Summary of Biomedical Treatments for Autism

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Overview

This document is intended to provide a simple summary of the major biomedical treatments available to help children and adults with autism/Asperger's. Biomedical treatments will not help every child, but they have helped thousands of children improve, sometimes dramatically.

This summary is primarily based on the excellent book "Autism: Effective Biomedical Treatments" by Jon Pangborn, Ph.D., and Sidney Baker, MD,. published by the Autism Research Institute. That book provides much more depth on the testing and treatments which are briefly summarized in this document. Another good source of information is "Children with Starving Brains," by Jaquelyn McCandless, MD. After reading this document, it is highly recommended that you go to those sources for more information.

This summary generally follows the DAN! philosophy, which involves trying to treat the underlying causes of the symptoms of autism, based on medical testing, scientific research, and clinical experience, with an emphasis on nutritional interventions. Many of the DAN! treatments have been found by listening to parents and physicians.

ARI Survey of Parent Ratings of Treatment Efficacy

Most of the treatments listed on the following pages were evaluated as part of the Autism Research Institute (ARI) survey of over 23,000 parents on their opinion of the effectiveness of various treatments for children with autism. For a full copy of the latest ARI Survey, see the last page. (For Asperger's see www.autism.com)

Other Interventions:

Behavioral interventions, such as Applied Behavior Analysis (ABA), can also be very helpful to children with autism, and are recommended to be used in conjunction with biomedical treatments. Similarly, speech therapy, sensory integration, physical therapy, occupational therapy, and a good educational program can be very important. Finally, social interventions (such as Relationship Development Intervention) and social groups can be very helpful in building social relationships and skills. Biomedical therapy may help improve the efficacy of these other interventions, by improving brain and body health and making it easier for the child to learn.

Note about Author: James Adams is a professor at ASU researching the biological causes of autism and how to treat it. His research has included studies of vitamins, minerals, essential fatty acids, amino acids, neurotransmitters, heavy metal toxicity, detoxification, gastrointestinal bacteria, immune system regulation, and sleep disorders in children and adults with autism. He is the lead author of the 2005 DAN! Consensus Report on Treating Mercury Toxicity in Children with Autism, and serves on the Executive Committee of Defeat Autism Now!. He has a Ph.D. in Materials Engineering, but now focuses his research on autism. He is an adjunct professor at Southwest College of Naturopathic Medicine. He is also the President of the Autism Society of America – Greater Phoenix Chapter, and father of a teen-age girl with autism.

Treatment Order:
We have listed the various treatments in approximate order of what is typically recommended, but every child is different, and initial assessment by a physician may suggest a different order. Also, some physicians have their own preferences as to order of treatment. The key point to remember is to observe the effect of each treatment on your child, both behaviorally and through testing where possible.

This Summary includes the following sections:

- Improve Diet
- Food Sensitivities
- GFCF Diet
- Vitamin/Mineral Supplements
- High-Dose Vitamin B6 and Magnesium
- Essential Fatty Acids
- Gut Treatments
    - Antifungals
    - Probiotics
    - Digestive Enzymes
- Amino Acids
- Melatonin
- Thyroid Supplements
- Sulfation
- Glutathione
- Chelation
- Immune System Regulation

Note: This summary is not intended as individual medical advice, and people should consult their physician for how to best treat their individual child. Autism is a spectrum disorder, and a treatment that helps one child may not help others.

Note: This summary represents the personal views of James B. Adams, and does not necessarily represent the views of Arizona State University, Autism Society of America, Defeat Autism Now!, or any other organization.

Acknowledgements

I would like to thank the many DAN! doctors, researchers, parents, and others who have helped provide information on treatments for autism, with special thanks to Jon Pangborn, Ph.D., and Tapan Audhya, Ph.D.

Dedication

This summary is dedicated to the memory of Bernard Rimland, Ph.D., for his pioneering work on autism research and advocacy, and for inspiring many others to follow in his footsteps. Thank you Bernie.

Your Personal Checklist for Biomedical Treatments

Currently Doing It – what effects?	Tried It In Past – what effect?	Considering for Future – any questions?	**Treatments**
			Improve Diet
			Food Sensitivities
			GFCF Diet
			Vitamin/Mineral Supplements (or Juicing)
			High-Dose Vitamin B6 & Magnesium
			Essential Fatty Acids
			Gut Treatments **Antifungals** **Probiotics** **Digestive Enzymes**
			Amino Acids
			Melatonin
			Thyroid Testing/Supplementation
			Sulfation
			Glutathione
			Chelation
			Immune System Regulation

Improving Diet

Rationale: Humans need certain essential nutrients for their bodies to function, including vitamins, minerals, essential fatty acids, and amino acids (from protein). A balanced diet rich in vegetables, fruits, and protein is important to help provide those key nutrients.

Explanation of Diet:

- Consume 3-4 servings of nutritious vegetables and 1-2 servings of fruit each day. (Corn is not a vegetable, it is a grain; potatoes have only limited nutritional value, especially if fried). Fruit juice is less healthy than eating the whole fruit, but better than soda.
- Consume at least 1-2 servings/day of protein (meat, chicken, eggs, nuts, beans). If child shows periods of irritability between protein meals, consider smaller protein snacks given more frequently.
- Greatly reduce or avoid added sugar (soda, candy, etc.).
- Avoid "junk food" – cookies, fried chips, etc. – they contain empty calories.
- Greatly reduce or avoid fried foods or foods containing transfats.
- Avoid artificial colors, artificial flavors, and preservatives.
- If possible, eat organic foods as they do not contain pesticides, and have more nutrients (vitamins and minerals). If eating non-organic food, wash fruit and vegetables well if eating the outside.

Benefits:

- Vegetables and fruits contain essential vitamins, minerals, and phytonutrients to improve and maintain mental and physical health.
- Protein is needed to provide amino acids, which are the building blocks for neurotransmitters and many other key amino acids and proteins in the body.
- Reduction in sugar intake can prevent rapid rises and falls in blood sugar, which can cause irritability and difficulty concentrating.
- Artificial colors and flavors can irritate some sensitive individuals, causing behavioral and other problems.
- Pesticides often contain toxic metals, and are suspected as a possible cause of some cases of autism.

Duration: Lifelong

Research:

ARI Survey of Parent Ratings of Treatment Efficacy:

	% Worse	% No Change	% Better	Number of Reports
Removed Sugar	2%	51%	48%	3695
Feingold Diet	2%	45%	53%	758

For more information, go to: www.feingold.org

Food Sensitivities

Rationale: Many children with autism have food sensitivities, due to abnormalities in their digestive and/or immune systems. If food is not fully-digested into individual sugars, amino acids, etc., then the partly digested food can pass from the gastrointestinal tract into the bloodstream, especially if the child has a "leaky gut" due to inflammation. The immune system recognizes those foods as foreign, and may launch an immune response to those foods, resulting in an allergic response.

Explanation of treatment:

- Avoid allergic foods.
- Consider digestive enzymes to more fully digest foods.
- Consider other methods to heal the gut – many food allergies will disappear when gut inflammation is healed.
- Consider using a 4-day diet rotation, in which a given food is only eaten 1 day every four days, so that there is less likelihood of developing an allergy to it.

Testing:

Some allergic reactions are immediate, and some are delayed by hours or days; the latter are much harder to detect. Some responses are very strong, such as rashes or even anaphylactic shock, whereas other reactions are milder such as headaches or stomachaches.
Testing can include observations, diet log, skin testing, and blood testing.
Observations: Look for red cheeks, red ears, and dark circles under eyes which may indicate allergies. Also look for changes in behavior.
Diet Log: Keep a diet log, and look for a pattern between symptoms and foods eaten in the last 1-3 days.
Blood testing: IgE and IgG testing is offered by many commercial labs. IgE related to an immediate immune response, and IgG relates to a delayed immune response.
Skin testing: less useful than blood testing, as it only checks for immediate response.
All allergy testing is limited, in that IgE tests can be negative even if there are clinical symptoms of food allergy. IgG and IgE tests can be positive but not correlate to a clinical symptom. Use allergy testing to suggest foods to avoid, and then observe the effects.

If you cannot afford or do not wish to do the testing, another option is to try an elimination diet of the most common reactive foods which include gluten (in wheat, rye, barley, possibly oats), dairy, cane sugar, corn, soy, yeast, peanuts, egg, artificial colors and preservatives. If there is improvement, then try challenging the children with one pure food every 4 days, to see if any can be added back in. Gluten and dairy are the last challenged.

Benefits:

Removing allergic foods can result in a wide range of improvements in some children, especially improvements in behavior and attention.

