

Viewing Time

The program will take up to one hour to complete.

Target Audience

This program is designed for primary care physicians.

Other health care professionals working with patients and their families may also find this program of interest.

Faculty Disclosure

It is the policy of Children's Hospitals and Clinics of Minnesota to ensure balance, independence, objectivity, and scientific rigor in all its educational programs. Our faculty have been asked to disclose to our program audience any real or apparent conflicts of interest related to the content of their presentation. They have also been requested to let you know when any product mentioned in their presentation is not labeled for the use under discussion or is still under investigation.

Faculty Disclosure

Lawrence Rosen, MD has disclosed no actual or potential conflict of interest in relation to this educational activity.

During this educational activity **Dr. Rosen** will not be discussing the use of any commercial or investigational product not approved for any purpose by the FDA.

Integrative Approaches to Autism

Lawrence Rosen, MD

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Integrative Approaches to Autism

*A lecture about the use of
complementary and alternative
medicine in children with Autism*

Program Objectives

Upon completion of this program, participants should be able to:

- Recognize the role of integrative medicine in the care of autism
- Identify key biomedical issues in children with autism
- Describe ethical principles in CAM use in children

Disclaimer

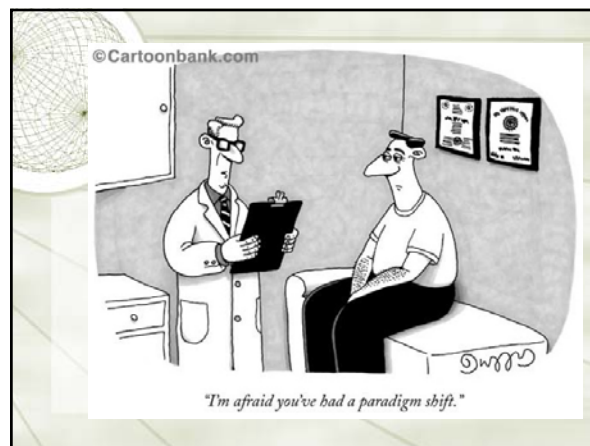
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Accreditation

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Receiving CME Credit

To receive CME credit you must view the entire program and complete the evaluation form at the end.



A U T I S M A L A R M .

Autism is preventable

- 1 out of 16 children are diagnosed with a developmental disorder relative behavioral problems
- 1 in 100 children are diagnosed with an autism spectrum disorder
- Developmental disorders have subtle signs and may be easily missed

Listen to parents

- Early signs of autism are often present before 18 months
- Parents usually DO have concerns that something is wrong
- Parents generally DO give accurate and quality information
- Don't ignore the not spontaneously raise concerns, ask if they have any

Act early

- Make screening and surveillance an important part of your practice (as endorsed by the AAP)
- Screen for subtle differences in behavior type and degree of development
- Learn to recognize red flags
- Use validated screening tools and identify problems early
- Improve the quality of life for children and their families through early and appropriate interventions

Refer

- To Early Intervention or a local school program (do not wait for a diagnosis)
- To an autism specialist, or team of specialists, immediately for a definitive diagnosis
- To audiologists and talk to a hearing impairment
- To local community resources for help and family support

Monitor

- Monitor a follow-up appointment to discuss concerns more thoroughly
- Look for other features known to be associated with autism
- Advise parents, and provide them with up to date information on autism
- Advise for families with a child who receives a diagnosis of autism, bipolar, or depression, and substance abuse
- Continue surveillance and search for additional or late signs of autism and/or other developmental disorders

