Nature versus Nurture Genetics and the Autism Epidemic

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Autism Spectrum Disorders and Beyond

"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)

Epidemic of Autism

- Latest US stats 1 in 150 children
- Genetic Epidemic?
- Where are all the autistic adults?
- Is Autism really that difficult to diagnose?
- What is happening to our children?
- What is happening to our environment?

Traditional Theories

- Refrigerator Mothers, poor parenting
- Purely a genetic disorder
- Hardwired malfunction of the brain
- Life long condition with no cure
- Diagnosis based on symptoms
- Treatment based on symptoms
- Medical treatment involves psychotropic drugs, with potential serious side effects

Biomedical Approach – Basic Tenets

- Genetic predisposition followed by environmental insult
- Genetic predisposition is multifactorial
- Environmental insult is multifactorial
- Genetic predisposition in families with immune issues
- Genetic predisposition involved in poor detoxification, especially methylation
- Software malfunction
- Can be reversed, not hard wired
- Diagnosis based on symptoms, signs, and lab testing
- Treatment based on symptoms, signs and laboratory data
- Medical treatment involves dietary, gastrointestinal, immune, anti-inflammatory, and detoxification strategies

Autism is a MEDICAL disorder, not a MENTAL disorder.

Most Autistic patients have environmentally-induced toxicity.

Autism is therefore preventable, reversible, and treatable.

Predispostion

- 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 – Corproporphyrin Oxidase
    - PON1 – Paroxonase

New Genetics

- New Genomics –
  - Human Genome Project, decoded 40,000 genes
  - Interplay between Genes and Environment
  - Genes can be turned on and off
- Nutragenomics
  - 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 (-/-)

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

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

Catecholamine -O- Methyl Transferase (COMT)

- Enzyme transfers methyl groups to catecholemines, (dopamine, NE, and Epi)
- Enzyme involved in neurotransmitter breakdown
- Cofactors include Magnesium, SAMe
- If enzyme is weak (COMT +/+), methyl groups are not used effectively may accumulate
- If enzyme is efficient (COMT -/-), methyl groups are used up rapidly and SAMe is depleted
- In both cases, methylation is impaired

Inciting Factors

- 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)

Vaccines and Mercury Exposure

- 1950 - 50 mcg
- 1970 - 75 mcg
- 1992 - 187.5 mcg
- EPA safe limit is 0.4 mcg/day for average newborn
- Hep B at birth has 12.5 mcg
- 2 month shots have 62.5 mcg/day
- Hep B, HIB, DTaP, flu, Td, Rhogam contain 25 mcg each
- Thimerosal removed from vaccines 2003, except flu vaccine
- Vaccines still contain the metal, Aluminum

Lead (Pb) Toxicity

- Low level toxicity associated with deliquency, criminal behavior, learning disorders, developmental delays, ADHD, hearing defects, and growth delays
- Deficiency of protein, Ca, Zinc, Se, Fe, or Vit E cause increase Pb absorption. Fluoride increases Pb absorption. Children absorb Pb more readily than adults
- Causes poor heme synthesis, decreased reduced glutathione, increased oxidative stress, and increased lipid peroxidation
- Reduces glutamine synthase and glutamic acid dehydrogenase
- Reduces GABA, increases glutamate, and increases ammonia
- Synergy with Hg increases toxicity exponentially. Safe threshold changed from 80ug/dl to 10ug/dl
- Children with blood levels of 10 mcg/dl, the upper limit of the "safe range", have IQs 7.5 points below those of kids whose blood Pb levels are 0-1mcg/dl

Aluminum (Al) Toxicity

- No physiologic need. 3rd most prevalent element.
- Fluoride increases ability of Al to cross blood brain barrier.
- Competitive inhibitor of Magnesium, Calcium, Iron
- Causes poor heme synthesis, decreased reduced glutathione, increased oxidative stress, and increased lipid peroxidation
- Reduces glutamic acid decarboxylase (GAD), inhibits acetylcholinesterase
- Reduces GABA, Increases Acetylcholine
- Synergy with Hg increases toxicity exponentially.
- Excess deposited in brain, bone, muscle, kidney, liver

Lead and ADHD Symptoms

Lead Exposure Tied to ADHD Symptoms

Significant effect seen in children with particular gene types, study reports By Serena Gordon

HealthDay Reporter

MONDAY, May 1 (HealthDay News) -- It's known that lead exposure poses serious health risks, including cognitive function problems.