ARI Survey of Parent Ratings of Treatment Efficacy:

	% Worse	% No Change	% Better	Number of Reports
Food Allergy Treatment	3%	37%	61%	560
Rotation Diet	2%	50%	48%	792
Removed Chocolate	2%	49%	49%	1721

Removed Eggs	2%	58%	40%	1096

Duration: Some food allergies (like peanuts) seem to be lifelong, whereas others can disappear when gut inflammation is healed and/or the immune system is normalized.

Research:

A study by Vojdani et al. found that many children with autism have food allergies.
Vojdani A, et al., Immune response to dietary proteins, gliadin and cerebellar peptides in children with autism. Nutr Neurosci. 2004 Jun;7(3):151-61.

There are also 3 studies by Jyonouchi et al, which found that children with autism had more hypersensitivities to food allergens that did typical children, which seemed to contribute to gut problems.
Jyonouchi et al., Dysregulated innate immune responses in young children with autism spectrum disorders: their relationship to gastrointestinal symptoms and dietary intervention. Neuropsychobiology. 2005;51(2):77-85.
Jyonouchi et al., Evaluation of an association between gastrointestinal symptoms and cytokine production against common dietary proteins in children with autism spectrum disorders. J Pediatr. 2005 May;146(5):605-10.
Jyonouchi et al., Innate immunity associated with inflammatory responses and cytokine production against common dietary proteins in patients with autism spectrum disorder. Neuropsychobiology. 2002;46(2):76-84.

A study by Lucarelli et al found that an 8-week diet which avoided allergic foods resulted in benefits in an open study of 36 children. Lucarelli et all, Food allergy and infantile autism. Panminerva Med. 1995 Sep;37(3):137-41.

A study by Kushak and Buie found that children with autism may have low levels and/or underactive digestive enzymes for complex sugars, which reduces the ability to fully digest starches and sugars.

Several studies by Horvath, Wakefield, Buie, and others have demonstrated that gut inflammation is common in autism. This may result in a “leaky gut” that may allow partly-digested food to pass into the blood, potentially causing an allergic response..
Horvath K et al, Gastrointestinal abnormalities in children with autistic disorder,” J. Pediatrics 135 no. 5 (1999) 559-563.
Horvath K and Perman JA “Autistic disorder and gastrointestinal disease,” Curr. Opinion in Pediatrics, 14 (2002) 583.
Wakefield et al., Enterocolitis in children with developmental disorders. Am J Gastroenterol. 2000 Sep;95(9):2285-95.
Kushak R and Buie T “Disaccharidase deficiencies in patients with autistic spectrum disorders,” presented at DAN! New Orleans Jan 2004.

Gluten-Free, Casein-Free Diet (and often corn-free and soy-free)

Rationale: Human digestive systems have not evolved on a diet containing high amounts of wheat and dairy products. Humans are the only animal who drink milk as adults, and the only animal to drink the milk of another animal. Cows milk is a perfect food for baby cows, but not for humans, especially past age of nursing.

Over the last several hundred years, wheat has been bred to greatly increase its gluten content, and a typical US diet contains far higher amounts of wheat than humans were eating 1000-10,000 years ago. Gluten (in wheat, rye, barley, and possibly oats) and casein (in all dairy products, including milk, yogurt, cheese, ice cream, caseinate) can cause two problems:

1. They are common food allergens (see previous section), especially in children and adults with autism.
2. Certain peptides from gluten and casein can bind to opioid-receptors in the brain, and can have a potent effect on behavior (like heroin or morphine), causing problems including sleepiness, giddiness, inattention/"zoning out", and aggressive and self-abusive behavior. Like opioids, they can be highly addictive, and a lack of them can cause severe behaviors.

These problems appear to be due to:

1) A failure of the digestive tract to fully digest the gluten and casein peptides into single amino acids
2) Inflammation of the gut, allowing the gluten and casein peptides to enter the bloodstream and reach opioid receptors in the brain.

Explanation of Treatment:

- Total, 100% avoidance of all gluten products and all dairy products. Even small amounts, like a bite of a cookie, can cause allergic and/or opioid problems. Many foods have trace contamination with gluten, such as dusting French fries and raisins with wheat powder to keep them from sticking, so it can be very difficult to avoid all foods and contaminated foods.
- Digestive enzymes can also be helpful, especially if there is an accidental exposure, but they are probably not as helpful as a total avoidance of casein and gluten.
- Many children with autism also benefit by removing corn and/or soy products.

Benefits:

Children who most crave dairy and/or wheat, and who eat a lot of it, are most likely to benefit. Casein-free diets usually produce benefits within a month, and sometimes within a week. Gluten free diets usually take 1-3 months to produce benefits. In some children there is a worsening of symptoms for a few days (similar to a drug withdrawal) followed by improvement.

ARI Survey of Parent Ratings of Treatment Efficacy:

	% Worse	% No Change	% Better	Number of Reports
Gluten- and Casein-Free Diet	3%	32%	65%	1446
Casein-Free Diet	2%	49%	49%	5574
Wheat-Free Diet	2%	50%	48%	3159

Duration: At least until problems in the gut are addressed, and possibly lifelong.

Safety Note: It is important that a **calcium supplement** be taken while on a dairy-free diet unless a child has an exceptionally nutritious diet rich in calcium.

Testing: There are tests available for allergies to wheat and dairy. However, a negative allergy test does not mean that dairy and wheat are ok, as they can also cause problems due to opioid action. **A trial of avoiding the foods is the best test.**

Research:
Reichelt has conducted several studies which have found abnormal peptides in the urine of people with autism, and he has conducted long-term treatment studies which found significant improvement from a GF/CF diet. Cade found that long-term use of digestive enzymes was beneficial, but that the GFCF diet was even more helpful.

Cade's large study of 150 children with autism found that 87% had IgG antibodies (allergy) to gluten, vs. 1% of the age and gender-matched controls, and 90% had IgG antibodies to casein, vs. 7% of the controls. He also studied 70 autistic children who followed a GFCF diet for 1-8 years, and found that 81% improved significantly by the third month, with improvements continuing over the next 12 months. Large improvements were observed in social isolation, eye contact, mutism, learning skills, hyperactivity, stereotypic activity, and panic attacks. Among the 19% who did not improve, about 1/3 of them were not following the GFCF diet, and had lots of gluten and casein peptides still in their blood. Cade R, Privette M et al. "Autism and Schizophrenia: Intestinal Disorders" Nutr. Neurosci 3 (2000) 57-72. Published by Overseas Publishers Association, (OPA) N.V.

Reichelt et al., Biologically active peptide-containing fractions in schizophrenia and childhood autism.
Adv Biochem Psychopharmacol. 1981;28:627-43. Review.

Knivsberg AM, Reichelt KL, Nodland M. Reports on dietary intervention in autistic disorders. Nutr Neurosci. 2001;4(1):25-37. Review.

Single-blind study of 10 children with autism found that 8 benefitted from a GFCF diet. Knivsberg AM, Reichelt KL, Hoien T, Nodland M. A randomised, controlled study of dietary intervention in autistic syndromes. Nutr Neurosci. 2002 Sep;5(4):251-61.

A 12-week, double-blind, cross-over study of a GFCF diet in 15 children with autism did not find significant benefits, but parents reported benefits that were not identified by the testing. Elder et al, The gluten-free, casein-free diet in autism: results of a preliminary double blind clinical trial. J Autism Dev Disord. 2006 413-420.

Other Diets:
Several other diets are being investigated currently. One alternative diet is the Specific Carbohydrate Diet (SCD), which involves avoiding all carbohydrates and most sugars (except monosaccharides in fruit). For more information on this diet, see www.pecanbread.com

For more information, go to:

Autism Network for Dietary Intervention: www.autismndi.com

Vitamin/Mineral Supplements

Rationale: In order to be classified as a "vitamin" or "essential mineral", many studies were conducted that showed that the lack of that vitamin or mineral resulted in disease or even death. The RDA is the minimum amount required to prevent disease, but may be less that the amount needed for optimal mental and physical health. Most people in the US consume less than the Required Daily Allowance (RDA) of one or more vitamins and minerals. For example, many women lack enough calcium and iron, leading to osteoporosis and anemia, respectively.

