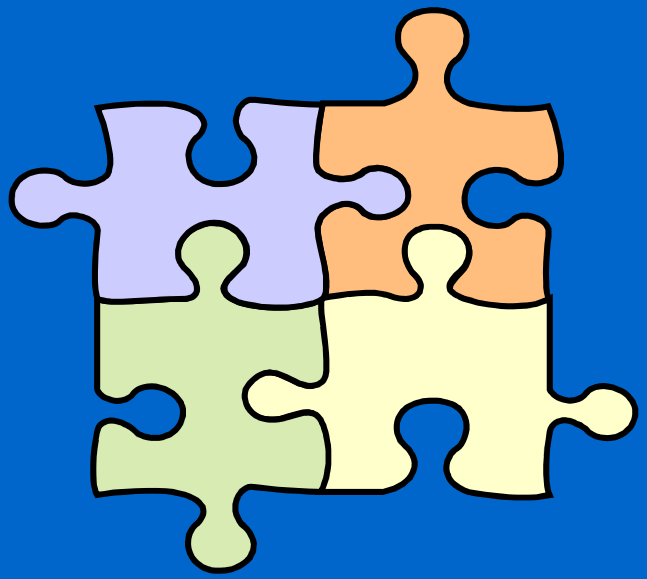
Detoxification, Chelation and Hyperbaric Oxygen Treatment in Autism—

Great Plains Laboratory
Autism Conference
Warsaw, Poland
October 17, 2009

John L. Kucera, MD
Colorado Springs, Colorado, USA

Overview

- More on Heavy Metals, Mercury, Thimerosal
- The Vaccine Issue
- Treatments
  - Detoxification
  - Chelation
  - Hyperbaric Oxygen



Biomedical Treatment for Autism

Detoxification / Chelation

For Children with Autism

WHY ?

Because it works!!

Modified CGI – Combined Parent/Clinician

Courtesy Dr Rimland, Autism Research Institute, San Diego, CA

Liz Mumper MD, Medical Director Defeat Autism Now!

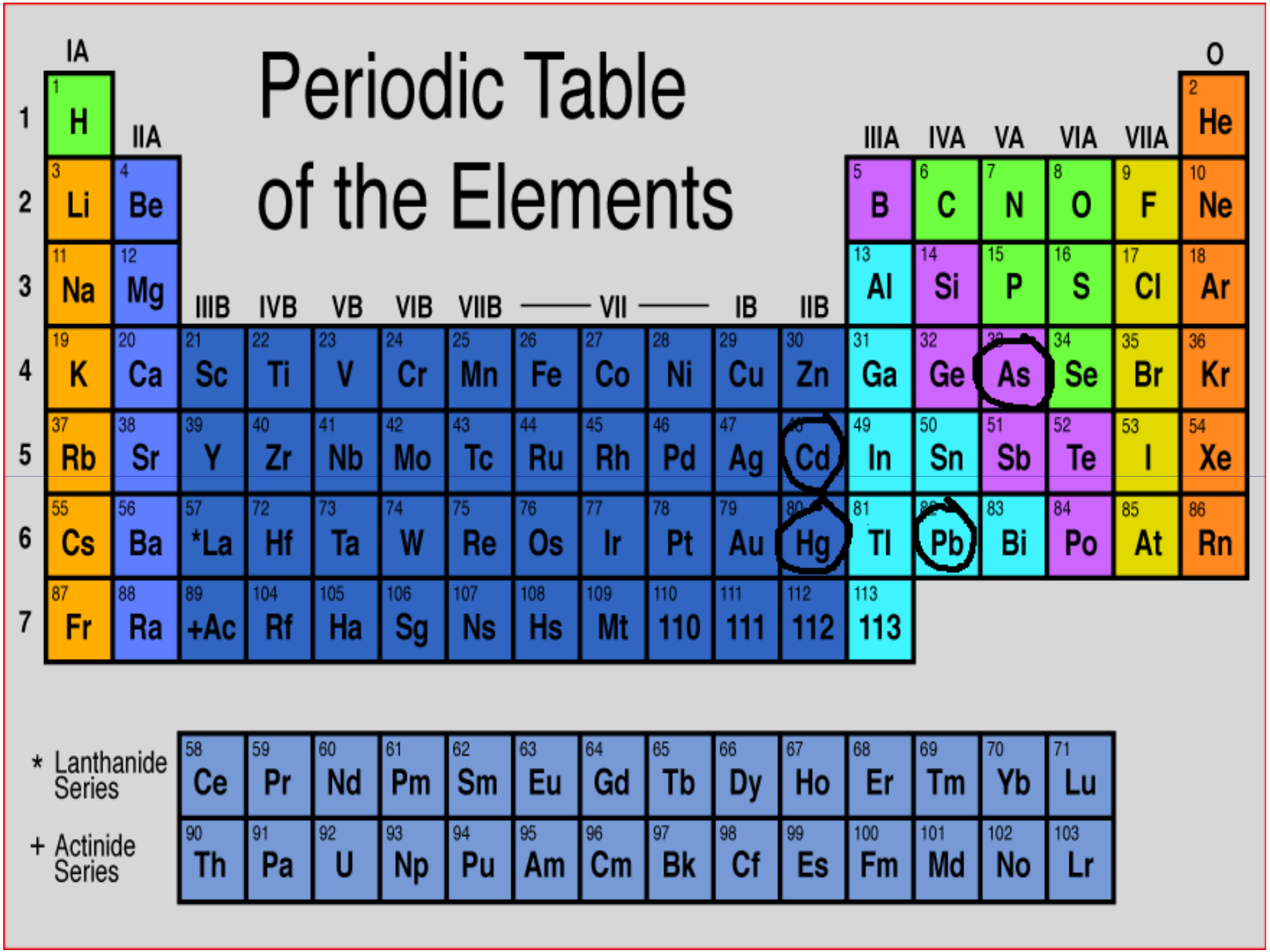
		Got Worse [A]	No Effect	Got Better	Better: Worse	No. of Cases [B]
1	**Chelation**	2%	22%	**76%**	38::1	324
2	**Gluten- Casein-Free Diet**	3%	32%	65%	22::1	1446
3	**MethylB12**	4%	33%	63%	16::1	192
4	**Food Allergy Treatment**	3%	37%	61%	21::1	560
5	**Melatonin**	8%	30%	61%	8::1	573
6	**Digestive Enzymes**	3%	42%	56%	19::1	737
7	**Fatty Acids**	2%	42%	55%	28::1	626
8	**Diflucan**	5%	41%	55%	11::1	330
9	**Candida Diet**	3%	44%	54%	18::1	756
10	**Risperidal**	18%	28%	54%	3::1	616
11	**Feingold Diet**	2%	45%	53%	27::1	758
12	**P5P (Vit. B6)**	13%	37%	51%	4::1	213
13	**Cod Liver Oil**	3%	47%	50%	17::1	818
14	**Nystatin**	5%	46%	49%	10::1	986
15	**Secretin IV**	7%	44%	48%	7::1	333
16	**Zinc**	2%	51%	47%	24::1	1244
17	**VitB6 w/Mg**	4%	49%	47%	12::1	5780
18	**Clonidine**	21%	31%	47%	2::1	1280
19	**IVIG**	7%	51%	42%	6::1	45
20	**DMG/TMG**	7%	51%	42%	6::1	5153
21	**Secretin TD**	10%	49%	41%	4::1	132
22	**Paxil**	29%	30%	41%	1.4::1	283
23	**Prozac**	31%	32%	36%	1.2::1	1123

What are Heavy Metals?

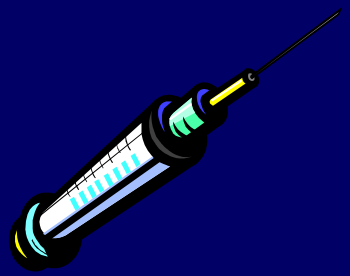
- Basic Definition: a group of elements between copper and bismuth on the periodic table of the elements having specific gravities greater than 4.0.

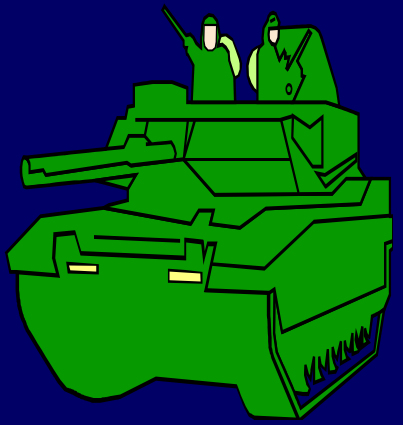
- Stricter Definition: those metals heavier than the rare earth metals, at the bottom of the periodic table.
- None are essential elements in biological systems
- **All** of the more well-known elements with the exception of bismuth and gold are **toxic**.

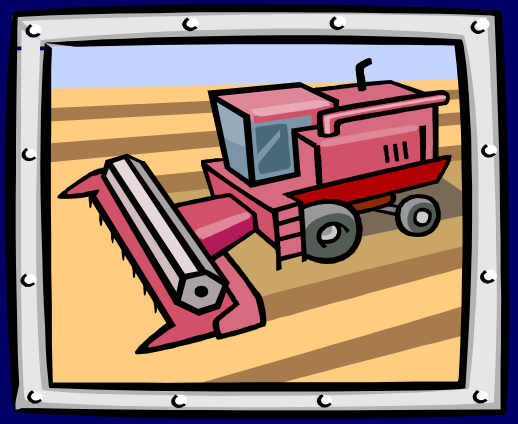
Reference: Wikipedia Website at http://en.wikipedia.org/wiki/Heavy_metals


Periodic Table of the Elements
IA
IIA
IIIB
IVB
VB
VIB
VIIB
VII
IB
IIB
IIIA
IVA
VA
VIA
VIIA
O
1 H
2 He
3 Li
4 Be
5 B
6 C
7 N
8 O
9 F
10 Ne
11 Na
12 Mg
13 Al
14 Si
15 P
16 S
17 Cl
18 Ar
19 K
20 Ca
21 Sc
22 Ti
23 V
24 Cr
25 Mn
26 Fe
27 Co
28 Ni
29 Cu
30 Zn
31 Ga
32 Ge
33 As
34 Se
35 Br
36 Kr
37 Rb
38 Sr
39 Y
40 Zr
41 Nb
42 Mo
43 Tc
44 Ru
45 Rh
46 Pd
47 Ag
48 Cd
49 In
50 Sn
51 Sb
52 Te
53 I
54 Xe
55 Cs
56 Ba
57 *La
72 Hf
73 Ta
74 W
75 Re
76 Os
77 Ir
78 Pt
79 Au
80 Hg
81 Tl
82 Pb
83 Bi
84 Po
85 At
86 Rn
87 Fr
88 Ra
89 +Ac
104 Rf
105 Ha
106 Sg
107 Ns
108 Hs
109 Mt
110 110
111 111
112 112
113 113
* Lanthanide Series
+ Actinide Series
58 Ce
59 Pr
60 Nd
61 Pm
62 Sm
63 Eu
64 Gd
65 Tb
66 Dy
67 Ho
68 Er
69 Tm
70 Yb
71 Lu
90 Th
91 Pa
92 U
93 Np
94 Pu
95 Am
96 Cm
97 Bk
98 Cf
99 Es
100 Fm
101 Md
102 No
103 Lr

Sources of Heavy Metals







Why Should We Test for and Treat Heavy Metals?

- Bind "irreversibly" to proteins
- Cause gross denaturation of tertiary structures of proteins (enzymes)
- Destroy functional configuration of proteins (i.e., prevents biological activity)
- Bind covalently at active site of enzymes

M Yudkin, R Offord: Biochemistry; U of Oxford, 1975

Why Should We Test for and Treat Heavy Metals?

Heavy Metals Denature Proteins

- Enzymes, e.g., Kreb's Cycle, Digestive enzymes
- Structural Proteins, e.g.,Tubulin--U of Calgary Study
  - Inactivate hormones
  - Impair cell receptor sites
  - Destroy or impair neuronal function
  - Impair myriad of metabolic functions

Why Should We Test for and Treat Heavy Metals?

- Impair immune function
- Impair gastrointestinal function
- Inhibit normal bacterial flora
- Impair DNA and RNA repair and replication
- Synergistic Toxicity

Why Should We Test for and Treat Heavy Metals?

Synergistic Toxicity

Makes Heavy Metals

Much More Toxic!

