

Why Biomedical?

Common Medical Issues Seen in Clinical Practice

Treating Autism Conference
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Developmental Delays

Traditional Approach

Diagnosis/Disease Based

- Subjective
- DSM IV-R criteria
- Lack of objective findings
- Lack of unifying framework
- Current research focuses on improving diagnosis and classification
- Research impaired
- Classification provides management strategies

- Mental Disorder
- Genetic

Emerging Model

Individual/Patient Based

- Symptoms and Objective physical and chemical findings
- Biochemical, Metabolic, Immunologic, and Gastrointestinal Abnormalities
- Unifying framework
- Research based on treatment
- Treatment is individualized

- Medical Illness
- Genetics and Environment define Phenotype

Autism is a **MEDICAL** disorder,
not a MENTAL disorder.

Most Autistic patients have
environmentally-induced toxicity.

Autism is therefore preventable,
reversible, and **treatable.**

Scientific Foundations of a Biomedical Approach to ASD

Dr. Bernie Rimland – Autism Research Institute

<http://www.autismwebsite.com/ARI/treatment/b6studies.htm>

Studies of High Dosage Vitamin B6 (and often with Magnesium) in Autistic Children and Adults, 1965 - 2005

Twenty-one of twenty-two studies yielded positive results, including 13 double-blind placebo-controlled trials; even minor adverse effects rarely were seen

Autism: Effective Biomedical Treatments, by Jon B. Pangborn, Ph.D. and Sidney M. Baker, M.D., Oct. 2005, this manual has revolutionized the biomedical approach in the diagnosis and treatment of autism, PDD and related disorders.

<http://www.autismwebsite.com/ARI/dan/scientificfoundations.htm>

Compilation of Studies Supporting the Biomedical Approach

Vitamin B6 (pyridoxine)

- Pyridoxal 5-phosphate (P5P) active form of vitamin B6
- Conversion of B6 to P5P requires: ATP, Mg, Zn, Vit B2
- Used by 112 enzymes
- Transamination reactions
- Decarboxylation (L-Dopa to Dopamine, 5HTP to Serotonin, Glutamic Acid to GABA)
- Tryptophan metabolism (breakdown of hydroxykynurenin, niacin production)
- Glycogenolysis (breakdown of glycogen)
- B6 deficiency may be caused by kryptopyrroles or pyroluria

Pyroluria

- Hx: (Pfeiffer, Walsh)
 - Morning nausea
 - Frequent mood swings
 - Difficult handling transitions
 - Poor short term memory
 - Poor stress handling
 - Avoidance
 - Seclusion
 - Over reaction, meltdowns
 - Overly dramatic
 - Sensory issues (light, sound, touch, taste, smell)
 - Burn easy in sun, do not tan
 - Poor dream recall
 - Vivid dreams, nightmares
 - Nervousness
 - Panic, Anxiety
 - Irish ancestry
 - Seizure disorder
- PE: (Pfeiffer, Walsh)
 - Glossitis, mouth ulcers
 - Dry skin, cracked lips and nails
 - Spleen tenderness
 - China doll skin
 - Spider veins
 - Sweet breath
 - Crowded upper front teeth
 - Red hair, blue eyes
 - Peripheral neuropathy
- Labs:
 - Urine Kryptopyrrole
 - 10-20 mild
 - 20-50 moderate
 - > 50 severe

“Virtually **all human diseases** result from the interaction of genetic susceptibility factors and modifiable environmental factors, broadly defined to include infections, chemical, physical, nutritional, and behavioral factors.”

– Office of Genetics and Disease Prevention (**CDC**)

Causation Theories

Web of Interactions

- Genetics
- Environmental Toxicity and Heavy Metal Burden
- Biologic / Immunological Triggers

Predisposition

- Genetics

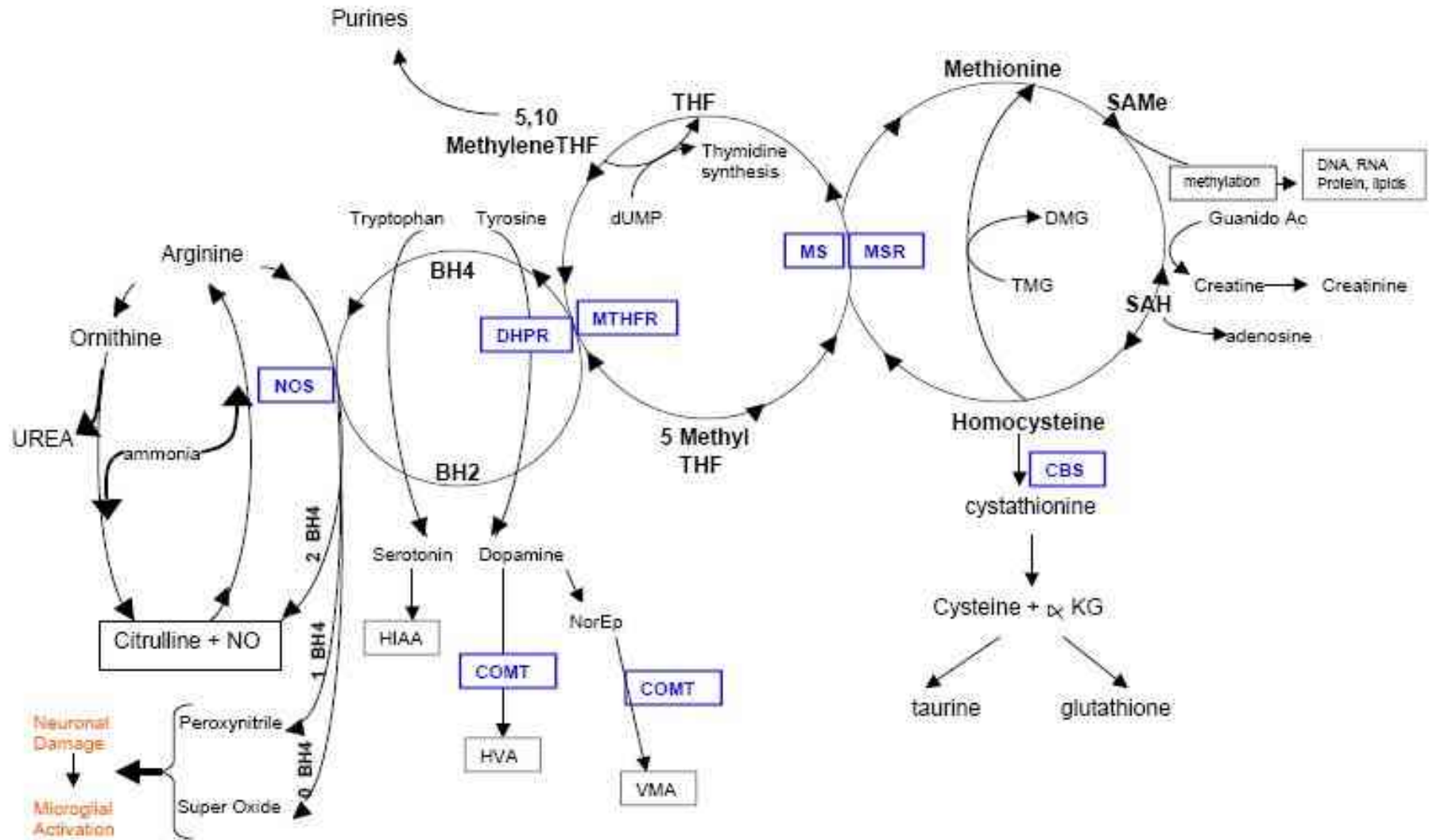
- Male Gender
- HLA- Type (C4B null allele)
- Family History of Autoimmunity (Hornig, 2004)
 - Allergies, asthma, diabetes, arthritis, colitis, celiac, thyroiditis
- Single Nucleotide Polymorphisms (SNP)
 - MTHFr- Methylene Tetrahydrofolate Reductase
 - COMT- Catecholamine O- Methyltransferase
 - MTRR/MTR- Methionine Synthase and Methionine Synthase Reductase (Deth, 2004)
 - BHMT – Betaine Homocysteine Methyltransferase
 - TCII – Transcobalamin
 - GABRB3- Gaba Receptor
 - ADA - Adenosine Deaminase
 - Mutant UBE3A (ubiquitin ligase)
 - CPOX – Coproporphyrin Oxidase
 - PON1 – Paroxonase

