

A Comprehensive Approach to Treating Autism and Attention-Deficit Hyperactivity Disorder: A Pre-pilot Study

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ABSTRACT

Objectives: The purpose of this study was to observe the effects of a multi dimensional treatment plan involving nutrition, environmental control, chelation, and behavioral/educational/physical/speech therapy to treat children with autistic spectrum disorder and attention-deficit hyperactivity (ADHD) disorder. This study is only a preliminary study, and its small size (10 patients) precludes statistical analysis of simultaneous multiple modal treatment regimes.

Design: This was an open-label observational study.

Settings/location/subjects: This study examined 10 children aged 4–10 years old who had been diagnosed with both autistic spectrum disorder and ADHD by outside physicians or psychologists. These 10 children presented consecutively in an environmental medicine clinic in Buffalo, New York. The children were given comprehensive nutritional/environmental/chelation treatment for 3 to 6 months in addition to their usual behavioral, educational, speech, and physical therapies.

Outcome measures: Study outcomes were measured by objective/subjective improvement as judged by physicians/parents/teachers. Outcomes were also measured by changes in urinary heavy metal burdens over time.

Results: All 10 children showed significant improvement in many areas of social interaction, concentration, writing, language, and behavior. Urinary lead burden dropped significantly in all 10 children.

Conclusions: Autistic spectrum disorders and ADHD are complicated conditions that probably require multidimensional treatment strategies. Larger studies are needed to determine optimum treatment plans involving nutrition, environmental control, medication, and behavioral/education/speech/physical therapies.

INTRODUCTION

Autism is a chronic disorder with onset before 3 years of age, which presents with a wide range of behavioral, social, and language problems.^{1–3} The recent total prevalence of autism, Asperger's syndrome, and related developmental disorders is estimated at between 40 and 60 per 10,000 children.⁴ Attention-deficit hyperactivity disorder (ADHD) is a very common condition affecting 8%–12% of children worldwide.⁵ About 40%–80% of autistic spectrum children also have ADHD as a comorbid disorder.^{6–9} Autism

and ADHD also are known to affect many adults, although there are few prevalence studies of these disorders in adults. Interviews with 3199 randomly selected U.S. adults ages 18–44 years found an ADHD prevalence rate of about 4.4%.¹⁰

Many approaches have been tried to treat autism. Many studies have reported that behavioral therapy and pharmacotherapy are often moderately helpful for many children on the autistic spectrum.^{11–13} Intensive behavioral interventions beginning at an early age seem to have considerable future promise in treating autism.¹² However, most current

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behavioral and pharmacotherapies usually produce only a partial improvement in autistic symptoms and behaviors.^{12,14} Autistic spectrum disorders are complicated conditions that may require an integrative treatment protocol involving many factors including behavioral and social therapy, pharmacotherapy, environmental control, and nutritional therapy.¹⁴

Likewise, ADHD is a multifactorial disorder that is usually treated with stimulants and other medications plus behavioral/educational therapy.^{15–17} A recent review of a wide range of treatments for ADHD found that many, but not all, studies reported that combinations of both psychosocial interventions and medications produced superior results than either intervention alone.¹⁸ Current ADHD treatments usually produce only partial benefits, and development of better multidimensional treatment protocols are clearly needed.^{17,19,20}

A review by the same authors has summarized previous research on the environmental and nutritional factors relating to autism and ADHD.* This study examined 10 children who all had a diagnosis of autism or Asperger's syndrome and all also had a diagnosis of ADHD. The patients were all given detailed history taking, physical examinations, and series of laboratory tests. The patients then were entered into a comprehensive multidimensional treatment program, which included behavioral treatments (physical/speech/occupational therapy, special education), environmental control, chelation therapy, immunotherapy, a good organic rotary diet (a diet in which specific foods are consumed only 1 day out of 4 days), and broad-based nutritional supplementation. None of the children were on stimulant medication during the study period.

It should be emphasized that this study was not a definitive study but only a preliminary study. The sample size of 10 patients precludes statistical analysis of the multiple treatment modalities for autism and ADHD. Larger, well-funded studies are needed to sort out which of the various treatment modalities produce statistically significant improvement. It is hoped that this study will provide a starting point for larger studies of multiple mode treatments for autism and ADHD.