Synergistic Toxicity of Heavy Metals

Lethal Dose Concept—lab animals

- LD-1 = no killing
- LD-50 = half of group of animals died
- LD-100 = **all** animals died

Example with Heavy Metals:

Feeding an LD-1 of a mercury salt with *1/20th* of an LD-1 of a lead salt killed ***all*** test animals = LD-100

Shubert et al. Combined Effects in Toxicology—A Rapid Systematic Testing Procedure: Cadmium, Mercury and Lead. J of Toxicol & Environ Health 4:763,1978

Synergistic Toxicity of Heavy Metals

ALUMINUM (Al) -- powerful Brain toxin, like Mercury, has no physiologic use in body

Al hydroxide, Al Phosphate, Potassium Al Phosphate (alum)

- Accumulates in brain, bone, liver, kidneys, muscles
- Competes with Calcium, Magnesium, Iron
- Poisons important cellular enzymes (e.g., Krebs Cycle)
- Inhibits brain cell neurotubule (structural) function
- Triggers "excitotoxicity" (overstimulation) in brain cells resulting in "apoptosis" cell death
- Overstimulates, damages immune system in brain
- Symptoms: muscle pain, weakness, difficulty thinking, memory loss, visual deficits, Multiple Sclerosis in adults

from Dr. Russell Blaylock, "The Blaylock Wellness Report", February 2007

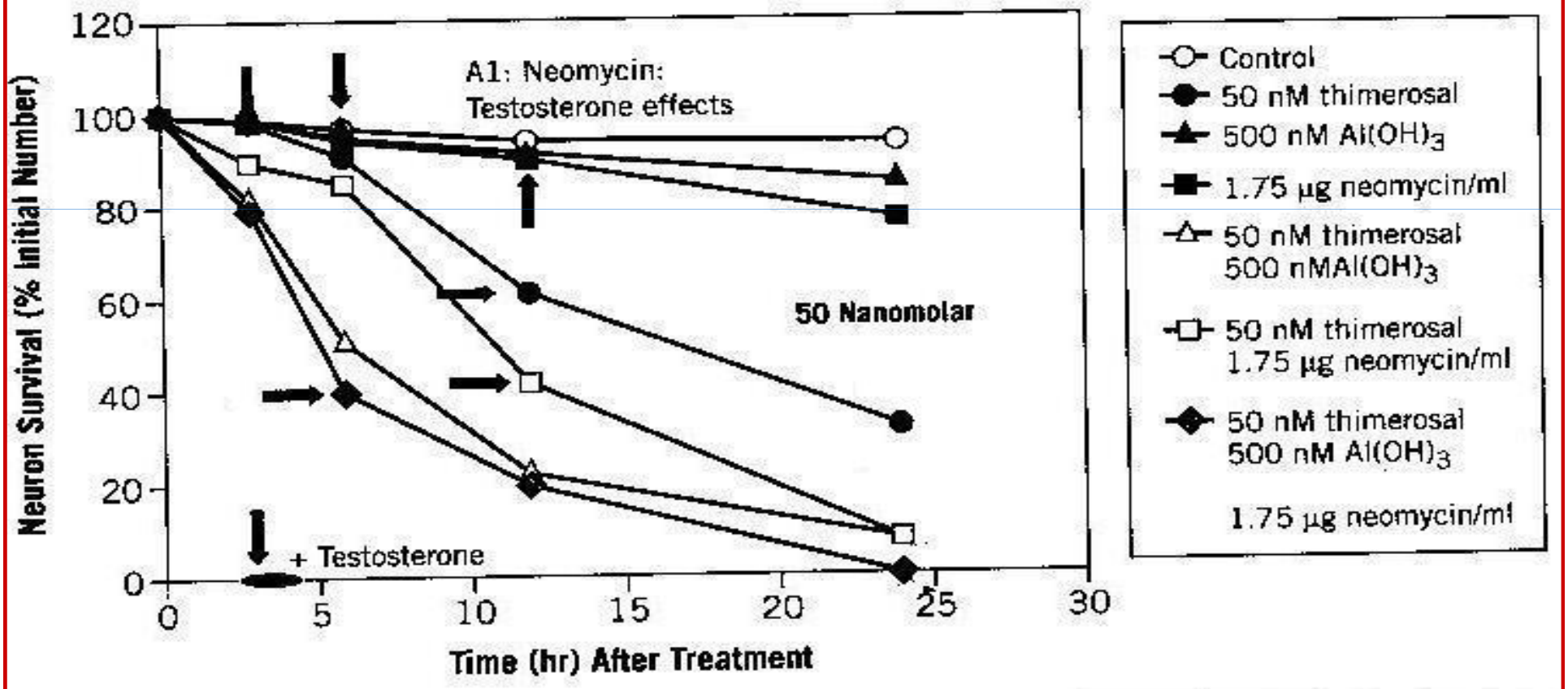
Aluminum in Vaccines

Fiejka M, Aleksandrowicz J., Zakladu Badania Surowic, Warszawie. Rocz Panstw Zakl Hig. 1993;44(1):73-80

"ALUMINUM AS AN ADJUVANT IN VACCINES & POST-VACCINE REACTIONS"

- Added to vaccine as an "**ADJUVANT"—**
  - stimulates immune system to enhance antibody production
- Antigen-Aluminum complex
  - Produces more intense immune reaction than free antigen
  - Produces longer stimulus
  - Can result in local nodule ("granuloma") in 5-10%
  - More frequent cause of local skin reactions than plain vaccines
  - May last for weeks
  - May indicate development of aluminum hypersensitivity
  - Induces production of IgE antibodies

Synergistic Toxicity-- Mercury, Aluminum, Neomycin



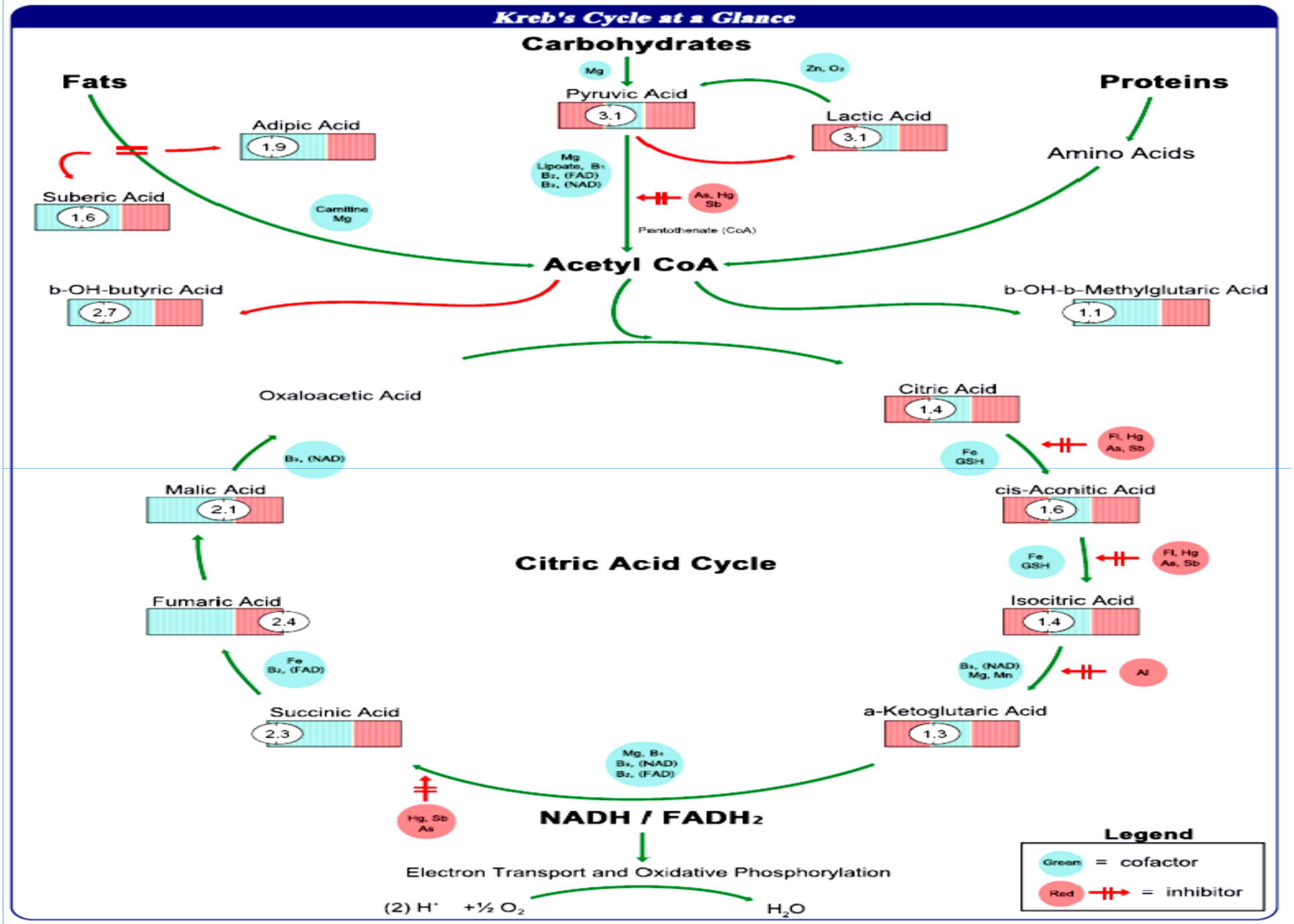
Source: Dr. Boyd Haley and Dr. Mark Lovell, University of Kentucky.

Effects of Heavy Metals-- Mitochondrial Damage

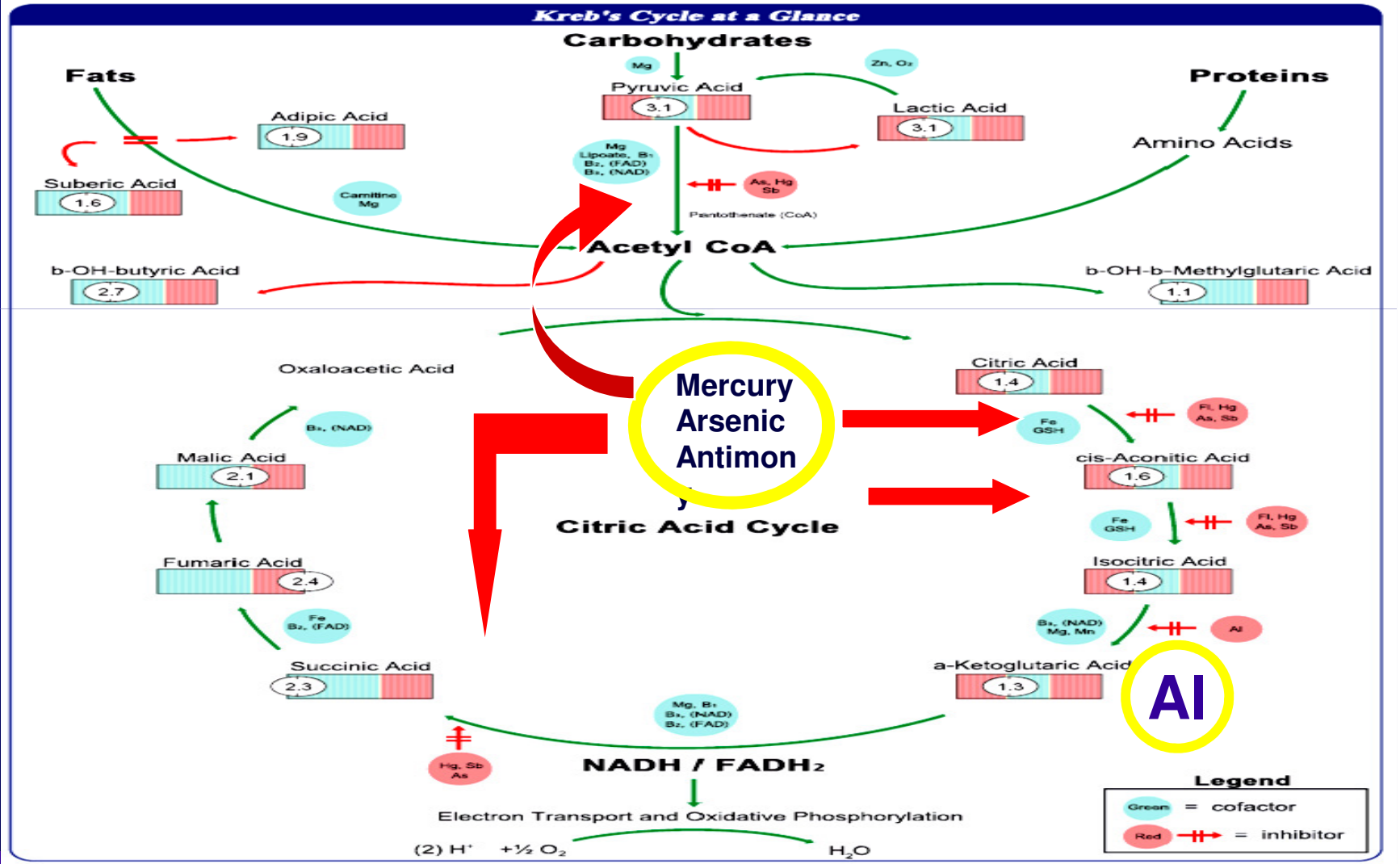
- Heavy metals poison activity of *mitochondria*
  - Inactivate specific steps of Krebs cycle
  - Sulfhydryl-reactive metals, especially Mercury, Lead, Arsenic and Cadmium, bind to sulfhydryl-containing antioxidant, **lipoic acid**
    - make it unavailable in Krebs Cycle
    - vital for production of Acetyl Co-A from pyruvate, keto acids

      Quig DW. Cysteine Metabolism & Metal Toxicity. Alt Med Review.3(4):262-270;1998

- Krebs Cycle dysfunction associated with
  - Cellular dysfunction
  - Specific and generalized tissue & organ dysfunction



Heavy Metal Effects in Kreb's Cycle



Heavy metals—Potentiating factors

- Presence of other heavy metals
  - Cadmium (from smoking), lead, and other heavy metals enhances the toxicity of mercury
    Dr Boyd Haley (Testimony before US Congress, 2001) See Shubert et al.
- ***Excess*** of ***essential minerals***
  - Zinc—excess supplementation associated with increased toxicity of mercury Dr. Boyd Haley, 2001

Heavy metals— Potentiating factors

- **Deficiencies** of essential trace minerals
  - Zinc, selenium, calcium, iron
    - **Zn or Fe** deficiency results in 4-fold increase of intestinal cadmium absorption from food
      Sowa B, Steibert E Arch Toxicol, 56:256-262,1985
    - **Iron** deficiency increases absorption of cadmium, lead and aluminum
      Goyer RA,Toxic & essential metal interactions, Ann Rev Nutr, 17:37-50,1997

It's More Than Mercury !

