

Monday Morning Tools for Your Autism Treatment Toolbox

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78th UWI/BAMP Annual Conference

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Disclaimer

- I am not dispensing medical advice, information provided is without warranty
- I have no financial relationships to disclose
- Some of the discussed treatments are considered “off label” by the FDA

Objectives

- To become acquainted with autism as a complex medical disease
- To understand its signs and symptoms in this context
- To acquire treatment tools that are useful on Monday morning.
- References are included here that will not be addressed during the live presentation due to time constraints.

Suggested Pre-Reading

- Buie, T et al. Evaluation, Diagnosis, and Treatment of Gastrointestinal Disorders in Individuals With ASDs: A Consensus Report. *Pediatrics*. 2010 Jan;125 (1):S1-S18. doi:10.1542/peds.2009-1878C
- Whiteley, P et al. Gluten- and casein-free dietary intervention for autism spectrum conditions. *Front Hum Neurosci*. 2012 Nov; 6: 344. doi: 10.3389/fnhum.2012.00344
- Herbert, M and Buckley, J. Autism and Dietary Therapy: Case Report and Review of the Literature *J Child Neurology*. 2013 Aug;28(8):973 - 980. doi 10.1177/0883073813488668
- Rossignol, D et al. Hyperbaric oxygen treatment in autism spectrum disorders. *Med Gas Res*. 2012; 2:16. doi: 10.1186/2045-9912-2-16
- Agrawal, A et al. Thimerosal induces TH2 responses via influencing cytokine secretion by human dendritic cells. *J Leukoc Biol*. 2007 Feb;81(2):474-82. doi: 10.1189/jlb.0706467
- Rossignol, D and Frye R. Evidence linking oxidative stress, mitochondrial dysfunction, and inflammation in the brain of individuals with autism. *Front. Physiol.*, 2014 Apr; 5() | <http://dx.doi.org/10.3389/fphys.2014.00150>

New survey finds 1 in 45 kids has autism: What's behind the alarming number?

 Maggie Fox
TODAY

Nov. 13, 2015 at 8:01 AM



A new government survey finds that more than 2 percent of U.S. kids have been diagnosed with autism — or 1 in 45 children aged 3 and older.





Toolbox Slides for Monday Morning

- "It is more important to know what patient has the disease than to know what disease the patient has." – Osler
 - If you've met one child with autism, you've met one child with autism
 - **Please PRESUME THEIR COMPETENCE!!**
- Health as a positive vitality – not merely the absence of disease.
- Promotion of organ reserve as the means to enhance health span.

Remembering How It All Works

The Inner Life of the Cell

Our Reality

- Autism in 1943- Kanner's initial description of 11 cases
- Autism in 1980- 1:2500
- Autism in 2007 – 1: 150 for children born 1994
- Autism in 2009- 1:100 for children born in 1996- a 50% increase
- Autism in 2013- 1:50 for school aged children
- Add in PDD-NOS, Asperger's, ADHD, LD- 1:6

Our Reality- Autism per CDC

- CDC----1% of children in US are on the spectrum
- 730,000 children nationwide
- 4 times as many boys as girls
- 25% are regressive
- Genes and environment involved

www.cdc.gov

Autism as a Whole Body Medical Illness- Not A New Concept

- Leo Kanner
- Describes 11 cases of autism in 1943
- Sick children with unusual behaviors



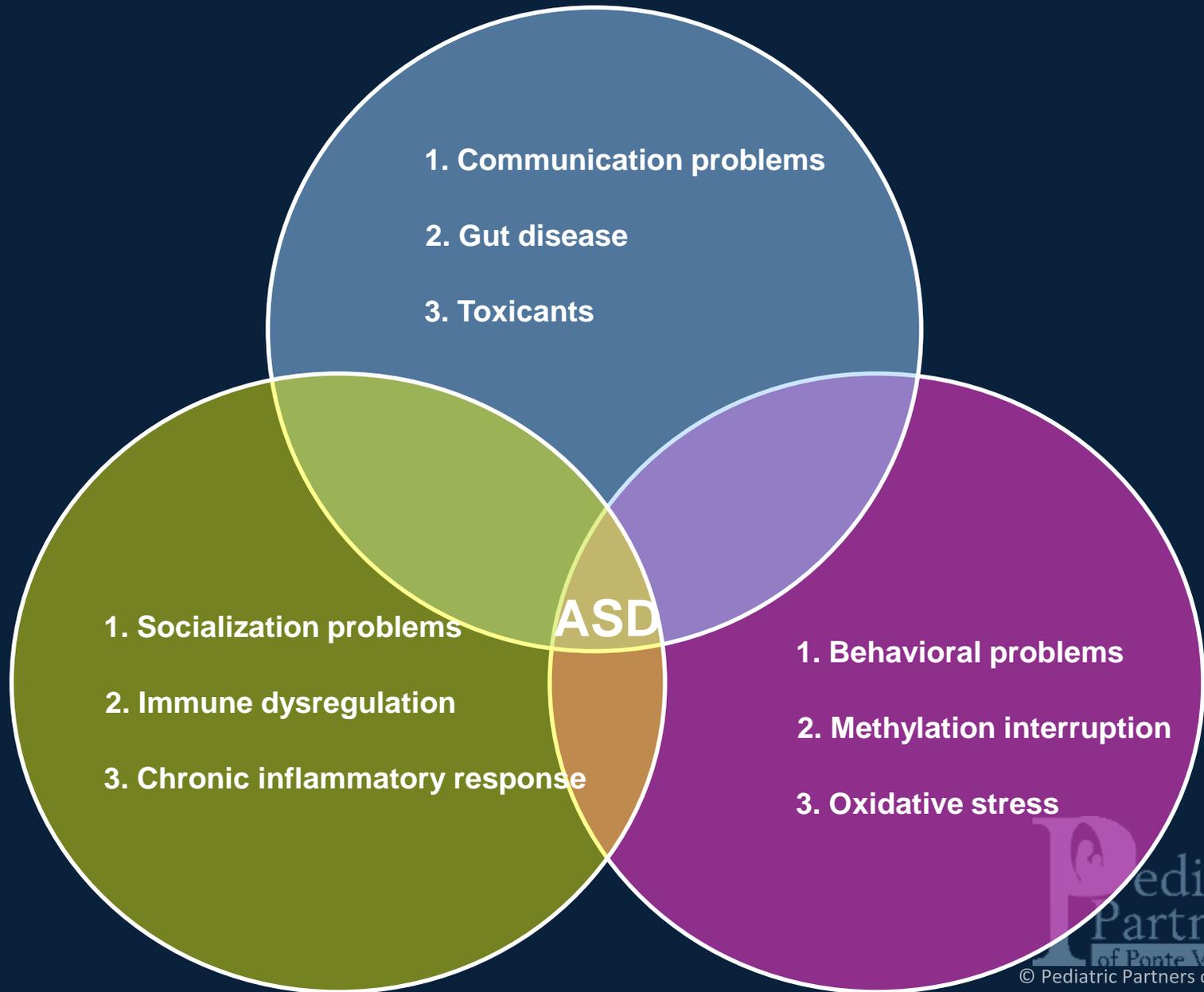
Kanner Describes Whole Body Illness

- **Case 1:** “Eating has always been a problem for him. He has never shown a normal appetite.”
- **Case 2:** “...large and ragged tonsils.”
- **Case 3:** diarrhea and fever following smallpox vaccination healthy except for large tonsils and adenoids.
- **Case 4:** vomited a great deal during his first year... feeding formulas were changed frequently ... tonsils were removed...
- **Case 5:** nursed very poorly ... quit taking any kind of nourishment at three months... tube-fed five times daily up to one year of age...At camp she slid into avitaminosis and malnutrition but offered almost no verbal complaints.”
- **Case 7:** vomited all food from birth through the third month....
- **Case 8:** feeding formula caused ...concern. ... colds, bronchitis, streptococcus infection, impetigo...
- **Case 9:** none of the usual children’s diseases.”
- **Case 10:** frequent hospitalizations because the feeding problem ... repeated colds and otitis media
- **Case 11:** was given anterior pituitary and thyroid preparations for 18 months

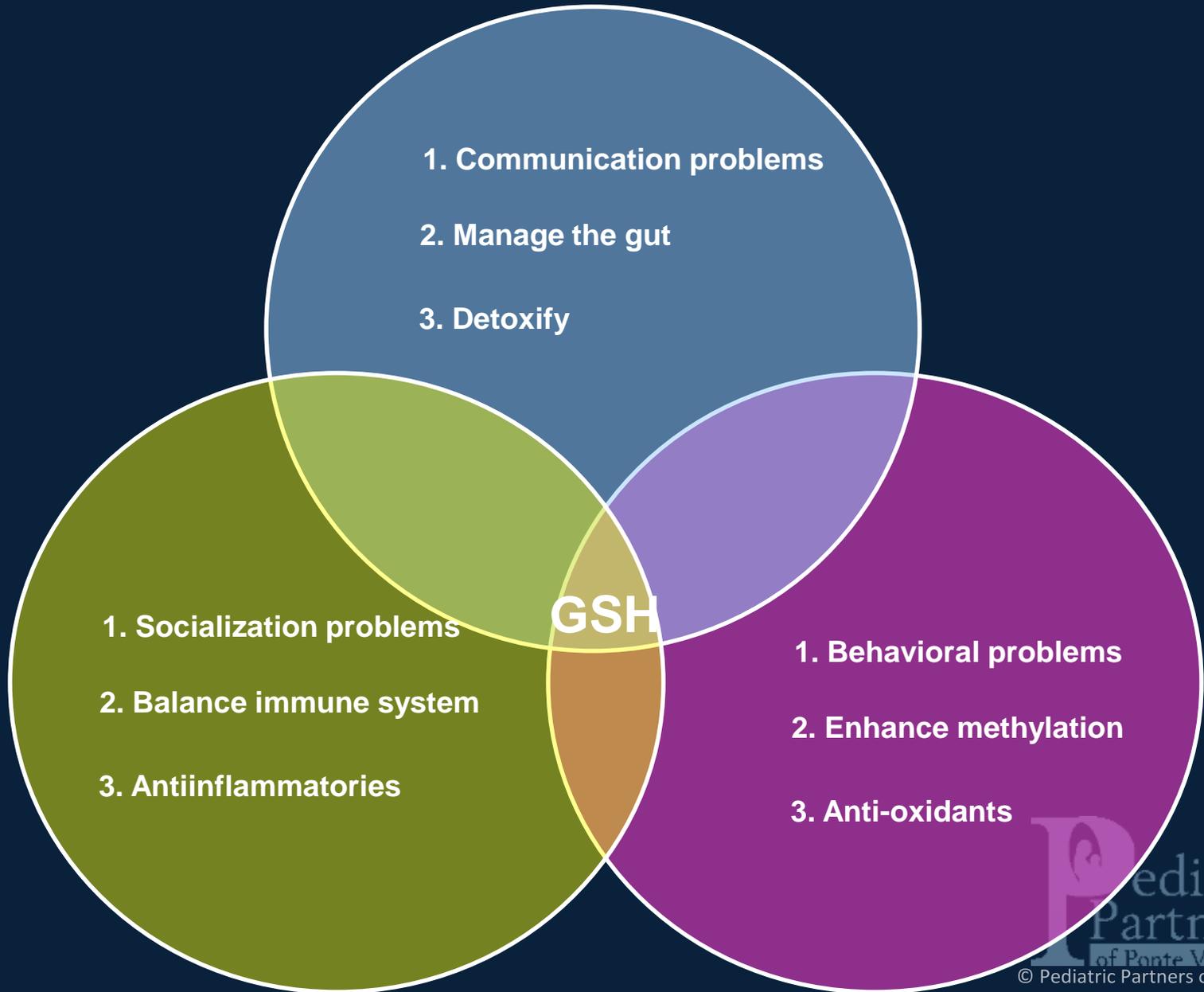
And Yet...

- Golnik A, Ireland M, Borowsky IW. Mar 2009. **Medical homes for children with autism: a physician survey.** Pediatrics. 123(3), 966-71.
- ...Physicians reported significantly lower overall self-perceived competency, a greater need for primary care improvement, and a greater desire for education for children with autism compared with both children with other neurodevelopmental conditions and those with chronic/complex medical conditions.
- ...barriers to providing primary care
 - lack of care coordination,
 - reimbursement and physician education,
 - family skeptical of traditional medicine and vaccines
 - patients using complementary alternative medicine.
 - CONCLUSIONS: Physician education is needed to improve primary care for children with autism.

Comprehensive Model for Autism

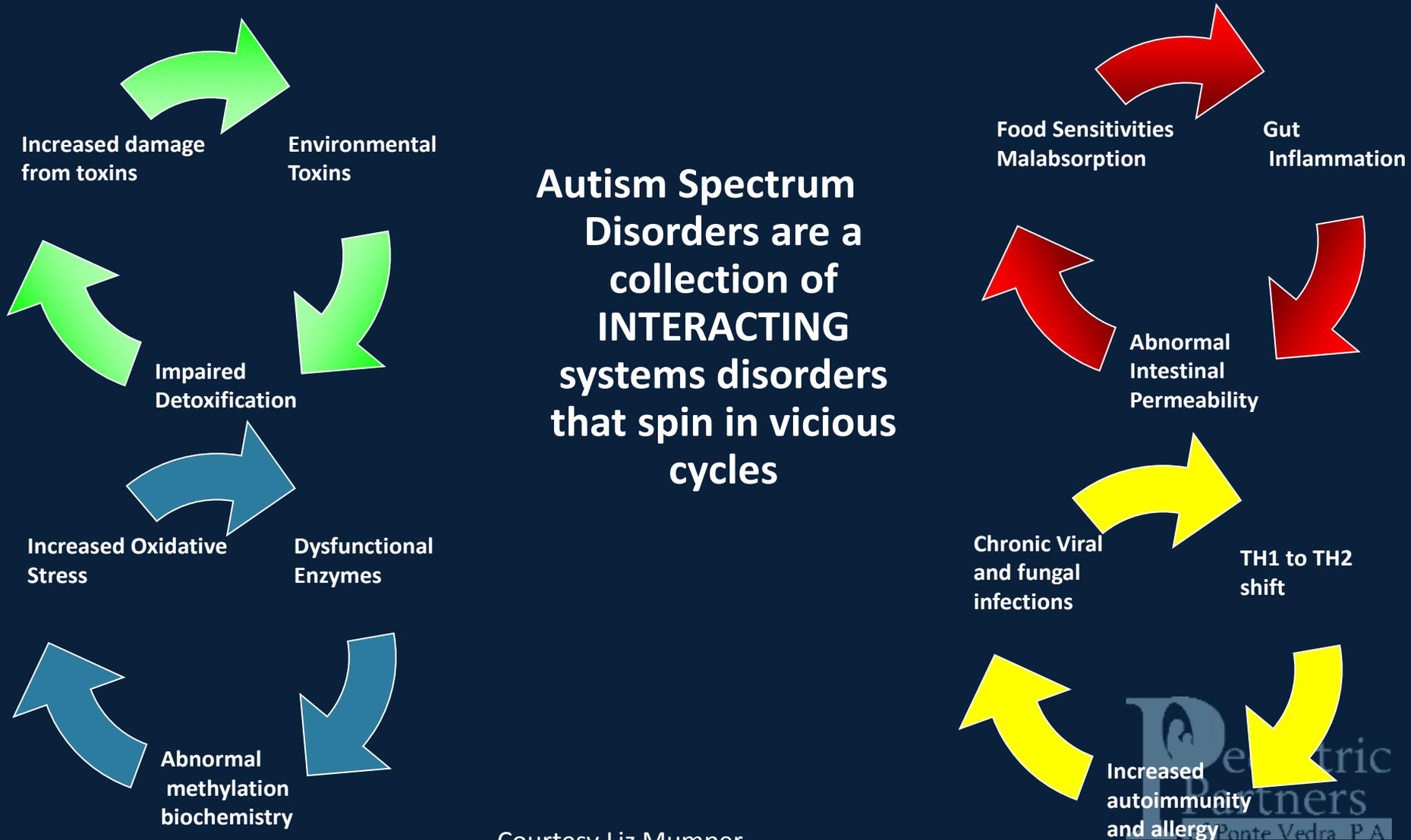


Managing Autism, Managing All Disease



New ways of thinking about Autism Spectrum Disorders- Vicious Cycles

Autism Spectrum Disorders are a collection of **INTERACTING** systems disorders that spin in vicious cycles



Courtesy Liz Mumper

Vicious Cycles - What It Looks Like In Our Homes

- Seizures- in up to 40% of our children
- Chronic Constipation and/or diarrhea
- Sleep problems
- Pica- eating non food items
- Low muscle tone- fine and gross motor skill impact
- Sensory disturbances
- Language and communication problems
- Repetitive behaviors, stimming
- Need for sameness, stereotypia

Environmental Exposure

- Role of environmental toxicity in disease no longer discounted
- Adult medicine accepted this long before pediatricians did
- Myriad articles

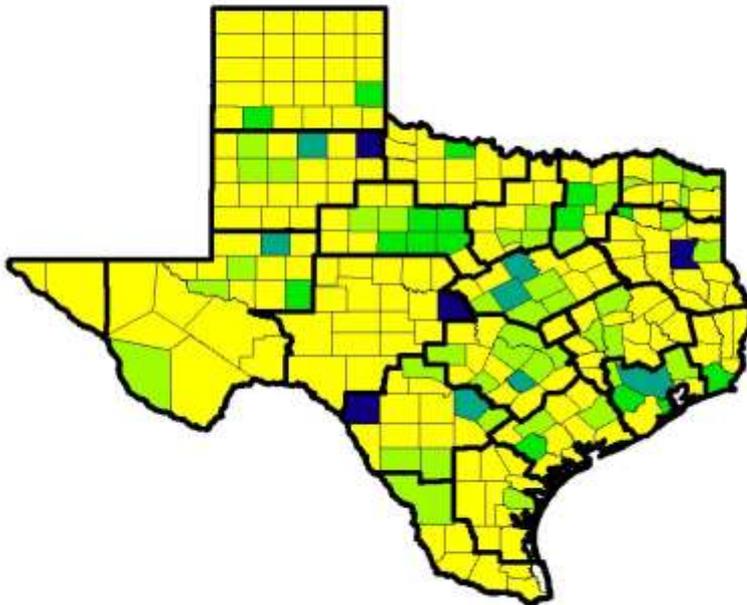


Texas autism rates, by school districts

Potential association between autism rates, environmental mercury other toxins in Texas

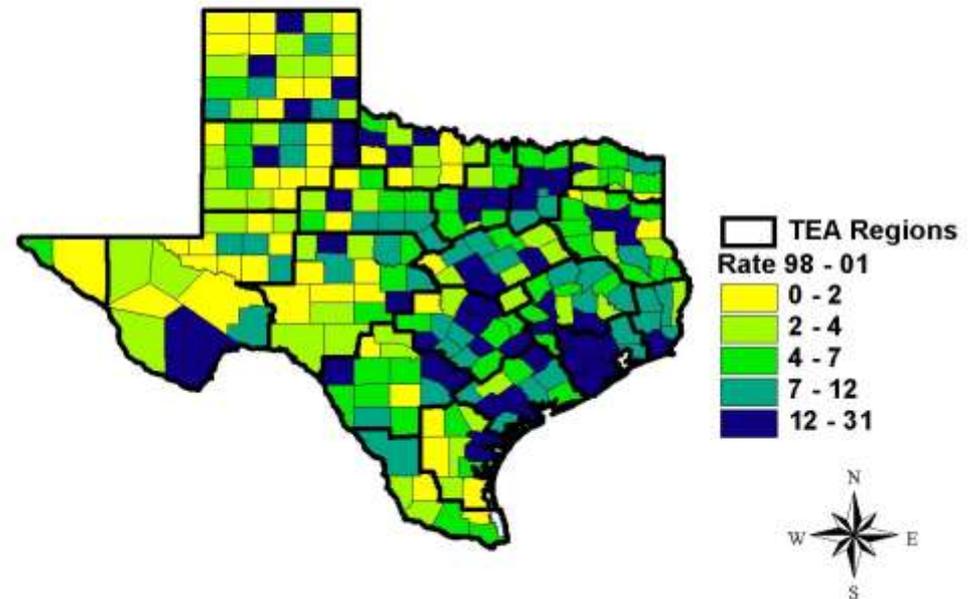
Palmer, et al., 2006 *Health and Place*, 12, 203-209

Observed Rate of Autism 1990 - 1993 By County of Texas
Aggregated from School Districts
With Texas Education Agency Districts



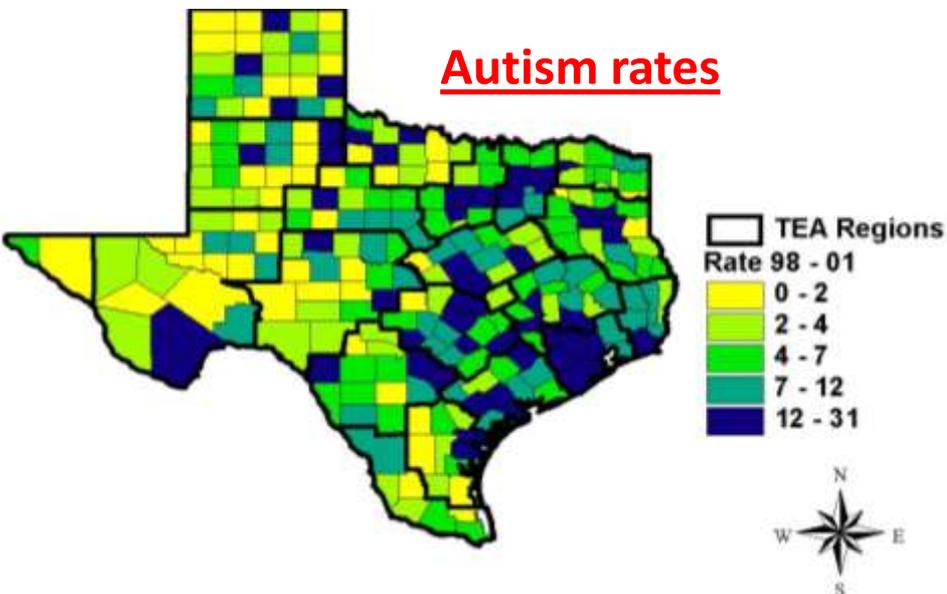
1990-1993

Observed Rate of Autism 1998 - 2000 By County of Texas
Aggregated from School Districts
With Texas Education Agency Districts



1998-2000

Observed Rate of Autism 1998 - 2000 By County of Texas
 Aggregated from School Districts
 With Texas Education Agency Districts

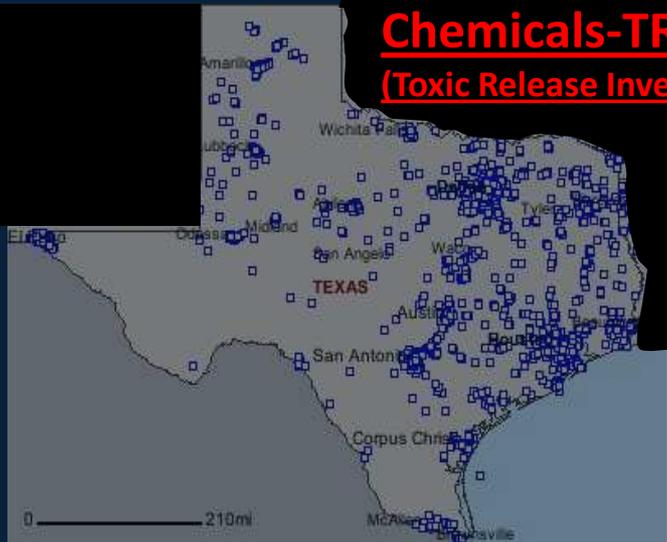


On average, for each 1000 lb of environmentally released mercury, there was a 43% increase in the rate of special education services and a 61% increase in the rate of autism.

