Anti-nutrients and Their Detoxification in Neurodivergence

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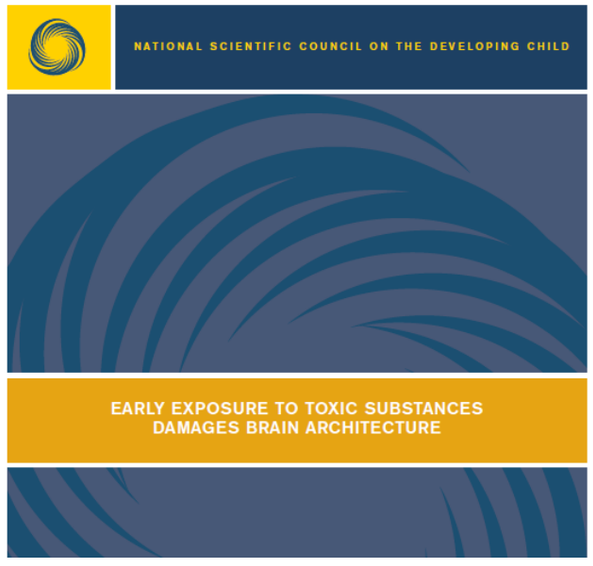


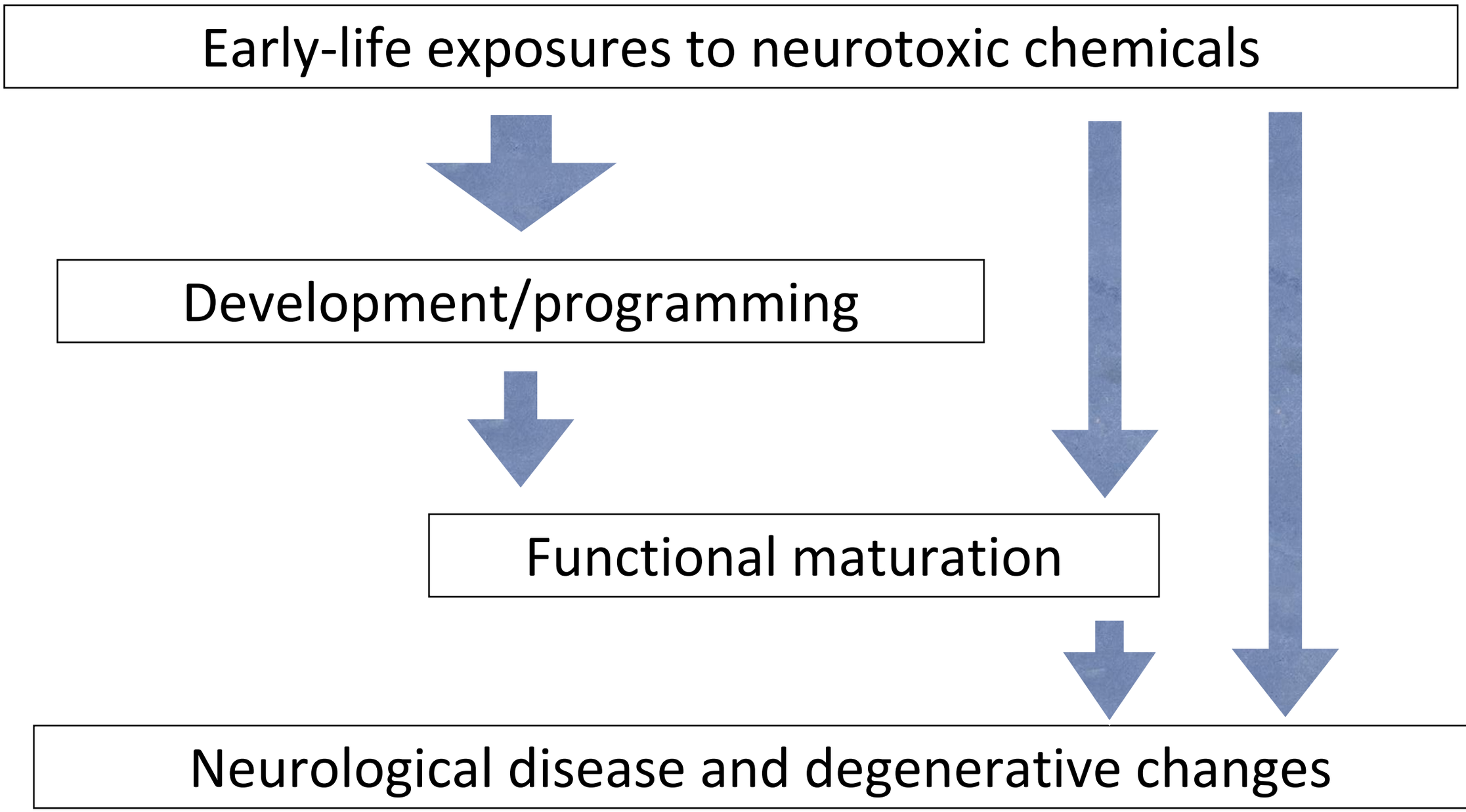
Environmental Exposure - National Scientific Council on the Developing Child

- A multidisciplinary collaboration of leading scientists in early childhood & early brain development
  www.developingchild.net

- The issue: Children develop in an environment of chemicals
- Brains are built over time— the circumstances in which they are built are as important as the initial architectural framework handed down by genetics
- Neurotoxicity may produce changes in architecture & function of brain
- Chemicals that disrupt brain architecture enter through contaminants in air, water, food
- Of greatest consequence: **timing of exposure during developmental process**

- Early assaults can lead to a broad range of physical and mental health problems
- Physical and mental health problems can be lifelong—devastating human and financial cost
- During pregnancy: **extreme sensitivity of developing brain to many chemicals**
- Substances are widely available and highly damaging to immature brains at doses that are tolerated with minimal to no adverse affects in adults

Environmental Exposure



Grandjean, P. and Landrigan, P. (2014). Neurobehavioural effects of developmental toxicity. The Lancet, 13(3), p. 330-338.

Environmental Exposure - Department of Toxic Substances Control

- most of the 80,000+ chemicals registered for use today have not been tested for safety or toxicity by any government agency
- USA: **2000** new chemicals introduced into commerce each year; **7 new chemicals a day**
- **2500** produced in quantities that exceed one million pounds annually
- Only **45%** of these high volume chemicals have been tested for human toxicity
- **Only 7% have been evaluated for potential effects on development (National Scientific Council on the Developing Child)**

- Toxic metals: lead, mercury, cadmium, arsenic, aluminum
- Auto exhaust
- PCB’s
- PBDE’s
- Plasticizers: Phthalates, BPA
- Dioxins
- Pesticides
- Polyaromatic hydrocarbons

THE LANCET Neurology

Neurobehavioural effects of developmental toxicity

Dr Philippe Grandjean, MD, Philip J Landrigan, MD
Published Online: 14 February 2014

- Industrial chemicals that injure the developing brain among known causes for rise in prevalence of ASD, ADHD, dyslexia, etc.
- 5 industrial chemicals identified as developmental neurotoxicants: Lead, methylmercury, PCBs, arsenic, toluene (2006).
- Since 2006, 6 additional developmental neurotoxicants documented: manganese, fluoride, chlorpyrifos, DDT, tetrachloroethylene, PBDEs.
- Even more neurotoxicants remain undiscovered.
- To control the pandemic of developmental neurotoxicity, a global prevention strategy is proposed.

THE LANCET Neurology

Volume 13 · Issue 3 · March 2014 www.thelancet.com/neurology

Articles

Rifampicine in patients with multiple system atrophy

See page 268

Articles

New autoimmune encephalitis with refractory seizures

See page 276

Review

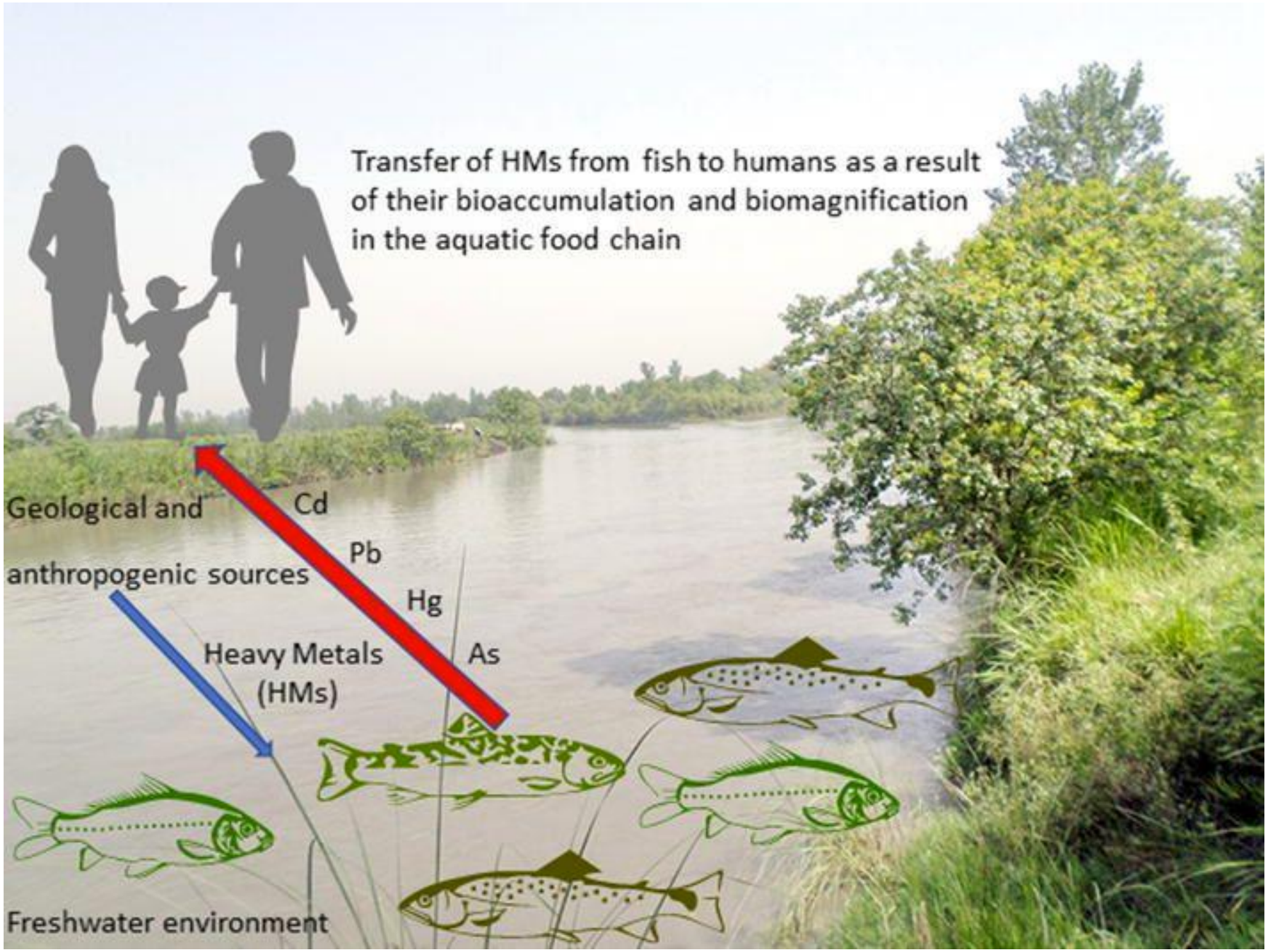
Neurotoxicity in the developing brain

See page 330

Also consider:

- The **air** children breathe
- Their usable **water** supply
- The **foods** children eat
  - fast foods
  - processed snack foods
  - soft drinks and sugar-added beverages
- Food **additives** and artificial sweeteners

Food Contaminants - Bioaccumulation



Ali, H. & Khan, E. **Bioaccumulation of non-essential hazardous heavy metals and metalloids in freshwater fish. Risk to human health**. Environ Chem Lett (2018) 16: 903.

European Commission

How mercury can enter our bodies

Volcanoes and other natural sources

Artisanal and small scale gold mining

Urban sewage system

Waste incineration and cremation

Products

Landfill

Coal power plants

Cement plants

Chlor-alkali plants

Vinyl chloride monomer plants

Landfill leachate

Soil contamination

Deposition to water

Larger fish

Humans

Biomagnification

Smaller fish

Bioaccumulation over time

Tiny plants and animals

which is taken up by

Anaerobic bacteria *convert mercury* to methylmercury

Methylmercury

- Causes majority of harmful mercury exposures.
- Easily absorbed by the gut.
- Binds strongly to proteins in fat, nerves and brain.
- Too much can build up and cause neurological damage.

For more information on mercury, read the Science for Environment Policy In-Depth Report, Tackling mercury pollution in the EU and worldwide.

Maternal-Fetal Transfer

- Virtually all pregnant women have chemicals in their bodies that might harm fetal development.
- Monitoring of pregnant women found about 100 different chemicals, with 43 of them in all women tested.
- Lead, mercury, toluene, perchlorate, bisphenol A, flame retardants, perfluorinated compounds, organochlorine pesticides and phthalates are among the chemicals

  (according to the U.S. Centers for Disease Control and Prevention's nationwide testing program)

Metals in Baby Food

- Toxic heavy metals like lead and arsenic are found in 94% of homemade and store-bought baby foods.

- A Healthy Babies Bright Futures (HBBF) 2019 study found that 95% of baby foods tested were contaminated with toxic heavy metals

- A 2021 Congressional investigation found baby foods to be tainted with “dangerous levels” of toxic heavy metals like lead and arsenic

healthybabyfood.org

Metals in Baby Food

- Rice cakes and crisped rice cereal are heavily contaminated with arsenic

- Lead, arsenic, and cadmium levels are high in some fresh carrots and sweet potatoes

- SKIP 4 foods heavily contaminated with heavy metals: Crisped rice cereal; Puffs (rice-based); Brown rice with no extra cooking water used; Rice cakes

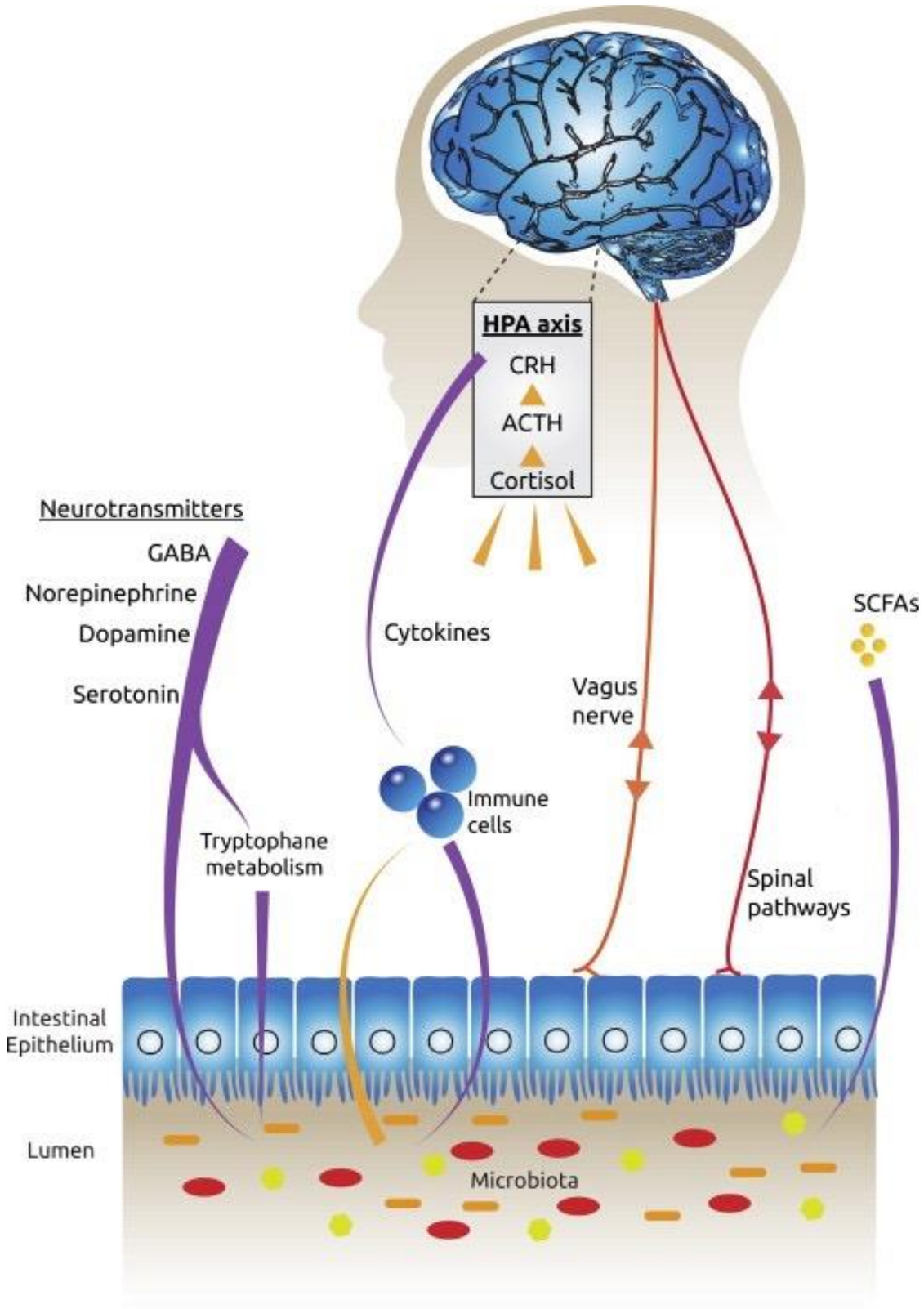
- Choose basmati rice from California and white over brown for lower metals. Rotate rice with other grains— try amaranth, quinoa, buckwheat, millet, and polenta (all gluten-free)

healthybabyfood.org

Toxic Chemicals as Anti-Nutrients

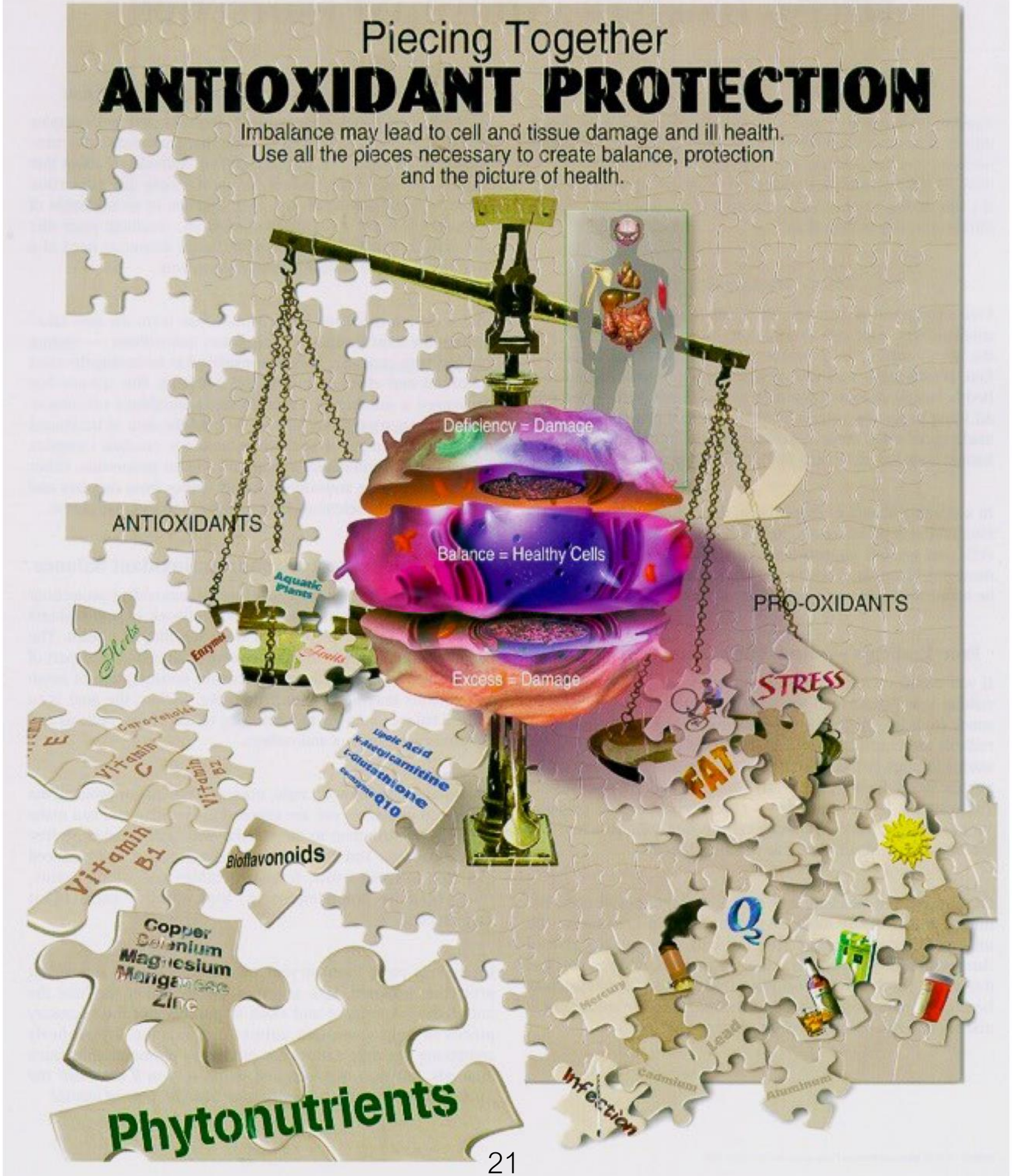
Toxic Chemicals as Anti-Nutrients: How?