NUTRIENT DEFICIENCIES—
increase vulnerability to toxins

- Vitamins—C, B-vitamins, A, D, E, K
- Bioflavonoids, Carotenoids
- Minerals—Magnesium, Selenium, Zinc
- Proteins (amino acids)
- Essential Fatty Acids
- Cholesterol

Mercury Issues

Let's Review!

It's More Than Mercury !

- Other Heavy Metals—Pb, As, Al, Sb, Ur, etc.
- Solvents, cleaning agents, fragrances
- Dyes, Cosmetics (phthalates, etc.)
- Pesticides, Petrochemicals
- Viruses, Bacteria, Molds--waste products
- Food Additives—preservatives, colors, flavors
  - Excitotoxins—Glutamates, aspartates
- Hormones, Contraceptives, Xenohormones
- Antibiotics, Pharmaceuticals

Why focus on Mercury ?

- Most toxic of heavy metals
- Very prevalent in our environment
- Treatment of mercury also removes other toxic heavy metals
- Treatment of mercury effectively helps reactivate other metabolic, enzymatic, and detoxification functions throughout the body
- Treatment, therefore, helps body remove other toxic substances (e.g. pesticides)

ELSEVIER

Health Place. 2006 Jun;12(2):203-9.

HEALTH & PLACE

www.elsevier.com/locate/healthplac

Environmental mercury release, special education rates, and autism disorder: an ecological study of Texas

Raymond F. Palmer[a,*], Steven Blanchard[b], Zachary Stein[a], David Mandell[c], Claudia Miller[a]

[a] *University of Texas Health Science Center, San Antonio Department of Family and Community Medicine, 7703 Floyd Curl Drive, San Antonio, Texas 78229-3900, USA*

[b] *Department of Sociology, Our Lady of the Lake University, San Antonio, Texas, USA*

[c] *University of Pennsylvania Center for Mental Health Policy and Services Research, USA*

Accepted 1 November 2004

Findings:
For every 100 pounds of mercury that is emitted from Texas smokestacks, there is a 6% increase in Autism rates in that state.
The regions of Texas with the highest mercury release had the highest incidence of Autism

A Case-Control Study of Mercury Burden in Children with Autistic Spectrum Disorders

Jeff Bradstreet, M.D.
David A. Geier, B.A.
Jerold J. Kartzinel, M.D.
James B. Adams, Ph.D.
Mark R. Geier, M.D., Ph.D.

Journal of American Physicians and Surgeons Volume 8 Number 3 Summer 2003

ABSTRACT

Large autism epidemics have recently been reported in the United States and the United Kingdom. Emerging epidemiologic evidence and biologic plausibility suggest an association between autistic spectrum disorders and mercury exposure.

This study compares mercury excretion after a three-day treatment with an oral chelating agent, meso-2,3-dimercaptosuccinic acid (DMSA), in children with autistic spectrum disorders and a matched control population. Overall, urinary mercury concentrations were significantly higher in 221 children with autistic spectrum disorders than in 18 normal controls (Relative Increase (RI) = 3.15; $P < 0.0002$). Additionally, vaccinated cases showed a significantly higher urinary mercury concentration than did vaccinated controls (RI = 5.94; $P < 0.005$). Similar urinary mercury concentrations were observed among matched vaccinated and unvaccinated controls, and no association was found between urinary cadmium or lead concentrations and autistic spectrum disorders.

The observed urinary concentrations of mercury could plausibly have resulted from thimerosal in childhood vaccines, although other environmental sources and thimerosal in Rh_o(D) immune globulin administered to mothers may be contributory.

Regardless of the mechanism by which children with autistic spectrum disorders have high urinary mercury concentrations, the DMSA treatment described in this study might be useful to diagnose their present burden of mercury.

Population Type	Number of Boys	Number of Girls	Mean Age in Years (Range)	Mean Urinary Mercury (mcg/ g) creatinine (Range)
Cases	183	38	6.25 (3 to 15)	4.06 ± 8.59 (0 to 58.65)
Controls	14	4	8.85 (3 to 16)	1.29 ± 1.54 (0 to 6.2)

With DMSA chelation, ASD children excrete > 3 x more Mercury suggesting an increased body burden.

Mercury and Amalgam

World Health Organization Assessment in 1991:

Dental amalgam is the number one source of mercury in humans.

Mercury in saliva & feces after removal of amalgam fillings

Björkman L, et al. Toxicol Appl Pharmacol. 1997 May;144(1):156-62.
Department of Basic Oral Sciences, Karolinska Institutet, Stockholm, Sweden.

- **Purpose: to obtain data on Hg concentrations in saliva & feces before & after removal of dental amalgam fillings.** Hg concentrations in urine, blood, and plasma were also determined. Ten subjects had all amalgam fillings removed at one session.
- **Before removal, median Hg fecal concentration > 10 X that of samples from amalgam-free reference group 10 subjects (2.7 vs 0.23 mumol Hg/kg dry weight, p < 0.001).**
- **A large increase in fecal Hg concentration 2 days after amalgam removal (median 280 mumol Hg/kg dry weight) was followed by a significant decrease.**
- **Sixty days after removal the median Hg concentration was still slightly higher than in fecal samples from the reference group.**
- **In plasma, initial median Hg concentration was 4 nmol/liter. 2 days after removal; Hg concentration increased to 5 nmol/liter, but declined to 1.3 nmol/liter by Day 60.**
- **In saliva, there was an exponential decline in the Hg concentration during the first 2 weeks after amalgam removal (t 1/2 = 1.8 days).**
- **Hg levels in all media decrease considerably after amalgam removal. Uptake of amalgam mercury in the GI tract after removal of amalgam fillings is low.**

- **Conclusion: amalgam fillings are a *significant* source of Hg in saliva & feces.**

Courtesy of Dr. Boyd Haley, Ph.D, Emeritus Professor, Chairman, Department. of Chemistry, University of Kentucky, USA

"Mercury in saliva & feces after removal of amalgam fillings"

Conclusions:

1. **Amalgam fillings are a *significant* source of Hg in saliva & feces.**
2. **After amalgam removal, mercury levels decrease significantly in all medias (urine, blood & plasma, as well as saliva and feces).**

Courtesy of Dr. Boyd Haley, Ph.D

A Revised Probabilistic Estimate of the Maternal Methyl Mercury Intake Dose Corresponding to a Measured Cord Blood Mercury Concentration

Alan H. Stern

Division of Science Research and Technology, New Jersey Department of Environmental Protection, Trenton, New Jersey, USA; and Division of Environmental and Occupational Health, University of Medicine and Dentistry of New Jersey–School of Public Health, Piscataway, New Jersey, USA

Published in final edited form as:
Neurotoxicol Teratol. 2006 ; 28(3): 363–375.

Impact of prenatal methylmercury exposure on neurobehavioral function at age 14 years

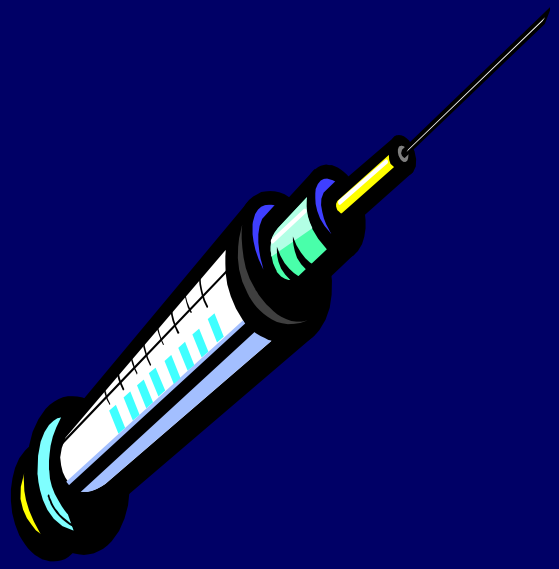
Frodi Debes[a], Esben Budtz-Jørgensen[b,c], Pal Weihe[a,c], Roberta F. White[d], and Philippe Grandjean[c,e]

In structural equation model analyses, the neuropsychological tests were separated into five groups; methylmercury exposure was significantly associated with deficits in motor, attention, and verbal tests. These findings are supported by independent assessment of neurophysiological outcomes. The effects on brain function associated with prenatal methylmercury exposure therefore appear to be multi-focal and permanent.

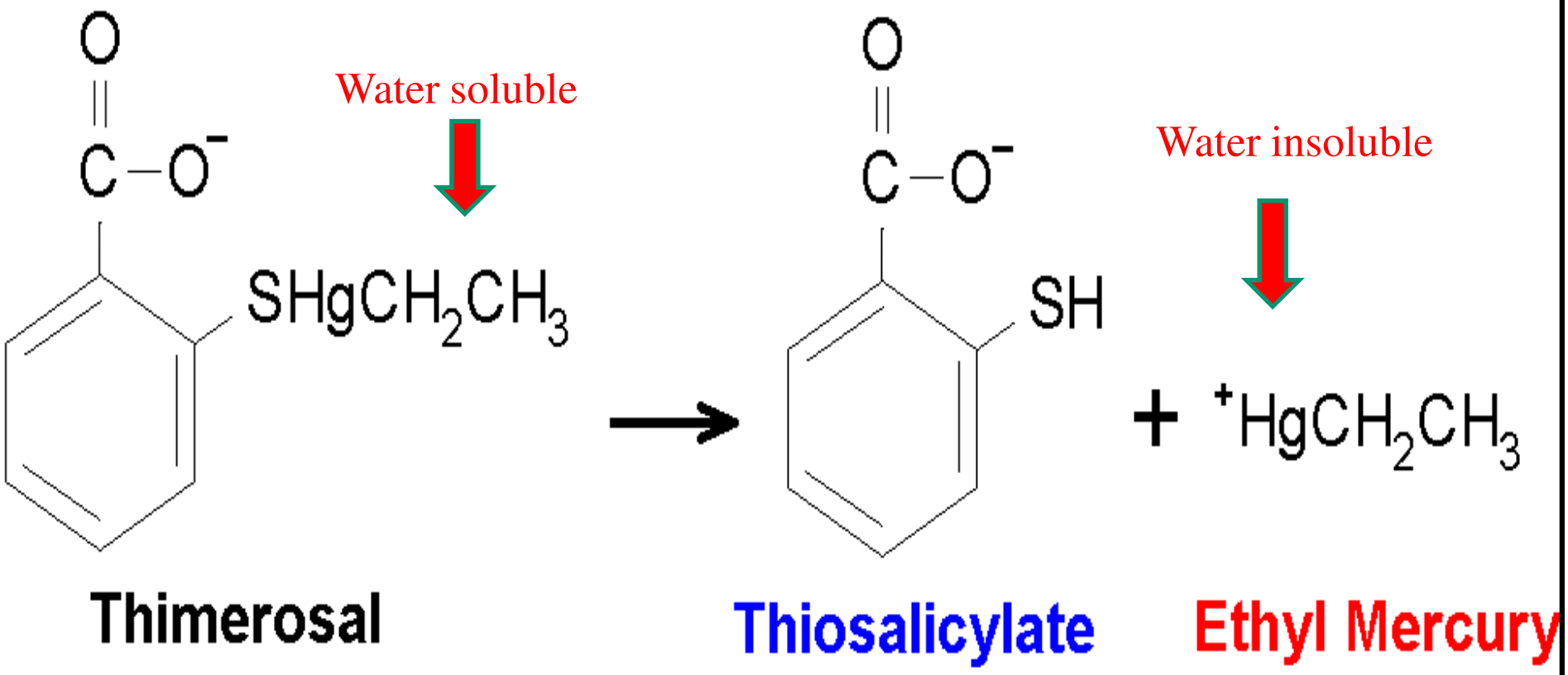
Presented by: Anna Choi, DSc, Harvard School of Public Health

Prenatal Methylmercury exposure affects neurobehavioral function at age 14

Thimerosal in Vaccines—
Another Very Toxic Form of Mercury



Thimerosal Is Composed of Thiosalicylic Acid And Ethyl Mercury, A Known Neurotoxicant



1. The Merck Index, 12th ed., p. 1590, #9451 (1996).
2. Martindale The Extra Pharmacopoeia, 30th ed., 804 (1993).

Thimerosal, Vaccines and Autism

Thimerosal--in most vaccines (until 2002 in US)

- Antibacterial, antifungal
- Used as "preservative", added to each vial
- Toxicity well-established and admitted by Eli Lilly
- Removed from animal vaccines many years ago
- Banned from most over-the-counter products in 1998, but left in vaccines--WHY?
- Vaccine requirements for children birth to age 2 increased from 8 in 1980 to **22** in 2001 in USA
- Children could have received >100x EPA safe daily dose in vaccines given on one day!!