Palmer et al. 2006 Health & Place 12, 203-209

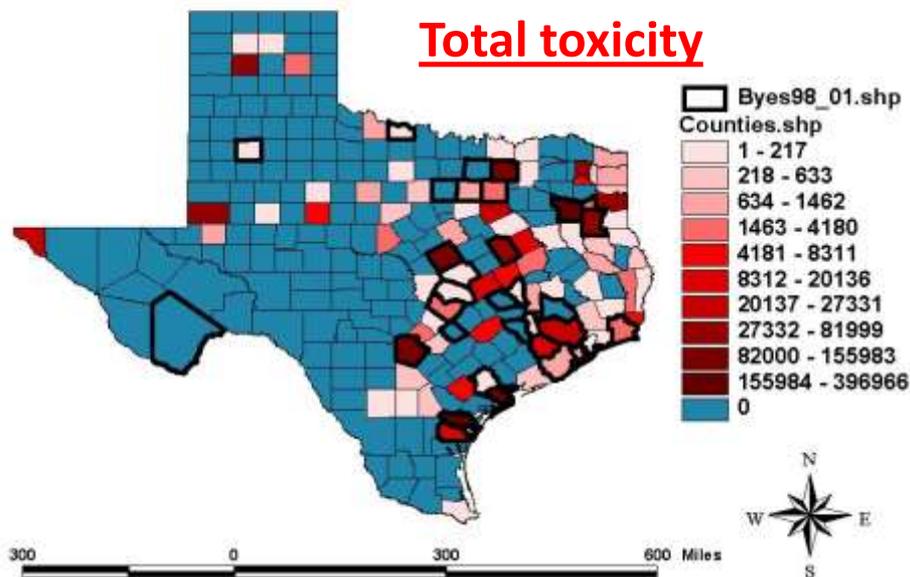
All Reporting Facilities, All Chemicals TRI-(1987-2002)
 Map shows 3,683 of 48,205 facilities reporting nationwide

**Chemicals-TRI
 (Toxic Release Inventory)**



Draft (21204) Levels of Total Toxicity by County for 2001
 with Top Two Deciles of Bayesian Autism Rates (98 - 01)
 Texas

Total toxicity



The Role of Environmental Exposure- The Foods We Eat

- AAP Grand Rounds 2008; 19;17
 - <http://aapgrandrounds.aappublications.org/cgi/content/full/19/17>
- “... the overall findings of the study are clear and require that even we skeptics, who have long doubted parental claims of the effects of various foods on the behavior of their children, admit we might have been wrong.”



Environmental Exposure- Remove and Avoid Toxicities

www.cpsc.gov www.atsdr.cdc.gov

- Eliminate toxins in food, water, environment
- Filter water, use air purifier/ionizer
- Avoid
 - Plastics/phthalates (#3,6,7)
 - Pesticides, chemicals
 - Flame retardants
 - Lead painted toys, jewelry
 - Mercury containing fish, amalgams, vaccines, factories, crematoriums
 - Acetaminophen (Schultz et al, *Autism*, 2008)



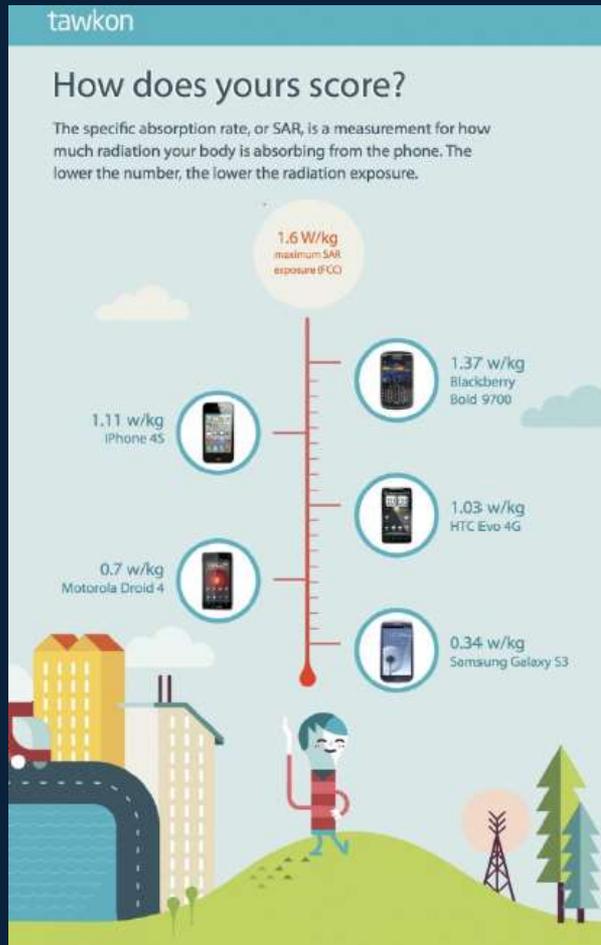
Avoiding Environmental Exposures

- Prevention
 - Creative a healthy foundation through diet, nutrition
 - MVI/EFA/Probiotic/Diet
 - Avoid dietary and environmental triggers
 - Websites
 - www.thegreenguide.com
 - www.cpsc.gov
 - www.leadcheck.com
 - www.atsdr.cdc.gov
 - www.ced.org
 - Ensure natural ongoing detoxification
 - Sweat
 - Treat constipation



For your
toolbox

Avoid EMF Exposure



- Use airplane mode
- No laptops on laps
- Choose a lower EMF phone
- Turn routers off in home at night
- Charge phones away from beds and bedrooms

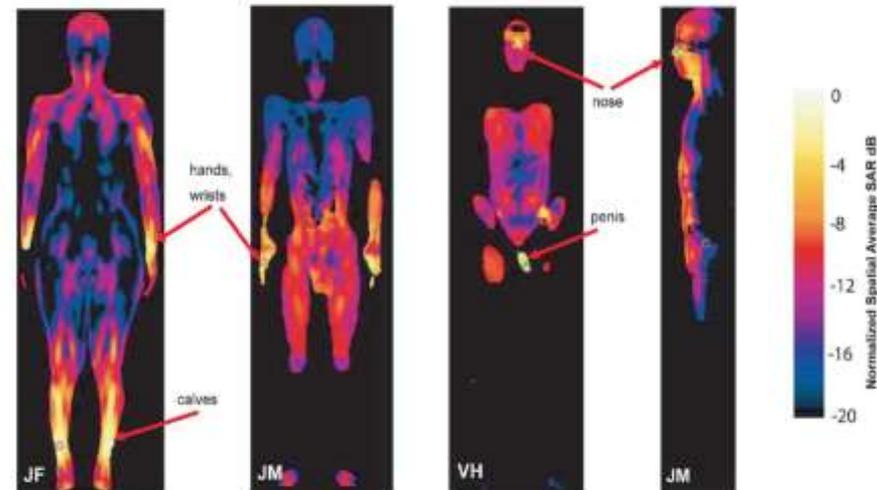
What Does EMF impact?

Fine Print Warnings (iPhone 4)

For optimal mobile device performance and to be sure that human exposure to RF energy does not exceed the FCC, IC, and European Union guidelines, always follow these instructions and precautions: When on a call using the built-in audio receiver in iPhone, hold iPhone with the dock connector pointed down toward your shoulder to increase separation from the antenna. When using iPhone near your body for voice calls or for wireless data transmission over a cellular network, keep iPhone at least 15 mm (5/8 inch) away from the body, and only use carrying cases, belt clips, or holders that do not have metal parts and that maintain at least 15 mm (5/8 inch) separation between iPhone and the body.

iPhone's SAR measurement may exceed the FCC exposure guidelines for body-worn operation if positioned less than 15 mm (5/8 inch) from the body (e.g., when carrying iPhone in your pocket).

Penis gets highest exposure



Workplace exposures, Gosselin et al, 2009 IEEE Transact.

New ways of thinking about Autism Spectrum Disorders

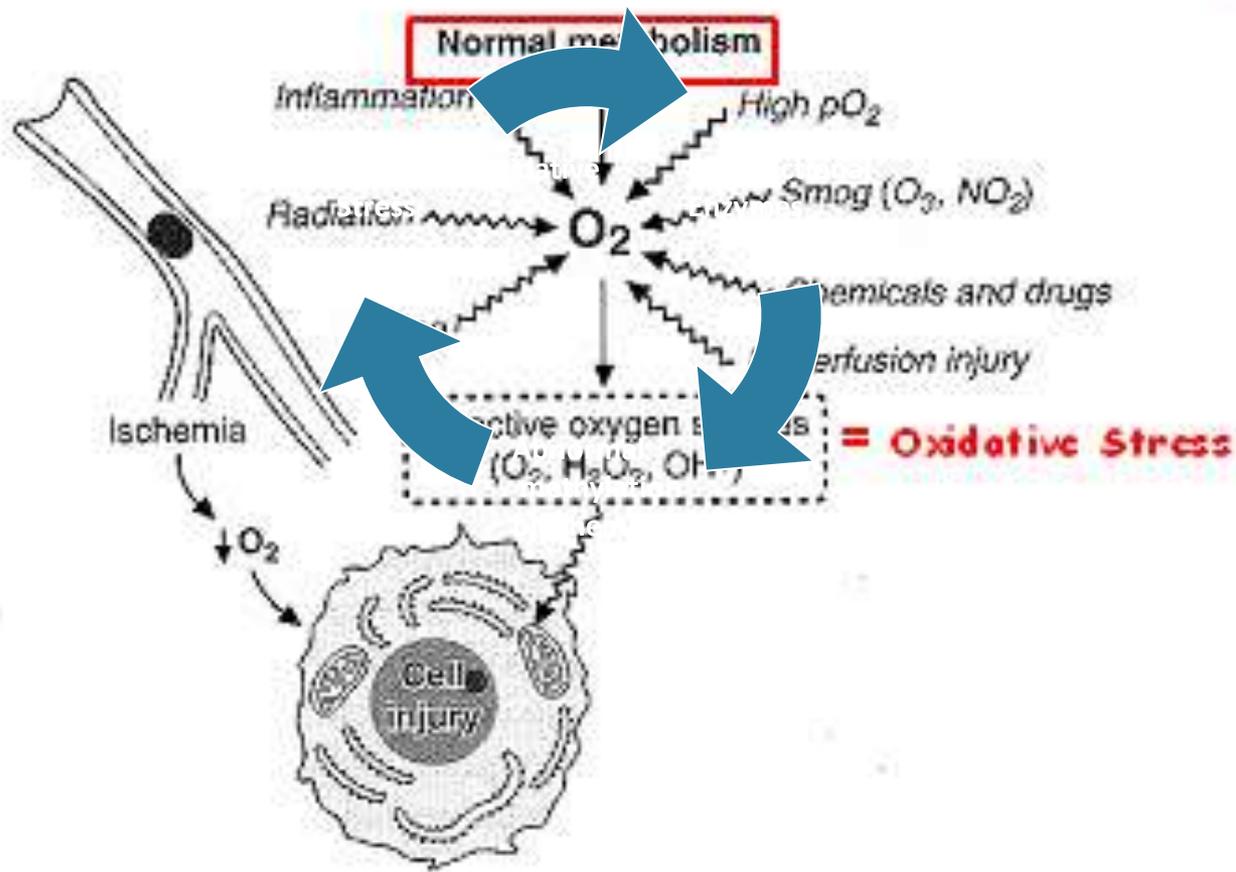
Autism Spectrum Disorders are a collection of **INTERACTING** systems disorders that spin in vicious cycles



Courtesy Liz Mumper

Impaired Detoxification: Mechanisms of Cell Injury

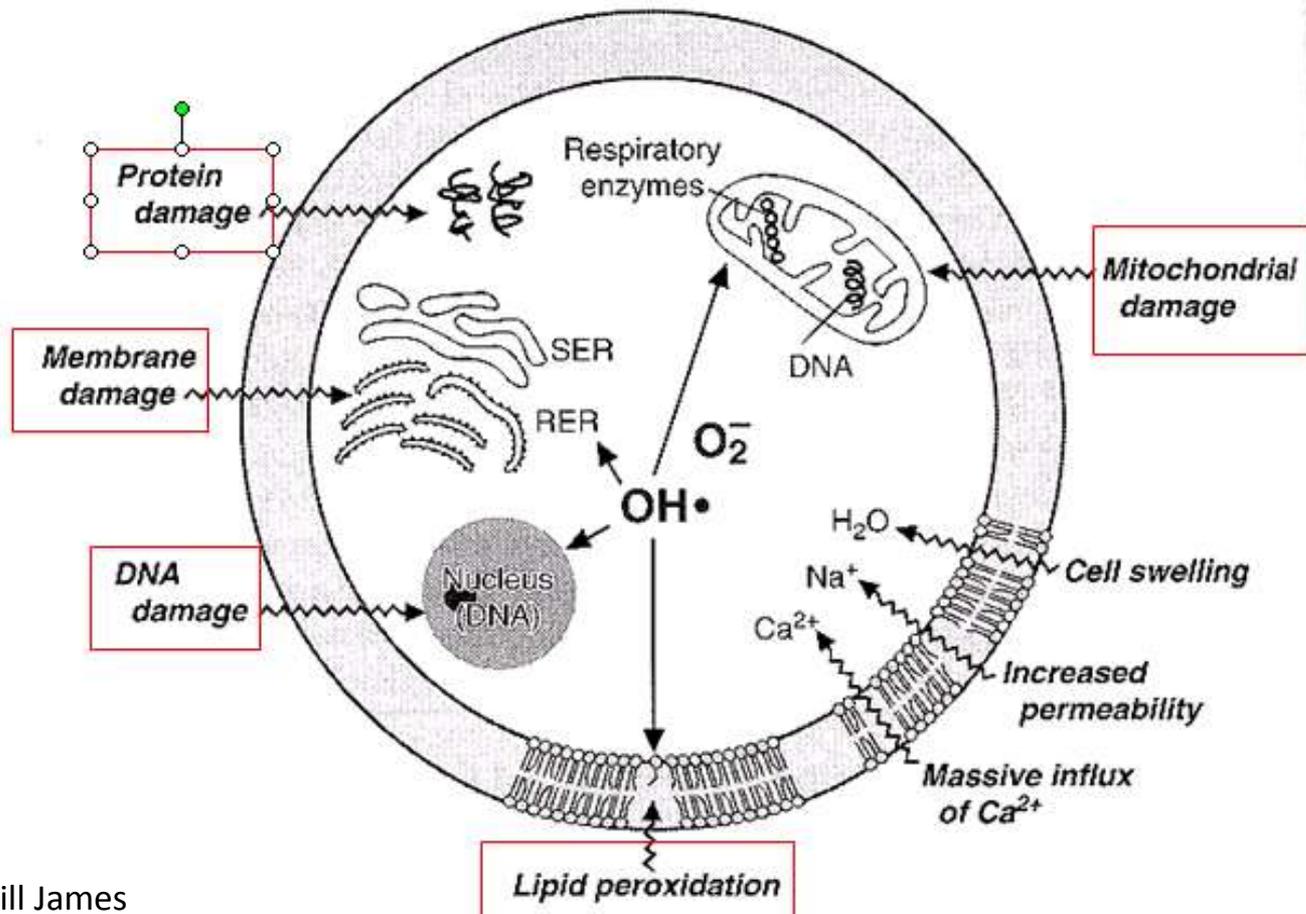
SOURCES OF OXYGEN FREE RADICALS AND CELL INJURY



Courtesy S. Jill James

Impaired Detoxification: Impact on Cell Function

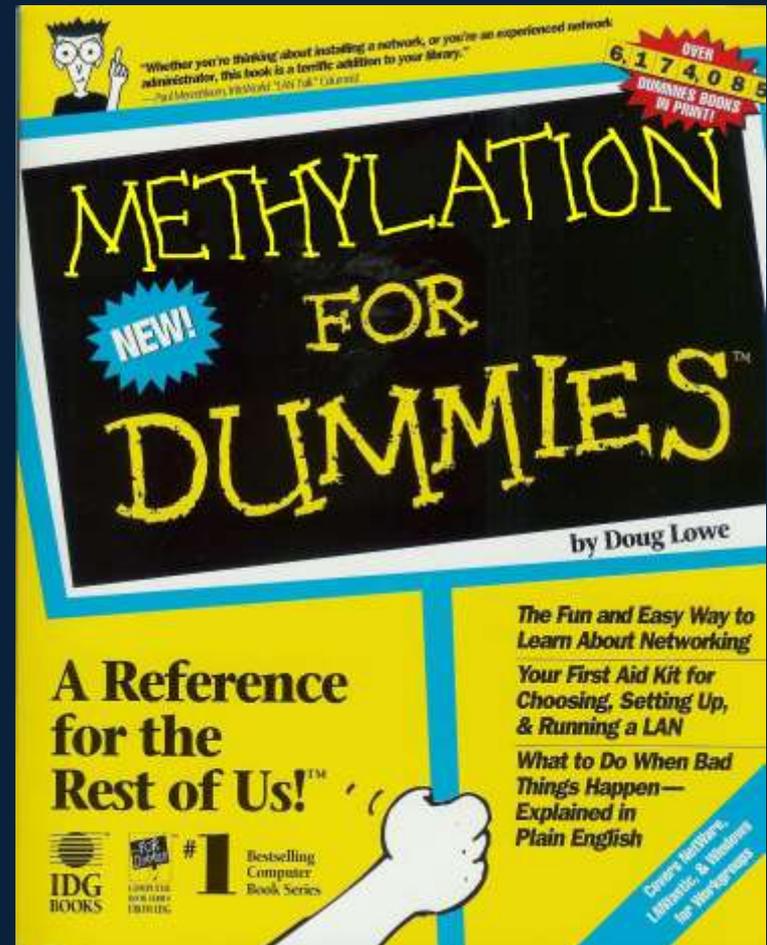
MECHANISMS OF FREE RADICAL-MEDIATED CELLULAR INJURY



Courtesy S. Jill James

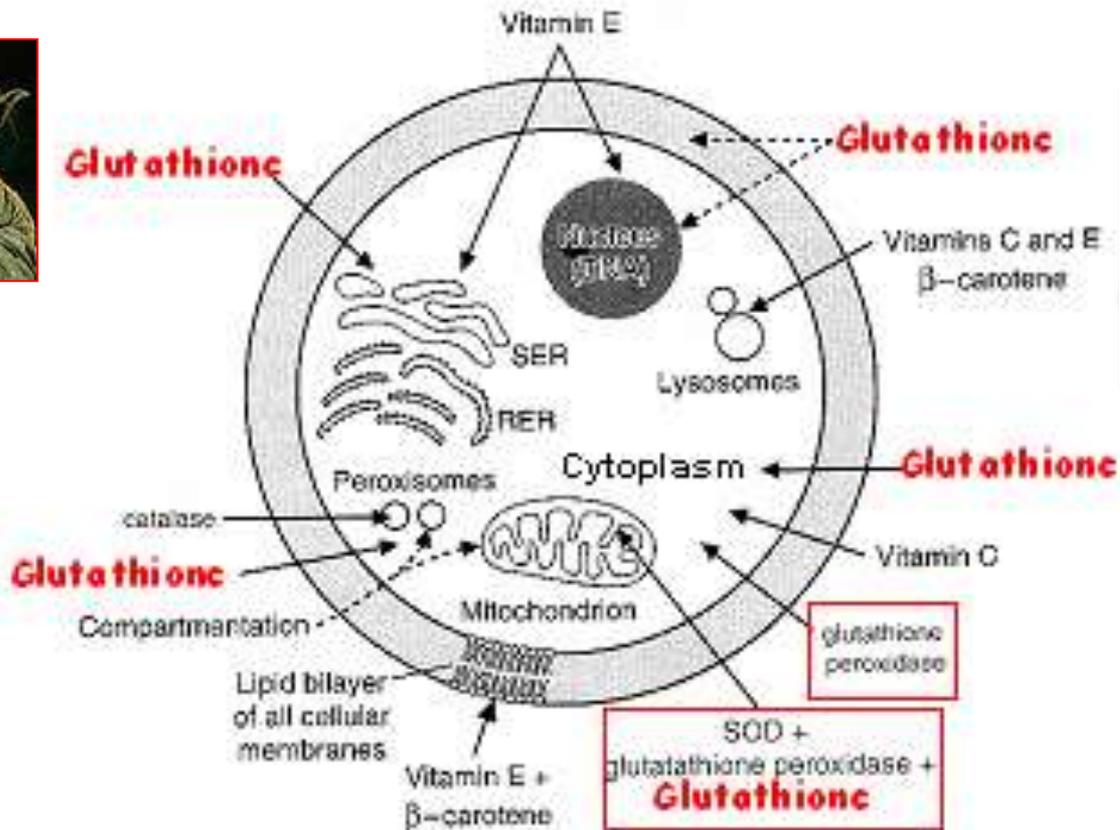
Without adequate methylation

- cannot make normal neurotransmitters
- cannot make creatine (a power currency of the cell)
- cannot control gene expression (epigenetics)
- cannot make cell membranes