METHODS

Patient selection and demographics

A total of 10 patients with a diagnosis of autism/Asperger's disorder and ADHD were chosen from patients at a busy environmental medicine/pediatric clinic. All 10 of these patients had earlier received diagnoses of both autism/Asperger's disorder and ADHD by institutions, neurologists, or developmental physicians. None of the patients were taking any psychotropic medicine (such as stimulants

or antidepressants) during the course of the study. The demographic and clinical characteristics of the patients are presented below in Table 1.

Multidimensional treatment protocol

Patients were treated for a total of 3–6 months. Treatment was multidimensional and included:

1. *Environmental control and avoidance of triggers.* This included extensive instruction to the parents including mite control, moisture/mold control, avoidance of tobacco smoke and pesticides, and use of less toxic cosmetics and cleaners. Inspection for lead paint and remediation if indicated was suggested for homes over 30 years old.
2. *An organic diet, which was rotated over a 4-day cycle.* This diet was low in refined sugar and free of food additives, salicylates, and artificial coloring. The diet was also free of casein and/or gluten in patients who had sensitivity to these proteins.
3. *Gastrointestinal support.* This included digestive enzymes, probiotics, and Tricycline (Nutricology Labs, Alameda, CA) supplement (Tricycline contains berberine, artemisinin, citrus extract, and walnut hulls) to improve leaky gut.
4. *Antigen injection therapy.* This was to address dust mite allergens, molds, foods, and chemicals.
5. *Nutritional supplements.* This included vitamins (A, B-complex), minerals (calcium, magnesium, manganese, zinc, molybdenum, selenium, iron), amino acids and peptides (glutathione, *N*-acetyl cysteine, taurine, glycine, glutamine, *S*-adenosyl methionine), omega 3/6 fatty acids, milk thistle, coenzyme Q10, α -lipoic acid, digestive enzymes, and probiotic bacteria.

TABLE 1. CHARACTERISTICS OF THE 10 PATIENTS

<i>Characteristics</i>	<i>Result: number of patients</i>
Demographics	
Patient selection	Random (10)
Age	4–10 years (10 patients; mean 5.9 years)
Gender	9 male/1 female
Mean age at diagnosis	3 years (10)
Age first seen by environmental physician	5–8 years (10)
Diagnosis	
Autism/PDD	5/10
Asperger's syndrome	5/10
Speech delay	10 (expressive speech delay 2/10)
Verbal problems	8/10
ADHD	10/10
Aggressive behavior	3/10 (hitting, biting)
Neurologic problems	3/10
Seizure history	1/10 (Febrile)
Housing	
House 70+ years old	6/10

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PDD, pervasive developmental disorder; ADHD, attention-deficit hyperactivity disorder.

6. *Chelation therapy.* This included intravenous chelation with calcium EDTA, DMPS (2,3-dimercaptopropane-1-sulfonate) and glutathione once or twice weekly for a total of 10–20 treatments. Also included were transdermal DMPS, glutathione ± TTFD (thiamine tetrahydro furfuryl disulfide), and oral DMSA (2,3 dimercaptosuccinic acid)/glutathione/α-lipoic acid.
7. *Injections 1–3 times per week with glutathione and methylcobalamin (vitamin B₁₂).* This was dosed 0.10–0.25 mL of a solution containing 10,000 units methylcobalamin and 100 mg of glutathione per mL.
8. *Usual therapies.* All 10 patients continued their usual behavioral/educational therapies, including special education, speech therapy, occupational therapy, and physical therapy.

Clinical and laboratory analysis

Detailed assessments of motor, behavioral, and educational capabilities were made by parents, teachers, and the physician both before and after the 3–6-month multifactorial treatment. Such assessments included both subjective ratings and records of each child’s ability to perform motor, social, and academic

tasks. Subjective changes in symptoms of autism and ADHD (improvement or deterioration) were measured by a questionnaire completed by the parents of the children before and after the 3–6-month multidimensional treatment.