For More Information: www.medicinfo.com/autism

CDC
MMWR
Morbidity and Mortality Weekly Report

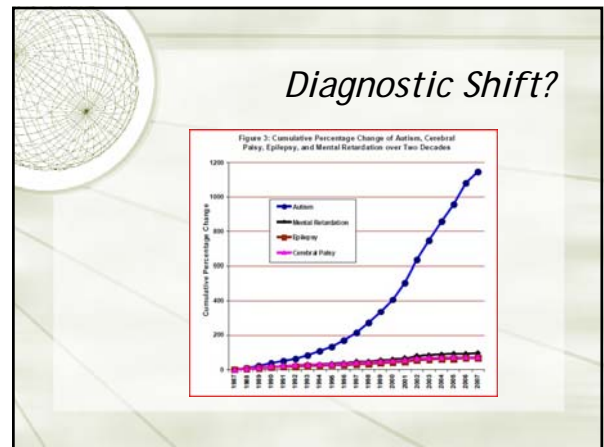
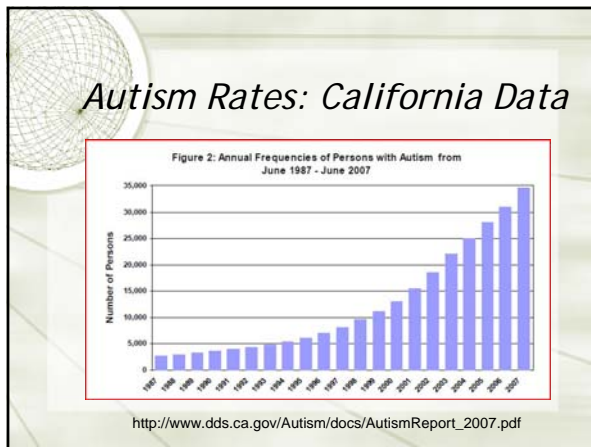
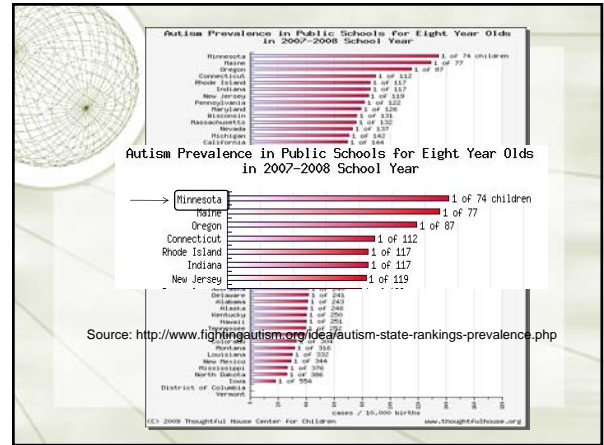
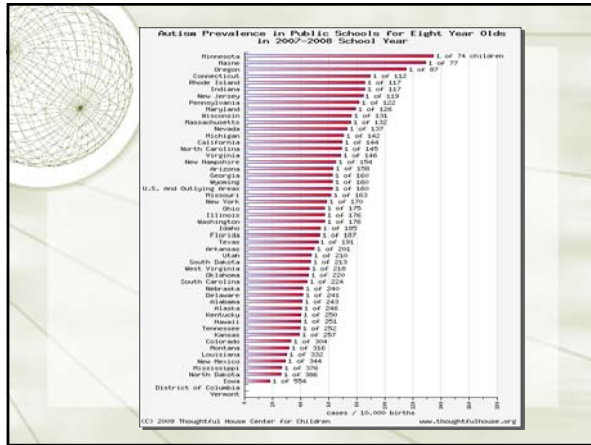
Supplement 5, November 5, 2009 / Vol. 58, No. SS-5

Prevalence of Autism Spectrum Disorders — Autism and Developmental Disabilities Monitoring Network, Six Sites, United States, 2000

Prevalence of Autism Spectrum Disorders — Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2005

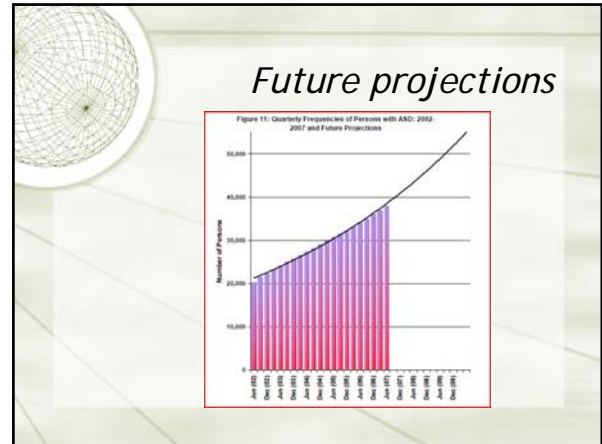
Evaluation of a Methodology for a Collaborative Multiple Source Surveillance Network for Autism Spectrum Disorders — Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2005

DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION



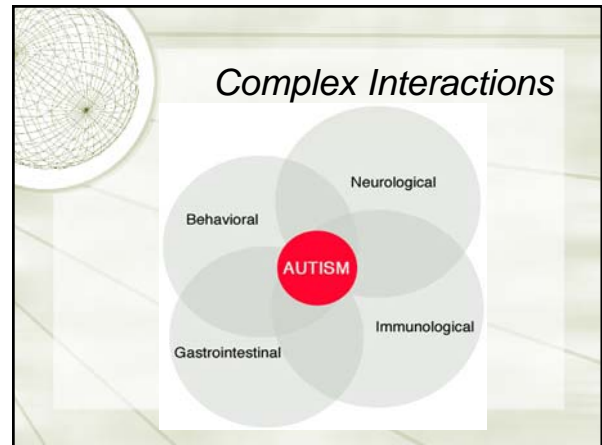
Hertz-Picciotto I, Delwiche L: The rise in autism and the role of age at diagnosis. Epidemiology 2009

- CONCLUSIONS: Autism incidence in California shows no sign yet of plateauing. Younger ages at diagnosis, differential migration, changes in diagnostic criteria, and inclusion of milder cases do not fully explain the observed increases. The rise in autism and the role of age at diagnosis.



What is Autism?

- 1943: Kanner
- 1964: Rimland
- 1994: DSM-IV
- 2009: A New Model?



One response

Autism Spectrum Disorder
A New Paradigm for Integrative Management

Lawrence Rosen, MD

Alternative & Complementary Therapies, October 2006

Pediatric Integrative Medicine

- The Whole Child ideal
- Family-centered care
- Focus on wellness and prevention
- Individualized therapies
- Relationships are the key
- Respectful, multidisciplinary collaboration

Integration: "Conventional" Therapies

- ✦ What are conventional therapies?
 - ✦ Education
 - ✦ Applied Behavioral Analysis
 - ✦ Other Behavioral Therapies (Floortime, RDI)
 - ✦ Speech/Communication Therapies
 - ✦ Occupational and Physical Therapies
 - ✦ Social Skills Groups
 - ✦ Psychotherapy/CBT
 - ✦ Medications

Integration: CAM Therapies

- ✦ Biomedical - main focus, most data
 - ✦ DAN/ARI, IFM
 - ✦ Eclectic
- ✦ Other - will cover briefly

Use of CAM in ASD

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Parental Perceptions and Use of Complementary and Alternative Medicine Practices for Children with Autistic Spectrum Disorders in Private Practice

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92% Use of CAM Therapies

Why ASD and PIM?

- ✦ Family beliefs and use of CAM
- ✦ ASD is a complex, multi-systemic medical disorder with no conventional cure

Family Beliefs

- ✦ Mercer L, et al: *Parental Perspectives on the Causes of an Autism Spectrum Disorder in their Children.* J Genet Couns 15: 41-50, 2006.
 - ✦ 90% genetic influences
 - ✦ 68% perinatal factors
 - ✦ **51% nutrition**
 - ✦ 44% prenatal factors
 - ✦ 40% vaccines

Liptak GS, et al: *Satisfaction with primary health care received by families of children with developmental disabilities.* J Pediatr Health Care. 2006

- ✦ "Physicians' knowledge about complementary and alternative medicine and their qualifications to manage developmental disabilities ranked worse than neutral. Families with a child with autism had more spontaneous negative comments and rated their primary care physicians lower on several aspects of care. They requested more information on complementary and alternative medicine and more support in the community."