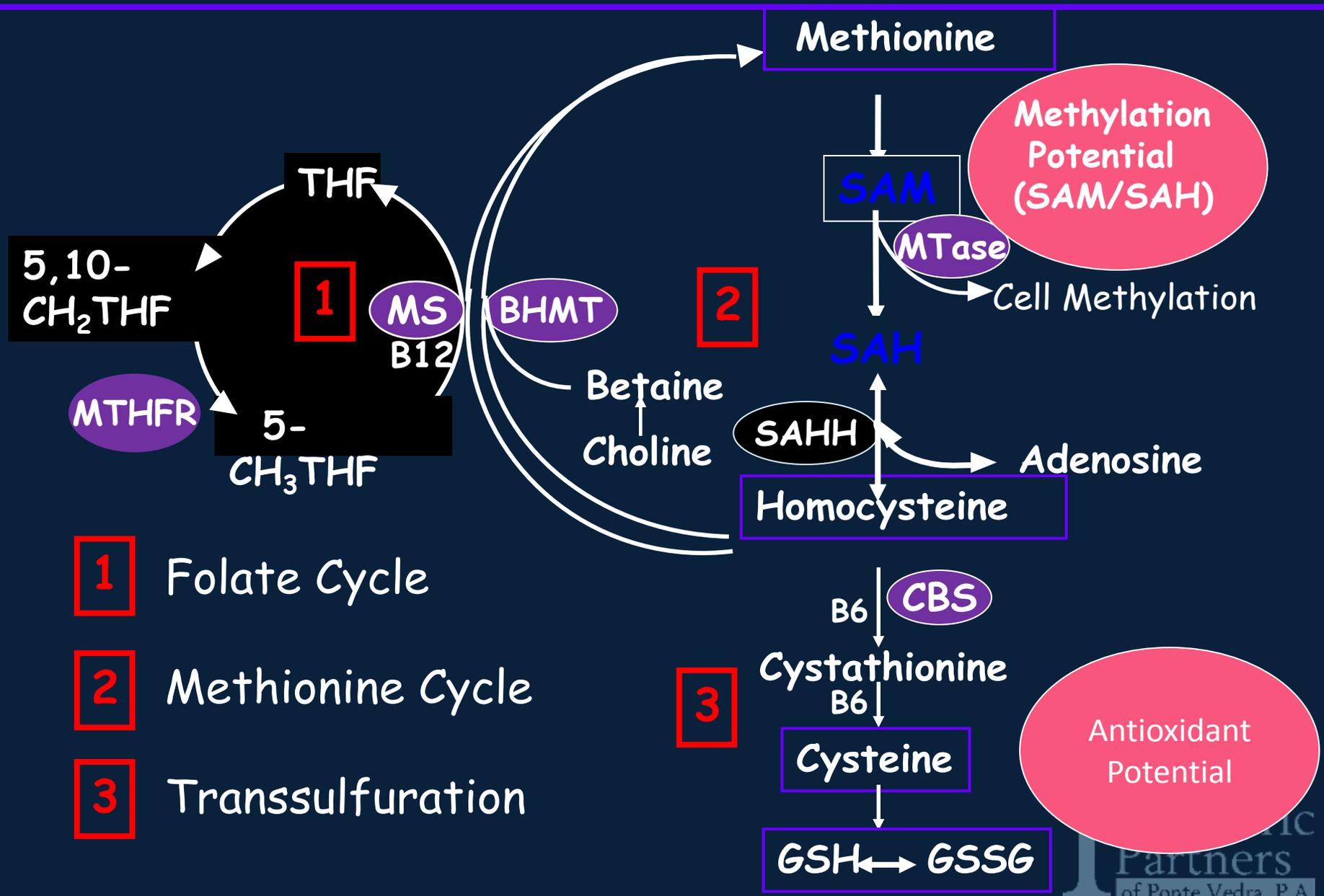
Managing Detoxification: Cellular Defense Mechanisms

FREE RADICAL CELLULAR DEFENSE MECHANISMS



Courtesy S. Jill James

Methionine Transsulfuration to Cysteine and Glutathione



- 1** Folate Cycle
- 2** Methionine Cycle
- 3** Transsulfuration

Methyl

Methyl Turns Genes on and off



Genes Methyl Affects



- Glutathione Reductase-*Redox Status*
- Insulin-like Growth Factor 2- *Development*
- Paroxonase 1- *stress response, redox status*
- Tumor Necrosis Factor-*inflammation*

Comparison of methionine cycle and transsulfuration metabolites between autistic children and control children¹

	Control children (n = 33)	Autistic children (n = 20)
Methionine ($\mu\text{mol/L}$)	31.5 \pm 5.7 (23–48)	19.3 \pm 9.7 (15–25) ²
SAM (nmol/L)	96.9 \pm 12 (77–127)	75.8 \pm 16.2 (68–100) ³
SAH (nmol/L)	19.4 \pm 3.4 (16–27)	28.9 \pm 7.2 (14–41) ²
SAM:SAH	5.2 \pm 1.3 (4–8)	2.9 \pm 0.8 (2–4) ²
Adenosine ($\mu\text{mol/L}$)	0.27 \pm 0.1 (0.1–0.4)	0.39 \pm 0.2 (0.17–0.83) ⁴
Homocysteine ($\mu\text{mol/L}$)	6.4 \pm 1.3 (4.3–9.0)	5.8 \pm 1.0 (4.0–5.8) ³
Cystathionine ($\mu\text{mol/L}$)	0.17 \pm 0.05 (0.1–0.27)	0.14 \pm 0.06 (0.04–0.2) ⁵
Cysteine ($\mu\text{mol/L}$)	202 \pm 17 (172–252)	163 \pm 15 (133–189) ²
tGSH ($\mu\text{mol/L}$)	7.6 \pm 1.4 (3.8–9.2)	4.1 \pm 0.5 (3.3–5.2) ²
Oxidized glutathione (nmol/L)	0.32 \pm 0.1 (0.11–0.43)	0.55 \pm 0.2 (0.29–0.97) ²
tGSH:GSSG	25.5 \pm 8.9 (13–49)	8.6 \pm 3.5 (4–11) ²

¹ All values are $\bar{x} \pm \text{SD}$; range in parentheses. SAM, S-adenosylmethionine; SAH, S-adenosylhomocysteine; tGSH, total glutathione; GSSG, oxidized glutathione.

^{2–5}Significantly different from control children: ² $P < 0.001$, ³ $P < 0.01$, ⁴ $P < 0.05$, ⁵ $P < 0.002$.

James SJ 2004. Am J Clin Nutr. 80,1611–17.

Healing Our Autistic Children- Managing Oxidative Stress

Efficacy of methylcobalamin and folic acid treatment on glutathione redox status in children with autism

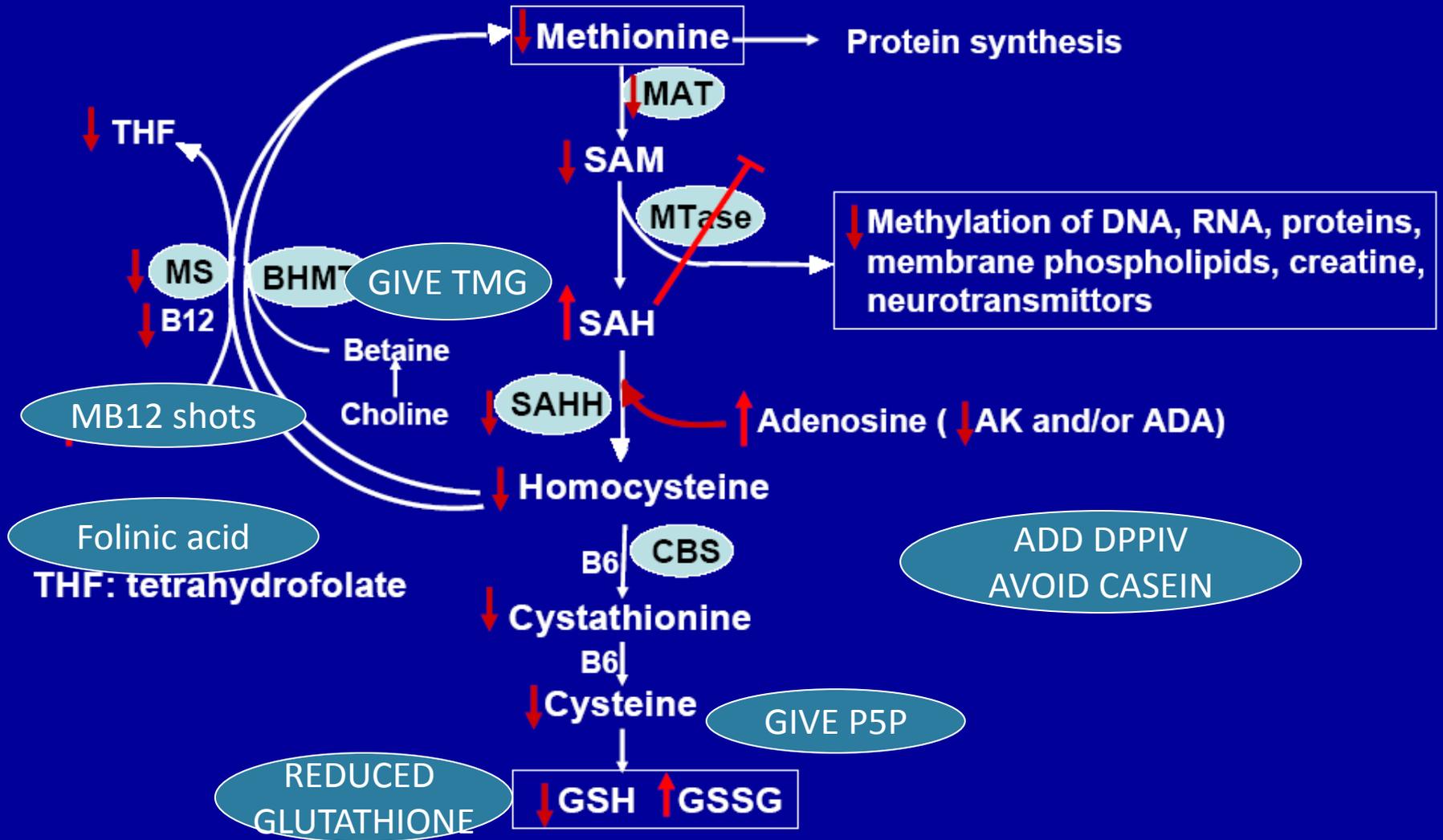
S Jill James et. al. Am J Clin Nutr 2009;89:1-6.

	Autism Pre Tx	Autism Post Tx	ASD Post Tx	p value
Total GSH	7.5 ± 1.8	5.4 ± 1.3	6.2 ± 1.2	0.001
Free GSH	2.8 ± 0.8	1.5 ± 0.4	1.8 ± 0.4	0.008
GSSG	0.13 ± 0.07	0.28 ± 0.08	0.22 ± 0.06	0.001
Total GSH/GSSG	47 ± 18	21 ± 6	30 ± 9	0.001
Free GSH/GSSG	17 ± 6	5 ± 2	8 ± 2	0.001
GM-Cys	11 ± 3	10 ± 2	10 ± 2	ns
Cys-Gly	11 ± 3	10 ± 2	10 ± 2	ns
Cysteine	210 ± 18	191 ± 24	215 ± 19	0.001
Homocys	5.0 ± 1.2	4.8 ± 1.8	5.3 ± 1.1	0.04
Methionine	24 ± 3	21 ± 4	22 ± 3	ns

The 3-mo intervention resulted in significant increases in cysteine, cysteinylglycine, and glutathione concentrations.

Conclusions: The significant improvements observed in transmethylation metabolites 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.

Effect of Oxidative Stress on Methionine Transsulfuration



MB12 Injections

- Insulin syringes- 31 gauge
- 30 degree angle in buttocks fat
 - Allows for slower release than arm or thigh fat
- Dose 65-75 mcg/kg q 3 days
 - Some patients have a diminishing effect towards third day and may benefit from qod or qd dosing
- Concentration 25 mg/ml MB12
 - We do not recommend the stock solution of 12.5 mg/ml

Web Resources for MB12

- <http://www.drneubrandner.com/Files/Methyl-B12;%20Myth,%20Masterpiece,%20or%20Miracle.pdf>
- <http://www.drneubrandner.com/pageVid.html>
– Videos
- Lee Silsby Compounding- Cleveland, OH
- Well Health Pharmacy- Jacksonville, FL
- Hopewell Pharmacy- Hopewell, NJ

Value of Activated Forms of Folate

- Folic acid has to be broken down to active form for utilization by tissues
- Wang, X and Fenech, M. A comparison of folic acid and 5-methyltetrahydrofolate for prevention of DNA damage and cell death in human lymphocytes *in vitro*. Oxford Journals, Life Sciences and Medicine Mutagenesis 18:1; 81-86.

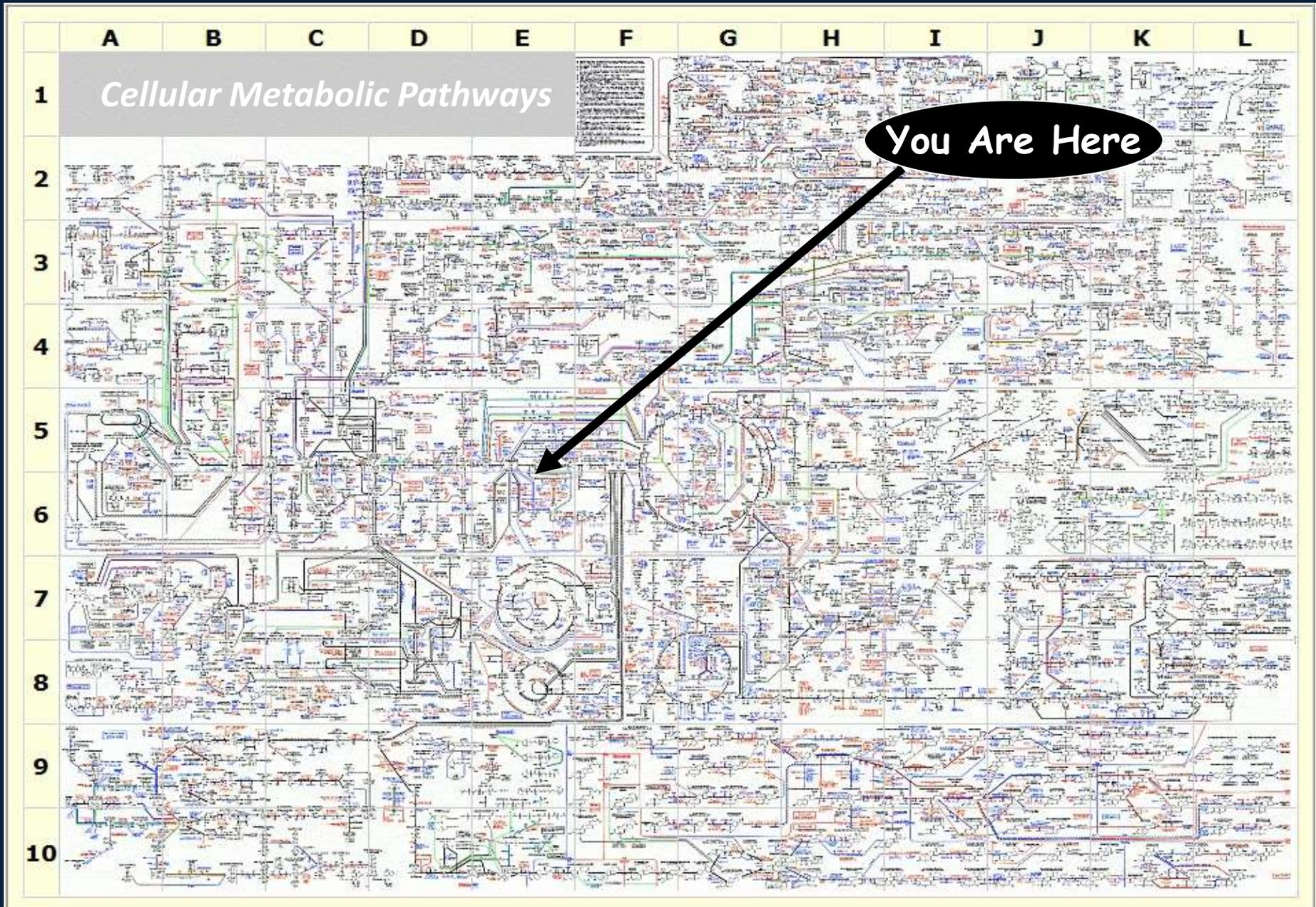


For your
toolbox

Supporting Folate Pathways

- Folinic acid
 - 5 formyl tetrahydrofolate – form found in foods
- 5 methyl tetrahydrofolate- (L methylfolate)- Deplin
 - Metabolically active form utilized by tissues
 - 40% of population has trouble activating folate (MTHFR SNP)
 - 90-99% of our ASD population has MTHFR SNP
- Cerefolin NAC
 - L methylfolate/B12/NAC
 - Reduces oxidative stress
 - Improves cognitive function
 - Off label use to lower homocysteine

Putting it all into Perspective...



