
Biological Treatments for Autism and PDD

Third Edition

Dr. William Shaw

With contributions by Bernard Rimland Ph.D., Bruce Semon M.D. Ph.D., Lisa Lewis Ph.D., Karyn Seroussi, and Pamela Scott

DISCLAIMER

This book is a summary of current research and medical therapies in use for the treatment of autism and PDD. The authors have written this book to serve as a guide to therapies and as a reference source for both professionals and nonprofessionals. All of this information is meant to be used under the care of the patient's health care professional and the authors do not intend that the information in this book be considered as a prescription for medical therapy for anyone. Many of the therapies discussed in this book are relatively new and may be associated with risks that may not be known for decades. Every medical therapy has inherent risks. The reader and the medical professional who treats himself or his children are responsible for weighing the risks involved in any of the therapies reviewed in this book before instituting such therapies. Although the authors have exhaustively researched all sources to ensure the accuracy of the information in this book, we assume no responsibility for errors, inaccuracies, or omissions.

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William Shaw Ph.D.

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PREFACE

Many new developments have occurred in the field of autism since the first edition of *Biological Treatments for Autism and PDD* in 1998. The most significant developments have been the discovery of significant abnormalities in the structure and function of the gastrointestinal tract in children with autism by Andrew Wakefield at the Royal Free Hospital in London and by Karoly Horvath at the University of Maryland School of Medicine. Wakefield's hypothesis is that these gastrointestinal abnormalities are due to the infection of the gastrointestinal tract by the vaccine strain of the measles virus. The presence of this virus in the intestinal biopsy samples of children with Autism while not being present in the controls is powerful evidence supporting his hypothesis. In addition, high concentrations of numerous heavy metals found in many children with Autism and the reduction of autistic symptoms after their removal points to multifactorial causes for autism. The marked increase in the incidence of autism has been confirmed in almost every state in the United States as well as in numerous other nations as well. The work of Ted Page, Mary Coleman, and others that research the genetic diseases which cause disordered purine metabolism, is very exciting because a simple dietary supplement of uridine can reverse almost all autistic symptoms in this subgroup of people. Confirmation of the effectiveness of many other therapies introduced in the first edition such as gluten and casein restriction, antimicrobial therapy, gamma globulin treatment, and use of secretin have now been confirmed by both additional scientific studies and the experience of tens of thousands of parents and physicians who have utilized them.

As in the first edition, the purpose of writing this book is to integrate information from the fields of biochemistry, immunology, genetics, nutrition, and microbiology about autism, ADD, and PDD into a form that could be assimilated by both parents, professionals such as nutritionists, dietitians, and physicians who deal with children with these disorders. Long conversations with hundreds of parents of children with autism and PDD, including many who are themselves physicians, have provided me with many clues to these disorders.

The information in this book may be useful not only for people with autism, but also for those with other disorders that share in some of the symptoms of autism including pervasive developmental disorder (PDD), Rett's syndrome, Williams disease, neurofibromatosis, tuberous sclerosis, Fragile X, Down's syndrome, Tourette's syndrome, Prader-Willi syndrome, and attention deficit disorder (ADD). Many of the same abnormalities in autism are also present in these disorders and the therapies suggested in this book for autism may also help children and adults with these other disorders as well. My objectives are to describe the abnormalities in autism and related disorders and to discuss some of the therapies that have frequently been beneficial for many children and adults. Although a few children have completely recovered from autism using the therapies outlined in this book (and the parents of two of them include their accounts in this book), I am not suggesting that all children will benefit but hope that many will benefit to some degree. *Biological Treatments for Autism and PDD* has now been translated into Spanish, German, and Dutch and many other languages. The feedback I have received is that the therapies covered in this book have been effective worldwide.

The accounts of the two mothers whose children completely recovered are very significant because of the similarities of the therapies they used. Both mothers obtained information and instituted therapy independently. Both children were diagnosed early about the age of two years. Both mothers independently began using antifungal therapy, an antiyeast diet low in sugar and free of yeast, treatment of food allergies, and a gluten and casein-free diet as key cornerstones of their therapy, both also used intensive behavioral interventions as well. You will note that there are significant differences in the nutritional and antifungal approaches presented by different authors in this book. I realize that this may be confusing, but this information honestly reflects the

fact that there are still many unknowns. You may wish to experiment with several of the different nutritional and antifungal approaches to determine which ones are most beneficial for your patient or child.