Urinary metals were tested by the postprovocation inductively coupled plasma mass spectrometry (ICP-MS) method by Doctor’s Data (St. Charles, IL). Organic acid analysis was performed by MetaMetrix Labs (Norcross, GA). Other laboratory data were gathered via standard laboratory techniques.

Statistical analysis

Statistical analysis of urinary metal concentrations before and after treatment were made by using a paired *t*-test (2-tailed) on the Statistical Program for Social Sciences (SPSS) 6.1 Software (SPSS Inc., Chicago, IL).

RESULTS

Results are presented below in Table 2 (histories, review of systems, and physical examinations), Table 3 (laboratory

TABLE 2. PAST HISTORIES, REVIEW OF SYSTEMS, AND PHYSICAL EXAMINATIONS

<i>Characteristics</i>	<i>Number of patients</i>
Past histories	
MMR vaccine (with thimerosal)	2/10
Allergic rhinitis/asthma	10/10
Infantile colic	3/10
Milk/milk formula intolerance	2/10
Recurrent respiratory/ear infections	5/10
Chronic constipation	5/10
Chronic diarrhea	4/10
Developmental disorders	
Autism	5/10
Asperger’s syndrome (high-functioning autism)	5/10
Attention-deficit hyperactivity disorder	8/10
Attention-deficit disorder (with inattention)	10/10
Systems review	
Atopic dermatitis/eczema	5/10
Head banging/headache	2/20
Itchy eyes, dark circles, allergic “shiners”	8/10
Ear infections/clucking throat sounds	5/10
Nasal symptoms	8/10
Asthma	4/10
“Picky” eating habits, abdominal pain, bloating–gas, chronic constipation or diarrhea	9/10
Physical examinations	
Poor eye contact	10/10
Dark circles under eyes	8/10
Allergic “shiners”	7/10
Nasal mucosal membranes, swollen, boggy and inflamed	8/10
Low peak respiratory flow	4/10
Abdomen, bloated	9/10
Neurologic, poor concentration, repetitive or stereotyped movements	10/10
Global developmental delay	2/10
Low to minimal speech	2/10

MMR, measles, mumps, rubella.

TABLE 3. LABORATORY RESULTS

<i>Test</i>	<i>Number of patients testing positive</i>
Blood	
Low hemoglobin	2/10
Increased serum eosinophils	3/10
Low T ₄ cells	2/6
Low T ₈ cells	3/6
Low natural killer cell activity	2/2
Low Iga and high IgE	3/4
Toxic metals	
Urine—high levels of lead, mercury, cadmium, and nickel	10/10
Hair—high levels of lead, mercury, tin, and arsenic	2/3
Ion panel	
Fasting plasma amino acids decreased	4/4
Red blood cell zinc low	7/7
Red blood cell magnesium low	4/7
Red blood cell selenium low	2/10
Vitamin A/beta carotene/vitamin E/coenzyme Q10 low	2/4
Omega 3 low	3/6
Abnormal detoxification markers (organic acid panel)	4/4
Intestinal dysbiosis	4/4
Biotin low	2/4
Vitamin B ₆ , B ₁₂ , folate low	3/4
IgG ₁₋₄ -90 Food allergen test positive	8/10
High level urine caserorphine	2/4
High level urine gliadorphine	3/4

Ig, immunoglobulin.

results), Table 4 (intradermal testing results), and Table 5 (urinary levels of metals before and after treatment). Note the significant ($p < 0.001$) drop in urinary lead levels following treatment as well as statistically marginal drops in urinary cadmium and mercury levels. Table 6 displays behavioral, motor, and educational improvements after 3 months of treatment. Figure 1 shows the dramatic drop in urinary lead levels seen in all 10 patients. The results of the parental questionnaire study showed an average improvement of $70 \pm 19\%$ in concentration and attention problems (range 40%–100%) and an average $46 \pm 31\%$ decrease of hyperactivity-related problems (range 0%–95% improvement).

