

EXPLORING THE MYSTERIES OF AUTISM

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Massive Autism Database

- **6,500 ASD patients,**
- **More than 1.5 million chemical assays of blood and urine,**
- **Striking biochemical differences between ASD children and non-affected children.**

Clinical Highlights

(6,500 ASD Patients)

- Outcome studies show 85% of families report major improvement following biochemical therapy and special diets,
- Hundreds of recoveries,
- Early intervention essential.

Conclusion

Autism is treatable and recovery is possible.

Autism Database Highlights

- **Autism chemical imbalances more severe than in violent criminals and schizophrenics,**
- **Discovery of undermethylation in more than 95% of ASD patients (1999),**
- **Clear evidence of oxidative stress overload and metallothionein depletion in autism patients (2000),**
- **Chemical studies of autism brain tissues.**

Pervasive Biochemical Abnormalities in Autism

- Depressed Glutathione & Cysteine
- Elevated toxic metals
- Hypomethylation
- Copper/Ceruloplasmin dysregulation
- Depleted Zinc & Metallothionein
- Elevated Pyrroles
- Low B-6, C, and Selenium
- Elevated Urine Isoprostanes

*Note: Each of these imbalances is associated with elevated **OXIDATIVE STRESS**.*

What is Oxidative Stress?

A harmful condition in which reactive oxygen species (free radicals) exceed the body's antioxidant defenses.

Some Consequences of Severe Oxidative Stress

- 1. Hypersensitivity to Hg & other toxic metals,**
- 2. Hypersensitivity to casein, and gluten,**
- 3. Poor immune function,**
- 4. Inflammation of the brain & G.I. tract,**
- 5. Depletion of glutathione & metallothionein.**

Consequences of Oxidative Overload in the G.I. Tract

- ❑ **Destroys digestive enzymes needed to break down casein & gluten,**
- ❑ **Increases candida/yeast levels,**
- ❑ **Diminishes Zn levels and production of stomach acid,**
- ❑ **Produces inflammation,**
- ❑ **Results in a “leaky intestinal barrier, allowing toxics to enter the bloodstream.**

Many Popular Autism Therapies Have Antioxidant Properties

- **Methyl B-12**
- **Metallothionein Promotion**
- **Transdermal or Injected Glutathione**
- **Zn, Se, CoQ-10, Vitamins A,C,D,E**
- **Chelation with DMSA, DMPS, EDTA.**
- **Alpha Lipoic Acid**
- **Risperdal**

CONCLUSION



**OXIDATIVE STRESS OVERLOAD IS A
DISTINCTIVE FEATURE OF AUTISM**

Methylation and Oxidative Stress

- **Undermethylation is a distinctive feature of autism,**
- **Undermethylation results in reduced synthesis of glutathione and cysteine – and weakened ability to cope with toxic metals and other sources of oxidative stress,**
- **An undermethylation environment during pregnancy may alter gene regulation of antioxidant protectors.**