Explanation of Treatment:
Vitamins and minerals are available in vegetables, fruits, meat, and other sources. However, the typical U.S. diet is lacking in key vitamins and minerals, so many people need to take a supplement.
Juicing: One option is to use a juicer to make fresh vegetable/fruit juice, and storing it for up to a few days in an airtight glass container. Fresh vegetable/fruit juice is a rich source of vitamins, minerals, and other nutrients. Commercial juices are "pasteurized" or heated to destroy bacteria, which also causes a loss of some nutrients. Grinding vegetables/fruit one time provides only about half of the original vitamins/minerals, so after the first juicing it is useful to soak the pulp for about 15 minutes in a small amount of pure water (about 10% of the amount of liquid initially squeezed out), and then grind the pulp again – this will yield most of the remaining vitamins/minerals. The only small disadvantage to juicing is a loss of insoluble fiber, but the soluble fiber remains, and that is the most important fiber. However, the advantage of juicing is that it is often a very easy and tasteful way to get healthy nutrients into children who don't eat fruits/vegetables. Some of the healthiest vegetables to use include cabbage, spinach, carrots, broccoli, parsley, oregano, mixed with a small amount of fresh fruit for flavor and other nutrients. Organic vegetables and fruits are preferred, as they have a higher amount of vitamins and minerals and less toxic pesticides. 8 ounces/day should be enough for most children and adults, depending on their intake of other vegetables and fruits.
Supplements: Vitamin/mineral supplements are largely unregulated, and some supplements do not contain what they claim, or use forms that are poorly absorbed. Some companies choose to participate in the Dietary Supplement Verification Program (DSVP) of the United States Pharmacopeia (USP) - that program verifies that the contents of the supplement match the label. Check for a USP or DSVP label, or go to http://www.usp.org/USPVerified/ to check a product.

- Also, most supplements do not contain all the essential vitamins and minerals, or do not contain enough of them.
- Several good choices for broad-spectrum vitamin/mineral supplements include Kirkman's Super Nu Thera (very high in vitamin B6), Kirkman's Spectrum Complete, Brainchild's Spectrum Support, and Awaken Nutrition. However, most of those supplements do not contain enough calcium, which is also very important to supplement, and they do not contain iron, which some children may need.
- Calcium supplements are especially important if a person is on a dairy-free diet.
- Iron supplements are needed by some typical children as well as children with autism, but should only be given if a test indicates a need, as too much iron can also be a problem.
- In general, nutritional supplements are a good way to boost key nutrients lacking in the diet.

Testing:
Most vitamin and mineral levels can be tested using blood samples taken while fasting. Vitamin Diagnostics is one of very few companies that can measure the level of all vitamins. Several commercial labs can measure the level of most minerals, most of which can be measured reliably in Red Blood Cells (RBC). Calcium is best measured in the urine, preferably with a 24-hour urine collection. Some laboratories also offer functional assessments of the need for vitamins and minerals based on blood and/or urine testing. Measure iron with serum ferritin.

Recommended Dosages:
We recommend the following dosages for people with autism as a reasonable level to start with. However, some individuals may need more or less depending on their diet and metabolic needs, and testing can help determine optimal supplement levels.
Note that vitamin and minerals can have a potent effect on body function and behavior, and so start at a low dose (1/10 of that below) and then gradually increasing over 3-4 weeks.

Iron should be added only if a test indicates a need for iron – this is common, and worth testing for. Low iron is a leading cause of mental retardation in the US, and 40% of infants under the age of 2 have low iron (and so do 40% of women of child-bearing age).

The dosage below should be adjusted up or down by bodyweight; ie, half for a 30 lb child, and for 90 pounds and above give 50% more.

VITAMINS	**Proposed Supplement (for 60 lb child)**	**RDA (4-8 yr)**	**Upper Limit**
Vitamin A (as mixed carotenoids)	6000 IU carotenoids (equivalent to 3000 IU Vit. A)	400 mcg (1333 IU)	900 mcg (3000 IU)
Vitamin C (ascorbic acid)	1000 mg	25 mg	650 mg
Vitamin D (cholecalciferol)	150 IU	5 mcg (200 IU)	50 mcg (2000 IU)
Vitamin E (mixed tocopherols)	200 IU	7 mg (10.5 IU)	300 mg (450 IU)
Vitamin K	0	55 mg	ND
B1 (thiamin HCl)	30 mg	0.6 mg	ND
B2 (riboflavin)	20mg	0.6 mg	ND
B3 (niacin/niacinamide)	15 mg niacin 20 mg niacinamide	8 mg	15 mg
B5 (calcium d-pantothenate)	25 mg	3 mg	ND
B6 (pyridoxal HCl)	40 mg*****	0.6	40 mg
B12 (cyanocobalamin)	800 mcg	1.2 mcg	ND
Folic Acid	400 mcg	200 mcg	400 mcg
Folinic Acid	400 mcg		
Biotin (d-biotin)	300 mcg	12 mcg	ND
Choline (choline bitartrate)	250 mg	250 mg	1000 mg
Inositol (inositol monophosphate)	100 mg	n/a	n/a
MINERALS			
Calcium (calcium citrate)	50 mg	800 mg	2500 mg
Chromium (chromium chelate)	70 mcg	15 mcg	ND
Copper	0	440 mcg	3000 mcg
Iodine (potassium iodine)	100 mcg	90 mcg	300 mcg

Iron **	0	10 mg	40 mg
Lithium (lithium amino acid chelate)	500 mcg	n/a***	n/a
Magnesium (magnesium glycinate or citrate)	150 mg	130 mg	110 mg*
Manganese (manganese taurate)	10 mg	1.5 mg	3 mg
Molybdenum (molybdenum chelate)	125 mcg	22 mcg	600 mcg
Phosphorus	0	500 mg	3000 mg
Potassium (potassium citrate)	50 mg	1500 mg	n/a
Selenium (selenium chelate)	85 mcg	30 mcg	150 mcg
Sulfur (MSM)	500 mg	n/a	n/a
Zinc (zinc citrate)	10-30 mg****	5 mg	12 mg

*** for Magnesium, the UL is the amount for supplements and does not count food sources**
**** Iron should be added on an individual basis only if serum ferritin tests reveal a need for iron. Suggest 5-10 mg of iron chelate for 4 weeks, followed by half that dosage afterwards**
***** Estimated daily intake of lithium in food is 1900 mcg/day for adults.**
****** Some children may need even higher levels of zinc.**
******* Some children and adults may benefit from much higher dosages, see section on High Dose Vitamin B6.**

Duration: Lifelong, although improving diet and healing gut may reduce the need for supplementation.

Safety Note: Most vitamins are water soluble, and excess amounts of them will be safely excreted in the urine. Some vitamins (vitams A, D, E, K) are fat soluble, and excess amounts of those can build up in the body and cause toxicity if taken at high levels (above what we recommend) for a long time.
Excess amounts of minerals can cause problems, and the upper limits listed above should not be exceeded without consultation with a physician or nutritionist.

ARI Survey of Parent Ratings of Treatment Efficacy:

	% Worse	% No Change	% Better	Number of Reports
Vitamin A	2%	58%	41%	618
Calcium[E]:	2%	62%	36%	1378
Folic Acid	3%	54%	42%	1437
Magnesium	6%	65%	29%	301
P5P (Vit. B6)	13%	37%	51%	213
Vitamin B3	4%	55%	41%	659
Vitamin B6 alone	8%	63%	30%	620
Vitamin B6 with Magnesium	4%	49%	47%	5780
Vitamin B12	4%	33%	63%	192
Vitamin C	2%	57%	41%	1706
Zinc	2%	51%	47%	1244

Research:

One small double-blind, placebo-controlled study published by Adams et al. found that a strong, balanced multi-vitamin/mineral supplement resulted in improvements in children with autism in sleep and gut function, and possibly in other areas. Adams JB et al., Pilot study of a moderate dose multivitamin-mineral supplement for children with autistic spectrum disorder. J Altern Complement Med. 2004 Dec;10(6):1033-9.

One study found that high-dose vitamin C (1.1 g per 10 kg bodyweight) helped children with autism.
Dolske MC et al., A preliminary trial of ascorbic acid as supplemental therapy for autism. Prog Neuropsychopharmacol Biol Psychiatry 1993 Sep;17(5):765-74.

Several studies have demonstrated that children with autism have substantial oxidative stress, suggesting either a low level of key antioxidants or an increased need for them.

For more information, go to: http://autism.asu.edu

High-Dose Vitamin B6 and Magnesium

Rationale: There are over 20 studies of vitamin B6 with Magnesium for autism, including 12 double-blind, placebo-controlled studies, making it one of most studied treatments for autism. Almost all of these studies found that 45-50% of children and adults with autism benefited from high-dose supplementation of vitamin B6 with magnesium. Vitamin B6 is required for over 100 enzymatic reactions, including the production of major neurotransmitters (serotonin, dopamine, and others) and glutathione (needed for detoxification). Magnesium is used to prevent the possibility of hyperactivity, which can occur if the vitamin B6 is taken by itself.

