

The Evidence on Complementary and Alternative Medical Interventions for Autism

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Why should behavior analysts be informed about CAM interventions for autism?

- Recent surveys show high rates of use of “alternative” interventions with this population.
- These interventions can affect behavior and influence effectiveness of behavior analytic procedures.

Why know about CAM?

- 52% of parents of children with ASD reported using at least one CAM intervention vs. 28% of parents of typically developing children (Wong & R. Smith, 2006)
- 43% of parents of children with ASD reported using vitamin supplements; 27% reported using special diets (Green et al., 2006)
- Of 121 parents whose children were receiving ABA, 61% reported also using megavitamins; 50% reported using special diets (T. Smith & Antolovich, 2000)

Relevant sections of BACB Guidelines for Responsible Conduct

- **1.01 Reliance on Scientific Knowledge.** Behavior analysts rely on scientifically and professionally derived knowledge when making scientific or professional judgments in human service provision, or when engaging in scholarly or professional endeavors.
- **1.04 Professional Development.** Behavior analysts who engage in assessment, therapy, teaching, research, organizational consulting, or other professional activities maintain a reasonable level of awareness of current scientific and professional information in their fields of activity, and undertake ongoing efforts to maintain competence in the skills they use.

Relevant sections of BACB Guidelines for Responsible Conduct

■ 2.09 Treatment Efficacy.

- (a) The behavior analyst always has the responsibility to recommend scientifically supported most effective treatment procedures. Effective treatment procedures have been validated as having both long-term and short-term benefits to clients and society.
- (b) Clients have a right to effective treatment (i.e., based on the research literature and adapted to the individual client).
- (c) Behavior analysts are responsible for review and appraisal of likely effects of all alternative treatments, including those provided by other disciplines and no intervention.

Relevant sections of BACB Guidelines for Responsible Conduct

- **3.02 Environmental Conditions that Hamper Implementation.**

If environmental conditions hamper implementation of the behavior analytic program, the behavior analyst seeks to eliminate the environmental constraints, or identifies in writing the obstacles to doing so.

- **4.0 THE BEHAVIOR ANALYST AND THE INDIVIDUAL BEHAVIOR CHANGE PROGRAM.**

The behavior analyst designs programs that are based on behavior analytic principles, including assessments of effects of other intervention methods, involves the client or the client-surrogate in the planning of such programs, obtains the consent of the client, and respects the right of the client to terminate services at any time.

- **10.01 Promotion in Society.**

The behavior analyst should promote the application of behavior principles in society by presenting a behavioral alternative to other procedures or methods.

From “The Ethical Behavior Analyst,”
BACB Newsletter, January 2007, p. 10:

- “...it is absolutely unethical for a behavior analyst to be trafficking in unproven approaches...”

- J.S. Bailey & M. Burch

Consensus-Based Interventions for Autism (NRC recommended)

- Intensive Applied Behavior Analysis (ABA)
 - Most rigorous, evidence-based.
- TEACCH program: Visual strategies
- Denver Model: developmental psychology + ABA Discrete Trials (D.T.) or Pivotal Response Training (P.R.T.).

The limits of teaching: Natural Extensions of Behavior (or Not!!!)