The Three Musketeers of Antioxidant Protection

Glutathione: First line of defense,

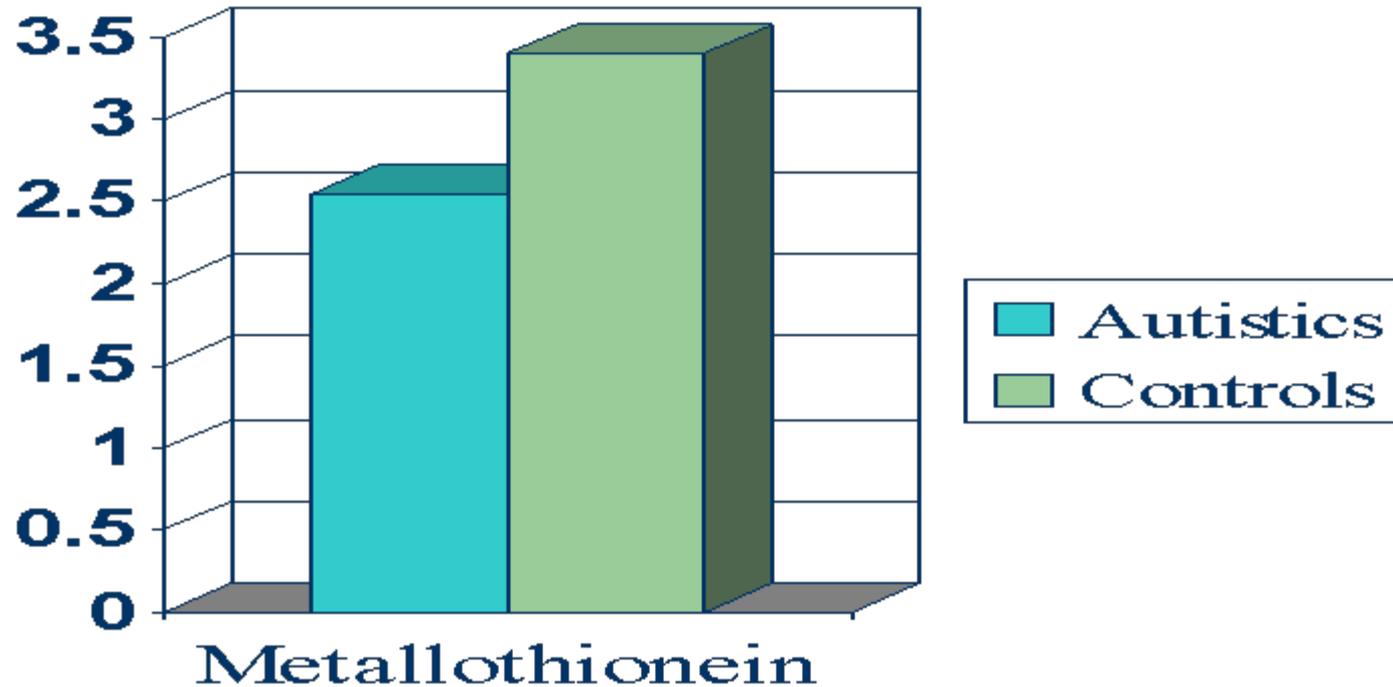
Metallothionein: Nature's back-up system,

Selenium: Speeds up the process.

This protection system appears weakened in ASD resulting in hypersensitivity to toxic metals, viruses, and other sources of oxidative stress.

Low Metallothionein Levels in Autism

$p < 0.0092$



Why is Metallothionein Important?

- Required for pruning, growth, and growth inhibition of developing neurons,
- Prevents Hg, and other metal toxics from passing intestinal and blood/brain barriers,
- Teams with glutathione to protect the brain,
- Required for effective immune function,
- Required for regulation of Copper and Zinc.

Note: MT functioning can be disabled by severe oxidative stress.

Autism Brains Are Different

- **Poverty of brain dendrites and synapses,**
- **Narrowed minicolumns in brain cortex,**
- **Incomplete maturation in cerebellum, amygdala, pineal gland and hippocampus,**
- **Brain inflammation,**
- **Damaged fats in autism brains,**
- **Abnormal levels of calcium and iron,**
- **Reduced structural connectivity between brain regions.**

Brain-Directed Therapies

- **The final battlefield in autism is the brain.**
- **Autism brains are different.**
- **Improved cognition, speech, and socialization depend on effective brain function.**

Brain-Directed ASD Approaches

- **Eliminate brain inflammation, toxic metals, and oxidative overload,**
- **MT-Promotion to stimulate development of immature neurons,**
- **Enhance brain plasticity to establish new dendrites and synapses: BDNF, Reelin, histone modification, occupational therapies, etc.**

The Bermuda Triangle of Autism



Undermethylation

Oxidative Stress

Epigenetics

Autism Rates

A Continuing Medical Mystery

- **Clear inborn predisposition: Greater than 60% concordance in identical twins; Less than 10% concordance in fraternal twins,**
- **Dramatic increase in autism cases over the past 50 years.**
- **Autism rates continue to escalate.**

How can there be an epidemic of a genetic condition?