Most of the studies used dosages of about 8-15 mg/pound of B6 (maximum of 1000 mg). Only 1 study used a lower dosage (1.3 mg/pound), and that is one of the few studies that found no benefit.

A dosage study by T. Audhya steadily increased the dosage of vitamin B6 from 1 to 10 mg/pound. They found that at least 3 mg/pound was needed to begin to see benefits, and 6 mg/pound was enough for most children to see benefit.

The reason why many children and adults benefit from high-dose vitamin B6 is still unclear, but a possible explanation is that many children and adults with autism have both 1) a decreased ability to convert vitamin B6 to its active form, and 2) defective enzymes for making key neurotransmitters that require an unusually high amount of the active form of vitamin B6. (For more explanation see Adams et al, Abnormally high plasma levels of vitamin B6 in children with autism not taking supplements compared to controls not taking supplements. J Altern Complement Med. 2006 Jan-Feb;12(1):59-63).

Treatment: Based on a review of all the research, Dr. Bernard Rimland has recommended a dosage of about 8 mg/pound of vitamin B6 (maximum of 1000 mg) and half as much magnesium. However, he emphasized that some individuals with autism need somewhat more or less.

It should be noted that all the treatment studies involved children and adults who were generally not following DAN! interventions, and it is possible that the other DAN! interventions may reduce the need for high-dose vitamin B6 in some children and adults.

Test: There is not yet a lab test to determine who will benefit from high-dose vitamin B6, although measurements of low neurotransmitters might be a possible clue. The best test is simply a 2 month trial, slowly increasing the dose from 1 mg/pound bodyweight to 8 mg/pound bodyweight of B6, and half as much magnesium.

Safety: High dose supplementation of vitamin B6 in children and adults with autism appears to be very safe. One study by Audhya compared 6 months of treatment with high-dose vitamin B6 in two forms (P5P or pyridoxine HCl) in 184 children with autism, and found adverse side-effects (worsening of behaviors) in 10% of those children receiving P5P (half the group) vs. none in those receiving pyridoxine HCl. However, a few children can do better on P5P. So, we suggest first starting with pyridoxine HCL, and then consider adding some P5P (5-25 mg) to see if further improvement occurs.

There is a small possibility that high dose vitamin B6 could cause temporary peripheral neuropathy (loss of feeling in fingers and toes), but this is extremely rare, and stopping supplementation generally results in full recovery.

For more info: A summary of vitamin B6 studies in autism is available at http://www.autismwebsite.com/ari/treatment/b6studies.htm

Essential Fatty Acids

Rationale: Essential fatty acids are critical nutrients for humans. They exist in the cell membrane of every cell, and roughly 20% of an infant's brain is composed of essential fatty acids. Mother's milk is very rich in essential fatty acids, but some infant formulas lack this key ingredient needed for brain development.
Two general categories of essential fatty acids are omega-3 and omega-6. Omega-3 fatty acids have relatively short shelf-lives, so commercial food processing often hydrogenates or partially hydrogenates them, which provides long shelf life but eliminates their nutritional value. Thus, over 80% of the US population has low levels of omega 3 fatty acids – this is one of the most widespread nutritional problems in the US.
Low levels of essential fatty acids are associated with a wide range of psychological disorders, including depression, post-partum depression, bipolar (manic/depression) and Rett's syndrome (similar to autism). Most importantly, two published studies have found that children with autism have lower levels of omega –3 fatty acids than the general population.
S. Vancassel et al., Plasma fatty acid levels in autistic children, Prostaglandins Leukot Essent Fatty Acids 2001 65:1-7.
Bell et al. (2002) Abnormal fatty acid metabolism in autism and Asperger's syndrome. In: Phospholipid Spectrum Disorder in Psychiatry and Neurology (2nd edition).

Explanation of Treatment:
One of the best sources of omega 3 fatty acids are fish, who obtain them from algae and plankton in the sea. Unfortunately, many fish are high in mercury and other toxins, especially the large predators (shark, swordfish, and tuna). Small fish, such as salmon and shrimp, tend to have lower levels of mercury, but it depends where they come from. So, it is generally safer for children to obtain essential fatty acids from fish oil, since little mercury is stored in the oil. Because fish oil (and fish) spoil readily, it is important to obtain a high-quality oil that does not smell or taste rancid, and it should be kept refrigerated.

Two of the major omega 3 fatty acids are EPA and DHA. DHA is critical for early brain development, and EPA is useful for later development.

Recommended dosages: (based on the amount of omega 3's, not the total amount of oil which will contain other oils) are:
Omega 3: 20-60 mg/kg (600-1800 mg for a 30 kg, or 60 lb, child). For younger children, use a supplement richer in DHA, and for older children and adults, use a supplement richer in EPA.
Omega 6: ¼ as much omega 6 as omega 3; so, if taking 1000 mg of omega 3's, then 250 mg of omega 6. It is important to maintain a balance of omega 3 and omega 6, so although most people in the US have enough omega 6, those taking an omega 3 supplement usually should take more.

Flax seed oil is also a source of omega 3 fatty acids, but the form it provides (alpha linolenic acid) must be converted by the body to the active form (EPA and DHA). There have been some reports that children with autism respond poorly to flax seed oil, so we generally recommend fish oil instead.

Cod liver oil (or other fish liver oil) is a good source of omega 3 fatty acids, and also provides good amounts of vitamin A and vitamin D. However, vitamin A intake from all supplements should not greatly exceed the RDA intake (see vitamin/mineral section) for extended periods, since excess amounts will be stored in the liver and could affect liver function. (Carotenes are pre-vitamin A and are not a problem).

Testing: The level of essential fatty acids can be measured in the red blood cell membrane. However, because most people in the US have low levels of omega 3's, it is desirable to reach levels at the top of the "normal" range for omega 3's. Also, it is better to measure the absolute amount of each fatty acid, rather than just the percentage of each.

ARI Survey of Parent Ratings of Treatment Efficacy:

	% Worse	% No Change	% Better	Number of Reports
Fatty Acids	2%	42%	55%	626

Research:
There is a huge number of scientific studies showing that humans need essential fatty acids, and that most people in the US do not consume enough. As mentioned above, 2 studies found that children with autism have lower levels of omega 3 fatty acids than do typical children.

There have been four treatment studies for children/adults with autism.

A 90-day open trial of essential fatty acids in 18 children with autism found significant increases in language and learning skills. Patrick L and Salik R, The Effect of Essential Fatty Acid Supplementation on Language Development and Learning Skills in Autism and Asperger's syndrome. Autism/Asperger's Digest: Research Article – Jan/Feb 2005.

One small double-blind, placebo-controlled treatment study by Amminger et al. found that fish oil might have some benefit in reducing hyperactivity, but the numbers were too small to be statistically significant.
Amminger et al. Omega-3 Fatty Acids Supplementation in Children with Autism: A Double-blind Randomized, Placebo-controlled Pilot Study. Biol Psychiatry. 2006 Aug 22.

One study by Adams et al. found that 2 months supplementation of fish oil (rich in DHA) led to significant improvements in sociability and other areas, especially in children and adults who consumed 0-1 servings of fish/month.

One open study by Audhya et al. was a 9-month treatment study. They found little improvement by 6 months, but substantial improvements by 9 months. The largest improvement was in gut function (verified by pre and post endoscopies in many cases), but also improvements in other areas.

For more info: see www.nordicnaturals.com

Digestive Enzymes

Rationale: The body normally produces a variety of digestive enzymes to break large food molecules into smaller ones which can be absorbed. Different enzymes are needed for different types of protein, carbohydrates, and fats. Children with autism sometimes have low levels of certain enzymes, or less active enzymes, or both – enzyme problems are especially common in children with gut problems (chronic constipation or diarrhea).

One digestive enzyme, DPP4, is easily deactivated by small amounts of toxins including mercury and organophosphates (pesticide sprays). DPP4 is needed to digest some peptides from casein and other substances that can have an opioid-like effect.

Treatment: Take a digestive enzyme with each meal, usually at the start of the meal. Use enzymes that are as complete as possible. Proteases are needed for protein, lipases for fats, and disacharidases and other enzymes for carbohydrates.
Note that we recommend digestive enzymes in addition to special diets, and should not be used instead of special diets. If a child has a problem digesting wheat or dairy products, it is best to just avoid them, and use the digestive enzymes as a precaution against unknown exposures.