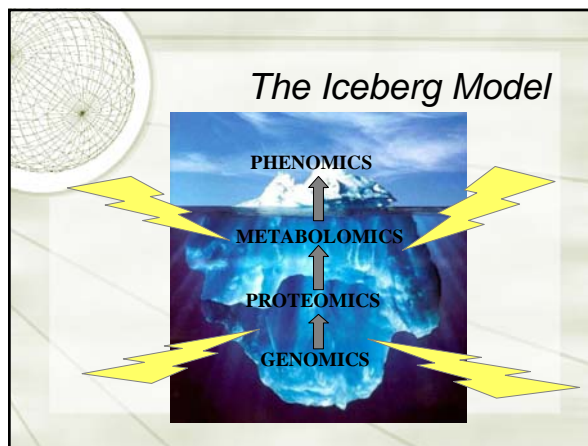
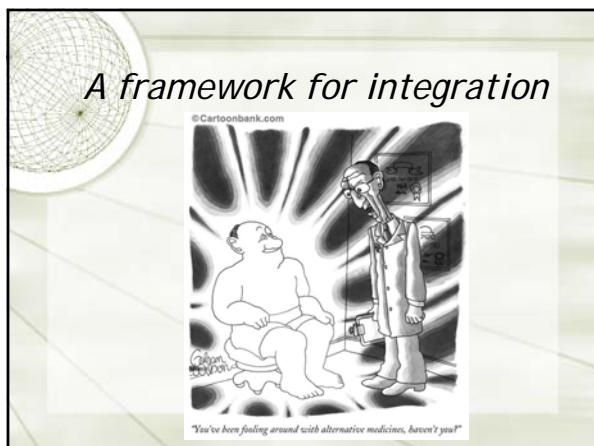
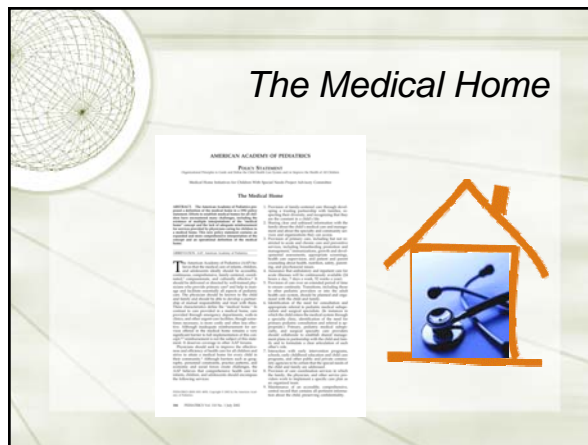


Ethical Issues


		Effective	
		Yes	No
Safe	Yes	Use/Recommend	Tolerate/Monitor
	No	Caution/Monitor	Advise against

Adapted from Cohen MH, Eisenberg DM; Ann Intern Med 2002

- ### AAP Guidelines
- + Kemper KJ, Vohra S, Walls R; AAP Task Force on Complementary and Alternative Medicine; Provisional Section on Complementary, Holistic, and Integrative Medicine: *The use of complementary and alternative medicine in pediatrics*. Pediatrics 122: 1374-1386, 2008.
 - + Myers SM, Johnson CP; AAP Council on Children with Disabilities: *Management of children with autism spectrum disorders*. Pediatrics 120: 1162-1182, 2007.
 - + AAP Committee on Children with Disabilities: *Counseling families who choose complementary and alternative medicine for their child with chronic illness or disability*. Pediatrics 107: 598-601, 2001.



Epigenetics




Environmental Health Perspectives Volume 114, Number 3, March 2008

Focus


Epigenetics: The Science Of Change

LDDI Scientific Consensus Statement

- ✦ Scientific Consensus Statement on Environmental Agents Associated with Neurodevelopmental Disorders, 2007
- ✦ *“The scientific evidence we have reviewed indicates environmental contaminants are an important cause of learning and developmental disabilities.”*



Biomedical Approaches



Neurometabolic Disorders and Dysfunction in Autism Spectrum Disorders

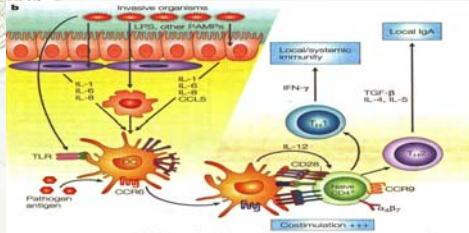
Neurometabolic Disorders and dysfunction in autism spectrum disorders. *Curr Neurol Neurosci Rep.* 2009.

Pediatrics and Developmental Neuropsychiatry Branch, National Institute of Mental Health, 10 Center Drive, Bethesda, MD 20892, USA.