The Role of Environment

- **Concordance of only 60-80% in identical twins indicates that environment plays a significant role.**
- **Since DNA mutations can take centuries to develop, the autism epidemic has been attributed to changes in environment.**

The Recipe for Autism



1. Inborn Predisposition

2. Environmental Insult

Environmental Insults: A Multitude of Possibilities

- 1. Attention has been focused on direct insults to the child from conception to age three.**
- 2. More than 30 environmental insults have been proposed, including mercury exposures, vaccines, changes in diet, viruses, increased Cu in the water supply, etc, etc.**

Other Autism Mysteries

- **Regression – Why does autism often appear suddenly after 18 months of typical development?**
- **Why doesn't autism go away easily after onset, despite aggressive therapies? Why can this condition persist a lifetime?**
- **Why does this heritable condition violate the classic laws of genetics?**
- **Why do a very high percentage of regressions occur between 16-22 months?**

A New Explanation - Epigenetics

- **There is growing evidence that autism is an epigenetic gene-regulation disorder.**
- **An epigenetic model neatly explains the autism epidemic, regression, persistence after onset, the numerous classic symptoms, the roles of undermethylation and oxidative stress, and increased regression incidence after 16 months of age.**

Mounting Evidence that Autism is an Epigenetic Disorder

1. **Nguyen et al; Identical twin study (FASEB Journal, April 2010): Finding: Abnormal methylation at DNA CpG sites.**
2. **Beaudet (2007), Nat. Med. 13, 534-536.**
3. **Schanen (2006), Hum. Mol. Genet. 15(2), R138- R150.**
4. **Nakayama, et al (2006), NSSYZ Journal.**

A Clue From Cancer Research

- **Severe oxidative stress can permanently alter epigenetic regulation of certain genes,**
- **Altered epigenetics can turn on a cancer gene or silence cancer-protective genes, initiating a cancer condition,**
- **Autism may arise from a similar mechanism – severe oxidative stress that permanently alters gene regulation.**

A Clue From the Past -- Thalidomide Babies

- ❑ Deformed thalidomide babies of the 1960's had a high incidence of autism,
- ❑ Autism occurred only if the anti-nausea pill was taken between days 20-24 of gestation,
- ❑ Most epigenetic decisions regarding gene expression or inhibition are established at this time,
- ❑ This suggests the greatest vulnerability to autism-causing environmental insults may be during in-utero epigenetic bookmarking.

Epigenetic Processes During Early Fetal Development

- **In utero chemical environment determines which genes will be expressed or inhibited throughout life (bookmarking),**
- **Gene expression errors can be transmitted to future generations by a process called transgenerational epigenetic inheritance (TEI),**
- **Methylation is a dominant factor in TEI, and is abnormally low in autistic children.**

Apparent Epigenetic Gene-Regulation Disorders

- **Cancer**
- **Heart Disease**
- **Autism**
- **Schizophrenia**
- **PTSD**

Characteristics of an Epigenetic Disorder

- ❑ **Cases of sudden onset after normalcy,**
- ❑ **Persistence of condition after onset,**
- ❑ **A multitude of characteristic symptoms,**
- ❑ **Heritable illness that violates laws of genetics,**
- ❑ **Abnormal methylation,**
- ❑ **Severe oxidative overload.**

The Walsh Theory of Autism

- **Autism predisposition results from genetics or in-utero insults that result in vulnerability to oxidative stress,**
- **Environmental insults eventually overwhelm antioxidant protectors and alter epigenetic gene regulation.... resulting in autism,**
- **Since epigenetic changes survive cell divisions, autism can persist a lifetime.**

Epigenetics and Autism

- **Epigenetic disorders typically involve sudden onset of symptoms after a period of relative wellness.**
- **Epigenetic disorders usually involve altered regulation of numerous genes and a variety of distinctive symptoms and traits.**
- **Epigenetic disorders violate Mendelian laws of genetics.**
- **Altered gene regulation can be transferred to future generations, contributing to increased incidence.**

Undermethylation Enclaves and Increasing Autism Rates

- Undermethylation is associated with OCD, perfectionism & high career accomplishment,
- High frequency for doctors, lawyers, CEO's, scientists, great athletes; also in affluent neighborhoods and universities,
- Increased social mobility in the past 50 years has resulted in increasing numbers of undermethylated persons who marry each other,
- Undermethylated in-utero environments are more vulnerable to epigenetic insults that can cause autism.