TABLE 4. INTRADERMAL TESTING RESULTS

<i>Test</i>	<i>Number of patients testing positive</i>
Neurotransmitters—histamine, serotonin, acetylcholine, dopamine, <i>N</i> -epinephrine	8/8
Inhalants—dust mites and molds	8/8
Inhalants—Pollens	6/8
Chemicals—ethanol, phenol, perfumes, chlorine	4/4
Foods—soy, eggs, rice, potatoes, beans, apples, bananas, peanuts, etc.	8/8

DISCUSSION

The 10 patients in this study with autism/Asperger's syndrome and ADHD had high urinary levels of lead in the presence of many nutritional and detoxification deficiencies. All 10 of these patients had serious deficits in educational, social, verbal, and motor abilities. In addition, abnormal immune functions, gastrointestinal (GI) symptoms, and allergies to many foods, inhalants, and chemicals were also seen in these patients.

This study found that a broad-based program of environmental control, immunotherapy, chelation, and comprehensive nutritional treatments were associated with both significant reductions in urinary lead levels and significant clinical improvements in all 10 children with autism and ADHD. Especially encouraging was the fact that there was some improvement in behavior, social skills, motor skills, and GI symptoms in all 10 children (Table 6). Four (4) of the children were able to return to regular classes from special education (Table 6). Verbal skills improved dramatically in the 8 patients who had some verbal skills prior to the comprehensive 3–6-month treatment (Table 6).

As noted above, the use of improved diets and/or nutritional supplements have been shown to be somewhat helpful to many children with autistic spectrum and/or ADHD. Use of alternative and complementary diet therapy is very common practice in patients with autistic spectrum disorder.

TABLE 5. LEVELS OF URINARY HEAVY METALS BEFORE AND AFTER 3–6 MONTHS OF COMPREHENSIVE TREATMENT (ALL 10 PATIENTS TESTED)

<i>Metal</i>	<i>Before treatment— mean level as µg metal/g creatinine</i>	<i>After treatment— mean level as µg metal/g creatinine</i>	<i>p-Value difference by paired t-test</i>
Aluminum	86.2	35.3	0.104
Arsenic	74.1	51.6	0.191
Cadmium	1.14	0.87	0.083
Lead	48.0	20.3	<0.001
Mercury	16.7	7.3	0.076
Nickel	24.8	14.9	0.185
Tin	18.0	9.0	0.168

Several studies have found that about 30%–50% of autistic spectrum children receive some form of dietary or dietary supplement therapy and about 41%–76% of these children seem to benefit from such therapy.^{21,22} Much more research is needed on nutritional treatments for children with autistic spectrum disorders and ADHD so that effective nutritional therapies can be used and ineffective nutritional therapies discontinued. Doses of supplements used often vary considerably from study to study. Future nutritional work needs to focus more on determining the ideal dosage of nutritional supplements for patients depending upon such factors as size, age, nutritional status, and degree of autism/ADHD problems.

As noted in Table 5, patients undergoing 3–6 months of comprehensive treatment had a large and significant drop in mean urinary lead levels as well as large but statistically insignificant declines in mean urinary mercury, cadmium, and aluminum levels. Published studies that report the effects of chelation therapy and/or environmental control on autism and ADHD are sparse. A case study was presented of a 4-year-old autistic boy with a high blood lead level who im-

proved greatly with succimer chelation therapy and whose autistic symptoms returned when chelation therapy was stopped.²³ Another study of 6 adults with high urine mercury levels found that treatment with oral DMPS (2,3-dimercaptopropane-1-sulfonate) and DMSA, coupled with intravenous glutathione/vitamins/minerals, significantly reduced urinary mercury levels.²⁴ Some studies have reported that home remediation of lead paint can produce modest reductions in blood lead levels in children.²⁵ Much more study on the possible health benefits of improved environmental control and/or chelation on autistic spectrum/ADHD patients is needed.