New Genetics

Human Genome Project, decoded 40,000 genes

- **Epigenetics**
 - Reversible gene expression
 - Interplay between Genes and Environment
 - Genes can be turned on and off
- **Nutrigenomics**
 - Study of how human genome is affected by nutrition
- **Pharmacogenomics**
 - Study of how the human genome affects the efficacy and metabolism of drugs
- **SNPs**
 - Single Nucleotide Polymorphisms are a slight variation in the genetic code resulting in abnormal protein or enzyme production
 - Measurable, Modifiable
 - Reported as homozygous (+/+), heterozygous (+/-), normal (-/-)
 - Common in the population

Amy Yasko Diagram (2005)



Methylation Genomics



INTEGRATIVE THERAPEUTICS INC.



Enhanced Cardio Panel

Healthy Lipid Metabolism	CETP-G	Cholesteryl Ester Transferase	Basic Support
Healthy Lipid Metabolism	LPL	Lipoprotein Lipase	Maximum Support
Vascular Integrity	IL-6	Interleukin 6, Beta-interferon	Added Support
Vascular Integrity	MTHFR_H	5, 10 Methylene tetrahydrofolate Reductase	Maximum Support
Vascular Integrity	MTR_A	5-Methyltetrahydrofolate-homocysteine S-M	Maximum Support
Vascular Integrity	MTRR	Methionine Synthase Reductase	Maximum Support
Vascular Integrity	NOS3	Endothelial Nitric Oxide Synthase (ENOS)	Added Support
Vascular Integrity	PON-1	Paraoxonase 1	Basic Support
Vascular Integrity	SELE	Endothelial Adhesion Molecule 1	Basic Support
Vascular Integrity	TNF-a	Tumor Necrosis Factor Alpha	Basic Support

High-dose vitamin therapy stimulates variant enzymes with decreased coenzyme binding affinity (increased K_m): relevance to genetic disease and polymorphisms¹⁻³

Bruce N Ames, Ilan Elson-Schwab, and Eli A Silver

ABSTRACT As many as one-third of mutations in a gene result in the corresponding enzyme having an increased Michaelis constant, or K_m , (decreased binding affinity) for a coenzyme, resulting in a lower rate of reaction. About 50 human genetic diseases due to defective enzymes can be remedied or ameliorated by the administration of high doses of the vitamin component of the corresponding coenzyme, which at least partially restores enzymatic activity. Several single-nucleotide polymorphisms, in which the variant amino acid reduces coenzyme binding and thus enzymatic activity, are likely to be remediable by raising cellular concentrations of the cofactor through high-dose vitamin therapy. Some examples include the alanine-to-valine substitution at codon 222 (Ala222→Val) [DNA: C-to-T substitution at nucleotide 677 (677C→T)] in methylenetetrahydrofolate reductase (NADPH) and the cofactor FAD (in relation to cardiovascular disease, migraines, and rages), the Pro187→Ser (DNA: 609C→T) mutation in NAD(P):quinone oxidoreductase 1 [NAD(P)H dehydrogenase (quinone)] and FAD (in relation to cancer), the Ala44→Gly (DNA: 131C→G) mutation in glucose-6-phosphate 1-dehydrogenase and NADP (in relation to favism and hemolytic anemia), and the Glu487→Lys mutation (present in one-half of Asians) in aldehyde dehydrogenase (NAD⁺) and NAD (in relation to alcohol intolerance, Alzheimer disease, and cancer). *Am J Clin Nutr* 2002;75:616-58.

Enzymes implicated in ASD:

Methylenetetrahydrofolate reductase (MTHFR)

Methyltransferases

Adenosine Deaminase

Methionine Synthase(MTR)

DPPIV

Methylenetetrahydrofolate Reductase (MTHFr)

- Enzyme converts MethyleneTHF to MethylTHF
- If Enzyme is weak, methyl groups are trapped and unable to convert homocysteine to methionine
- Enzyme is dependent on Vitamin B3
- Methyl-folate supplementation may help to bypass SNP