High Regression Incidence Between 16-22 Months

- **Breast feeding provides considerable protection against immune insults and oxidative stress.**
- **Most children transition to solid food between 12 and 18 months of age.**
- **Loss of this protection renders an autism-prone child more vulnerable to oxidative stress that can trigger a regression.**

Epigenetics and Autism

A Summary

- **Autism appears to be an epigenetic gene-regulation disorder,**
- **The role of epigenetics deserves a major increase in autism research funding,**
- **This could lead to vastly improved therapies and effective prevention.**

Brain Tissue Studies

Very limited amount of autism brain tissue available for research,

Conventional chemical analysis for zinc, copper, mercury, lead, calcium, etc requires significant sample size,

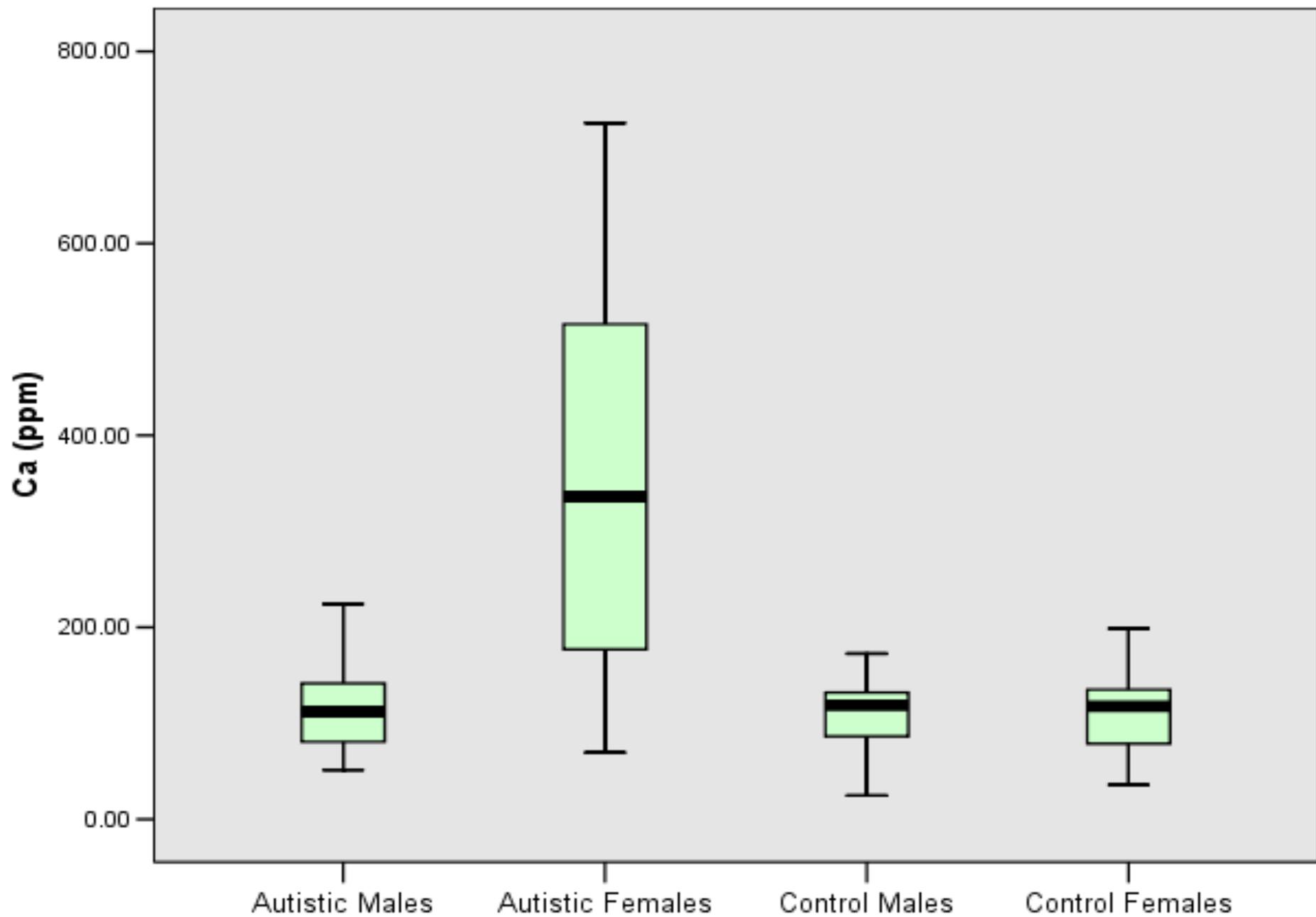
Until now, little or no data for levels of most elements in ASD brains.