- Pesticides and heavy metals can interfere with the absorption and utilisation of essential nutrients in the body. For example, lead can interfere with calcium absorption and cadmium can interfere with zinc and iron absorption.
- Cause harm to beneficial bacteria in the gut microbiome. An imbalanced gut microbiome can lead to reduced nutrient synthesis (i.e. post-biotic production), absorption, and increased inflammation
- Induce damage the gut lining leading to increased intestinal permeability or leaky gut syndrome. A leaky gut can reduce nutrient absorption and lead to nutrient deficiencies.



Toxic Chemicals as Anti-Nutrients: How?

- Toxic chemicals can impair liver and kidney function which are critical for detoxification and nutrient metabolism
- Increase oxidative stress and inflammation in the body. Chronic inflammation can interfere with normal digestion and absorption of nutrients. **Oxidative stress drains antioxidant reserves**
- Pesticides and heavy metals can deplete the body's antioxidants, including glutathione, vitamin C, and vitamin E. Lower antioxidant levels can increase inflammation and oxidative damage
- Pesticides and metals can interfere with energy metabolism in the **mitochondria**. Mitochondrial dysfunction can lead to low energy levels and compromised cellular function.



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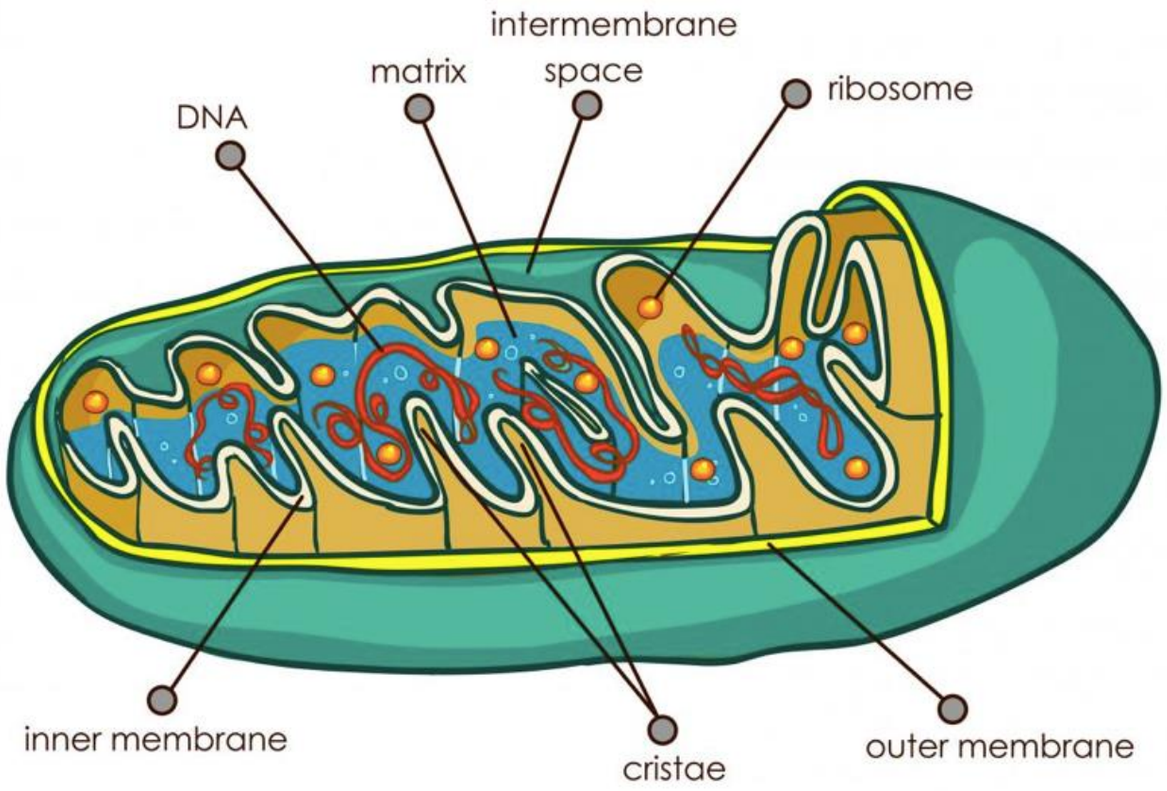
Mitochondria

- Produce 90% of a cell's energy
- Found in most cells - a few hundred per cell
- Abundant in metabolically active cells - brain, cardiac and skeletal muscle, liver, kidney – can contain thousands
- 10% of our body weight; number a million billion
- Have their own DNA - mtDNA



Secondary mitochondrial dysfunction: Toxins, medications

- Heavy metals - mercury, lead, arsenic, aluminum, cadmium
- Pesticides
- Auto exhaust
- Gut organism biotoxins
- Hypoxia - and functional hypoxia
- Meds: valproic acid, risperidone, acetaminophen, SSRI’s
- Lowered glutathione

Mitochondria - key points

- Primary source of free radicals (prooxidants) is by electron leakage from the electron transport chain
- Protection from damage to mtDNA and from oxidative stress by **Glutathione**
- Mitochondria cannot produce GSH – import it from cytoplasm
- Other critical nutrients for mitochondrial function: iron, magnesium, CoQ10; carnitine, lipoid acid; B vitamins
- Output: energy and free radicals

Mitochondrial dysfunction and ASD

- Children with ASD are more likely to have deficits in their ability to produce cellular energy than are typically developing children.
- Cumulative damage and oxidative stress in mitochondria might influence both the onset and severity of autism, suggesting a significant link between autism and mitochondrial problems.
- Several studies have documented a significantly lower mean glutathione (GSH) concentration and a lower mitochondrial GSH reserve in children with ASD compared to controls.

Mitochondrial dysfunction and autism spectrum disorders: A simplified approach

Autism Science Digest: The Journal of Autism One Issue. 2012 2.

Mitochondrial dysfunction and ASD continued

- These findings suggest that mitochondria from children with ASD may be **more vulnerable to damage from environmental toxicants** than mitochondria from typically developing children.
- Several studies have reported that nutritional supplements and/or antioxidants may be beneficial in some children with ASD who have mitochondrial dysfunction.
- Six studies have reported various improvements (including language and coordination) with the **use of carnitine** in children with ASD and mitochondrial disease.

Mitochondrial dysfunction and autism spectrum disorders: A simplified approach

Autism Science Digest: The Journal of Autism One Issue. 2012 2.

Pesticides

von Ehrenstein Ondine S, Ling Chenxiao, Cui Xin, Cockburn Myles, Park Andrew S, Yu Fei et al. (2019).

Prenatal and infant exposure to ambient pesticides and autism spectrum disorder in children: population based case-control study.

BMJ. 364 doi: https://doi.org/10.1136/bmj.l962

- 2961 individuals with diagnosis of autism spectrum disorder, including 445 with intellectual disability comorbidity, in California's main agricultural region
- Controls derived from birth records matched to cases 10:1 by sex and birth year
- Data from California state mandated Pesticide Use Reporting to estimate prenatal and infant exposures to pesticides
- 11 high use pesticides selected for examination according to previous evidence of neurodevelopmental toxicity in vivo or in vitro

von Ehrenstein Ondine S, Ling Chenxiao, Cui Xin, Cockburn Myles, Park Andrew S, Yu Fei et al. (2019).

Prenatal and infant exposure to ambient pesticides and autism spectrum disorder in children: population based case-control study.

BMJ. 364 doi: https://doi.org/10.1136/bmj.l962

- Risk of autism spectrum disorder was associated with prenatal exposure to glyphosate, chlorpyrifos, diazinon, malathion, avermectin, and permethrin.
- For autism spectrum disorder with intellectual disability, estimated odds ratios were higher (by about 30-40%) for prenatal exposure to glyphosate, chlorpyrifos, diazinon, permethrin, methyl bromide, and myclobutanil.
- Exposure in the first year of life increased the odds for the disorder with comorbid intellectual disability by up to 50% for some pesticide substances.

von Ehrenstein Ondine S, Ling Chenxiao, Cui Xin, Cockburn Myles, Park Andrew S, Yu Fei et al. (2019).

Prenatal and infant exposure to ambient pesticides and autism spectrum disorder in children: population based case-control study.

