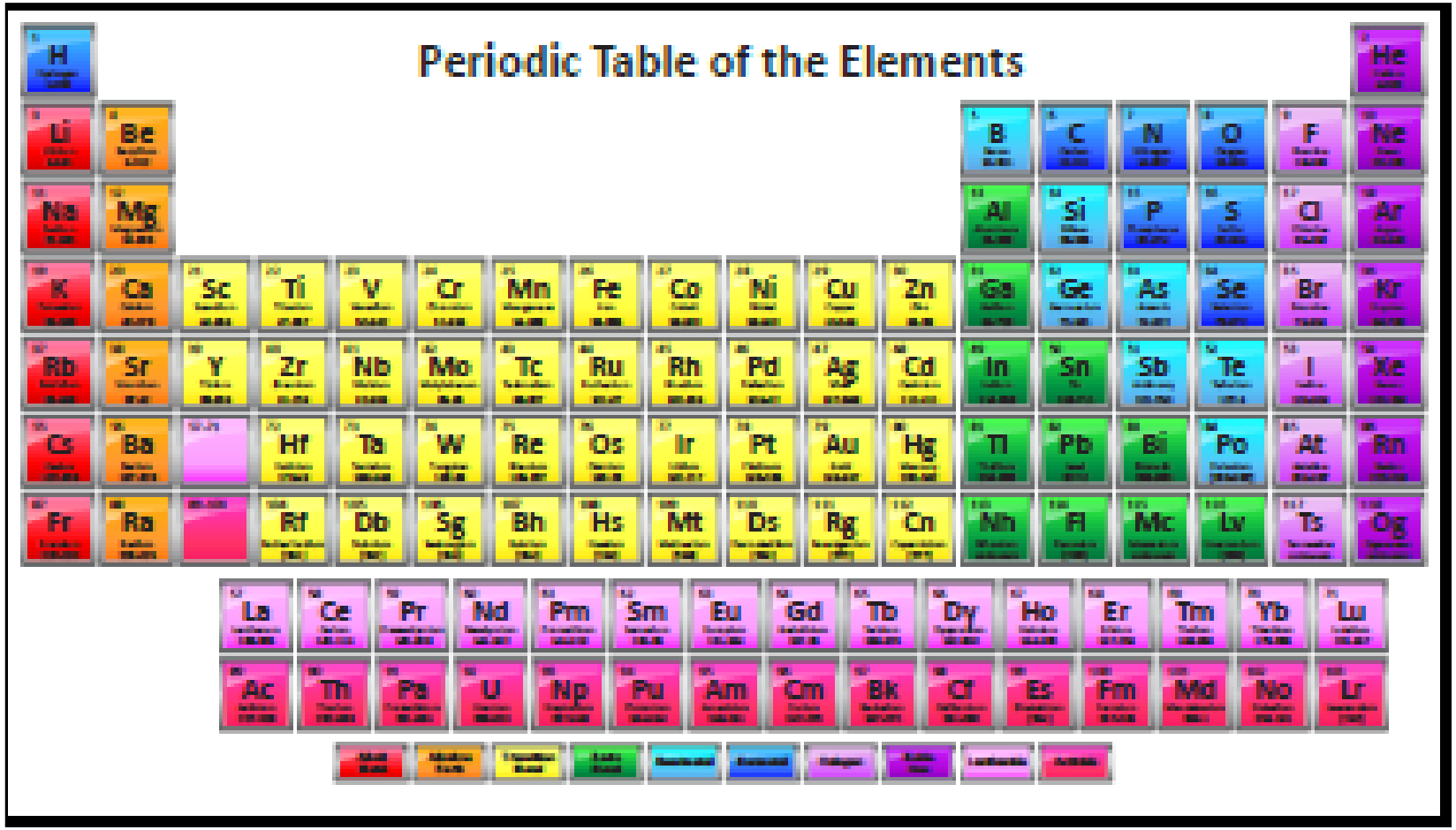
Periodic table -



J Occup Med Toxicol. 2006

The toxicity of cadmium and resulting hazards for human health

Renal insufficiency cough

Prostate cancer carcinogenic

Bone diseases - demineralization

Ovarian dysfunction - progesterone / testosterone

Occup Environ Med. 1998 Jul;55(7):435-9.

Cadmium may be a risk factor for osteoporosis

The Scientific World Journal - Volume 2013

Review Article

Cadmium Toxicity and Treatment

Cadmium Toxicity Effects / Symptoms:

Zinc deficiency - antagonizes zinc (more than 300 enzymes)

Infertility in men - low sperm count

DNA / RNA processing - Defective gene expression

Copper accumulation / dominance

Mental / Behavioral - ADHD, violence, anti-social , hardened personality

Degenerative - premature aging and hardening of tissue - arteries and kidneys renal insufficiency

High blood pressure

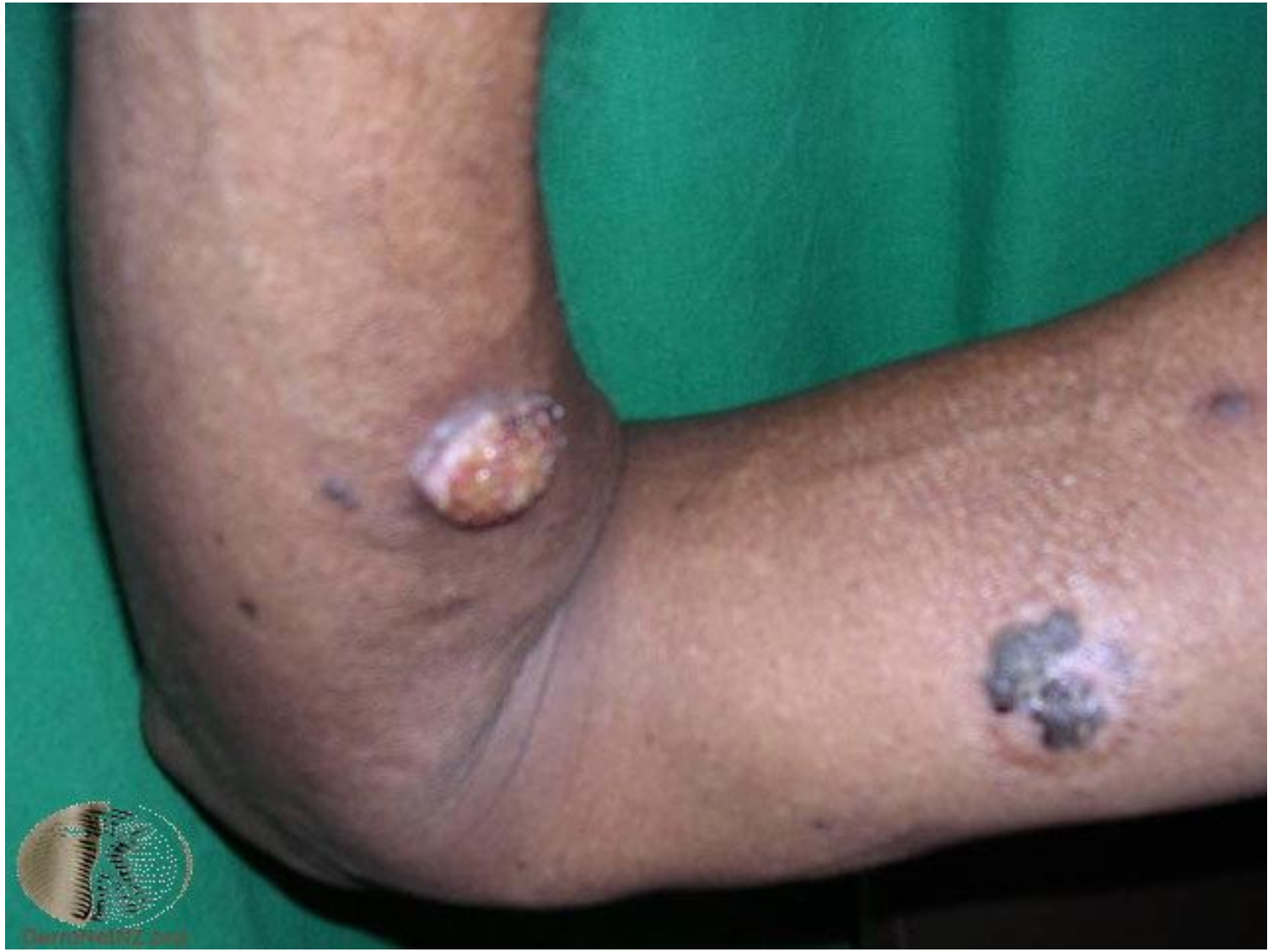
Chronic cough, lung cancer

Birth Defects

Inhalation of vapor / particles during industrial exposure (welding or soldering) - chemical pneumonitis

