

The Gut-Brain-Nutrient Connections to Autism:

Prevention and Treatment Options

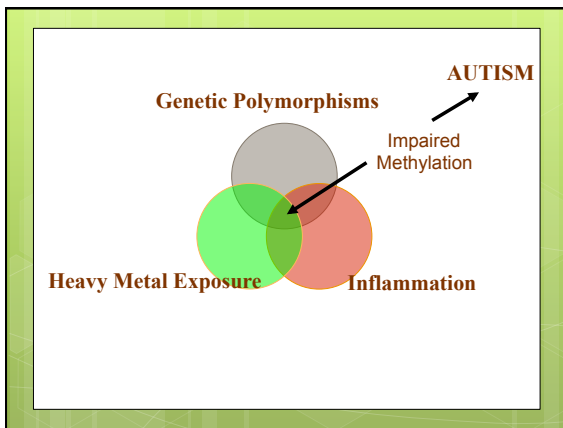
Presented by:
 Brenda Watson, CNC, co-founder
 RenewLife & Advanced Naturals
 Leonard Smith MD, FACS Faculty
 Univ. Miami Integrative Medicine.

PARADIGM SHIFT

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

Most Autistic patients have environmentally-induced toxicity.

Autism is therefore preventable, treatable and reversible.

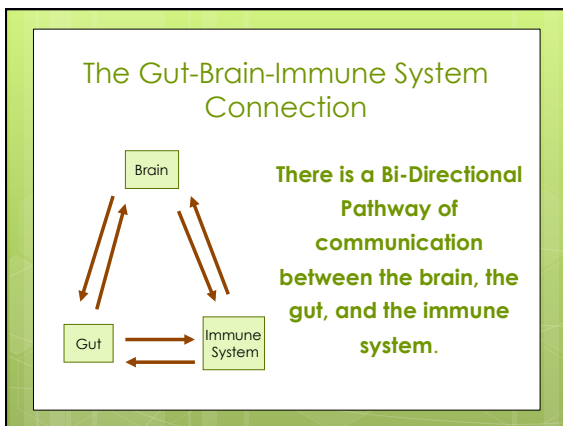


Pre-disposition

Genetics

- Male Gender 4:1
- Family History of Autoimmunity (Homig, 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
 - GST M1/T1 double null**

Experimental Biology 2005. April 2, Jill James PhD




American Academy of Pediatrics

"...there is emerging evidence relevant to ASDs in the areas of immune function, **the relationship between signaling pathways of the gut and brain, and genome-GI microbiome interactions.**

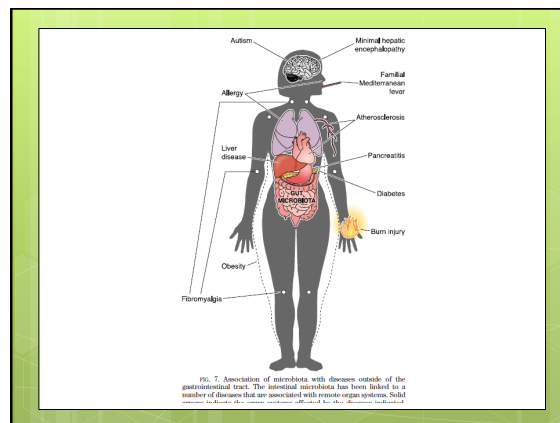
Increasingly, evidence supports a combination of changes in gut microflora, intestinal permeability, inappropriate immune response, activation of specific metabolic pathways, and behavioral changes in genetically predisposed individuals."

*Gastrointestinal Conditions in Children With Autism Spectrum Disorder: Developing a Research Agenda
 Pediatrics 2012;130:S160*



Body – 10 trillion cells

Microbiome – 100 Trillion Bacteria Are We a Bus for our Bacteria?



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**.

PANDAS

JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 20, Number 4, 2010
© Mary Ann Liebert, Inc.
Pp. 317-331
DOI: 10.1089/jcap.2010.0043

The Immunobiology of Tourette's Disorder, Pediatric Autoimmune Neuropsychiatric Disorders Associated with *Streptococcus*, and Related Disorders: A Way Forward

Tanya K. Murphy, M.D.,¹ Roger Kurlan, M.D.,² and James Leckman, M.D.³

PANDAS

Predominating theory to explain the pathophysiology behind PANDAS:

Molecular mimicry whereby antibodies intended to target Group A Strep target brain proteins instead.