BMJ. 364 doi: https://doi.org/10.1136/bmj.l962

- Findings suggest that an offspring's risk of autism spectrum disorder increases following **prenatal exposure** to ambient pesticides within 2 km of mother's residence during pregnancy, compared with offspring of women from the same agricultural region without such exposure.
- **Infant exposure** could further increase risks for autism spectrum disorder with comorbid intellectual disability.

Mercury

CDC: Mercury and Newborns

- An estimated 300,000 newborns each year—**one out of every 14— are exposed to levels of methylmercury that exceed guidelines** that the EPA set to avoid neurological effects in fetuses.
- Mercury in the womb has been tied to reduced IQ and other effects on developing brains

The value of ecologic studies: mercury concentration in ambient air and the risk of autism

Rev Environ Health 2011;26(2):111–118
K. Stephen Blanchard1,*, Raymond F. Palmer2 and Zachary Stein3

- Given that they are particularly susceptible to the adverse neurologic effects of mercury, **children can be particularly at risk** from environmental mercury exposure.
- **The body burdens of mercury accumulation can begin in utero**
- Wide range of environmental sources:
  -Industrial emissions to air, land, water
  -Consumption of fish, various other foods
  -Dental amalgams

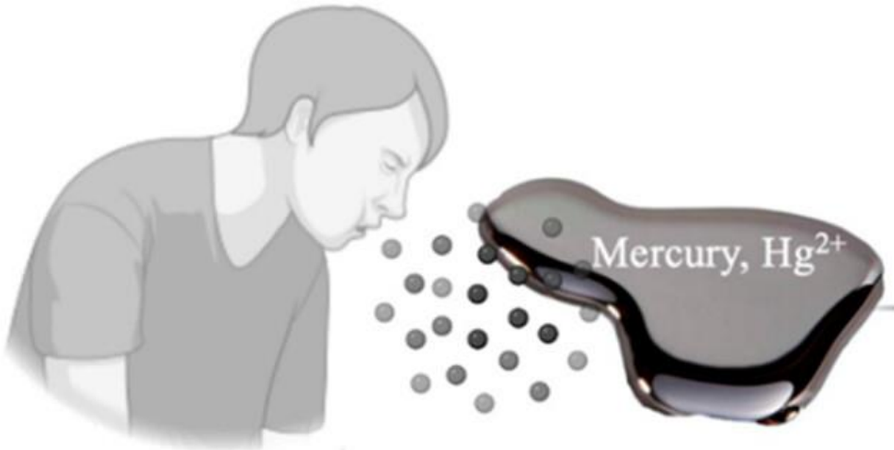
The value of ecologic studies: mercury concentration in ambient air and the risk of autism

Rev Environ Health 2011;26(2):111–118

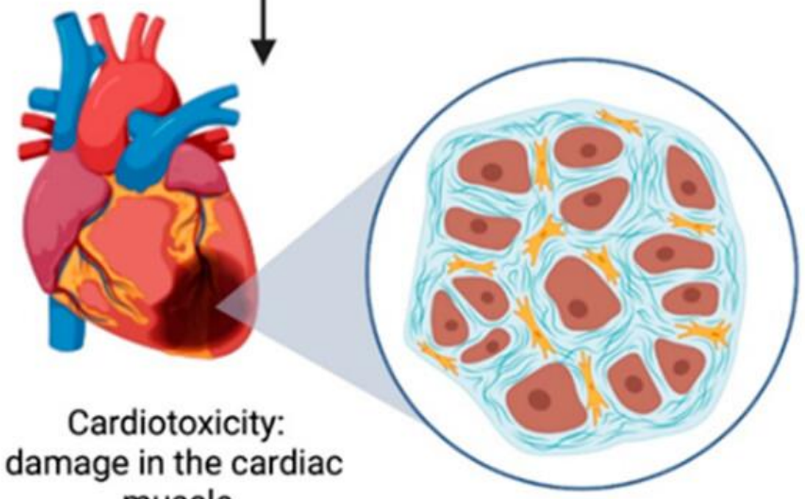
K. Stephen Blanchard1,*, Raymond F. Palmer2 and Zachary Stein3

Recent reports implicate mercury in the etiology of metal-induced neurodegeneration and oxidative damage, suggesting that mercury exposure could have a role in the etiology of various developmental and cognitive disorders.

1. **The Toxicity of Mercury and Its Chemical Compounds: Molecular Mechanisms and Environmental and Human Health Implications: A Comprehensive Review**
   Yuan-Seng Wu et al; *ACS Omega* **2024** *9* (5), 5100-5126
   DOI: 10.1021/acsomega.3c07047



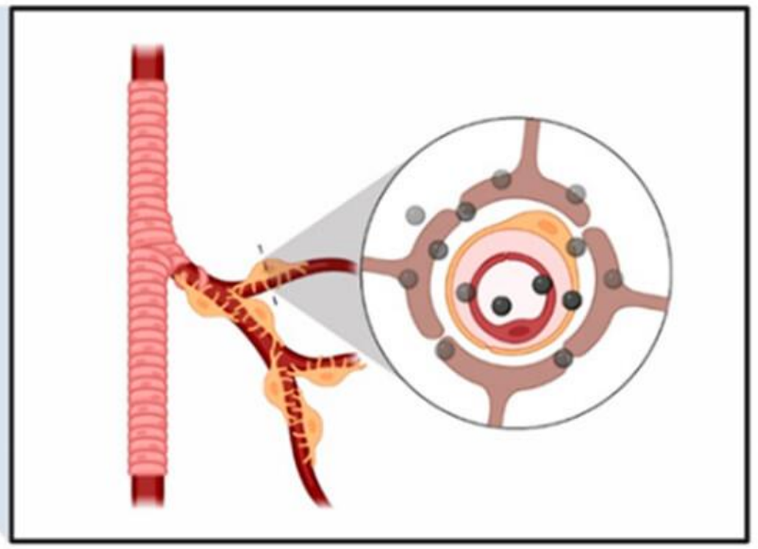
Exposure



Cardiotoxicity:
damage in the cardiac muscle
• Pumping problem

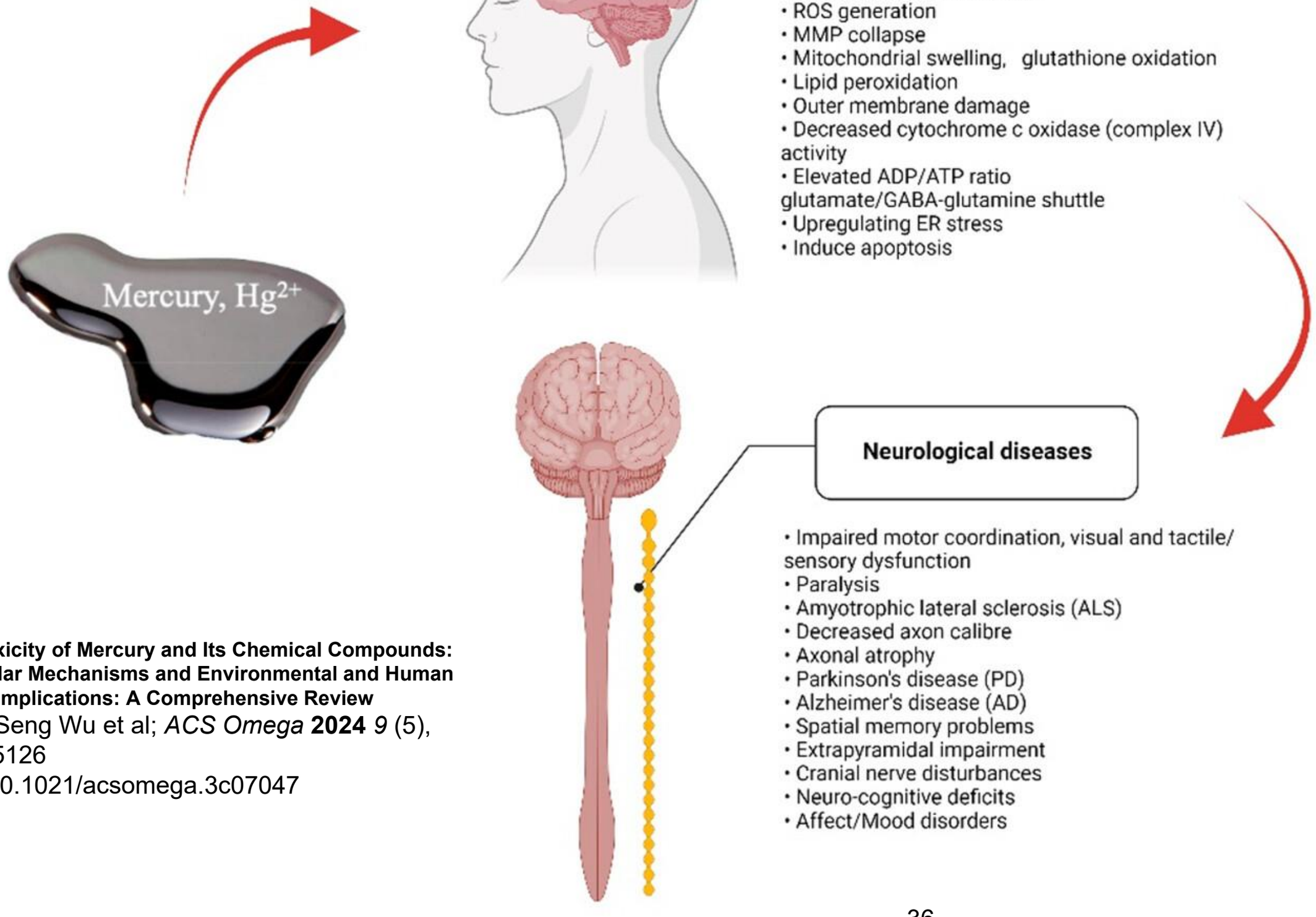
- Coronary heart disease
- Cerebrovascular accident
- Myocardial infarction
- Hypertension
- Carotid artery obstruction
- Cardiac arrhythmias
- General atherosclerosis

Mercury is present in breast milk and builds rapidly in the placenta and embryonic cells.



Mercury rapidly traverses the blood-brain barrier and the placenta, then into the foetal brain.