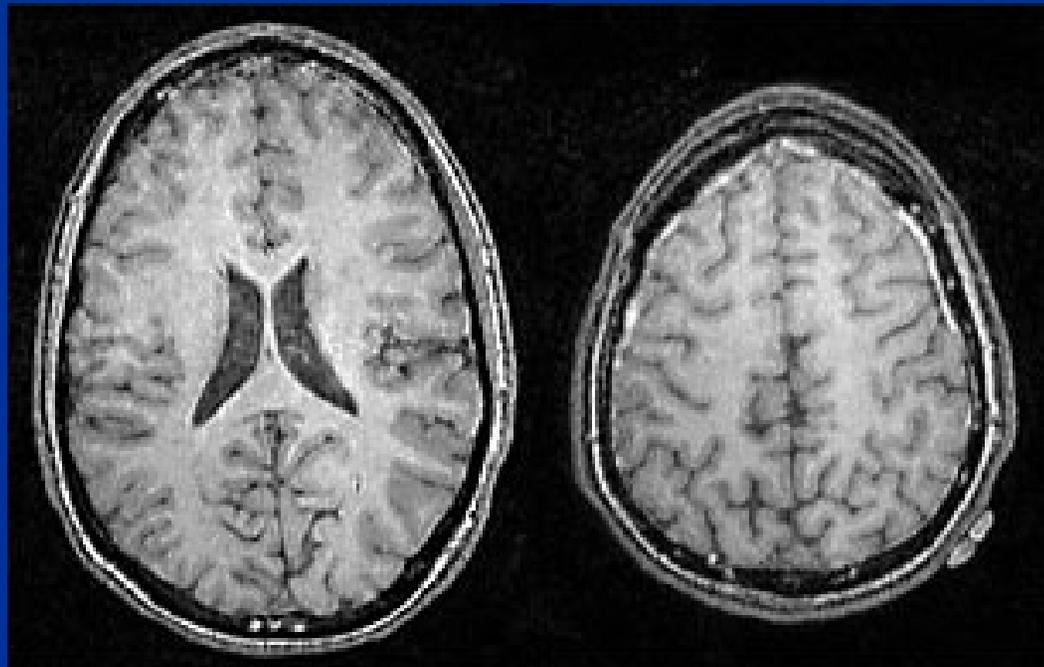
Laboratory evaluation: Evidence-based

- Lead, thyroid, blood count, iron, CO2
- Chromosomes & Fragile X, blood chemistry panel, urine organic acids & plasma amino acids, other.
- Avoid Non-evidence based, for-profit labs.



Other Diagnostic Tests at discretion of Medical Specialists

- EEG
- MRI
- Sleep lab
study



Risk of Co-Morbid Conditions in Autism

- Mental Retardation
 - Eating/GI disorders
 - Seizures
 - Sleep disorders
 - Psychiatric
 - Other
- The disability and co-morbid conditions are motivators for parents to be tempted by advertised, unproven tests & treatments.

Pharmacologic Treatment of Co-Morbidities Need More Study

- Stimulants (e.g. Ritalin); Strattera for ADD/ADHD symptoms.
- SSRIs (Prozac, Paxil, Zoloft, Celexa, etc.) for anxiety; panic attacks; depression).
- Antipsychotics like Risperdal or Abilify for aggressive & self-injurious behavior, psychosis.

Risperidone (Risperdal)

- FDA gave recent official approval.
- Used for > 10 years to treat aggression in autism but risk of diabetes/movement disorders
- **NEJM study** 8/1/2002: 82 boys, 19 girls ages 5-17: 69% showed marked improvement in aggression vs. 12% in placebo group: highly statistically significant. Single most effective medication study ever in autism.

Susan Levy M.D. & Susan Hyman M.D.

- *Pediatric Annals* 32:10. 685-691. 2005
“Use of Complementary and Alternative Treatments for Children with Autistic Spectrum Disorders is Increasing”.
- * *Contemporary Pediatrics*. October 1, 2000
“Autistic Spectrum Disorders: When traditional medicine is not enough”

Scientific approaches:

- Medical, pharmacologic & epidemiologic studies seek large sample sizes for statistical significance & randomized, double-blind, placebo controlled trials (GOLD STANDARD).
- Behavior Analysis uses other scientific research designs: Single subject design with reversal or multiple baseline.

For researching medical interventions:

- Evidence-based, scientific principles
 - Standard diagnosis critical.
(cognitive/behavioral/adaptive skill measures; ADOS, ADI-R, DSM-IV TR criteria).
 - All experimental subjects have same treatment exposure.
 - Standardized tests to measure outcomes.
 - Randomized/placebo-controlled trials.

Hierarchy of quality of evidence: Medical & Pharmacologic Studies

- Meta-analysis of multiple Randomized Clinical Trials (RCTs) in people
- Randomized, double-blind/ placebo-controlled trials in people.
- Single blind trial/other research designs.
- Open label trial
- Animal models
- Anecdotal/testimonial

Unproven Medical Interventions: CAM



Complementary and Alternative Medical Treatments (CAM):

- “Strategies that have not met the standards of clinical effectiveness, either through randomized controlled clinical trials or through the consensus of the biomedical community” (AAP, 2001)
- Strategies not scientifically evidence-based.