Mechanisms by which autoantibodies cause clinical symptoms in central nervous system (CNS) diseases include:

- **Direct stimulation or blockade of D2 receptors in the basal ganglia with marked increase in Dopamine & increase in TNFalpha results in more Brain Inflammation and Hyperactivity**
- Immune complexes promoting inflammation of various brain regions

Fecal Transplant for CDiff.

- Review predominantly comprised of single center case series and case reports,^[30-41] a meta-analysis^[42] and one systematic review.^[20]
- **In all, about 92% of patients were cured of their RCDI, with a range of 81-100%.¹**
- FMT has been found to be quite acceptable to patients. In the recent multicenter study, **97% of patients with RCDiff reported willingness to undergo another FMT** if they were to have a repeat CDI episode, and 53% stated that they would choose FMT as first-line therapy before antibiotics

Curr Opin Gastroenterol. 2013;29(1):79-84

FECAL MICROBIAL TRANSPLANTS (FMT) AUTOIMMUNE & NEUROLOGIC DISORDERS

Patient with ulcerative colitis and idiopathic thrombocytopenic purpura (ITP). FMT not only resulted in remission of ulcerative colitis but also reversal of ITP with platelet counts that increased from a mean of 97K to 195K / microliter

Normal defecation was achieved in three patients with multiple sclerosis, who underwent FMT for chronic constipation and who also noted improvement of motor symptoms and urinary function, resulting in a regained ability to walk and removal of indwelling catheters.¹⁵⁵

Curr Opin Gastroenterol. 2013;29(1):79-84.

Physiol Rev 90: 600-664, 2010.
doi:10.1152/physrev.00042.2009

Gut Microbiota in Health and Disease

INNA SEKIROV, SHANNON L. RUSSELL, L. CAETANO M. ANTUNES, AND B. BRETT FINLAY

Michael Smith Laboratories, Department of Microbiology and Immunology, and Department of Biochemistry and Molecular Biology, The University of British Columbia, Vancouver, British Columbia, Canada

AUTISM - DAMAGED MICROBIOME And/Or ANTIBIOTIC INDUCED GUT DYSBIOSIS WITH IMMUNE DEFECTS?

1) Extensive antibiotic use is commonly associated with late-onset autism (18-24 mo. of age), & often follows antimicrobial therapy,

2) Gastrointestinal abnormalities also often present at the onset of autism and frequently persist.

3) Autistic symptoms have sometimes been reduced by oral Vancomycin treatment & relapse occurs following cessation of treatment - due to spores?

Physiol Rev • VOL 90 • JULY 2010 • www.prv.org

AUTISM - DAMAGED MICROBIOME And/Or ANTIBIOTIC INDUCED GUT DYSBIOSIS WITH IMMUNE DEFECTS?

4. Trimethoprim/sulfamethoxazole (TMS) antibiotics - much more likely to precede diagnosis of late-onset autism than exposure to any other antibiotic regimen.

5. TMS Tx Gm-, and are not effective against *Clostridium* spp., suggesting that early exposure to these drugs may promote an overgrowth of *Clostridium* spp. that could contribute to the etiology of autism.

6. Oral vancomycin targets Gm+ organisms. (*Clostridium* spp.) *Clostridia* spores that remain viable after vancomycin Tx may be responsible for relapses that occur in autistic patients /sibs after discontinuation of vancomycin.

Propionic Acid

- o A by-product of bacterial fermentation with carbohydrates in intestine. A Short Chain Fatty Acid.
- o Helps regulate the release of bad fatty acids from VAT and the liver.
- o Helps regulate the production of cholesterol.
- o Have broad effects on cellular systems
- o Actively taken up into the brain.
- o Some is good – More is NOT Better. Always a question of balance! Too much fermentation creates "Leaky Gut".