Biomedical Theory and Practice

- ✦ Gastrointestinal/Nutrition
- ✦ Immune Dysregulation
- ✦ Metabolism/Mitochondria
- ✦ Oxidative Stress/Detoxification

Gastrointestinal Issues



Invasive organisms, LPS, other PAMPs, IL-1, IL-6, IL-8, IL-12, TNF-α, CCL5, TLR1, TLR2, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, TLR11, TLR12, TLR13, TLR14, TLR15, TLR16, TLR17, TLR18, TLR19, TLR20, TLR21, TLR22, TLR23, TLR24, TLR25, TLR26, TLR27, TLR28, TLR29, TLR30, TLR31, TLR32, TLR33, TLR34, TLR35, TLR36, TLR37, TLR38, TLR39, TLR40, TLR41, TLR42, TLR43, TLR44, TLR45, TLR46, TLR47, TLR48, TLR49, TLR50, TLR51, TLR52, TLR53, TLR54, TLR55, TLR56, TLR57, TLR58, TLR59, TLR60, TLR61, TLR62, TLR63, TLR64, TLR65, TLR66, TLR67, TLR68, TLR69, TLR70, TLR71, TLR72, TLR73, TLR74, TLR75, TLR76, TLR77, TLR78, TLR79, TLR80, TLR81, TLR82, TLR83, TLR84, TLR85, TLR86, TLR87, TLR88, TLR89, TLR90, TLR91, TLR92, TLR93, TLR94, TLR95, TLR96, TLR97, TLR98, TLR99, TLR100.

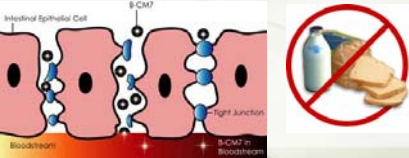
- ✦ Valicente-McDermott M et al: Frequency of gastrointestinal symptoms in children with autistic spectrum disorders. *J Dev Behav Pediatr* 27: S128-S136, 2006.

Evidence of GI Inflammation

- ✦ Horvath K et al: Gastrointestinal abnormalities in children with autistic disorder. *J Pediatr* 135: 559-563, 1999
- ✦ Wakefield AJ et al: Enterocolitis in children with developmental disorders. *Am J Gastroenterol* 95: 2285-2295, 2000.
- ✦ Ashwood P et al: Intestinal lymphocyte populations in children with regressive autism: evidence for extensive mucosal immuno-pathology. *J Clin Immunol* 23: 504-17, 2003.

Nutritional Therapies: Food

- ✦ GFCF diet
- ✦ Other elimination diets
- ✦ Food allergies/sensitivities



The diagram illustrates the intestinal epithelial cell structure, highlighting the tight junctions and the presence of B-CM7 protein. A red prohibition sign is overlaid on a glass of milk and a slice of bread, indicating the elimination of these foods in a GFCF diet.

Nutritional Therapies: Supplements

- ✦ Vitamins
- ✦ Minerals
- ✦ Amino, Organic, and Fatty Acids
- ✦ Probiotics
- ✦ Enzymes

Vitamins and Minerals

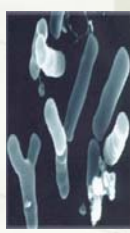
- ✦ Vitamin B6 and Magnesium
- ✦ Vitamin B12 and Folic Acid
- ✦ Vitamin A
- ✦ Vitamin D and Calcium
- ✦ Vitamins C, E and Selenium
- ✦ Iron
- ✦ Zinc and Copper

Amino, Organic, and Fatty Acids

- ✦ Aldred S, et al: Plasma amino acid levels in children with autism and their families. *J Autism Dev Disord* 33: 93-7, 2003.
- ✦ Vancassel S, et al: Plasma fatty acid levels in autistic children. *Prostaglandins Leukot Essent Fatty Acids* 65:1-7, 2001.
- ✦ Bell JG et al: Essential fatty acids and phospholipase A(2) in autistic spectrum disorders. *Prostaglandins Leukot Essent Fatty Acids* 71: 201-204, 2004.

Probiotics

- ✦ Finegold SM et al: Gastrointestinal microflora studies in late-onset autism. *Clin Infect Dis* 35 (Suppl 1): S6-16, 2002.
- ✦ Bruzzese E, et al: Microflora in inflammatory bowel diseases: a pediatric perspective. *J Clin Gastroenterol* 38: S91-S93, 2004.
- ✦ O'Mahony L, et al: Lactobacillus and bifidobacterium in irritable bowel syndrome: symptom responses and relationship to cytokine profiles. *Gastroenterology* 128: 541-551, 2005.