But new research suggests that certain children are more likely to develop attention-deficit hyperactivity disorder (ADHD) when exposed to lead in their environment.

The study found that youngsters with a specific genetic variation in a dopamine receptor, dubbed DRD4-7, had more problems with tasks that required attention and flexibility. The researchers also found that boys exposed to lead were at greater risk of attention problems than girls.

"Lead exposure leads to problems with attention and executive function. And certain kids are going to be more affected by the adverse effects of lead," said study author Dr. Tanya Froehlich, a developmental, behavioral and pediatric specialist at Cincinnati Children's Hospital Medical Center.

Lead Sources are Everywhere

Grandma gets lead out of baby bibs

By Steve Zalusky
Daily Herald Staff Writer

These vinyl bibs pose a lead poisoning threat to infants and toddlers who are at the most vulnerable age, said Caroline Cox, research director at the Center for Environmental Health and author of a report on lead in baby bibs released by the center this week. As every parent knows, young children commonly chew and suck on their bibs, so if the bib is contaminated, children are being directly exposed to lead.

Let's start with a straightforward fact:
Mercury is unimaginably toxic and dangerous.
A single drop on a human hand can be irreversibly fatal.
A single drop in a large lake can make all the fish in it unsafe to eat.

Often referred to as quicksilver, mercury is the only common metal that is liquid at room temperature. Alchemists, including the young Sir Isaac Newton, believed it was the source of gold. In the modern era, it became a common ingredient of paints, diuretics, pesticides, batteries, fluorescent lightbulbs, skin creams, antifungal agents, vaccines for children, and of course, thermometers. There is probably some in your mouth right now: So-called silver dental fillings are half mercury.

Mercury is also a by-product of many industrial processes. In the United States coal-fired power plants alone pump about 50 tons of it into the air each year. That mercury rains out of the sky into oceans, lakes, rivers, and streams, where it becomes concentrated in the flesh of fish, shellfish, seals, and whales. Last year the Food and Drug Administration determined there is so much mercury in the sea that women of childbearing age should severely limit their consumption of larger ocean fish. The warning comes too late for many mothers. A nationwide survey by the Centers for Disease Control shows that one in 12 women of childbearing age *already* have unsafe blood levels of mercury and that as many as 600,000 babies in the United States could be at risk. But that begs a critical question: At risk for what?

POPs (Persistant Organic Pollutants)

Phthalates, Pesticides, Herbicides, Bisphenol A, PCBs, PBDE, DDT…

- Endocrine Disruptors – substances that may at tiny doses interfere with hormonal signals that regulate human organs, development, metabolism, and other functions.
- Low Dose Hypothesis – No safe levels (pp trillion have biologic effects)
- Damage DNA - 90% inherited
  - Harm developing nervous system
  - Alter brain structure, neurochemistry, behavior, reproduction and immune response in animals
  - Carcinogenic
  - Gender bending chemicals
  - Damage sperm and cause genital malformations
  - Precocious Puberty
  - Allergies, Asthma, Diabetes, Heart Disease, Thyroid disease
- Used in flexible plastics, cosmetics, perfumes, food packaging
- Found in breast milk, cord blood, and infants

Allergies and POPs

- Environmental Estrogens Induce Mast Cell Degranulation and Enhance IgE-Mediated Release of Allergic Mediators