Propionic Acid & Gut Bacteria

- o Gut Bacteria *Clostridia* and *Desulfovibrio* produce PPA from fermentation of dietary carbohydrates. Urine biomarker - HydroxyphenylHydroxypropionic Acid (HPPA)
- o High levels of these bacteria are often found in children with ASD or Schizophrenia.
- o Avoid Beta lactam antibiotics (penicillin, cephalosporins, monobactams and carbapenems), may promote *Clostridia* growth
- o Common antibiotics kill these bacteria. (Flagyl/Vancocin), also add probiotics and *S. Boulardii* may suppress or kill strains of *Clostridia*.
- o Remove refined carbohydrates from diet.

FMT & AUTISM

Single case series, the intestinal microbiota of 13 children with autism were compared with 9 children without the disease. The autistic children were found to have greater numbers and different types of clostridial species when compared with controls.

Published observations of improvement in autistic symptoms in two children after FMT and in five children who received daily cultured *Bacteroidetes* and *Clostridia* for several weeks (T. Borody, personal correspondence).

Curr Opin Gastroenterol. 2013;29(1):79-84

Inciting Factors

Environmental Toxicity

Mom

- o Amalgams – Portugese Study (JAMA)
- o Fish consumption (tuna, swordfish, king mackerel)
- o Vaccines (Yazbak, 2004)
- o Environmental and Occupational Exposures
 - o Heavy Metals
 - o Persistent Organic Pollutants (POPs)
- o Pharmaceuticals (oral contraceptives, antibiotics)
- o Viral, Bacterial, or Fungal Infections
- o Diet and Stress

Antidepressant use during pregnancy and childhood autism spectrum disorders

Found a 2-fold increased risk of ASD associated with treatment with selective serotonin reuptake inhibitors by the mother during the year before delivery with the strongest effect associated with treatment during the first trimester

Arch Gen Psychiatry. 2011 Nov;68(11):1104-12. doi: 10.1001/archgenpsychiatry.2011.73. Epub 2011 Jul 4.

Inciting Factors

Environmental Toxicity

Patient

- o Thimerosal Exposure From Vaccines
- o Mercury Exposure Other
 - o Amalgams, Food, Coal burning plants, Breast Milk...
- o Other Heavy Metals
 - o Lead, Antimony, Arsenic, Aluminum, Cadmium
- o Environmental Toxins
 - o Persistent Organic Pollutants (POPs)
- o Dietary Sources
- o Pharmaceuticals
- o Live Virus Vaccines (MMR)
- o Multiple Vaccines at one time (up to 7)

Mercury in Breast Milk

- o Results indicated that there was an efficient transfer of inorganic mercury from blood to milk and that, in this population, mercury from amalgam fillings was the main source of mercury in milk.
- o Exposure of the infant to mercury from breast milk was calculated to range up to 0.3 microg/kg x d, of which approximately one-half was inorganic mercury.
- o This exposure, however, corresponds to approximately one-half the tolerable daily intake for adults recommended by the [World Health Organization](#)
- o Should we measure Hg++ & filter Breast Milk as needed?

Arch Environ Health. 1996 May-Jun;51(3):234-43

Environment-induced Disease: Everyone is exposed to these chemicals

The exposure rate (based on meconium analysis) and the median concentration of the pollutants in the positive samples were as follows (426 infants, Philippines):

- 1) lead *neurotoxic carcinogen insecticide n* (26.5%: 35.77 microg/ml),
 - 2) cadmium *carcinogen* (8.5%: 13.37 microg/ml),
 - 3) mercury *neurotoxin* (83.9%: 3.17 ng/ml),
 - 4) Chlordane (12.7%: 22.48 microg/ml),
 - 5) chlorpyrifos *insecticide* (11.0%: 8.26 microg/ml),
 - 6) diazinon *insecticide* (34.3%: 12.96 microg/ml),
 - 7) DDT *insecticide* (26.5%: 12.56 microg/ml),
 - 8) lindane *insecticide* (73.5%: 2.0 microg/ml),
 - 9) malathion *insecticide* (53.0%: 6.80 microg/ml),
 - 10) parathion *insecticide* (32.0%: 2.30 microg/ml)
 - 11) pentachlorophenol *insecticide* (16.1%: 90.00 microg/ml) "Aplastic anemia, pure red cell aplasia, leukemia, lymphoma and other hematologic disorders have followed exposure to products containing the pesticide."
- Neurotoxicology.* 2002 Sep;23(3):329-39

Cerebral Folate Deficiency

- Folate is extremely important to the brain and the rest of the CNS.
- A deficiency within the brain will produce neurological disorders beginning around age 4-6 months.
- Symptoms include delayed development, speech difficulties, spasticity, ataxia, epilepsy, unusual movements or writhing and other ASD symptoms.