Arsenic

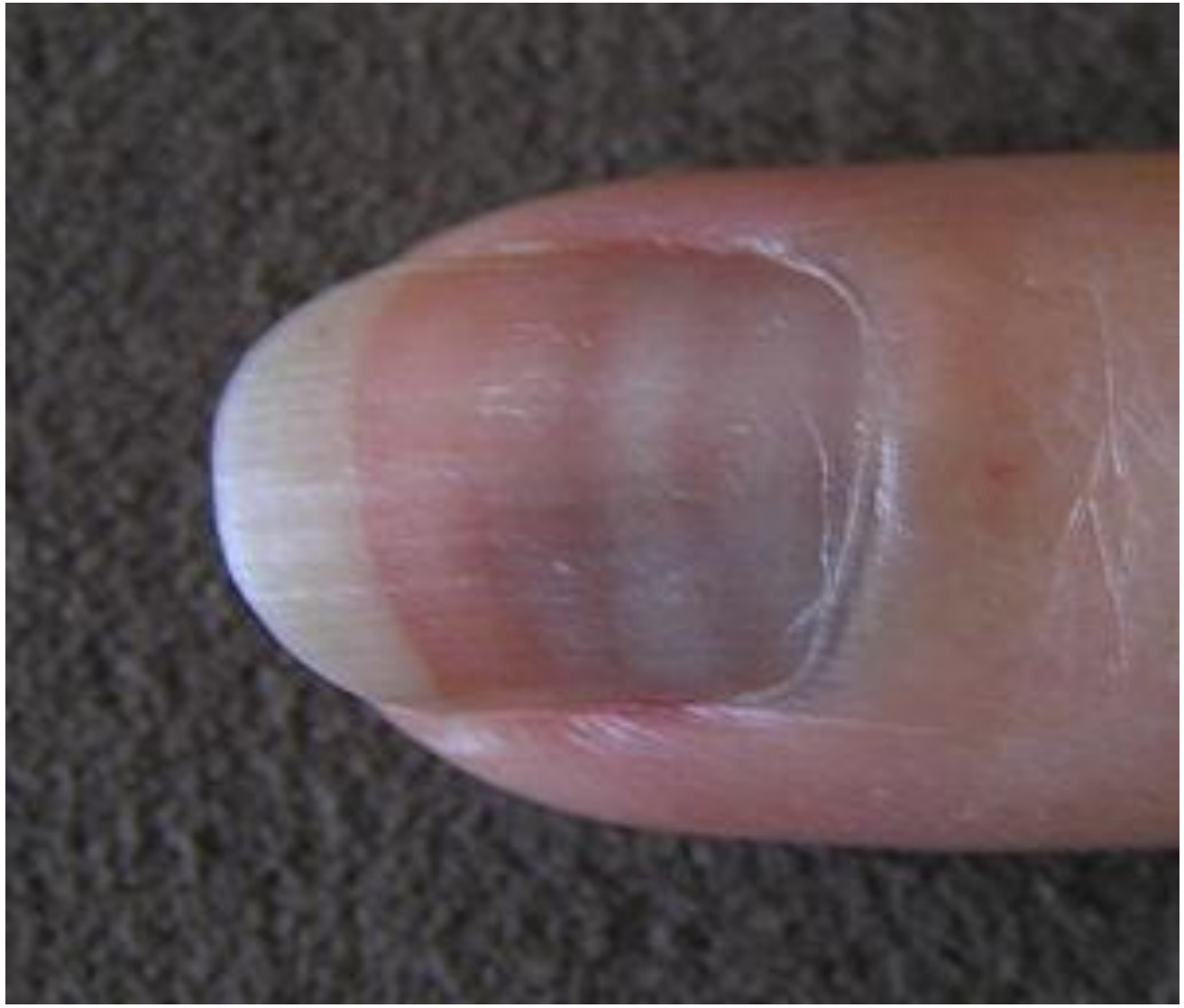
Induced Skin Cancer



Arsenic

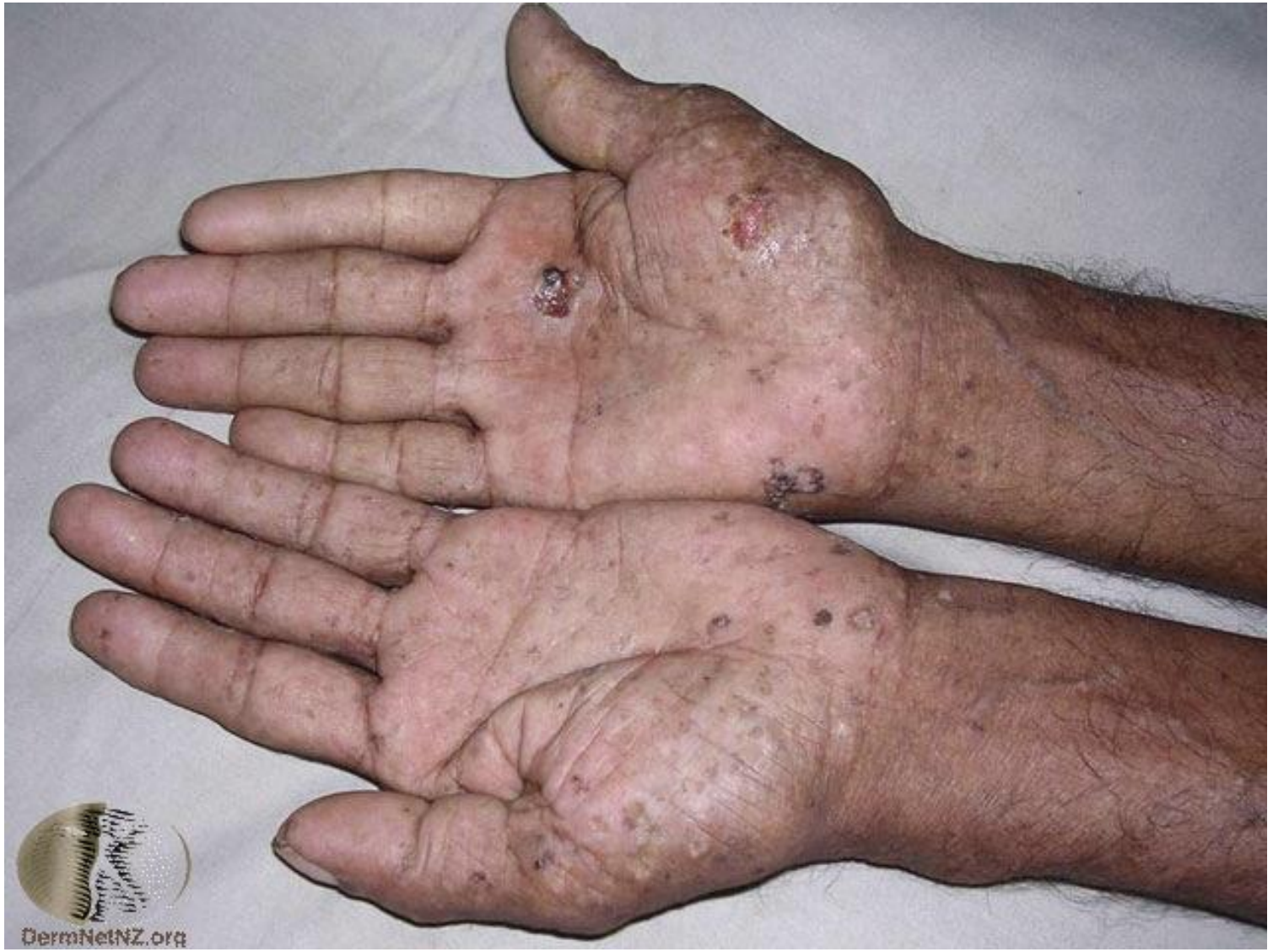
Mees Lines

White Discoloration



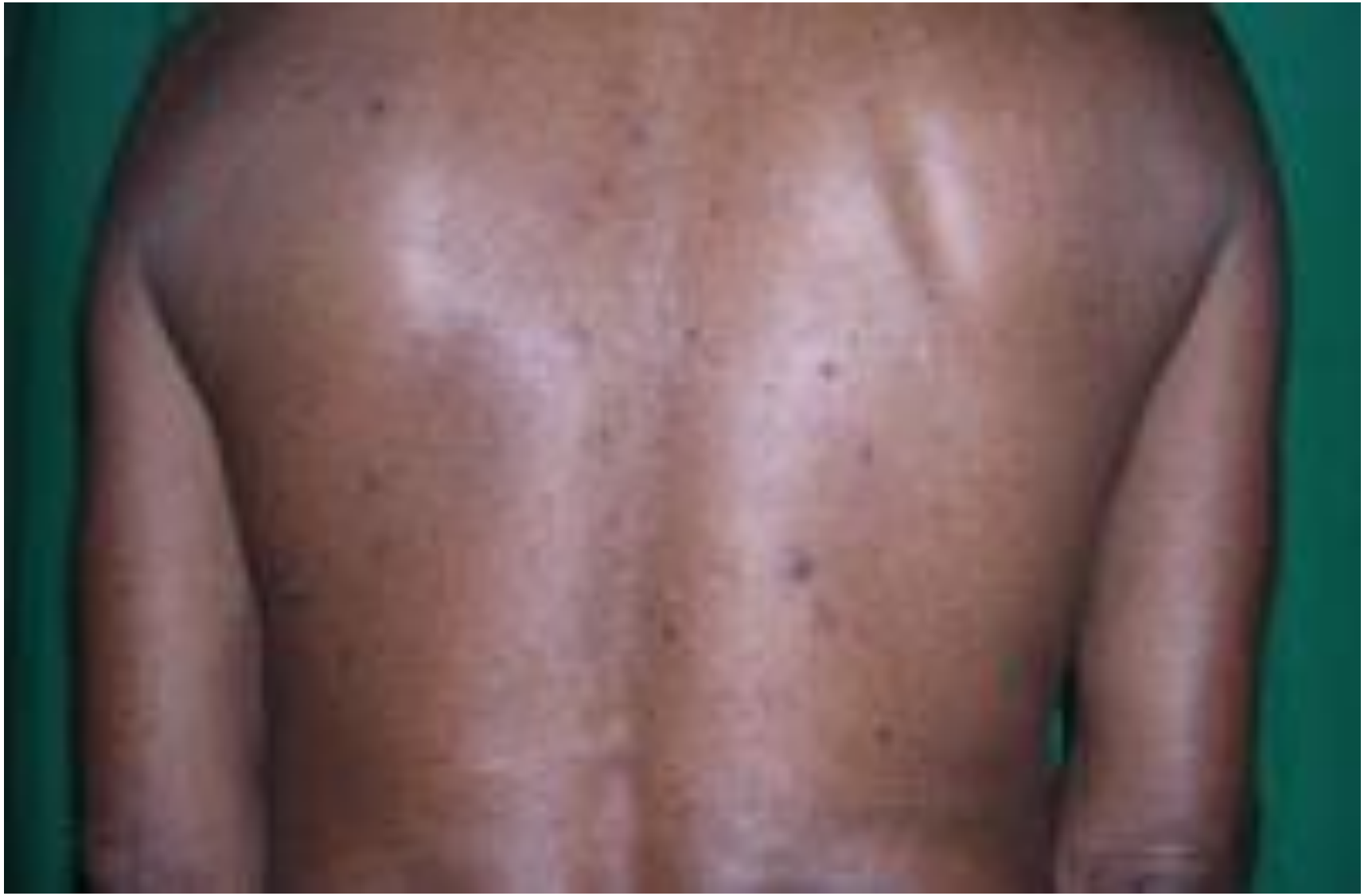
Arsenic

Keratosis



Arsenic

Skin



Arsenic

PTW Wood

Laboratory indicators / changes in Heavy Metal Toxicity

Laboratory indicators/changes in Heavy Metal Toxicity

Urine Tests

Indications of Mitochondrial Dysfunction

Uncoupling of oxidative phosphorylation

Elevated fatty acid metabolites

Elevated lactate

Elevated hydroxymethylglutarate

Multiple partial blocks in Krebs cycle

Elevated 3-methyl histidine

Elevated sarcosine

Elevated pyroglutamate

Elevated vanilmandellate

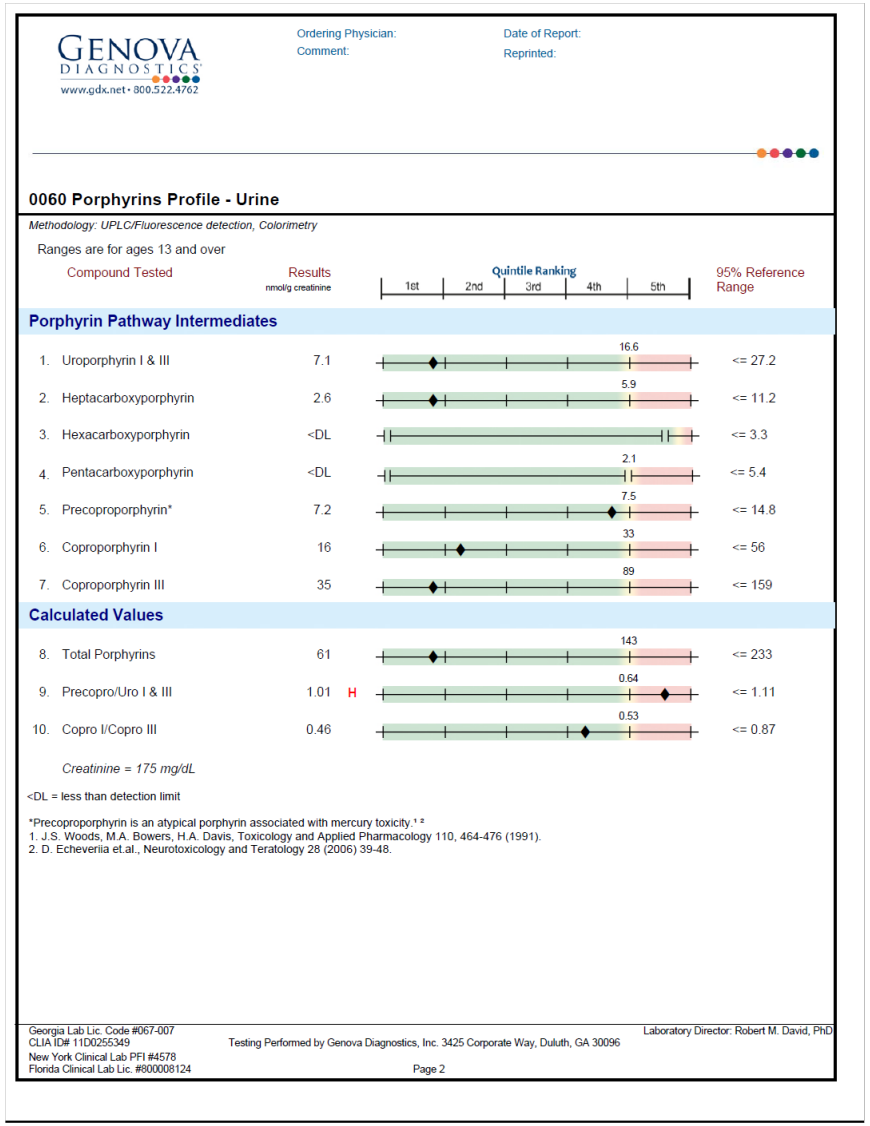
Elevated homovanillate

Fractionated urine porphyrins

Elevated coproporphyrin

Elevated precoproporphyrin

Porphyrins Profile



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Ordering Physician:
Comment:

Date of Report:
Reprinted:

0060 Porphyrins Profile - Urine

Methodology: UPLC/Fluorescence detection, Colorimetry

Ranges are for ages 13 and over

Compound Tested	Results nmol/g creatinine		Quintile Ranking 1st 2nd 3rd 4th 5th	95% Reference Range
Porphyrin Pathway Intermediates				
1. Uroporphyrin I & III	7.1		16.6	<= 27.2
2. Heptacarboxyporphyrin	2.6		5.9	<= 11.2
3. Hexacarboxyporphyrin	<DL			<= 3.3
4. Pentacarboxyporphyrin	<DL		2.1	<= 5.4
5. Precoproporphyrin*	7.2		7.5	<= 14.8
6. Coproporphyrin I	16		33	<= 56
7. Coproporphyrin III	35		89	<= 159
Calculated Values				
8. Total Porphyrins	61		143	<= 233
9. Precopro/Uro I & III	1.01	H	0.64	<= 1.11
10. Copro I/Copro III	0.46		0.53	<= 0.87

Creatinine = 175 mg/dL

<DL = less than detection limit

*Precoproporphyrin is an atypical porphyrin associated with mercury toxicity.[1,2]
1. J.S. Woods, M.A. Bowers, H.A. Davis, Toxicology and Applied Pharmacology 110, 464-476 (1991).
2. D. Echeveriia et.al., Neurotoxicology and Teratology 28 (2006) 39-48.

Georgia Lab Lic. Code #067-007
CLIA ID# 11D0255349
New York Clinical Lab PFI #4578
Florida Clinical Lab Lic. #800008124

Testing Performed by Genova Diagnostics, Inc. 3425 Corporate Way, Duluth, GA 30096

Laboratory Director: Robert M. David, PhD

Page 2

Immune System Tests

High IgE

Low IgG

Low IgG subclasses

Low CD8

Low NK

High CD3/CD26

Tests for Oxidative Stress

Low SOD
Low reduced GSH
Low GSH peroxidase
High lipid peroxides

Tests for Neurotransmitters

High blood / platelet serotonin

High epinephrine / norepinephrine

Urine wasting of sulfur / sulfate

Low plasma sulfate with normal urine sulfate / creatinine

Heavy Metal Testing

Heavy Metal Testing

Options

- Blood
- Urine
- Hair
- Stool
- BioEnergetic

Additional considerations

- Minerals
- GSH
- Sulfur - cysteine

Testing for Mercury / Metal Toxicity

Which metal and which method

Current vs Past Exposure

Blood, hair, unprovoked urine - NOT a good method for testing for past exposures

Mercury and other metals - short half-life (weeks) in the blood

Hair and unprovoked urine

Measure of recent exposure - days (urine) / weeks (hair)
Reflect ability to excrete toxic metals
Affected by heavy metal body burden
Body's glutathione level (controls excretion)

Blood and Unprovoked Urine - measure of recent exposure

Provocation Test: - IV / oral / rectal / topical chelators before and during collection of urine or stool sample

1) metal was present in the body
2) increased body burden
3) demonstrates that the detoxification agent can promote its excretion
4) not equivalent to body burden (CNS / brain)

Testing for Mercury / Metal Toxicity

Blood - antibodies - very specific / auto-immune

Urine Porphyrins - more accepted test for chronic metal toxicity in the traditional medical community

Bio-energetic - clinical AK / computer biofeedback - least accepted TMC / growing prevalence in CAM

Testing for Mercury / Metal Toxicity

Blood, hair, and unprovoked urine mercury

- reflect recent exposure
- does not correlate with total body burden

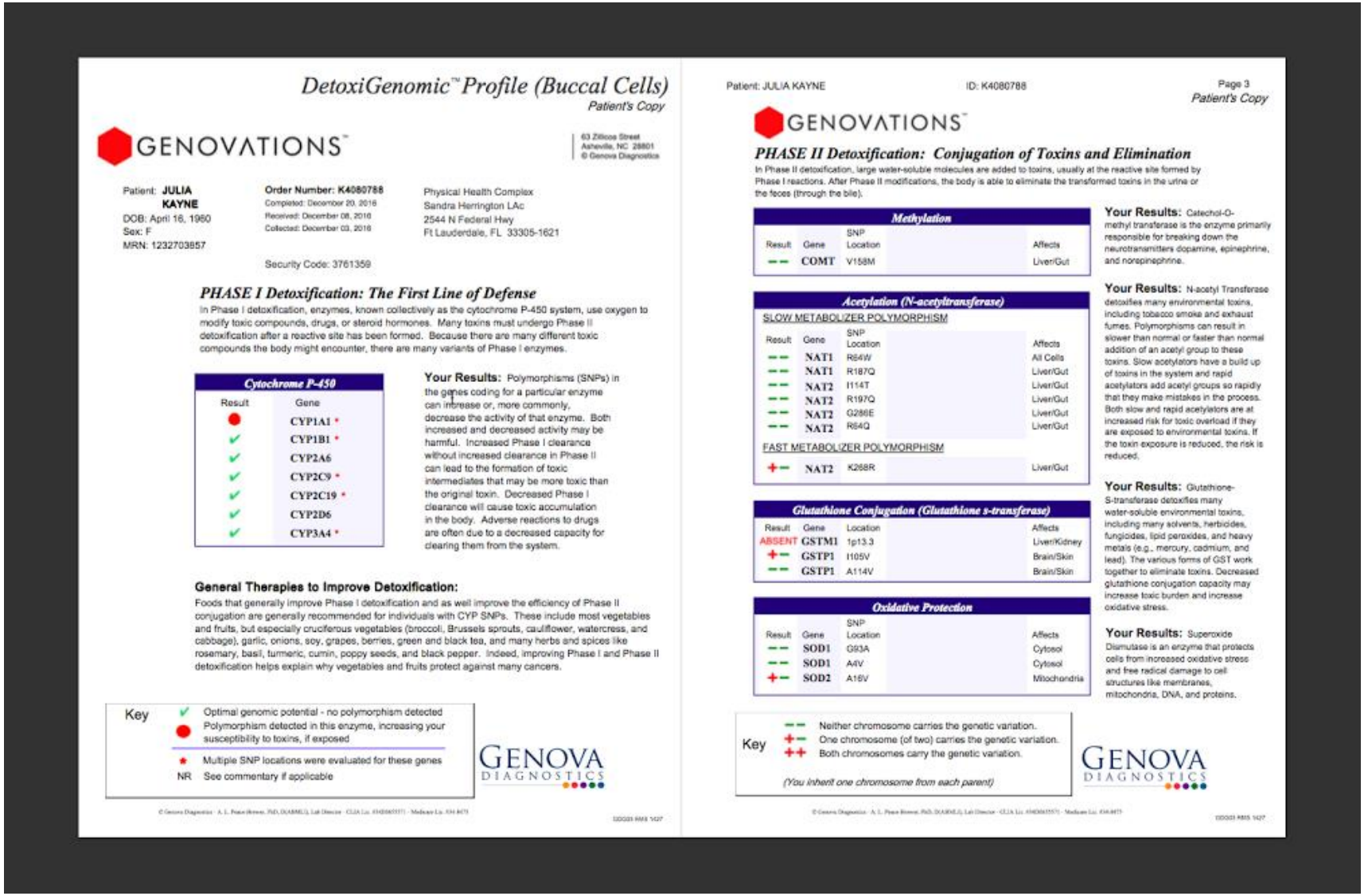
Hair - Maternal scalp hair may be the best indicator of fetal brain levels

Blood and unprovoked urine levels correlate fairly well to each other

Kazantzis, "it has not been possible to set a level for mercury in blood or urine below which mercury related symptoms will not occur"

Mercury symptoms can occur at any blood or urine level, blood and urine levels often usually under reflect tissue levels and even more so CNS levels

Genovations Lab



DetoxiGenomic™ Profile (Buccal Cells)

Patient's Copy

GENOVATIONS™

63 Zillicoa Street
Asheville, NC 28801
© Genova Diagnostics

Patient: **JULIA KAYNE**
DOB: April 16, 1960
Sex: F
MRN: 1232703857

Order Number: K4080788
Completed: December 20, 2016
Received: December 08, 2016
Collected: December 03, 2016

Security Code: 3761359

Physical Health Complex
Sandra Herrington LAc
2544 N Federal Hwy
Ft Lauderdale, FL 33305-1621

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.

Cytochrome P-450

Result	Gene
●	CYP1A1 *
✔	CYP1B1 *
✔	CYP2A6
✔	CYP2C9 *
✔	CYP2C19 *
✔	CYP2D6
✔	CYP3A4 *

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.

General Therapies to Improve Detoxification:

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

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

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PHASE II Detoxification: Conjugation of Toxins and Elimination

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

Methylation

Result	Gene	SNP Location	Affects
– –	COMT	V158M	Liver/Gut

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

Acetylation (N-acetyltransferase)

SLOW METABOLIZER POLYMORPHISM

Result	Gene	SNP Location	Affects
– –	NAT1	R64W	All Cells
– –	NAT1	R187Q	Liver/Gut
– –	NAT2	I114T	Liver/Gut
– –	NAT2	R197Q	Liver/Gut
– –	NAT2	G286E	Liver/Gut
– –	NAT2	R64Q	Liver/Gut

FAST METABOLIZER POLYMORPHISM

Result	Gene	SNP Location	Affects
+ –	NAT2	K268R	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.

Glutathione Conjugation (Glutathione s-transferase)

Result	Gene	Location	Affects
ABSENT	GSTM1	1p13.3	Liver/Kidney
+ –	GSTP1	I105V	Brain/Skin
– –	GSTP1	A114V	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.

Oxidative Protection

Result	Gene	SNP Location	Affects
– –	SOD1	G93A	Cytosol
– –	SOD1	A4V	Cytosol
+ –	SOD2	A16V	Mitochondria

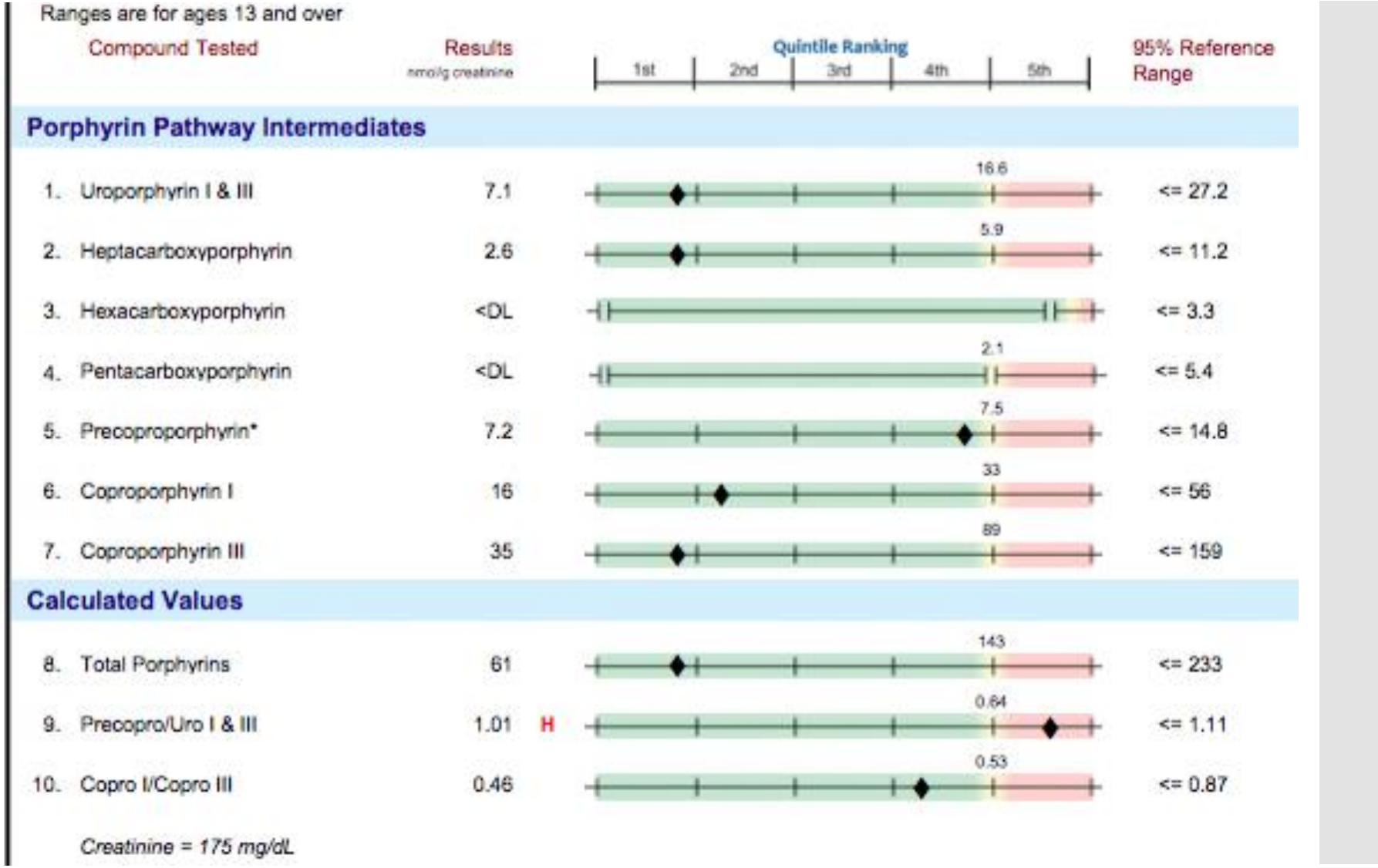
Your Results: Superoxide Dismutase is an enzyme that protects cells from increased oxidative stress and free radical damage to cell structures like membranes, mitochondria, DNA, and proteins.

Key
– – Neither chromosome carries the genetic variation.
+ – One chromosome (of two) carries the genetic variation.
+ + Both chromosomes carry the genetic variation.