Action and Toxicity of Thimerosal Animal Studies

- Composed of Thiosalicylic Acid and Ethyl Mercury
  - *Ethyl* Mercury—released from Thimerosal
    - Known neurotoxicant The Merck Index, 12th ed., p.1590, #9451 (1996)
    - Acts differently than Methyl Mercury
- Thimerosal clears rapidly from blood Gasset et.al, Ophth.1975
  - CDC, IOM & AAP use this fact to claim thimerosal is not toxic enough to cause autism Pichichero et al, Lancet 360: 1737, 2002
  - Primate Studies—Ethyl Hg converted to inorganic form, Hg2+, which **persists in brain** Burbacher, et al, *2005*

"RAPID BLOOD TO BRAIN MOVEMENT OF [^{203}Hg]-THIMEROSAL"

Gasset et al. Tetratogenicities of Opthalmic Drugs. Arch. Opthalomol 93, 52-55, 1975

- Pregnant rabbits were injected subcutaneous with [^{203}Hg]-thimerosal.
- **From hour 1 post injection to hour 6 the cpm of ^{203}Hg in the blood decreased from 100,000 to less than 25,000 cpm, (over 75%.)**
- **From hour 2 post injection to hour 6 there was increased cpm of ^{203}Hg in the fetal brain (2 fold),** liver (4 fold) and kidney (3 fold).

Courtesy of Dr. Boyd Haley, Dept. of Biochemistry, Univ. of Kentucky

Two-fold increase in brain mercury from 2 to 6 hours post-injection of Thimerosal

Comparison of Blood and Brain Mercury Levels in Infant Monkeys Exposed to Methylmercury or Vaccines Containing Thimerosal

Thomas M. Burbacher,[1,2,3] Danny D. Shen,[4] Noelle Liberato,[1,2,3] Kimberly S. Grant,[1,2,3] Elsa Cernichiari,[5] and Thomas Clarkson[5]

[1]Department of Environmental and Occupational Health Sciences, School of Public Health and Community Medicine, [2]Washington National Primate Research Center, [3]Center on Human Development and Disability, and [4]Departments of Pharmacy and Pharmaceutics, School of Pharmacy, University of Washington, Seattle, Washington, USA; [5]Department of Environmental Medicine, University of Rochester School of Medicine, Rochester, New York, USA

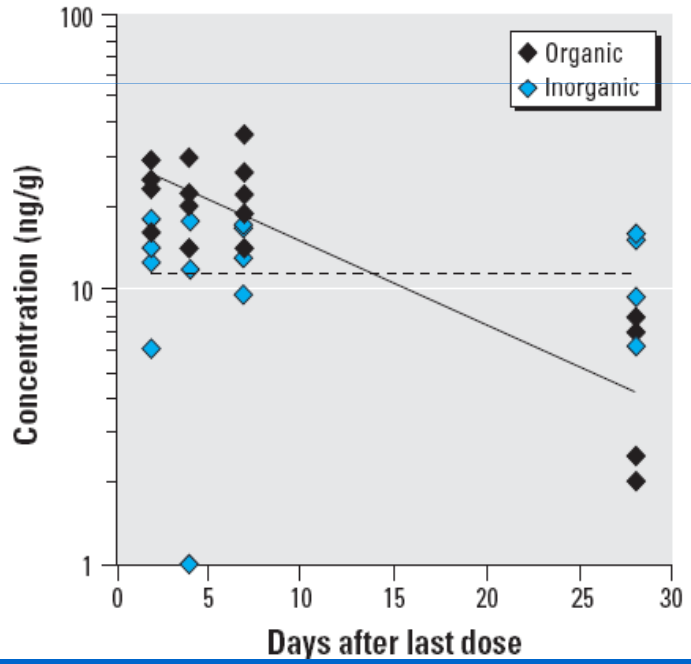


Figure 7. A semilogarithmic plot of washout of organic and inorganic Hg in the brain after four weekly im injection of vaccines containing thimerosal (20 µg/kg Hg). The data were collected from groups of infant monkeys sacrificed at 2, 4, 7, and 28 days after the last dose. The lines represent nonlinear regression fit of the data to a monoexponential model. The regression estimate (± SE) of $T_{1/2}$ for organic Hg is $T_{1/2} = 14.2 \pm 5.2$ days ($r = 0.76$). The half-life of inorganic Hg is too long (> 120 days) to be accurately estimated from the present data (i.e., r is not significantly different from 0).

Inorganic Mercury persists indefinitely in brains of infant monkeys

Changes in the number of astrocytes and microglia in the thalamus of the monkey Macaca fascicularis following long-term subclinical methylmercury exposure.

Neurotoxicology. 1996 Spring;17(1):127-38.

Charleston JS, Body RL, Bolender RP, Mottet NK, Vahter ME, Burbacher TM.

Department of Pathology, School of Medicine, University of Washington, Seattle 98195-7470, USA.

Autometallographic determination of the distribution of IHg by cell type indicates that both the astrocytes and microglia contain substantially elevated IHg deposits relative to all other cell types. The data suggest that the inorganic mercury present in the brains, may be a proximate toxic form of mercury responsible for the changes within the astrocyte and microglial populations.

Summary: Inorganic Mercury collects in monkey brains after long-term, low-dose Methylmercury exposure, and is likely to be the form of mercury responsible for the toxic changes in brain cells.

Molecular Psychiatry (2004), 1–13

www.nature.com/mp

IMMEDIATE COMMUNICATION

Neurotoxic effects of postnatal thimerosal are mouse strain dependent

M Hornig[1], D Chian[1] and WI Lipkin[1,2]

[1]*Jerome L and Dawn Greene Infectious Disease Laboratory, Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA;* [2]*Departments of Neurology and Pathology, Columbia University College of Physicians and Surgeons, New York, NY, USA*

The developing brain is uniquely susceptible to the neurotoxic hazard posed by mercurials. Host differences in maturation, metabolism, nutrition, sex, and autoimmunity influence outcomes. How population-based variability affects the safety of the ethylmercury-containing vaccine preservative, thimerosal, is unknown. Reported increases in the prevalence of autism, a highly heritable neuropsychiatric condition, are intensifying public focus on environmental exposures such as thimerosal. Immune profiles and family history in autism are frequently consistent with autoimmunity. We hypothesized that autoimmune propensity influences outcomes in mice following thimerosal challenges that mimic routine childhood immunizations. Autoimmune disease-sensitive SJL/J mice showed growth delay; reduced locomotion; exaggerated response to novelty; and densely packed, hyperchromic hippocampal neurons with altered glutamate receptors and transporters. Strains resistant to autoimmunity, C57BL/6J and BALB/cJ, were not susceptible. These findings implicate genetic influences and provide a model for investigating thimerosal-related neurotoxicity.
Molecular Psychiatry advance online publication, 8 June 2004; doi:10.1038/sj.mp.4001529

"…following thimerosal challenges that mimic routine childhood immunizations … mice showed growth delay; reduced locomotion; exaggerated response to novelty [and brain changes consistent with] thimerosal-related neurotoxicity."

Toxicity of Thimerosal

Active suppressor of Immune System

- **Hg inhibits WBC division** by disrupting mitotic spindle (tubulin-like structure similar to axons of neurons)
- Very potent **inhibitor of phagocytosis** by monocytes
  - Inhibits process at nanomolar levels
    Rampersad, et al., Transfusion 45(3): 384-93, 2005
  - Prevents removal of microbes, Ethyl-Hg damaged cells and proteins
  - **Leads to greater susceptibility for microbe infections, autoimmunity, chronic inflammation**

    From Boyd Haley, PhD, Mercury Biochemistry and its Relationship to Neurological Disease, USAAA International Conference, August 11, 2006, Park City, UT

Autism -- Biomedical Perspective

Potential mercury toxicity in some children

- Thimerosal in most vaccines until 2002
- ***Synergistic*** toxicity with aluminum, formaldehyde in many vaccines
- Immaturity / vulnerability of hepatic detoxification
  - Sulfation impaired by mercury
  - Glutathione decreased
- Immaturity / vulnerability of Blood Brain Barrier & neurons
- Genetic susceptibility?
  - Children with autism appear to have an impaired ability to excrete mercury compared to neurotypical children
  - Confirmed by scientists at MIT, ASU, and Pfieffer Research Center

Autism & Mercury Poisoning

"**Autism: A Unique Type of Mercury Poisoning"**,Bernard, Enayati, Binstock, et. al., published in Medical Hypothesis, 2001

- Gastro-intestinal Problems
- Immune System Abnormalities
- Biochemical Abnormalities
- Central Nervous System Lesions

“Autism: A Unique Type of Mercury Poisoning”

Bernard, Enayati, Binstock, Roger, Redwood, McGinnis

Medical Hypothesis, 2001

available on Autism Research Institute Website:

www.autism.com/ari

www.defeatautismnow.com

Effects of Mercury in Autism

- Inhibits DPP-IV enzyme
- Increases Th2 Lymphocytes (allergy/inflammation)
- Decreases Th1 Lymphs (viral/fungal defense)
- Induces Autoantibodies to Myelin Basic Protein
- Decreases **Glutathione** in liver & brain

Treatment of Heavy Metals

OVERVIEW

- Alleviating Factors
- Preparing for Chelation/Detoxification
- Chelating Agents
- Glutathione
- OSR—Benefits with Heavy Metals

Heavy Metals—Alleviating Factors

Zinc—

- Promotes renal cadmium elimination

  Sowa B, Steibert E Arch Toxicol, 56:256-262,1985

- Improves placental blood supply in subjects with increased cadmium load Gerhard et al, 1998

- Reduced fetotoxic effects of cadmium-containing drinking water in pregnant rat studies Sorell TL and Gaziano JH, Toxicol Appl Pharmacol, 102:537-545,1990

Heavy Metals—Alleviating Factors

Selenium—

- Protects from mercury and methylmercury toxicity

  Goyer RA,Toxic & essential metal interactions, Ann Rev Nutr, 17:37-50,1997

- Essential factor in the elimination of mercury

  Schrauzer GN *Erfahrungsheilkd, 10:561-564,1990*

- Completely inhibits cytotoxic effects of mercury in in-vitro and in-vivo studies

  Wu XQ et al, The antagonistic effect of selenium on the toxicity of mercury. Trace Elements 7:40-44, 1990

Heavy Metals--Alleviating Factors

Magnesium—

- Blocks intestinal absorption of lead

  Fine BP et al. Influence of magnesium on the intestinal absorption of lead. Environ Res 12:224;1976.

- Increases urinary excretion of lead

  Krall AR et al. Effects of magnesium infusions on the metabolism of calcium and lead, in M Cantin, MS Seelig, Eds. Magnesium in Health and Disease. Spectrum Publications, 941-48;1980

- Deficiency may predispose to Pb intoxication

  Werbach, MR Nutritional Influences on Illness. Third Line Press, Tarzana, CA;549;1996

- Increases activity of glucuronyl transferase--
  - Involved in hepatic glucuronidation

    Brown RC, Bidlack WR. Regulation of glucuronyl transferase by intracellular magnesium, in Proceed Int Sympos Magnesium and its Relationship to Cardiovascular, Renal and Metabolic Disorders. Los Angeles, CA, 1985:24

Heavy Metals—Alleviating Factors

Vitamin C Has antioxidant protection and "chelating" ability

- Lead retention directly reduced Flanagan P et al. The relationship between iron and lead absorption in humans. Amer J of Clin Nutr 36(5):823-829,1982
- Lead content in breast milk decreased Altman P et al, Lead detoxication effect of a combined calcium phosphate and ascorbic acid therapy in pregnant women with increased lead burden. (German) Wiener Medizinische Wochenschrift 131(12):311-314,1981
- Spermatocytes protected from lead-induced toxic effects Hsu P et al, Effects of vitamin E and/or C on reactive oxygen species-related lead toxicity in the rat sperm. Toxicology 128(3):169-179,1998

Heavy Metals—Alleviating Factors

Vitamin C--(continued)

- Mercury—reduces organic (more toxic) forms to safer inorganic and elemental forms, but may not directly remove Hg from body

  Gage J. Mechanisms for the biodegradation of organic mercury compounds: the actions of ascorbate and of soluble proteins. Toxicol and Applied Pharmacol 32(2):225-238;1975

- Cadmium—limits lipid peroxidation

  Hudecova A, Ginter E. The influence of ascorbic acid on lipid peroxidation in guinea pigs intoxicated with cadmium. Food and Chem Toxicol 30(12):1011-1013;1992

- Arsenic—ovaries protected

  Chattopadhyay S et al. Protection of sodium arsenite-induced ovarian toxicity by coadministration of L-ascorbate in mature Wistar strain rat. Arch Environ Contam and Toxicol 41(1):83-89;2001

Basic Labs before Detoxification

- Basic laboratory studies
  - Complete Blood Count
  - Comprehensive Metabolic Profile
  - Iron Studies, Thyroid Profile, Lipid Profile
  - Immune: Immunoglobulins IgG,A,M,E; ANA
- Expanded blood tests
  - Vitamin levels—D, B-6, B-12, Folic Acid
  - Markers for toxicity