A weakness of our study was that the patient group was small (10) and did not contain a control group. To analyze the possible effects of all of the individual diet, supplementation, chelation, and environmental interventions would require a large study with 100s or 1000s of children. Such a

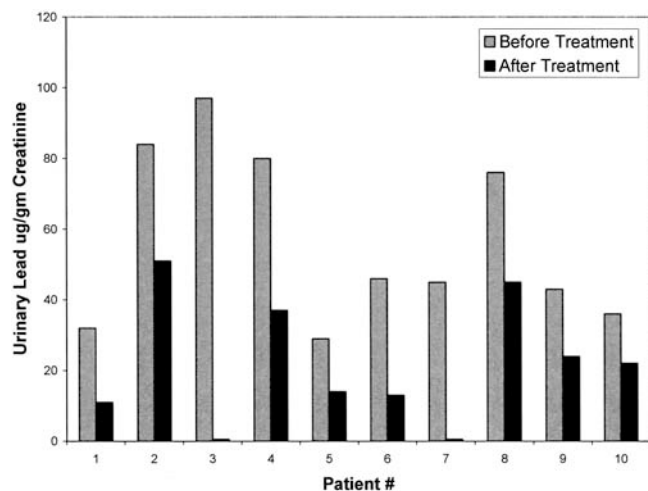


FIG. 1. Urinary lead levels before and after 3–6 months of multidimensional treatment.

TABLE 6. BEHAVIORAL, MOTOR, AND EDUCATIONAL IMPROVEMENTS AFTER 3–6 MONTHS OF MULTIDIMENSIONAL TREATMENT

<i>Characteristics</i>	<i>Number of patients</i>
Improved eye contact and social interaction	10/10
Improved focusing and concentration	10/10
Reduction in stereotyped tactile activities	10/10
Reduced respiratory infections and otitis media	4/4
Improved writing, drawing, expression, and initiating play activity	10/10
Improvements in expressive language	8/10
Reduction in adverse GI symptoms such as gas, bloating, pain, diarrhea, constipation	10/10
Reduction in ADHD symptoms	7/10
Improved cooperativeness	9/10
Reduced behavior problems	9/10
Reduced tactile/auditory sensitivity	6/10
Reduction in total urinary heavy metal levels in provocation tests	10/10
Returned to regular class	4/10

GI, gastrointestinal; ADHD, attention-deficit hyperactivity disorder.

large study would probably require considerable outside funding to conduct.

Another weakness of this study and many other published autism studies is that they were not performed in a double-blind manner. Few randomized controlled treatments of autism have been made to date.^{12,26,27} Development of double-blind studies are particularly difficult if multiple treatment modes (such as drugs, nutrition, behavioral, and environmental interventions) are employed. Another possible shortcoming of this study is that blood nutrient analyses were not performed on all patients due to lack of outside funding for the study.

All 10 patients in this study had a dual diagnosis of both autistic spectrum and ADHD. For future studies of multimodal treatment, it would be interesting to have several patient groups including patients with a single diagnosis of autistic spectrum or ADHD, as well as patients with dual diagnosis. Better diagnosis of patients with single or dual diagnosis of autistic spectrum and/or ADHD may lead to better multimodal treatment plans.⁹

This study involved a parental before-and-after questionnaire of autism/ADHD symptoms. Future studies would do best to use more structured and validated instruments for assessment such as the Gilliam Autism Rating Scale, Autism Diagnostic Observation Schedule Generic, and Autism Diagnostic Interview-Revised for autism²⁸ and the Conners Rating Scales for ADHD symptoms.²⁹

CONCLUSIONS

Both autism and ADHD appear to involve a broad range of genetic, prenatal, social, developmental, nutritional, and environmental factors, and it is unlikely that only one single cause will be found for either disorder.^{14,20,30-32} Future studies of autism etiology should concentrate on a variety of genetic and environmental factors. Recently, a California study has begun that will examine 360 autistic children for such multiple factors as genotypes, immunology, and many types of chemical and biological exposures.³¹ Several other studies are currently under way that are studying the effects of genetic and prenatal and postnatal environmental exposures and the development of autism.³³ Future autism treatment will probably require many different interventions per patient. Therefore, large, well-controlled studies of multiple interventions for autism (behavioral and social therapy, drugs, nutrition, environmental control) are needed in order to develop better treatment protocols. Additional studies employing multidimensional treatment for ADHD are also needed.^{16,20}

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