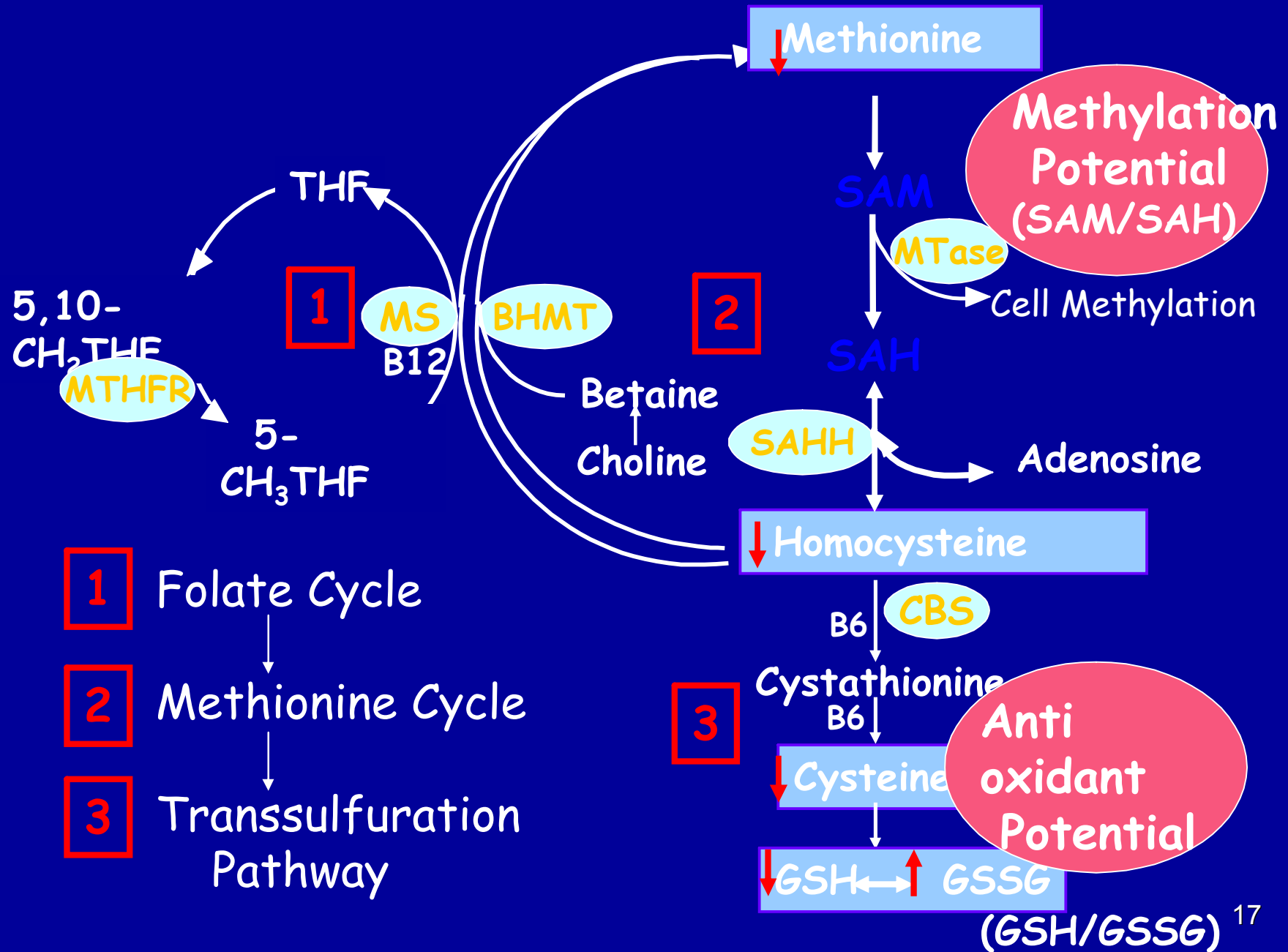
Methionine Synthase (MTR, MTRR)

- Enzyme converts Homocysteine to Methionine
- Enzyme involved in Dopamine methylation
- Dopamine Receptor (DRD4) methylation necessary for attention and focus
- Enzyme may be weak, genetically
- Enzyme inhibited by Cu, Pb, Al, and Hg
- Enzyme is dependent on Methyl B12
- Methyl B12 is a promising treatment

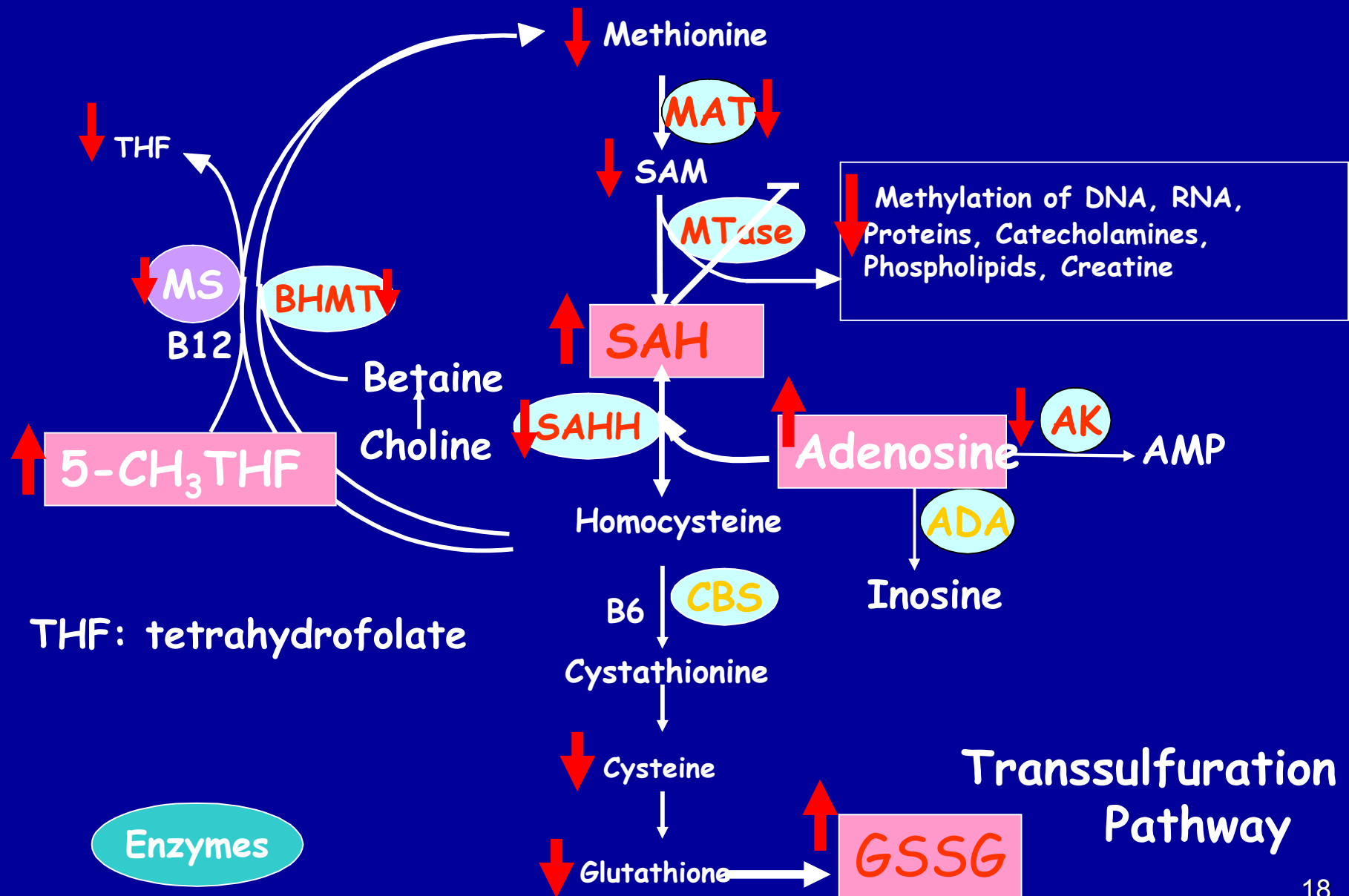
Methylcobalamin (B12)

- Cofactor for Methionine Synthase and Methionine Synthase Reductase in the methylation cycle.
- Bypasses impairments along folate pathway.
- Methylates Dopamine-4 Receptor(DRD4).
- Shown to help cognitive ability, abstract thinking, attention, focus, awareness, language, behavior, OCD, anxiety,(Neubrandner, 2004).
- Given by injection, highly concentrated, injected subcutaneous in gluteal tissue, slow release, painless, no toxicity associated with high dose vitamin B12.
- May give intranasal, sublingual, transdermal preparations, but not as effective
- No test for methylB12 deficiency.
 - ❖ Side effects – increased energy, hyperactivity, agitation, insomnia.