- **1Department of Pediatrics, Child Health Research Center; and 2Department of Biochemistry and Molecular Biology, University of Texas Medical Branch,** Galveston, Texas, USA
  Background: Prevalence and morbidity of allergic diseases have increased over the last decades. Based on the recently recognized differences in asthma prevalence between the sexes, we have examined the effect of endogenous estrogens on a key element of the allergic response. Some lipophilic pollutants have estrogen-like activities and are termed environmental estrogens. These pollutants tend to degrade slowly in the environment and to bioaccumulate and bioconcentrate in the food chain ; they also have long biological half-lives.
- **Objectives: Our goal in this study was to identify possible pathogenic roles for environmental estrogens in the development of allergic diseases.**
- **Methods: We screened a number of environmental estrogens for their ability to modulate the release of allergic mediators from mast cells. We incubated a human mast cell line and primary mast cell cultures derived from bone marrow of wild type and estrogen receptor (ER-) –deficient mice with environmental estrogens with and without estradiol or IgE and allergens. We assessed degranulation of mast cells by quantifying the release of hexosaminidase.**
- **Results: All of the environmental estrogens tested caused rapid, dose-related release of ?-hexosaminidase from mast cells and enhanced IgE-mediated release. The combination of physiologic concentrations of 17?-estradiol and several concentrations of environmental estrogens had additive effects on mast cell degranulation. Comparison of bone marrow mast cells from ER- –sufficient and ER- –deficient mice indicated that much of the effect of environmental estrogens was mediated by ER- .**
- **Conclusions: Our findings suggest that estrogenic environmental pollutants might promote allergic diseases by inducing and enhancing mast cell degranulation by physiologic estrogens and exposure to allergens.**
- **Key words:** allergy, asthma, ?-hexosaminidase, environmental estrogen, estradiol, estrogen receptor , IgE, mast cells. ***Environ Health Perspect*** **115:48–52 (2007) . doi:10.1289/ehp.9378 available via** http://dx.doi.org/ **[Online 3 October 2006]**

In harm's way: toxic threats to child development.

Stein J, Schettler T, Wallinga D, Valenti M.

J Dev Behav Pediatr. 2002 Feb;23(1 Suppl):S13-22

The developing brain is uniquely susceptible to permanent impairment by exposure to environmental substances during time windows of vulnerability. Lead, mercury, and polychlorinated biphenyls (PCBs) have been extensively studied and found to impair development at levels of exposure currently experienced by significant portions of the general population. High-dose exposures to each of these chemicals cause catastrophic developmental effects. More recent research has revealed toxicity at progressively lower exposures, illustrating a "declining threshold of harm" commonly observed with improved understanding of developmental toxicants. For lead, mercury, and PCBs, recent studies reveal that background-population exposures contribute to a wide variety of problems, including impairments in attention, memory, learning, social behavior, and IQ. Unfortunately, for most chemicals there is little data with which to evaluate potential risks to neurodevelopment. Among the 3000 chemicals produced in highest volume (over 1 million lbs/yr), only 12 have been adequately tested for their effects on the developing brain. This is a matter of concern because the fetus and child are exposed to untold numbers, quantities, and combinations of substances whose safety has not been established.

PMID: 11875286 [PubMed - indexed for MEDLINE]