Restoring Balance

- Interventions have far reaching effects
 - Rather than one substance having one effect, one substance has a 360° effect
 - Beware the law of unforeseen consequences
- All about restoring balance and letting nature's pathways operate the way they were intended

Health- a Vital Reserve

Sick



Well



Health- a Vital Reserve

Sick

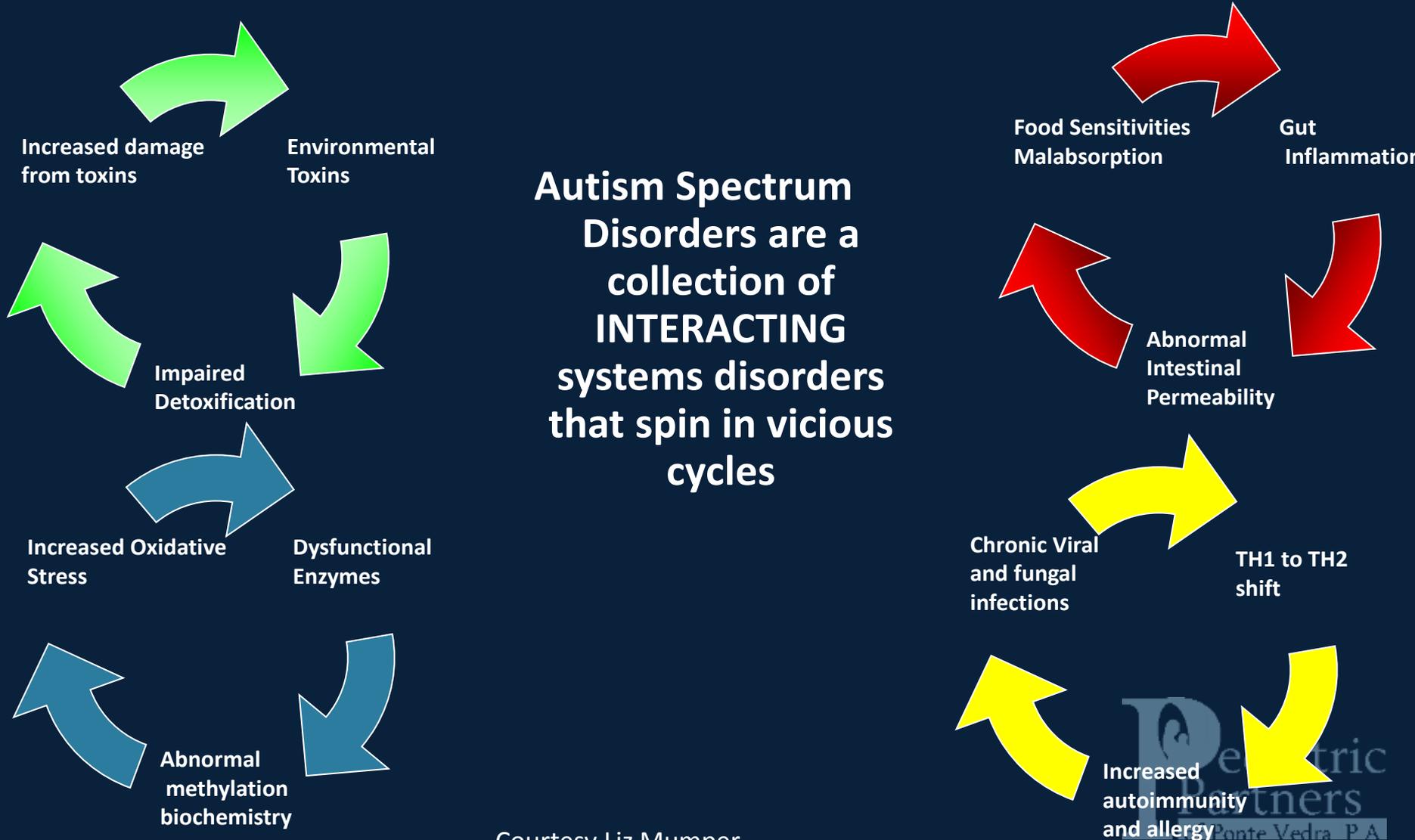


Well



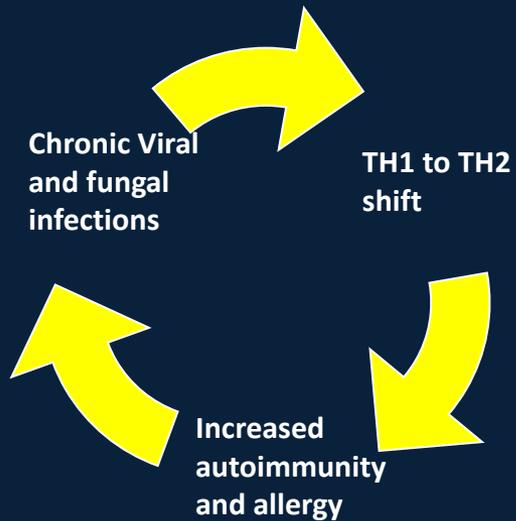
New ways of thinking about Autism Spectrum Disorders

Autism Spectrum Disorders are a collection of **INTERACTING** systems disorders that spin in vicious cycles



Courtesy Liz Mumper

Vicious Cycle of Immune Dysregulation



Vicious Cycle of Immune Dysregulation

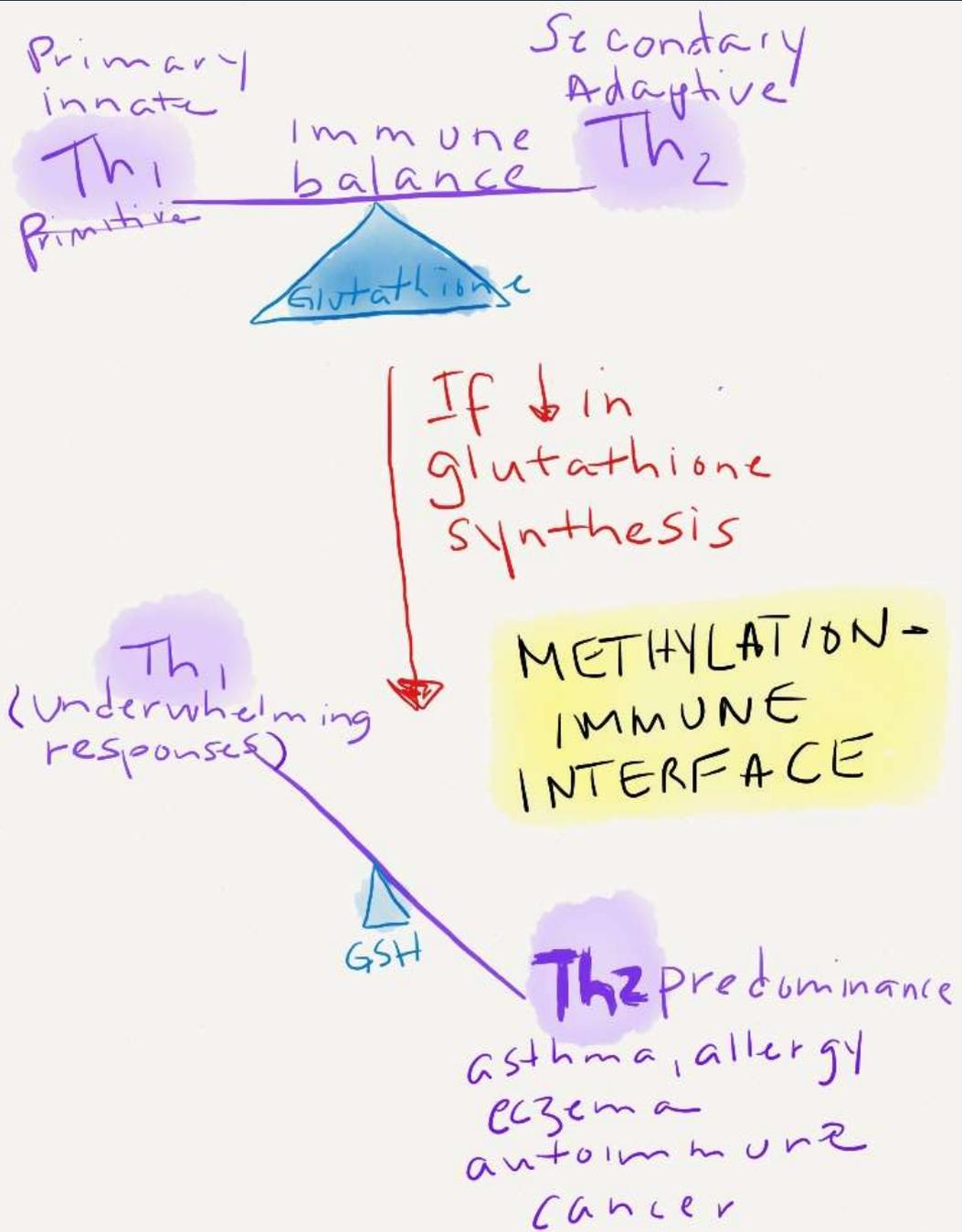
Clinical Clues

- Allergic shiners
- Asthma
- Eczema/atopy
- Fungal skin infections
- Chronic fungal and parasitic infections
- Oral thrush
- Molluscum contagiosum
- Warts

Physical Evidence

- Increased IgE
- Autoimmunity markers
- Abnormal NK cell function
- IgA deficiency
- Low IgG
- Lymphopenia
- T-cell abnormalities
- Increased TNF-alpha
- “itis” - gut, brain, skin
- PANDAS

Methylation Immunologic Interface

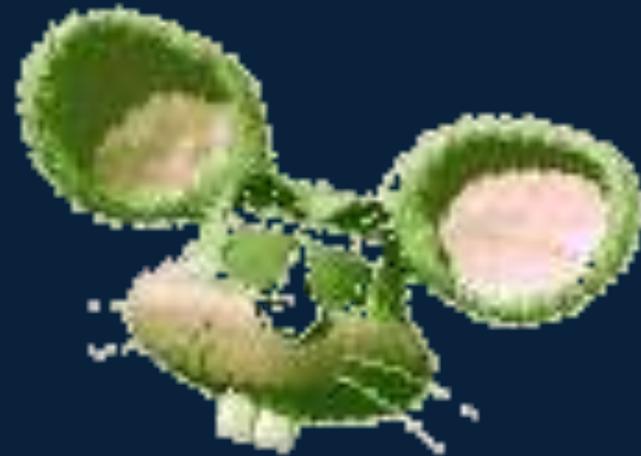


Vicious Cycle of Immune Dysregulation Response to Leishmaniasis Major

Genetically restricted
 T_H1 response



Genetically restricted
 T_H2 response



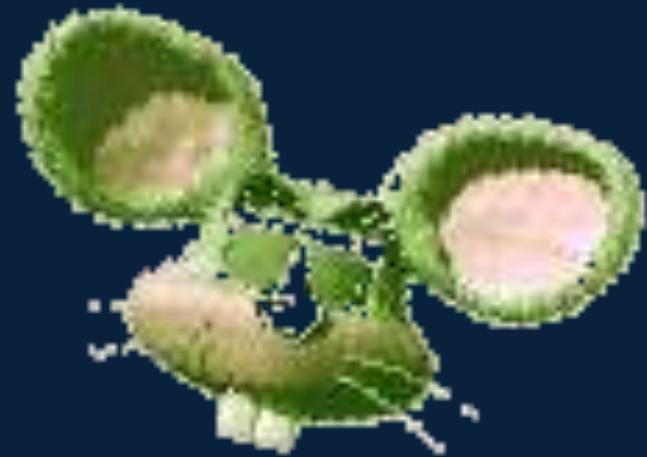
Courtesy Andy
Wakefield

Bagenstose LM., et al . Mercury enhances susceptibility to murine
Leishmaniasis. Parasite Immunology 2001;23:633-640

Vicious Cycle of Immune Dysregulation Response to Leishmaniasis Major



Resistant mouse given
sub-toxic doses of
mercuric chloride



Previously resistant mouse
exposed to L. major

Autoimmunity, IL-4 production, IgG1 and IgE

Non healing and parasite persistence

Courtesy Andy
Wakefield

Vicious Cycle of Immune Dysregulation in Autism

Elevated cytokine levels in children with autism spectrum disorder
J Neuroimmunol. 172:198-205, March 2006

Cynthia A. Molloy^{a,b,d,*}, Ardythe L. Morrow^{a,d}, Jareen Meinzen-Derr^a, Kathleen Schleifer^c,
Krista Dienger^c, Patricia Manning-Courtney^{b,d}, Mekibib Altaye^{a,d}, Marsha Wills-Karp^{c,d}

^a Center for Epidemiology and Biostatistics, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, MLC 5041, Cincinnati, OH 45229-3039, United States

^b Division of Developmental and Behavioral Pediatrics, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, MLC 4002, Cincinnati, OH 45229-3039, United States

^c Division of Immunobiology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, MLC 7038, Cincinnati, OH 45229-3039, United States

^d Department of Pediatrics, University of Cincinnati College of Medicine, United States

Vicious Cycle of Immune Dysregulation in Autism

Imani, F., Kehoe, K. 2001. **Infection of Human B Lymphocytes with MMR Vaccine Induces IgE Class Switching.** *Clinical Immunology*, 100(3), 355-361.

Our data suggest that a potential side effect of vaccination with live attenuated viruses may be an increase in the expression of IgE.

Vicious Cycle of Immune Dysregulation in Autism

TESTING PERFORMED AT ASSOCIATED REGIONAL UNIVERSITY PATHOLOGISTS, INC
500 CHIPETA WAY SALT LAKE CITY, UTAH 84108
CAP NO. 40963-01 CLIA NO. 46D0523979

IMMUNOGLOBULIN E (IGE)	959.8	IU/ML	<150
IMMUNOGLOBULIN PROFILE			
IMMUNOGLOBULIN A (IGA)	197	MG/DL	69-382
IMMUNOGLOBULIN G (IGG)	1053	MG/DL	723-1685

UNLESS OTHERWISE INDICATED, ALL TESTING PERFORMED AT
CLINICAL PATHOLOGY LABORATORIES, INC. 9200 WALL ST AUSTIN, TX 78754
CLIA NUMBER 45D0505003 CAP ACCREDITATION NO. 21525-01

Vicious Cycle of Immune Dysregulation in Autism



Uncoupling of ATP-mediated Calcium Signaling and Dysregulated IL-6 Secretion in Dendritic Cells by Nanomolar Thimerosal

Samuel R. Goth, Ruth A. Chu, Jeffrey P. Gregg,
Gennady Cherednichenko, and Isaac N. Pessah

doi:10.1289/ehp.8881 (available at <http://dx.doi.org/>)
Online 21 March 2006

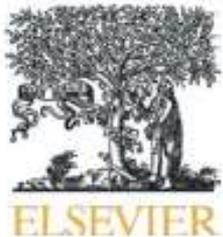
Vicious Cycle of Immune Dysregulation in Autism

Thimerosal induces TH2 responses via influencing cytokine secretion by human dendritic cells

Anshu Agrawal,¹ Poonam Kaushal, Sudhanshu Agrawal, Sastry Gollapudi, and Sudhir Gupta
Division of Basic and Clinical Immunology, University of California, Irvine, California, USA

Journal of Leukocyte Biology 2007;81:474-482

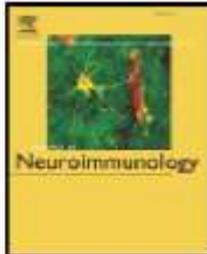
Vicious Cycle of Immune Dysregulation in Autism



Contents lists available at ScienceDirect

Journal of Neuroimmunology

journal homepage: www.elsevier.com/locate/jneuroim



Low natural killer cell cytotoxic activity in autism: The role of glutathione, IL-2 and IL-15

Aristo Vojdani ^{a,*}, Elizabeth Mumper ^b, Doreen Granpeesheh ^c, Lynne Mielke ^d, David Traver ^e, Kenneth Bock ^f, Karima Hirani ^g, James Neubrandner ^h, Kurt N. Woeller ⁱ, Nancy O'Hara ^j, Anju Usman ^k, Cindy Schneider ^l, Frank Hebroni ^a, Joshua Berookhim ^a, Jaquelyn McCandless ^m

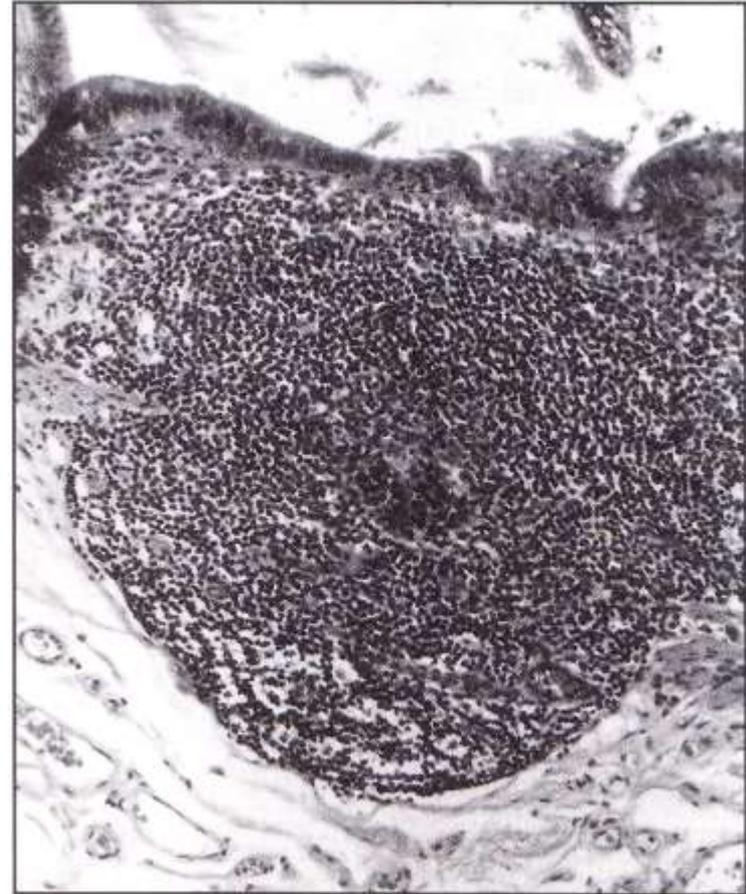
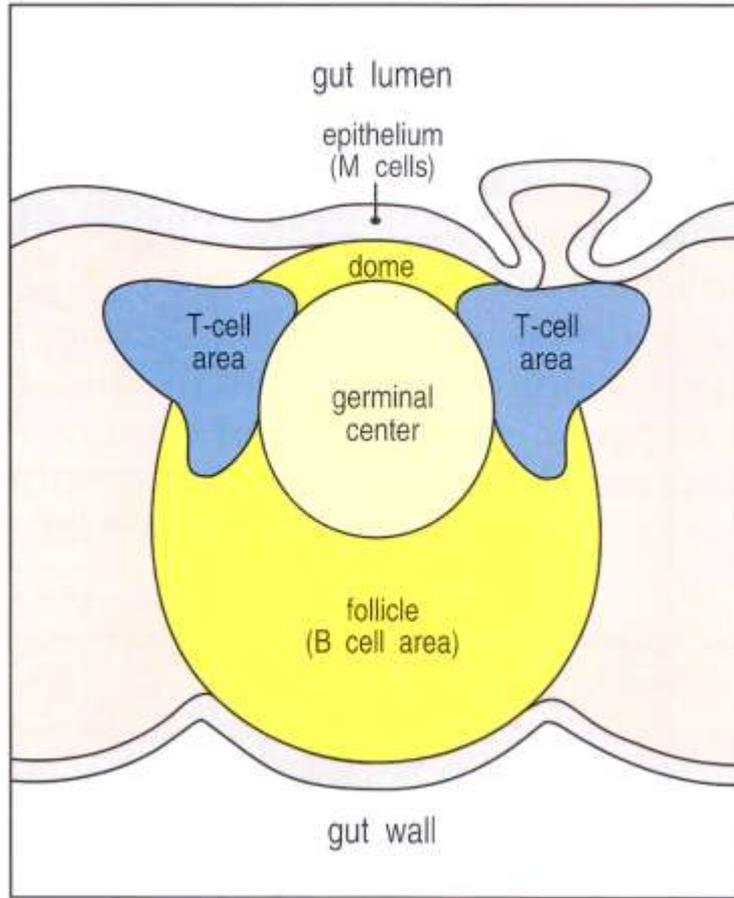


For your
toolbox

Immune Regulation

- Probiotics- Dairy Free! Strep Free!
- Flossing teeth!
- Curcumin- preferably with bioperine
- Larchwood extract- Arabinex
- Quercitin
- Beta-glucans- Immunotix
- Low dose Naltrexone
www.lowdosenaltrexone.org
- PPARS modulation- Isoprinosine, CBD