Methionine Transsulfuration to Cysteine and Glutathione



Impact of Oxidative Stress on Methionine Metabolism



Inciting Factors

- Environmental Toxicity

- Mom

- Amalgams
- Fish consumption (tuna)
- Rhogam
- Vaccines (Yazbak, 2004)
- Environmental and Occupational Exposures
- Pharmaceuticals (oral contraceptives, antibiotics)
- Comorbid Conditions

Inciting Factors

- Toxicity

- Patient

- Thimerosal Exposure From Vaccines
 - Mercury Exposure, Other
 - Other Heavy Metals
 - Environmental Toxins
 - Dietary Sources
 - Pharmaceuticals
 - Comorbid Conditions
 - Gastrointestinal Permeability
 - Immune Issues

Mercury (Hg) Toxicity

- Potent Neurotoxin
- Exposure is common
 - Seafood, Amalgams, Air, Thimerosal (vaccines)
- Symptoms of toxicity similar to autistic symptoms (Bernard, 2000)
- Glutathione is the primary mechanism of excretion
- Autistics have low glutathione levels (James, 2004)
- Tylenol and Antibiotics decrease excretion of mercury
- Baby teeth study found 3x higher Hg in autism vs. control (Adams, 2005)
- Baby hair study found very low levels of Hg in autism vs. control consistent with poor excretion of Hg (Holmes, 2003)
- On DMSA challenge testing autistics excreted 5.8x higher Hg than controls (Bradstreet, 2003)
- Recovery is possible with Mercury Detox (Holmes, Buttar)

Inciting Factors

- **Biologic and Immunologic Triggers**

- **Virus** (Measles, Rubella, Polio, CMV...)

(Viral Model for Developmental Disorders- Borna Virus, Hornig 1999)

- Measles (Wakefield, Singh)
- HHV6
- CMV

- **Bacteria** (Clostridia, Streptococcus, Gram Negative Rods...)

- **Fungal** (Yeast [candida], Mold)

- **Other** (Lymes)

- Some of these biologic agents produce **neurotoxins**.

- Our body may produce antibodies to these agents. These antibodies may cross react with our own tissue creating an autoimmune reaction. This is called **molecular mimicry**.

Impaired transsulfuration and oxidative stress in autistic children: Improvement with targeted nutritional interventions.

S. Jill James, PhD.

Am J Clin Nutr. 2004 Dec;80(6):1611-7.

Results of a targeted nutritional intervention trial with folic acid and betaine (trimethylglycine) in children with autism

In an attempt to improve baseline plasma methionine/cysteine/glutathione levels and increase antioxidant and methylation capacity, the 20 autistic children were given supplements of 800 μg of folic acid b.i.d. and 1000 μg betaine (trimethylglycine) b.i.d. for a period of 3 weeks. Folic acid (5-formylTHF) enters the folate pathway in a reduced form which is more easily assimilated into folate metabolism than the synthetic vitamin form, folic acid. Folic acid is converted to 5, 10-methyleneTHF which will support purine and thymidylate synthesis and also methionine synthesis. Betaine provides a folate-independent pathway for methionine regeneration via the betaine-homocysteine methyltransferase (BHMT in figure 1) that occurs primarily in the liver.

After nutritional intervention for only 3 weeks, a highly significant increase in plasma methionine, cysteine, and glutathione levels were associated with almost 2-fold increase in the ratio of reduced to oxidized glutathione (GSH/GSSG). These results would suggest that supplementation with folic acid and betaine had a strong positive impact on antioxidant capacity in the autistic children. Although SAM levels were significantly increased, the decrease in SAH and adenosine levels did not reach statistical significance due to high inter-individual variability. Eight of the 20 children continued the intervention with betaine and folic acid for an additional 3-4 months. After the extended intervention period, SAM levels increased to 112 nmol/L, SAH levels decreased to 17 nmol/L, and adenosine levels decreased to 0.18 $\mu\text{mol/L}$; all well within normal ranges.

Table 2

	<u>Baseline</u>	<u>After Intervention</u>	<u>p value</u>
Methionine ($\mu\text{mol/L}$)	19.3 \pm 9.7	28.0 \pm 7.2	<0.001
SAM (nmol/L)	75.8 \pm 16.2	81.4 \pm 10	<0.03
SAH (nmol/L)	26.1 \pm 5.4	25.1 \pm 8.4	NS
Homocysteine ($\mu\text{mol/L}$)	5.4 \pm 0.9	7.0 \pm 1.0	<0.002
Adenosine ($\mu\text{mol/L}$)	0.39 \pm 0.2	0.33 \pm 0.1	NS
Cysteine ($\mu\text{mol/L}$)	163 \pm 14.6	225 \pm 37	<0.002
Total glutathione ($\mu\text{mol/L}$)	4.1 \pm 0.5	5.7 \pm 1.0	<0.001
Oxidized Glutathione (nmol/L)	0.55 \pm 0.2	0.48 \pm 0.2	NS
GSH/GSSG Ratio	8.6 \pm 3.5	13.8 \pm 4.8	<0.001

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

S. Jill James, PhD ,et al

Am J Med Genet B Neuropsychiatr Genet. 2006 Dec 5;141(8):947-56

- Autism is a behaviorally defined neurodevelopmental disorder usually diagnosed in early childhood that is characterized by impairment in reciprocal communication and speech, repetitive behaviors, and social withdrawal. Although both genetic and environmental factors are thought to be involved, none have been reproducibly identified. The metabolic phenotype of an individual reflects the influence of endogenous and exogenous factors on genotype. As such, it provides a window through which the interactive impact of genes and environment may be viewed and relevant susceptibility factors identified. Although abnormal methionine metabolism has been associated with other neurologic disorders, these pathways and related polymorphisms have not been evaluated in autistic children. Plasma levels of metabolites in methionine transmethylation and transsulfuration pathways were measured in 80 autistic and 73 control children. In addition, common polymorphic variants known to modulate these metabolic pathways were evaluated in 360 autistic children and 205 controls. The metabolic results indicated that **plasma methionine and the ratio of S-adenosylmethionine (SAM) to S-adenosylhomocysteine (SAH), an indicator of methylation capacity, were significantly decreased in the autistic children relative to age-matched controls. In addition, plasma levels of cysteine, glutathione, and the ratio of reduced to oxidized glutathione, an indication of antioxidant capacity and redox homeostasis, were significantly decreased.** Differences in allele frequency and/or significant gene-gene interactions were found for relevant genes encoding the reduced folate carrier (RFC 80G > A), transcobalamin II (TCN2 776G > C), catechol-O-methyltransferase (COMT 472G > A), methylenetetrahydrofolate reductase (MTHFR 677C > T and 1298A > C), and glutathione-S-transferase (GST M1). **We propose that an increased vulnerability to oxidative stress (endogenous or environmental) may contribute to the development and clinical manifestations of autism.** (c) 2006 Wiley-Liss, Inc.
- PMID: 16917939 [PubMed - in process]