DOI: (10.1021/acsomega.3c07047)



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DOI: 10.1021/acsomega.3c07047

DOI: (10.1021/acsomega.3c07047)

New science challenges old notion that mercury dental amalgam is safe

Biometals (2014) 27:19–24, DOI 10.1007/s10534-013-9700-9
Kristin G. Homme • Janet K. Kern •
Boyd E. Haley • David A. Geier • Paul G. King • Lisa K. Sykes • Mark R. Geier

Amalgam load and mercury

- Animal and human studies reveal that mercury is transferred to breast milk in proportion to maternal dental amalgam load.
- **The developing neuron is the most sensitive target for mercury** (Berlin et al. 2007). Studies on neurons in culture find growth impairment at the same mercury concentrations that are found in neonatal infants of amalgam-bearing mothers with no other known exposures.

Lead

ehp ENVIRONMENTAL HEALTH PERSPECTIVES
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Environ Health Perspect. 2011 June; 119(6): 873–877.
Published online 2010 December 16. doi: 10.1289/ehp.1002835
PMCID: PMC3114825
Research
Children's Health

Residential Proximity to Freeways and Autism in the CHARGE Study

Heather E. Volk,[1] Irva Hertz-Picciotto,[2] Lora Delwiche,[2] Fred Lurmann,[3] and Rob McConnell[4]

Author information ► Article notes ► Copyright and License information ►

See "A Research Strategy to Discover the Environmental Causes of Autism and Neurodevelopmental Disabilities" in volume 120 on page a258.

This article has been cited by other articles in PMC.

Abstract

Go to:

Background Little is known about environmental causes and contributing factors for autism. Basic science and epidemiologic research suggest that oxidative stress and inflammation may play a role in disease development. Traffic-related air pollution, a common exposure with established effects on these pathways, contains substances found to have adverse prenatal effects.

Study: Living Near a Highway May Contribute to Autism Risk

Environmental Health Perspectives:

children who lived near highways at birth had twice the risk of autism as those who live farther way.

The impact of low-level lead toxicity on school performance among children in the Chicago Public Schools: a population-based retrospective cohort study

Anne Evens, Daniel Hryhorczuk, Bruce P Lanphear, Kristin M Rankin, Dan A Lewis, Linda Forst, and Deborah Rosenberg.

Environmental Health 2015, 14:21 doi:10.1186/s12940-015-0008-9; 7 April 2015

- These results clearly indicate that **early childhood lead exposure has a negative impact on school performance**, even at blood lead concentrations below 5 µg/dL.
- The impact of low-level lead exposure on children's school performance is substantial.

The impact of low-level lead toxicity on school performance among children in the Chicago Public Schools: a population-based retrospective cohort study

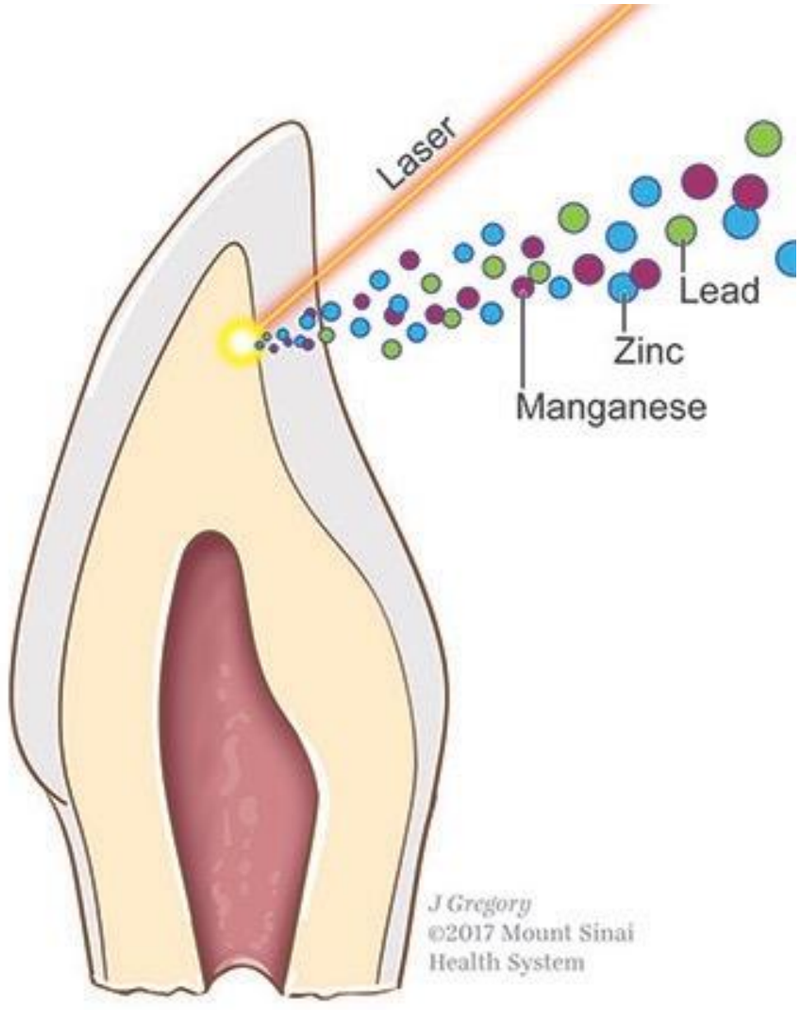
Anne Evens, Daniel Hryhorczuk, Bruce P Lanphear, Kristin M Rankin, Dan A Lewis, Linda Forst, and Deborah Rosenberg. Environmental Health 2015, 14:21 doi:10.1186/s12940-015-0008-9; 7 April 2015

- Among all children, a 5 µg/dL increase in B-Pb within a B-Pb range of 2 – 9 µg/dL resulted in a **32%** increase in the risk of failure.
- Childhood lead exposure at levels ≥5 µg/dL accounted for as much as **25%** of children failing in reading and math.
- While various risk factors are associated with school failure, lead exposure is a particularly important one.
- Moreover, it is entirely preventable.

Manish Arora, Abraham Reichenberg, Charlotte Willfors, Christine Austin, Chris Gennings, Steve Berggren, Paul Lichtenstein, Henrik Anckarsäter, Kristiina Tammimies & Sven Bölte. 2017. **Fetal and postnatal metal dysregulation in autism.** Natural Communications. https://doi.org/10.1038/ncomms15493

- Fetal and early childhood exposure to toxic metals and deficiencies of nutritional elements linked with several adverse developmental outcomes frequently associated with ASD
- Previous research shows methodological shortcomings e.g. **elemental exposure has frequently been estimated using concentrations in blood post-diagnosis**
- Arora et al: tooth-matrix biomarkers that directly measure fetal and postnatal exposure to multiple metals, and recruited twins from population-based cohorts

Manish Arora, Abraham Reichenberg, Charlotte Willfors, Christine Austin, Chris Gennings, Steve Berggren, Paul Lichtenstein, Henrik Anckarsäter, Kristiina Tammimies & Sven Bölte. 2017. **Fetal and postnatal metal dysregulation in autism.** Natural Communications. https://doi.org/10.1038/ncomms15493



- Cross-section of tooth showing laser removal of the dentine layer, in tan, for analysis of metal content.

Manish Arora, Abraham Reichenberg, Charlotte Willfors, Christine Austin, Chris Gennings, Steve Berggren, Paul Lichtenstein, Henrik Anckarsäter, Kristiina Tammimies & Sven Bölte. 2017. **Fetal and postnatal metal dysregulation in autism.** Natural Communications. https://doi.org/10.1038/ncomms15493

- **In ASD cases, higher lead levels** were observed over the prenatal period and first 5 months postnatally
- **Zinc levels were lower** in cases during the third trimester
- Manganese levels were consistently lower in cases both pre- and postnatally, and this deficiency was highest 4 months after birth
- Correlated tooth-matrix biomarkers with the severity of autistic traits a decade later using established clinical assessments. **Lead and manganese showed statistically significant associations with ADOS-2 or SRS-2**

Modern Exposure of Major Significance: Gasoline

Source: Kitman; The Secret History of Lead; The Nation, Mar 2002

- Burning of gasoline has accounted for 90 percent of lead placed in the atmosphere since the 1920s
- Most of the estimated 7 million tons of lead burned in gasoline in the United States in the twentieth century remains -- **in the soil, air and water and in the bodies of living organisms**

A Civilization Exposed

According to a 1988 report to Congress on childhood lead poisoning in America by the government's Agency for Toxic Substances and Disease Registry about

68 million young children had toxic exposures to lead from gasoline from 1927 to 1987.

Source: Jamie Lincoln Kitman, The Nation. March 2000.

Environmental Research. 2017.

Background lead and mercury exposures: Psychological and behavioral problems in children.

Brooks B. Gumpa, Matthew J. Dykasb, James A. MacKenzie, Amy K. Dumasa, Bryce Hruskaa, Craig K. Ewart, Patrick J. Parsons, Christopher D. Palmere, Kestutis Bendinskasg.

https://doi.org/10.1016/j.envres.2017.06.033

- Potential harm from exposure to nonessential metals, particularly mercury (Hg) and lead (Pb), has been the focus of research for years.
- Initial interest focused on relatively high exposures; however, **recent evidence suggests that even background exposures might have adverse consequences for child development**
- Measured Pb and Hg, psychological outcomes, and vagal responses in children ages 9-11.

Environmental Research. 2017.

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https://doi.org/10.1016/j.envres.2017.06.033

- Pb levels were associated with hostility, ODD, and poor emotional regulation.
- These significant associations were found within a range of blood Pb levels from 0.19 to 3.25 µg/dL, **well below the "reference value" for children of >5 µg/dL**.
- Increasing Hg was associated with increasing autism spectrum behaviours for those children with sustained vagal tone during acute stress.