Indirect Markers for Metal Toxicity

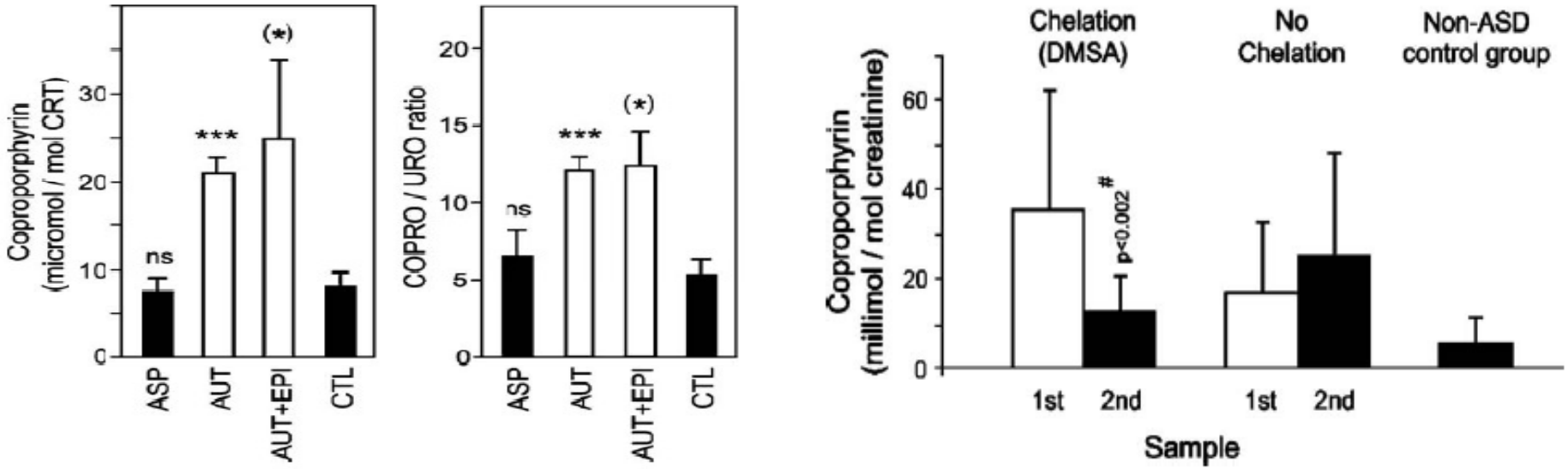
- Haptoglobin—may be increased
- Beta-2 Microglobulin—elevated with Mercury
- Immunoglobulins—Ig M may be increased
- Urinary Porphyrins—Possible biomarker for environmental toxicity

Available online at www.sciencedirect.com
SCIENCE DIRECT
Toxicology and Applied Pharmacology 214 (2006) 99–108
Toxicology and Applied Pharmacology

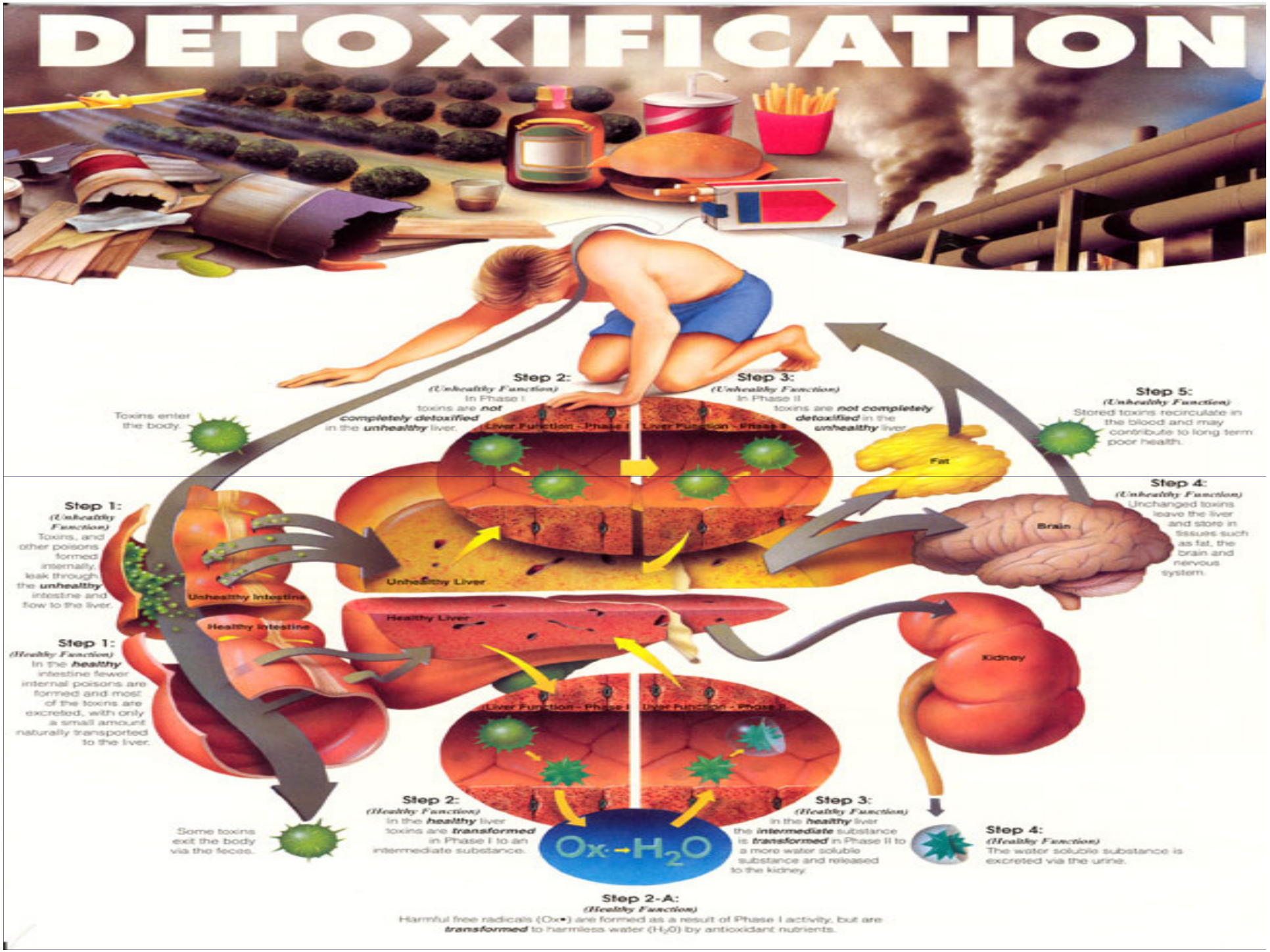
Porphyrinuria in childhood autistic disorder: Implications for environmental toxicity

Robert Nataf [a], Corinne Skorupka [b], Lorene Amet [b], Alain Lam [a], Anthea Springbett [c], Richard Lathe [d,*]

[a] *Laboratoire Philippe Auguste, Paris, France*
[b] *Association ARIANE, Clichy, France*
[c] *Department of Statistics, Roslin Institute, Roslin, UK*
[d] *Pieta Research, PO Box 27069, Edinburgh EH10 5YW, UK*



Increased Coproporphyrins in ASD


DETOXIFICATION
Step 2:
(Unhealthy Function)
In Phase I toxins are not completely detoxified in the unhealthy liver.
Step 3:
(Unhealthy Function)
In Phase II toxins are not completely detoxified in the unhealthy liver
Step 5:
(Unhealthy Function)
Stored toxins recirculate in the blood and may contribute to long term poor health.
Toxins enter the body.
Liver Function - Phase I
Liver Function - Phase II
Fat
Step 4:
(Unhealthy Function)
Unchanged toxins leave the liver and store in tissues such as fat, the brain and nervous system.
Brain
Step 1:
(Unhealthy Function)
Toxins, and other poisons formed internally, leak through the unhealthy intestine and flow to the liver.
Unhealthy Liver
Unhealthy Intestine
Healthy Intestine
Healthy Liver
Kidney
Step 1:
(Healthy Function)
In the healthy intestine fewer internal poisons are formed and most of the toxins are excreted, with only a small amount naturally transported to the liver.
Liver Function - Phase I
Liver Function - Phase II
Step 2:
(Healthy Function)
In the healthy liver toxins are transformed in Phase I to an intermediate substance.
Step 3:
(Healthy Function)
In the healthy liver the intermediate substance is transformed in Phase II to a more water soluble substance and released to the kidney.
Step 4:
(Healthy Function)
The water soluble substance is excreted via the urine.
Some toxins exit the body via the feces.
Ox· → H2O
Step 2-A:
(Healthy Function)
Harmful free radicals (Ox·) are formed as a result of Phase I activity, but are transformed to harmless water (H2O) by antioxidant nutrients.

Preparation for Detoxification/Chelation

DETOXIFY YOUR Child's LIVING AREAS

– <u>Locate, remove, avoid toxic sources</u>

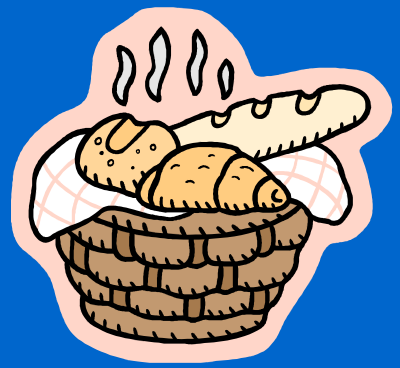
Heavy metals:

- Clothing/bedding -- fire retardants (antimony)
- Wooden playground equipment (arsenic)
- Toys—painted with lead, cadmium paints
- Light bulbs—mercury, tungsten
- Dental fillings (amalgams)
- (also dental sealants)

Preparation for Detoxification/Chelation

Pure water, food, drinks

- Heavy metals (mercury, tin, aluminum)
- Pesticides
- Artificial flavorings (esp. monosodium glutamate MSG)
- Artificial sweeteners (esp. aspartame (Nutrasweet ™)
- Artificial colorings (especially reds and yellows) and preservatives
- Hydrogenated oils
- Food allergens, spices
- Other cooking ingredients
- Cookware and utensils (glass and iron best)
- Gas stove, oven fumes
- MEDICATIONS AND SUPPLEMENTS!



Preparation for Detoxification/Chelation

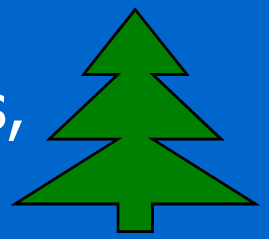
DETOXIFY YOUR LIVING AREAS

- Evaluate home, school, daycare environment
- construction materials
- carpeting/fabrics
- glues/adhesives
- cleaning materials, air fresheners
- laundry detergents, bleaches, etc.
- paints, varnishes, painting materials
- plants, pets
- Other substances around house—contaminated clothing or materials from work, materials stored in basement, garage

Preparation for Detoxification/Chelation

DETOXIFY YOUR LIVING AREAS

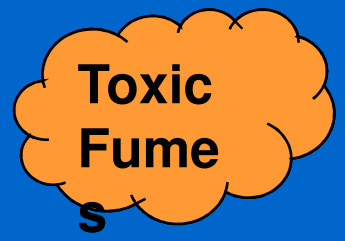
- Outside--play areas at home & school, daycare
  - Fertilizers, herbicides, pesticides, paints
  - Airborne allergens (weeds, flowers, trees, grasses)
  - Toxic fumes (factories, cars/trucks, etc.)
  - Swimming areas—contaminants, pollutants in ponds/lakes; chlorine or other antiseptics in pools



Preparation for Detoxification/Chelation

DETOXIFY YOURSELVES!

Yourselves and child's siblings
- soaps, shampoos
- perfumes, hairsprays, colognes
- hair coloring, gels, "after-shaves"
- cosmetics (lipsticks, mascara, etc.)
- food you eat that child should not



Measuring Heavy Metals

- **Hair** – reflects successful removal which may not be optimal
  - most reliable if detox function intact
  - less reliable for Mercury in infants/children with immature or impaired detoxification; good for Lead
- **Blood** –
  - Serum – useful only for recent exposure
  - RBC – 90-120 day turnover; good for recent toxic exposure or ongoing exposures and for essential mineral assessment
- **Stool** – hepatic detoxification, specimen quality; more useful if recent exposure/ingestion or during chelation
- **Urine** – baseline unchallenged collection not reliable alone

  Arch Environ Health 6:480-3;1963

  – useful if compared to timed collection after oral or IV challenge with chelating agent (e.g., DMSA, DMPS, EDTA, etc.)