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

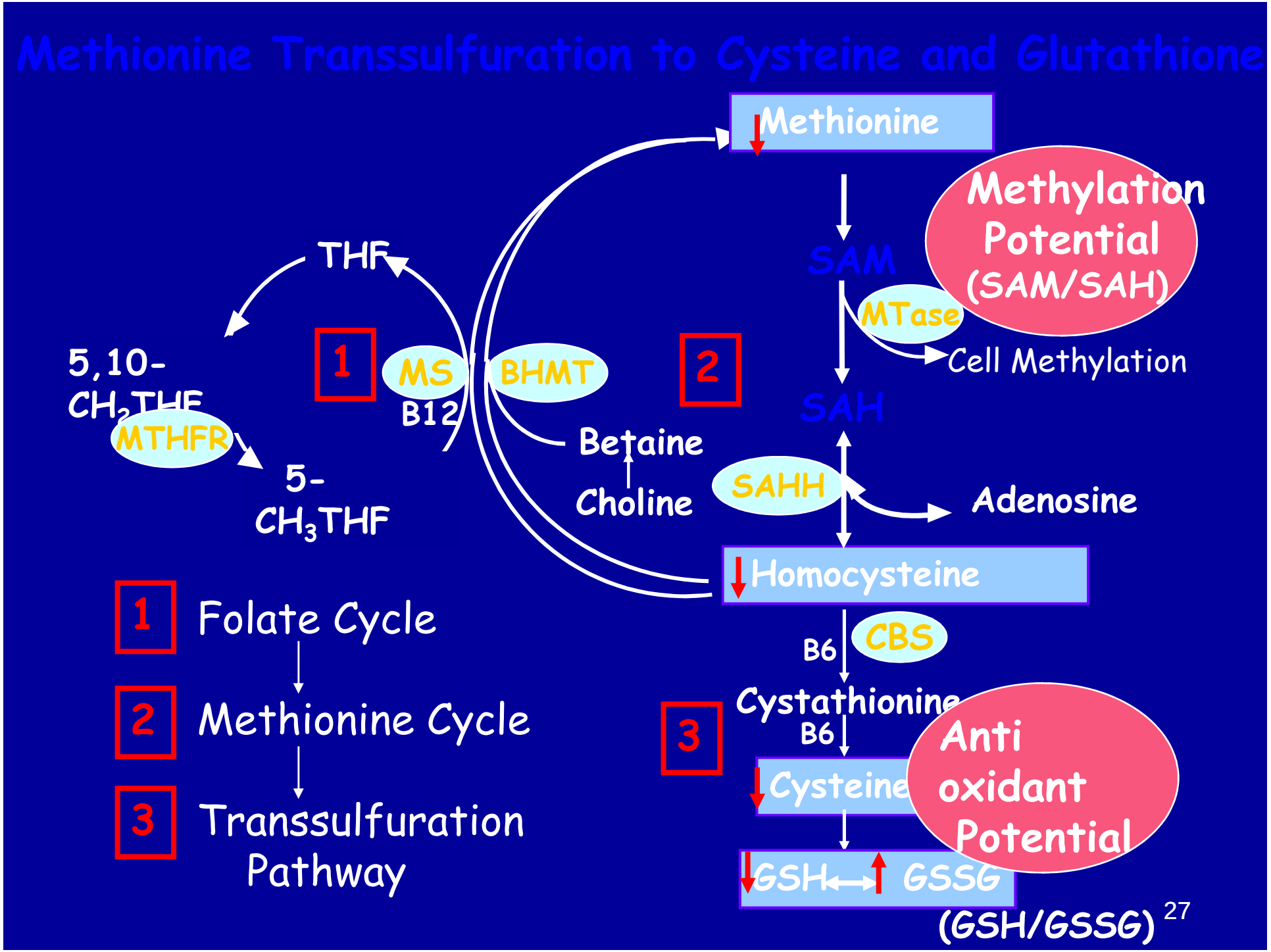
Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism.