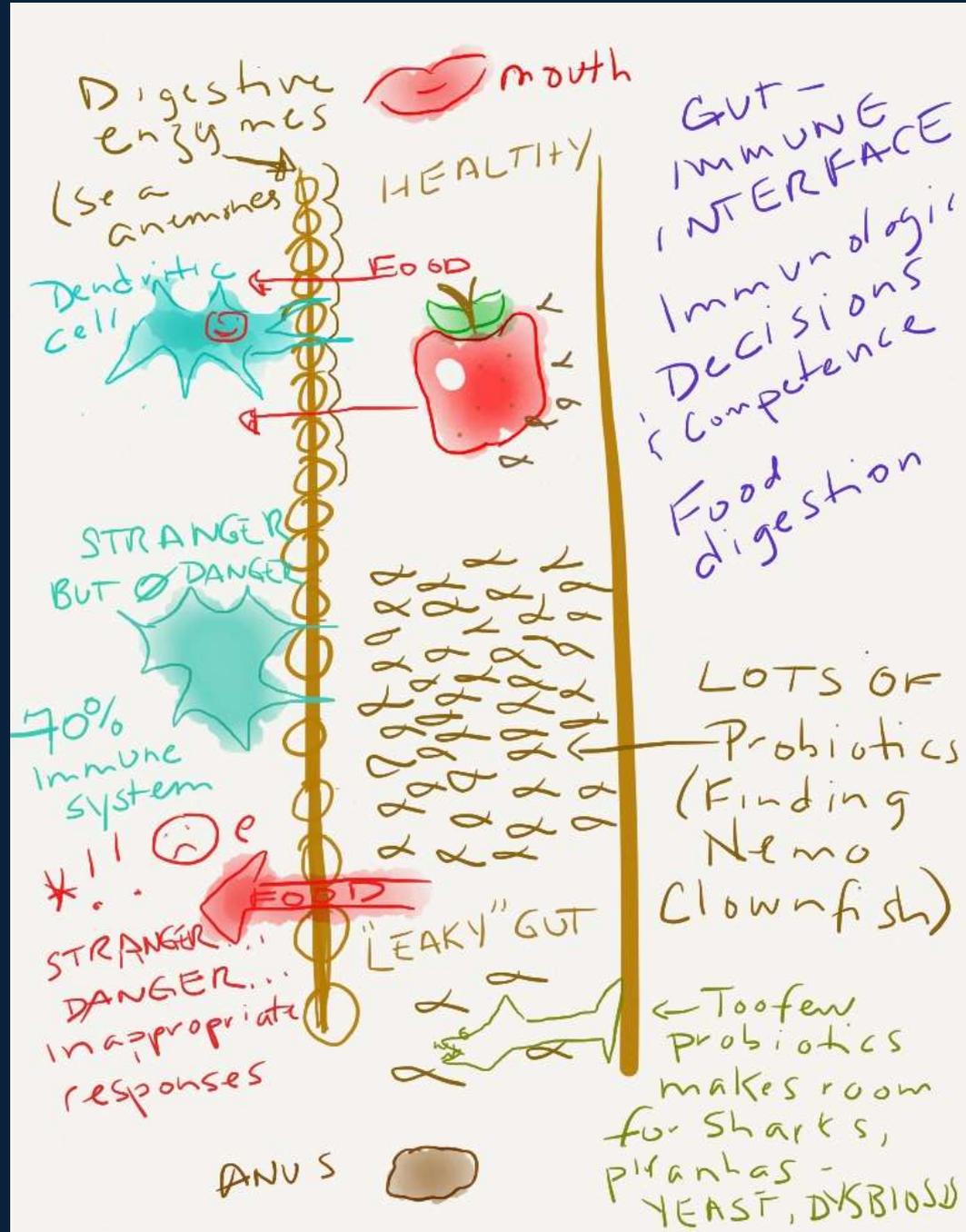
Vicious Cycles Intersecting- 70% of the Immune System is in the Gut



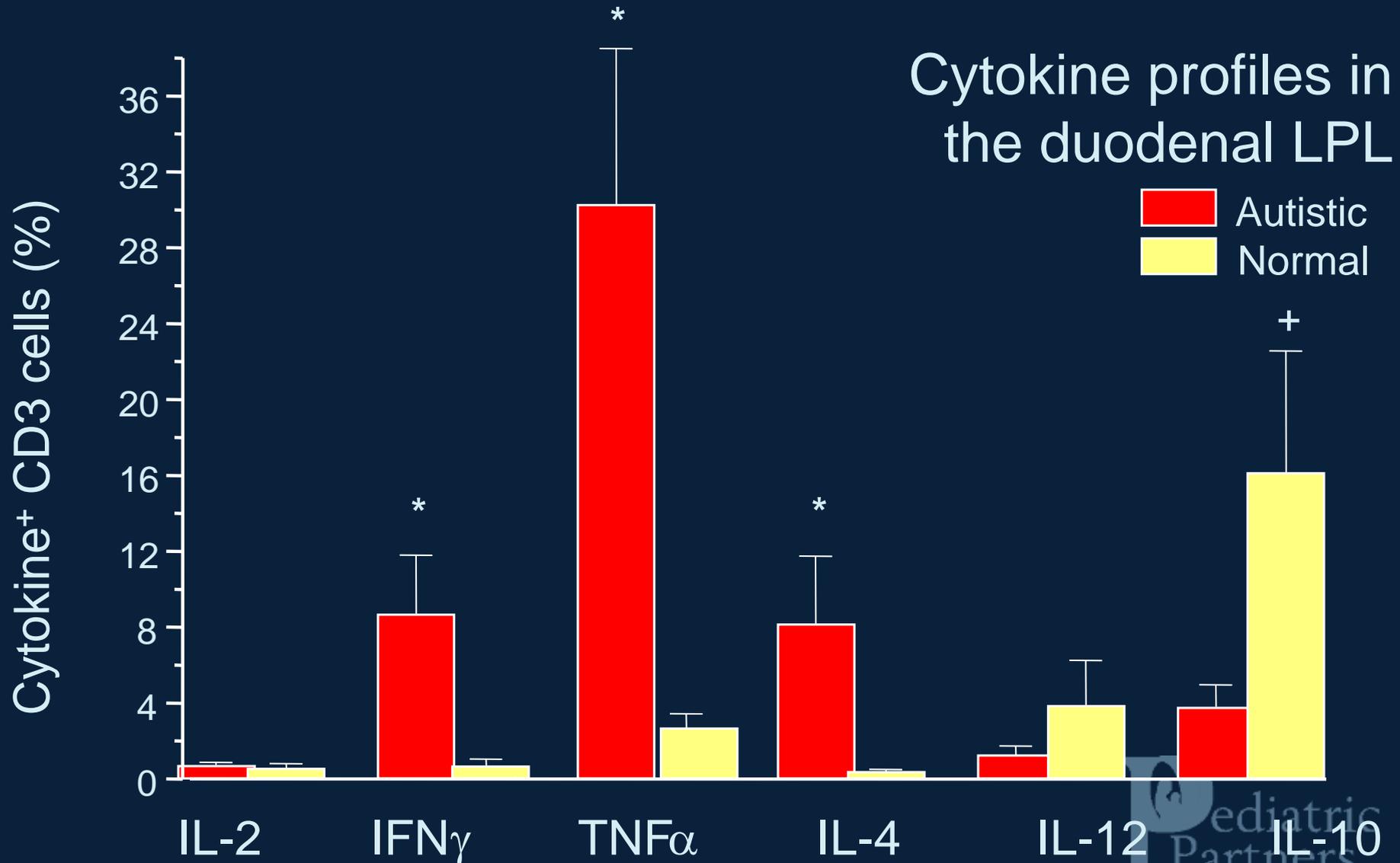
Gut-Immune Interface



70% of Immune System is "in" the gut



Immune Dysregulation in the ASD Bowel



Gut Problems in ASD

- Buie, T et al “Children with autism spectrum disorders can benefit from adaptation of general pediatric guidelines for the diagnostic evaluation of abdominal pain, chronic constipation, and gastroesophageal reflux disease. “

Buie T et al, *Pediatrics* vol 125 Suppl January, 2010 S19-S29

Vicious Cycles- Gut Disorders in Autism- It's Not Just A Poop Issue!

Historical clues:

- Difficulty breastfeeding
- Persistent Colic
- Gastro-esophageal reflux
- Infantile eczema
- Food sensitivities
- Failure to thrive
- Frequent antibiotics (abnormal flora)
- Abnormal posturing
- Self injurious behavior
- Poor sleep
- Insatiable appetite

Food Sensitivities
Malabsorption

Gut
Inflammation

Abnormal
Intestinal
Permeability

Physical/Lab clues:

- Abnormal stools
- Abdominal pain
- Lymphonodular hyperplasia of ileum
- Esophagitis
- Gastritis
- Distended abdomen

Clues for Specific Bowel Problems

Historical and Physical Exam Clues for Dysbiosis

- Parasites
 - Anal itching and probing
 - Picking, biting, licking, grinding
- Yeast
 - Rash/peeling feet/ridged, discolored nails
 - Inflamed cheeks/red anus
 - Ring worm/tinea corporis or capitis

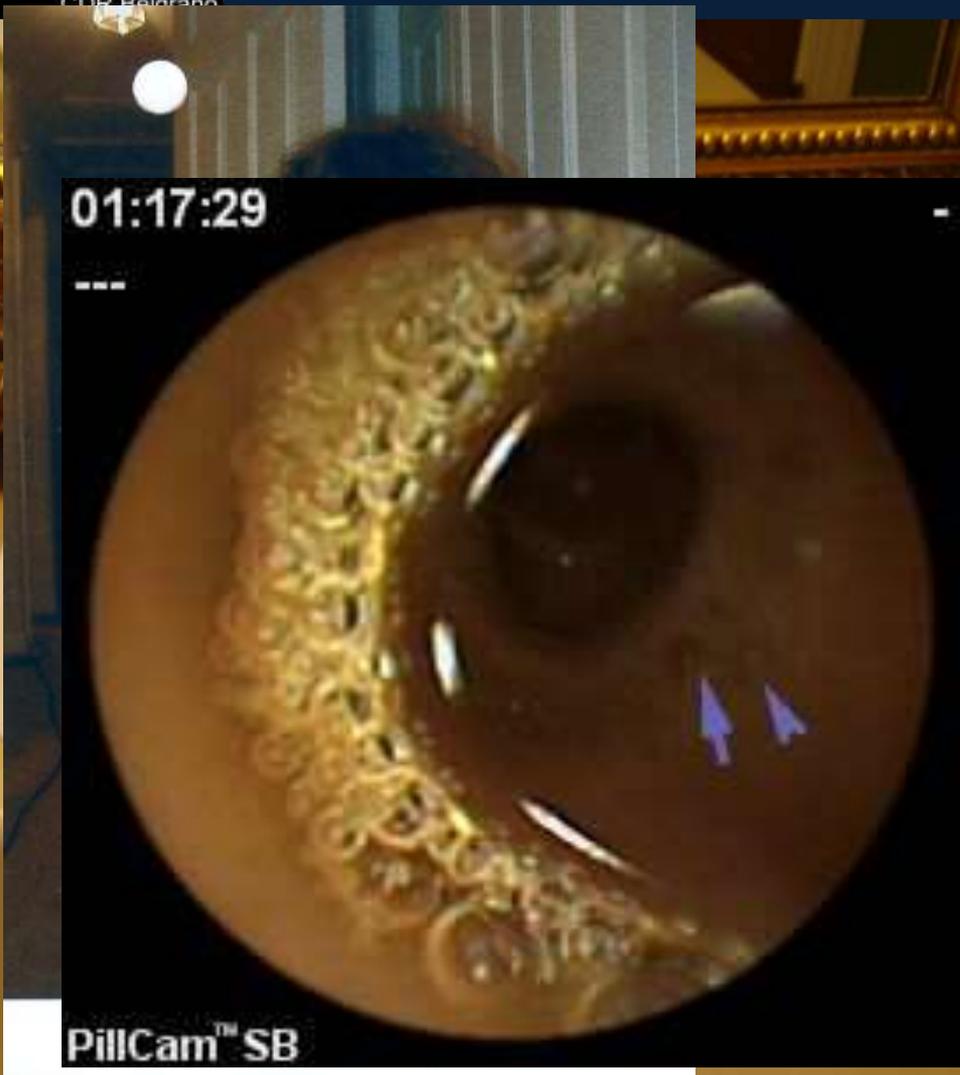
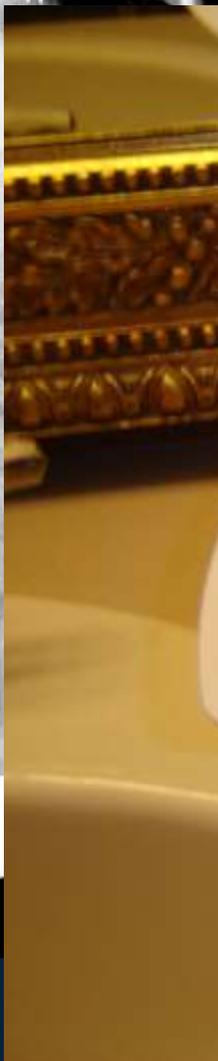
Signs and Symptoms of Malabsorptive Deficiencies

- Zinc Deficiency
 - Acne/sparse hair/psoriasis
 - White spots/lines on nails
 - Canker sores
- Essential Fatty Acid Deficiency
 - Keratosis pilaris
 - Dry, coarse hair
- Magnesium deficiency
 - Muscle twitches/tingling
 - Sighing
 - Salt craving

Lab Options for Gut Issues

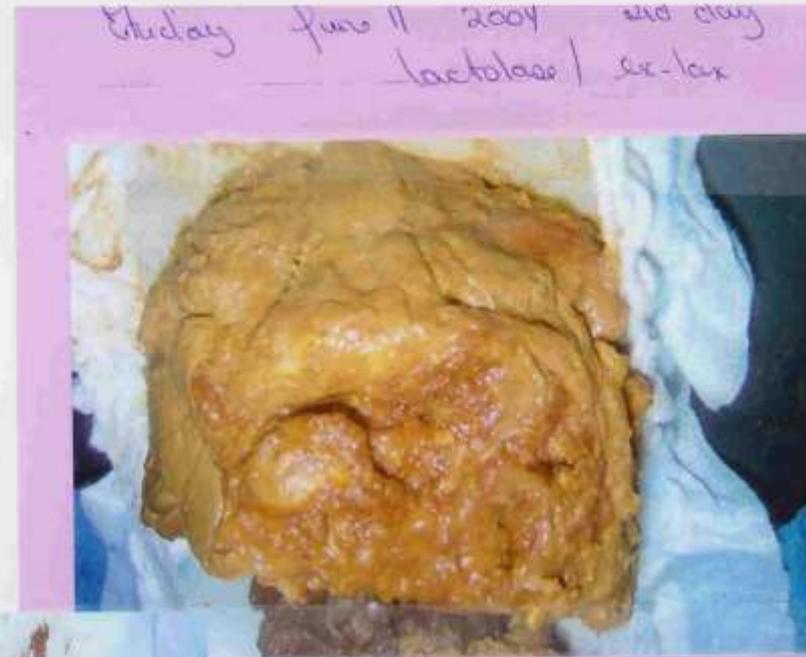
- Urine Organic Acids Test (OATS, MAP)
- Stool Microbiology
- Stool Mycology
- Stool Parasitology
- IgG/IgE Food Panel
- Celiac Panel
- Fecal Fat
- Breath Test for Fructose Malabsorption
- Inflammatory Markers (ESR, CRP, calprotectin,...)
- Ammonia - blood
- IBD Serology (prometheus testing)
- Endoscopy, Colonoscopy if necessary

What Is Wrong With These Children?



Vicious Cycles: Gut Disorders in Autism- Constipation

One bowel movement



Vicious Cycles- Gut Disorders in Autism- Constipation

Normal Belly X-Ray



X-Ray of Constipation in Autism

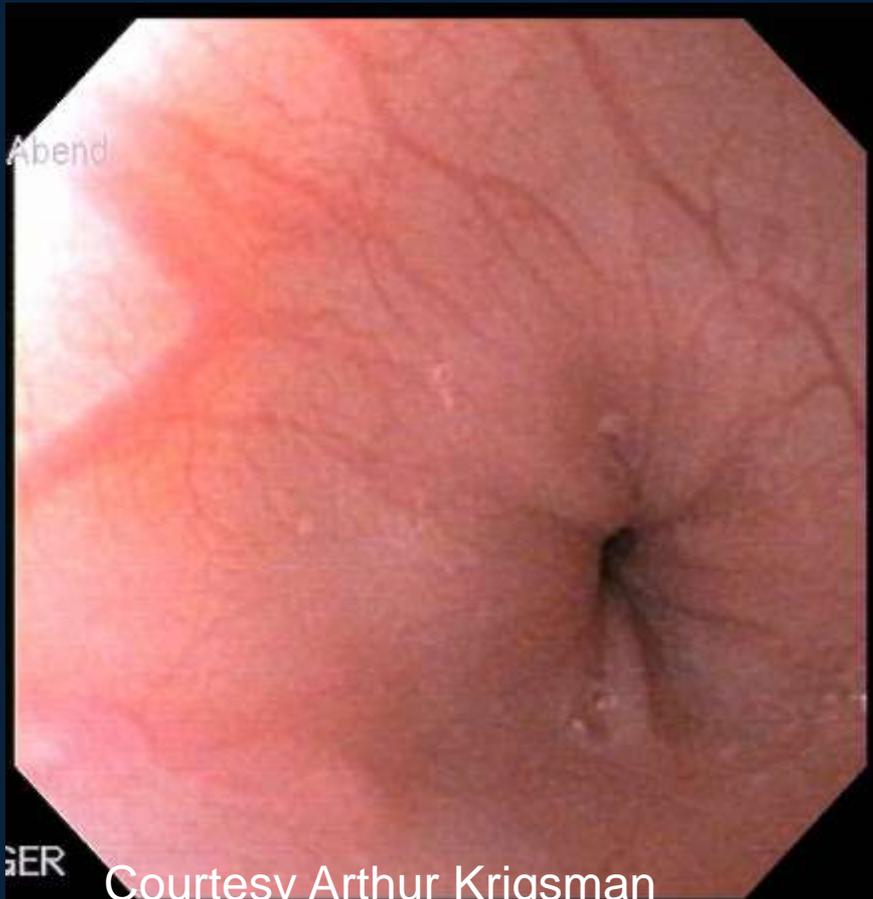


Vicious Cycles- Gut Disorders in Autism- Diarrhea



Vicious Cycles- Gut Disorders in Autism- Reflux

Normal Esophagus



Eosinophilic Esophagitis



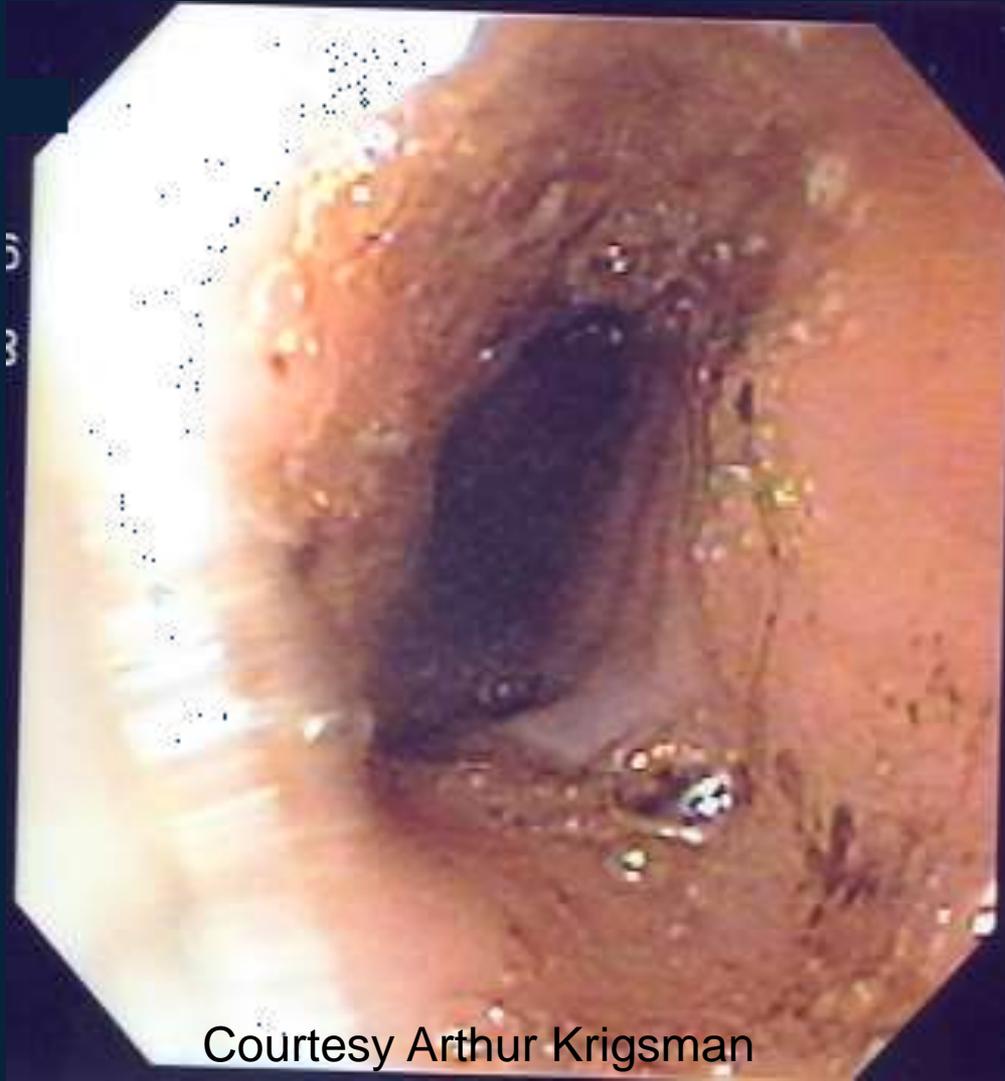
Vicious Cycles- Gut Disorders in Autism- LNH