The image shows a microscopic view of probiotic bacteria, likely Lactobacillus and Bifidobacterium, used in the studies mentioned in the text.

Enzymes

- ✦ Theory: Gut inflammation and DPPiV
- ✦ Reichelt KL, et al: Gluten, milk proteins and autism: dietary intervention effects on behavior and peptide secretion. *J Applied Nutrition* 42 :1-11, 1990.
- ✦ No RCT's

Immune Dysregulation

- ★ Recurrent and/or Chronic
 - ✦ URI's
 - ✦ LRTI's
 - ✦ AOM and/or CSOM
- ★ Niehus R, Lord C: Early medical history of children with autism spectrum disorders. *J Dev Behav Pediatr* 2006.
- ★ Heuer L, et al: Reduced levels of immunoglobulin in children with autism correlates with behavioral symptoms. *Autism Res* 2008.

Th1/Th2 Imbalance

Figure 7 - Model of the role of the intestinal microenvironment in polarizing immune functions.

Source: A. Vojdani (ISL)

Early Warning Signs?

- ★ Spergel JM, Paller AS: *Atopic dermatitis and the atopic march*. *J Allergy Clin Immunol* 112S: 118-127, 2003.
 - ✦ Eczema
 - ✦ GE Reflux
 - ✦ Allergic rhinitis
 - ✦ Asthma
- ★ Croen LA, et al: Maternal autoimmune diseases, asthma and allergies, and childhood autism spectrum disorders: a case-control study. *Arch Pediatr Adolesc Med* 159:151-157, 2005.

The Gut-Immune System

- ★ Ashwood P et al: Intestinal lymphocyte populations in children with regressive autism: evidence for extensive mucosal immunopathology. *J Clin Immunol* 23: 504-17, 2003.
- ★ DeFelice ML, et al: Intestinal cytokines in children with pervasive developmental disorders. *Am J Gastroenterol* 98: 1777-1782, 2003.
- ★ Vojdani A, et al: Immune response to dietary proteins, gliadin and cerebellar peptides in children with autism. *Nutr Neurosci* 7: 151-161, 2004.
- ★ Jyonouchi H, et al: Dysregulated innate immune responses in young children with autism spectrum disorders: their relationship to gastrointestinal symptoms and dietary intervention. *Neuropsychobiology* 51: 77-85, 2005.

Biochemical/Metabolic Txts

Metabolic Dysregulation

Source: James SJ, et al: *Metabolic biomarkers of increased oxidative stress and impaired methylation capacity in children with autism*. *Am J Clin Nutr* 80: 1611-1617, 2004.

Metabolic Treatment

Efficacy of methylcobalamin and folic acid treatment on glutathione redox status in children with autism¹⁻³

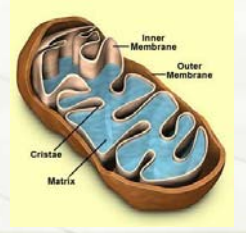
S. Jill James, Susan Mielnik, George Fuchs, Zora Kolic, Sagar Arjunan, Okonkwo Paul, Amanda Mahalik, and David W. Gaylor

ABSTRACT
Background: Metabolic abnormalities and impaired immune skills have been reported for several neurodevelopmental disorders but are relatively understudied in autism.
Objective: The objective of this study was to determine whether or not treatment with the metabolic precursors, methylcobalamin and folic acid, would improve plasma concentrations of intracellular antioxidant glutathione and glutathione redox ratio in autistic children.
Design: In an open-label trial, 40 autistic children were treated with 75 µg methylcobalamin (1000xVitamin B12) and 400 µg folic acid (10xVitamin B9) for 7 wks. Metabolites in the homocysteine/methionine cycle and glutathione redox pathway were measured before and after treatment and compared with values measured in age-matched control children.
Results: The results indicated that pretreatment metabolic concentrations in autistic children were significantly different from values in the control children. The 7-wk intervention resulted in significant increases in cysteine, creatinine, folate, and glutathione concentrations (P < 0.0001). The redox ratio of glutathione was decreased and the glutathione redox ratio increased after treatment (P < 0.0001). Although mean metabolic concentrations were not significantly different after treatment, they remained below those in unaffected control children.
Conclusions: The significant improvements observed in homocysteine, methionine and glutathione redox status after treatment suggest that targeted nutritional intervention with methylcobalamin and folic acid may be of clinical benefit in some children who have autism. This trial was registered at clinicaltrials.gov as NCT00442115. *Am J Clin Nutr* 2009;89:422-30.