Glutathione (GSH) Action

- Tripeptide (glutamate, glycine, and cysteine)
- Potent **Antioxidant** – quelches free radicals and reactive oxidative species (ROS)
- Recycles Antioxidants – Vit C, Vit E, CoQ10
- **Detoxification** Phase I, Phase II
 - Chemicals, Peroxides, Alcohol, and Heavy Metals
- **Immune Enhancer** – Increases Natural Killer Cell Activity
- GSH Conserves Vitamin C and Vitamin C conserves GSH
- Alpha Lipoic Acid helps to regenerate reduced GSH
- Metallothionein helps to regenerate reduced GSH

Glutathione Support

- TMG, Folinic, Methyl B12
- Glutathione precursors
 - N- Acetyl Cysteine
 - Glycine
 - Glutamate (do not give)
- Vitamin C, Vitamin E, Selenium, Zinc, Metallothionein, Alpha Lipoic Acid
- Reduced L-Glutathione
 - transdermal, oral, intranasal, nebulized, suppository, lipocetical, intravenous preparations

Methylation Support

- Trimethylglycine
- Dimethylglycine
- S-adenosyl Methionine
- Methionine
- NADH
- Vitamin B2
- Active Folates (folinic, methylTHF)
- Methylcobalamin (methyl B12)
- Creatine, CoQ10
- Jill James Study (TMG, folinic, methyl B12)

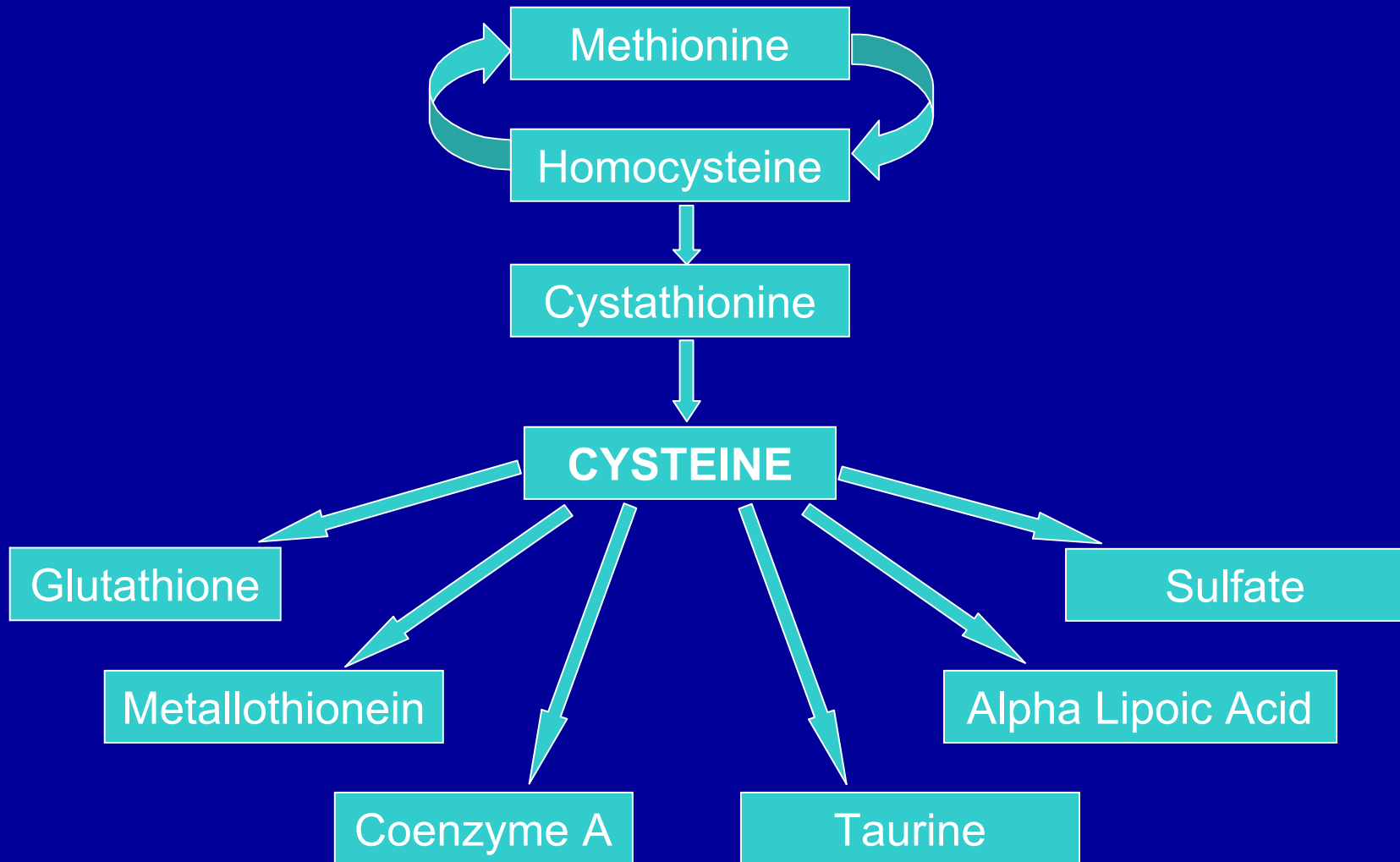
Bradstreet, J., et. Al

Clinical Evaluation of Plasma Cysteine and Plasma Sulfate Concentrations Among Children with ASD

Presentation DAN Conference Oct. 2003

- Children with ASD had 21% lower plasma cysteine levels ($p < .0001$) compared to controls
- Children with ASD had 11% lower plasma sulfate levels ($p < .006$) compared to controls

Cysteine Makes Detox Happen



Sulfation Support

- Magnesium Sulfate (Epsom Salts)
- Molybdenum, Biotin
- Vitamin B1, Allithiamine (TTFD), Benfotiamine
- Vitamin C
- N- Acetyl Cysteine (NAC)
- Reduced Glutathione (GSH)
- Glucosamine Sulfate, Chondroitin Sulfate
- Taurine
- Alpha Lipoic Acid

Aftermath of Genetics, Toxins, and Biologic Triggers ... the Metabolic Train Wreck...