(You inherit one chromosome from each parent)

GENOVA DIAGNOSTICS

Porphyrin Pathway Lab



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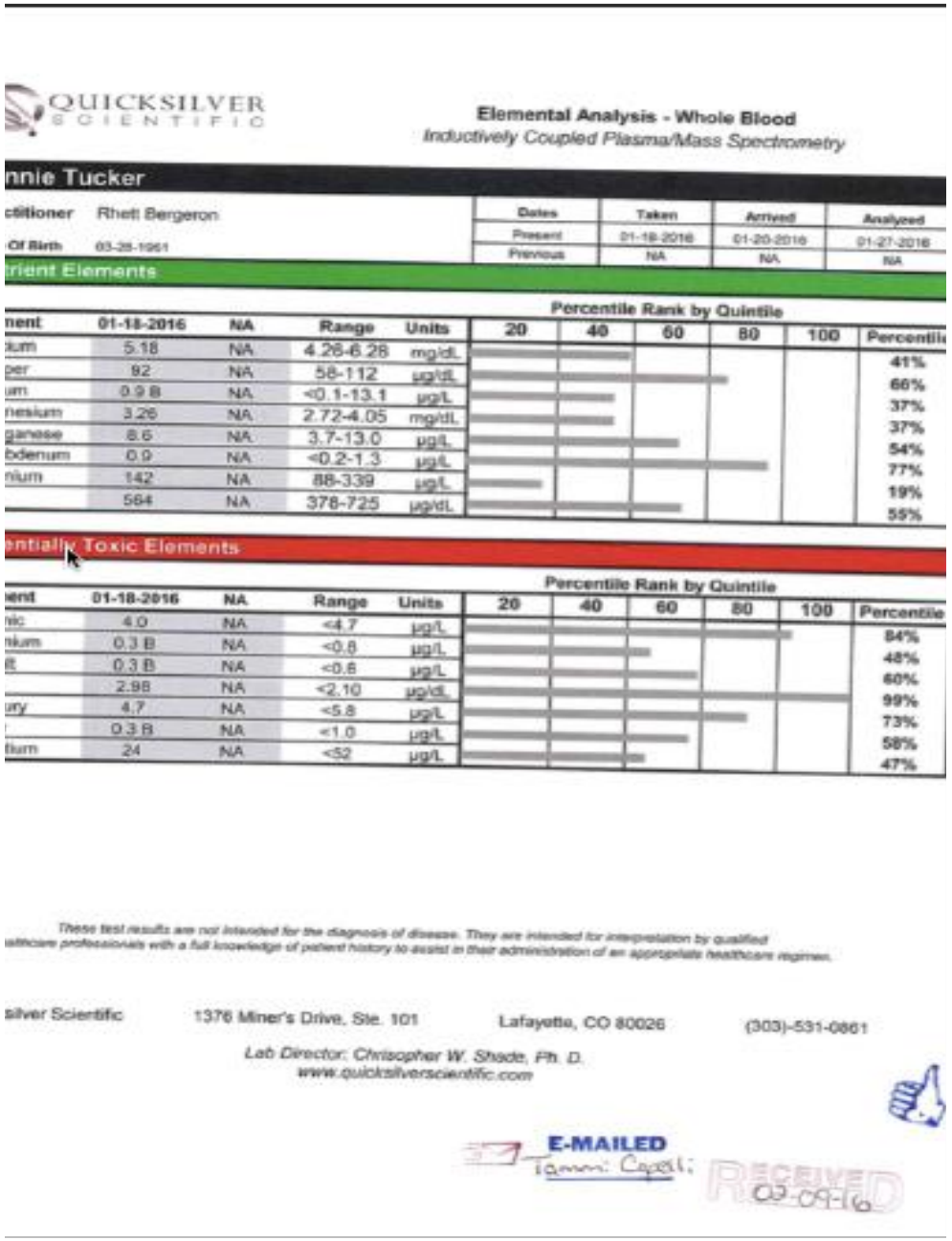
Quick Silver Lab



QUICKSILVER SCIENTIFIC

Elemental Analysis - Whole Blood
Inductively Coupled Plasma/Mass Spectrometry

nnie Tucker

ctitioner Rhett Bergeron
Of Birth 03-28-1961

Dates	Taken	Arrived	Analyzed
Present	01-18-2016	01-20-2016	01-27-2016
Previous	NA	NA	NA

rient Elements

nent	01-18-2016	NA	Range	Units	Percentile Rank by Quintile 20	40	60	80	100	Percentile
ium	5.18	NA	4.26-6.28	mg/dL						41%
per	92	NA	58-112	µg/dL						66%
um	0.9 B	NA	<0.1-13.1	µg/L						37%
nesium	3.26	NA	2.72-4.05	mg/dL						37%
ganese	8.6	NA	3.7-13.0	µg/L						54%
bdenum	0.9	NA	<0.2-1.3	µg/L						77%
nium	142	NA	88-339	µg/L						19%
	564	NA	378-725	µg/dL						55%

entially Toxic Elements

ent	01-18-2016	NA	Range	Units	Percentile Rank by Quintile 20	40	60	80	100	Percentile
nic	4.0	NA	<4.7	µg/L						84%
nium	0.3 B	NA	<0.8	µg/L						48%
t	0.3 B	NA	<0.8	µg/L						60%
	2.98	NA	<2.10	µg/dL						99%
ury	4.7	NA	<5.8	µg/L						73%
	0.3 B	NA	<1.0	µg/L						58%
tium	24	NA	<52	µg/L						47%

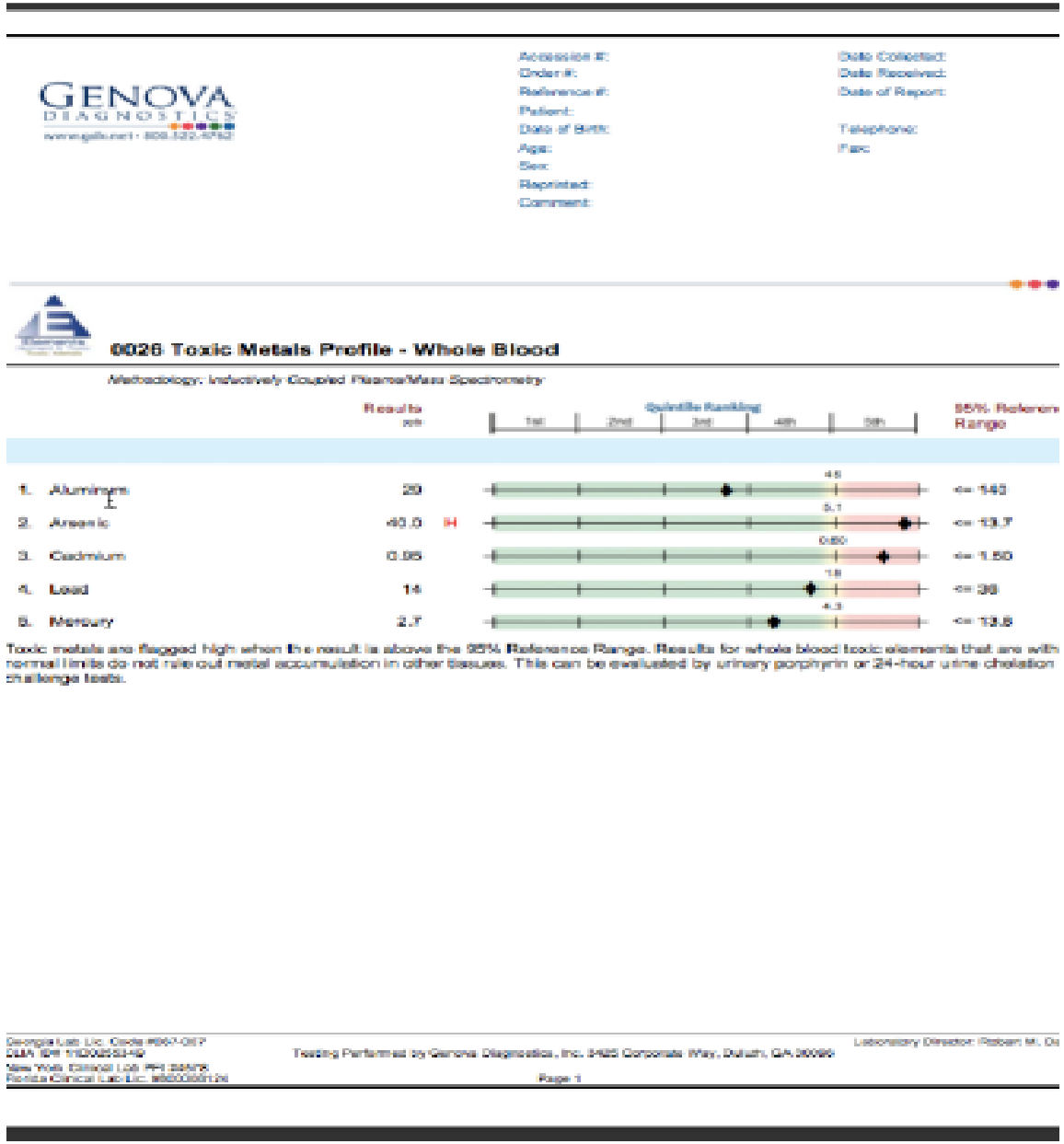
These test results are not intended for the diagnosis of disease. They are intended for interpretation by qualified healthcare professionals with a full knowledge of patient history to assist in their administration of an appropriate healthcare regimen.

Silver Scientific 1376 Miner's Drive, Ste. 101 Lafayette, CO 80026 (303)-531-0861

Lab Director: Christopher W. Shade, Ph. D.
www.quicksilverscientific.com

E-MAILED
Tamm: Capell: RECEIVED 02-09-16

Genova Lab Toxic Metals



GENOVA DIAGNOSTICS

Accession #:
Order #:
Reference #:
Patient:
Date of Birth:
Age:
Sex:
Reprinted:
Comment:

Date Collected:
Date Received:
Date of Report:

Telephone:
Fax:

0026 Toxic Metals Profile - Whole Blood

Methodology: Inductively Coupled Plasma/Mass Spectrometry

		Results µg/g		Quintile Ranking 1st 2nd 3rd 4th 5th	95% Reference Range
1.	Aluminum	29		45	<= 143
2.	Arsenic	40.0	H	5.1	<= 13.7
3.	Cadmium	0.95		0.60	<= 1.50
4.	Lead	14		1.8	<= 38
5.	Mercury	2.7		4.3	<= 13.8

Toxic metals are flagged high when the result is above the 95% Reference Range. Results for whole blood toxic elements that are with normal limits do not rule out metal accumulation in other tissues. This can be evaluated by urinary porphyrin or 24-hour urine chelation challenge tests.

Georgia Lab Lic. Cert# 9997-017
CLIA ID# 11D0653349
New York Clinical Lab PFI 35478
Florida Clinical Lab Lic. #800008124

Testing Performed by Genova Diagnostics, Inc. 3450 Corporate Way, Duluth, GA 30096

Laboratory Director: Robert M. Ou

Page 1

Testing for Mercury / Metal Toxicity

Provoked urine challenges - DMSA / DMPS / EDTA

Extensive history, literature, controversy, and ignorance

Limited danger - but real - dosing and compatibility is important

Heavy Metal Testing

- Heavy Metal Testing - provoked urine
- Example - nurse with memory concerns
- ex. oral DMSA (Chelex) urine lead - 60
- ex. IV DMPS urine lead - 120
- lead levels were 2x the levels after DMPS

Testing for Mercury / Metal Toxicity - basic considerations of urine provoked testing

DMSA - methylmercury or organic mercury

DMPS - inorganic mercury

DMSA - does not effect or pull from amalgams

DMPS - pulls from amalgams

Consider using both compatibly

Testing for Mercury / Metal Toxicity - basic considerations of urine provoked testing

- Decreased glutathione level can mask a high body burden of metals
- Repeated detoxification and supporting therapy (minerals, sulfur) - before significant excretion occurs
- Lower doses of chelator agents may fail to increase excretion significantly
- Higher doses may be needed for provocation testing vs. lower doses for long-term treatment
- Detoxification / chelating agent may preferentially bind to one metal first - hide the presence of other metals
- Mercury can be tightly bound to body tissue - may not be removed until significant amounts of other toxic metals have been removed

Warning - Na2EDTA - provoking and treatment

Na2EDTA - EDTA (slow) vs. CaNaEDTA (fast)

Acute fatal hypocalcemia have been reported following the improper administrations

Pediatrics. 2006 Aug;118(2):e534-6.

Deaths resulting from hypocalcemia after administration of edetate disodium: 2003-2005

From 2003 to 2005, deaths of 3 individuals as a result of cardiac arrest caused by hypocalcemia during chelation therapy were reported to the Centers for Disease Control and Prevention. Two were children.

Clin Toxicol (Phila). 2008 Dec;46(10):1083-4. doi: 10.1080/15563650701261488.

Pediatric fatality secondary to EDTA chelation.

CASE REPORT:

A five-year-old autistic male - while receiving his third treatment he went into cardiac arrest - had been given edetate disodium rather than edetate calcium disodium - profound hypocalcemia / cardiac arrest - that led to his death.

American College of Medical Toxicology Position Statement on Post-Chelator Challenge Urinary Metal Testing

American College of Medical Toxicology

Heavy metals are ubiquitous in the environment

Exposure is constantly occurring

Chelating agents

- Bind metallic and metalloid elements
- Have been shown to increase their elimination from the body.
- Mobilize metals in healthy individuals who have a body burden considered normal for a standard reference population
- Mobilize metals in those who are determined to have a high body burden

Chelating agents may

- Increase the elimination of certain essential elements (zinc, copper, iron)
- Promote target organ redistribution of metallic elements of concern such as mercury

Position of the American College of Medical Toxicology - post-challenge urinary metal testing has not been scientifically validated

- Has no demonstrated benefit
- May be harmful when applied in the assessment and treatment of patients in whom there is concern for metal poisoning

Testing for Antibodies - Metals and Their Binding Proteins

Metals can bind to different amino acids and become antigenic

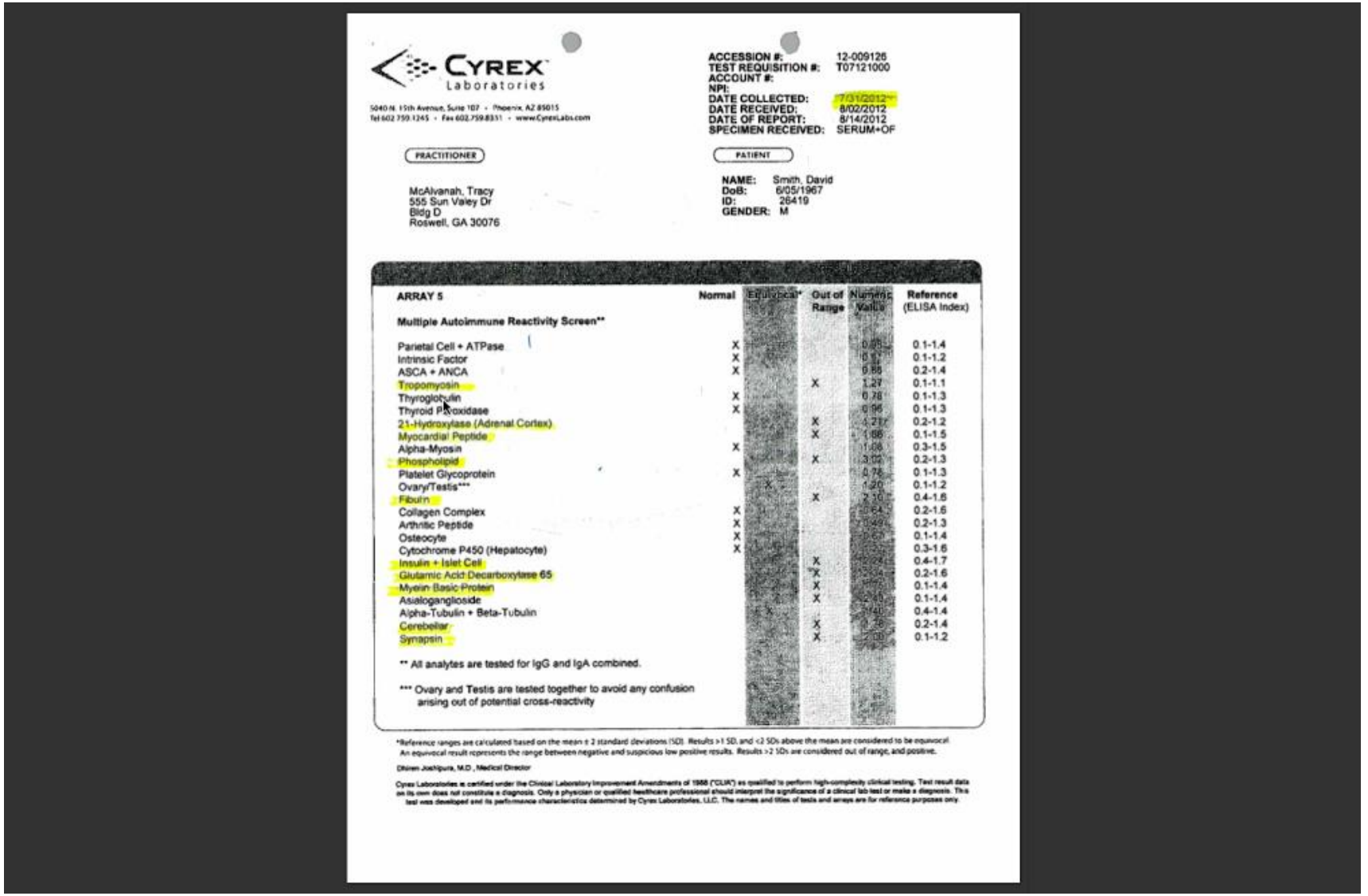
Activate T-cells - production antibody (IgG, IgM, IgA) - auto-immune

Ex. nuclear proteins - fibrillarin and chromatin (30-50% of children with autism + Abs)

Cyrex - Neurological Autoimmune Reactivity Screen

- IgG and IgA
- Myelin basic protein
- Asialoganglioside
- Alph and Beta Tubulin
- Cerebellar
- Synapsin

Cyrex Lab



CYREX Laboratories

5040 N. 15th Avenue, Suite 107 • Phoenix, AZ 85015
Tel 602.759.1245 • Fax 602.759.8331 • www.CyrexLabs.com

ACCESSION #: 12-009126
TEST REQUISITION #: T07121000
ACCOUNT #:
NPI:
DATE COLLECTED: 7/31/2012
DATE RECEIVED: 8/02/2012
DATE OF REPORT: 8/14/2012
SPECIMEN RECEIVED: SERUM+OF

PRACTITIONER

McAlvanah, Tracy
555 Sun Valey Dr
Bldg D
Roswell, GA 30076

PATIENT

NAME: Smith, David
DoB: 6/05/1967
ID: 26419
GENDER: M

ARRAY 5 Multiple Autoimmune Reactivity Screen**	Normal	Equivocal*	Out of Range	Numeric Value	Reference (ELISA Index)
Parietal Cell + ATPase	X			0.05	0.1-1.4
Intrinsic Factor	X			0.61	0.1-1.2
ASCA + ANCA	X			0.85	0.2-1.4
Tropomyosin			X	1.27	0.1-1.1
Thyroglobulin	X			0.78	0.1-1.3
Thyroid Peroxidase	X			0.96	0.1-1.3
21-Hydroxylase (Adrenal Cortex)			X	1.21	0.2-1.2
Myocardial Peptide			X	1.66	0.1-1.5
Alpha-Myosin	X			1.06	0.3-1.5
Phospholipid			X	3.02	0.2-1.3
Platelet Glycoprotein	X			0.78	0.1-1.3
Ovary/Testis***		X		1.20	0.1-1.2
Fibulin			X	2.10	0.4-1.6
Collagen Complex	X			0.64	0.2-1.6
Arthritic Peptide	X			0.49	0.2-1.3
Osteocyte	X			0.63	0.1-1.4
Cytochrome P450 (Hepatocyte)	X			0.73	0.3-1.6
Insulin + Islet Cell			X	2.24	0.4-1.7
Glutamic Acid Decarboxylase 65			X	2.34	0.2-1.6
Myelin Basic Protein			X	1.64	0.1-1.4
Asialoganglioside			X	2.18	0.1-1.4
Alpha-Tubulin + Beta-Tubulin		X		1.40	0.4-1.4
Cerebellar			X	1.78	0.2-1.4
Synapsin			X	1.00	0.1-1.2

** All analytes are tested for IgG and IgA combined.

*** Ovary and Testis are tested together to avoid any confusion arising out of potential cross-reactivity

*Reference ranges are calculated based on the mean ± 2 standard deviations (SD). Results >1 SD, and <2 SDs above the mean are considered to be equivocal. An equivocal result represents the range between negative and suspicious low positive results. Results >2 SDs are considered out of range, and positive.

Dhiren Jashpura, M.D., Medical Director

Cyrex Laboratories is certified under the Clinical Laboratory Improvement Amendments of 1988 ("CLIA") as qualified to perform high-complexity clinical testing. Test result data on its own does not constitute a diagnosis. Only a physician or qualified healthcare professional should interpret the significance of a clinical lab test or make a diagnosis. This test was developed and its performance characteristics determined by Cyrex Laboratories, LLC. The names and titles of tests and arrays are for reference purposes only.

Heavy Metal Testing - Autoimmune Antibody

Environ Health Perspect; 2015

Mercury Exposure and Antinuclear Antibodies among Females of Reproductive Age in the United States: NHANES

1,352 females from the National Health and Nutrition Examination Survey (NHANES) 1999–2004

Examined associations between mercury biomarkers and antinuclear antibody (ANA) positivity and titer strength.