S. Jill James, PhD ,et al

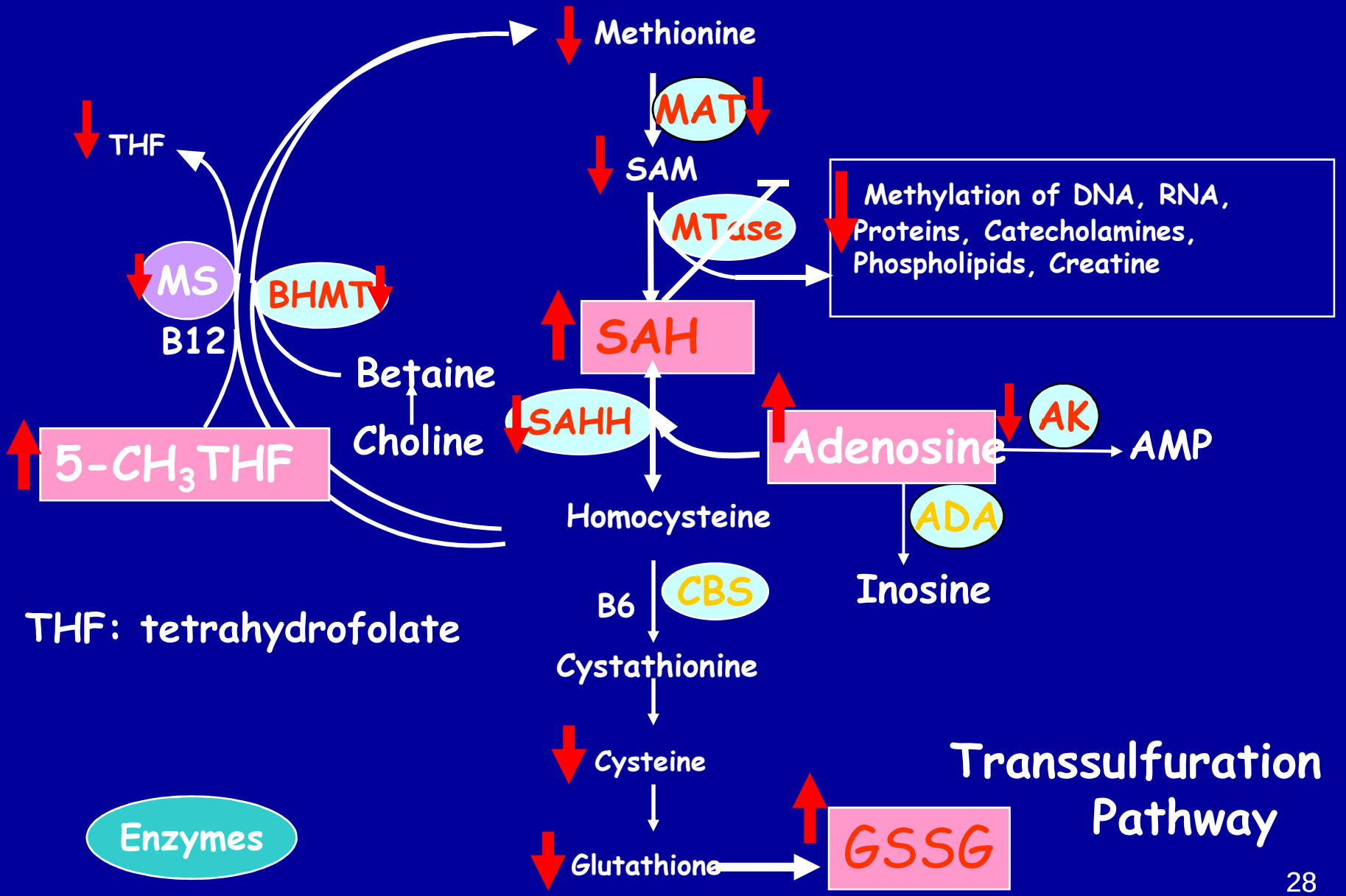
Am J Med Genet B Neuropsychiatr Genet. 2006 Dec 5;141(8):947-56