The Changing Reference Value - CDC

Previous Definitions for Interpreting Childhood Blood Lead Levels

Conversion factor = 0.0483

Year	Blood lead level (µg/dL)		Interpretation*
1960	60		Not applicable
1970	40		Undue or increased lead absorption
1975	30		Undue or increased lead absorption
1978	30		Elevated blood lead level
1985	25		Elevated blood lead level
1991	10	**0.48**	Level of concern
2012	5	**0.24**	Reference value
2021	3.5	**0.17**	Reference value

*https://stacks.cdc.gov/view/cdc/61820

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CS 335659-A November 2022

Lead Facts

- Lead toxicity is a multisystem disease
- Risk factor for fetal loss and neurologic impairment of the infant after delivery
- Major risk to children today: lead-based paints, the food supply and contaminated soil
- Lead = cumulative toxicant; very prolonged residence in bone
- Evaluating sources of exposure requires evaluating lifelong events

Lead Facts

- Blood lead levels increase at times of high bone turnover i.e. prolonged immobilization; menopause; fracture; pregnancy; lactation; vitamin D deficiency
- Fetal exposure – maternal lead stores are mobilized to the fetus during pregnancy
- In children lead levels increase from ages 9 – 36 months due to increased hand-mouth activity
  -- peak hand-mouth age is 18 – 24 mos.
- Children retain **40-50 %** of lead they are exposed to (Adults retain 10%)

Susceptibility of Children

- Fetal exposure
- Undeveloped blood brain barrier (up to 6 months of age)
- Immature detoxification - prolonged half life in children
- Synergy with other contaminants
  –> more than 200 chemicals found in cord blood
- Avenues of exposure and entry
- The age of neurodevelopment

Aluminum

… and Glyphosate

Aluminum and Glyphosate Can Synergistically Induce Pineal Gland Pathology: Connection to Gut Dysbiosis and Neurological Disease

Agricultural Sciences, 2015, 6, 42-70
Stephanie Seneff, Nancy Swanson, Chen Li

- Al is invariably toxic to living systems
- No known beneficial role in any biological systems
- Humans increasingly exposed to Al from food, water, medicinals, cosmetics, industrial occupational exposure
- Al forms toxic complexes with other elements, such as fluorine, and interacts negatively with mercury, lead, and glyphosate
- Negatively impacts CNS in all species that have been studied, including humans

Aluminum and Glyphosate Can Synergistically Induce Pineal Gland Pathology: Connection to Gut Dysbiosis and Neurological Disease

Agricultural Sciences, 2015, 6, 42-70. Stephanie Seneff, Nancy Swanson, Chen Li

- Many neurological diseases, including autism, depression, dementia, anxiety disorder and Par-kinson's disease, are associated with abnormal sleep patterns, which are directly linked to pineal gland dysfunction.
- The pineal gland is highly susceptible to environmental toxicants.
- Glyphosate chelates aluminum, allowing ingested aluminum to bypass the gut barrier. This leads to anemia-induced hypoxia, promoting neurotoxicity and damaging the pineal gland.

Aluminum and Glyphosate Can Synergistically Induce Pineal Gland Pathology: Connection to Gut Dysbiosis and Neurological Disease

Agricultural Sciences, 2015, 6, 42-70. Stephanie Seneff, Nancy Swanson, Chen Li

- Glyphosate and aluminum disrupt cytochrome P450 enzymes, involved in melatonin metabolism.
- Melatonin is derived from tryptophan, whose synthesis in plants and microbes is blocked by glyphosate
- **Pineal gland is outside of the blood brain barrier (BBB) and is highly perfused**—receiving a blood flow rate that is second only to that of the kidney.
- Likely explains why it is especially susceptible to exposure to environmental toxicants such as aluminum, mercury, cadmium and fluoride

Perinatal Toxicity Of Aluminum

The Internet Journal of Toxicology Volume 3 Number 1
P Nayak. 2005.

- At the perinatal age, aluminum is highly neurotoxic and **inhibits prenatal and postnatal brain development**.
- In addition, maternal dietary exposure to excess aluminum during gestation and lactation which did not produce maternal toxicity would be capable of causing permanent neurobehavioral deficits in weanling mice and rats
- "Elevated aluminum exposure level at this vulnerable age might produce **a lifelong toxicological consequence."**

Aluminum-Induced Entropy in Biological Systems: Implications for Neurological Disease

Journal of Toxicology, Volume 2014, Article ID 491316

Christopher A. Shaw, Stephanie Seneff et al

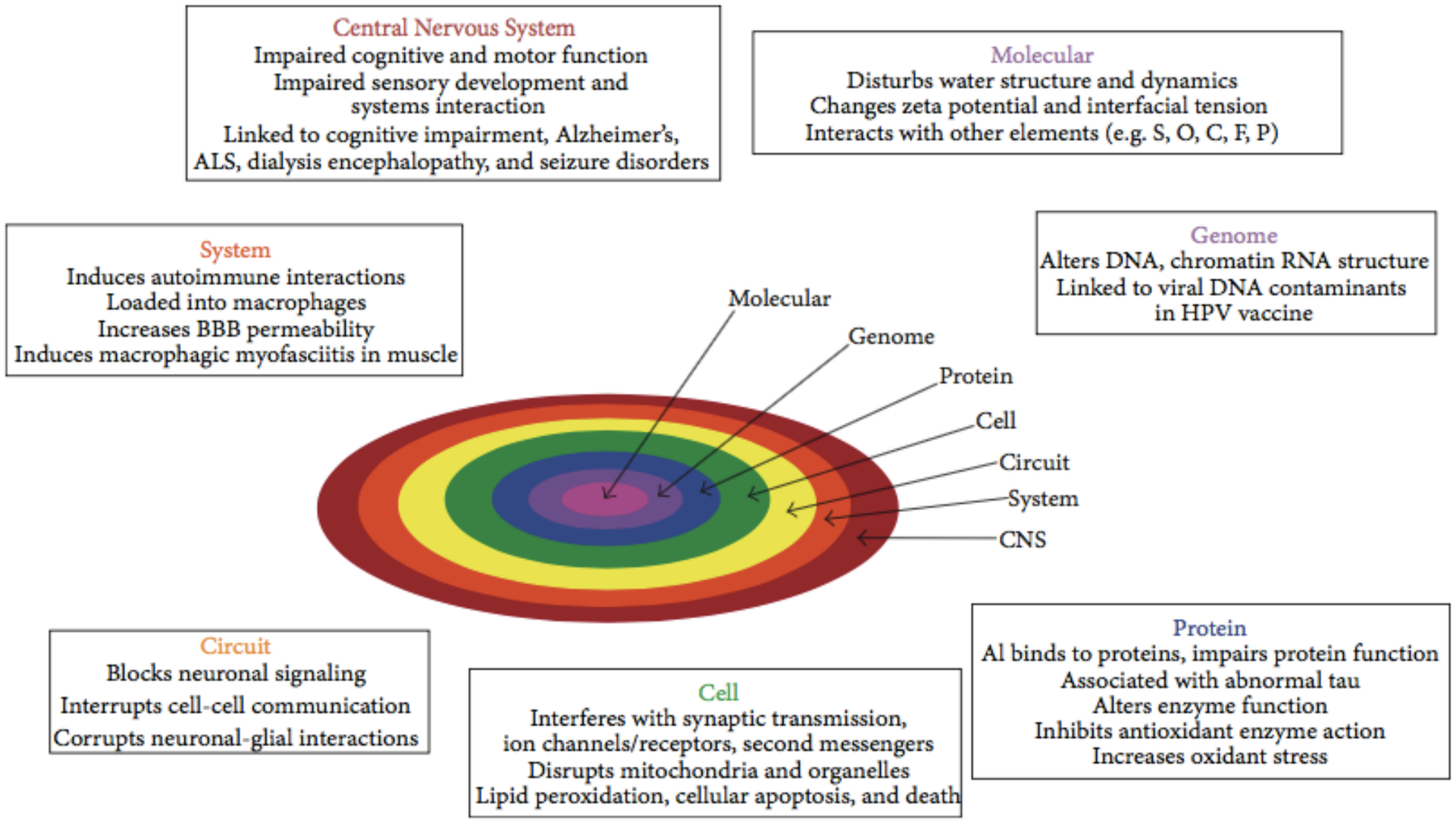

FIGURE 4: Schematic of the biosemiotic levels at which Al can impact the body and CNS.

Aluminum in Brain Tissue in Autism

Journal of Trace Elements in Medicine and Biology, Volume 46, March 2018, Pg 76-82.
Matthew Mold, Dorcas Umar, Andrew King, Christopher Exley.

- Measured, for the first time, the aluminium content of brain tissue from donors with a diagnosis of autism.
- Some of the highest values for aluminium in human brain tissue yet recorded.
- Appeared to be present intracellularly in microglia-like cells and other inflammatory non-neuronal cells in the meninges, vasculature, grey and white matter.

Aluminum in Brain Tissue in Autism

Journal of Trace Elements in Medicine and Biology, Volume 46, March 2018, Pg 76-82.
Matthew Mold, Dorcas Umar, Andrew King, Christopher Exley.

"We have made the first measurements of aluminium in brain tissue in ASD and we have shown that the brain aluminium content is extraordinarily high. We have identified aluminium in brain tissue as both extracellular and intracellular with the latter involving both neurones and non-neuronal cells.

The presence of aluminium in inflammatory cells in the meninges, vasculature, grey and white matter is a standout observation and could implicate aluminium in the aetiology of ASD."