Hair, blood, urine

16% ANA positive - speckled staining pattern

The higher the ANA, the stronger the correlation with mercury levels

Methylmercury, at low levels generally considered safe, was associated with subclinical autoimmunity among reproductive-age females

Autoantibodies may predate clinical disease by years

Heavy Metal Testing - Porphyrins

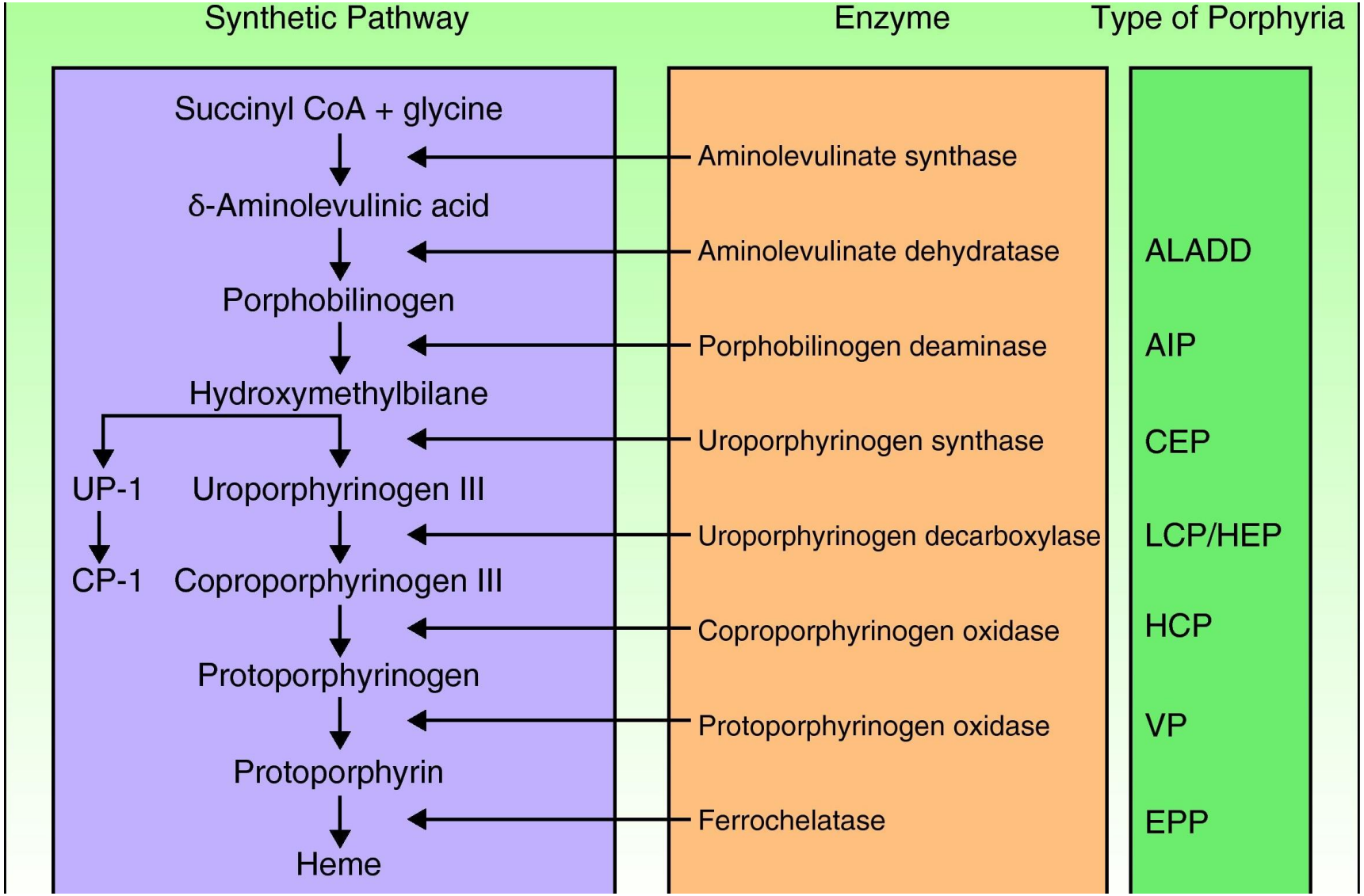
Porphyrin pathway - eight enzymes - 4 steps in mitochondrial / 4 steps in cytosol

Important in heme and cytochromes synthesis

Effects energy and detoxification

Urinary porphyrin testing - 1940s

Porphyrin Pathways



Heavy Metal Testing - Porphyrins

Urine porphyrins - biomarkers of toxins

1. Pathway is highly active - large accumulations of intermediates

2. Enzymes of the porphyrin pathway are widely distributed in body

3. Highly sensitive to the presence of various toxins

Conditions That Can Cause Porphyria

Conditions That Can Cause Porphyria	
Genetic Disorders	
Hereditary hyperbilirubinemias	– Dubin–Johnson syndrome – Rotor's syndrome
Bronze baby syndrome	
Erythrohepatic protoporphyria	
Hereditary tyrosinemia	
Diabetes mellitus	
Myocardial infarction	
Hematologic diseases	– Hemolytic, sideroachrestic, sideroblastic, aplastic anemias – Ineffective erythropoiesis (intramedullary hemolysis) – Pernicious anemia – Thalassemia – Leukemia – Erythroblastosis
Disturbance of iron metabolism	– Hemosiderosis – Idiopathic and secondary hemochromatosis – Iron de ciency anemia
Diseases	
Infectious diseases	– Mononucleosis – Acute poliomyelitis
Liver diseases	– Cirrhosis – Active chronic hepatitis – Toxic and infectious hepatitis – Fatty liver – Alcoholic liver syndromes – Drug injury – Cholestasis – Cholangitis – Biliary cirrhosis
Malignancies	– Hepatocellular tumors – Hepatic metastases – Pancreatic carcinoma – Lymphomatosis
Other Conditions	
Pregnancy	
Carbohydrate fasting	

Heavy Metal Testing - Porphyrins

Inherited porphyrin enzyme deficiencies - 90% are healthy throughout adulthood until their porphyria is triggered

1. Toxic chemicals or drugs
2. An acute illness or worsening chronic condition
3. Major dietary change

Heavy Metal Testing - Porphyrins

Altered porphyrin metabolism as a biomarker of mercury exposure and toxicity

Can J Physiol Pharmacol 1996 Feb;74(2):210-215

Urinary Porphyrin Profiling

Environmental Toxin-induced Porphyrinurias	
Environmental toxin	Urinary porphyrin elevation (or as noted)
Arsenic	Uroporphyrins Coproporphyrin I High Copro I/III ratio
Mercury	Precoproporphyrin Pentacarboxyporphyrin Coproporphyrin (total)
Lead	Aminolevulinic acid (ALA) Coproporphyrin III Coproporphyrin I (sometimes) Zinc protoporphyrin
Hexachlorobenzene	Uroporphyrins
Methyl chloride	Coproporphyrins
Dioxin	Uroporphyrins
Polyvinylchloride	Coproporphyrins
Polybrominated biphenyl	Coproporphyrins (Uroporphyrins)

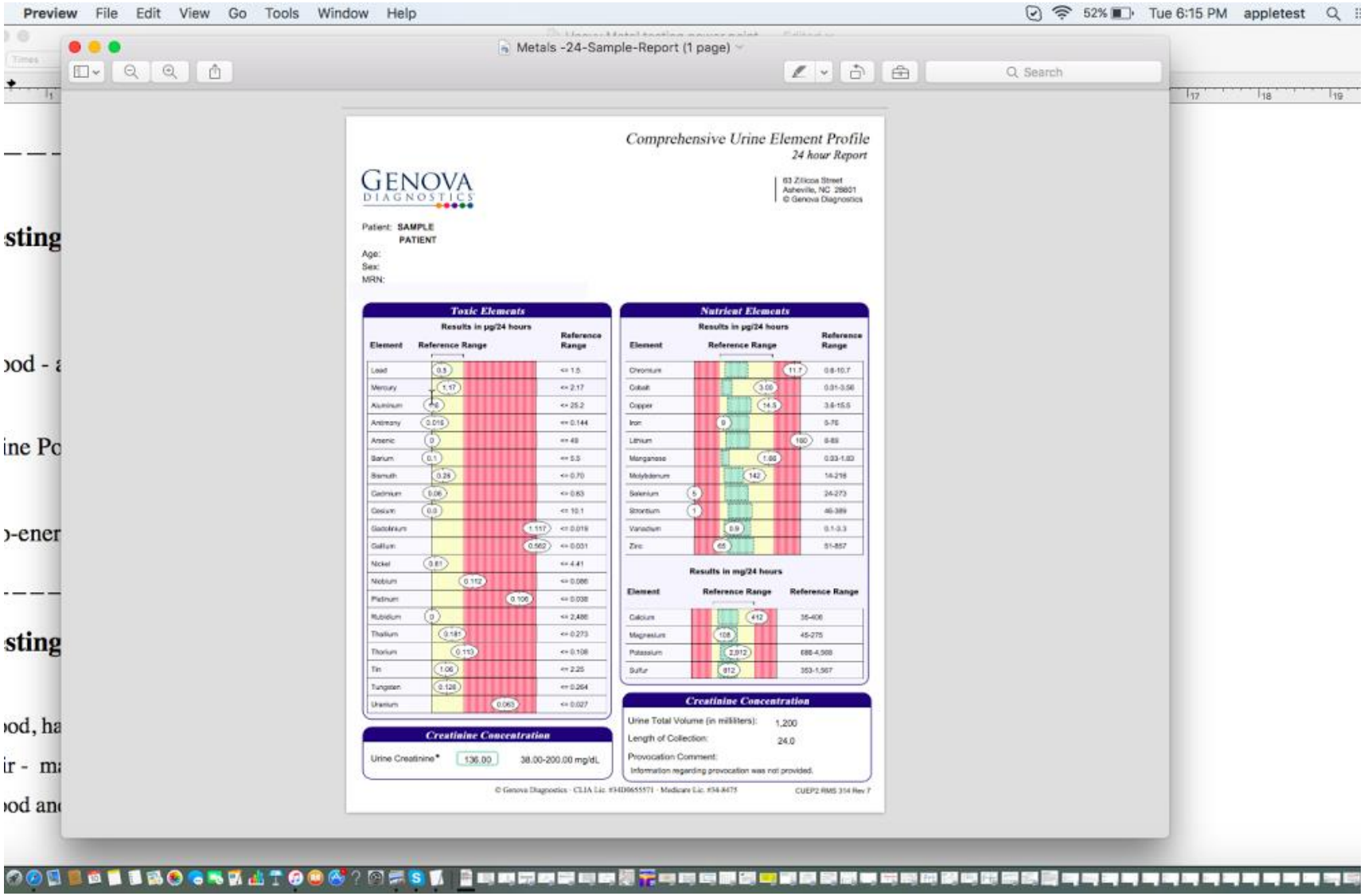
Heavy Metal - evaluation / testing - additional considerations:

Mineral

Anti-oxidant markers / detoxification - Sulfur status

Detoxification pathways - genetics and functional

Genova Lab


Preview File Edit View Go Tools Window Help
Tue 6:15 PM appletest
Metals -24-Sample-Report (1 page)
Search
Comprehensive Urine Element Profile
24 hour Report
GENOVA DIAGNOSTICS
Patient: SAMPLE PATIENT
Age:
Sex:
MRN:
Toxic Elements
Results in µg/24 hours
Element
Reference Range
Reference Range
Lead
Mercury
Aluminum
Antimony
Arsenic
Barium
Bismuth
Cadmium
Cesium
Gadolinium
Gallium
Nickel
Niobium
Platinum
Rubidium
Thallium
Thorium
Tin
Tungsten
Uranium
Creatinine Concentration
Urine Creatinine*
136.00
38.00-200.00 mg/dL
Nutrient Elements
Results in µg/24 hours
Element
Reference Range
Reference Range
Chromium
Cobalt
Copper
Iron
Lithium
Manganese
Molybdenum
Selenium
Strontium
Vanadium
Zinc
Results in mg/24 hours
Element
Reference Range
Reference Range
Calcium
Magnesium
Potassium
Sulfur
Creatinine Concentration
Urine Total Volume (in milliliters):
1,200
Length of Collection:
24.0
Provocation Comment:
Information regarding provocation was not provided.

Heavy Metal - evaluation / testing - Minerals

sample - genova mineral metal sample report

Quick Silver Sample Report Minerals Metals – Page 1

Elemetal Analysis - Whole Blood

Inductively Coupled Plasma/Mass Spectroscopy

QUICKSILVER SCIENTIFIC

Lab ID: 127261-20
Client ID: DORMAN NANCY 03/15/47 F
Collection Date: 10/08/2015
Date Received: 10/15/2015
Date Analyzed: 11/01/2015
Batch: WG693751

ACZ Laboratories, Inc

Element	Result	Units	Reference Range	Percentile Rank by Quintile (20 / 40 / 60 / 80 / 100)
Nutrient Elements				
Calcium	4.79	mg/dL	4.00 - 6.52	30%
Chromium	8	µg/L	< 1 - 11	64%
Copper	97	µg/dL	65 - 116	55%
Lithium	<1	µg/L	< 1 - 10	N/A
Magnesium	4.25	mg/dL	2.84 - 4.32	94%
Molybdenum	0.4 B	µg/L	< 0.5 - 1.9	27%
Selenium	486	µg/L	108 - 495	98%
Zinc	636	µg/dL	465 - 825	48%
Potentially Toxic Elements				
Antimony	5.5	µg/L	< 11	38%
Arsenic	1.2 B	µg/L	< 5.1	41%
Barium	3.6	µg/L	< 4.1	89%
Cadmium	0.8 B	µg/L	< 0.8	92%
Cobalt	0.9 B	µg/L	< 0.5	N/A
Lead	1.04	µg/dL	< 2.51	32%
Mercury	3.1	µg/L	< 5.8	62%
Silver	<0.5	µg/L	< 0.8	N/A
Strontium	32	µg/L	< 43	73%
Titanium	6 B	µg/L	< 25	N/A

RECEIVED
DEC 05 2015

These test results are not for the diagnosis of disease. They are intended to provide nutritional guidelines to qualified healthcare professionals with a full knowledge of patient history to assist in their administration of an appropriate healthcare regimen.

Quicksilver Scientific 1375 Miner's Drive, Ste. 101 Lafayette, CO 80026 (303) 531-0861
Lab Director: Christopher W. Shade, Ph.D.
www.quicksilverscientific.com

Quick Silver Sample Report Minerals Metals- Page 2

Elemetal Analysis - Whole Blood

Inductively Coupled Plasma/Mass Spectroscopy

QUICKSILVER SCIENTIFIC

Lab ID: L27261-20
Client ID: DORNAN NANCY 03/15/47 F
Collection Date: 10/08/2015
Date Received: 10/15/2015
Date Analyzed: 11/05/2015
Batch: WG393731

ACZ Laboratories, Inc.

Report Comments and Interpretation

Reference ranges compiled from laboratory generated data to reflect 5th-95th (or <95th) percentile ranking of sample population with the following exceptions:
-Upper limit of reference range for Antimony, Arsenic, Cadmium and Lead reflect the 90th percentile of population data.
-Upper reference range for Mercury reflects EPA specified guidelines.

The Blood Lead reference level for children ages 1-5 is 5 ug/dL which represents the highest 2.5% of the tested population (97.5 percentile).
-CDC Update October 30, 2012

Due to solubility issues specifically associated with Silver in this high pH matrix, results are estimated and typically have a low bias when detected.

Results for elements not detected are reported as "< method detection limit"

Percentile Rankings are only plotted for elements with sufficient population data and only for results greater than the element's detection limit.

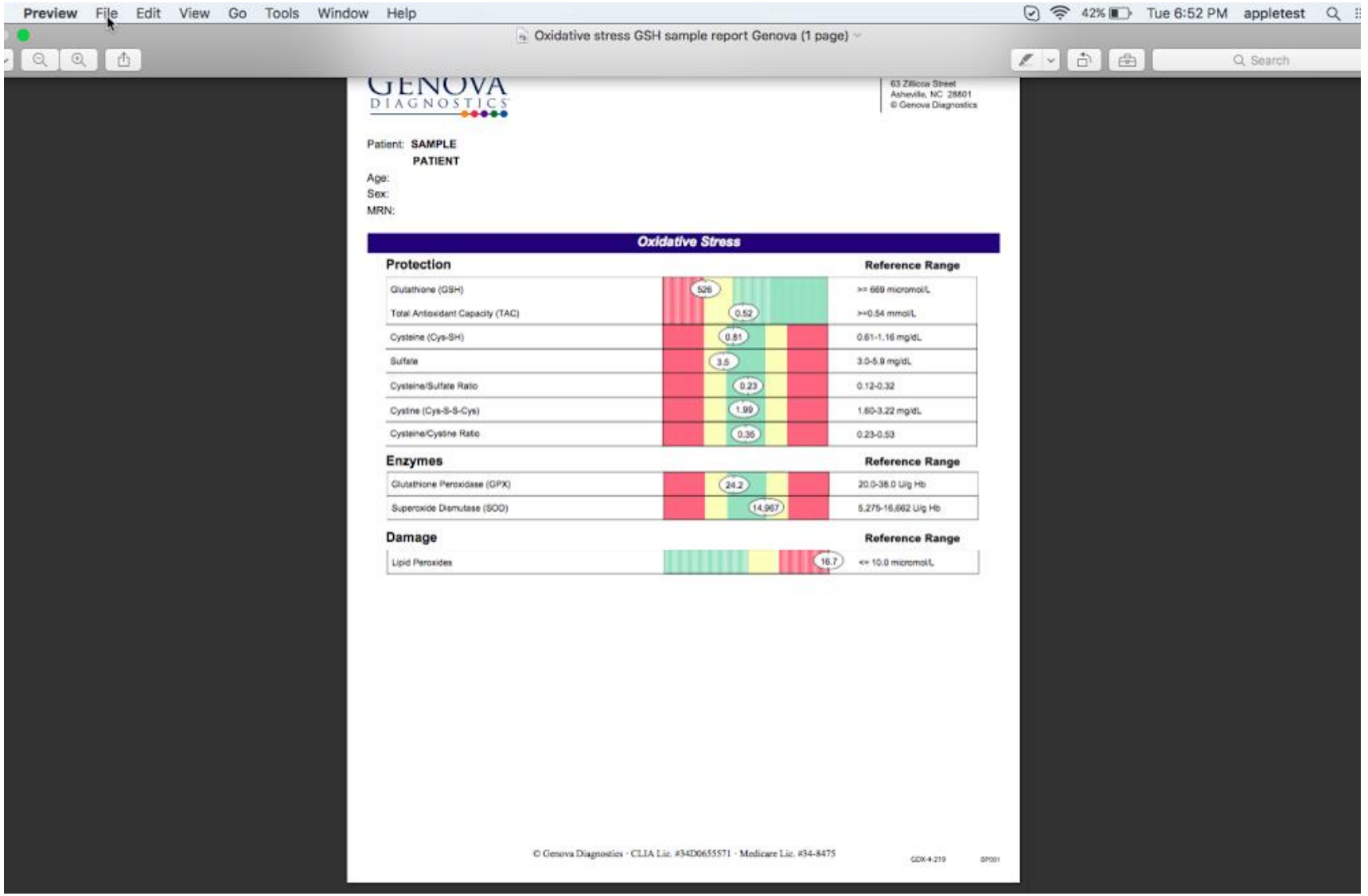
Results containing a "B" indicate that the reported value is between the method's detection and quantitation limit and should be considered estimated. These results are reported with 99% confidence that the result is greater than zero but the data is not quantifiable and the uncertainty is +/- 100%.