Sometimes during detoxification treatments, toxic elements such as mercury are freed from sequestration inside cells and they are "removed" via bile. However, once in the small intestine, these toxics (mercury) can bind to and inactivate digestive enzymes such as peptidases (DPP4) and disaccharidases which are needed to break down complex sugars. There are reports of "no evidence of need" for digestive enzymes until detoxification was started. The message is that there can be several reasons for use of digestive aids and that "things change".

Testing: A Comprehensive Digestive Stool Analysis can reveal if some types of foods are not being digested well, suggesting a problem with specific digestive enzymes.

ARI Survey of Parent Ratings of Treatment Efficacy:

	% Worse	% No Change	% Better	Number of Reports
Digestive Enzymes	3%	42%	56%	737

Research:
Studies by Horvath et al. and Kushak/Buie have found that many children with autism have defective carbohydrate digestion:
Horvath K et al, Gastrointestinal abnormalities in children with autistic disorder," J. Pediatrics 135 no. 5 (1999) 559-563.
Horvath K and Perman JA "Autistic disorder and gastrointestinal disease," Curr. Opinion in Pediatrics, 14 (2002) 583.
Kushak R and Buie T "Disaccharidase deficiencies in patients with autistic spectrum disorders," presented at DAN! New Orleans Jan 2004.

Gut Treatments: Anti-fungals and Probiotics

Rationale: The human gut contains a large number of bacteria (10x more gut bacteria than cells in the entire body). Most of these gut bacteria are beneficial, and help with food digestion, water balance, and limiting the growth of harmful bacteria and yeast.

Some children with autism have low levels of beneficial bacterial, and high levels of harmful bacteria and yeast. The harmful bacteria and yeast produce toxins that can severely affect mental functioning and behavior; alcohol is just one of many toxins that yeast can produce, and is a good example of a yeast toxin that can severely affect behavior. It seems that the best way to treat these problems is with a combination of antifungal diet, antifungal medications (if yeast are present) and probiotics (beneficial bacteria). These can help restore normal gut function.

Treatment:
Anti-fungal Diet: Yeast feed on sugar and simple carbohydrates, so reducing or avoiding those foods is important. Also, it can be helpful to avoid foods containing yeast or yeast products, including fruit juice, vinegar (in ketchup and other foods), leavened foods (bread, pizza, bagels, rolls), cheese, and mushrooms (a type of yeast/fungus).
Duration: Dr. Sidney Baker recommends a trial for 5-14 days, followed by a high exposure to see if the diet makes a difference. If so, continue long-term.

Anti-fungal Medications: There are several prescription and non-prescription anti-fungal treatments, and sometimes several need to be tried before finding an effective one for a given strain of yeast. Nystatin is the safest because it is not absorbed, but many yeast are now resistant to it. Diflucan, Sporanox, Lamisil, and Nizoral are alternatives which yeast are less likely to be resistant to, but since they are absorbed into the body they have a very small chance of overtaxing the liver, so liver enzymes should be checked every few months if they are used long-term. Some non-prescription antifungal treatments include capryllic acid, oregano concentrate, citrus seed extract, undecylenic acid, and pau d'arco. An unusual treatment is saccharomyces boulardii, a harmless yeast that will kill off other yeast and promote beneficial bacteria, but will disappear within a few weeks when you stop taking it, often leaving behind a now healthy gut.
Duration: Dr. Sidney Baker recommends a series of high-dose trials of 2-3 weeks for each antifungal, followed by the next one until you find one that works.
Die-off reaction: When yeast are killed, they can release all their toxins at once. This can cause a temporary "die-off" reaction lasting a few days, followed by good improvement when the toxins leave the body. Activated charcoal can be taken to absorb these toxins and reduce side-effects.

Probiotics: Probiotics are mixtures of one or more beneficial bacteria which are normally present in the gut. Many probiotics contain only a few billion or less Colony Forming Units (CFU's), but some strong probiotics contain 30-75 billion CFU's, and some prescription probiotics contain up to 500 billion CFU's. The higher-dose products are more likely to be able to reach the gut and recolonize it with good bacteria. If high-dose probiotics continue to be needed, this may suggest pancreatitis or other serious dysfunction may be present.
Duration: Use a high dose initially, and then consider a lower maintenance dose.
Testing: One simple and very useful test is to look at the stool, since half of the stool is bacteria. The stool should be a medium/dark brown and well-formed, with 1-3 bowel movements/day.

Use Antibiotics only with great caution: One round of oral antibiotics typically kills off over 99% of beneficial gut bacteria, but has little or no effect on yeast or many types of bad bacteria, which then thrive due to lack of competition from beneficial bacteria. Oral antibiotics often cause overgrowths of bad bacteria and yeast, and are suspected as the cause of many of the gut problems in autism. Several studies have shown that children with autism had, on average, a much higher usage of oral antibiotics than typical children in their first few years of life.

Lab Testing: A Comprehensive Digestive Stool Analysis (available from Great Smokies or Doctor's Data) will reveal the amount of some types of normal and abnormal bacteria and yeast. A sensitivity analysis can suggest which anti-fungals are most likely to be beneficial, but often just a series of trials of different antifungals is the best approach.
Urinary organic acid testing can be done to check for abnormally high levels of metabolites from yeast, although the reliability of this test is somewhat unclear.

ARI Survey of Parent Ratings of Treatment Efficacy:

	% Worse	% No Change	% Better	Number of Reports
Antifungals[C]: Diflucan	5%	41%	55%	330
Antifungals[C]: Nystatin	5%	46%	49%	986
Antibiotics (not recommended)	31%	57%	12%	1799

Research:
A large study by Rosseneau et al. found that 95% of 80 children with regressive autism and chronic constipation had roughly 10,000x the normal amount of E. Coli, and many also had similarly high levels of other types of Aerobic Gram Negative Bacilli (AGNB). A 3-month treatment study of 11 children found that a potent antibiotic (not available in the US) resulted in complete elimination of the bacteria and a great improvement or total cure of the gut problems, and a large improvement in behavior. However, when the antibiotics were stopped, the AGNB returned within a month, and the improvements in gut function and behavior were lost. A similar small treatment study by Sandler et al with another potent antibiotic (Vancomycin) again found temporary improvement in gut function and behavior, but again the gains were lost when the treatment was stopped.
Sander et al, Short-term benefit from oral vancomycin treatment of regressive-onset autism. J Child Neurol. 2000 Jul;15(7):429-35.

Two small studies by Finegold et al found some limited evidence of abnormal anaerobic bacteria, primarily increases in clostridia. They did not test for AGNB. A study by Parracho et al also found increased amounts of clostridia.
Song Y, Liu C, Finegold SM. Real-time PCR quantitation of clostridia in feces of autistic children. Appl Environ Microbiol. 2004 Nov;70(11):6459-65.
Finegold et al, Gastrointestinal microflora studies in late-onset autism. Clin Infect Dis. 2002 Sep 1;35 (Suppl 1):S6-S16.
Parracho HM et al., Differences between the gut microflora of children with autistic spectrum disorders and that of healthy children. J Med Microbiol. 2005 Oct;54(Pt 10):987-91.

Amino Acids

Rationale: Protein is made of long strands of individual amino acids. When protein is digested properly, digestive enzymes split the long protein molecule into small peptides and individual amino acids, which the body can absorb. Those amino acids can then be reassembled to make a wide array of critical substances, such as neurotransmitters, hormones, enzymes, antibodies, immunoglobulins, glutathione, and many other substances. Amino acids are the "building blocks" of life.

Some children with autism have self-limited diets that are low in protein, and some have digestive problems that limit their ability to digest protein into individual amino acids. Either of these problems can lead to insufficient amino acids.

Treatments:

1) Ensure diet contains sufficient protein (two 4-oz servings/day).
2) Consider digestive enzymes to more completely digest the protein into individual amino acids
3) Give "free-form" amino acids; "free-form" means that the amino acids exist as individual molecules, rather than part of a large protein molecule that needs to be digested. General amino acid supplements are available, and they can also be customized by a compounding pharmacy.

Testing:

Amino acids can be tested either from blood (when fasting for 10 hours) or from a urine sample (24 hour is best). Fasting blood plasma reveals circulating levels of amino acids related more to metabolism than to diet/digestion. 24-hour urine amino acid analysis shows what's in excess or not usable and what's deficient, if kidney transport is normal. Urine has to be interpreted carefully, as high levels in the urine can indicate "wasting" or excessive excretion, resulting in a low body level.