- **Heavy Metal Overload**
 - Elevated levels of Mercury, Lead, Aluminum...
 - Mineral Deficiencies
 - Abnormal Porphyrins (Nataf)
- **Oxidative Stress** (James, Salomon, Pratico)
 - Impaired Methylation
 - Sulfation Abnormalities
 - Impaired Detoxification
 - Depletion of antioxidants, vitamin cofactors
 - Depletion of reduced Glutathione
- **Gastrointestinal Dysfunction**
- **Immune System Dysregulation**

AND LOTS and LOTS of INFLAMMATION

Gastrointestinal Dysfunction

- **Maldigestion**

- Decreased activity of digestive enzymes (Horvath,1999. Buie, 2004)
- High levels of opioid peptides found in urine of autistics. (Reichelt, 1997)
- IgG Food Sensitivities

- **Malabsorption**

- Fat Soluble Vitamin Deficiencies
- Essential Fatty Acid Deficiencies
- Essential Amino Acid Deficiencies

- **Dysbiosis**

- Dysbiosis or altered bowel flora (Rossenau, 2004)
- Clostridial overgrowth (Sandler, 2002)
- Persistent measles virus (Wakefield, Krigsman)

- **Inflammation**

- Autistic Enterocolitis, Lymphoid Hyperplasia (Wakefield,1998)
- Increased intestinal permeability leading to food sensitivities and autoimmunity (Vodjani, 2002)
- Increased pro-inflammatory cytokines – LP, TNF alpha, IFN gamma (Ashwood, 2004)
- Proinflammatory response to dietary proteins (Jyonuchi, 2004)

Immune Dysregulation

- **Th1 and Th2 skewing**
 - Abnormal cell-mediated immunity
 - Abnormal T-cell subsets, decreased NK cells, abnormal cytokines, Th2 skewing (Zimmerman, 1998)
 - Decreased secretory IgA
 - Pro-inflammatory Factors in the Gut (Ashwood, Jyonuchi)
- **Pro-inflammatory Cytokines in the Brain**
 - MCP-1, TGF beta-1 (Vargas, 2005)
 - Abnormal EEG, Seizure activity
 - Microglial Activation
- **Increased Autoimmunity**
 - Autoantibodies to neural antigens (Connolly, 1999)
 - Myelin basic protein and Neuronal Axonal Filament Protein Antibodies (Gupta, 1996 /Singh, 1997)

Abnormal Metal-Metabolism Observed in Test Subjects

Pfeiffer Treatment Center Data, May 2001

- 99% of test subjects had abnormal Cu/Zn ratios (499/503)
- Extremely disordered levels of Cu and Zn, indicating absence of blood homeostasis for these metals in 428 subjects (85%),
- Moderately disordered Cu/Zn levels despite ongoing zinc therapy in 41 subjects (8%),
- Severe pyrrole disorder in an additional 30 subjects (6%), indicating severe zinc depletion,
- Only 4 of the 503 autism-spectrum patients did not exhibit a serious metal-metabolism disorder.

Signs and Symptoms of Zinc Deficiency

- **Hx:**
 - Poor appetite, anorexia
 - Taste sensitivities
 - Poor wound healing
 - Frequent infections
 - Stunted growth
 - Night blindness
 - Light sleeper
 - Irritability, episodic anger
 - Chronic diarrhea
 - Fly hx of leukemia
 - H2 blockers, antacid, prednisone, or OCP use
- **PE:**
 - Sparse head hair
 - Groove across nails or white spots
 - Nasal polyps
 - Dark skin
 - Canker sores
 - Acne
 - Psoriasis
 - Body odor
- **Labs:**
 - Plasma zinc (<90ug/dl)

Signs and Symptoms of Copper Excess

- **Hx:**
 - **Hyperactivity**
 - **Jekyll- Hyde behavior**
 - **Temper, Rage, Tantrums**
 - **Frequent yeast infections**
 - **Poor short term memory**
 - **Night blindness**
 - **Light sleeper**
 - **Speech delays**
 - **Learning disabilities**
 - **Depression**
 - **Hx of Oral Contraceptive Use**
- **PE:**
 - **Red Hair**
 - **Kaiser-Fleisher Rings**
- **Labs:**
 - **Serum Copper (>100mcg/dl)**

Treatment of High Cu/Zinc Ratios

Treat Zinc deficiency until Zinc level optimized (100mg/dl)

Goal is 1:1 ratio of Cu/Zn

Support Metallothionein (MT) production

Add Manganese and Molybdenum

Provide adequate amounts of vitamin B6/Magnesium

Optimize Vitamin C dose

Avoid Sources of Copper

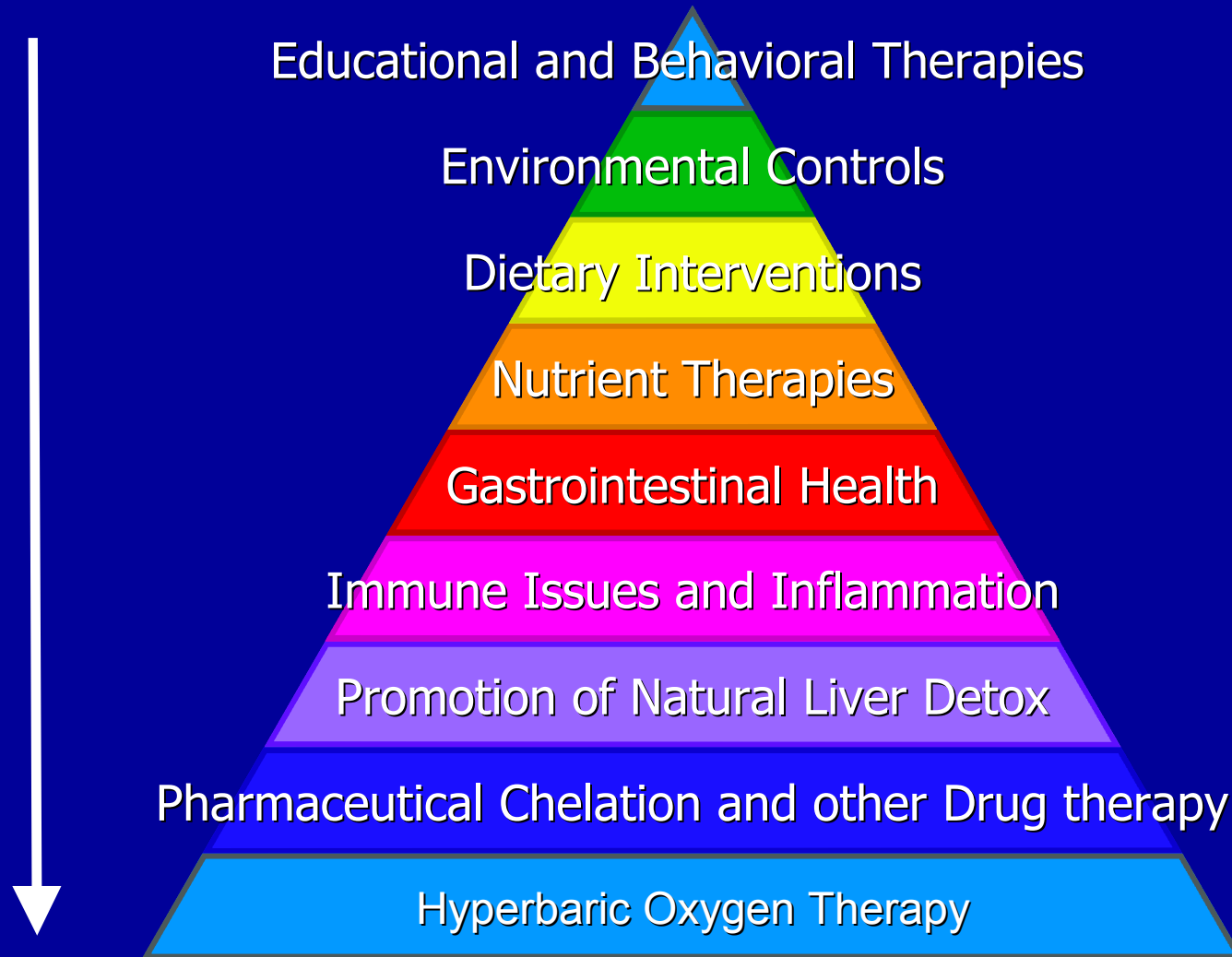
- Tap water (Cu pipes)
- Swimming pools and hot tubs (Cu algaecide)
- Chocolate, Carob, Soy, Shellfish, Liver