ASD Guidelines for Effective Intervention

- California Dept. Dev. Services (DDS) project to publish evidence-based guidelines for effective interventions for ASD.
- Collaboration with the National Standards Project (Susan Wilczynski Ph.D. BCBA, Director): www.nationalautismcenter.org.
- Evidence-Base for Pharmacologic and CAM treatments in ASD: Lynne Huffman M.D.

Evidence-Base for Pharmacology

Evidence-Base for CAM

- DDS Guidelines Project: Structured, systematic review of scientific research with common elements. Pharm/CAM section directed by Lynne Huffman M.D.'s team at Stanford.
- Criteria for scientific studies included/excluded: ASD studies ages 0-22 published in peer-reviewed journals 1994-2007; single subject research included. 835 studies found; 109 studies met inclusion criteria; 726 excluded from review.

109 Scientific Papers: Full Review

Results Pending

- 85 studies on Pharmacologic therapy.
- 24 studies on CAM therapy: 7 on Vitamins, 6 on Whole Diet, 5 on Proteins & Amino Acids, 1 on Fatty Acids, 1 on Minerals, 1 on Chelation, 1 on HBOT, 2 on “mind-body medicine”.
- Excluded editorials, comments, letters, reviews, if had only 1 adult subject, if not on treatment, if no human subjects or not in English.

Atypical Antipsychotics: Effect on Social Interaction

- Scientific Quality Scores from 0 (unsatisfactory) to 5 (Rigorous).
- No studies scored 5 (Rigorous). 2 studies scored 4 (solid) and of these, 0 showed significant improvement.
- 4 studies scored 3 (Adequate). 2 of 4 showed significant improvement in social interaction.

Poison Risks

- Dietary supplements carry risk of injury & death.
- Children particularly vulnerable.
- American Association of Poison Control Centers annual data.
- Poisonings from vitamins, minerals, essential oils and dietary supplements has increased 9 fold since 1983. The supplements linked to the most reactions in 2005 were Vitamins.

Non-conventional Treatments:

- Categorize by proposed action on:
 - 1. Neurotransmitters.
 - 2. G.I. function.
 - 3. Immunologic system.
 - 4. “Detoxifying”.

Neurotransmitter Function:

- 1. Vitamin B6 & Magnesium; Vitamin B12
- 2. Vitamin C: risk of kidney stones
- 3. DMG/TMG : Pantethenic acid food supplement: dimethyl or trimethyl glycine.
- 4. Omega-3, fish oils, other essential fatty acids.

Neurotransmitters: Vitamin B6 & Magnesium

- 14 studies : “Success” in improving attention span or language in autistic kids, BUT:
- Scientific Cochrane review concluded existing studies NOT adequate to show efficacy due to significant design flaws; inability to rule out alternative explanations (Nye C, Brice A. *Cochrane Database Syst. Rev.* 2000;(4):CD003497).

Vitamin B6 & Magnesium:

- 1. Most Frequent Doses:
 - 30 mg/kg/day Vitamin B6.
 - 10 mg/kg/day Magnesium.
- 2. Two double-blind/placebo-controlled studies did not show positive effect.
- 3. Side effects: hand numbness and tingling.

DMG/TMG

- Pantethenic acid : prior marketing as Vitamin B 15; Now as DiMethylGlycine (DMG).
- Russian study showed increased expressive language skills in DD children (not clear how expressive language was measured).
- Recent small, double-blind study: Negative results in autistic boys treated with modest doses. Hyperactivity side effect in 1 boy.

Changes in G.I. Function:

- 1. Gluten-free/casein-free diet.
- 2. Pepcid antacid- No efficacy studies
- 3. Secretin.
- 4. Probiotic agents that change gut flora.
 - acidophilus; lactobacillus.



Changes in G.I. Function:

- Gluten-free/casein-free diet:

Wheat-free & Milk-free

Hypothesis of increased intestinal permeability: increased absorption of morphine-like compounds from gluten and casein lead to autistic symptoms. NOT PROVEN.

Guidelines Project: Whole Diets (Preliminary Results)

- No studies given a scientific quality score of 5 (rigorous) or 4 (solid).
- Only 1 study had quality score of 3 (adequate). This study failed to show significant improvement for ASD subjects in their social interaction with special diet.