Photon Beam Nanoanalysis of Autism Brain Tissues

- **Double blind, controlled study of 176 brain tissues from U. of Maryland's Autism Brain Bank,**
- **Elemental analysis for Hg, Pb, Cu, Zn, Ca, and other elements using high-brilliance photons,**
- **More than 35,000 individual assays obtained for autism & control brain tissues.**

Results of Brain Tissue Study

- 1. Testing of 153 intact samples,**
- 2. Abnormal overloads of specific elements found throughout autism brains and not in the controls,**
- 3. Major chemical differences between male and female ASD brains, suggesting that male and female autism may represent distinctly different conditions.**



What About Mercury?

- **All ASD brain tissues tested were from children exposed to Thimerosal,**
- **Strong evidence that mercury insults can initiate autism,**
- **Are brain mercury levels high in ASD brains several years after exposure to Thimerosal?**

“Normal” Hg Levels in Brain

- Hg present in brains of all humans,
- Some Hg enters and departs the brain daily,
- Hg concentrations of 5 to 25 ppb considered typical for healthy persons,
- Hg levels exceeding 75 ppb considered a serious health risk.

Mercury Results

- **Mercury not detected in any of the autism or control samples, in any brain region,**
- **Detection limit in this experiment believed to be 40-50 ppb.**

Autism and Neurodegeneration

- **Recent evidence of neurodegeneration in autism.... attributed to severe oxidative stress,**
- **Gradual loss of brain cells and IQ may occur if antioxidant therapy is not provided,**
- **Young autistics appear very bright despite behavioral, speech, and socialization deficits,**
- **Most adult autistics exhibit mental retardation (exception: Aspergers Disorder).**

Antioxidant therapy may be needed throughout life.

Risperdal and Abilify Warning

- Risperdal & Abilify are atypical antipsychotic drugs that can produce improved behavior in ASD children, and are frequently prescribed by mainstream doctors.
- Recent studies indicate that Risperdal and Abilify gradually shrink the cortex area of the brain.
- Ho, et al. Arch Gen Psych, 68:2

Summary

- **Autism appears to be an epigenetic disorder triggered by environmental insults,**
- **Epigenetic disorders are treatable and potentially preventable,**
- **Epigenetic science is providing a roadmap for advanced therapies that can benefit patients challenged by autism-spectrum disorders.**

A Look at the Future

- **Identification of misbehaving genes in autism will be achieved in the near future. Therapies to normalize deviant gene expression will eventually be developed.**
- **Epigenetic therapies of the future may represent a superior therapy for autism.**
- **Future newborn babies may be screened for epigenetic errors and receive treatment to prevent autism.**

Thank You!



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Over his impressive career, Dr. Walsh has worked with 30,000 patients with conditions ranging from autism to schizophrenia to Alzheimer's. His book is an essential tool for anyone who would prefer to heal the brain with nutrients rather than drugs.

Teri Arranga, editor-in-chief, *Autism Science Digest*

NUTRIENT POWER

HEAL YOUR BIOCHEMISTRY
AND HEAL YOUR BRAIN



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