It may also be useful to measure levels of neurotransmitters in platelets (blood), as low levels of neurotransmitters can be treated by supplementing with amino acids, allowing the body to build their own.

Research:

One study by Aldred et al. found that patients with autism or Asperger syndrome and their siblings and parents all had raised glutamic acid, phenylalanine, asparagine, tyrosine, alanine, and lysine ($p < .05$) than age-matched controls, with reduced plasma glutamine. Other amino acids were at normal levels. This suggests a general disorder of amino acid metabolism in their families.

Aldred S, Moore KM, Fitzgerald M, Waring RH. Plasma amino acid levels in children with autism and their families. J Autism Dev Disord. 2003 Feb;33(1):93-7.

Melatonin

Rationale: Many children and adults with autism have sleep problems, including falling asleep, nighttime waking, and early waking. These sleep problems have a strong correlation with gut problems, and healing the gut seems to reduce many of those sleep problems.
However, if sleep problems continue, supplementation with melatonin can help. Melatonin is the hormone the body naturally produces at nighttime to regulate sleep. It is formed from the neurotransmitter serotonin, so low serotonin levels can cause low melatonin levels.

Testing: The best test for melatonin is simply a trial of it if a person has continuing sleep problems not due to other causes (see below).

Treatment: Melatonin production is greatly reduced by light, and even a simple nightlight can greatly decrease melatonin production. So, first try eliminating all sources of light.

For problems falling asleep, first try a behavioral approach of a regular nighttime routine (at a fixed time, begin bath/shower, brush teeth, story, etc.). Also, be sure to eliminate caffeine and reduce sugar intake at nighttime.

If sleep problems persist, start with 1 mg of melatonin (0.5 mg for children), and increase up to 2-5 mg if necessary (1-3 mg for children). If waking occurs during the night, then try a time-release form rather than increasing the dose. 2 mg time-release can be better than 5 mg all at once.

Safety: Melatonin seems to be exceptionally safe, and high dosages in animals produce no toxicity, and a study of 1400 women taking 75 mg/day for up to 4 years with no adverse effects. In fact, animal studies suggest that long-term use of melatonin can increase lifespan 20%, presumably due to its strong antioxidant effect.

ARI Survey of Parent Ratings of Treatment Efficacy:

	% Worse	% No Change	% Better	Number of Reports
Melatonin	8%	30%	61%	573

For more info, go to www.melatonin.com

Thyroid Supplementation

Rationale: About 5-10% of the general population has a thyroid disorder requiring supplementation, and that percentage may be higher in autism. Poor thyroid function due to lack of iodine is the major cause of mental retardation in the world, resulting in over 80 million cases of mental retardation. Poor thyroid function can be caused by other factors as well.

Testing:
A simple initial assessment can be done by measuring body temperature before waking. A low body temperature is a good indicator of too low a level of thyroid function. Overall low energy/activity level can also be a possible indicator of a thyroid problem, but could be caused by other factors also.

A blood thyroid test can also be done. However, some laboratory reference ranges may be too broad, and should be interpreted carefully.

A very sensitive urinary thyroid test is available from Vitamin Diagnostics.

Treatment:
If iodine levels are low, then one can begin with iodine supplementation. If that does not normalize thyroid levels, then one can consider thyroid supplements. We recommend natural thyroid supplements derived from animals, as they will provide a complete thyroid source. Synthetic thyroid supplements are NOT recommended, as they are incomplete.

Duration:
Usually 1-2 months of supplementation is needed to observe an increase in energy level and body temperature. Supplementation may be needed long-term unless the problem with thyroid development is resolved.
CAUTION: Too much thyroid hormone can cause weight loss and other problems, so thyroid levels should be monitored regularly if taking a supplement.

Research:
One study by Adams et al found that many children with autism have unusually low levels of iodine in their hair, which possibly suggests a low level in their body and need for more.
Adams JB et al., Analyses of toxic metals and essential minerals in the hair of Arizona children with autism and associated conditions, and their mothers. Biol Trace Elem Res. 2006 Jun;110(3):193-209.

Sulfation

Rationale: Sulfate is used for many functions in the body, including detoxification, maintaining the lining of the gut, and hormone production. Some children with autism have a low level of sulfate in their bodies, due to a variety of reasons including poor absorption in the gut, excess loss in the urine, poor recycling of sulfate by the kidney, or oxidant stress and inflammation can shut down cysteine dioxygenase, which throttles the cysteine -> sulfate route.

Testing: Blood testing can be used to check for levels of free and total plasma sulfate, and this is probably the more reliable test. Plasma cysteine can also be informative. (Urine testing of free and total sulfate may be useful to look for excessive loss of sulfate, but this is only one of several possible causes of low sulfate in the body, and should not be solely relied on to assess sulfate status).

Alternatively, since Epsom salt baths are very safe, one could simply try them for up to several weeks and look for improvements in behavior and functioning (see below).

Treatment:
Tapan Audhya evaluated many different ways to increase plasma sulfate levels in children with autism who had low levels. The two most effective methods were oral MSM (500-2000 mg depending on size and sulfate level) and Epsom Salt (magnesium sulfate) baths – 2 cups of Epsom salts in warm/hot water, soak for 20 minutes, 2-3x/week. A few children did not tolerate MSM, but Epsom salt baths are generally very well tolerated. (T. Audhya, Role of Sulfation, presentation at Autism/Asperger's Conference in Anaheim, CA, February 2007.)

Many parents and physicians have anecdotally reported that Epsom salt baths were beneficial to their children. However, there is less experience with MSM for children with autism, and more research is needed.

Research:
A small pilot study by Alberti et al found that children with autism had a reduced sulfation capacity compared to controls.
Alberti A, Pirrone P, Elia M, Waring RH, Romano C. Sulphation deficit in "low-functioning" autistic children: a pilot study. Biol Psychiatry. 1999 Aug 1;46(3):420-4.

Glutathione Therapy

Rationale: Many children with autism have low levels of active glutathione, which is needed to protect the body from many toxins including toxic metals.

Treatment: There are many ways to increase active glutathione levels. They include:
1) Oral glutathione: Only about 10% of oral glutathione is absorbed, so this method is not very effective at raising body levels, but it may improve levels in the gut.
2) IV glutathione: The IV form is highly effective, but temporary, and it can be difficult to administer regularly to the child.
3) Vitamin C: 500 mg of vitamin C was found to raise RBC glutathione levels 50% in college students.
Johnston et al, Vitamin C elevates red blood cell glutathione in healthy adults. Am J Clin Nutr. 1993 Jul;58(1):103-5.
4) TMG/Folinic Acid/methyl-B12: A study by James et al. found that 800 mcg of folinic acid and 1000 mg of TMG somewhat improved plasma glutathione levels in children with autism. Adding subcutaneous injections of methyl-Vitamin B12 (methyl-cobalamin) resulted in normalization of plasma glutathione levels.
James et al, Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism. Am J Med Genet B Neuropsychiatr Genet. 2006 Dec 5;141(8):947-56.
5) DMSA (chelation): Toxic metals such as mercury can greatly decrease the body's ability to make glutathione, so removing toxic metals by chelation seems to greatly help glutathione production.

Research:
A large study by James et al confirmed her original finding of low glutathione in children with autism due to abnormalities in their methionine pathway. She also found that children with autism were more likely to have genetic polytypes associated with abnormalities in the methionine pathway.
James et al.Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism. Am J Med Genet B Neuropsychiatr Genet. 2006 Dec 5;141(8):947-56.

A study by Adams et al. found that DMSA (chelation) resulted in a great improvement or normalization of RBC (red blood cell) levels of glutathione after just 1 round (3 days) of DMSA treatment, with benefits lasting at least 1-2 months.
Adams et al, Preliminary results of DMSA treatment study, presentation at Fall DAN! Conference 2006.

Chelation: Removal of Toxic Metals

Rationale: Many children with autism have a low amount of active glutathione, and a higher fraction of their glutathione is oxidized (inactive). Glutathione is the body's primary defense against mercury, toxic metals, and many toxic chemicals, so a low level of glutathione results in a higher body burden of toxins. Also, many children with autism had increased use of oral antibiotics in infancy, which alter gut flora and thereby almost completely stop the body's ability to excrete mercury. Normalizing glutathione, restoring gut flora, and removing toxic metals often results in reduction of the symptoms of autism.

Preparation for Treatment: Prior to beginning chelation, it is important to first prepare the body for it. This includes:
1) Reducing exposure to toxins (organic food, reverse osmosis water, no mercury fillings, avoiding pesticides, etc.).
2) Improving levels of essential vitamins and minerals – see section on vitamins and minerals.
3) Improving glutathione levels - see section on glutathione.
4) Treating gut dysbiosis – see sections on gut treatments.