Report Qualifiers

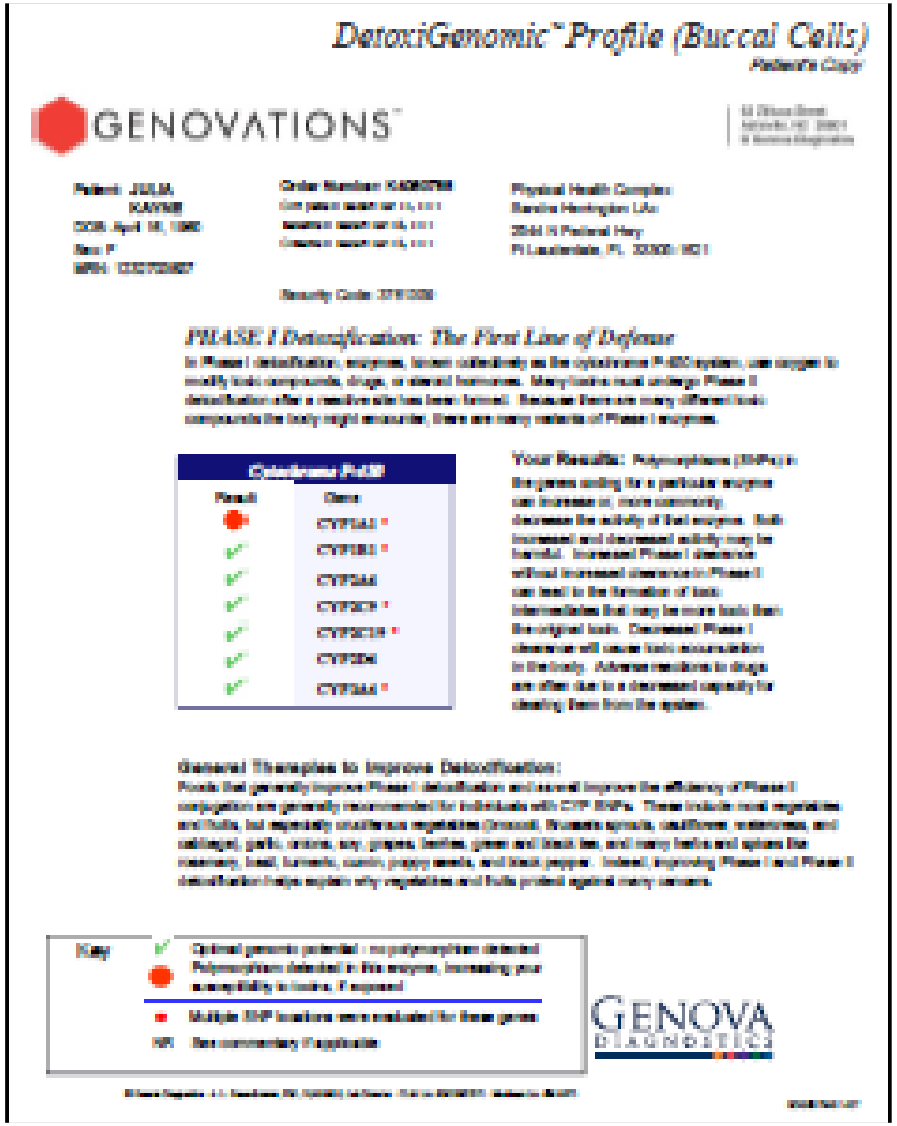
Cobalt
CH = Analyte concentration verified by repeat analysis.

Quicksilver Scientific 1376 Miner's Drive, Ste. 101 Lafayette, CO 80026 (303) 531-0861
Lab Director: Christopher W. Steele, Ph.D.
www.quicksilverscientific.com

Genova Lab


Preview File Edit View Go Tools Window Help
42% Tue 6:52 PM appletest
Oxidative stress GSH sample report Genova (1 page)
Search
GENOVA DIAGNOSTICS
63 Zillicoa Street
Asheville, NC 28801
© Genova Diagnostics
Patient: SAMPLE PATIENT
Age:
Sex:
MRN:
Oxidative Stress
Protection
Reference Range
Glutathione (GSH) 526 >= 669 micromol/L
Total Antioxidant Capacity (TAC) 0.52 >=0.54 mmol/L
Cysteine (Cys-SH) 0.81 0.61-1.16 mg/dL
Sulfate 3.5 3.0-5.9 mg/dL
Cysteine/Sulfate Ratio 0.23 0.12-0.32
Cystine (Cys-S-S-Cys) 1.99 1.60-3.22 mg/dL
Cysteine/Cystine Ratio 0.36 0.23-0.53
Enzymes
Reference Range
Glutathione Peroxidase (GPX) 24.2 20.0-36.0 U/g Hb
Superoxide Dismutase (SOD) 14,967 5,275-16,662 U/g Hb
Damage
Reference Range
Lipid Peroxides 16.7 <= 10.0 micromol/L
© Genova Diagnostics · CLIA Lic. #34D0655571 · Medicare Lic. #34-8475
GDX-4-219
BP001

Genomic Profile



DetoxiGenomic™ Profile (Buccal Cells)

Patient's Copy

GENOVATIONS™

PHASE I Detoxification: The First Line of Defense

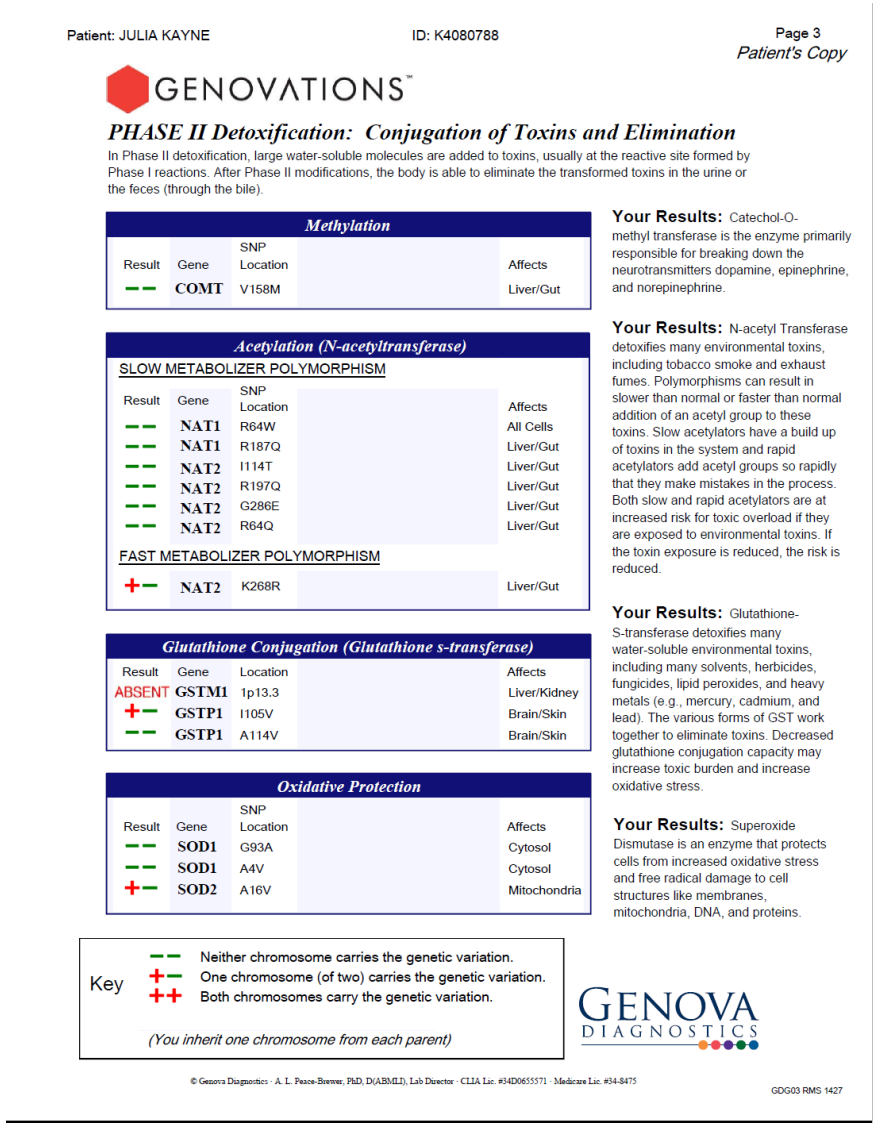
Your Results:

General Therapies to Improve Detoxification:

Key

GENOVA DIAGNOSTICS

Genomic Profile



Patient: JULIA KAYNE ID: K4080788 Page 3
Patient's Copy

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).

Methylation

Result	Gene	SNP Location	Affects
−−	COMT	V158M	Liver/Gut

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

Acetylation (N-acetyltransferase)

SLOW METABOLIZER POLYMORPHISM

Result	Gene	SNP Location	Affects
−−	NAT1	R64W	All Cells
−−	NAT1	R187Q	Liver/Gut
−−	NAT2	I114T	Liver/Gut
−−	NAT2	R197Q	Liver/Gut
−−	NAT2	G286E	Liver/Gut
−−	NAT2	R64Q	Liver/Gut

FAST METABOLIZER POLYMORPHISM

Result	Gene	SNP Location	Affects
+−	NAT2	K268R	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.

Glutathione Conjugation (Glutathione s-transferase)

Result	Gene	Location	Affects
ABSENT	GSTM1	1p13.3	Liver/Kidney
+−	GSTP1	I105V	Brain/Skin
−−	GSTP1	A114V	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.

Oxidative Protection

Result	Gene	SNP Location	Affects
−−	SOD1	G93A	Cytosol
−−	SOD1	A4V	Cytosol
+−	SOD2	A16V	Mitochondria

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

Key
−− Neither chromosome carries the genetic variation.
+− One chromosome (of two) carries the genetic variation.
++ Both chromosomes carry the genetic variation.

(You inherit one chromosome from each parent)

GENOVA DIAGNOSTICS

Cadmium - Toxicity – " Cd - female personality"

Tough cowgirl or "tom" girl

Older physical appearance memory impairment

Unhappy or anger demeanor crudeness
Increased libido critical or negative regarding males
Aggressiveness / violence lack of compassion

Energy vampires

Cadmium - Exposure

Cigarette smoking Marijuana
Tap water Coffee
Hydrogenated vegetable oils Cigarette paper
Shellfish Large ocean fish - tuna, cod, haddock
Maternal transfer Water contamination
Braking systems

Manufacturing / Industrial:

Plating, galvanizing, semiconductor, links, pigments in dyes and paints
Television screens, lasers, batteries, paint pigments
Cosmetics
Barrier in nuclear fission
Used with zinc to weld seals in lead water pipes < 1960s

Detection / Assessment for Cadmium:

Tissue Hair Analysis - can be under reflected

Accumulates more in bones, kidneys, and brain

Urinary (unprovoked) cadmium - not reflective of body burden

Blood cadmium - indicator of recent exposure - 3 month

Provoked urine challenge - deposited stores in kidneys and rough estimate of body burden

Reasonable to screen high risk individuals (smokers, persons with industrial exposure)

Cadmium Toxicity Effects / Symptoms:

- Zinc deficiency - antagonizes zinc (more than 300 enzymes)
  - Infertility in men - low sperm count
  - DNA / RNA processing - Defective gene expression
- Copper accumulation / dominance
- Mental / Behavioral - ADHD, violence, anti-social , hardened personality
- Degenerative - premature aging and hardening of tissue - arteries and kidneys
- Renal insufficiency
- High blood pressure
- Chronic cough, lung cancer
- Birth Defects
- Inhalation of vapor / particles during industrial exposure (welding or soldering) - chemical pneumonitis

Cadmium - Toxicity - " Cd - Female Personality"

Tough cowgirl or "tom" girl

Older physical appearance

Unhappy or anger demeanor

Increased libido

Aggressiveness / violence

Energy vampires

memory impairment

crudeness

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lack of compassion

Cadmium - Exposure

Cigarette smoking

Tap water

Hydrogenated vegetable oils

Shellfish

Marijuana

Coffee

Cigarette paper

Large ocean fish - tuna, cod, haddock

Water contamination

Maternal transfer

Braking systems

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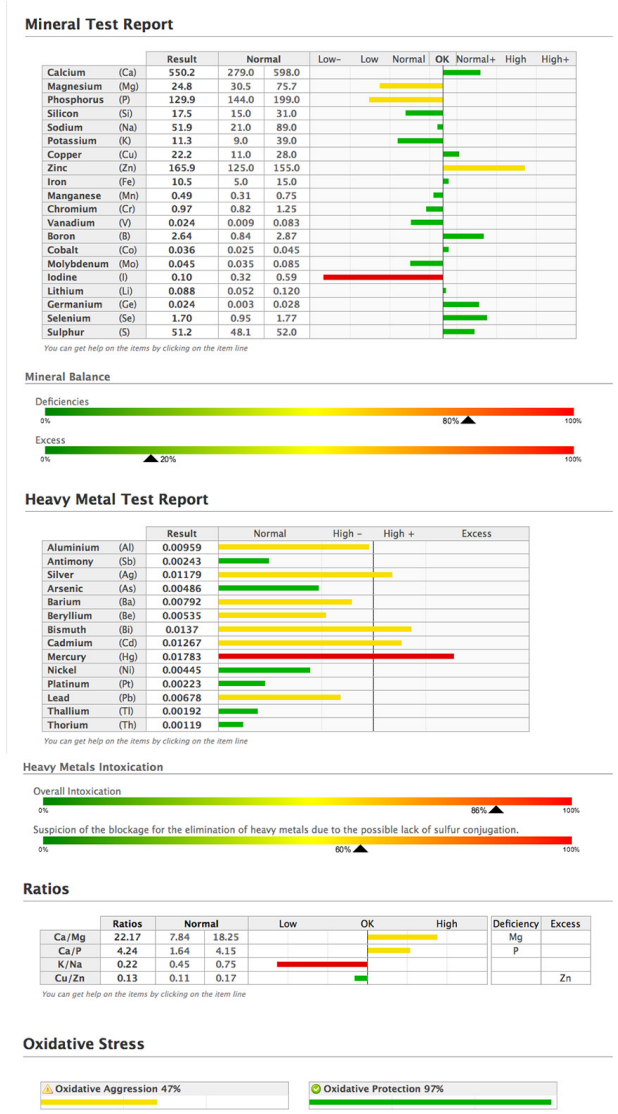
OligoScan – Spectro-Photometry

- Using light to measure absorbance level or optical density of specific molecule
- Every molecule reflects light in a unique way - measurable
- Based on Beer-Lambert law - absorbance or light interaction - directly proportional to concentration of molecules
- Surface of the hand - epidermis analysis
- Tissue / intracellular levels

OligoScan – Sample report



Mineral Test Report

		Result	Normal		Low–	Low	Normal	OK	Normal+	High	High+
Calcium	(Ca)	550.2	279.0	598.0							
Magnesium	(Mg)	24.8	30.5	75.7							
Phosphorus	(P)	129.9	144.0	199.0							
Silicon	(Si)	17.5	15.0	31.0							
Sodium	(Na)	51.9	21.0	89.0							
Potassium	(K)	11.3	9.0	39.0							
Copper	(Cu)	22.2	11.0	28.0							
Zinc	(Zn)	165.9	125.0	155.0							
Iron	(Fe)	10.5	5.0	15.0							
Manganese	(Mn)	0.49	0.31	0.75							
Chromium	(Cr)	0.97	0.82	1.25							
Vanadium	(V)	0.024	0.009	0.083							
Boron	(B)	2.64	0.84	2.87							
Cobalt	(Co)	0.036	0.025	0.045							
Molybdenum	(Mo)	0.045	0.035	0.085							
Iodine	(I)	0.10	0.32	0.59							
Lithium	(Li)	0.088	0.052	0.120							
Germanium	(Ge)	0.024	0.003	0.028							
Selenium	(Se)	1.70	0.95	1.77							
Sulphur	(S)	51.2	48.1	52.0							

You can get help on the items by clicking on the item line

Mineral Balance

Deficiencies

0% 80% 100%

Excess

0% 20% 100%

Heavy Metal Test Report

		Result	Normal	High –	High +	Excess
Aluminium	(Al)	0.00959				
Antimony	(Sb)	0.00243				
Silver	(Ag)	0.01179				
Arsenic	(As)	0.00486				
Barium	(Ba)	0.00792				
Beryllium	(Be)	0.00535				
Bismuth	(Bi)	0.0137				
Cadmium	(Cd)	0.01267				
Mercury	(Hg)	0.01783				
Nickel	(Ni)	0.00445				
Platinum	(Pt)	0.00223				
Lead	(Pb)	0.00678				
Thallium	(Tl)	0.00192				
Thorium	(Th)	0.00119				

You can get help on the items by clicking on the item line

Heavy Metals Intoxication

Overall Intoxication

0% 86% 100%

Suspicion of the blockage for the elimination of heavy metals due to the possible lack of sulfur conjugation.

0% 60% 100%

Ratios

	Ratios	Normal		Low	OK	High	Deficiency	Excess
Ca/Mg	22.17	7.84	18.25				Mg	
Ca/P	4.24	1.64	4.15				P	
K/Na	0.22	0.45	0.75					
Cu/Zn	0.13	0.11	0.17					Zn

You can get help on the items by clicking on the item line

Oxidative Stress

Oxidative Aggression 47%

Oxidative Protection 97%

- J Occup Med Toxicol. 2006
- The toxicity of cadmium and resulting hazards for human health
- Renal insufficiency cough
- Prostate cancer carcinogenic
- Bone diseases - demineralization
- Ovarian dysfunction - progesterone / testosterone
- Occup Environ Med. 1998 Jul;55(7):435-9.
- Cadmium may be a risk factor for osteoporosis
- The Scientific World Journal - Volume 2013
- Review Article
- Cadmium Toxicity and Treatment

Journal of Toxicology Volume 2011

Review Article

- Heavy Metal Poisoning and Cardiovascular Disease
- Cardiovascular disease (CVD) is an increasing health problem and traditional risk factors fail to account for all deaths from CVD
- Environmental, dietary and lifestyle behavioral factors that are the control keys in the progress of this disease
- Evidence for the link between heavy metals with CVD and the proposed mechanisms of toxicity

Metal Detox Treatment

Heavy Metal Detoxification - Chelation Therapy:

Heavy Metals - Basic Facts

Exposure - unavoidable / low grade / continuous

Levels - accumulation

Toxicity - non-specific and subtle changes - unrecognized

Every person needs heavy metal assessment - at some time

Response - Responsibility - Detoxify or Die

Metal Detoxification - safe and effective

Heavy Metal - BASIC TREATMENT STRATEGY

Identify / remediate exposure

Comprehensive strategy - more successful / better tolerated

- Chelation
- Minerals
- Anti-oxidants
- Supporting elimination
- Energetic - biocompatibility testing

The earlier in life, the better the outcomes

The slower, the better

Repeat / on-going maintenance protocols

Heavy Metal-

BASIC TREATMENT STRATEGY

- Identify exposure and discontinue / eliminate –
  fish, amalgams, vaccines, lead pain and pipes, treated wood
- Optimize minerals - ZINC, selenium
- Support Anti-oxidant pathways
- Support sulfur based biochemistry
- Support optimal elimination / excretion in liver-bile, colon, kidneys, skin
- Target - Detoxify loosely bound / systemic metals - 1st
- Detoxify CNS - last
- Oral chelation can be effective ALONE and enhances IV chelation

Metal Detox Treatment - Components

- Elimination / Drainage Support - lymph, kidney, liver, skin
- Herbal, Homeopathic, Laser-assisted, Sauna
- Minerals - zinc, magnesium, selenium
- Sulfur - MSM, garlic, methionine, NAC
- Rx chelators - DMPS, DMSA, EDTA
- Nutraceutical / Metabolic chelators- GSH, ALA, PC
- Plant / Herbal based - chlorella, cilantro, garlic
- BioEnergetic - Homeopathic, Laser assisted
- IV Therapy - Vit C, PC, GSH, NAC, ALA, DMPS, EDTA, Minerals

Basics of Treatment

1. Diet - reduce inflammatory / processed foods / increase fiber
   - Optimize minerals and sulfur - baseline mineral assessment
   - Deficiencies of minerals and sulfur - risk factor in metal accumulation / poor response to treatment
   - MSM 1/8 - 1 tsp. 1 - 2x daily
   - Fresh garlic 1-2 cloves per day

2. Mineral Replacement
   - Multi mineral - without copper
   - Zinc 25 - 100 mg daily
   - Liquid/ Ionic minerals

3. Enhance mineral / nutrient uptake
   - HCL / Digestive enzyme
   - Repair leaky gut

4. Support intestinal elimination
   - HCL / Fiber / Vit C / Magnesium
   - Whole flaxseed - 1 - 2 tbsp. - freshly ground - add to yogurt / smoothie / oatmeal

Types of Chelators

Pharmaceutical Rx

Dietary

Plant / Herbal

Plant Nutraceutical

Nutritional / Metabolic Chelators

Homeopathic

Metal Detoxification

Pharmaceutical Chelation Therapy

- Well studied - through world
  - Effective
  - Safe
- Metal mobilization does not always equal metal excretion
- Risk of redistribution
- Can increase the excretion of minerals / induce or worsen mineral deficiencies
- Possibility of side effects - kidney damage, death, allergic reactions,
- Worsening of neurological symptoms from redistribution

Metals - History of heavy metal detoxification / chelation therapy

- Chelation was developed to combat arsenic based gas; then was gradually applied to other heavy metals
- Cant Lewis PhD - U.S. researcher - developed Lewisite - arsenic based chemical weapon, but then the Germans obtained it and threatened to use it
- **British developed British anti-lewisite (BAL) - dimercaprol - sulfur / thiol based molecule**
- BAL increased urinary excretion of Ar and significantly decreased the time of dermatitis (60 to 20 days)
- Arsenic based antibiotics in treatment of syphilis - dermatitis and hepatotoxicity
- Charity Hospital, New Orleans - Ar expose children
- BAL in the treatment of arsenic ingestion of children. Pediatrics. **1948;1**(3):372–378
- **Side effects** of BAL / Dimercaprol: Nausea and vomiting (most common), hypertension, excessive sweating and tears, pain at intramuscular injection sites

Metals - History of heavy metal detoxification / chelation therapy

Early studies on di-thiols: 1940s

Dithiol compounds as antidotes for arsenic

Biochem J. 1946; 40:535–548.