Cerebral Folate Deficiency

- Folate transport into the brain is blocked resulting in low levels of active folate in cerebrospinal fluid, but normal levels in RBCs & serum
- Exposure to folate receptors found in cow and goat milk cause the body to produce antibodies that will bind to folate receptors in the brain and block transport of methyl folate into brain and cerebrospinal fluid.
- In addition, synthetic folic acid (added to bread and grains) competes with natural methyl folate for brain receptor and proves toxic once inside.

Suggestions

- Remove milk and dairy from the diet as early in age as possible.
- Remove grains from the diet as early in age as possible.
- Supplement with 5-Methyl Folate not folic acid.
- Test for MTHFR genetic mutations.

Note: If your child has responded favorably to a dairy-free, grain-free diet it is a possible CFD is a factor.

"A milk-free diet downregulates folate receptor autoimmunity in cerebral folate deficiency syndrome".

Developmental medicine and child neurology. May 2008;50(5):346-352

NUTRITION - Setting the Stage

Half the US population is deficient in at least one of the following:

Vitamins – B12, B6, C, D, E,
or Folic Acid

Minerals – Iron, Zinc, and Selenium

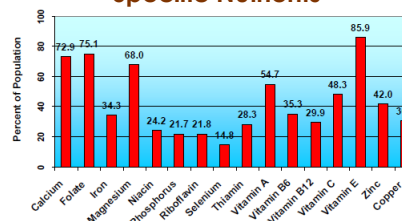
Ames B. Arch Biochem Biophys. 2004;423:227-234.

Essential Nutrient Insufficiencies Linked with Top Causes of Death in U.S.

- Heart Disease: Ca, Mg, Zn, Se, K, Cr, Cu, Vit D
- Malignant Neoplasms: Ca, Mg, Zn, Se, Cu, Vit D
- Chronic Respiratory Diseases: Mg, Se
- Diabetes: Ca, Mg, Zn, Se, Cr, Vitamin D
- Alzheimer's: Mg, Se, Cu
- Nephritis, Nephrotic Syndrome: Zn, Se
- Liver Disease: Zn, Se
- Hypertension: Ca, Mg, Zn, Se, K, Cr, Cu, Vit D

Lord RS, Bralley JA. *Laboratory Evaluations for Integrative and Functional Medicine*, 2nd edition. Duluth, GA: Metametrix Institute; 2008. Adapted from Table 3.4-reports showing associations of essential element insufficiency with the top causes of death in the United States (2005). P.71.


Percent of U.S. Population NOT Meeting the Dietary Reference Intake (DRI) for Specific Nutrients



<http://www.ba.ars.usda.gov/cnrg/services/cnmapfr.html> Aug 10, 2009

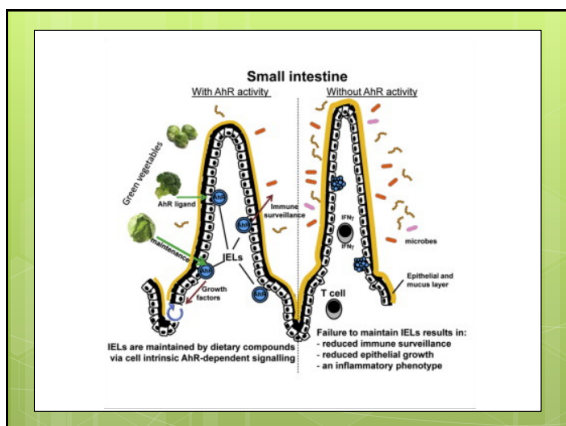
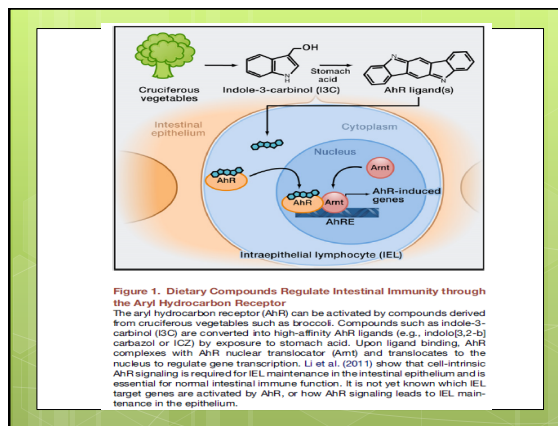
Green Veggies Vaccinate the Immune System