Testing:
There are several good ways to test for heavy metal toxicity. They include:
1) **Urinary porphyrins:** This test checks for abnormal levels of porphyrins in the urine, where different porphyrin levels appear to correlate with body burden of mercury, lead, or other toxic metals. See http://www.labbio.net
2) **Challenge dose:** Give a trial of DMSA or DMPS, and measure the level of toxic metals in the urine before and after taking it. A large increase indicates that the metals are present, and that the medication is helpful in removing them.

Hair, blood, and unprovoked urine testing only indicate recent exposure to toxic metals, and are NOT useful in determining past exposure. Children may have a high body burden but a low level in their current hair, blood, or urine.

Treatment: The chelation treatments recommended by DAN! include DMSA, DMPS, and TTFD.
DMSA: Oral DMSA is approved by the FDA for treating lead poisoning in children. Some of the compounded rectal suppositories also appear to increase excretion of toxic metals, but the transdermal forms do not measurably increase excretion of toxic metals.
Safety: DMSA only slightly affects excretion of most essential minerals, so a basic mineral supplement can compensate for this. The exception is that the first dose of DMSA removes a significant amount of potassium (equivalent to that in a banana), and that is not included in mineral supplements, so 1-2 servings of fresh fruit or vegetables should be consumed to restore potassium levels. DMSA also significantly increases excretion of cysteine, so that should be supplemented before and/or during therapy.
DMSA has a small chance of increasing liver enzymes or decreasing blood cell count, so those should be monitored during treatment.

DMPS: DMPS is not approved by the FDA, but a physician may have it legally compounded for IV, oral, and rectal use, all of which increase excretion of toxic metals. The transdermal form does NOT appear to increase excretion of toxic metals.
Safety: DMPS slightly increases the excretion of some essential minerals, so a basic mineral supplement is recommended to compensate for this loss. It is unknown if it causes a loss of potassium. DMPS has a small chance of increasing liver enzymes or decreasing blood cell count, so those should be monitored during treatment.

TTFD: A small pilot study of TTFD (used as a rectal suppository) resulted in some increase in excretion of arsenic and possibly other metals, and also significant reduction of autistic symptoms. The transdermal form may also work, although more study is needed.
Safety: TTFD appears to be very safe, with animal studies at high doses finding no evidence of toxicity.

More info: Anyone considering chelation therapy is urged to read the DAN! Consensus Report on Treating Mercury Toxicity in Children with Autism, available at www.autismresearchinstitute.com. This report provides more detailed advice on pre-treatments, treatments, dosages, and safety.

ARI Survey of Parent Ratings of Treatment Efficacy:

	% Worse	% No Change	% Better	Number of Reports
Chelation	2%	22%	76%	324

Research:
There is substantial evidence to suggest that many children with autism suffer from exposure to mercury, and probably other toxic metals and toxic chemicals. The data includes:

1) A literature review by Bernard et al showing that the symptoms of autism were very similar to those of people suffering from infantile exposure to mercury poisoning.
   Bernard S et al, Autism: a novel form of mercury poisoning. Med Hypotheses. 2001 Apr;56(4):462-71.
2) A study by James et al. found that children with autism had low levels of glutathione, which is the body's primary defense against mercury.
   James et al, Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism. Am J Med Genet B Neuropsychiatr Genet. 2006 Dec 5;141(8):947-56.
3) A large study by Nataf et al. found that over half of children with autism had abnormal levels of a porphyrin in their urine that highly correlates with a high body burden of mercury.
   Nataf R et al., Porphyrinuria in childhood autistic disorder: implications for environmental toxicity. Toxicol Appl Pharmacol. 2006 Jul 15;214(2):99-108
4) A study by Bradstreet et al. found that children with autism excreted 3-6x as much mercury as did typical children when both were given DMSA.
   Bradstreet J., Geier DA, Kartzinel JJ, Adams JB, Geier MR, A Case-Control Study of Mercury Burden in Children with Autistic Spectrum Disorders, J. Am. Phys. Surg 8(3) 2003 76-79.
5) A baby hair study by Holmes et al. found that children with autism had unusually low levels of mercury in their baby hair (1/8 normal), suggesting a decreased ability to excrete mercury. A replication study by Adams et al. found similar, although less dramatic, differences. The Adams et al study also found that children with autism had much higher usage of oral antibiotics than did typical children, which is important because usage of oral antibiotics almost completely stops the body's ability to excrete mercury.
   Holmes AS, Blaxill MF, Haley BE. Reduced levels of mercury in first baby haircuts of autistic children. Int J Toxicol. 2003 Jul-Aug;22(4):277-85.
6) A small pilot study by Adams et al found that children with autism had 2x more mercury in their baby teeth than did typical children, suggesting that they had a higher body burden of mercury during their infancy when the teeth formed. That study also found that children with autism had a much higher usage of oral antibiotics during their infancy, similar to their baby hair study.
7) Two studies of airborne mercury, in Texas and in the San Francisco Bay area, found that the amount of mercury in the air correlated with the incidence of autism.
   Windham et al, Autism spectrum disorders in relation to distribution of hazardous air pollutants in the San Francisco bay area. Environ Health Perspect. 2006 Sep;114(9):1438-44.
   Palmer RF et al., Environmental mercury release, special education rates, and autism disorder: an ecological study of Texas. Health Place. 2006 Jun;12(2):203-9.
8) There have been nine epidemiological studies of the link between thimerosal in vaccines and autism. Four published studies by the Geiers have consistently found that children who received thimerosal in their vaccines had a 2-6x higher chance of developing autism than those who received thimerosal-free vaccines. Four published studies by groups affiliated with vaccine manufacturers have failed to find a link, and one was inconclusive. Three of the studies were conducted in other countries where the usage of thimerosal is much less and the incidence of autism is much lower, so those results have limited relevance to the US.

Immune System Regulation

Rationale: Several studies have found abnormal immune systems in autism, generally with shift to Th-2, and some evidence for auto-immunity.
Molloy et al., Elevated cytokine levels in children with autism spectrum disorder, J. Neuroimmunol 172 (2006) 198-205.

Treatments: More research on effective treatments for normalizing the immune system in children with autism are needed. If lab testing reveals abnormal immune system, current possible treatments include Actos (pioglitazone), intra-venous immunoglobulins (IVIG), and low-dose naltrexone.

Research:
IVIG: Gupta et al., found IVIG benefited 4 of 10 children, with 1 case of marked improvement. This is an expensive treatment, as the immunoglobulins need to be collected from hundreds or thousands of human donors.
Gupta et al., Treatment of children with autism with intravenous immunoglobulin. J Child Neurol. 1999 Mar;14(3):203-5. No abstract available.

Twenty six autistic children received intravenous gamma globulin (IVIG) every 4 weeks for 6 months at a dose of 400mg/Kg. Aberrant behaviors, speech, hyperactivity,inappropiate stims and social interactions significantly improved. However 22 of the 26 children regressed within 4 months after discontinuing IVIG.
Boris m, Goldblatt A, Edelson SM; Improvement in children with autism treated with intravenous gamma globulin. Journal of Nutritional & Environmental Medicine, Dec 2005; 15(4): 169-176.

ACTOS: ACTOS (pioglitazone) has multiple effects, including the ability to decrease inflammation. An open study of ACTOS in 25 children with autism for 3-4 months found substantial improvements in irritability, lethargy, stereotypy, and hyperactivity, with greater benefits in the younger children. Doses were 30 mg (younger children) and 60 mg (older children)
Boris et al., Effect of pioglitazone treatment on behavioral symptoms in autistic children, accepted in J. Neuroinflammation 2007.

Low-dose naltrexone:
There have been 14 clinical trials of naltrexone for children with autism. A review paper by Elchaar et al. reported “Naltrexone has been used most commonly at doses ranging from 0.5 to 2 mg/kg/day and found to be predominantly effective in decreasing self-injurious behavior. Naltrexone may also attenuate hyperactivity, agitation, irritability, temper tantrums, social withdrawal, and stereotyped behaviors. Patients may also exhibit improved attention and eye contact. Transient sedation was the most commonly reported adverse event.”
Elchaar et al., Efficacy and safety of naltrexone use in pediatric patients with autistic disorder. Ann Pharmacother. 2006 Jun;40(6):1086-95. Epub 2006 May 30. Review.

It has been suggested that low-dose naltrexone, at about 3-5 mg/day (much lower than the doses mentioned above) may be beneficial to children with autism and may improve the regulation of their immune system. More research is needed.