British anti-lewisite (BAL)

Nature. 1945; 156:616–619

Diagnosis and treatment of lesions due to vesicants.

Br Med J. 1944;2(4359):109–112

The effect of BAL on the excretion of arsenic in arsenical intoxication.

J Clin Investig. 1946;25(4):534–540

Metals - History of heavy metal detoxification / chelation therapy

J Med Toxicol. 2013 Dec; 9(4): 347–354.

The Role of Chelation in the Treatment of Arsenic and Mercury Poisoning

DMPS, DMSA, Dimercaprol - mainstay of chelation treatment of arsenic and mercury intoxication for more than half a century

Animal experiments and some human data: dithiol chelators enhance arsenic and mercury excretion

Controlled animal experiments support a therapeutic role for these chelators in the prompt treatment of acute poisoning by arsenic and inorganic mercury salts.

Metals - History of heavy metal detoxification / chelation therapy

1st studies –

Mice injected with arsenic - DMPS or DMSA or saline injected intraperitoneal

Rabbits - single injection of BAL

Injection given 5 min after arsenic exposure:

100 % survival

Delayed treatment > 6 h: 0% survival

Established principle -

Efficacy of chelation is greatest when administered promptly (minutes to hours) after arsenic exposure delayed chelation is diminished chelation

History of metal detoxification - chelation

Chelation and Mercury

1949 Longcope and Luetscher, John Hopkins

Oral mercuric chloride (commonly used for suicide 1920-40s)

Before availability of chelation BAL / only supportive treat - 30% mortality with BAL within 4 hour - 0% mortality

Ann Intern Med. 1949; 31:545–553

The use of BAL (British Anti-Lewisite) in the treatment of the injurious effects of arsenic, mercury, and other metallic poisons

Chelation Protocols - by National Physician Associations

1) International College of Integrative Medicine, "Diagnostic and treatment protocols for safer, effective mercury human biohazard management," Tech. Rep., Consensus Development Working Group of the International College of Integrative Medicine, Bluffton, Ohio, USA, 2003.

2) American College for Advancement in Medicine, Chelation Module, American College for Advancement in Medicine, Irvine, Calif, USA, 2010.

3) Advanced Medical Education and Services Physician Associatio, Introduction To Clinical Metal Toxicology, Advanced Medical Education and Services Physician Association, San Antonio, Tex, USA, 2007.

Autism Research Institute, Clinician Seminar Level 1, Autism Research Institute, San Diego, Calif, USA, 2010.

Acute Exposure / Toxicity of Heavy Metals - Mercury

1990 rat studies - Mercuric Chloride

Immediate high dose chelation with inj. BAL or oral DMPS or oral DMSA vs control

90% mortality in controls

High survival in treated groups

100% survival in DMPS

Chelation is effective if started promptly

Delayed treatment - loose the benefit

Hum Exp Toxicol. 1991; 10:423–430

Effect of four thiol-containing chelators on disposition of orally administered mercuric chloride.

Acute Exposure / Toxicity of Heavy Metals - mercury

Lower dose chelation in rats - examining acute nephrotoxicity of mercuric chloride with DMPS iv:

Immediate treatment with DMPS (54 mg/kg iv) - 100% protecting against oliguric renal failure delayed treatment (>24 hr.), 0% protective effect

Acta Pharmacol Toxicol. 1980; 46:81–88.

The effect of immediate and delayed treatment with DMPS on the distribution and toxicity of inorganic mercury in mice and in fetal and adult rats

DMPS – Mercury Detox Test - Standardized procedure for urine metal testing

Occupational and Environmental Medicine. 2004;61(6):535–540

Evaluation of the mercury exposure of dental amalgam patients by the Mercury Triple Test.

Hg levels in scalp hair, urine (pre-and post-challenge DMPS 200-400 mg oral), Hg release from amalgams after chew test

#2223

1.3 µg Hg/g creatinine in basal urine

32 µg Hg/g creatinine after DMPS = 32x

Conclusions:

A standardized procedure for evaluation of the magnitude and origin of the Hg burden of individuals has been developed, which, by comparison with the database presented here for the first time, can serve as a diagnostic tool.

Metal Detoxification - Rx chelators

DMSA

DMPS

EDTA

Mercury
Compartmentalization

Metals are stored in different body compartments

Intracellular	Extracellular (connective tissue)
Intravascular	Kidneys / liver
Intestinal wall	Central nervous system

Each compartment requires different detoxification approaches

Priority of compartments

1. Intestinal / kidneys / liver	Chlorella / Garlic
2. Extracellular / connective tissue	Chlorella / DMPS
3. Central nervous system	DMSA / cilantro / ALA

Metal Detoxification - Therapeutics - Pharmaceutical Chelators

DMPS

2 free sulfhydryl groups

Water-soluble complexing / chelation agent

Developed in the 1950s in the Soviet Union

Chelates - heavy metals / minerals - zinc, copper, arsenic, mercury, cadmium, lead, silver, and tin

Used effectively treat metal intoxication since the 1960s

Extensive international research / excellent safety record

Registered / approved in Germany - treatment of mercury poisoning

Not FDA approved in U.S.

Patients should be informed of the unapproved / experimental status full disclosure/informed consent document in the medical chart

DMPS - Efficacy

"Treatment mercury toxicity is well established and accepted"

"Clearly demonstrated elimination effects on the connective tissue"

59. Hurlbut KM, Maiorino RM, Mayersohn M, Dart RC, Bruce DC, Aposhian HV Determination and metabolism of dithiol chelating agents. XVI: Pharmacokinetics of 2,3-dimercapto-1-propanesulfonate after intravenous administration to human volunteers. J Pharmacol Exp Ther 1994 Feb;268(2):662-668

60. Zheng W, Maiorino RM, Brendel K, Aposhia HV. Determination and metabolism of dithiol chelating agents. Fundam Appl Toxicol 14:598-607 (1990)

61. Aposhian HV Environ Health Perspect Mobilization of mercury and arsenic in humans by sodium 2,3-dimercapto-1-propane sulfonate. 1998 Aug;106 Suppl 4:1017-1025

58. Sallsten G, Barregard L, Schutz A Clearance half-life of mercury in urine after the cessation of long term occupational exposure: influence of a chelating agent (DMPS) on excretion of mercury in urine. Occup Environ Med 1994 May;51(5):337-342

73. Aposhian HV, Maiorino RM, Gonzalez-Ramirez D, et al. Mobilization of heavy metals by newer, therapeutically useful chelating agents. Toxicology 1995 Mar 31;97(1-3):23-38

DMPS

DMPS is primarily excreted in the urine

Oral

- 40% absorption - better than DMSA
- Lower dosages / better absorption
- Less GI side effects

Clinical Patient Monitoring - during DMPS

CBC

CMP

RBC Minerals

Serum copper / Plasma zinc

Serum iron

DMPS -

74. Promotes maximal excretion of heavy metals within 2-3 hours after infusion

- Combining with Chlorella may increase the amount of mercury / metals mobilized and excreted
- U.S. - Compounded Rx - injectable, oral, topical, suppository
- Oral 100 - 400 mg daily
- IV 3-5 mg/kg - injected slowly intravenously over 5 - 15 minutes
- Repeat every1 - 4 weeks - depending on tolerability….
- After IVC 25 grams
- ** Should not be used for on-going treatment in patients that still have amalgam fillings **
- Can mobilize mercury from amalgams
- May cause seizures, cardiac arrhythmias, fatigue
- Not mutagenic, teratogenic or carcinogenic

DMPS: Safety Side Effects

DMPS Safety:

Hurlbut - volunteers were given large dose of DMPS (3 mg/kg intravenously over 5 minutes) ex. 150 mg

Transient 20 mmHg drop in systolic blood pressure during infusion

DMPS Side Effects:

Use with great caution - biocompatibility

Hypotensive effects, allergic reactions and skin rashes

High affinity for copper and zinc - replenishment

DMPS - Studies

H. V. Aposhian, "Mobilization of mercury and arsenic in humans by sodium 2,3-dimercapto-1-propane sulfonate (DMPS)," Environmental Health Perspectives, vol. 106, no. 4, pp. 1017–1025, 1998.

H. V. Aposhian, R. M. Maiorino, D. Gonzalez-Ramirez et al., "Mobilization of heavy metals by newer, therapeutically useful chelating agents," Toxicology, vol. 97, no. 1–3, pp. 23– 38, 1995.

"2,3 Dimercapto-1-propane sulfonic acid (DMPS) in the treatment of heavy metal poisoning," FDA Docket 98-n- 0182 entry for DMPS and Nguyen H. T., 1999, http://www .fda.gov/ohrms/dockets/DOCKETS/98n0182/nom005b.pdf. G. Sallsten, L. Barregard, and A. Schutz, "Clearance half-life of mercury in urine after the cessation of long term occupational exposure: influence of a chelating agent (DMPS) on excretion of mercury in urine," Occupational and Environ-mental Medicine, vol. 51, no. 5, pp. 337–342, 1994.

O. Torres-Alanis, L. Garza-Ocanas, and A. Pineyro-Lopez, "Evaluation of urinary mercury excretion after administration of 2,3-dimercaptol-propane sulfonic acid to occupation- ally exposed men," Journal of Toxicology—Clinical Toxicology, vol. 33, no. 6, pp. 717–720, 1995.

D. Gonzalez-Ramirez, M. Zuniga-Charles, A. Narro-Juarez et al., "DMPS (2,3-dimercaptopropane-1-sulfonate, dimaval) decreases the body burden of mercury in humans exposed to mercurous chloride," Journal of Pharmacology and Experimental Therapeutics, vol. 287, no. 1, pp. 8–12, 1998.

DMSP – Safety / Efficacy

Science of the Total Environment, vol. 307, no. 1–3, pp. 71–82, 2003.

"The Mt. Diwata study —Treatment of mercury intoxicated inhabitants of a gold mining area with DMPS

Workers in gold mine - chronic exposure to elemental mercury

Fish eaters - methyl mercury

Controls without significant known mercury exposure

Lab - blood, urine and hair mercury levels

Symptoms (tremor, sleepless- ness, memory loss, etc.)

106 # - oral DMPS 400 mg per day - 14-day trial - only complication was an allergic rash in one patient

Blood mercury did not decrease during the trial, despite increases in urine mercury up to 85-fold

Significant improvements - objective measures of neurological function / symptoms

Most reported subjective improvement in memory, sleeplessness, metallic taste, fatigue, anxiety, and paresthesias

Treatment efficacy - similar in both groups

DMPS Study - Challenge / Treatment - Mexico

DMPS Decreases the Body Burden of Mercury in Humans Exposed to Mercurous Chloride (topical)

Journal of Pharmacology and Experimental Therapeutics October 1998, 287 (1) 8-12

Workers involved in the production of calomel skin-bleaching lotion
In direct contact with mercurous chloride
Elevated baseline urine levels of mercury

#8 workers

All the subjects responded to the challenge dose of DMPS by increased urinary excretion of mercury.

Before 333 ug/l (50-1000)

After 4282ug/l (2000-8000)

10x fold increase in urinary elimination

Metal Detoxification - Therapeutics - Pharmaceutical Chelators

DMSA

Am Fam Physician. 1993 Dec;48(8):1496-502.

DMSA Succimer: the first approved oral lead chelator.

DMSA - Succimer effective oral lead chelating agent

Approved for outpatient treatment of children with elevated blood lead levels higher

Side effects: gastrointestinal symptoms, rash and transient elevations of serum aminotransferase levels, are uncommon and mild

Isolated cases of neutropenia have been reported.

Weekly monitoring - CBC, LFT - recommended during treatment

Blood lead levels should be checked weekly to identify rebound from bone and soft tissue mobilization

Heavy Metal Detoxification / Chelation Therapy –

DMSA / NaCaEDTA

J Pediatr. 1992 Jan;120(1):133-9.

Controlled study of DMSA for the management of childhood lead intoxication.

19 children with BPb concentrations of 50 to 69 micrograms/dl

5-day inpatient oral course of DMSA (1050 mg/m2 per day)

BPb concentration decreased by 61%

#4 children

5 day coarse of IV Na2CaEDTA

BPb concentration decreased by 45%

Treatment with DMSA was more effective CaNa2EDTA in reducing blood lead and in restoring metabolic activity to the heme pathway

Well tolerated

A comparison of NaCaEDTA and DMSA in the treatment of inorganic lead poisoning

Clin Toxicol (Phila). 2009 Nov;47(9):841-58

DMSA - more effective in reducing the kidney lead concentration

Sodium calcium EDTA - more effective in reducing bone lead concentrations

No consistently observed effect of chelation therapy on brain lead concentrations

DMSA and sodium calcium edetate - comparable impact on lowering blood lead concentrations

A comparison of NaCaEDTA and DMSA in the treatment of inorganic lead poisoning

Clin Toxicol (Phila). 2009 Nov;47(9):841-58

ADVERSE EFFECTS:

EDTA can cause dose-related nephrotoxicity

Both agents deplete zinc and copper (zinc / sodium calcium edetate)

Transient increase in LFT - more common with DMSA

No significant hepatic toxicity

Skin lesions during treatment with EDTA are unusual - attributed to zinc deficiency.

DMSA has occasionally been associated with a severe mucocutaneous reaction necessitating discontinuation of therapy

A comparison of NaCaEDTA and DMSA in the treatment of inorganic lead poisoning

Clin Toxicol (Phila). 2009 Nov;47(9):841-58

CONCLUSIONS:

Oral DMSA and IV sodium calcium edetate are both effective chelators of lead.

Both antidotes resolve the symptoms of moderate and severe lead toxicity rapidly

Description of 3,180 courses of chelation with DMSA in children ≤ 5 y with severe lead poisoning

PLoS Med. 2014 Oct 7;11(10)

Extensive lead poisoning impacting several thousand children in rural northern Nigeria

400 fatalities had occurred over 3 mo.

(CDC) confirmed widespread contamination from lead-rich ore being processed for gold

1,156 children ≤ 5 y of age who underwent between one and 15 courses of chelation treatment.

Overall improvement - 74.5%

Oral DMSA effective chelating agent for the treatment of severe childhood lead poisoning in a resource-limited setting.

Controlled study of DMSA for the management of childhood lead intoxication

J Pediatr. 1992 Jan;120(1):133-9.

Abstract

Efficacy and safety of meso-2,3-dimercaptosuccinic acid (DMSA) in children with markedly elevated blood lead (BPb) concentrations.

19 children with BPb concentrations of 50 to 69 micrograms/dl

5-day inpatient oral course of DMSA (1050 mg/m2 per day)

BPb concentration decreased by 61%

#4 children

5 day coarse of IV Na2CaEDTA

BPb concentration decreased by 45%

Treatment with DMSA was more effective CaNa2EDTA in restoring metabolic activity to the heme pathway

Well tolerated

Metal Detoxification - Chelation therapy - EDTA

CaNaEDTA and Na2EDTA

Na2EDTA - slow, continuous intravenous infusion

CaNaEDTA - slow IVP or 15 min infusion

Indications: lead, aluminum, cadmium

Side effects - malaise, headache, fatigue, chills or fever, myalgia, anorexia, nasal congestion, watery eyes, anemia, transient hypotension, clotting abnormalities, and kidney failure (Jang 2011)

Chelate essential trace metals, such as zinc, copper, and manganese (Flora 2010)

Sodium EDTA (without calcium) can cause life-threatening hypocalcemia (Brown 2006), death

Lab - monitor kidney function

Informed consent

Metal Detoxification - Chelation therapy - EDTA

Dosing:

IV - 50 mg / kg body weight

70 Kgm person - 3.5 Gm dose

2 - 3 grams are usual - detoxification therapy

1.5 - 2 grams for maintenance

Caution - start with lower dose - 1 gram in elderly or low body weight - gradually increase dose

Oral- 500 mg to 6000 mg daily

Oral EDTA enhances elimination of metals during IV therapy

EDTA - Chelation Therapy - TACT trial

TACT - Trial to Assess Chelation Therapy

Large scale, multi-center study - 20x larger than any previous study

safety and effigy of EDTA chelation for CHD

placebo-controlled, double blind

1708 #

Results

- Modestly reduced the risk of some cardiac events in adults who had previously had a heart attack
- Treatment effect lasted over the 5-year follow-up period
- 18% reduced risk of subsequent cardiac events such as heart attack, stroke, hospitalization for angina, or coronary revascularization
- Greater benefit - diabetes and CHF
- Side effects - Events occurred in 25% of the patients with diabetes who received EDTA chelation and in 38% of those who received placebo.
- Death from any cause was 43% lower in those patients with diabetes who received chelation

EDTA - Chelation Therapy - TACT trial

TACT - Trial to Assess Chelation Therapy

38 people (16%) receiving chelation and 41 people (15%) receiving placebo cited an adverse event as the cause of discontinuing study infusions.

4 unexpected severe adverse events that were possibly or definitely attributed to study therapy

2 in the chelation group (1 death)

2 in the placebo group (1 death)

Heart failure was reported in 57 (7%) chelation patients, and 71 (8%) placebo patients.

55,222 infusions

330 (0.6%) were administered at least 30 minutes too rapidly

EDTA - chelation therapy - Publications from the TACT Studies

The effect of an EDTA-based chelation regimen on patients with diabetes mellitus and prior myocardial infarction in the Trial to Assess Chelation Therapy (TACT). Circulation: Cardiovascular Quality and Outcomes. 2014;7(1):15–24.

EDTA chelation therapy alone and in combination with oral high-dose multivitamins and minerals for coronary disease: the factorial group results of the Trial to Assess Chelation Therapy. American Heart Journal. 2014;168(1):37–44. e5.

Oral high-dose multivitamins and minerals after myocardial infarction: a randomized trial. Annals of Internal Medicine. 2013;159(12):797–805.

Design of the trial to assess chelation therapy (TACT). American Heart Journal. 2012;163(1):7–12.

Effect of disodium EDTA chelation regimen on cardiovascular events in patients with previous myocardial infarction: the TACT randomized trial. JAMA. 2013;309(12):1241–1250.