Avoid Red/ Yellow dyes (deplete Zn)

Basic Strategy

- History and Physical Examination
- Laboratory Testing
- Clean Up
 - Environmental Controls
 - Dietary Interventions
 - Address Gastrointestinal Health
- Foundational Nutrients
- Treat underlying Immune Issues and Inflammation
- Support Detoxification Pathways
- Heavy Metal Detoxification
- Hyperbaric Oxygen Therapy

Intensity of Symptoms = Intensity of Treatment



History - Heavy Metals

- **Mercury (Hg)**

- Oral ulcers, tremors, failure to thrive, abdominal distention, red lips, red finger tips, increased salivation, pale stools, watery stools, detached, disconnected, disinterested, poor eye contact

- **Lead (Pb)**

- Allergies, ADD symptoms, constipation, coordination, delinquency, dyslexia, headaches, hyperactivity, hypothyroidism, insomnia, irritability, mood swings, muscle weakness, dyspraxia, low muscle tone, visual and auditory processing issues, pica

- **Aluminum (Al)**

- Anemia, poor appetite, odd behaviors, constipation, dry mouth, dry skin, fatigue, hyperactivity, poor memory, numbness, weak upper body muscles

Mineral Interactions and Symptoms

- **Zinc (Zn)**
 - Deficiency can cause immune, language, attention/ focus issues
- **Magnesium (Mg)**
 - Deficiency can cause hyperactivity, anxiety, muscle spasms, enuresis
 - Reduces Aluminum, Antagonizes Calcium
- **Calcium (Ca)**
 - Excess leads to hyperexcitability
 - Deficiency leads to poor bone mineralization, rigidity in muscles
 - Reduces Lead and Aluminum
- **Molybdenum (Mb)**
 - Deficiency leads to yeast and sulfation issues
 - Reduces Tungsten and Copper
- **Copper (Cu)**
 - Excess can cause erratic behavior, hyperactivity, poor focus, yeast issues
 - Reduces Zinc and Molybdenum

History - Gastrointestinal

- History of Colic, Reflux
- Frequent Antibiotics
- Dairy Intolerance, Sugar Cravings
- History of frequent Otitis Media or Sinusitis
- History of Thrush, Severe Diaper Rash
- Poorly Formed Stools, Odd Color, Consistency, Odor, Mucus, "Soft Serve"
- Undigested Food in Stools, Floating Stools
- Constipation, Chronic Diarrhea, Both
- Abnormal Posturing
- Self Injurious Behavior
- Poor Sleeping Habits

History - Immune

- Eczema, Allergic Rhinitis, Asthma
- Seizure Disorder
- Frequent Viral Infections
 - Cold sores, Warts, Molluscum Contagiosum...
- Frequent Bacterial Infections
 - Otitis, Sinusitis, ...
- Chronic Diarrhea
 - Gastroenteritis
- Food Sensitivities
- Rare Fever
- Family History of Autoimmunity

Physical

- Pale skin, spider veins, long eyelashes
- Skin rash, sand paper skin, eczema
- Dilated pupils
- Lack of eye contact, divergent gaze
- Poor visual tracking
- Allergic shiners
- Nails – spots, ridges
- Coated tongue or thrush
- Lymphadenopathy
- Spleen tenderness
- Abdominal bloating
- Hypotonia
- Ligamentous laxity (double jointed)
- Signs of precocious puberty

Laboratory Testing Options

- CBC
- Comprehensive Metabolic Panel
- Serum Copper
- Plasma Zinc
- Ceruloplasmin
- Hair Analysis
- Thyroid profile
- Blood Lead

- Intracellular Minerals and Metals
- Urine Essential Minerals
- Essential Fatty Acids
- Amino Acids
- Plasma cysteine, sulfate, rGSH

- Urine Organic Acids
- Stool Microbiology
- Stool Mycology
- Stool Parasitology

- Immune Markers
 - Immunoglobulin Levels
 - T lymphocyte Panel
 - Natural Killer Cell Activity
 - PANDA's Profile
 - Anti MBP Ab, Anti NAFP Ab
 - IgG Food Ab Panel
 - Vaccine Titers
 - Viral Titers