Changes in G.I. Function:

United Kingdom General Practice Database did not show higher incidence of GI problems in autism than in general population.

Gluten/Casein-free diet studies

- Whitely et. al. *Autism*. 1999; 3:45-65. small case series reporting improvement in autistic children over time.
- Knivsberg et. al. *Nutritional Neuroscience* 2002; 5(4):251-261. randomized trial showed subjective improvement (parents aware of dietary status of child): Open label trial. No standardized measurement of behavioral change
- Sponheim. E. *Tidsskr Nor Laegeforen* 1991;111(6):704-707: Gluten-free diet not effective.

Gluten/Casein-free diet studies

- Studies did NOT address issues of maturation/other interventions as confounding factors.
- Counsel family on nutritional risks & dietary sufficiency; risk of inducing eating disorder.
- Need other sources of calcium/Vitamin D.
- soy, rice or potato substitutes for milk products may decrease protein intake.

GI function: continued

- Secretin: UC Davis MIND Institute study and others (more than 10) showed no efficacy. (Susan Levy M.D. conducted one of these studies).

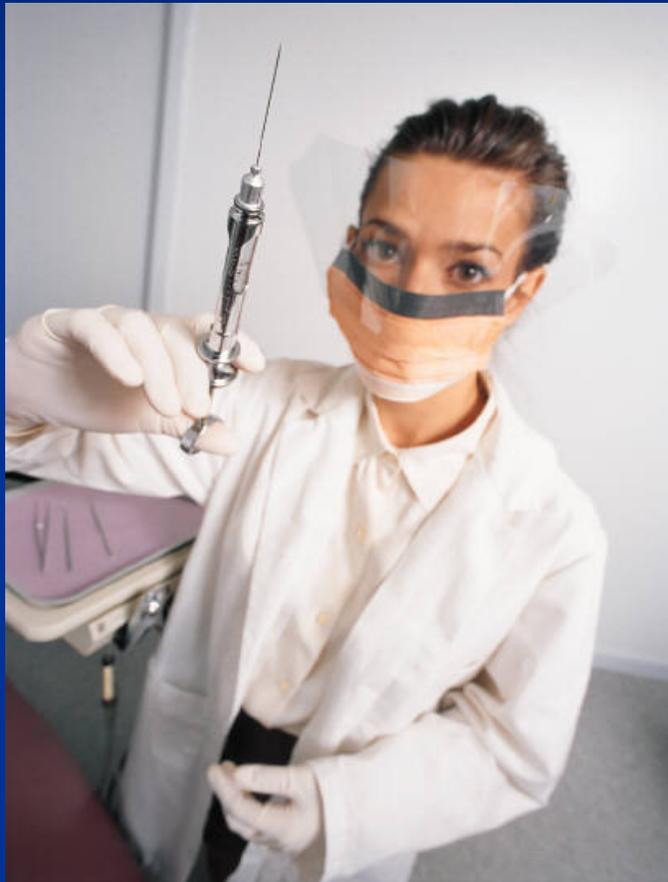
Immune system Modulation:

- 1. Antibiotic/Antifungal treatments :lack of outcome measures; toxic side effects, drug resistant bacteria: Sandler et. al. J Child Neurology, 2000) / Nystatin or Fluconazole to decrease gut yeast-No controlled trials.
- 2. Intravenous Immunoglobulin (IVIG).
- 3. Vitamin A (risk of toxic dosing)
- 4. Withholding/altering Immunizations.

Intravenous Immunoglobulin (IVIG)

- Indirect evidence of immune system changes in autism.
- IVIG : a plasma-derived product used to treat severe neurologic disorders of presumed immune origin (e.g. MS, Kawasaki Disease).
- Open-trial treatment noted subjective plus other improvements across a range of measures but was not standardized or compared to a control group.

IVIIG: continued:



- Small risk of aseptic meningitis, kidney failure, infection.
- Costly, in short supply & needed for proven efficacy in life-threatening diseases (Kawasaki Disease).
- No double-blind, placebo-controlled trials done yet in autism.