Cutler Metal Detox Protocol

Low dose / higher frequency

DMSA or DMPS alone, followed by adding ALA

DMSA / DMPS - extracellular metals

ALA - brain / intracellular metals

- Added later, after lowering systemic levels

- Avoiding redistribution to brain

Cutler Metal Detox Protocol

DMSA 4 hours
DMPS 8 hours
ALA 3 hours
Combination 3 hours

Cycle 3 days on / 11 days off
Variation - 3 days on / 4 days off
Longest 14 days on

DMSA 1/16 - 1/2 mg / # BW / dose
DMPS 1/4 - 1 mg / # BW / dose
ALA 1/16 - 1/2 mg / # BW / dose

Cutler Metal Detox Protocol

Monitor Copper (ALA) - it may tend to increase

When combing with ALA, decrease DMPS 50% (taking every 3 hours)

Basic supplements
Zinc B complex
Magnesium Molybdenum

Epsom Salt baths (sulphate/magnesium)
Sauna

Metal Detoxification - Therapeutics - Pharmaceutical Chelators

Low Dose / Frequent Dosing Protocol - Cutler Protocol

Start with DMSA or DMPS, later add ALA

1/8 mg / # BW - increase slowly to 1/2 mg / # BW

Increase every 5 cycles - 3 days on / 11 days' off

DMSA	4 hours
DMPS	8 hours
ALA	3 hours

6 months to 2 years

Metal Detoxification - Therapeutics - Pharmaceutical Chelators

Low Dose / Frequent Dosing Protocol - Cutler Protocol

Supportive:

Vit C	500 - 2000 mg daily	3x daily
Magnesium	100 - 200 mg	3x daily
Zinc	25 - 50 mg	1-2x daily
Mineral	1	2x daily

Not advised:

IV chelation

Cilantro and chlorella

Metal Detoxification - Therapeutics - Natural Chelators Chlorella

Algae

Cell wall absorbs toxic metals - bind cadmium (in animal models) and zinc, copper, and lead (in vitro)

Detoxify wastewater of metal contaminants (Almaguer Cantu 2008; Shim 2008; Uchikawa 2010).

Accelerated the excretion of methylmercury (Uchikawa 2010)

Accelerated the excretion of cadmium (Shim 2009)

Reduced lead-induced bone marrow toxicity (Queiroz 2011)

Enhances mobilization of mercury in connective tissues

(muscles, ligaments, connective tissue, and bone)

Enhances biliary - intestinal excretion (particularly important - mercury - 90%)

Metal Detoxification - Therapeutics - Natural Chelators

Dose: 1 - 3 grams' daily

Dose: 500 mg tablet 1/4 tsp. 1x daily - check tolerability

Gradually increase dose 3x daily - 1 tsp. or 6 tablets

Pulse large doses 1 tbsp. or 16 tablets 500 mg

Radioactive metals or exposure

Amalgam tattoos - topical application

47. Ahner, AB, Kong KS, Morell MM, 1995 Phytochelatin production in marine algea: An interspecies comparison. Limnol Oceanograph 40: 649-657

48. Carr HP, et al. Characterization of the cadmium-binding capacity of Chlorella vulgaris. Bull Environ Contam Toxicol. 1998 Mar; 60(3): 433-440.

Metal Detoxification - Therapeutics - Natural Chelators

Cilantro

Chinese parsley

Mercury and Tin

CNS and the brain

Use later in process - after other body stores are minimized / cleared

Fresh cilantro

daily on food

pesto - blend: fresh organic cilantro, small amount of water, sea salt and olive oil

1 tsp. - tbsp. 1-3 times / day with meals

Garlic (sulfur) and Metal Detoxification

Garlic sulfur rich compounds

Metal-chelating properties

Anti-oxidants

Protect from metal-catalyzed oxidative damage

J Korean Med Sci 1987 Dec;2(4):213-224 [SEP]Cha CW A study on the effect of garlic to the heavy metal poisoning of rat.

Garlic (sulfur) and Metal Detoxification

Food Chem Toxicol. 2012;50(2):222–6

Comparative study on the efficacy of Allium sativum (garlic) in reducing some heavy metal accumulation in liver of wistar rats.

Rats fed garlic as 7% of their diet for 1 week - before, after, or during exposure to heavy metal toxins

Significantly reduced lead, cadmium, or mercury accumulation in their livers for 6 weeks

Garlic (sulfur) and Metal Detoxification

Basic Clin Pharmacol Toxicol. 2012 May;110(5):476-81

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

Previous studies on animals - garlic (Allium sativum) is effective in reducing blood and tissue lead concentrations.

investigate therapeutic effects of garlic and compare it with d-penicillamine in patients with chronic lead poisoning.

117 workers at a car battery plant

3x daily * 4 weeks

garlic 1200 µg allicin

d-penicillamine 250 mg

Clinical improvement was significant in both groups

Lead levels decreased	Garlic	426	to	347µg/L
D-penicillamine	417	to	315ug/L	

Garlic - safer clinically and as effective as d-penicillamine

Metal Detoxification - Therapeutics - Natural Chelators

Porphorazyme

Chlorophyll (Biotics Labs)

Group of different porphyrins

Facilitates metal excretion

1 - 3 tablets 1 - 3x / day for extended periods of time

Metal Detoxification - Therapeutics – Natural Chelators

Modified Citrus Pectin

Three studies - mobilization / excretion of metals from body stores -

Arsenic, Mercury, Cadmium, and Lead

5 - 20 grams / day

1. 15 g of MCP daily for 5 days and 20 g of MCP on day 6

Significant urinary excretion of arsenic, mercury, cadmium, and lead

150% increase in cadmium excretion

560% increase in lead excretion on day 6 (Eliaz 2006).

Essential minerals such as calcium, zinc, and magnesium did not increase in the urinary analysis.

2. Series of case reports, 5 patients with different illnesses took MCP alone or in combination with alginate for up to 8 months. The patients showed a 74% average decrease in toxic heavy metals after treatment (Eliaz 2007).

3. 7 children with blood lead levels >20 µg/dL received 15 g/day of MCP for 2 to 4 weeks. Blood lead levels dropped an average of 161%, and urinary lead excretion increased by an average of 132% (Zhao 2008).

Metal Detoxification - Therapeutics - Natural Chelators

Silica / silicon - Orthosicilate and Zeolite

Studies:

- Decreased aluminum absorption from GI trace
- Decreased accumulation in brain
- Increased aluminum excretion in urine
- Decreased lead levels in tissues

In human subjects, soluble silicon (orthosilicic acid) decreases aluminum absorption from the digestive tract and decreases its accumulation in the brain (Jurkic 2013).

Alzheimer's patients drank up to 1 L of mineral water daily (containing up to 35 mg of silicon/L) for 12 weeks. Over the study period, urinary excretion of aluminum increased without affecting urinary excretion of the essential metals iron and copper. In addition, there was a clinically relevant improvement in cognitive performance in at least 3 out of 15 individuals (Davenward 2013).

Inclusion of zeolite (clinoptilolite) in high-lead diets of laboratory mice reduced tissue lead concentration by 77-91%, increased the percentage of healthy red blood cells, and reduced chromosomal damage (Topashka-Ancheva 2012; Beltcheva 2012).

Flowers JL, Lonsky SA, Deitsch EJ. Clinical evidence supporting the use of an activated clinoptilolite suspension as an agent to increase urinary excretion of toxic heavy metals. Nutrition and Dietary Supplements. 2009:11-18.

Biological and therapeutic effects of ortho-silicic acid and some ortho-silicic acid-releasing compounds: New perspectives for therapy. Nutr Metab. 2013;10(1):2

Metal Detoxification - Supporting

Therapy / Natural chelators

Sulfur - Biochemical Neutraceuticals

Methionine	Cysteine
NAC	SAM
ALA	GSH
Redoxal	

Alpha-Lipoic Acid / Glutathione

Sulfur- compounds complex with heavy metals chelate a number of metals in cell culture

Cadmium, lead, zinc, cobalt, nickel, iron, and copper - (Patrick 2002)

In a rat model, ALA and glutathione reduced some of the adverse changes in blood parameters, including drops in red blood cell number and size as well as reductions in hemoglobin concentration brought about by intoxication with lead, cadmium, or copper (Nikolic 2013).

ALA and glutathione in a rat model both reduced cadmium-associated oxidative stress and improved the activity of the antioxidant enzyme catalase in kidney tissue (Veljkovic 2012)

Metal Detoxification - Supporting Therapy / Natural chelators

N-Acetyl Cysteine

N-acetyl cysteine (NAC) provides a source of sulfur for glutathione production

Effective at reducing oxidative stress due to heavy metal toxicity (Patrick 2006).

Capable of binding and sequestering divalent copper (II), trivalent iron (III), lead, mercury, and cadmium ions (Samuni 2013).

Chronic exposure to toxic metals can decrease cysteine levels (Quig 1998).

In animal models and cell culture experiments

Enhanced renal excretion of lead (Pb IV)

Lowered concentrations of mercury

Protected against cadmium-induced liver cell damage (Samuni 2013)

600 - 2400 mg daily

Metal Detoxification - supporting therapy - minerals

Selenium

Animal models - selenium blocks the effects of lead when administered before exposure and reduces mercury toxicity (Patrick 2006)

Human studies - selenium increases mercury excretion in humans (Li 2012; Zwolak 2012)

100-200 mcg/day reduced blood and hair levels of arsenic in Chinese farmers with arsenic poisoning (Zwolak 2012)

Mitigate the toxicity of heavy metals - cadmium, thallium, inorganic mercury, and methylmercury (Whanger 1992)

100 mcg of selenium (selenomethionine) daily for 4 months: 34% reduction in hair levels of mercury (Seppanen 2000).

Metal Detoxification - supporting therapy - Folate

Cofactor in sulfur-containing amino acid metabolism

Cysteine / methionine - precursors to internal detoxifiers / anti-oxidants - alpha-lipoic acid and glutathione

Nutrition. 2013;29(3):514–8

Relation between serum folate status and blood mercury concentrations in pregnant women

1105 pregnant women

Higher blood folate levels were associated with lower blood mercury levels during pregnancy

Metal Detoxification - supporting therapy - Folate

Cadmium, lead and mercury exposure in nonsmoking pregnant women.

173 pregnant non-smokers

Not supplementing folic acid or iron supplements during pregnancy was associated with higher blood cadmium levels (Hinwood 2013)

Folate supplementation: 1 - 5 mg

Metal Detoxification - supporting therapy - Probiotics

Trapping and metabolizing xenobiotics or heavy metals

Lactobacillus rhamnosus (LC-705 and GG), Lactobacillus plantarum (CCFM8661 and CCFM8610), and Bifidobacterium breve Bbi 99/E8 - bind both cadmium and lead in laboratory studies (Ibrahim, Halttunen 2006; Halttunen 2008).

In mouse models, two different Lactobacillus plantarum strains reduced tissue accumulation of cadmium and lead and protected against oxidative stress (Zhai 2013; Tian 2012).

Metal Detoxification - Therapeutics - Supporting Remedies

Homeopathic / Herbal Drainage and Organ Support –

Liver, Lymph, Kidney

Solidago

Burbur

Heavy Metal
Detoxification / Chelation –

Glutathione

Glutathione

Mobilizes metals - promotes excretion

Anti-oxidant - cell and enzyme protection

Recycle antioxidants - C, E

- Oral - capsules, liposomal liquid
- IM
- IV
- Topical
- Nebulizer

Dose - 200 - 5000 mg

129,000 PubMed articles

The role of intracellular glutathione in inorganic mercury-induced toxicity in neuroblastoma cells. Neurochemical Research. 2009;34(9):1677–1684.

Glutathione modulation influences methyl mercury induced neurotoxicity in primary cell cultures of neurons and astrocytes. Neuro Toxicology. 2006;27(4):492–500.

Anti-oxidant and anti-atherogenic properties of liposomal glutathione: studies in vitro, and in the atherosclerotic apolipoprotein E-deficient mice. Atherosclerosis. 2007;195(2):e61–e68

Liposomal-glutathione provides maintenance of intracellular glutathione and neuroprotection in mesencephalic neuronal cells. Neurochemical Research. 2010;35(10):1575–1587

Recent advances in the treatment of neurodegenerative diseases based on GSH delivery systems. Oxidative Medicine and Cellular Longevity. 2012;2012:12 pages.240146

Metallothioneine Induction Therapy

William Walsh, Ph.D. / Pfeiffer Treatment Center

1,200 published articles describing MT synthesis, activation, and redox mechanisms

Cysteine rich protein on Golgi apparatus - 1/3 AA = cysteine

Each molecule of MT requires 7 atoms of zinc (Zn) for proper functioning

Zn-MT = "magnet" for toxic metals

Autism risk - congenital / acquired deficiency (toxicity, deficiencies)

Metallothonein - Function:

Binding of metals

Storage site for zinc / copper

Ccavenger of reactive oxygen species / free radicals

Controls oxidative stress

Protect cells from apoptosis induced by oxidative stress and metals

Regulates zinc and copper concentration in the blood.

Development and functioning of our immune system.

Development of nerve cells (neurons) in the brain together with Omega-3 fatty acids.

Protects against excessive yeast growth in the intestines.

Prevents intestinal infections.

Involved in gastric acid production.

Influences taste and texture sensation of food in the mouth.

Regulating influence on hippocampal behaviour.

Emotional development and socialization (amygdala).

Metallothionein Induction Therapy

Phase 1

Zinc preloading 4-8 weeks; start low, gradual increase'

Goal Zn > 100 (reference range 60 - 100 umol/L)

Daily dosage = mg / lb + 20 mg

Also - P6P, Mn gluconate, C, E

Add - taurine - if seizure tendency

Phase 2

Add Glutathione, Selenium, SH-AA

Heavy Metal Toxicity –

Interaction - Potentiation of Toxicity

"Interaction Profiles" - US Agency for Toxic Substances and Disease Registry report

1. Renal toxicities are greater - mixtures of lead plus mercury

2. Neurological toxicities of mixtures of lead plus arsenic, lead plus methylmercury, and lead plus cadmium are supra-additive

Agency for Toxic Substances and Disease Registry. Interaction Profiles Home Page, http://www.atsdr.cdc.gov/ interaction profiles/index.asp.

Mercury Toxicity - Hypertension

Recommendation: mercury assessment in all patients presenting with hypertension or any vascular disease

M. C. Houston, "Role of mercury toxicity in hypertension, cardiovascular disease, and stroke," Journal of Clinical Hypertension, vol. 13, no. 8, pp. 621–627, 2011.

Metal Detoxification -

Sauna Therapy

Journal of Environmental and Public Health Volume 2012

Review Article

Arsenic, Cadmium, Lead, and Mercury in Sweat: A Systematic Review

No person is without some level of toxic metals in their bodies - circulating and accumulating

Children and the fetus are most at risk of harm - lower IQ and dysfunctional behavior

Older populations - low grade metal exposure / life time accumulation - at risk:

Early cognitive decline

Kidney and cardiovascular disease

Diabetes

Osteoporosis

Agency for Toxic Substances and Disease Registry. Toxicological Profile: Mercury. US Department of Health and Human Services. Public Health Service, 1999

Metal Detoxification - Sauna Therapy

Blood flow to the skin increasing from baseline of 5–10% to 60–70% of the cardiac output

5 - 10 x increase in blood flow

Maximal sweating can occur within 15 minutes

Primarily decreases metals - blood / extracellular space - ? intracellular

Fluid loss may be as high as 2 L/h ("acclimatized" person who regularly sweats)

Adult sweat: 1 quart sweat (2 #) = 100 mg DMSA every 4 hours that day

A. Eisalo and O. J. Luurila, "The Finnish sauna and cardiovascular diseases," Annals of Clinical Research, vol. 20, no. 4, pp. 267–270, 1988

Metal Detoxification - Sauna

Reviewed Medical Literature

Significantly increased excretion of lead, cadmium, mercury, arsenic

Sweat - 10x increase in lead (lead-exposed workers)

Sauna Detoxification - added benefit

Increases excretion of toxic chemicals

Observed in New York rescue workers

Persistent flame retardants

Bisphenol-A

"Methamphetamine expo- sure and chronic illness in police officers: significant improvement with sauna-based detoxification therapy," Toxicology and Industrial Health

"Persistent organic pollutants in 9/11 world trade center rescue workers: reduction following detoxification," Chemosphere, vol. 69, no. 8, pp. 1320–1325, 2007.

"Human detoxification of perfluorinated compounds," Public Health, vol. 124, no. 7, pp. 367–375, 2010.

"Human excretion of bisphenol-A: blood, urine and sweat (BUS) study," Journal of Environmental and Public Health, 2012.

Sauna Detoxification –

Added benefit - Combination therapies

Overall detoxification of metals and chemicals can be enhanced

GSH, NAC, Vit C, Minerals, Garlic, Chlorella, Rx Chelating agents

Sauna Detoxification – Support / Enhancement

Autonomic nervous system / heat regulatory mechanism - decreased sweating ability

- Hydration
- Brushing the skin
- Niacin - vasodilation
- Exercise prior to sauna use
- Persistence and ample hydration patients do eventually start to sweat.

Metal Detoxification - Sauna

With acclimatization and regular use - generally well tolerated by all ages

Medical supervision - considered / recommended - initial sessions for children and elderly

Contraindications (R) - unstable angina pectoris, recent myocardial infarction, severe aortic stenosis, and pregnancy

"Health effects and risks of sauna bathing," International Journal of Circumpolar Health, vol. 65, no. 3, pp. 195–205, 2006.

"Benefits and risks of sauna bathing," American Journal of Medicine, vol. 110, no. 2, pp. 118–126, 2001

Metal Detoxification –

Sauna - Historical

Spanish Era and its colonies - significant mercury exposure

Ill workers sent to warmer climes

- Away from the exposure
- Drink weak beer

Alcohol inhibited hydrogen peroxide / catalase oxidation of elemental mercury to ionic mercury

- Increasing mercury in exhaled breath
- Work in the heat to sweat out toxins

Effective strategy - tremors, salivation, and mouth ulcers resolved within a few weeks

"A small dose of ethanol increases the exhalation of mercury in low-level- exposed humans," Journal of Toxicology and Environmental Health, Part A, vol. 60, no. 2, pp. 89–100, 2000.

"Workers' health and colonial mercury mining at Huancavelica, Peru," The Americas, vol. 57, no. 4, pp. 467– 496, 2001.