AhR Receptor



- AhR/Ligand is vital for the correct functioning of immune cells in the gut & skin known as intraepithelial lymphocytes (IELs).
- Dec. AhR = Dec. IEL = Dec in anti-microbial peptides

Cell. 2011, October 13.



- ### Autism Treatments % of effectiveness 23,000 DAN Parent Surveys
- Detox. (Chelation)C: 76%
 - Gluten- /Casein-Free Diet 65%
 - Vitamin B12 63%
 - Food Allergy Treatment 61%
 - Melatonin 61%
 - Digestive Enzymes 56%
 - Fatty Acids 55%
 - Candida Diet 54%
 - Feingold Diet 53%
 - PSP (Vit. B6) 51%
 - Cod Liver Oil 50%
 - Removed Chocolate 49%
 - Removed Milk Products/Dairy 49%
 - Removed Sugar 48%
 - Removed Wheat 48%
 - Rotation Diet 48%
 - Zinc 47%
 - Vitamin B6 with Magnesium 47%
 - Folic Acid 42%

- ### Autism Treatments % of effectiveness 23,000 DAN Parent Surveys
- DMG 42%
 - TMG 42%
 - Vitamin A 41%
 - Vitamin C 41%
 - Vitamin B3 41%
 - Removed Eggs 40%
 - Transfer Factor 39%
 - 5 HTP 39%
 - Cod Liver Oil with Bethanecol 39%
 - Colostrum 37%
 - CalciumE: 36%
 - Vitamin B6 alone 30%
 - Magnesium 29%
 - Pepcid 28%
 - St. Johns Wort 21%
 - SAME 19%

Elemental Red Blood Cell Analysis

Element	Reference Range	Reference Range	Element	Reference Range	Reference Range
Chromium	0.004	0.002-0.062 mcg/g	Lead	0.057	<= 0.048 mcg/g
Copper	0.538	0.466-0.721 mcg/g	Mercury	0.0315	<= 0.0039 mcg/g
Magnesium	38.0	30.1-56.5 mcg/g	Arsimony	0.002	<= 0.002 mcg/g
Manganese	0.009	0.007-0.038 mcg/g	Arsenic	0.030	<= 0.071 mcg/g
Potassium	2.729	2.220-3.626 mcg/g	Cadmium	0.000	<= 0.001 mcg/g
Selenium	0.25	0.25-0.76 mcg/g	Thallium	<8	<= 0.000000 mcg/g
Vanadium	0.003	0.001-0.014 mcg/g	Tin	<8	<= 0.0009 mcg/g
Zinc	4.1	7.8-13.1 mcg/g			

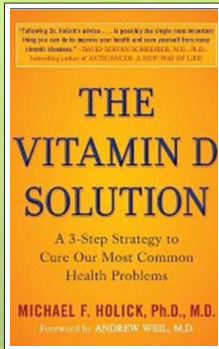
Chronic Disease Nutritional Problems

- **Low Vitamin D** 30-80% Population
- **Low Calcium** 30-80% Population

(46 different studies worldwide)

Peterlik M, et al. *Int J Environ Res Public Health*. 2009;6:2585-2607.

© 2010, The Institute for Functional Medicine



Sunshine 11AM – 2PM 20 min-60 min

Sunlamps

Supplement Vit D3

1000 iu/d up to 12 months

2000 iu/d 12 mo to 3-4 years

3000 iu – 10,000 iu/day based on testing with 25 OH Vit D serum level.