Normal
Colonoscopy

Lymphonodular
Hyperplasia



Vicious Cycles- Gut Disorders in Autism- Bile Reflux Esophagitis



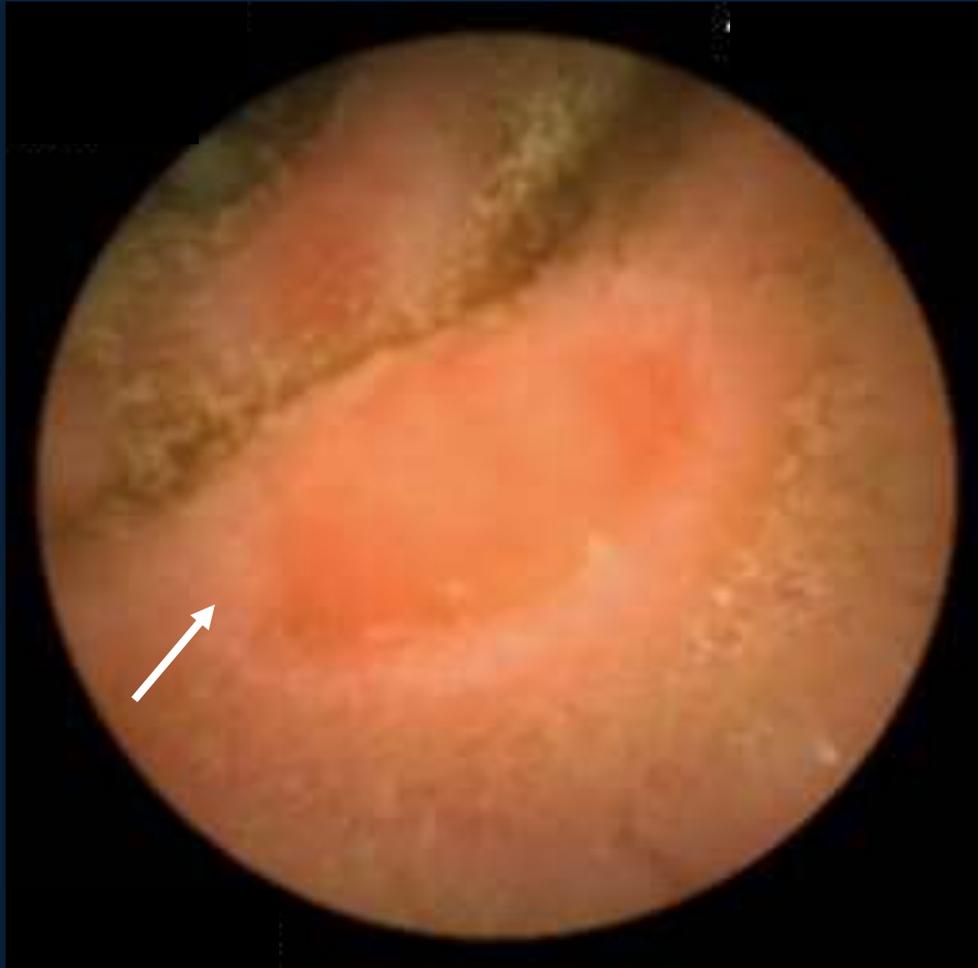
Courtesy Arthur Krigsman

Vicious Cycles- Gut Disorders in Autism- Small Bowel Aphthous Ulcerations



Pill Cam
photos
courtesy
Arthur
Krigsman

Vicious Cycles- Gut Disorders in Autism- Small Bowel *Erosive* Ulcerations (with enteric protein loss)



Pill Cam
photos
courtesy
Arthur
Krigsman

Vicious Cycles- Gut Disorders in Autism- Pain



Photo
courtesy
Arthur
Krigsman

pediatric
partners
Ponte Vedra, P.A.
Partners of Ponte Vedra

Vicious Cycles- Gut Disorders in Autism- Pain



Photo
courtesy
Arthur
Krigsman

Vicious Cycles- Gut Disorders in Autism- Pain



Photo
courtesy
1/25/03 Arthur
Krigsman

Vicious Cycles- Gut Disorders in Autism- Pain



Photo
courtesy
Arthur
Krigsman

diatric
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e Veda, P.A.
rs of Ponte Veda

Vicious Cycles- Gut Disorders in Autism- Pain



after 48 hr hospital admission for abdominal pain.
September, '04 - Age 3

Photo
courtesy
Arthur
Krigsman

Abnormal Bowel Flora- Yeast

- Candida mannans impair host immune response
- Candida overgrowth compromises mucosal integrity
- Candida produce toxic organic acids--- arabinose, citramalic acid, tartaric acid, and Beta ketoglutaric acid
- Toxins affect child's mood and behavior

Abnormal Bowel Flora- Clostridia

- May involve abnormal flora
- Clostridial counts higher than controls
- Oral Vancomycin significantly effective in some
- Autistics had 9 Clostridial species not found in controls

Clostridium—propionic acid can precipitate symptoms of autism (MacFabe, D, *Behav Brain Res.* 2007 Jan 10; 176(1) 149-69

Bowel Flora Disruption in ASD

- “These studies demonstrate significant alterations in the upper and lower intestinal flora of children with late-onset autism and may provide insights into the nature of this disorder.”

Finegold, SM, Molitoris, D, et al (2002) “Gastrointestinal microflora studies in late-onset autism” *Clin Infect Dis* **35** (Suppl 1): S6-S16.

Vicious Cycles- Gut Disorders in Autism

Dysbiosis, Dysbiosis, Parasitosis

Parasitology

Few white blood cells
Many *Dientamoeba fragilis* trophozoites

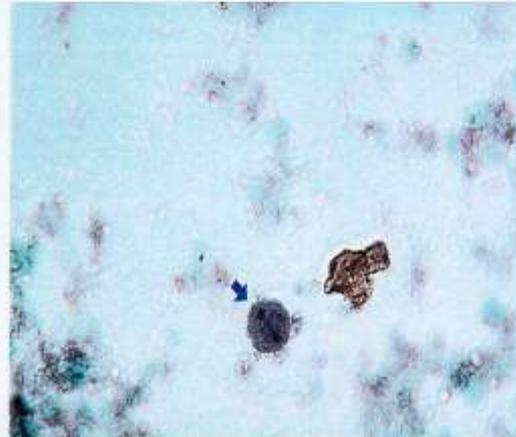
Giardia antigen (EIA): Negative

Cryptosporidium antigen (EIA): Negative

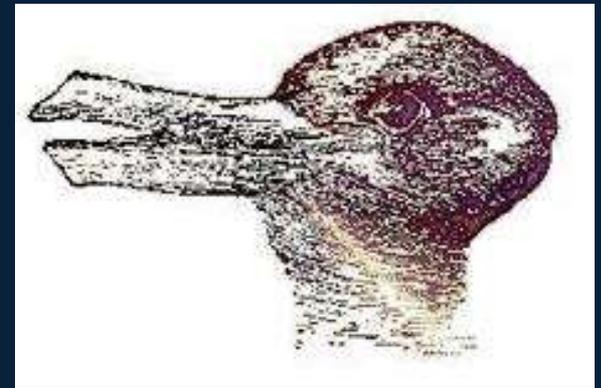
Entamoeba histolytica/dispar antigen (EIA): Negative



Dientamoeba fragilis trophozoites



Autism- Brain Disorder or Disorder Affecting Brain?



“Autism is less a brain disorder (structure) and more a disorder that affects the brain (function) - the brain is attached to the body and it is wet!” - Martha Herbert, MD, PhD

- Metabolic abnormalities
 - Vitamin D3 influences serotonin synthesis
 - Low methylfolate production impacts neurotransmitter function
- Chronic activation of neuroinflammation- Vargas
- SPECT scans show diminished blood flow to regions of the brain- and this is correctable

Healing Our Autistic Children- How Do We Help Our Patients?

Pertinent History

- Family –
 - Autoimmune (*Valicenti-McDermott*)
 - GI, allergies, IDDM
- Prenatal –
 - Maternal amalgams/vaccines/meds/diet
- Neonatal –
 - Birth trauma/meds/vaccines/antibiotics
 - Hyperbilirubinemia (*Croen et al, 2005, Pediatrics*)
 - Breastfeeding/colic/reflux/sleep
- Environmental – EMF (electromagnetic fields), water, mold, ticks, pesticides, plastics, metals

Healing Our Autistic Children- Pertinent History

- Neonatal period is critical
- GUT tolerance--adaptive immune mechanism
- Priming for allergic diseases
- Post natal development of mucosal immune homeostasis depends on development of normal commensal organisms

Brandtzaeg, PE (2002) "Current understanding of gastrointestinal immunoregulation and its relation to food allergy"
Ann N Y Acad Sci **964**: 13-45



For your
toolbox

Healing Our Autistic Children- How Do We Help Our Patients?

- Begin with the gut- The 3Rs
- REMOVE- Move to a GF/CF diet
- REPLENISH-Probiotics- need to be dairy free
- REPAIR and RESTORE
 - Enzymes- need to contain DPP-IV
 - Multivitamins- rich in B complex and B-6
 - Omegas- fish oil (from companies that remove organs before pressing flesh), flax
 - Minerals- calcium, zinc, magnesium
- REPAIR and RESTORE- yeast management

The Role of GFCF Diet

- It is a nutritional opportunity, not a penalty
- It removes an opiate source for some
- It removes an allergen (IgE *and* IgG) for some
- It removes autoimmune incitement for many
- It removes an inflammatory igniter for all
- It is helpful- whether it is behaviorally obvious or not

Whiteley, P et al. Gluten- and casein-free dietary intervention for autism spectrum conditions. *Front Hum Neurosci.* 2012 Nov; 6: 344.
doi: 10.3389/fnhum.2012.00344

Healing Our Autistic Children- Remove-Diet Options

ASD Diets Options	ARI Survey Results*
GFCF (Gluten-free and Casein-free) No gluten (wheat, rye, barley, spelt, kamut, and oats) or casein (dairy)	GFCF - 65% improved No Dairy - 50% improved No Wheat - 49% improved
Food Sensitivity Elimination Eliminating all other food sensitivities: Soy, corn, eggs, citrus, peanuts, chocolate, cane sugar	No Eggs – 49% improved No Chocolate – 49% improved No Sugar – 48% improved Rotation Diet – 49% improved
Feingold Diet/Low Phenols Restricts high phenolic foods, including all artificial ingredients and many fruits	54% - improved
SCD (Specific Carbohydrate Diet) Restricts carbohydrates to only fruits, non-starchy vegetables, and honey. No grains, starchy vegetables, or mucilaginous fibers	Candida Diet – 54% improved
Feast Without Yeast Standard anti-yeast diet with no sugar, yeast foods, etc.	
Body Ecology Diet Anti-yeast diet combining principles of anti-yeast diets including no sugar, acid/alkaline, fermented foods, etc.	
Low Oxalate Diet Restricts high oxalate foods, includes supplementation of calcium, probiotics, and other nutrients	

Courtesy of Julie Matthews, NC

* parents' reporting of noticeable symptomatic improvement

© Pediatric Partners of Ponte Vedra



The Role of Healthy Fat

Casein Free Cashew Nut/Coconut Oil Whipped Cream



Role of Diet- Modified (GFCF) Ketogenic Diet for Seizures

J Child Neurol. 2013 May 10. [Epub ahead of print]

Autism and Dietary Therapy: Case Report and Review of the Literature.

Herbert MR, Buckley JA.

¹Pediatric Neurology and TRANSCEND Research, Massachusetts General Hospital, Boston, MA, USA.

Abstract

We report the history of a child with autism and epilepsy who, after limited response to other interventions following her regression into autism, was placed on a gluten-free, casein-free diet, after which she showed marked improvement in autistic and medical symptoms. Subsequently, following pubertal onset of seizures and after failing to achieve full seizure control pharmacologically she was advanced to a ketogenic diet that was customized to continue the gluten-free, casein-free regimen. On this diet, while still continuing on anticonvulsants, she showed significant improvement in seizure activity. This gluten-free casein-free ketogenic diet used medium-chain triglycerides rather than butter and cream as its primary source of fat. Medium-chain triglycerides are known to be highly ketogenic, and this allowed the use of a lower ratio (1.5:1) leaving more calories available for consumption of vegetables with their associated health benefits. Secondary benefits included resolution of morbid obesity and improvement of cognitive and behavioral features. Over the course of several years following her initial diagnosis, the child's Childhood Autism Rating Scale score decreased from 49 to 17, representing a change from severe autism to nonautistic, and her intelligence quotient increased 70 points. The initial electroencephalogram after seizure onset showed lengthy 3 Hz spike-wave activity; 14 months after the initiation of the diet the child was essentially seizure free and the electroencephalogram showed only occasional 1-1.5 second spike-wave activity without clinical accompaniments.

KEYWORDS: autism, dietary therapy, ketogenic diet

PMID: 23666039 [PubMed - as supplied by publisher]



For your
toolbox

Healing Our Autistic Children- Remove- Dietary Recommendations

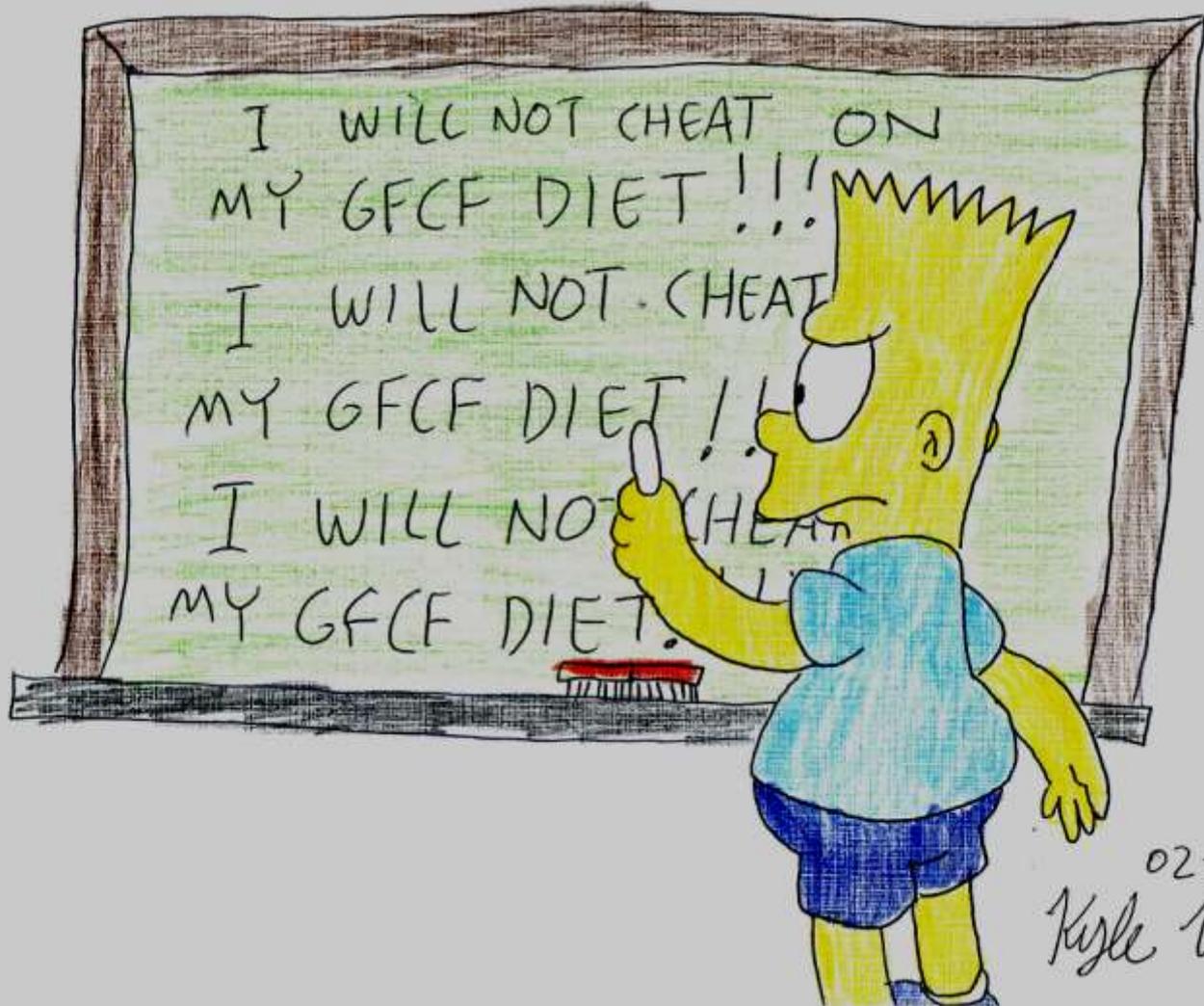
- Removal of dairy: anything that comes from an udder! No casein, whey, etc
- Removal of gluten: protein in wheat, oat, rye, barley
 - tacanow.org
 - gfcfdiet.com
- Selective removal of specific foods- sometimes soy, corn, et al.
- True addictions (gliado- and casomorphins) may make these transitions difficult!

Healing Our Autistic Children- Remove- Choosing A Diet

- There are many, many different diets
- The **best** diet: the one that works for your patient- GFCF is always a starting point
- Laboratory investigations can point direction
 - IgE food allergies
 - IgG food allergies
 - Caso and gliado morphin urinary measures
- As organic as possible, cook from “scratch”
- Medically prescribed diets are a tax deduction!!

FOR

DR. JULIE AND DR. JERRY



02-01-07

Kyle W.



Healing Our Autistic Children- Repair- Non-Prescriptive Yeast Management

- Garlic (1-2 fresh cloves or pills/day)
 - Caprylic acid (500-1000 mg with meals)
 - Oregano oil (0.2 ml 2x/day)
 - Grapefruit or citrus seed extract (1/3 adult dose)
 - Saccharomyces boulardii (3-6 capsules/day)
 - Candisol- hemicellulase digests yeast cell wall
- * Remember that pharmaceuticals are often made from herbs. Herbs are medicines- start low, go slow, not every thing is going to be a good thing, there can be behavioral Herxheimer's reactions

Healing Our Autistic Children- Repair- Prescriptive Yeast Management

- Non-absorbable prescriptions
 - Amphotericin b 250 mg four times daily 10 d, then 500mg four times daily for 10
 - Nystatin powder up to ¼ tsp (500 million units) at least 3 times daily
- Systemic prescriptions*:
 - Itraconazole (Sporanox)
 - Fluconazole (Diflucan)
 - Terbinafine (Lamisil)
 - Ketaconazole (Nizoral)

* need to be adjusted for weight, potential for “die-off” (behavioral Herxheimer’s), be aware of dyes, sugars, and fillers as potential problems



Remove- Parasites

- Parasites
 - Sources of parasites
 - Herbs—Artemesia, Black Walnut, Cloves
 - Antiparasitic drugs—Nitazoxanide, Metronidazole
 - Combinations of drugs followed by herbs



For your
toolbox

Repair- Managing Constipation

- George's Aloe Juice, Vitamin Fiber –start low, work up
- Fleets child size enema once
- Miralax (aka Glycolax) 2 tsp for 3 weeks





Repair- Fiber

- Soluble Fiber- apple pulp, rice bran, carrots, flaxseed, soy, peas, oranges
 - Glucose regulation, pH balance, bile acid binding, regulation of phase I and II liver detox
- Insoluble Fiber- Beets, green beans, leafy greens, nuts, seeds, whole grains (gluten free)
 - Promotes bowel regularity; provides substrate for Bifidobacterium to produce butyric acid; improves satiety; cancer protection

Gut Managed, Behavior Managed



06/03



12/03

Healing Our Autistic

Children-

Replace- Deficient Omega 3's



- Cod Liver Oil, start with $\frac{1}{2}$ tsp daily and work up to 2 tsp daily IF TOLERATED
- Remember that omegas are cox 2 inhibitors of inflammation....





For your
toolbox

Replace- Deficiencies Of Hibiscus, Vitamin A and DV

- Daily Value is the amount needed to prevent deficiency related disease, not to optimize health
- Individual needs vary person to person and from day to day
- Nutritional analysis- rich in iron, Vitamin C, fiber antioxidants, flavonoids, Thiamine, Vitamin A
- Hibiscus “pica” in a child with visual stimming and peripheral vision use- resolved by replacing Vitamin A



<http://link.springer.com/article/10.1023/B:AL.0000040310.80938.53>

<https://hort.purdue.edu/newcrop/ncnu02/f/bost-556.pdf>



Healing Our Autistic Children- How Can A Primary Care Practitioner Help?