RadioActive Elements / Metals

RadioActive Elements / Metals

RadioActive element - atom with unstable nucleus

Naturally emits energy to become more stable

High energy rays / high speed particles = ionizing radiation

Alpha / beta particles / gamma rays

Effects - alters / damage DNA and cellular molecules and processes

1. Directly ionizing DNA molecules
2. Indirectly by ionizing water in body cells - free radicals formed - damage DNA

Ionizing radiation - harmful / toxic to human tissue

In food radiation - change food structure - destroys or reduces nutrients creates radiolytic products - formaldehyde, benzene, formic acid, and quinone sex. Gamma Radiation - cobalt 60 / cesium 137

Radioactive Elements – Health Concerns

- Ionizing radiation - radiation damage
- Long half life in environment
- Increasing exposure - "no place to hide"
- Anti-oxidant and nutritional deficiencies - increase risk of toxic effects of low dose exposure
- One of primary concerns - increased risk of cancer

  ex. radon in lung cancer in non-smokers
  ex. radon in lung cancer - increasing risk in smokers

- Degenerative conditions - premature aging

RadioActive Elements –

Common uses

Iodine-131	Thyroid assessment
Bismuth-212	Cancer therapy
Technetium-99	Radiology imaging
Uranium -235	Nuclear energy production
Americium-241	Smoke detectors
Cobalt-60	Antibacterial in foods
Cesium-137	Antibacterial in food
Radon	Gas - environmental
Radium 88	Past exposure / cancer therapy
Strontium 90	Medical

RadioActive Elements – Common exposure

Iodine-131	Thyroid assessment / treatment, medical and laboratory
Bismuth-212	Cancer therapy
Technetium-99	Radiology imaging
Uranium -235	Nuclear energy waste, accidents
Americium-241	Smoke detectors
Cobalt-60	Antibacterial in foods
Cesium-137	Antibacterial in food, nuclear waste and accidents
Radon	Gas - environmental
Radium 88	Past exposure / cancer therapy / family exposure / medical occupational
Tritium H_3	EXIT signs improperly handled and manufacturing
Strontium 90	Nuclear waste / accident

RadioActive Elements –

Treatment - Standard / Conventional

Cesium 137	Prussian blue 1-3 grams 3x daily * 30-60 days - insoluble ferric hexacyanoferrate
Cobalt 60	DMSA, EDTA, NAC
Iodine 131	Potassium iodide / propylthiouracil
Radium 226	Aluminum hydroxide / sodium alginate / barium sulfate / calcium phosphate
Strontium 90	Aluminum hydroxide / sodium alginate / barium sulfate / calcium phosphate
	IV Calcium gluconate
Uranium 235	IV Sodium bicarb - facilitates renal excretion - urine pH 8-9 - 3 days
Tritium H-3	H_2O water diuresis - 3 to 4 liters daily * 3 weeks

Radium - 88

Discovered Marie and Pierre Curie in 1898

Radioactivity of isotope Ra226 - basis for historical unit for radioactivity - curie

Isotopes of radium are highly radioactive

The most stable isotope - Ra 226 - half life of 1600 yrs - decays into radon gas (Radon 222)

Radium isotopes - exist in environment - decay products from uranium and thorium

Radium - 88

Former use:

Self-luminous paints - watches, nuclear panels, aircraft switches, clocks, instrument dials

Instrument dial painters - licked their brushes to give them a fine point - ingesting radium

Oral mucosal sores, anemia, bone cancer

Acts like calcium - deposited in bones - effects bone marrow

Radium Girls lawsuit - awareness of radioactive risk and protection

Additive - toothpaste, hair creams, and even food items

Nasal radium irradiation - administered to children to prevent middle-ear problems or enlarged tonsils (1940 - 1970s)

Current Use:

- Oncology - nasopharyngeal irradiation (delayed risk of brain cancer and pituitary dysfunction)
- Oncology - 223Ra Xofigo - FDA approved 2013 for metastatic bone cancer (prostate)
- Treatment: aluminum hydroxide / sodium alginate / barium sulfate / calcium phosphate

Radon
Rn-222

Naturally occurring radioactive gas

Results from decay of Radium 226

Emits alpha radiation - similar to plutonium

Higher levels near spring waters and hot springs

Tends to collects in basements and crawl spaces - poor ventilation

Carcinogenic - highly

1000 times greater risk of death as any other EPA carcinogen

Radon
Rn-222

EPA action level = 4 pCi/L (Curie - unit of radioactivity)

Screening in seven states - 1 in 3 homes - levels over 4 pCi/L

1/15 U.S. homes - estimated to have elevated radon

Home level of 4 = 35x more than allowed level standing next to radioactive waste site - Nuclear Regulatory Comm

1000 times greater risk of death as any other EPA carcinogen

Action level DOES NOT EQUAL safe level

Ventilation lowers radon levels

#1 Cause of lung cancer among non-smokers

#2 Cause of lung cancer

21,000 lung cancer deaths every year

2,900 of these deaths occur among people who have never smoked

Treatment - ventilation / no conventional / Functional Med Tx - anti-oxidants

RadioActive Elements

Cobalt 60 –

Radioactive Element - manufactured isotope - nuclear power plants / radiation therapy / irradiated food

Cobalt 27

Metal / compounds - manufacturing - pigments (dyes, tattoos, paints), medical device (metal implants)

Cobalt Organic - B12

Methylcobalmin / hydroxycobalamin / s-adenosylcobalain methionine metabolism - Methionine aminopeptidase 2 - tissue repair

Cobalt 60 and 58 – Radioactive Element

Manufactured radioactive isotopes - produced in nuclear reactors

Ionizing radiation - gamma rays

Probable human carcinogen

Exposure - released to the environment

Result of nuclear accidents - water, air currents, soil

Radioactive waste dumping in the sea

Radioactive waste landfills

Nuclear power plant operations - contaminants in cooling water

Half life - moderately short-lived

Co60	5 yrs
Co 58	71 days

Occupational Exposure :

Workers at nuclear facilities, irradiation facilities, or nuclear waste storage sites

Sterilizing medical equipment and consumer products

Radiation therapy for treating cancer patients - brain

Food irradiation

Cobalt 60 and 58 - Radioactive Element

Probable human carcinogen

Genotoxic - oxidative damage / inhibition of DNA repair

Associated cancers - lung , upper GI , bone cancer

2012 USGS Minerals Yearbook: Cobalt [Advance Release]. http://minerals.usgs.gov/minerals/pubs/commodity/cobalt/myb1-2012-cobal.pdf.

1996. Incidence of lung cancer among cobalt-exposed women. Scand J Work Environ Health 22(6): 444-450

2000. Lung cancer mortality in a site producing hard metals. Occup Environ Med 57(8): 568-573

2005. Metals, toxicity and oxidative stress. Curr Med Chem 12(10): 1161-1208

Valko M, Rhodes CJ, Moncol J, Izakovic M, Mazur M. 2006. Free radicals, metals and antioxidants in oxidative stress-induced cancer. Chem Biol Interact 160(1): 1-40.

National Toxicology Program, Department of Health and Human Services

Cobalt -27

Heavy Metal / Compounds

National Toxicology Program, Department of Health and Human Services

Report on Carcinogens, Fourteenth Edition

Cobalt Metal and Cobalt Compounds That Release Cobalt Ions In Vivo

Reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity in experimental animals

Animal studies - rats and mice exposed to cobalt metal or cobalt compounds developed tumors at various tissue sites — lungs, adrenal glands, pancreas, and immune system

Cobalt - Co 27 - Metal and Compounds

Reasonably anticipated human carcinogen

Use / Exposure:

Rechargeable battery electrodes - smart phone and laptops

Cobalt nanoparticles

- Medical application sensors
- MRI contrast enhancement
- Drug delivery

Cobalt compounds

Pigments for glass, ceramics, enamels, paints, dyes, tattoos

- Driers for paints, varnishes, or lacquers
- Adhesives
- Trace mineral additives in animal diets

"Green" energy technology applications

Cobalt alloys - joint implants

Increasing exposure of a Reasonably anticipated human carcinogen

Cobalt - Co 27 –

Metal and Compounds

Excessive exposure / higher levels - cardiomyopathy, vision or hearing impairment, hypothyroidism, polycythemia

Urinary cobalt - higher in occupational exposure and failed hip implants

Cobalt ions may be released into the body throughout the lifetime of a cobalt-containing device (Sampson and Hart 2012, Devlin et al. 2013).

Blood cobalt > 10 µg/L Mayo Clinic (2015)

Recommended - further clinical investigation and action

Review of the Health Hazards Posed by Cobalt

DJ Paustenbach et al. - Crit Rev Toxicol 43 (4), 316-362. 4 2013.

RadioActive Elements –

Tritium H - 3

Radioactive hydrogen

Produced naturally in upper atmosphere when sun light interact with nitrogen

Most common form in water

Use:

Produced during nuclear weapons explosions

Byproduct in nuclear reactors

Government weapons production plants

EXIT signs - self luminating

Exposure:

Released as steam / leak into the underlying soil and ground water

Improper disposal / handling of EXIT signs

Treatment: water diuresis - 3 to 4 liters daily * 3 weeks

Cesium 133 Stable Heavy Metal

and

Cesium 134 / 137 Radioactive Element

Ce 133 - stable

Naturally occurring metal

By product of mining

Ce 134 and 137 - radioactive metal isotopes

From nuclear processing / degradation of uranium / nuclear accidents and explosions

Transported though air - 1000s of miles - then settles in water and soil - then food

Ce 137 half life = 30 yrs

RadioActive Elements –

Public Health and Environmental Contamination

2011 Fukushima nuclear power plant accident

Radiation leaked into sea and ground water

300 tons of radiation still leaking

Leak irreparable due to high temperatures

I-131 -	8 days
Ce 134 -	2 yrs
Ce 137 -	30 years
Strontium	90 - 20 yrs

Concern: Cesium 137 and 134

spread in air currents - globally

distributed in water, soil, fish, plant life

fish, produce, herbs transported internationally

Cesium-134	2 yr half life

Western U.S. offshore water

Canadian salmon

Cesium 137	30 yr half life

Recently detected higher levels on U.S. and Canadian west coast

Radiation levels are predicted to continue rising

RadioActive Elements –

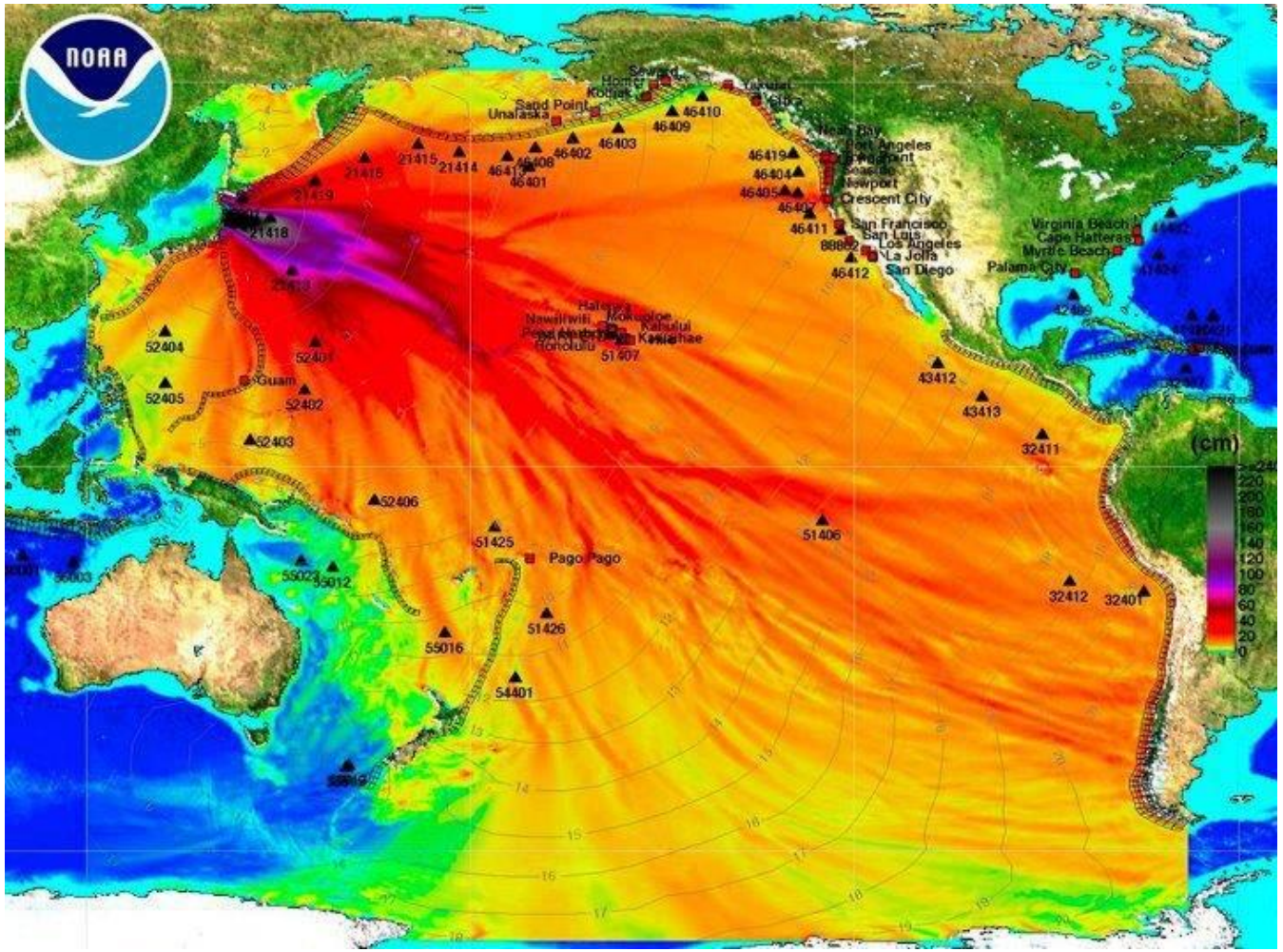
Public Health and Environmental Contamination

2011 Fukushima nuclear power plant accident

2014 radiation levels on West coast - increased by 300 to 500 percent

Pacific ocean 5-10x more radioactive than after nuclear bombs of WWII era

Fukushima Pacific Radiation picture



Cesium 133 Stable Heavy Metal

and

Cesium 134 / 137 Radioactive Element

Exposure:

Air, water, soil, food

Food - considered greatest exposure

Nuclear plants - waste and accidents

Effects:

Ce 133 GI symptoms, cardiac arrythmias, including prolonged QT syndrome, neurological, infertility

Ce134/137 Cancer -Leukemia

Acute radiation syndrome (vomiting, nausea, and diarrhea)

Skin and ocular lesions, compromised immune function, neurological signs, irrational behavior,

Circulatory system collapse, neuromuscular incoordination, followed by convulsions and death

Treatment: Conventional - Prussian blue

1-3 grams 3x daily * 30-60 days - insoluble ferric hexacyanoferrate

Functional - combination antioxidants

RadioActive Elements Strontium 90

Exposure - nuclear power plants and accidents

20 yr half life

Risk - bone cancer and hyperparathyroidism

Treatment - high exposure - conventional : aluminum hydroxide / sodium alginate / barium sulfate / calcium phosphate

IV Calcium gluconate

Functional : combination antioxidants

Treatment - low exposure - - combination antioxidants

Iodine 131 and 129 –

Radioactive Metal Isotopes

I 131 - occurs naturally - but short lasting

I 131 and 129 - by product nuclear processing of uranium and plutonium

Half life

131	8 days	Medical use, Nuclear by-product
129	1.6x107 year	Nuclear by-product

Use / Exposure:

Accidental release from nuclear accidents

Contamination water from nuclear power plants

Occupational - medical, laboratory, nuclear facilities

Patients undergoing medical nuclear imaging

Imaging - pheochromocytoma and neuroblastoma

Thyroid conditions -hyperthyroid, nodule, and cancer

Patients undergoing medical treatment of thyroid conditions I 131 capsules

Family members (children) of patients undergoing I131 treatment

Treatment:

Conventional - Potassium iodine (KI) 12 - 150 mg * weeks / months

Functional - combination antioxidants

RadioActive Elements –

Polonium-210 and 84

Highly radioactive element (alpha particles) and chemically toxic

Decay product of radioactive Lead PB 210

Increasing levels of Lead PB 210

- Calcium phosphate fertilizers
- Drinking water
- Tobacco and plants

Polonium in cigarette smoke - cancer in laboratory animals

"Tobacco Radioactivity and Cancer in Smokers," 63 American Scientist 404-412 (July-August 1975).

Treatment: Functional - combination anti-oxidants

Anti-oxidant Protection / Detoxification of Radiation

Adv Exp Med Biol. 2008 ; 614: 165–178

ANTIOXIDANTS REDUCE CONSEQUENCES OF RADIATION EXPOSURE

Department of Radiation Oncology, University of Rochester Medical Center

The ability of antioxidants to reduce the cytotoxic effects of radiation - 50 years

Sulfur-containing antioxidants - most beneficial therapeutic ratio

Capable of both scavenging oxygen radicals

Affecting chemical repair of some forms of DNA damage

Prevention of immediate radiation-induced genotoxicity requires that an antioxidant be present at the time of irradiation.

Anti-oxidant Protection / Detoxification of Radiation

Adv Exp Med Biol. 2008 ; 614: 165–178

ANTIOXIDANTS REDUCE CONSEQUENCES OF RADIATION EXPOSURE

Department of Radiation Oncology, University of Rochester Medical Center,

Immediate Radioprotective Effects

By scavenging of radicals ROS

Caffeine, melatonin, flavonoids, polyphenols

Chronic Radioprotective Effects by Antioxidants

1.increasing an-ox mechanisms

- glutathione peroxidase
- glutathione reductase
- increasing the synthesis of glutathione (GSH)
- reducing levels of oxygen radicals and peroxides in cells

2. activation of the redox-sensitive nuclear transcription factor, NFκB

Subsequent expression of the antioxidant enzyme, manganese superoxide dismutase (MnSOD)

3. Protection of membranes

Decreased lipid radical and peroxides

Pretreatment - flavonoid, luteolin, reduced lipid peroxidation

4-fold reduction in lipid peroxidation

Anti-oxidant Protection / Detoxification of Radiation

Adv Exp Med Biol. 2008 ; 614: 165–178

ANTIOXIDANTS REDUCE CONSEQUENCES OF RADIATION EXPOSURE

4. Mitochondrial protection / preservation

Melatonin - effective at protecting mitochondria

Increasing the efficiency of oxidative phosphorylation

Reducing the leakage of electrons from the electron transport chain

Decreases the formation of ROS from these electrons

Induces the levels of antioxidant enzymes GPx

Increases GSH levels within the cell

5. Inhibition ROS related apoptosis

SOD, green tea polyphenol, (–)-epigallocatechin

6. Protection against - reperfusion injury - ROS

7. Modulation of inflammatory response - cytokines

Epicatechin, trans-resveratrol, and theaflavin

NAC

8. Reducing ROS and inflammation in late radiation-induced tissue injury (scarring / fibrosis)

MnSOD , a-tocopherol

Anti-oxidant Protection / Detoxification of Radiation

Adv Exp Med Biol. 2008 ; 614: 165–178

ANTIOXIDANTS REDUCE CONSEQUENCES OF RADIATION EXPOSURE

HBOT - most effective treatment for many chronic radiation-induced soft tissue injuries

HBOT mechanisms of action - attributed to:

Induction of SOD and antioxidant systems - inhibition of inflammation

Improved tissue vascularization

Prevention of immediate radiation-induced genotoxicity requires that an antioxidant be present at the time of irradiation

in vitro and in vivo studies - antioxidants given in combination result in GREATER radioresistance than when given individually

RadioActive Elements - Protection / Detoxification Treatment

Turmeric	Spirulina	Green Tea
Astaxanthin	Chlorella	Melatonin
NAC	ALA	GSH
Potassium iodide	Vit C	Zinc
Selenium	Vit D_3	Melatonin
SOD	Vit E	

Radioactive Elements - Chernobyl Nuclear Accident

Radiation sickness

145k children

160k workers

Spirulina 5 grams daily

Reduced radiation sickness

Increased urinary excretion of radionuclides

Spirulina- natural sorbent of radionucleides Sep 1993. Research Institute of Radiation Medicine, Minsk, Belarus. 6th Int'l Congress of Applied Algology

ALA and Vit E - helped lower the amount of radioactivity found in the urine (Korkina, 1993)

RadioActive Elements - Protection against Radiation Exposure

Protective Effects of Vit C in Radiation Exposure

Mice study

Vit C therapy starting before radiation exposure vs starting after, and later bone marrow replacement

Pretreatment - 40% survival

Delayed treatment - 0% survival

Yanagisawa A: Orthomolecular approaches against radiation exposure.

40th Orthomolecular Medicine Today Conference. Toronto, Ontario. April 29, 2011

RadioActive Elements - Protection against Radiation Exposure

1. Vitamin C - Radioprotector against iodine-131 in vivo

   J Nucl Med, 1993; 34: 637-640.

2. Combination of anti- oxidants (ALA, C, E, Se, NAC, CoQ10)

   Improved the survival of mice after total body irradiation

   Antioxi-dant diet supplementation starting 24 hours after exposure reduces radiation lethality

   Radiat Res, 2010; 173: 462-468.

RadioActive Elements - Protection against Radiation Exposure

Astazanthin

Strongest carotenoid antioxidant

- 54x > C
- 14x > E
- 500x > E for singlet oxygen free radicals
- 11x > B-Carotene for singlet oxygen free radicals

Crosses BBB and BRB (blood retinal barrier)

Anti-inflammatory

Toxic Metals and RadioActive Elements - summary points

Toxic Metals and RadioActive Elements - summary points

Toxic Metals are UBIQUITOUS

Exposure is UNAVOIDABLE

Low Level Exposure - ACCUMULATION

METAL TOXICITY - subtle and non-specific

Effects of toxic metals - DEPLETING, INFLAMMATORY, DEGENERATIVE

MINIMIZING body burden = one of HIGHEST PRIORITIES of Preventive/Functional Med

OPTIMIZING nutrient levels is ESSENTIAL to protection / detoxification

Metal Detoxification with Pharmaceutical/Nutraceuticals - SCIENTIFIC, SAFE, EFFECTIVE