LOW VITAMIN D

Decreased neurotrophic factor levels, increased mitosis, decreased apoptosis, enhanced proliferation, and changes in brain morphology and altered behaviour patterns

Post-mortem human studies show that areas of the brain, e.g., the hippocampus, limbic system, pituitary, substantia nigra, diencephalon, cerebral cortex & white matter generally have high concentrations of vitamin D receptor (VDR)

Research in Developmental Disabilities 33 (2012) 1541–1550

Prevalence of Vitamin D Deficiency Among Healthy Infants and Toddlers

Catherine M. Gordon, MD, et. Al.

- About 40% had a 25OH vit D level < 20ng/ml
- Patients found to have 25OH vit D < 20 ng/ml (50 nmol/liter)] participated in a randomized clinical trial :
2,000 IU daily vitamin D2
50,000 IU vitaminD2 weekly
2,000 IU daily vitamin D3
- Yield equivalent outcomes in the short-term treatment (6 weeks) of low vitamin D.

J Clin Endocrinol Metab, July 2008, 93(7):2716–2721

Effect of a vitamin/mineral supplement on children and adults with autism

Oral vitamin/mineral supplementation is beneficial in improving the nutritional and metabolic status of children with autism, including improvements in methylation, glutathione, oxidative stress, sulfation, ATP, NADH, and NADPH.

Effect of a vitamin/mineral supplement on children and adults with autism

Most significant improvements were (in order) in the areas of Hyperactivity, Tantrumping, Overall, and Receptive Language.

We hypothesize that longer treatment may result in greater improvements. There was wide variation in degree of improvement - some participants experiencing little benefit, and some experiencing moderate or substantial benefit.

BMC Pediatrics 2011, 11:111 James B Adams, et al.

Natural Immune Modulators

- o Vitamins C, D, A, E, selenium, zinc, & magnesium really good hydration
- o Mushrooms Shiitake, Maitake, Reshi, Omega 3 with O6/O3 ratio < 4.0
- o Plant based diet, GF,CF, low sugar diet
- o Oral Chelation DMSA or DMPS
- o Exercise, Yoga, Meditation, CBT

Natural Immune Modulators

- Probiotics and Prebiotics
- Super Probiotics (Repopulate)
- Colon Hydrotherapy
- Infrared Sauna
- Hyperbaric Oxygen
- Stem Cell Liberation and/or Stem Cell Transplants - MSCs

BRIEF REPORT

Omega-3 Fatty Acids Supplementation in Children with Autism: A Double-blind Randomized, Placebo-controlled Pilot Study

G. Paul Amminger, Gregor E. Berger, Miriam R. Schäfer, Claudia Klier, Max H. Friedrich, and Martha Feucht

Background: There is increasing evidence that fatty acid deficiencies or imbalances may contribute to childhood neurodevelopmental disorders.

Methods: We conducted a randomized, double-blind, placebo-controlled 6-week pilot trial investigating the effects of 1.5 g/d of omega-3 fatty acids (1.84 g/d eicosapentaenoic acid, 7 g/d docosahexaenoic acid) supplementation in 13 children (aged 5 to 17 years) with autistic disorders accompanied by severe tantrums, aggression, or self-injurious behavior. The outcome measure was the Aberrant Behavior Checklist (ABC) at 6 weeks.

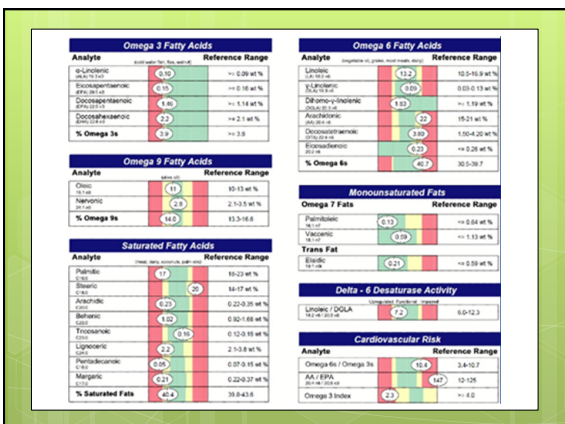
Results: We observed an advantage of omega-3 fatty acids compared with placebo for hyperactivity and stereotypy, each with a large effect size. Repeated-measures ANOVA indicated a trend toward superiority of omega-3 fatty acids over placebo for hyperactivity. No clinically relevant adverse effects were elicited in either group.