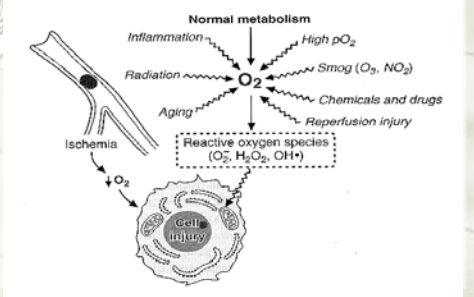
The American Journal of Clinical Nutrition

Mitochondrial dysfunction

★ A slight detour: "The Curious Case of Hannah Poling"



Oxidative Stress



Source: J. James

Antioxidant Defenses

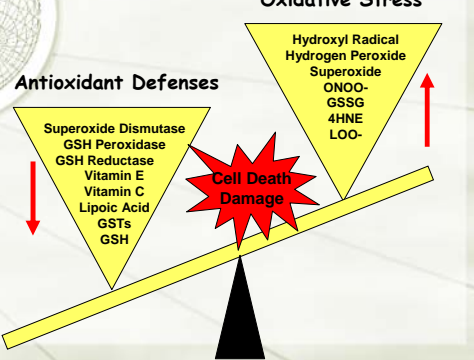
- Superoxide Dismutase
- GSH Peroxidase
- GSH Reductase
- Vitamin E
- Vitamin C
- Lipoic Acid
- GSTs
- GSH

Oxidative Stress

- Hydroxyl Radical
- Hydrogen Peroxide
- Superoxide
- ONOO-
- GSSG
- 4HNE
- LOO-
- NO

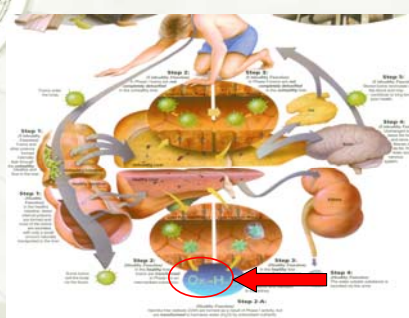
Source: J. James

Oxidative Stress



Source: J. James

Detoxification Theory



Detoxification Therapies

- ✦ Support natural defenses
 - ✦ Antioxidants (vitamins and minerals)
- ✦ Botanicals (herbal, homeopathy)
- ✦ Physical (sauna, baths)
- ✦ Chelation
- ✦ Biofilm theory

HBOT Theory

Autism	HBOT
▼ Cerebral perfusion	▲ Perfusion to brain tissue
▲ Inflammation	▼ Inflammation
▲ Oxidative stress	▼ Oxidative stress
Neurodegenerative disease	▲ Stem cells

Rossignol: Med. Hypotheses 2006

HBOT Evidence

- ✦ Rossignol DA, et al: Hyperbaric treatment for children with autism: a multicenter, randomized, double-blind, controlled trial. BMC Pediatr. 2009.
- ✦ "Children with autism who received hyperbaric treatment at 1.3 atm and 24% oxygen for 40 hourly sessions had significant improvements in overall functioning, receptive language, social interaction, eye contact, and sensory/cognitive awareness compared to children who received slightly pressurized room air."

Additional CAM Therapies

- ✦ Sensory Integration Therapies
- ✦ Hippotherapy
- ✦ Creative Arts/Expressive Therapies
- ✦ TCM/Acupuncture
- ✦ Manipulative Therapies (chiropractic, osteopathic, craniosacral, massage)
- ✦ Homeopathy
- ✦ Energy Medicine (Reiki)
- ✦ Yoga

New Paradigm: Integrative Medicine

Autism: Integrative Medicine as a New Paradigm

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May 2009

**Comments
and
Questions**

*Thanks for viewing
this presentation!*



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click the CME Eval button below
and complete the form.*

Autism: Integrative Approach

Selected Resources and References

May 2009

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General

AAP Committee on Children with Disabilities: *Counseling families who choose complementary and alternative medicine for their child with chronic illness or disability*. Pediatrics 107: 598-601, 2001.

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