Some of this material may be difficult but every attempt has been made to simplify it without distorting the meaning. Knowledge is power. Much of this information may not be familiar to parents or to medical practitioners. The parent who reads this book should assume that their family doctor or even their neurologist or other specialist may not know nearly as much as they do about autism after reading this book. Until recently, most of this information has been available only in the form of research papers accessible only to medical research specialists, and was essentially unknown by persons outside each narrow specialty. There has been a tremendous increase in the application of knowledge about autism and PDD that was stimulated by a group of physicians and scientists who met in Dallas in January 1995 as a part of Dr. Bernard Rimland's Defeat Autism Now! (DAN!) Conference.

My goal is that this book will enable your child to become healthier and function better so, as a result, both you and your child will have a better life. I am sure to be criticized for recommending therapies based on "incomplete" or "anecdotal" data. While acknowledging the great benefits of antibiotics and vaccines in treating disease, I think the overuse of antibiotics and vaccines have harmed substantial minorities of treated individuals. However, I think the dangers to our children are too great to wait until all the data is perfect, which could take a very long time. The Red Cross refused to act on behalf of the Jews in German concentration camps in World War II despite numerous reports of genocide because the evidence was "anecdotal" rather than "definitive." It has taken nearly 50 years from the time of the first research linking lung cancer and smoking to get restrictions on cigarette use for minors. It took 25 years from the initial discovery that folic acid supplementation prevented a birth defect called spina bifida until extra folic acid supplements were recommended for pregnant women. The stakes for the safety of our children are too high to wait forever.

William Shaw Ph.D.

ABOUT THE AUTHORS

William Shaw received a Ph.D. in biochemistry from the Medical University of South Carolina. He has board certifications in both the fields of Clinical Chemistry and Toxicology. He worked for six years in nutritional biochemistry, endocrinology, and immunology at the Centers for Disease Control; for twelve years in a large medical testing laboratory called Smith Kline Beecham Clinical Laboratories, involved with specialized medical testing for toxicology (poisons and drugs), chemistry, immunology, and endocrinology. The next five years, he was an associate professor at the University of Missouri at Kansas City (UMKC) School of Medicine and Director of Clinical Chemistry, Toxicology, and Endocrinology and the organic acid testing for metabolic diseases at Children's Mercy Hospital, the teaching hospital for the University of Missouri at Kansas City School of Medicine. Dr. Shaw has lectured throughout the world on autism and has been a keynote speaker at the Autism Society of America National Meeting, the National Meeting of the American Association for Environmental Medicine, and the National Meeting of the American College for Advancement of Medicine. He is actively involved with both the "Defeat Autism Now" (DAN) group and the "Cure Autism Now" (CAN) foundation. Dr. Shaw is the author of many scientific papers and the co-author of two book chapters dealing with laboratory medicine and nutritional biochemistry. Dr. Shaw can be reached by phone at (913)341-8949 or by e-mail at williamsha@aol.com. The website for The Great Plains Laboratory is www.greatplainslaboratory.com and the mailing address is The Great Plains Laboratory, 11813 W. 77th St, Lenexa, KS 66214.

Bernard Rimland Ph.D. passed away in 2006. He was a research psychologist and was the director of the Autism Research Institute since it was founded in 1967. He was the editor of the *Autism Research Review International* and was the founder of the Autism Society of America. His prize-winning book *Infantile Autism: the Syndrome and its Implications for a Neural Theory of Behavior* is credited with changing the field of psychiatry from its "blame the mother" orientation to its current recognition that autism is a biological disorder, not an emotional illness. He lectured on autism and related problems throughout the world, was the author of numerous publications and received many awards for his work on autism. Dr. Rimland served as primary technical advisor on autism for the film *Rain Man*. Dr. Rimland, who earned his Ph.D. in experimental psychology and research design at Penn State University, had also conducted research on the relationship between nutrition and behavior. He was a past officer of several societies devoted to research in this area, and had lectured and published extensively on this topic, as well as in the field of autism.