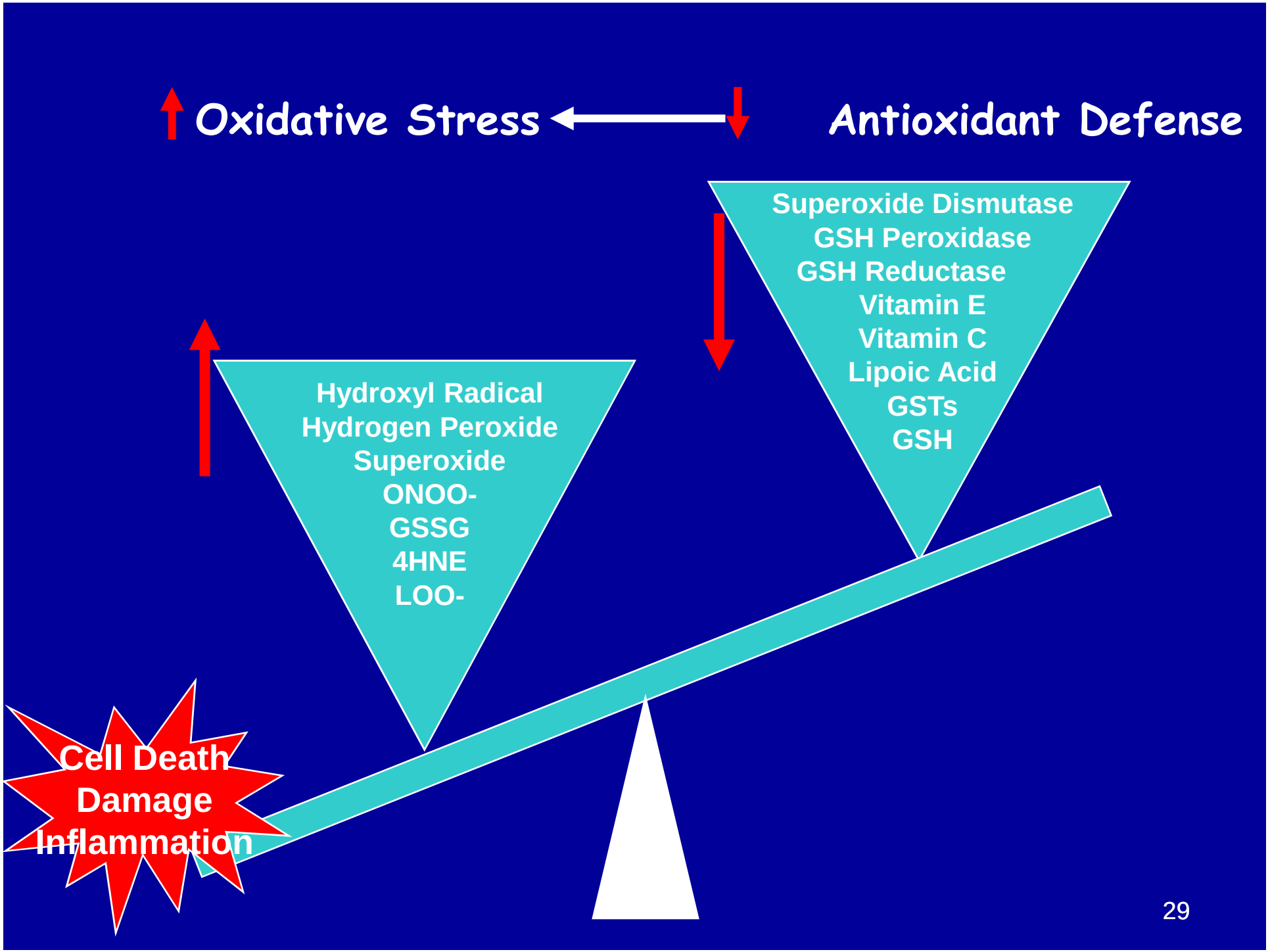
- Autism is a behaviorally defined neurodevelopmental disorder usually diagnosed in early childhood that is characterized by impairment in reciprocal communication and speech, repetitive behaviors, and social withdrawal. Although both genetic and environmental factors are thought to be involved, none 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]

Methionine Transsulfuration to Cysteine and Glutathione



Impact of Oxidative Stress on Methionine Metabolism




Oxidative Stress
Antioxidant Defense
Superoxide Dismutase
GSH Peroxidase
GSH Reductase
Vitamin E
Vitamin C
Lipoic Acid
GSTs
GSH
Hydroxyl Radical
Hydrogen Peroxide
Superoxide
ONOO-
GSSG
4HNE
LOO-
Cell Death
Damage
Inflammation

"Evaluation of subtoxic single exposures is misleading and meaningless. Toxic exposures in the environment interact to deplete Glutathione, damage DNA, and reach a threshold of toxicity sooner in the most genetically vulnerable individuals"

- Dr. Jill James

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
  - Lipid Peroxidation
- 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, Omega 3 Deficiencies
  - Essential Amino Acid Deficiencies
- Dysbiosis
  - Dysbiosis or altered bowel flora (Rossenau, 2004)
  - Clostridial overgrowth (Sandler, 2002)
  - Persistent measles virus (Wakefield, Krigsman)
- Gut 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; Jyonuchi 2005)
  - Proinflammatory response to dietary proteins (Jyonuchi, 2004)