Mental health disorders: Standard of care

- *"To include what's outside the box does not exclude what's inside."* Bo Jonnson
- History; Exam; **Lab work; Diagnosis**
- Psychiatry referral (Developmental Paediatrician)
- Psychoactive medication
- Psychotherapy; CBT (Autism: Applied Behaviour Analysis/ABA, Intensive Behavioural Intervention/IBI, Speech Therapy, Occupational Therapy)
- Professional and personal support network
- Institutional care

Diagnosis plus

"Normal"
Speech Disorder
Apraxia
Seizure Disorder
Learning Disability
Dyslexia
Oppositional Behaviour
Antisocial Personality
Hyperlexia
Hyperactivity Disorder
Attention Deficit Disorder
Attention Deficit & Hyperactivity Disorder
Asperger's Syndrome
Autism Spectrum Disorder
Pervasive Developmental Delay
Global Developmental Delay

The name game

GENETICS

Normal”
Speech Disorder
Apraxia
Seizure Disorder
Learning Disability
Dyslexia
Oppositional Behaviour
Antisocial Personality
Hyperlexia
Hyperactivity Disorder
Attention Deficit Disorder
Attention Deficit & Hyperactivity Disorder
Asperger’s Syndrome
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Pervasive Developmental Delay
Global Developmental Delay

The name game

GENETICS
TOXIN EXPOSURE

Disorder
Apraxia
Seizure Disorder
Learning Disability
Dyslexia
Oppositional Behaviour
Antisocial Personality
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Attention Deficit Disorder
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The name game

GENETICS
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The name game

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OXIDATIVE STRESS

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The name game

GENETICS
TOXIN EXPOSURE
DIET FACTORS
DYSBIOSIS
NUTRIENT DEFICIENCIES
FOOD INTOLERANCES
OXIDATIVE STRESS
MITOCHONDRIAL DYSFUNCTION

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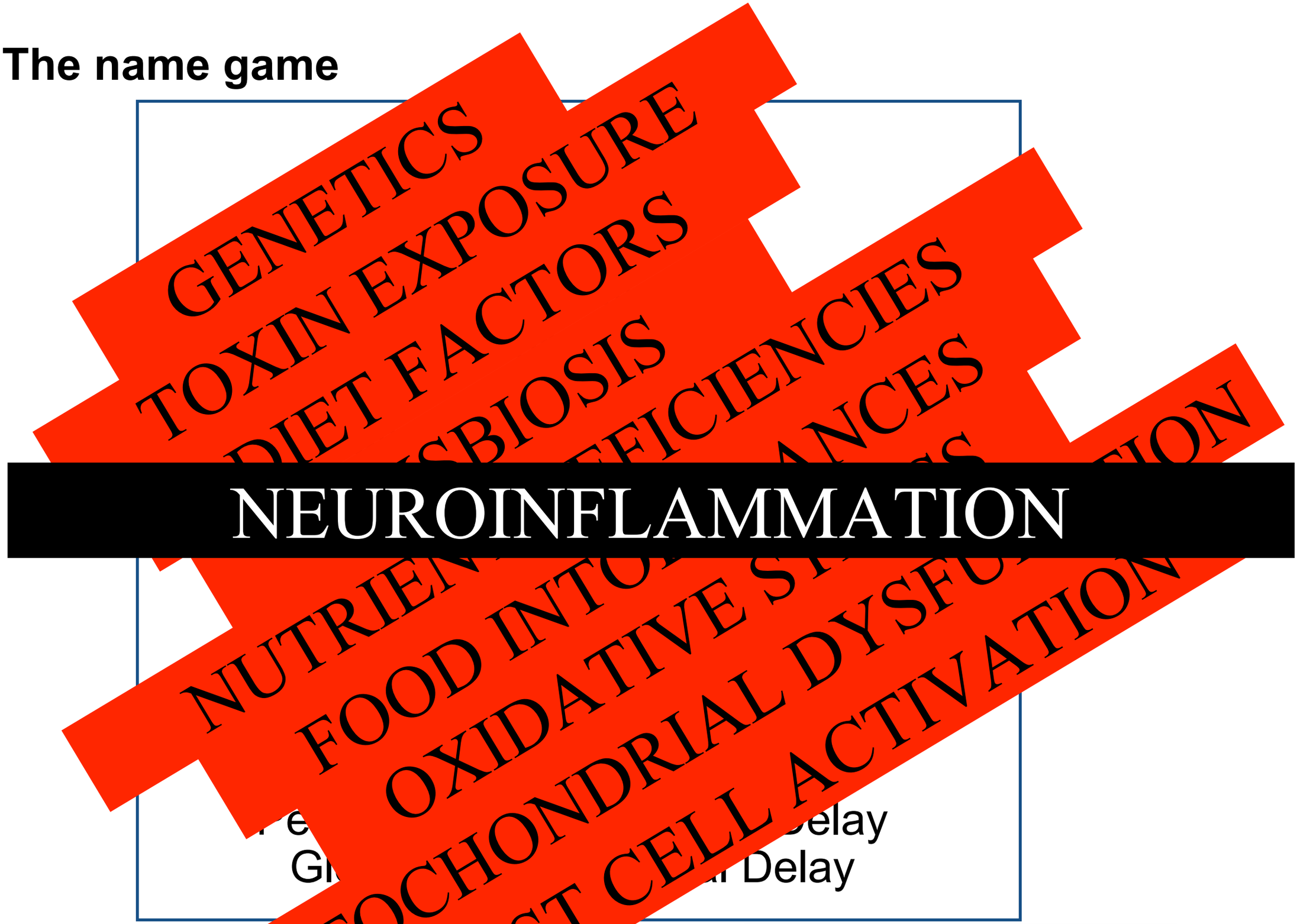
The name game

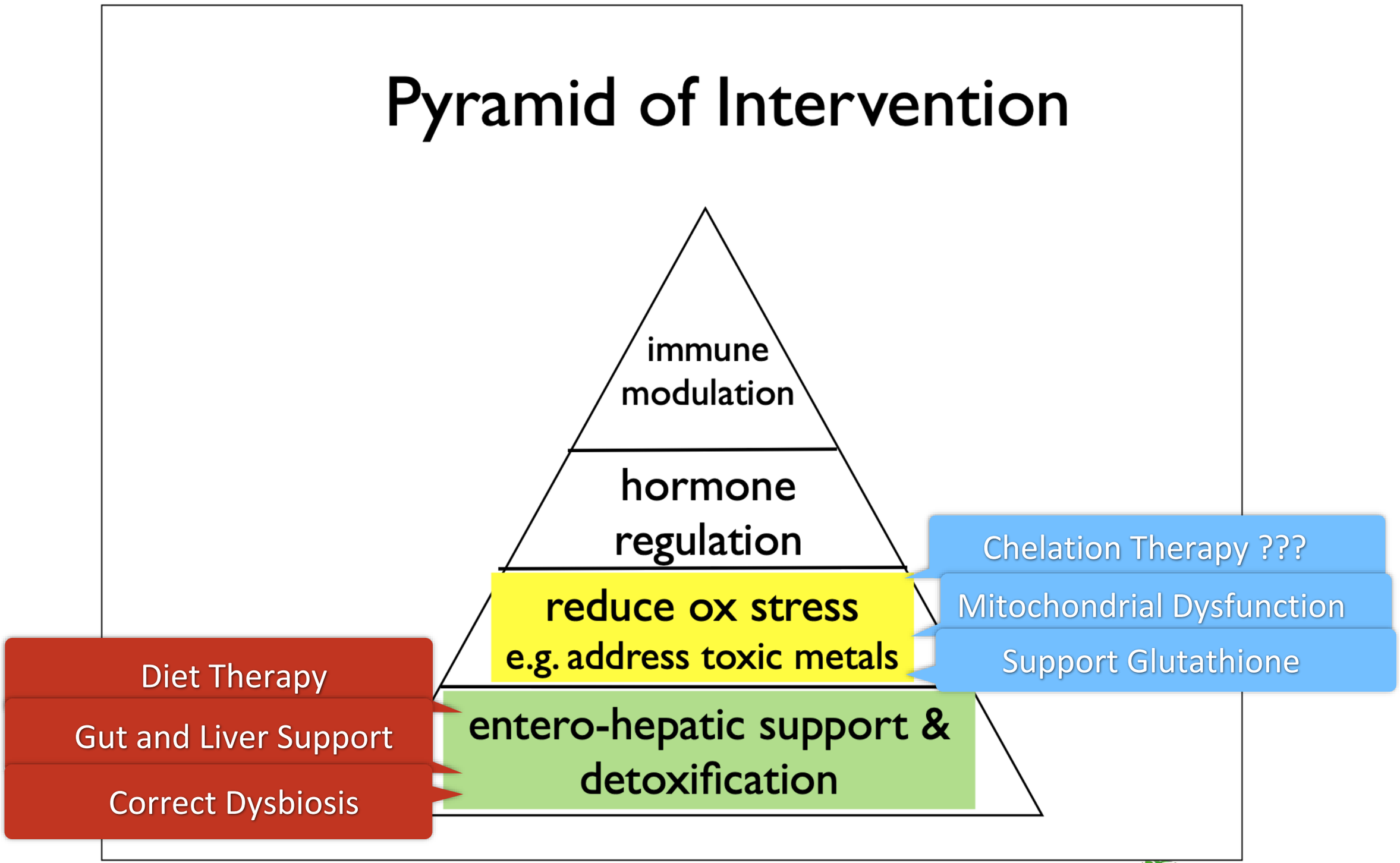
GENETICS
TOXIN EXPOSURE
DIET FACTORS
DYSBIOSIS
NUTRIENT DEFICIENCIES
FOOD INTOLERANCES
OXIDATIVE STRESS
MITOCHONDRIAL DYSFUNCTION
MAST CELL ACTIVATION

Pe Delay
Gl Delay

The name game



Pyramid of Intervention



Management - Tackling The Toxins

- AVOID EXPOSURE
- AVOID EXPOSURE
- **AVOID EXPOSURE**
- Clean up the diet
- Can they take supplements? = Nutrient therapy
  - Gut and liver - address dysbiosis - Candida / bacterial; protect from Herxing; botanical or pharmaceutical
  - No constipation
  - Can they do sauna therapy?
  - Metal binding and removal

➡ DIET DYSBIOSIS NUTRIENT THERAPY **METAL DETOXIFICATION**

Sears ME. **Chelation: Harnessing and Enhancing Heavy Metal Detoxification--a review.**
ScientificWorldJournal. 2013 Apr 18;2013:219840. doi: 10.1155/2013/219840. PMID: 23690738; PMCID: PMC3654245.

- “As research progresses, harms more subtle than acute poisoning are seen at lower and lower body burdens of heavy metals

- Chelation is central to natural detoxification of heavy metals, via formation of complexes, particularly with glutathione and other small molecules, and their excretion

- In this paper, measures to support natural detoxification pathways involving chelation, as well as use of pharmaceutical chelators are examined.”