- Urinary Peptides
- Hormone Studies
- Neurotransmitter Levels
- Genomics – SNPs

- Urine/ Fecal Toxic Metals
- Urinary Porphyrins
- Oxidative Stress Markers

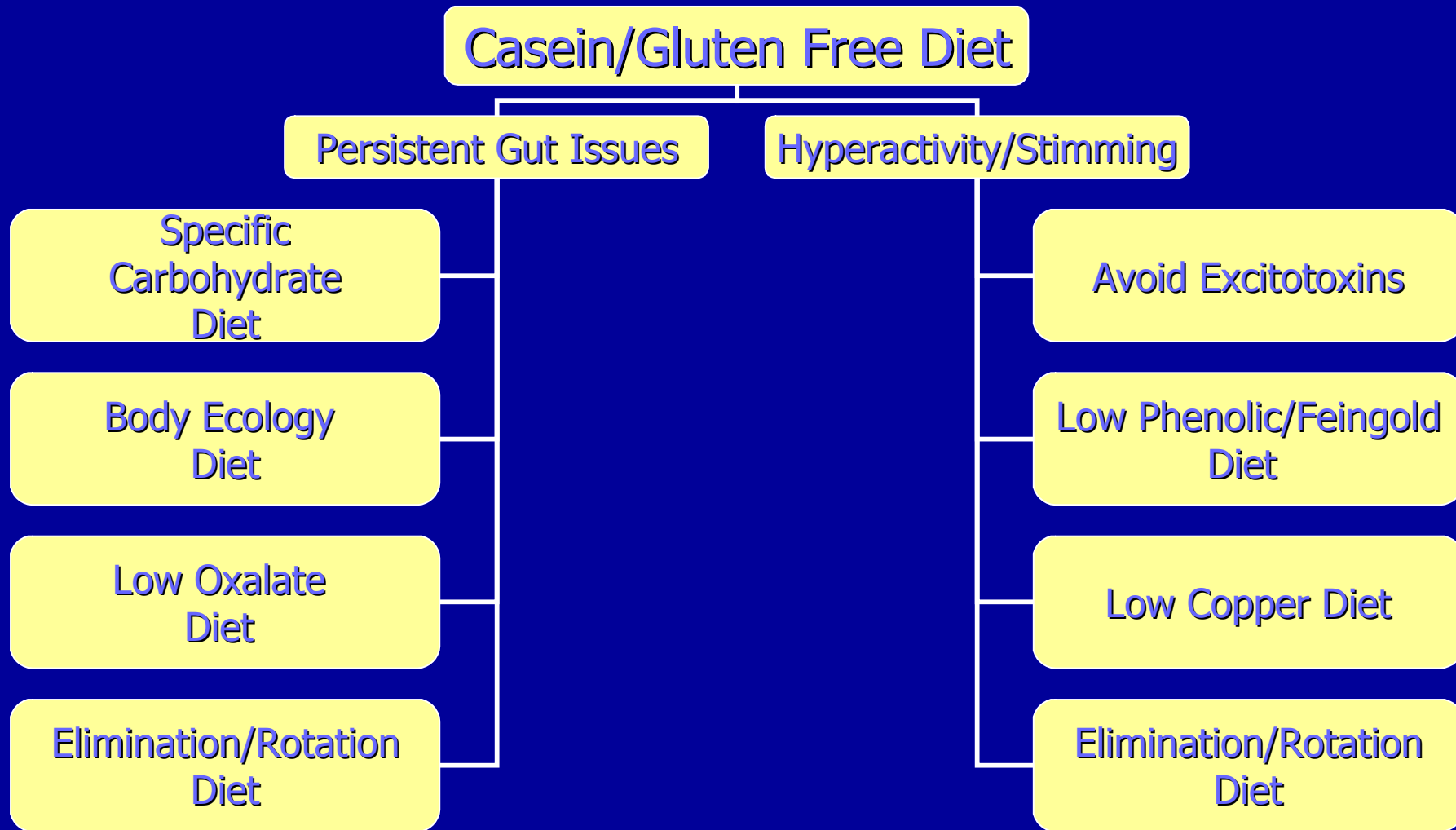
Clean up the Child's Environment

- Use natural, biodegradable and perfume free detergents and cleaning agents, do not dry clean clothes.
- Avoid chlorine: use water filters, limit pool and hot tubs.
- Wear 100% cotton clothes, avoid flame retardant materials (antimony).
- Use fluoride-free toothpaste (tin,titanium).
- Avoid playing on pressure treated wood (arsenic).
- Eliminate exposure to Mercury and thimerosal products.
- Use an air purifier, especially in the bedroom.
- Avoid prolonged exposure to batteries (light up shoes).
- No plastic furniture (polyvinyl chloride).
- Use aluminum-free baking powder, deodorant. Do not cook in aluminum foil or drink from aluminum cans.
- Avoid use of herbicides or pesticides, on lawns, garden, or home.
- Use natural shampoos, soaps, and make-up (lipstick-Pb, foundation-Bi).

Clean up the Child's Diet

- Casein-free/Gluten-free/Soy-free Diet Trial for 3-6 months.
- Avoid sugar and refined starch, high fiber diet, maximize antioxidants, cruciferous veggies, turmeric, garlic...
- Limit processed and preserved foods; organic is best.
- Avoid excitotoxins (ex. Caffeine, MSG, NutraSweet, red/yellow food dyes, nitrites, sulfites, glutamates, preservatives).
- Limit intake of phenolics (apples, grapes, strawberries).
- Limit sources of Copper (chocolate, shellfish, tap water, artificial food dyes).
- Drink plenty of filtered water.
- Never microwave in plastics or Styrofoam, do not store food in plastic or foil, or cook on Teflon coated pans.
- Eliminate seafood.
- Begin meals with raw fruits and veggies.
- Add good fats (olive, coconut, flax). Avoid hydrogenated and trans fats.
- Buy hormone-free, antibiotic-free, organic meat and eggs.
- Limit Genetically Modified Foods (GMO).
- Add fermented foods (coconut kefir, cabbage, goat milk yogurt)

Dietary Options



Clean up the Child's Gut

- Daily bowel movements are a goal.
- Add digestive **enzymes** with meals.
- Start high potency **probiotics** (acidophilus and bifidus).
- Start treatment for **dysbiosis** depending on symptoms and lab findings.
- If persistent symptoms:
 - Eliminate disaccharides from diet for 3-6 months
 - Specific Carbohydrate Diet
 - Consider referral to knowledgeable GI specialist
 - Consider trial of IV Secretin
 - Add natural anti-inflammatory agents.
- Keep close eye on gut during any detox regimen.

Foundational Nutrients

- Minerals
 - Zinc 2-3mg/kg
 - Magnesium 10-30mg/kg
 - Selenium 100-200mcg/day
 - Molybdenum 100-250mcg/day
 - Calcium 200-1000mg/day
- Antioxidants
 - Vitamin C 500-1500mg/day
 - Vitamin E 200-800iu/day
 - Vitamin A 2500-15,000iu/day
- EFA
 - Omega 3 EFA 1000mg
- Vitamins
 - B6 50-500mg or P5P 12.5-100mg
 - B Complex

Treat Underlying Nutritional and Biochemical Imbalances

- Anti-viral, Anti-parasitic, Anti-bacterial
- Essential Fatty Acids
 - Omega 6
 - Omega 3
- Immune Modulators
 - IVIG, oral immunoglobulins, transfer factor, colostrum, lauricidin, alpha and beta glycans, sterols, low dose naltrexone
- Anti-inflammatory Agents
 - Antihistamines, Singulair, Sulfasalazine
 - Curcumin, Boswellia, Green Tea
- Hormonal Regulation
 - Spironolactone, Oxytocin, Secretin, CCK

Support Natural Liver Detoxification

- Methylation
 - DMG, TMG, S-ame, methyl B12, B2
- Sulfation
 - B6, B1, Biotin, Molybdenum
- Glycine Conjugation
- Taurine Conjugation
- Glutathione Conjugation
 - Selenium, Zinc
- Glucuronidation
 - Calcium D-glucarate

Heavy Metal Detox Options

- **Chelators-** bind a free metal ion into a ring structure thereby neutralizing its reactive state
 - DMSA
 - EDTA
 - DMPS
- **Clathrating agents-** trap heavy metals within a colloid mesh
- **Zeolites** – trap heavy metals into a honeycomb structure
- **Natural Liver Detox Support**
 - Glutathione (IV, PO, Nebulized, Lipoceutical)
 - Methylcobalamin/methyl B12 (Subcutaneous injection, sublingual, transdermal, intranasal)
 - Alpha Lipoic Acid (PO, Transdermal)
 - N-Acetyl Cysteine (PO, Transdermal, IV)
 - TTFD/Allithiamine (Transdermal, Suppository)
- **Herbals** (garlic, cilantro, chlorella, spirulina)
- **RNA Therapy**
- **Homeopathics**
- **Far infra-red Sauna**

Additional Sources of Information

- "Autism, A Novel Form of Mercury Poisoning", Bernard, et al., 2000 (www.safeminds.org and autism.org)
- Children with Starving Brains, Jaquelyn McCandless MD
- Special Diets for Special Kids, Lisa Lewis
- Evidence of Harm, David Kirby
- Other websites
 - www.ddr.org
 - www.909shot.com
 - www.safeminds.org
 - www.cfgfdiet.com
 - www.autism.org
 - www.autismresearchinstitute.org
 - www.autismone.org
 - www.generationrescue.org

Thank You and Good Luck on your Journey

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