Vitamin A

- Vitamin A for 3rd-world children with diarrhea is standard care.
- Vitamin A facilitates immune response by modulation of G-protein function in cell membranes.
- Autistic children may have extended immune system response to Measles: a possible immune abnormality in G-protein function but no data on latter.

Vitamin A: continued:

- Proponents use Cod liver oil as source.
- Toxicity from excess Vitamin A: skin rash, liver enlargement & damage; increased pressure in brain.

Vitamin A: continued

- > 6,000 Retinol equivalents (RE) per day for >1 to 2 months: high toxicity risk. (Cod liver oil may be > 5000 REs per teaspoon)
- 3 year old autistic boy at UCDCMC with severe fatigue, swelling of hands and feet & distended belly with enlarged liver/liver failure.



Need for Informed Consent!

- Physician never informed parents about risks of Vitamin A toxicity.
- Parents didn't read the labels of all the products given to child, several of which contained Vitamin A.
- Set up for severe Vitamin A toxicity.



Withholding Immunizations: An idea with no data to support it!



- Is Immune system overwhelmed by exposure to multiple foreign substances?
- No data on this hypothesis!

Immunizations/MMR continued:

- Epidemiologic studies have not confirmed link between MMR & autism. (Stratton, et. al. , Editors: *Immunization Safety Review*. Washington, DC; Institute of Medicine, National Academies Press: 2000; Fombonne & Chakrabarti: *Pediatrics* 2001; 108(4))
- Theoretical concern: Measles has predilection for temporal lobes and abnormal anti-brain Measles antibodies have been reported in a small number of autistic children (Singh & Lin *J. Biomed. Sci* 2002 9 (4): 359-364). Replication studies are needed to better understand this.

“No Evidence for a New Variant of MMR-Induced Autism”

- Article by Eric Fombonne & Suniti Chakrabarti.

Pediatrics 2001; 108 (4). Located on the web at:
<http://www.pediatrics.org/cgi/content/full/108/4/e58>

Results refute hypothesis of a link between MMR vaccine and a regressive form of autism with GI symptoms supposedly occurring shortly after immunization.

Accumulating large-scale epidemiologic studies all fail to support an association between MMR and autism at a population level.

Immunizations: continued:

- “Overwhelmed immune system” hypothesis:
So withhold immunizations or splitting doses
into separate aliquots? : NOT evidence-based.
- Thimerosal was never in live virus vaccines
(MMR) and was removed from DPT, Hib and
Hepatitis vaccines ~ 1999-2000.

Thimerosal removed from vaccines in 1999-2000, but no definite decrease in prevalence of autism (appears to be increasing by ~17% per year) in some studies; in other studies rate has stabilized but remains high.

Thimerosal

- Thimerosal is a neurotoxin.
- Association and correlation do not prove causation; only guide toward what should be scientifically studied.
- CDC funds multiple studies on thimerosal related to autism & development:
Kaiser/UC Davis MIND Institute Studies.

Toxin Removal

- 1. Chelation for Mercury, Lead, other Heavy Metals.
- 2. Detoxification



Toxin Removal : Chelation

- Chelation for heavy-metal poisoning:
- Known to be effective for lead poisoning;
- Proposed in autism due to some similarities between mercury toxicity and autism.
- Evidence mostly circumstantial.

Chelating Agents:

- Lead study-children; mercury-adults.
- No other double-blind/placebo-controlled studies to support chelation specifically in autistic children.
- Toxicity: kidney & liver; essential mineral depletion, seizures, severe allergic reactions.

Side Effects of Chelation Therapy

- Recent Environmental Health Perspectives study (Strupp, B. et al., Cornell University) shows harmful effects of chelation in rats.
- Increased learning & behavior problems from chelation with succimer (Chemet) noted in lead-free rats.
- One death in 5 year old boy given I.V. chelation treatment for autism.

Detoxification

- Proposal: Autistic children do not fully process tylenol or chemicals in certain fruits/veggies, so need special diet/baths.
- N-dimethylglycine= pangamic acid or Epsom salt baths to detoxify chemicals containing sulfur and cysteine.
- No controlled trials on above. Epsom salt risk of magnesium toxicity.