Conclusions: The results of this study provide preliminary evidence that omega-3 fatty acids may be an effective treatment for children with autism.

Omega-3 Fatty Acids Supplementation in Children with Autism: A Double-blind Randomized, Placebo-controlled Pilot Study

- o A 6-week pilot trial investigating the effects of 840 mg/d eicosapentaenoic acid, 700 mg/d docosahexaenoic acid in 13 children (aged 5 to 17 years) with autistic disorders accompanied by severe tantrums, aggression, or self-injurious behavior.
- o Results of this study provide preliminary evidence that omega-3 fatty acids may be an effective treatment for children with hyperactivity

BIOLOGICAL PSYCHIATRY 2007;61:551-553



Journal of Translational Medicine

Review Open Access

Stem Cell Therapy for Autism

Thomas E Ichim¹, Fabio Solano², Eduardo Glenn², Frank Morales², Leonard Smith³, George Zabrecky³ and Neil H Riordan^{*1,4}

Address: ¹Meditem Laboratories Inc, Tempe, Arizona, USA; ²Institute for Cellular Medicine, San Jose, Costa Rica; ³American Medical Center, Ridgefield, Connecticut, USA and ⁴2027 E. Cedar Street Suite 102 Tempe, AZ 85281, USA

Email: Thomas E Ichim - thomas.ichim@gmail.com; Fabio Solano - doctorsolano@gmail.com; Eduardo Glenn - edglenn@yahoo.com; Frank Morales - ffrank05@aol.com; Leonard Smith - lsmith8@gmail.com; George Zabrecky - dozregg@aol.com; Neil H Riordan - riordan@mediteminc.com

* Corresponding author

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Hindawi Publishing Corporation
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 doi:10.1155/2012/480289

Review Article
Autism Spectrum Disorders: Is Mesenchymal Stem Cell Personalized Therapy the Future?

Dario Siniscalco,^{1,2} Anna Sapone,^{3,4} Alessandra Cirillo,⁵ Catia Giordano,¹ Sabatino Malone,¹ and Nicola Antonucci⁶

¹Division of Pharmacology "L. Donatelli", Department of Experimental Medicine, Second University of Naples, Via S. Maria di Costantinopoli, 16-80138 Napoli, Italy
²Centre for Autism, La Torre del Silenzio, Caserta, 80138 Napoli, Italy
³Department of Internal and Experimental Medicine "Magnano-Lanciani", Second University of Naples, 80138 Napoli, Italy
⁴Centre for Genetic Research and Muscular Biology Research Center, University of Maryland School of Medicine, Baltimore, MD 21201, USA
⁵Division of Biotechnology and Molecular Biology "A. Cascini", Department of Experimental Medicine, Second University of Naples, 80138 Napoli, Italy
⁶Biomedical Centre for Autism Research and Treatment, 70122 Bari, Italy

Correspondence should be addressed to Dario Siniscalco, dariosin@uniba.it

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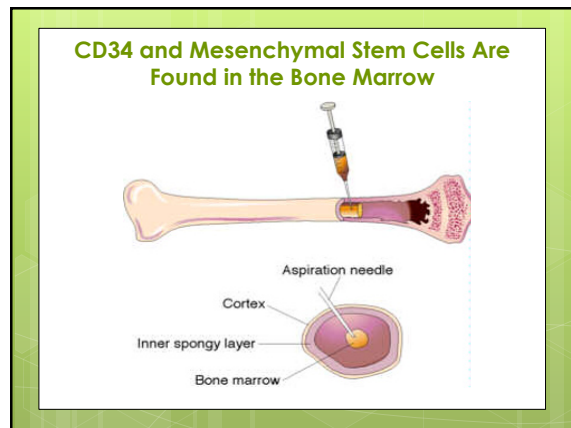
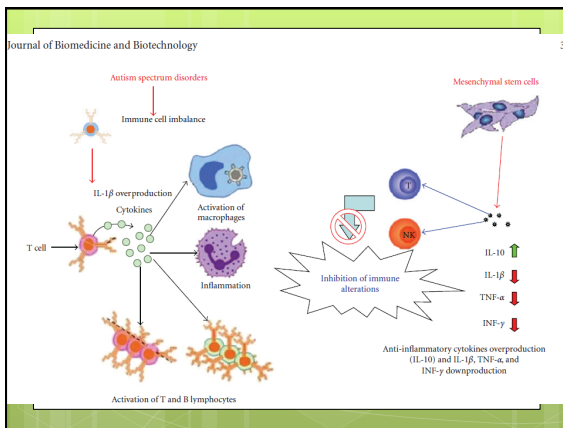
Mesenchymal Stem Cells