- Diet- a GF/CF diet, as organic as possible
- Multivitamin that is rich in B complex, and especially B6
- Minerals- especially Calcium, Zinc, and Magnesium
- Omegas- Fish Oils
- Probiotics- Dairy Free
- Enzymes- with DPP- IV
- Yeast management

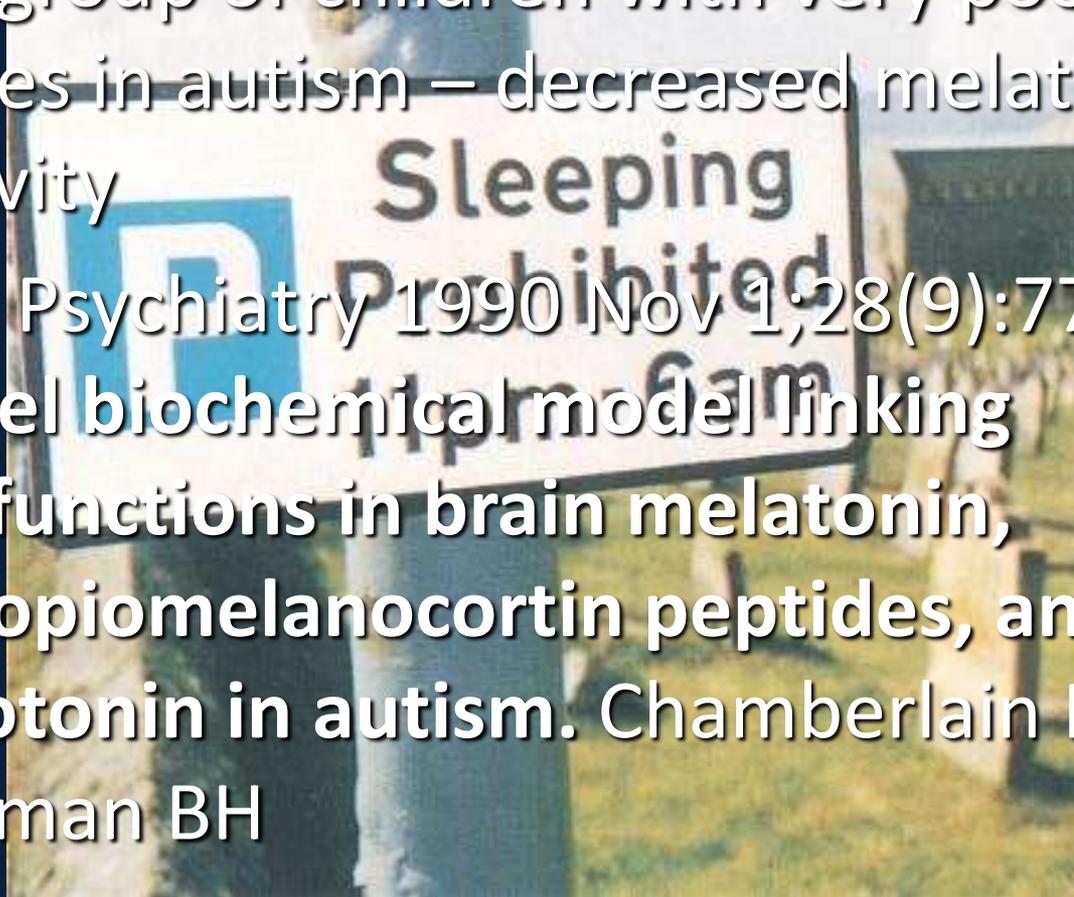


Healing Our Autistic Children- Management of Inflammation- Upper and Lower GI

- Ranitidine (Zantac)
Famotidine (Pepcid)
- Montelukast
(Singulair)
- Cromolyn sodium
(Gastrochrom)
- Changing diets
- Changing probiotics
- Changing enzymes
- Mesalamine
(Pentasa)
- Sucralfate
(Carafate)
- Moving bowels!
- Antibiotics- non-
systemic ideal
- Antifungals
- Antiparasitics
- Steroids

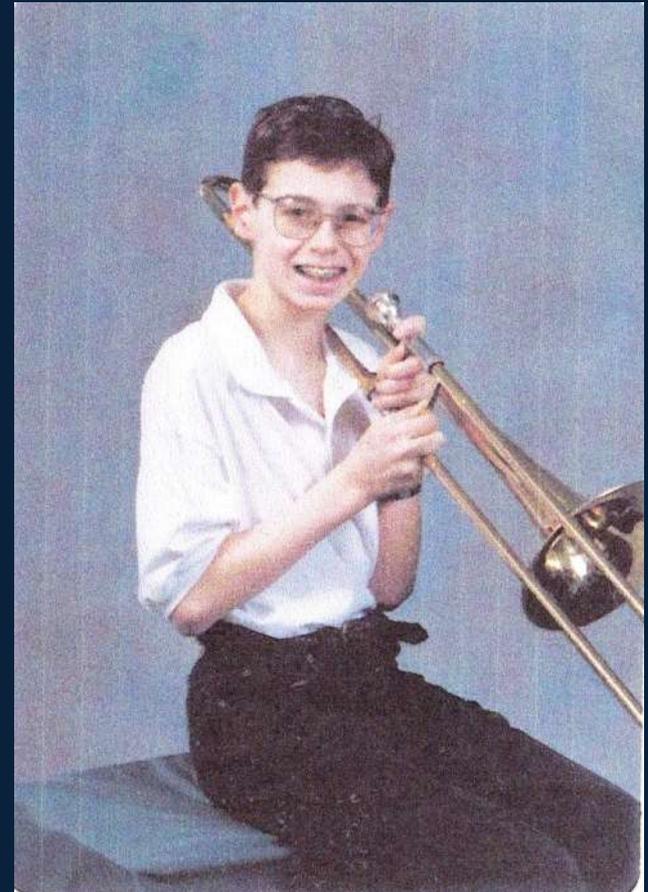
Healing Our Autistic Children- Managing Sleep

- Subgroup of children with very poor sleep cycles in autism – decreased melatonin activity
- Biol Psychiatry 1990 Nov 1;28(9):773-93. A novel biochemical model linking dysfunctions in brain melatonin, proopiomelanocortin peptides, and serotonin in autism. Chamberlain RS, Herman BH

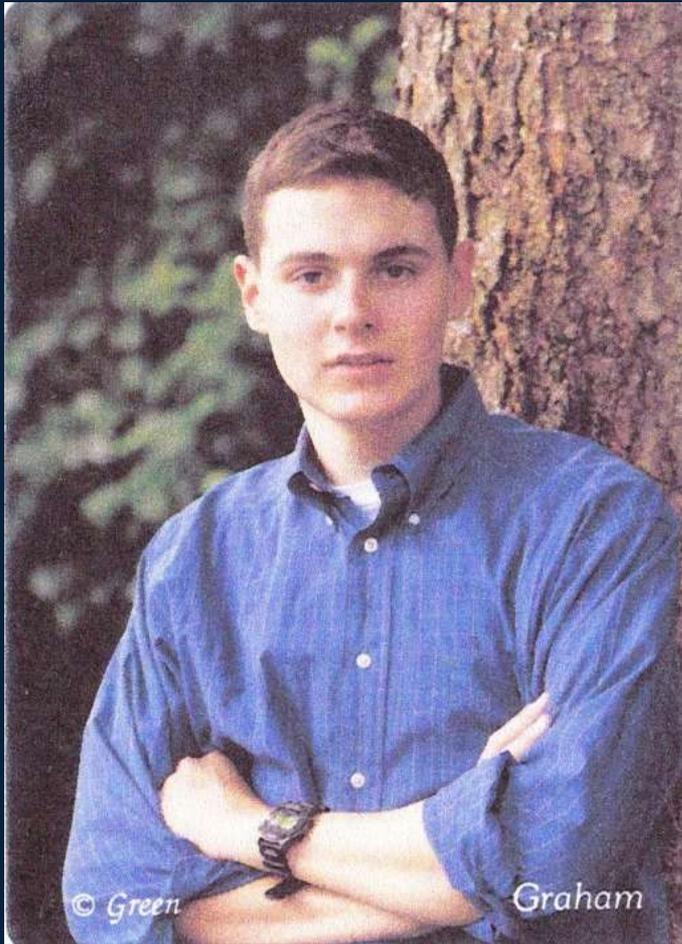


Sick

- 16 year old
- Multiple antipsychotics
- Chronic constipation
- Stool- NG Lactobacillus or Bifidobacterium, 4+ candida
- MTHFR ++ C677T
- Mercury and lead toxic



Well- Health a Vital Reserve



- Healthy GF/CF diet
- Drugs weaned off
- Supplements (to include amino acids)
- Magnesium citrate
- Diflucan, Enzymes, Prebiotics , Probiotics
- Removal of metals

Healing Our Autistic Children- How Do We Help Our Patients?

Manage the gut disease

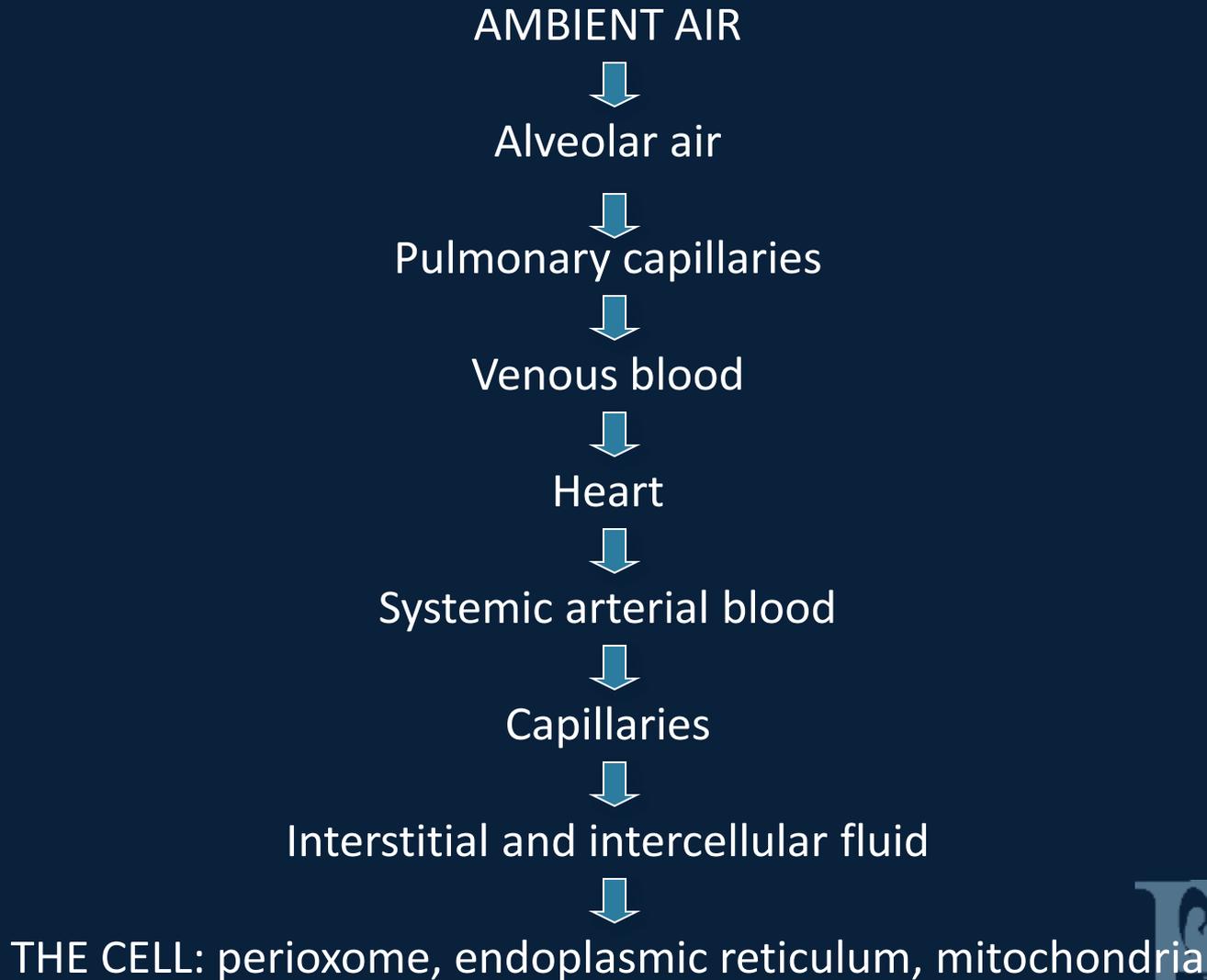
Manage the immune
dysregulation

Manage the inflammation

Manage the oxidative
stress

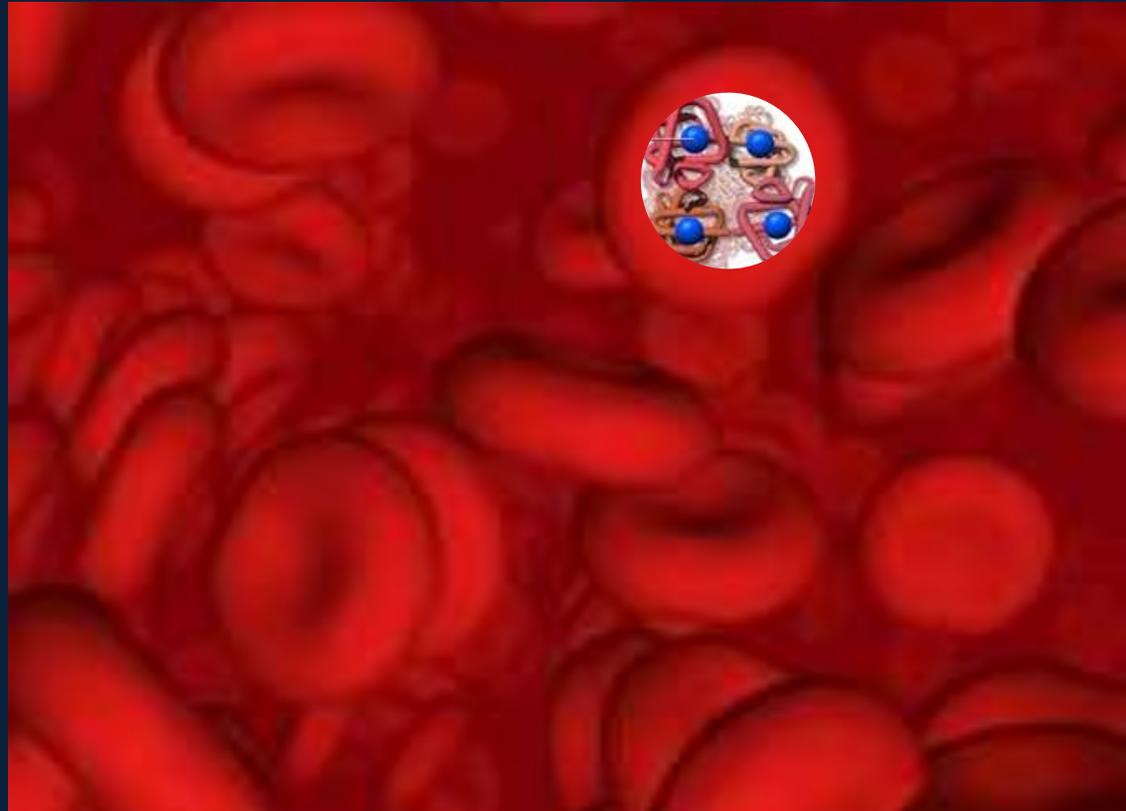


Basic Physiology of HBOT



Oxygen at Atmospheric Pressure- Attached to Red Blood Cell

- Travels attached to red blood cells
- Four molecules of Oxygen per red blood cell
- Oxygen only crosses a short distance into tissue when it arrives at its destination



Henry's Law- Defines What Happens With Hyperbaric Pressure

- The amount of any gas that will dissolve in a liquid at a given temperature is a function of the partial pressure of the gas in contact with the liquid and the solubility coefficient of the gas in that particular liquid.
- Simplified: As the pressure of any gas increases, more of that gas will dissolve into any solution with which it is in free contact.

$$\frac{V_G}{V_L} = aP_g$$

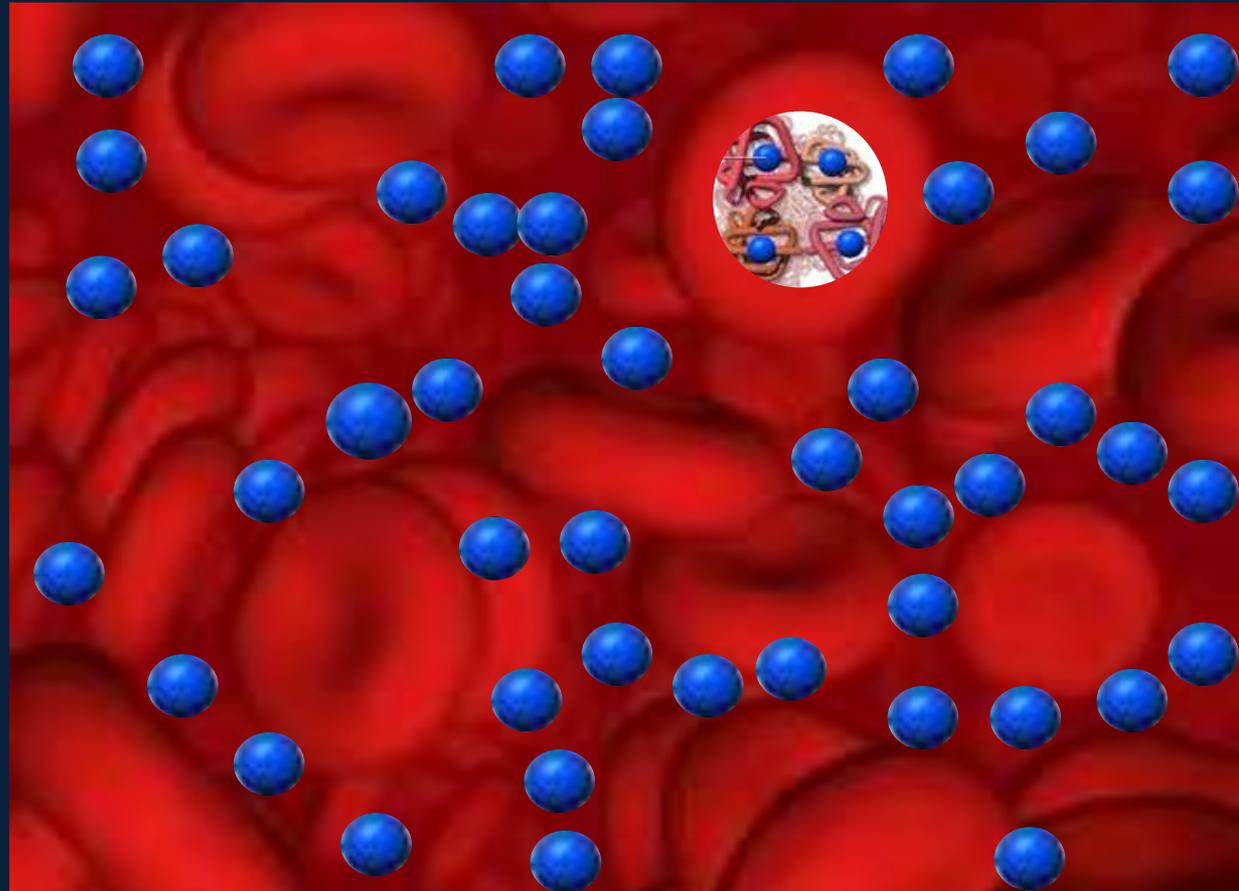
V_L

Henry's Law in Real Life



Oxygen-Under Pressure Dissolves Into Plasma

- Much more oxygen travels to the tissue
- Different laws of physics apply because the oxygen is floating freely, not bound
- When it arrives at tissue it floods into the damaged area, penetrating much further
- This speeds healing



Oxygen Washes Into Tissue...

At atmospheric pressure, it washes into tissue a short way



At hyperbaric pressure, it floods tissue, penetrating deeply



Physiology of Oxygenation

- Diffusion distance between the capillary wall and the cell is less than 50 micrometers (RBC is 8 micrometers), if the distance is larger, oxygen utilization is diffusion-limited – particularly true for cerebral white matter.

HBT and GI Issues

Reflux, Colitis, Obstruction

- Chronic Idiopathic Intestinal Pseudo-Obstruction: Case reported by Yokota *et al* (2000) demonstrated complete relief of obstruction and rapid decrease of abnormally accumulated intestinal gas

HBT and GI Issues

Reflux, Colitis, Obstruction

- Undersea Hyperb Med. 2002 Winter;29(4)
Hyperbaric oxygen improves healing in experimental rat colitis.

HBT and GI Issues

Reflux, Colitis, Obstruction

- Koloskow and Dumurov (1986): working with rat ulcers, 60% healed with HBOT
- Komarov *et al* (1985) reported 127/132 pts confirmed healing by endoscopy with 10-15 treatments at 2 ATA.
- Efuni *et al* (1986) 217 pts with peptic ulcer disease and HBOT 9-17 treatments at 2 ATA. 96% of PUD were healed in 19 days which, when compared to 350 controls, represented a shortened duration of illness by 7-28 days

HBT in Neuroinflammation

Neuroglial Activation and Neuroinflammation in the Brain of Patients with Autism

Diana L. Vargas, MD,^{1,2} Caterina Nascimbene, MD,¹⁻³ Chitra Krishnan, MHS¹
Andrew W. Zimmerman, MD,^{1,4} and Carlos A. Pardo, MD^{1,2,5}

Autism is a neurodevelopmental disorder characterized by impaired communication and social interaction and may be accompanied by mental retardation and epilepsy. Its cause remains unknown, despite evidence that genetic, environmental, and immunological factors may play a role in its pathogenesis. To investigate whether immune-mediated mechanisms are involved in the pathogenesis of autism, we used immunocytochemistry, cytokine protein arrays, and enzyme-linked immunosorbent assays to study brain tissues and cerebrospinal fluid (CSF) from autistic patients and determined the magnitude of neuroglial and inflammatory reactions and their cytokine expression profiles. Brain tissues from cerebellum, midfrontal, and cingulate gyrus obtained at autopsy from 11 patients with autism were used for morphological studies. Fresh-frozen tissues available from seven patients and CSF from six living autistic patients were used for cytokine protein profiling. We demonstrate an active neuroinflammatory process in the cerebral cortex, white matter, and notably in cerebellum of autistic patients. Immunocytochemical studies showed marked activation of microglia and astroglia, and cytokine profiling indicated that macrophage chemoattractant protein (MCP)-1 and tumor growth factor- β 1, derived from neuroglia, were the most prevalent cytokines in brain tissues. CSF showed a unique proinflammatory profile of cytokines, including a marked increase in MCP-1. Our findings indicate that innate neuroimmune reactions play a pathogenic role in an undefined proportion of autistic patients, suggesting that future therapies might involve modifying neuroglial responses in the brain.