Immune Dysregulation

- Th1 and Th2 skewing
  - Abnormal cell-mediated immunity (Molloy, 2006)
  - Abnormal T-cell subsets, decreased NK cells, abnormal cytokines, Th2 skewing (Zimmerman, 1998; Gupta, 1996)
  - Decreased secretory IgA
  - Pro-inflammatory cytokines,TNF alpha, IL-6 (Jyonuchi, 2001; Maes, 2001)
- Pro-inflammatory Cytokines in the Brain
  - MCP-1, TGF beta-1 (Vargas, Pardo, Laurence, 2005)
  - Abnormal EEG, Seizure activity
  - Microglial Activation
- Increased Autoimmunity
  - Autoantibodies to neural antigens (Connolly, 1999)
  - Mylein basic protein and Neuronal Axonal Filament Protein Antibodies (Gupta, 1996 /Singh, 1997)

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

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

Allergic shiners

- Allergic shiners, or dark circles beneath the eyes, in patient with autism and immune dysregulation.

Eczema as marker of Th2 shift in immune status

- Infantile atopic dermatitis or eczema
- A, This infant has an acute, weeping dermatitis on the cheeks and forehead.
- B and C, Involvement of the trunk and the extremities, with erythema, scaling, and crusting, are evident.

Eczema

- Childhood atopic dermatitis with lesions on the arms (A) and the legs (B). In childhood, eczema involves the flexural surfaces of the upper and lower extremities. The neck, ankles, wrists, and posterior thighs may also be severely affected.

Fungal dermatitis

- Widespread fungal dermatitis with Candida albicans.
- Note the dystrophic changes of the nails secondary to chronic infection (C).
- Normal immune surveillance usually prevents persistent infection with this ubiquitous organism.

Candidiasis

- A, Involvement of buccal mucosa with white plaque.
- B, Mucocutaneous infection of the commissures of the lips.

Molluscum contagiosum

- Severe molluscum contagiosum

  – (Courtesy of G. B. Scott, MD and M. T. Mastrucci, MD, Miami, Fla.)

Warts

- Verruca vulgaris. Dry, rough, and crusty, these common warts usually involve the hands. The periungual distribution in this girl was due in part to her habit of picking at her cuticles.

Laboratory Testing Options

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

- 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 Porphryins
- Urinary Neopterin
- Urinary 8-OH Guanosine
- PCB Levels

Lab Work-up Options for Heavy Metal Toxicity

- Hair Analysis
- Intracellular RBC Minerals and Toxic Metals
- Detoxification Markers
  - Reduced Glutathione, Cysteine, and Sulfate
- Urine Toxic Metals – provoked
- Fractionated Urinary Porphyrins
- Fecal Toxic Metals

Lab Work-up Options for Gut Issues

- Urine Organic Acids
- Stool Microbiology
- Stool Mycology
- Stool Parasitology
- IgG Food Antibody Panel
- Celiac Panel
- Inflammatory Markers (ESR, CRP, histamine)
- Ammonia, blood or urine

Lab Work-up Options for Immune Issues

- Immunoglobulin Levels
- T lymphocyte Panel
- Natural Killer Cell Activity
- PANDA's Profile
- IgG Food Antibody Panel
- Vaccine Titers
- Viral Titers
  - EBV, CMV, HSV, HHV6,
- Lymes Western Blot, FIA

“Small
things
done
with
great

LOVE
bring

JOY

and

PEACE”