MSCs - found principally in the bone marrow and fat of adults, giving rise to skeletal muscle cells, blood, fat, vascular, urogenital systems, & connective tissues throughout the body.

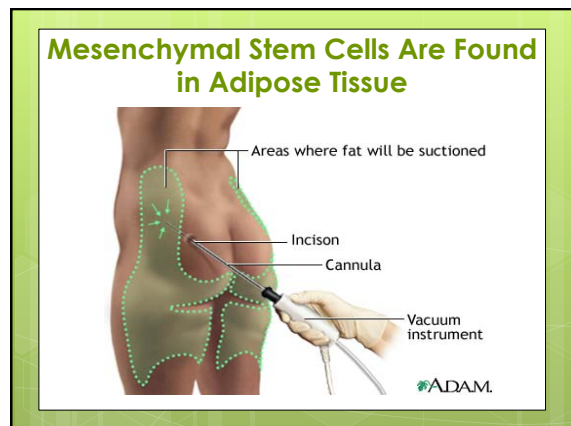
MSCs have two other extraordinary properties:

- migrate to sites of tissue injury, where they inhibit release of proinflammatory cytokines
- Strong immunosuppressive activity and successful autologous, as well as allogeneic, transplantations without requiring pharmacological immunosuppression

Journal of Biomedicine and Biotechnology
 Volume 2012, Article ID 480289, 6 pages



Mesenchymal Stem Cells Are Found in the Cord Blood



What is the rationale behind using stem cells to treat autism?

Mesenchymal stem cells (MSCs) can regulate the immune system. It is thought that they may help to reverse inflammatory conditions and is currently in the final stages of clinical trials in the US for Crohn's disease, a condition resembling the gut inflammation in autistic children.

Which types of stem cells are used to treat autism and how are they obtained?

The adult stem cells used to treat autism at the Stem Cell Institute come from human umbilical cord tissue (Wharton's Jelly, high in allogeneic Mesenchymal Stem Cells).

These stem cells are recovered from donated umbilical cords. Before they are approved for treatment all umbilical cord-derived stem cells are screened for viruses and bacteria to International Blood Bank Standards.

What are the advantages of treating with allogeneic umbilical cord tissue-derived stem cells?

- Because HLA matching is not necessary, anyone can be treated.
- Allogeneic stem cells can be administered multiple times over the course of days in uniform dosages that contain high cell counts.
- Umbilical cord tissue provides an abundant supply of mesenchymal stem cells.
- No need to collect stem cells from the patient's hip bone or fat under anesthesia, which especially for small children and their parents, can be an unpleasant ordeal.
- There is a growing body of evidence showing that umbilical cord-derived mesenchymal stem cells are more robust than mesenchymal stem cells from other sources.

How are the stem cells administered for autism treatment?

The umbilical cord-derived stem cells are administered intravenously by a licensed physician.

Depending upon the age and physical size of the patient, the stem cells might also be administered intrathecally (into the spinal fluid) by an experienced anesthesiologist. Intrathecal injection allows the stem cells to bypass the blood-brain barrier and migrate throughout the central nervous system.

The autism treatment protocol typically takes 5 days.
For More Information www.cellmedicine.com

WHAT TO DO BEFORE & AFTER RECEIVING STEM CELLS

- o Eat 80% organic plant based alkaline diet
- o Sleep at least 7-8 hours/day
- o Moderate aerobic/resistance exercise 3-4 times/week, include stretching 2-3X/week
- o Take Multivitamin, Vitamin D3, Fish Oil, Vit. C and Probiotics most every day
- o Consider toxic metal challenge and a Detoxification Program
- o Modify Lifestyle and lower stress

The End

Thank You Attending and Listening

Any Questions?