Natural Chelating Compounds and Micronutrients

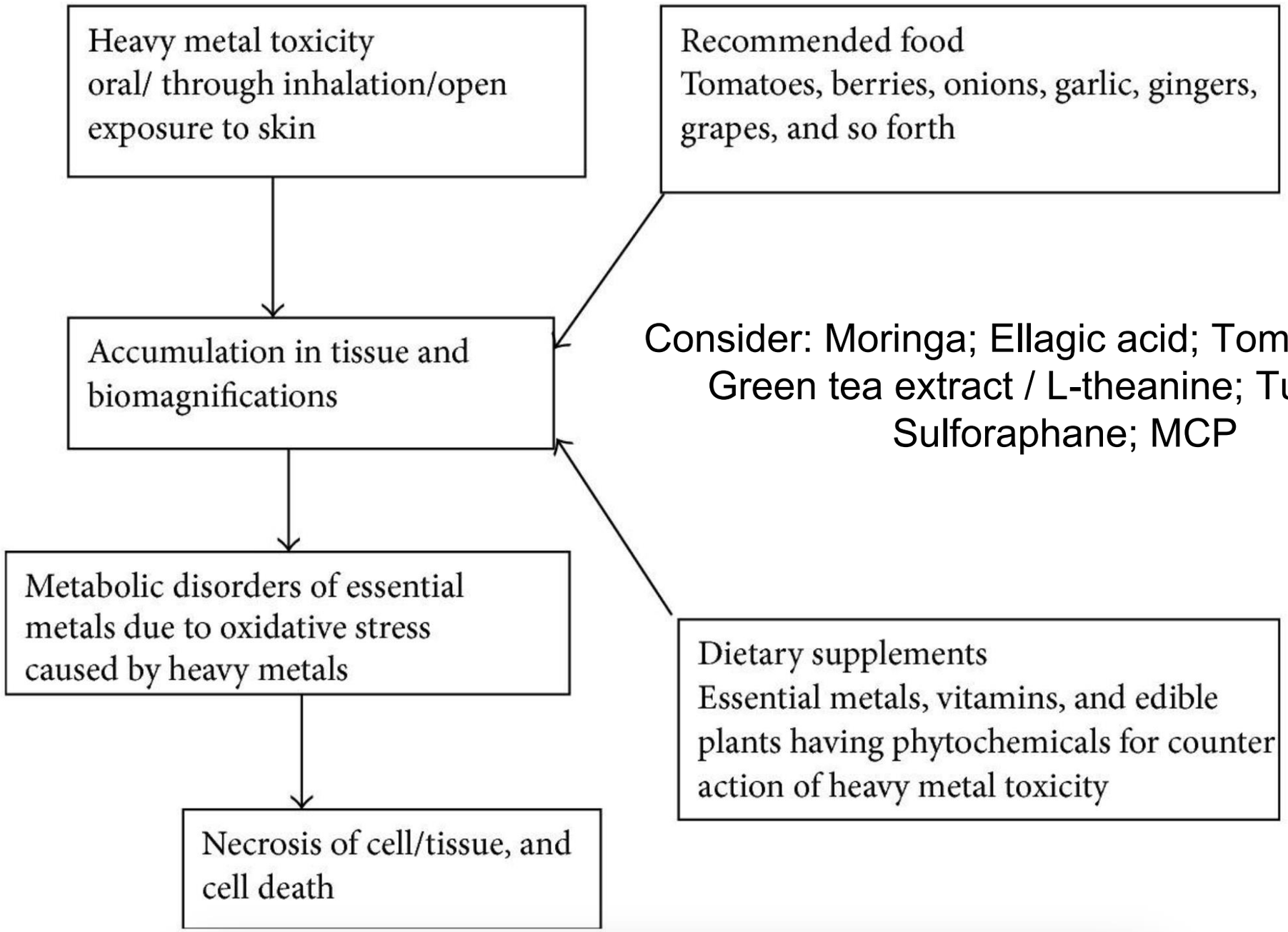
- Insoluble fibre
- Chlorella
- Modified citrus pectin
- Alginates
- Sulphur containing foods e.g. garlic
- Cilantro
- Glutathione - liposomal; S-acetyl; IV
- Taurine; methionine
- ALA
- NAC
- Selenium compounds
- Zeolite
- Calcium; iron; zinc; magnesium repletion

Natural Chelating Compounds and Micronutrients

NAC (N-Acetyl Cysteine)	150 mg	500 mg
L-Methionine	150 mg	
Apple Pectin	100 mg	
R+ Lipoic Acid	75 mg	25 mg
MSM (Methylsulfonylmethane)		500 mg
Chlorella		500 mg
Milk Thistle 80%		250 mg
Vitamin E (mixed)		200 IU
Selenium (L-Selenomethionine)		100 mcg

- **Clarke's Rule for Pediatric Dosage = Weight (kg) / 68 kg x Adult Dose**

Metal Detoxification - Phytochemicals



Gupta VK, Singh S, Agrawal A, Siddiqi NJ, Sharma B. **Phytochemicals Mediated Remediation of Neurotoxicity Induced by Heavy Metals.** Biochem Res Int. 2015;2015:534769. doi: 10.1155/2015/534769. Epub 2015 Nov 5. PMID: 26618004; PMCID: PMC4651672.

Metal Detoxification - Pharmaceutical Options (off-label)

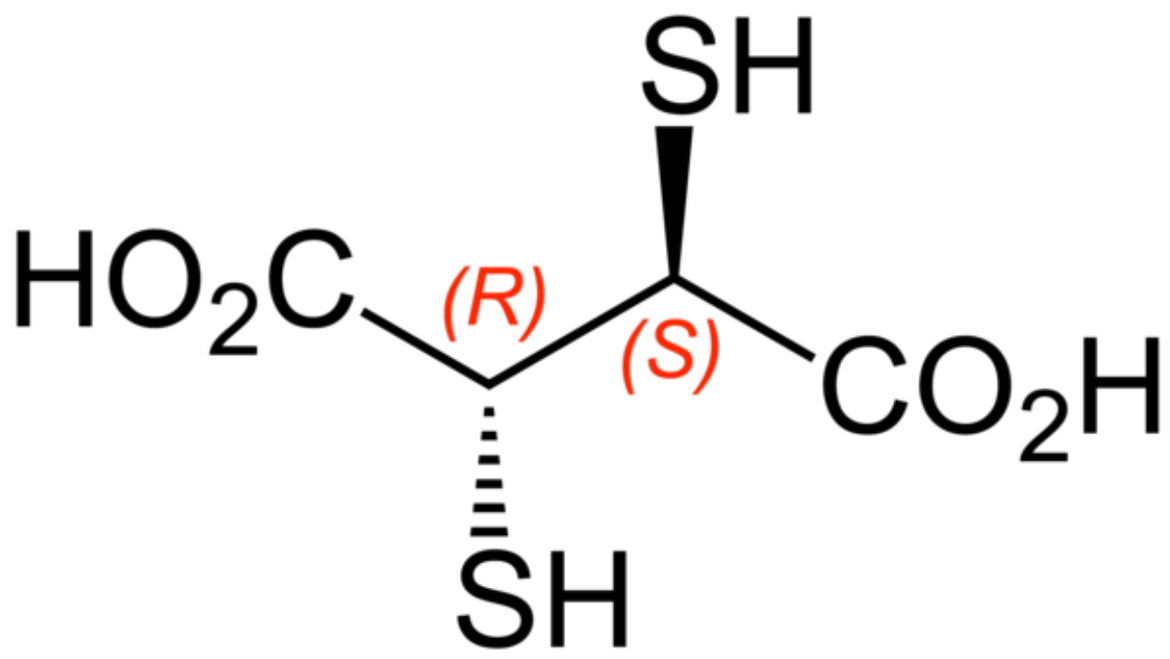
- DMSA - succimer
- DMPS
- EDTA - Calcium; Magnesium Disodium

Your best option (depending on your regulator):

oral DMSA for provocation and ongoing adjunctive treatment

- 20% absorption orally
- Limited by intestinal dysbiosis
- 10-25% excreted in urine; remainder in faeces

Metal Detoxification - DMSA (off-label)



- DMSA and DMPS are thiols; sulfhydryl groups are the basis for metal binding and complex stability
- Other thiols: metallothionein; ALA and Glutathione

Metal Detoxification - DMSA Protocol

- DMSA - 3 days on / 11 days off ; 30 mg / kg per day divided TID
- Blood surveillance - CBC; Creatinine; ALT; Zinc; Copper; others as appropriate - 1 and 3 months
- Supplement review - Zinc; multi-minerals; B complex; B12 and B9 support; GSH (or NAC); probiotic / prebiotic
- No minerals during ON days
- Monthly consults
- 3 months - re-test

Metal Depuration - Affinities

	Primary	Secondary	Tertiary	Negligible
DMSA	Lead; Arsenic	Aluminum*	Cadmium; Mercury	
DMPS	Mercury; Arsenic	Lead	Cadmium	Aluminum
CaEDTA	Cadmium; Aluminum	Lead		Mercury; Arsenic
MgNa2EDTA (3G)	Cadmium; Aluminum	Lead		Mercury; Arsenic

Translational Biomedicine - (2011) Volume 2, Issue 2

Efficacy of oral DMSA and intravenous EDTA in chelation of toxic metals and improvement of the number of stem/ progenitor cells in circulation. Nina Mikirova1*, Joseph Casciari1, Ronald Hunninghake1

Bradberry S, Vale A. **A comparison of sodium calcium edetate (edetate calcium disodium) and succimer (DMSA) in the treatment of inorganic lead poisoning.** Clin Toxicol (Phila). 2009 Nov;47(9):841-58. doi: 10.3109/15563650903321064. PMID: 19852620.

Anti-nutrients in Neurodivergence

– Key Points

Key Points:

- Toxic chemicals disrupt the development of all organ systems
- The nature and severity of the disruption dependent on type of substance, level and duration of exposure, and most important timing during the developmental process
- The exposures have started in utero and continue during infancy
- A child's immediate environment (and diet) can be a significant source of more toxic substance exposure
- Toxic chemicals act as anti-nutrients through various mechanisms
- The best strategies for toxic metal detoxification incorporate nutrients, phyotchemicals and pharmaceuticals where possible
- **Protection** has to come from nutrients

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Thank you

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