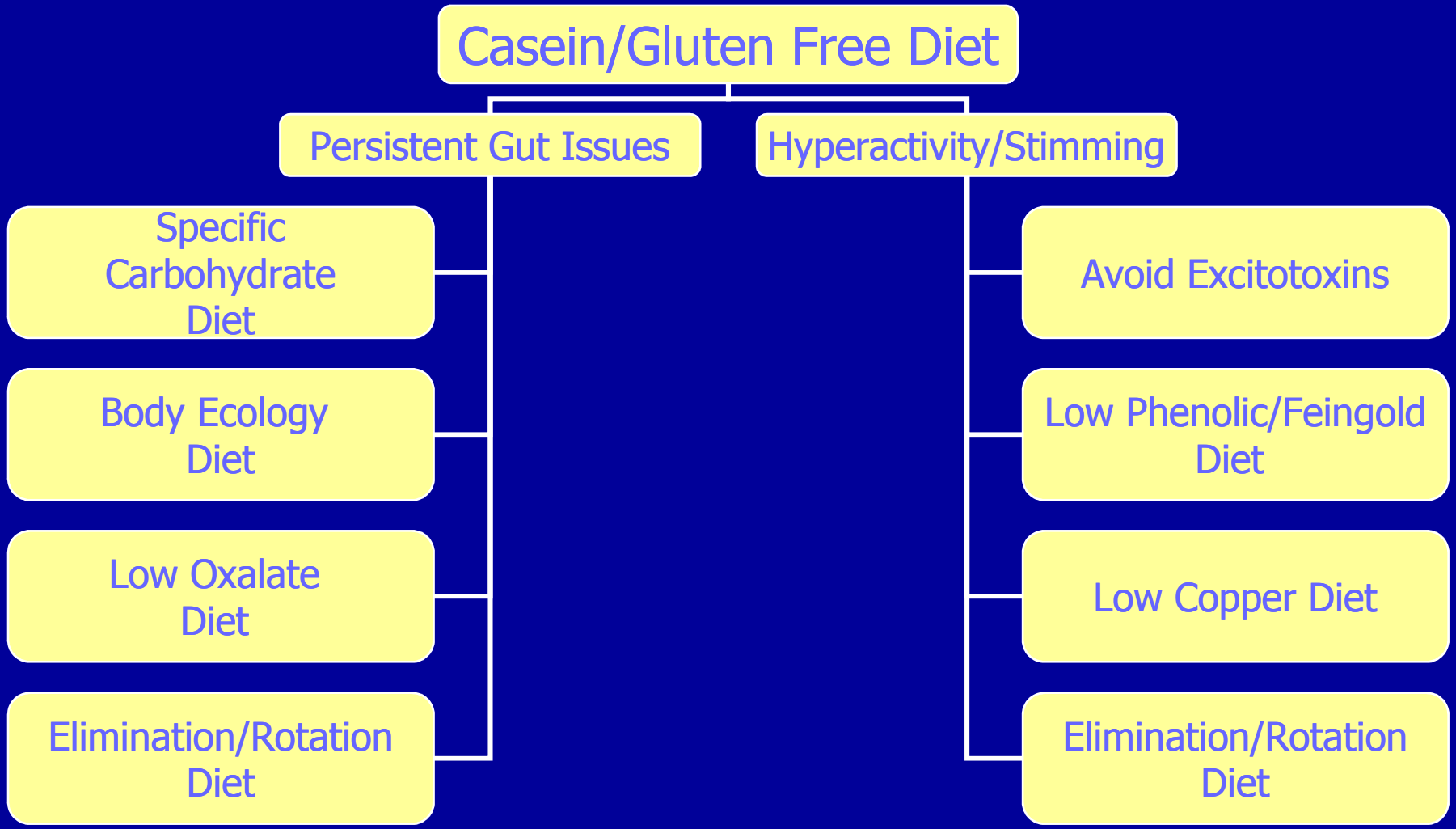
Clean up the Child's Environment

- 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
  - Molybenum 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 Immune Issues and Inflammation

- Eliminate food allergies
- Address chronic infections (yeast, bacteria, virus, parasites)
- 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, Ginger

Lead and Curcumin (Turmeric)

A new study shows that a component of the spice turmeric prevents lead-induced neuron death and memory loss in rats.

The cure for the effects of lead poisoning on learning and memory may lie in the roots of the plant *Curcuma longa*, the source of the Asian spice turmeric. That conclusion comes from a new study published online January 17 in the Journal of Agricultural and Food Chemistry**.**

Lead reduces levels of antioxidants—compounds that mop up toxic free radicals—in the brain. Free radicals kill neurons in the hippocampus, the brain region that controls learning and memory. When simultaneously treated with lead and curcumin—a chemical in turmeric and a powerful antioxidant—rat hippocampal neurons survived better than those treated only with lead. Curcumin also improved the performance of lead-poisoned rats in a learning and memory test, illustrating curcumin's therapeutic prowess.

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: Effective Biomedical Treatments, Pangborn and Baker
- "Autism, A Novel Form of Mercury Poisoning", Bernard, et al., 2000 (www.safeminds.org and autism.org)
- Healing the New Childhood Epidemics, Ken Bock, MD
- 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