METALLOTHIONEIN

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Walsh Research Institute

- **Nonprofit public charity**
- **Experimental research**
- **Expertise in biochemical therapy**
- **International physician training**

Human Metallothionein

- Family of zinc dependent cysteine-rich proteins,
- Short linear arrays of 61 to 68 amino acids,
- 20 cysteine residues,
- S-configuration with extraordinary metal-binding capability.

Metallothionein Family

- MT-I Found throughout body,
- MT-II Found throughout body,
- MT-III Expressed in brain (growth inhibition)
- MT-IV Squamous cells in GI tract, Skin

Genetic Expression of apo-Metallothionein I and II

- Housekeeping proteins,
- Induced by oxidative stress, toxic metals, radiation,
- Ample zinc, histidine, cysteine needed,
- Rapid binding to seven atoms of Zn after expression to form Zn-MT.

Genetic Expression of apo-Metallothionein III

- Growth-inhibition factor in brain,
- Rapidly binds to Cu and Zn atoms,
- Expression separate from MT-I and MT-II

Metallothionein Promotion Therapy

- Developed initially for autism patients
- Efficient removal of mercury and other toxic metals,
- Enhances homeostasis of Cu and Zn
- Excellent antioxidant properties
- Promising therapy for Alzheimer's Disease.

MT-Promotion Protocol

- 22 nutrients known to promote genetic expression and functioning of metallothionein,
- Step 1: Zinc normalization
- Step 2: MT-Promotion nutrients

Why is Metallothionein Important?

- Required for pruning, growth and growth-inhibition of brain cells in early development,
- Prevents Hg, and other metal toxics from passing intestinal and blood/brain barriers,
- Required for homeostasis of Cu and Zn,
- Supports immune function,
- Major antioxidant system in body & brain.

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

Teamwork Between Metallothionein, Glutathione, and Selenium

- GSH is first line of defense against toxic metals.
- When 10-20% of GSH is oxidized, toxic metals are transferred from GSH to MT.
- Se increases kinetics of the GSH/MT antioxidant system by more than 50%.
- Most toxic metals depart body in MT form.

MT & GSH Are Abundant in Intestinal Mucosa and Blood-Brain Barrier

- 95% of ingested Hg, Pb, Cd is stopped by MT & GSH at the intestinal mucosa.
- 80% of toxic metals entering portal blood stream become bound to MT/GSH in liver.
- 95% of remaining toxic metals are sequestered at B/B barrier by MT & GSH.
- Additional MT & GSH are present in the brain and provide antioxidant neuroprotection.

Oxidative Stress Can Impair Brain Development

- High oxidative stress depletes glutathione,
- Ample glutathione is required for proper functioning of metallothionein,
- Metallothionein is a key factor in early brain development.