Ann Neurol 2005;57:000-000

HBT in Neuroinflammation

Benson RM, Minter LM, Osborne BA, Granowitz EV. Clin Exp Immunol. 2003 Oct;134(1):57-62.

Hyperbaric oxygen inhibits stimulus-induced proinflammatory cytokine synthesis by human blood-derived monocyte-macrophages.

Hyperoxia alone and pressure alone did not affect cytokine production.

In summary, HBO exposure transiently suppresses stimulus-induced proinflammatory cytokine production and steady state RNA levels.

Neurologic Impact- SPECT Scan

Single Positron Emission Computed Tomography

- Takashi Ohnishi, et al. 2000. **Abnormal regional cerebral blood flow in childhood autism.** Brain, 123(9), 1838-1844.
- ...altered perfusion in the medial prefrontal cortex and anterior cingulate gyrus, ... altered perfusion in the right medial temporal lobe. The perfusion abnormalities seem to be related to the cognitive dysfunction observed in autism...

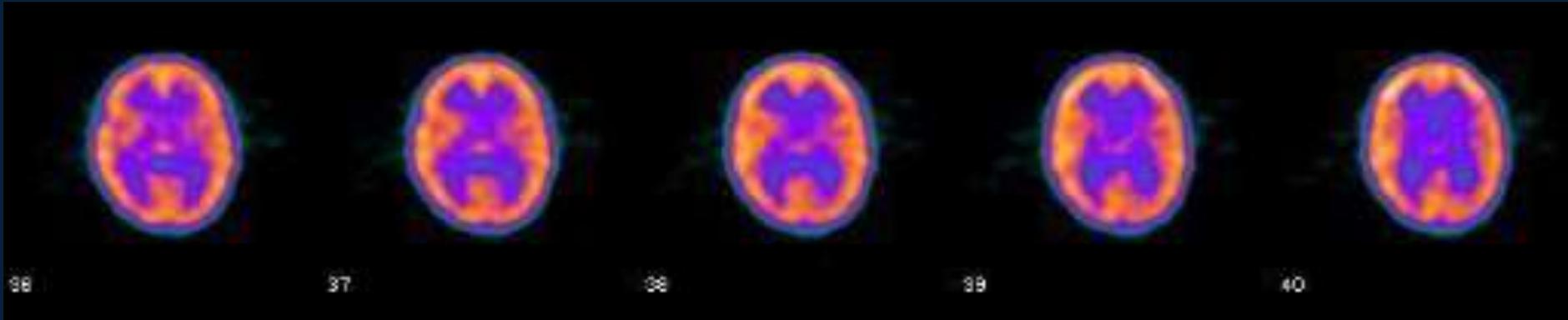
MHBT Research

62 autistic children randomly assigned to 40 (1 hour) treatments at 1.3 atm, 24% oxygen or a slightly pressurized room at 21% oxygen.

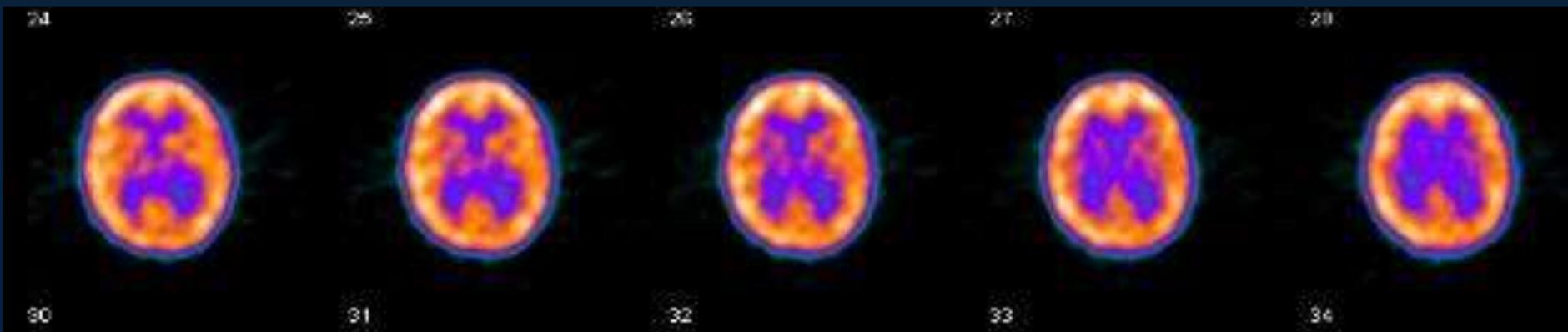
Significant improvements in overall functioning in the children who received 1.3 atm/24% O₂. Included language, social interaction, eye contact and others.

Rossignol, DA, et al “Hyperbaric treatment for children with autism: a multicenter, randomized, double-blind, controlled trial, *BMC Pediatrics*, 2009;9(21).

SPECT Scan Changes with HBT Pre

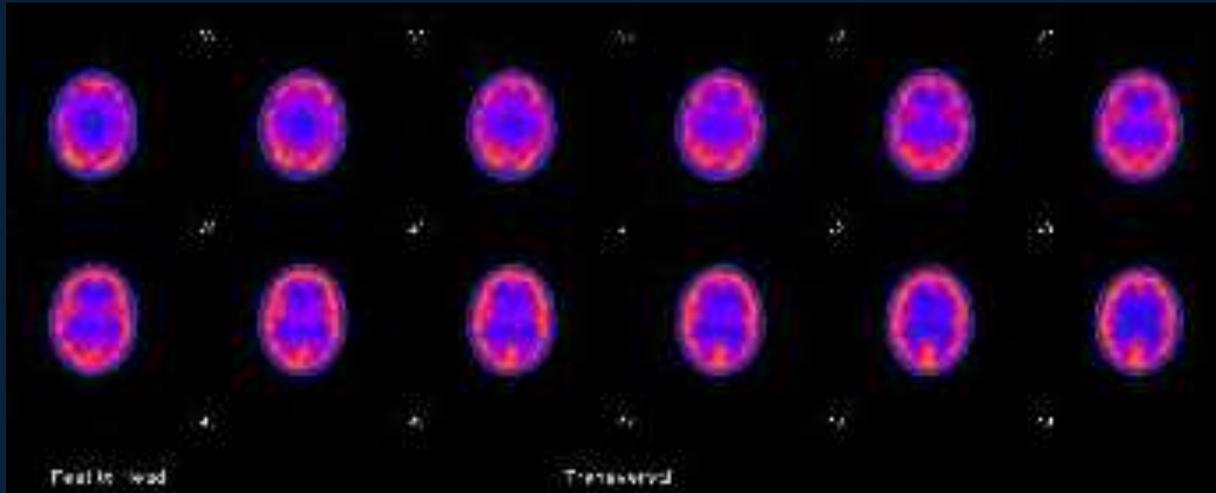


Post 40 hours 1.3 ATA

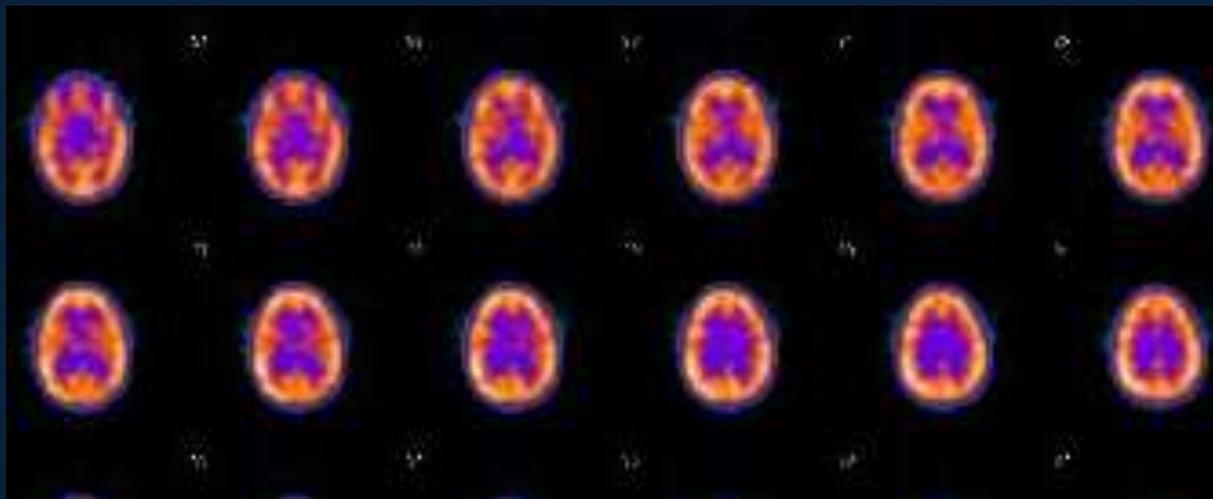


SPECT Scan Changes with HBT

Pre

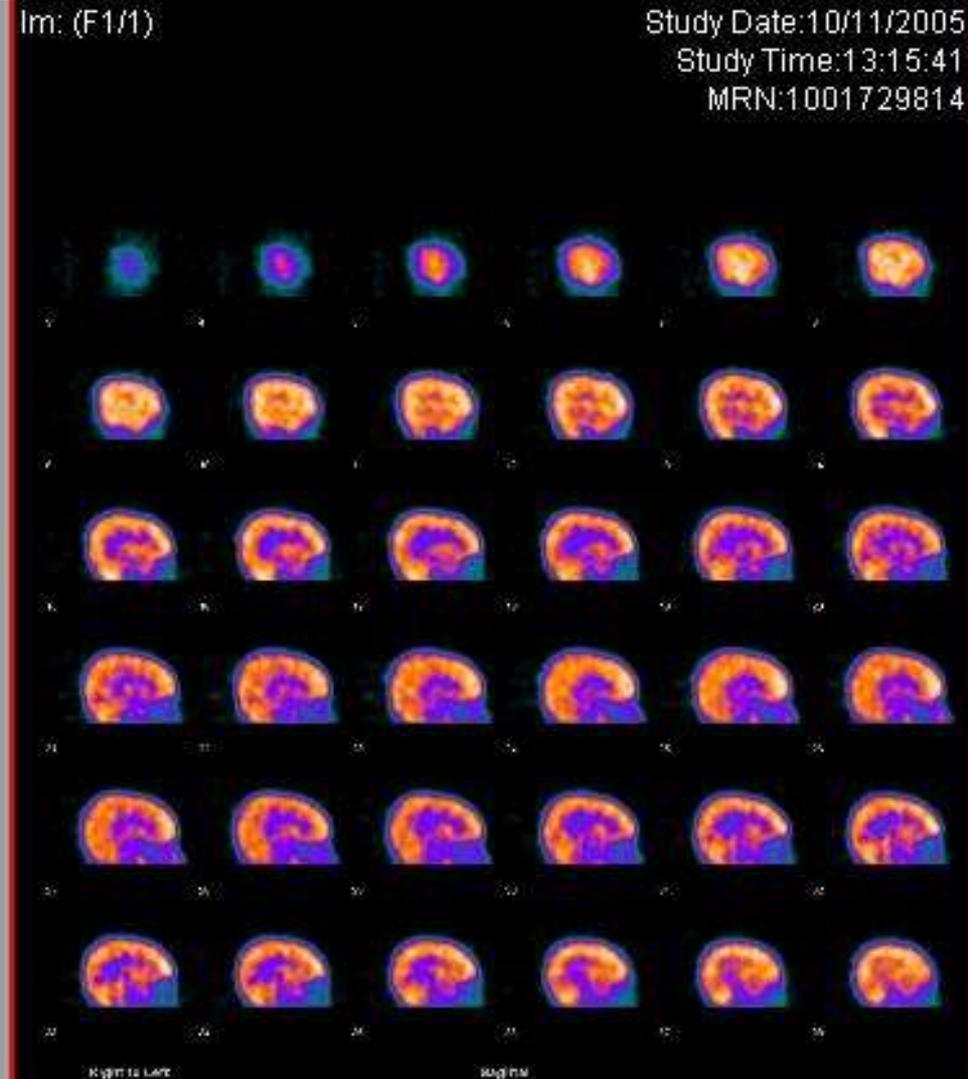
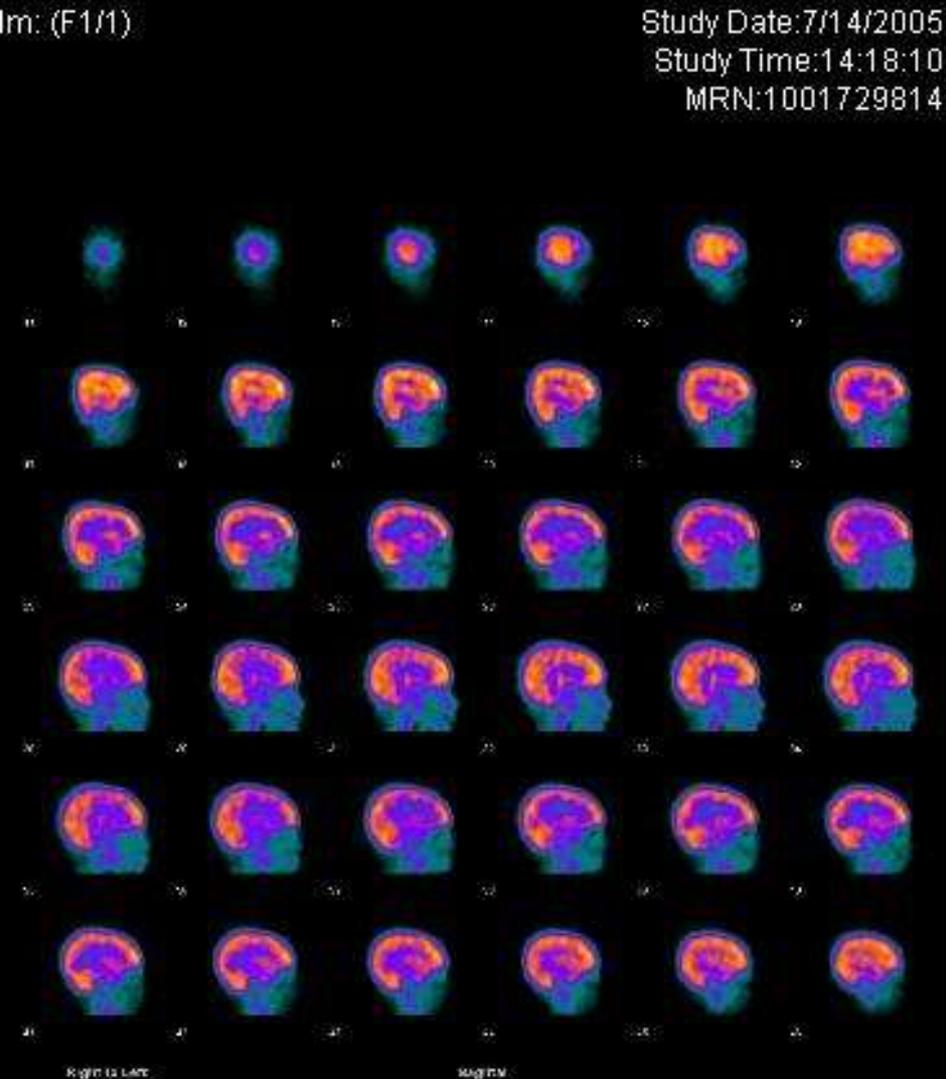


Post



SPECT Scan Changes with HBT

Pre Treatment Post Treatment



Summary of Research in MHBT

Rossignol et al. *Medical Gas Research* 2012, **2**:16
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REVIEW

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Hyperbaric oxygen treatment in autism spectrum disorders

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Abstract

Traditionally, hyperbaric oxygen treatment (HBOT) is indicated in several clinical disorders include decompression sickness, healing of problem wounds and arterial gas embolism. However, some investigators have used HBOT to treat individuals with autism spectrum disorders (ASD). A number of individuals with ASD possess certain physiological abnormalities that HBOT might ameliorate, including cerebral hypoperfusion, inflammation, mitochondrial dysfunction and oxidative stress. Studies of children with ASD have found positive changes in physiology and/or behavior from HBOT. For example, several studies have reported that HBOT improved cerebral perfusion, decreased markers of inflammation and did not worsen oxidative stress markers in children with ASD. Most studies of HBOT in children with ASD examined changes in behaviors and reported improvements in several behavioral domains although many of these studies were not controlled. Although the two trials employing a control group reported conflicting results, a recent systematic review noted several important distinctions between these trials. In the reviewed studies, HBOT had minimal adverse effects and was well tolerated. Studies which used a higher frequency of HBOT sessions (e.g., 10 sessions per week as opposed to 5 sessions per week) generally reported more significant improvements. Many of the studies had limitations which may have contributed to inconsistent findings across studies, including the use of many different standardized and non-standardized instruments, making it difficult to directly compare the results of studies or to know if there are specific areas of behavior in which HBOT is most effective. The variability in results between studies could also have been due to certain subgroups of children with ASD responding differently to HBOT. Most of the reviewed studies relied on changes in behavioral measurements, which may lag behind physiological changes. Additional studies enrolling children with ASD who have certain physiological abnormalities (such as inflammation, cerebral hypoperfusion, and mitochondrial dysfunction) and which measure changes in these physiological parameters would be helpful in further defining the effects of HBOT in ASD.

Keywords: Hyperbaric oxygen treatment, Autism, Oxidative stress, Inflammation, Behavior

Recovery, Improved Health, Optimizing Function Is Plausible...



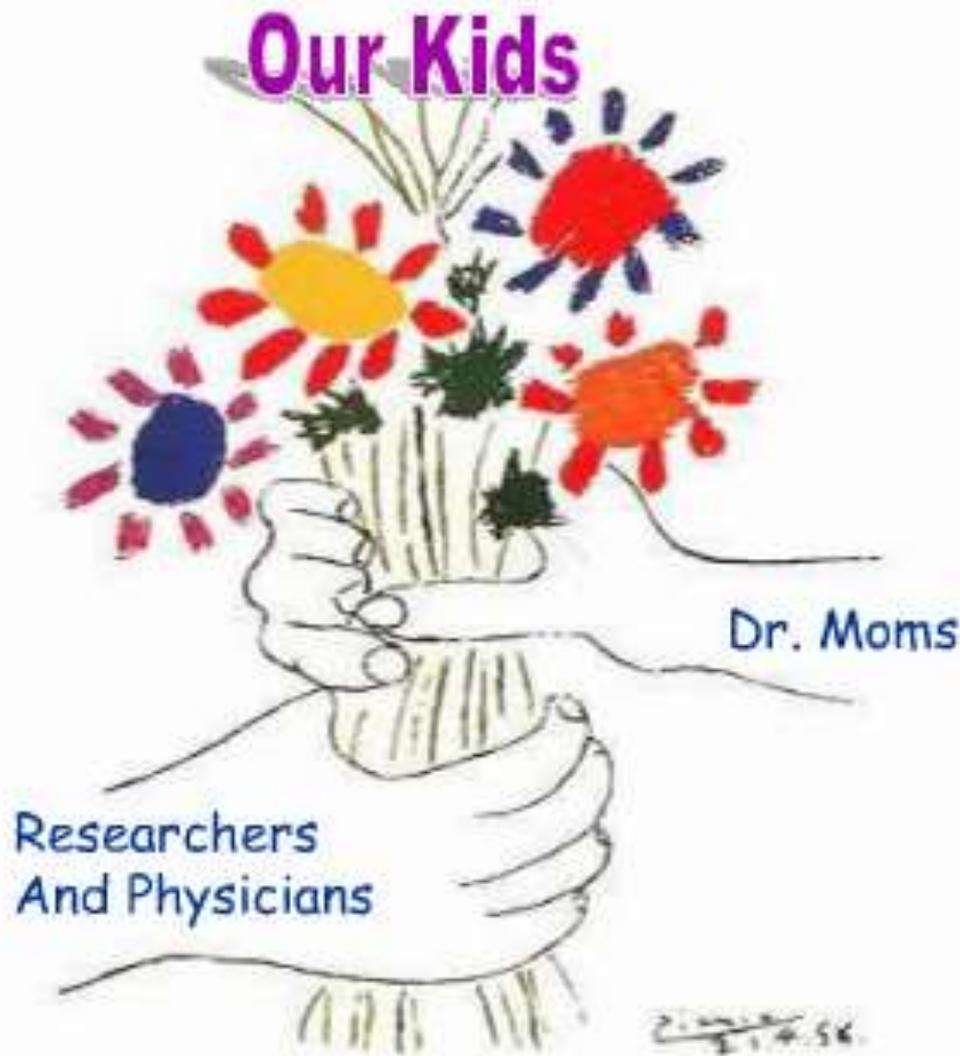
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