Example: Heavy Metals in Blood

- Heavy Metals in blood do not persist in the blood serum or plasma.
  - Bind to proteins, therefore not found in serum unless ongoing or recent isolated exposure
  - Carried to organs (liver, fatty tissue, bones)
- Metals bound in red blood cells cleared as blood cells die, are removed and replaced every three to four months

Reduced Levels of Mercury in First Baby Haircuts of Autistic Children

Amy S. Holmes,[1] Mark F. Blaxill,[2] and Boyd E. Haley[3]

[1]*Baton Rouge, Louisiana, USA*
[2]*SafeMinds, Cambridge, Massachusetts, USA*
[3]*Chemistry Department, University of Kentucky, Lexington, Kentucky, USA*

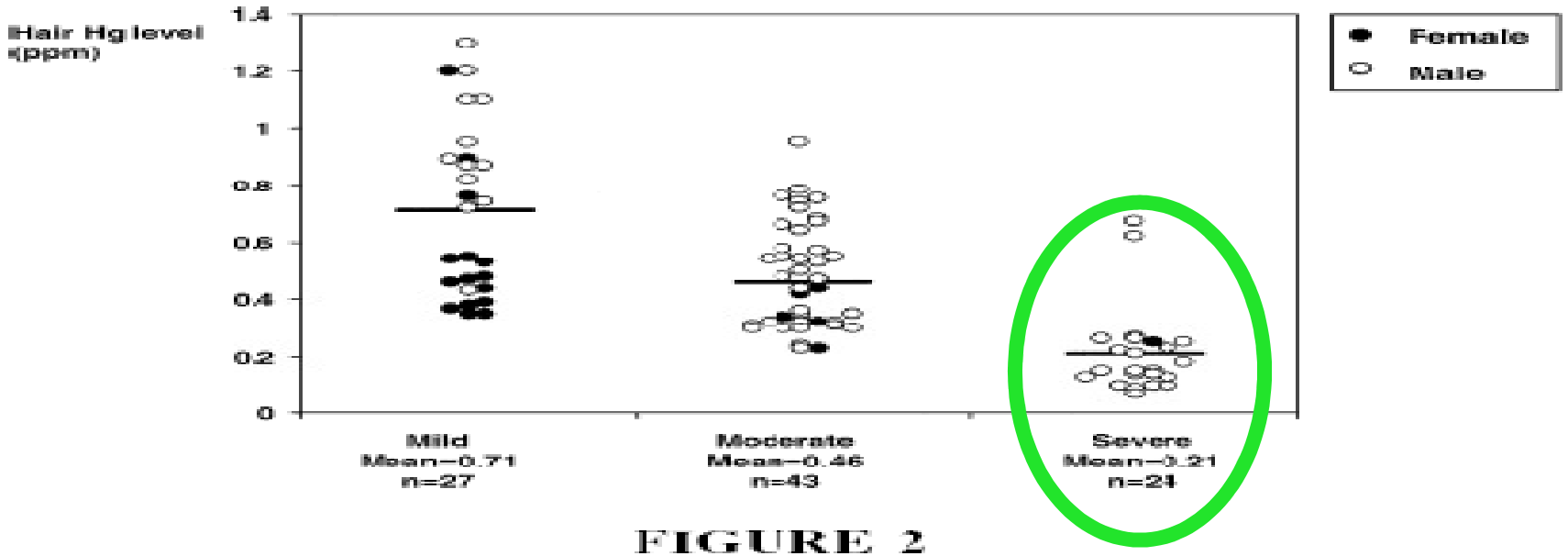


FIGURE 2
A plot of the birth hair mercury levels in autistic children based on the clinical severity of the disease. Solid circles represent individual female subjects and open circles represent individual male subjects.

Children with the most severe autistic symptoms had the lowest hair Mercury

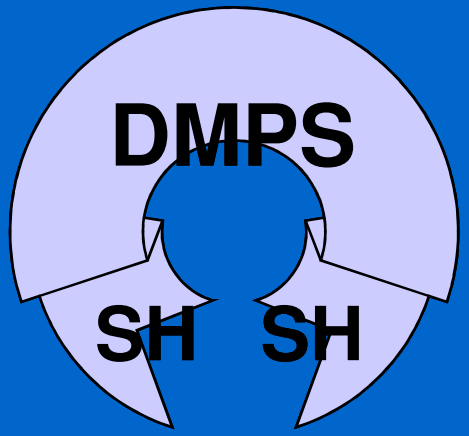
Measuring Heavy Metals

Urine

- Urine Challenge – controversial ; best available tool to evaluate excretion ability and estimate body burden
- Unchallenged urine –
  - not reliable alone as indicator of mercury exposure Arch Environ Health 6:480-3;1963
  - useful as baseline if compared to timed collection after IV or oral challenge with chelating agent (e.g., DMSA, DMPS, EDTA, etc.) Vas Aphosian, Ph.D
- Challenge (provocative) agents vary in affinities for each toxic metal and nutrient mineral
  1. **DMSA (meso-2, 3 dimercaptosuccinic acid)**
  2. **DMPS (sodium 2,3 dimercaptopropane-1-sulfonate)**
  3. **EDTA (ethylene diamine tetra-acetic acid)**
  4. **TTFD (thiamine tetrahydrofurfuryl disulfide)**
  5. **ALA (alpha-lipoic acid)**

What is Chelation?

- Comes from the Greek word for CLAW
- The binding of a substance by a chemical with at least two chemical bonds to the substance in a claw-like fashion
- Often used for removing unwanted minerals, metals



Why Chelation of Heavy Metals ?

Clearance of Mercury and other heavy metals helps restore both pathways—**Methylation** and **Transsulfuration**

- Necessary for detoxification and many critical pathways in growth and metabolism
- Helps prevent depletion of Glutathione, needed for detoxification
- Breaks the "vicious cycle", downward spiral of heavy metal toxicity and further inability to detoxify

Mercury/Heavy Metal Detoxification

DMSA -- Rx *Chemet* (Sanofi Pharmaceuticals), *Succimer* (Thorne), *DiSulfhydryl* (Kirkman)

- Sulfur-thiol, forms stable complex with metals
- Approved by FDA
- Long-term experience in US with pediatric lead toxicity
  (Safety and efficacy of DMSA in children with elevated blood lead concentration. J Toxicol Clin Toxicol 2000; 38(4):365-75)
- Majority (40-60%) remains in intestine; excreted in feces
- Three-day dosing before urine collection
- Good safety profile
- May promote dysbiosis

Mercury/Heavy Metal Detoxification

- **DMSA**--most often used in children in USA--DAN! Protocol for Mercury Detoxification
- Usually oral dosing; can be rectal, transdermal
  - –About every 6-8 hours; do not interrupt sleep
  - –Usually given for 3 days, then eleven days off
  - –More frequent dosing usually OK (2-3d on/4d off)
  - –Re-check CBC, biochemical profile and urine metal challenge after first two or three cycles
  - –Not effective for aluminum chelation

John L. Kucera, MD

Mercury/Heavy Metal Detoxification

DMPS--sodium 2,3 dimercaptopropane-1-sulfonate Dimaval (Heyl); generic available in US at compounding pharmacies

- Not FDA-approved for specific use; use not prohibited
- Rapidly absorbed orally; peaks in ~4 hours
- Majority (45-60%) excreted in urine; rest in feces
- **Greater affinity for Hg and Pb** than As & Cd
- Extensively researched in Europe for safety & efficacy
- Challenge test: one-time oral dose (5 mg/kg) followed by 6-hour urine collection
- Used for treatment of metal toxicity—IV, oral, transdermal, suppository

Mercury/Heavy Metal Detoxification

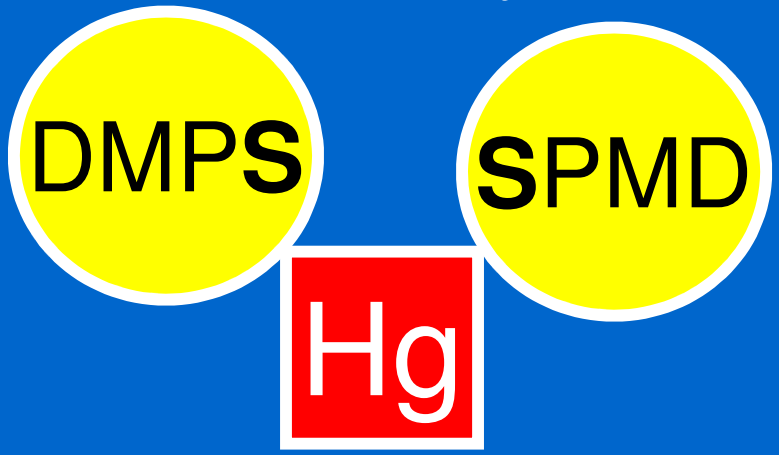
DMPS--usually reserved for persistently elevated mercury or other metals

- –More efficient chelator—fewer doses
- –***More effective chelator of mercury***
- –Can be used for challenge test after DMSA treatment. Can be *used as primary treatment.*
- –Less experience with IV use in young children, but safely used in adults
- –Transdermal forms available

John L. Kucera, MD

"Chelation"-like Effect of DMPS & DMSA

- Two DMPS used to inactivate one atom of Mercury for clearance by Liver or Kidney



Mercury/Heavy Metal Detoxification

Other Chelators

Mercury/Heavy Metal Detoxification

Other Chelators--**Alpha Lipoic Acid (ALA)**

- Naturally made by body (no RX needed)
- Potent antioxidant and hepatic aid in detox
- Improves neuropathy in diabetes
- Water soluble *and* lipid soluble
- Crosses blood brain barrier
- May be yeast promoting if used early
- Better used after body burden of metal lowered

Mercury/Heavy Metal Detoxification

Calcium EDTA

- Effective, safe, inexpensive
- Used as preservative in foods
- Many years of world-wide use in IV form
- Several forms
  - Disodium EDTA—can deplete intracellular Calcium
  - Calcium EDTA—various formulations
- Available in oral, IV, transdermal, and suppository form *(Detoxamin)*
- Used in Biofilm removal strategies in intestines

Mercury/Heavy Metal Detoxification

Other Chelators--

TTFD-Thiamine Tetrahydrofurfuryl Disulfide

- Pioneering work of Derrick Lonsdale, MD
- Sulfhydryl (SH) group (probable chelator)
- Removes SH-reactive metals
  - **Arsenic, mercury, cadmium, lead**
- Initial study used rectal suppositories
- Topical application effective, 50mg AM & PM
- Skin rash and odor common
- May also be treating thiamine deficiency

New Chelator Strategies

- Characteristics of ideal human heavy metal chelator
  - Non-toxic
  - Pass through cell membranes and mitochondria without damaging them
  - Pass readily through blood brain barrier
  - Bind mercury selectively and tightly (permanently)
  - Effectively cleared by hepatic and/or renal pathways

- **OSR** "Oxidative Stress Relief", Benzene bis-amido bis-thiol
  - Base compound binds Hg2+ tighter and more selectively than anything known to date

From Boyd Haley, PhD, Mercury Biochemistry and its Relationship to Neurological Disease, USAAA International Conference, August 11, 2006, Park City, UT

Review: Oxidative Stress & Autism

The single biochemical abnormality found in essentially all neurological, neurodegenerative, and neurobehavioral diseases is **the increased production of oxidative free radical compounds and low glutathione levels.**

This is reflective of oxidative stress.

Oxidative stress is strongly associated with modification of lipids, proteins, and DNA that can lead to:

- membrane structural problems,
- enzyme inhibition and
- genetic mutations.

Dr. Boyd Haley, PhD

Journal of Toxicology and Environmental Health, Part B, 9:485–499, 2006

ISSN: 1093–7404 print / 1521–6950 online
DOI: 10.1080/10937400600882079

Taylor & Francis

EVIDENCE OF TOXICITY, OXIDATIVE STRESS, AND NEURONAL INSULT IN AUTISM

Janet K. Kern, Anne M. Jones

Department of Psychiatry, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, USA

According to the Autism Society of America, autism is now considered to be an epidemic. The increase in the rate of autism revealed by epidemiological studies and government reports implicates the importance of external or environmental factors that may be changing. This article discusses the evidence for the case that some children with autism may become autistic from neuronal cell death or brain damage sometime after birth as result of insult; and addresses the hypotheses that toxicity and oxidative stress may be a cause of neuronal insult in autism. The article first describes the Purkinje cell loss found in autism, Purkinje cell physiology and vulnerability, and the evidence for postnatal cell loss. Second, the article describes the increased brain volume in autism and how it may be related to the Purkinje cell loss. Third, the evidence for toxicity and oxidative stress is covered and the possible involvement of glutathione is discussed. Finally, the article discusses what may be happening over the course of development and the multiple factors that may interplay and make these children more vulnerable to toxicity, oxidative stress, and neuronal insult.

"This article …describes the evidence for toxicity and oxidative stress … and the possible involvement of glutathione …"

Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism

James SJ, Melnyk S, Jernigan S, Cleves MA, Halsted CH, Wong DH, Cutler P, Bock K, Boris M, Bradstreet JJ, Baker SM, Gaylor DW (Goldblatt A)

Am J Med Genet B Neuropsychiatr Genet. 2006 Aug 17

"We propose that an increased vulnerability to oxidative stress (endogenous or environmental) may contribute to the development and clinical manifestations of autism."

Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism[1,2]

S Jill James, Paul Cutler, Stepan Melnyk, Stefanie Jernigan, Laurette Janak, David W Gaylor, and James A Neubrander

Am J Clin Nutr 2004;80:1611–7. Printed in USA.