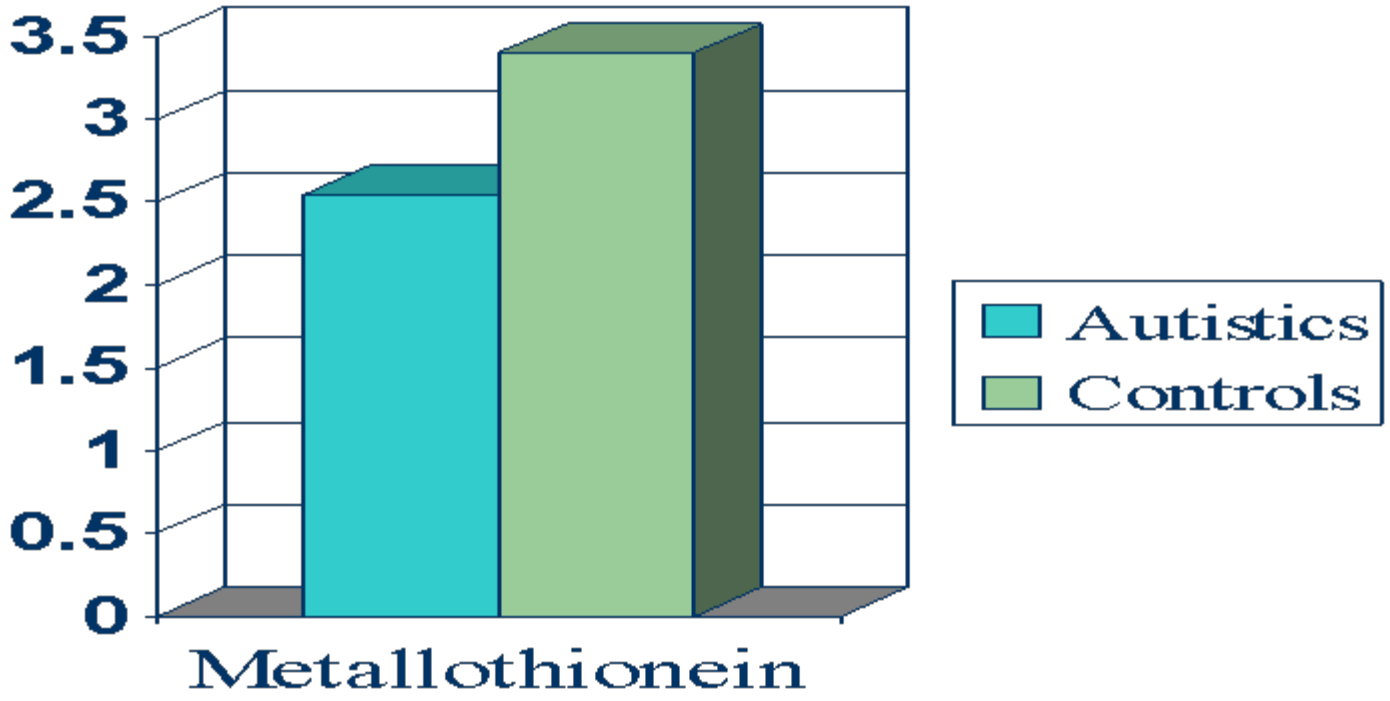
Unique Advantages of Metallothionein-Promotion Therapy

- Directly aimed at development of brain cells,
- Potential for permanently correcting the intestinal and blood/brain barriers,
- Restores a key antioxidant system.

Limitation: **Does not directly enhance development of dendrites and synapses.**

Low Metallothionein Levels in Autism

$p < 0.0092$



MT-Promotion Therapy Autism Outcome studies

- Clear improvement in autism outcomes shown in separate studies by Holmes, Walsh,
- Many cases of “recovery”,
- Best results for early intervention (ages 2-4).

Alzheimer's Disease

- Gradual degeneration of brain cells resulting in progressive senility and death,
- Amyloid plaque and neurofibrillary tangles,
- Severe oxidative stress and inflammation,
- Elevated toxic metals,
- Present treatments unable to stop death of brain cells: Average time between diagnosis and death is eight years.

Rationale for MT-Promotion Therapy for Treatment of Alzheimer's Disease

- Amyloid plaques are known to result from interaction of metal free-radicals with natural substances in the brain.
- Metallothionein proteins provide natural protection against free-radical metal ions,
- Metallothionein protein levels are less than 1/3 of normal levels in Alzheimer brains.

Initial Alzheimer's Results

- Most patients reported partial improvement of memory followed by stabilization of condition.
- Some patients exhibit continuing improvement after years of treatment,
- Several patients have lost the diagnosis of AD due to lack of progression of the disease after several years.
- Caretaker needed for effective compliance.

Explanation for Memory Improvements Following MT-Promotion Therapy

- Destroyed brain cells are lost forever,
- The untreated AD brain is afflicted by inflammation and oxidative stresses,
- MT-Promotion therapy has powerful antioxidant and anti-inflammation properties,
- Many Alzheimer researchers believe that memory and other brain functions would improve if the inflammation and oxidative stresses were reduced.

Reliable MT Assay Needed

- Early commercial MT assays badly flawed,
- Research lab assays involved radioactive mercury – A poor candidate for commercial lab test,
- MT assay development underway in Kansas City.

THANK YOU!

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