Hyperbaric Oxygen Treatment

- **HBOT**

- Publication in Medical Hypotheses, 2006; 67(2):216-218. March 22, 2006. “Hyperbaric Oxygen Therapy may improve symptoms in autistic children”.
- Hypothesis based on research showing decreased brain blood flow and brain inflammation in autism.

HBOT

- No current data on the use of HBOT for the treatment of developmental disorders.
- Now registered with NIH : An Open Label, Uncontrolled, Single group treatment study.
- Currently recruiting: Ages 2 to 10 with Autism, PDD or Asperger (n=30) at CAM treatment center (phase I clinical trial).
- Subjects: +/- receive behavioral intervention as confound. Primary outcome measure not clearly specified. Design Flaws!!!!!!

HBOT Challenges & Side Effects

- Claustrophobia; initial treatment compliance.
- Aggravation of ear and sinus infections.
- Fire hazard
- Expensive



Above all, Do No
HARM!!!!!!

Parent training in science &
critical thinking

Genetic Inheritance + Environmental Exposure

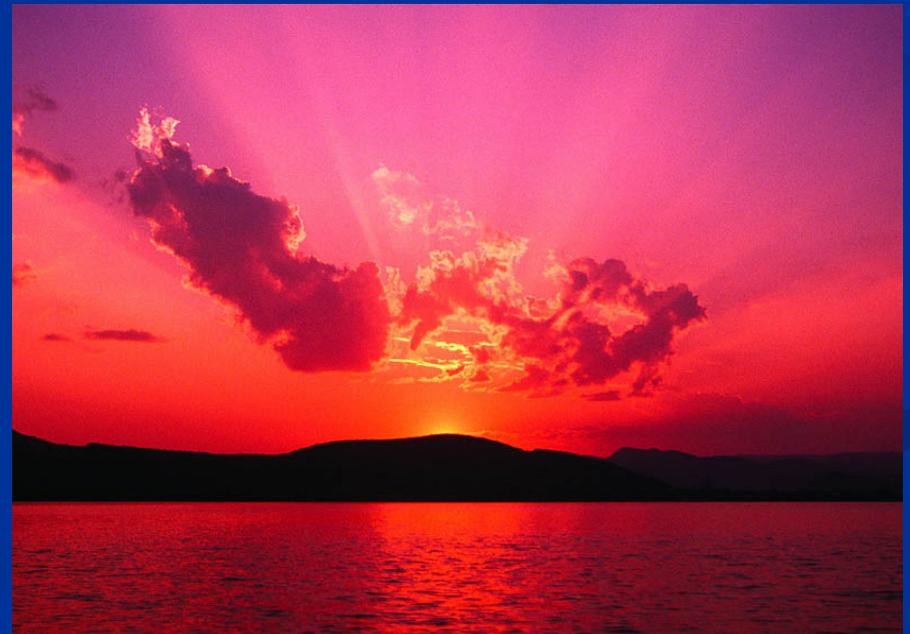
- We inherit gene-environment relationships.
- Human genetics changes slowly over generations: If recent increase in ASD is real, suggests environmental exposure as key to causation, in genetically susceptible individuals.

Newer prevalence surveys (slide from Eric Fombonne M.D.)

	Autism				PDD + AS			All PDD
	Age	rate/ 10,000	M/F ratio	% IQ normal	rate/ 10,000	M/F	% IQ normal	rate/ 10,000
<ul style="list-style-type: none"> ■ CDC, ■ 2000 	3-10	40.5	2.2	37	27.0	3.7	51	67.5
<ul style="list-style-type: none"> ■ Baird et al, ■ 2000 	7	30.8	15.7	60	27.1	4.5	-	57.9
<ul style="list-style-type: none"> ■ Chakrabarti ■ & Fombonne ■ 2001 	4-7	16.8	3.3	29	44.5	4.3	94	61.3

Gene Environment Relations

- Selection by consequences:
Galapagos Islands



- What are the possible Environmental Toxins or Exposures?

CHARGE Study

- **C**hild**H**ood **A**utism **R**isks from **G**enes and the **E**nvironment.
- Federally-funded epidemiologic study: UC Davis M.I.N.D. Institute, Kaiser & California Developmental Regional Centers.
- Environmental exposures of mother & child: Diet, Vaccines, Household Chemicals (**PBDEs**), Other.

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Thank you!