Comparison of methionine cycle and transsulfuration metabolites between autistic children and control children[1]

	Control children ($n = 33$)	Autistic children ($n = 20$)
Methionine (μmol/L)	31.5 ± 5.7 (23–48)	19.3 ± 9.7 (15–25)[2]
SAM (nmol/L)	96.9 ± 12 (77–127)	75.8 ± 16.2 (68–100)[3]
SAH (nmol/L)	19.4 ± 3.4 (16–27)	28.9 ± 7.2 (14–41)[2]
SAM:SAH	5.2 ± 1.3 (4–8)	2.9 ± 0.8 (2–4)[2]
Adenosine (μmol/L)	0.27 ± 0.1 (0.1–0.4)	0.39 ± 0.2 (0.17–0.83)[4]
Homocysteine (μmol/L)	6.4 ± 1.3 (4.3–9.0)	5.8 ± 1.0 (4.0–5.8)[3]
Cystathionine (μmol/L)	0.17 ± 0.05 (0.1–0.27)	0.14 ± 0.06 (0.04–0.2)[5]
Cysteine (μmol/L)	202 ± 17 (172–252)	163 ± 15 (133–189)[2]
tGSH (μmol/L)	7.6 ± 1.4 (3.8–9.2)	4.1 ± 0.5 (3.3–5.2)[2]
Oxidized glutathione (nmol/L)	0.32 ± 0.1 (0.11–0.43)	0.55 ± 0.2 (0.29–0.97)[2]
tGSH:GSSG	25.5 ± 8.9 (13–49)	8.6 ± 3.5 (4–11)[2]

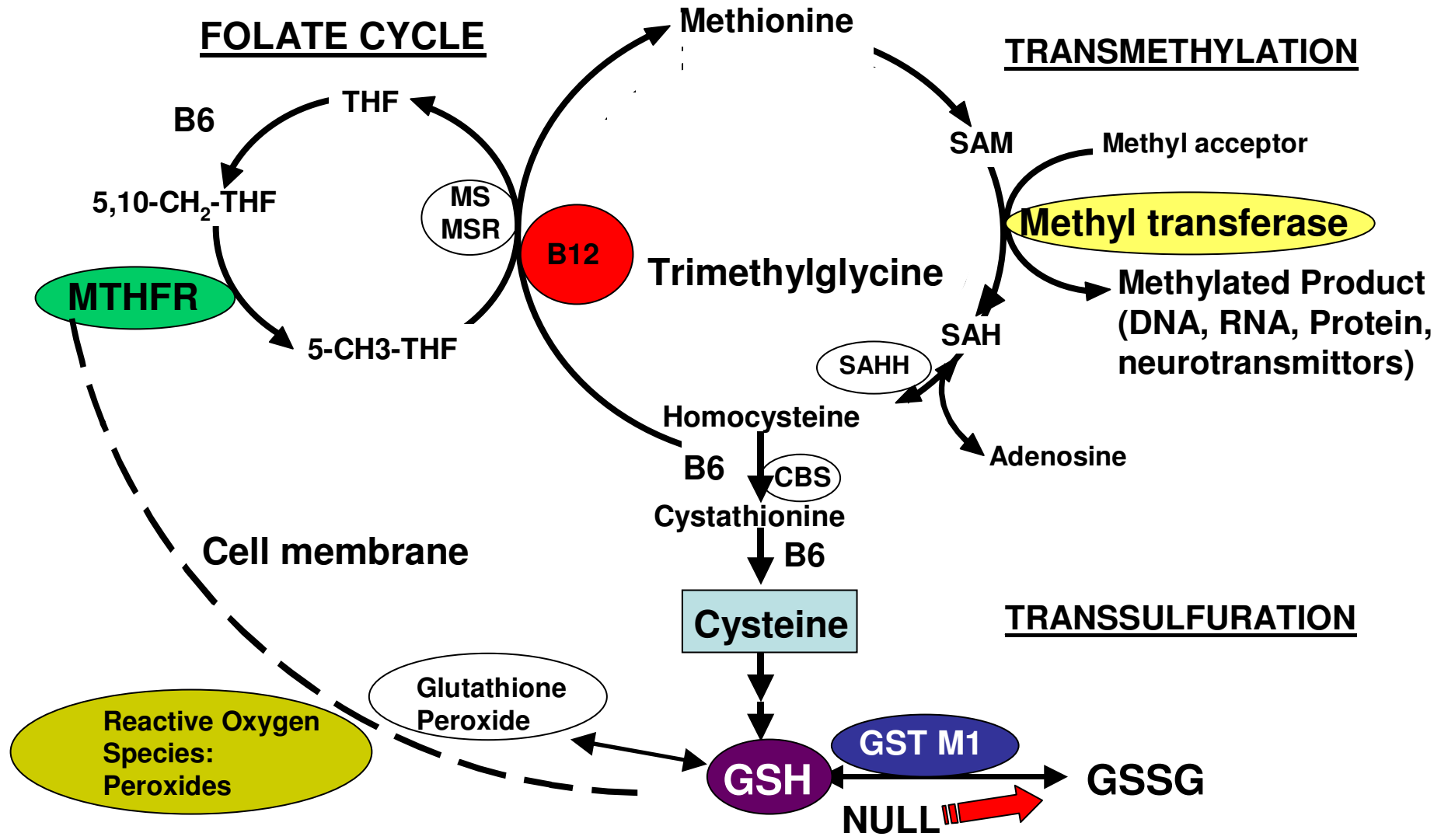
[1] All values are $\bar{x}$ ± SD; range in parentheses. SAM, *S*-adenosylmethionine; SAH, *S*-adenosylhomocysteine; tGSH, total glutathione; GSSG, oxidized glutathione.

[2–5]Significantly different from control children: [2] $P < 0.001$, [3] $P < 0.01$, [4] $P < 0.05$, [5] $P < 0.002$.

Biomarkers of Oxidative Stress—Methionine and Glutathione levels decreased in Autism

The Methylation and Transsulfuration Pathways provide the Reduced Glutathione (GSH) needed to repair Oxidative Damage.

The Methylation and Transsulfuration Pathways Provide the Reduced Glutathione (GSH) to Repair Oxidative Damage.



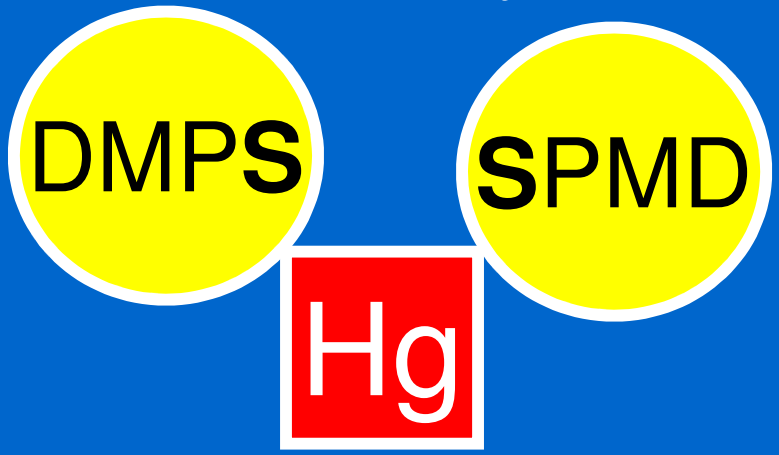
Courtesy of Jill James, PhD, University of Arkansas

Glutathione Deficiency

- Tri-peptide critical for Detoxification
- **Potent Antioxidant**
- Co-factor in Krebs Cycle
- Needed for intestinal function Martensson, Proc Natl Acad Sci 87:3-'90
- Modulates Th1/Th2 immune response Peterson, PNAS 95
- Anti-inflammatory (used in leucotriene synthesis)
- Hepatic biotransformation of toxins
- **Binding to heavy metals—Natural "Chelator"**
- **GSH production dependent on:**
  - **Functional methylation and trans-sulfuration pathways**
  - **Enzymes inhibited by mercury**
  - Adequate amounts of Cysteine (depleted in Autism)
- **Deficient in children with autism** Bradstreet study ICDRC p<.00001

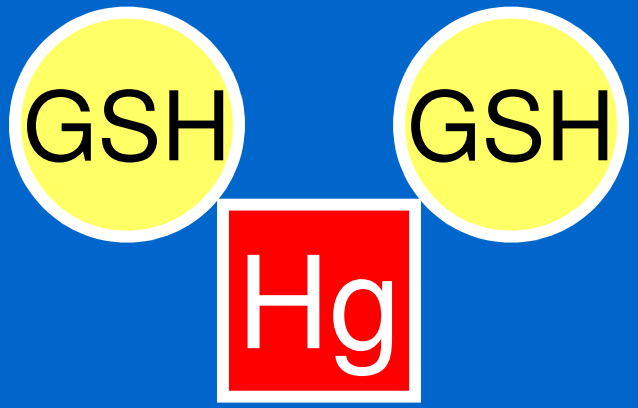
"Chelation"-like Effect of DMPS & DMSA

- Two DMPS used to inactivate one atom of Mercury for clearance by Liver or Kidney



"Chelation"-like Effect of Glutathione

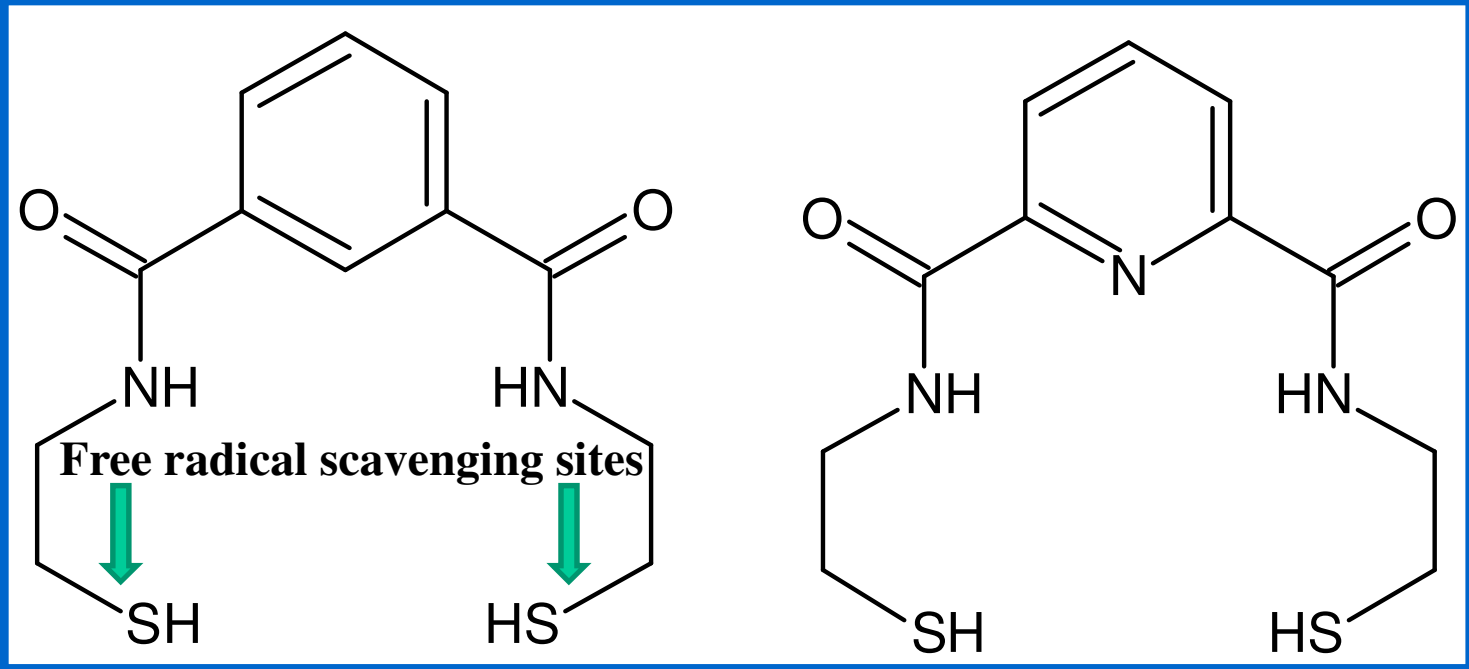
- Two Glutathione GSH needed to inactivate one atom of Mercury:



CONCEPT: WE NEED TO DIRECTLY TREAT OXIDATIVE STRESS BY:

1. REDUCING THE PRODUCTION OF FREE RADICALS OR SCAVENGING THEM TO **SALVAGE GSH**. **(ANTIOXIDANTS IN DIET, REMOVE TOXINS)**
2. INCREASE PRODUCTION OF GLUTATHIONE BY PROVIDING PRO-GLUTATHIONE NUTRIENTS (e.g CYSTEINE) AND **REMOVING ANY TOXICANTS (e.g. HEAVY METALS)** THAT PREVENT GSH SYNTHESIS.
3. PREVENT AND **REVERSE THE DAMAGE CAUSED BY OXIDATIVE STRESS** FACTORS.

OSR—New Lipophilic Agent: Relief for Oxidative Stress—Potent Antioxidant



Potent scavengers of hydroxyl radicals in lipophilic areas.