Summary

Autism is a very complex disorder, and we do not fully understand it. However, there are many biomedical abnormalities that have been identified, and most can be treated to some degree. By following the testing and treatments outlined above, many children will improve to some degree, and some will improve dramatically. Sometimes one treatment shows great benefit, but it is more common that each treatment helps a small amount. However, the cumulative effect of multiple treatments can be substantial. Younger children are the ones most likely to benefit, especially those who had a period of normal development followed by regression, but older children and adults can often benefit from the same treatments outlined here.

Much more research is needed to improve on these treatments and to determine who is most likely to improve, and to discover new treatments.

For more information, I encourage you to attend Defeat Autism Now! Conferences (www.autismwebsite.com) and read "Autism: Effective Biomedical Treatments" by Jon Pangborn, Ph.D., and Sidney Baker, MD, published by the Autism Research Institute, and "Children with Starving Brains," by Jaquelyn McCandless, MD. Those books will provide more detail on the treatments summarized in this document.

Please consider filling out the ARI Treatment Effectiveness Survey at www.autism.com, to share your experiences with other families.

To read case studies of children who have greatly improved from biomedical approaches, see "Recovering Autistic Children" by Stephen Edelson, Ph.D., and Bernard Rimland, Ph.D., available from www.autism.com.

Good luck in your journey.

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PARENT RATINGS OF BEHAVIORAL EFFECTS OF BIOMEDICAL INTERVENTIONS

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The parents of autistic children represent a vast and important reservoir of information on the benefits—and adverse effects—of the large variety of drugs and other interventions that have been tried with their children. Since 1967 the Autism Research Institute has been collecting parent ratings of the usefulness of the many interventions tried on their autistic children.

The following data have been collected from the more than 25,500 parents who have completed our questionnaires designed to collect such information. For the purposes of the present table, the parents responses on a six-point scale have been combined into three categories: "made worse" (ratings 1 and 2), "no effect" (ratings 3 and 4), and "made better" (ratings 5 and 6). The "Better:Worse" column gives the number of children who "Got Better" for each one who "Got Worse."

DRUGS	Parent Ratings: Got Worse[A]	No Effect	Got Better	Better: Worse	No. of Cases[B]
Aderall	42%	25%	33%	0.8:1	694
Amphetamine	47%	28%	25%	0.5:1	1286
Anafranil	32%	38%	30%	0.9:1	405
Antibiotics	32%	54%	14%	0.4:1	2039
Antifungals[C]					
Diflucan	5%	42%	53%	10:1	505
Nystatin	5%	46%	49%	9.4:1	1229
Atarax	25%	53%	22%	0.9:1	502
Benadryl	24%	51%	25%	1.1:1	2924
Beta Blocker	17%	51%	32%	1.9:1	276
Buspar	26%	44%	30%	1.1:1	369
Chloral Hydrate	41%	39%	20%	0.5:1	443
Clonidine	21%	31%	47%	2.2:1	1441
Clozapine	37%	43%	20%	0.5:1	140
Cogentin	19%	55%	27%	1.4:1	176
Cylert	45%	35%	20%	0.4:1	618
Deanol	15%	57%	29%	2.0:1	206
Depakene[D]					
Behavior	26%	43%	31%	1.2:1	1027
Seizures	12%	33%	55%	4.7:1	675
Desipramine	34%	33%	33%	1.0:1	82
Dilantin[D]					
Behavior	28%	49%	23%	0.8:1	1097
Seizures	15%	36%	49%	3.3:1	422
Felbatol	20%	56%	24%	1.2:1	50
Fenfluramine	20%	52%	27%	1.3:1	473
Halcion	37%	42%	22%	0.6:1	65
Haldol	38%	28%	34%	0.9:1	1186
IVIG	10%	46%	44%	4.4:1	70
Klonapin[D]					
Behavior	28%	39%	33%	1.1:1	224
Seizures	25%	60%	15%	0.6:1	60
Lithium	24%	45%	31%	1.3:1	441
Luvox	29%	37%	34%	1.2:1	203
Mellaril	28%	38%	33%	1.2:1	2088
Mysoline[D]					
Behavior	41%	45%	14%	0.3:1	146
Seizures	19%	56%	25%	1.4:1	75
Naltrexone	20%	45%	35%	1.7:1	273
Paxil	30%	33%	37%	1.3:1	374
Phenergan	29%	46%	24%	0.8:1	291
Phenobarb.[D]					
Behavior	47%	37%	16%	0.3:1	1099
Seizures	18%	43%	39%	2.2:1	508
Prolixin	30%	41%	29%	1.0:1	97
Prozac	31%	32%	36%	1.2:1	1240
Risperidal	19%	27%	54%	2.9:1	912
Ritalin	44%	26%	29%	0.7:1	4029
Secretin					
Intravenous	7%	48%	45%	6.3:1	422
Transderm.	10%	53%	37%	3.6:1	176
Stelazine	28%	45%	27%	0.9:1	431
Steroids	35%	33%	32%	0.9:1	111
Tegretol[D]					
Behavior	25%	45%	30%	1.2:1	1492
Seizures	13%	33%	54%	4.2:1	814
Thorazine	36%	40%	24%	0.7:1	933
Tofranil	29%	38%	33%	1.1:1	766
Valium	35%	41%	24%	0.7:1	851
Zarontin[D]					
Behavior	35%	45%	20%	0.6:1	148
Seizures	19%	55%	26%	1.4:1	104
Zoloft	32%	33%	34%	1.1:1	434

BIOMEDICAL/ NON-DRUG/ SUPPLEMENTS	Parent Ratings: Got Worse[A]	No Effect	Got Better	Better: Worse	No. of Cases[B]
Calcium[E]	2%	62%	35%	14:1	1871
Cod Liver Oil	4%	47%	49%	12:1	1389
Cod Liver Oil with Bethanecol	10%	50%	40%	4.2:1	105
Colostrum	6%	56%	38%	6.3:1	516
Detox. (Chelation)[C]	3%	24%	73%	25:1	627
Digestive Enzymes	3%	39%	57%	18:1	1223
DMG	8%	51%	42%	5.5:1	5601
Fatty Acids	2%	43%	55%	23:1	995
5 HTP	13%	51%	36%	2.8:1	254
Folic Acid	4%	54%	43%	11:1	1792
Food Allergy Trtmnt	3%	35%	62%	23:1	818
Hyperbaric Oxygen Therapy	6%	42%	52%	8.5:1	66
Magnesium	6%	65%	29%	4.6:1	301
Melatonin	8%	29%	63%	7.7:1	896
MT Promoter	13%	48%	38%	2.9:1	52
NAET	4%	52%	44%	11:1	77
P5P (Vit. B6)	13%	37%	50%	4.0:1	418
Pepcid	11%	60%	29%	2.6:1	143
SAMe	17%	62%	21%	1.2:1	115
St. Johns Wort	17%	68%	16%	0.9:1	127
TMG	15%	43%	42%	2.9:1	683
Transfer Factor	10%	51%	39%	3.9:1	142
Vitamin A	2%	59%	39%	19:1	990
Vitamin B3	4%	54%	41%	9.6:1	832
Vit. B6/Mag.	4%	48%	48%	11:1	6387
Vitamin B12	5%	34%	62%	14:1	688
Vitamin C	2%	56%	42%	17:1	2171
Zinc	2%	49%	49%	20:1	1736
SPECIAL DIETS					
Candida Diet	3%	43%	55%	19:1	867
Feingold Diet	2%	43%	55%	24:1	850
Gluten- /Casein-Free Diet	3%	32%	65%	20:1	2208
Removed Chocolate	2%	48%	50%	29:1	1944
Removed Eggs	2%	57%	41%	18:1	1290
Removed Milk Products/Dairy	2%	48%	51%	32:1	6113
Removed Sugar	2%	49%	49%	24:1	4014
Removed Wheat	2%	48%	50%	28:1	3565
Rotation Diet	2%	48%	50%	21:1	881
Specific Carbohydrate Diet	7%	28%	66%	10:1	195

A. "Worse" refers only to worse behavior. Drugs, but not nutrients, typically also cause physical problems if used long-term.
B. No. of cases is cumulative over several decades, so does not reflect current usage levels (e.g., Haldol is now seldom used).
C. Antifungal drugs and chelation are used selectively, where evidence indicates they are needed.
D. Seizure drugs: top line behavior effects, bottom line effects on seizures
E. Calcium effects are not due to dairy-free diet; statistics are similar for milk drinkers and non-milk drinkers.