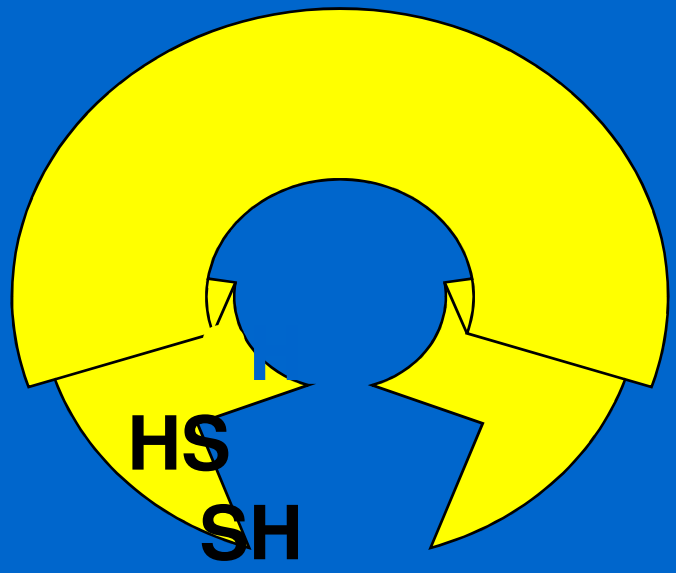
Benzene bis-amido bis-thiol

Pyridine bis-amido bis-thiol

A New Antioxidant called,

"OSR", Oxidative Stress Relief

Chelation Concept



OSR—Also Effective in Heavy Metal Detoxification

- Designed specifically to be lipid soluble
- Very potent antioxidant
- Also safely assists in removing heavy metals sequestered in fat-soluble areas
- No detectable toxicity, even at much higher doses than used in treatment
- Helps maintain health levels of Glutathione, which binds with heavy metals for removal

Mercury/Heavy Metal Detoxification

Precautions

- Make sure bowels moving
  - Some metals cleared through gut
  - Increase fiber – pears, oat bran, apples, legumes, and, if necessary, psyllium at bedtime
  - Magnesium citrate, vitamin C powder
  - Laxatives, if necessary - try *Cascara sagrada* or senna
- Support, protect liver, major detoxifying organ
  - Silymarin (extract of milk thistle), dandelion, artichoke, N-acetyl cysteine, antioxidants
- Monitor and supplement trace minerals
  - Chelators bind with nutritional minerals, too

Mercury/Heavy Metal Detoxification

Throughout treatment:

- Appropriate nutritional support
- Appropriate monitoring tests
  - CBC, CMP after one month
  - Recheck Toxic Metal Provocation Test
  - See DAN! Detoxification Consensus Paper
- Monitor for side effects and benefits
- Consider what supplements, diets, treatments may no longer be necessary!
- Trial careful, individual, slow tapering/discontinuance

Chelation — a Biomedical Treatment

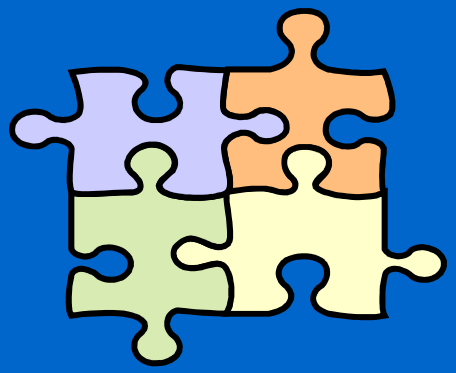
- Correct or compensate for abnormal biochemistry in children with autistic behaviors
- Help remove harmful substances or organisms found by biomedical testing
- Relatively very safe compared with most pharmacological treatments
- Generally easy to know if effective
- Can be utilized with other therapies – nutritional, behavioral, pharmacological
- Work synergistically with other therapies
- Complex! Optimal benefits if supervised by experienced clinician

The Biomedical (Defeat Autism Now!) Approach

"Science-Based Effective Treatments"

- Analyze the Problem—
- Look at the Child – Physical Exam, behaviors
- Listen to the Mom (and Dad/Family/Caregivers)
- Laboratory Testing—Blood, Stool, Hair, Urine, Saliva, Imaging
- Look at the Research, Encourage New Research
- Treatments—Diet, Medications, Minerals, Vitamins, Fatty Acids, Herbals, Natural Products
- Work with and enhance Behavior Therapies
- Explore, Evaluate, Consider "Alternative" Therapies and Routes of Administration
  1. IV therapies, Transdermal, Suppositories
  2. Homeopathy
  3. Hyperbaric Oxygen

Biomedical Approach to Autism

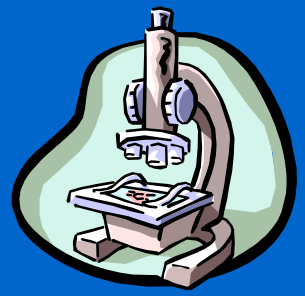


Hyperbaric Oxygen Therapy

Hyperbaric Oxygen (HBOT)

- What is HBOT?
  - A procedure to increase Oxygen in the body by means of a pressurized chamber.
- How does it work?
- What are benefits / risks of HBOT?
- Why is it useful in children with Autism?
- Are there risks of HBOT?

Hyperbaric Oxygen--HBOT



- Has well-defined effects on basic pathophysiologic processes
- Can be used as a drug
- Key mechanism: DNA Signal Induction
- Evidence for efficacy of low-pressure HBOT as a potential therapeutic agent in acute and chronic brain pathology

Hyperbaric Oxygen Therapy HBOT

- EDefinition:
- TThe use of greater than atmospheric pressure of oxygen as a medical intervention (drug) to treat pathological processes, and their associated diseases

Key Principle of HBOT

- Based on "Henry's Law" of Physics
  - Simplified: At a given temperature, the amount of gas that will dissolve in a liquid depends on the pressure of the gas in contact with the liquid.
  - As the pressure of the gas increases, more of it will dissolve into the solution with which it is in contact

HBOT Physiology

If the Gas is OXYGEN and the Liquid is BLOOD,

- The hemoglobin in red blood cells can hold more oxygen under higher pressures
- The hemoglobin will carry more oxygen to the tissues under higher pressures

HBOT Physiology

KEY PRINCIPLES:

- Primary Injury is followed, as a normal part of the body's response, by further Secondary Injuries

- Regardless of the type of PRIMARY insult in ACUTE brain injury, the Secondary Injuries will likely be the DOMINANT INJURIOUS PROCESS

  Harch, Paul G., MD, LSU New Orleans Hyperbaric Medicine and Wound Care Department (11/05 ACAM)

- Goal of treatment: minimize Secondary Injuries

HBOT Physiology

Primary injuries include:

- Ischemia—lack of adequate blood flow
- Hypoxia—lack of adequate oxygen
- Toxins
- Mechanical trauma
- Radiation
- Others

HBOT Physiology

Secondary Injuries

- Secondary injuries include: reperfusion injury, inflammation, hypoxia, oxidative damage, edema, ischemia
- The damaging effects of secondary injuries can be minimized or repaired by Hyperbaric oxygen therapy

HBOT in Chronic Neurological Conditions

Key Concept: **Ischemic Penumbra**

The adjacent dysfunctional brain tissue around an area of clearly and more severely damaged tissue, will retain vascularity and viability, and therefore has increased likelihood of recovering function.

HBOT in Chronic Neurological Conditions

Key Concept: **Ischemic Penumbra**

Stated simply: The less injured brain tissue surrounding the most injured area can survive and recover if given adequate conditions for recovery.

Benefits of Low Pressure (1.3 – 2.0 ATA) **"Mild" HBOT**

- Reduces edema
- Reduces infection
- Reduces inflammation
- Cleans up the extracellular matrix
- Helps restore the Blood-Brain Barrier
- Stimulates growth factors for new blood vessels and neurogenesis
- Reduces seizures
- Reduces spasticity

Potential Side Effects

- Pressure sensation in sinuses, pain in ears
- Irritability (transient)
- Increased hyperactivity (transient)
- Increase in seizures (very rare)
- No major adverse events seen in clinical studies and treatment centers

"Mild" Hyperbaric OxygenTherapy

- Uses low pressures up to 1.3 atmospheres
  - 10 to 12 feet below sea level
- Uses oxygen concentrator in chamber
  - 24% to 96% O2)
- No risk of oxygen toxicity as with High Pressure chambers at 100% oxygen
- Permits use of smaller, light-weight chambers
- Does not require direct medical monitoring

Softshell HBOT Chamber

- Advantages
  - Increased safety
  - Space requirements
  - No building/fire codes
  - Portable
  - Less expensive to purchase/maintain
  - Treatments cheaper
  - No treatment endpoint due to oxygen toxicity
  - After proper training, can be used at home

Softshell HBOT Chamber

- Possible Disadvantages
  - Claustrophobia
  - Less Pressure—1.3 ATA
  - Less O2 Concentration
  - Less Durable Chamber
  - May be less effective or require longer treatment time— 40 “dives” is considered minimal number. Some improve within 10; others after 60, 80, 100.

Reported HBOT Benefits in Autistic Children

Physiology

- Improved oxygenation to tissues/organs
- Increased perfusion to brain
- Improvements documented by SPECT scans
- Decreased markers of inflammation (C-Reactive Protein)
- Increased antioxidant enzymes (catalase, SOD)
- Improved neurological function
- Enhancement of immune system
- Decrease in chronic infections
- Improvement in persistent gut dysbiosis

Rossignol, DA, et. al. Hyperbaric treatment for children with autism: a multicenter, randomized, double-blind, controlled trial.
BMC Pediatr. 2009 Mar 13;9(1):21

Reported HBOT Benefits in Autistic Children

Behavior Changes

- Generally calmer
- Improved cognitive function
- Improved attention span and memory
- Improved sleep
- Improved socialization
- Improved learning of skills

Rossignol DA, et. al. Hyperbaric Oxygen Therapy may improve symptoms in autistic children. *Med. Hypothesis.* 2006; 67(2):216-28

HBOT Benefits in Autistic Children

- Improved behaviors also correlate with findings on SPECT scan
- Enhances benefits of other medical, nutritional and behavioral therapies

Negative Findings for HBOT Benefits in Autistic Children

- Double-blind, placebo-controlled study
- Conditions: 1.3 ATA, 24% Oxygen, 60 minutes, 80 dives—6 to 10 per week
- Small improvements in both groups
- No significant differences between the Experimental and Placebo groups

Granpeesheh, et. al. Randomized Trial of Hyperbaric Oxygen Therapy for Children with Autism. Presented at Defeat Autism Now! Conference, Dallas, TX; Oct 10, 2009

HBOT Response Variability in Autism

- Autism is a multifactorial condition
  - There are many types of autism and many causes of autism
  - Varying responses are expected and reasonable:

    "The Problem: Autism is an enormously heterogeneous disorder that has many causes. It is unlikely that the same preventions or treatments will be optimally effective for all types of autism."

    - David G. Amaral, PhD. "Dealing with the Heterogeneity of Autism: The Autism Phenome Project." Presented at the Defeat Autism Now! Conference; Dallas, TX: October 10, 2009

HBOT Response Variability in Autism

Factors that could influence outcome of HBOT

- Degree of inflammation, oxidative stress
- Number and type of metabolic abnormalities
- Number and type of nutritional deficits
- Variability of treatment chamber conditions
  - Low pressure 1.3 ATA vs. 1.5 or higher
  - Use of supplemental Oxygen vs. Room Air
- Number, length, frequency of treatments
- Number and type of concurrent therapies

HBOT—Summary

- Hyperbaric Oxygen Therapy (HBOT) has many years of worldwide use, documenting its' safety and efficacy
- The mechanisms by which HBOT exerts it's clinical effects are increasingly well understood.
- Short-term clinical studies and the clinical experience of numerous physicians have shown definite benefits of Low-Pressure, "Mild" HBOT.

HBOT—Summary

- After over 5 years of experience in children with autism, statistically significant benefits in cognition, awareness, motivation and speech have been documented.
- SPECT scans correlate improvements in behaviors with increased activity in appropriate brain mapped areas.
- Though few children have a negative response, not all children have a significant positive response. Reasons for the variability in response have been proposed.

HBOT—Summary

- HBOT is not a panacea! Improving diet, gut function, nutritional support and detoxification are necessary as well.
- HBOT works with and likely enhances therapeutic benefits of other treatments.
- Continuing clinical research and experience will help clarify the mechanisms and benefits of HBOT, and the optimal methods for its' use in Autism.

Defeat Autism Now!

IS DEDICATED TO

THE EXPLORATION, EVALUATION,

AND DISSEMINATION OF

SCIENTIFICALLY DOCUMENTED BIOMEDICAL INTERVENTIONS

FOR INDIVIDUALS

WITHIN THE AUTISM SPECTRUM,

THROUGH THE COLLABORATIVE EFFORTS

OF CLINICIANS, RESEARCHERS, AND PARENTS.

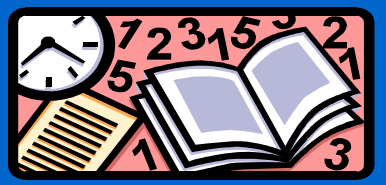
The Defeat Autism Now! Approach

"Science-Based Effective Treatments"

- Keep an open, humble mind—No one knows it all
- Subject new ideas to clinical trials
- Enlist the help and skill of willing scientists, experts
- Avoid prejudices, close-mindedness
- Respect and be guided, but not trapped, by "Scientific Method" or "Western Medicine" view of wellness, illness, physical, emotional and spiritual "health"
- Learn from the experiences and wisdom of others—parents, therapists, teachers, doctors of various disciplines
- Collaborate, share knowledge
- Prayer is okay if you wish to include it in your care of children with Autism

Suggestions for Practitioners/Parents

- Depend/build on knowledge, experience, genius of experts:
  - researchers, clinicians, **parents**
- Maintain intellectual and practical integrity; your motives for what you say and do are important
- Avoid needless, self-serving contradictions and controversies—other parents/practitioners findings, experience may be correct in some cases or for their child
- Avoid the obsession of trying to know it all—it's impossible



Suggestions for Practitioners/Parents

- Collaborate, share your experiences, get advice
- **Stay healthy yourself!**
  - Physical
  - Emotional
  - Spiritual

- **Try to maintain balance in your life and that of your children**

“Sometimes it is not enough to do our best; we must do what is required.”

--Sir Winston Churchill 1874-1965

Prayer of St. Francis of Assisi

Lord, make me an instrument of Thy peace…

- Where there is Hatred, let me so Love;
- Where there is Injury, Pardon;
- Where there is Doubt, Faith;
- Where there is Despair, Hope;
- Where there is Darkness, Light;
- Where there is Sadness, Joy.

O Divine Master, grant that I may not so much seek to be consoled as to console; to be understood as to understand; to be loved as to love;

For it is in giving that we receive; it is in pardoning that we are pardoned; and it is in dying that we are born to eternal Life.

Detoxification, Chelation and Hyperbaric Oxygen Treatment in Autism—

Thank You!

Great Plains Laboratory
Autism Conference
Warsaw, Poland
October 18, 2009

John L. Kucera, MD
Colorado Springs, Colorado, USA