Bruce Semon M.D. Ph.D. is both a child psychiatrist and nutritionist practicing in Milwaukee, Wisconsin. He has practiced nutritional medicine since 1991. He received his M.D. from University of Wisconsin-Madison in 1984 and his Ph.D. in Nutrition from University of California-Davis in 1989. He was a Fellow at the National Institute of Health, National Cancer Institute (Laboratory of Nutritional and Molecular Regulation) from 1989-1991. He completed an adult residency in psychiatry at the Medical College of Wisconsin in 1995 and a fellowship in child and adolescent psychiatry in 1997. Dr. Semon has published several academic papers relating to nutrition. Dr. Semon has treated many patients suffering from autism and other disorders in conventional ways, seeing very few positive changes. He has treated many patients for yeast-related illnesses, including eczema, psoriasis, depression and autism, with remarkable results. He is using the nutritional approach in his private practice in Milwaukee, as well as in a Milwaukee based mental health clinic with which he is affiliated. Dr. Semon and his wife, Lori Kornblum, have published a cookbook *Feast Without Yeast* with recipes for a diet free of yeast and fermented foods, casein, gluten, eggs, corn, and soy. Dr. Semon can be reached at: 250 W. Coventry Court, Suite 101, Glendale, Wisconsin 53217, (414) 352-6500.

Lisa S. Lewis Ph.D. is the mother of two children, one of whom was diagnosed with autism at the age of three. Her formal academic training is in biological anthropology and while earning a doctorate in that field, she studied genetic variation and performed studies of blood proteins in several species of non-human primates. This background in science laid the foundation for understanding the theories underlying dietary interventions. In additions, she has a great interest in baking and runs a small catering business which specializes in children's birthday cakes. For the last ten years, Dr. Lewis has been in the computing field. After her son's autism diagnosis, she found that doctors had little to offer in the way of information or treatment. As a result of doing her own research, dietary intervention, which began as a trial, has now become a way of life for her son. Having spent so much time and energy trying to understand the why's and the how's of this diet, she was able to put together an eighteen page information brochure that was widely distributed. She is the author of the recent book *Special Diets for Special Kids: Understanding and Implementing Special Diets to Aid in the Treatment of Autism and Related Developmental Disorders*.

Karyn A. Seroussi is the co-founder with Lisa Lewis of the Autism Network for Dietary Intervention, and a co-founder of the Rochester, NY chapter of Parents of Allergic Children. She lives with her husband and two children, all of whom have different dietary requirements. She has completed a very popular book, *Unraveling the Mystery of Autism and Pervasive Developmental Disorder, A Mother's Story of Research and Recovery*, which tells of her family's experience and her son's recovery from autism.

Pamela Scott is a parent first and an advocate for life. She is currently working as a Parent Training Consultant for The Parent Connection. The Parent Connection is devoted to making broad systems change in the way families access services through Missouri's Division of Mental Retardation and Developmental Disabilities. The Parent Connection offers educational workshops, training, and presentations. These services are available to families, parent groups, and the professionals who work with them.

FORWARD

Dr. Shaw has performed a great and much needed service for the parents of children with Autism--and the physicians who work with children with Autism--by publishing this book.

There are a great many parent guidebooks, which offer psychological and educational advice. There are also many books, which discuss esoteric medical and scientific issues. There are, however, very few books like this one which address the practical, here and now biomedical treatments that can bring about dramatic improvement in many autistic individuals.

The term autism (and the newer, quite confusing term "PDD") are umbrella words which cover a broad array of disorders sharing a number of overlapping symptoms, but having a large variety of different causes. No one knows how many causes of autism there are. But there are some causes we do know about, and about which we have a rudimentary understanding.

Children or adults with autism caused by some of the factors covered in this book can be treated with some success and often with quite dramatic success. And it is to some of these known causes, and their treatments, that this important new book is addressed.

The reader will quickly discover that this book is "user friendly". Its purpose is to clarify, to explain, to guide, and to encourage so that at long last the parents themselves can begin to do what they have always wanted to do—have a real hand in the healing of their child with Autism.

Thank you Dr. Shaw.

-----Bernard Rimland Ph.D., November 1997.

Infections, Antibiotics, Vaccines, and their Relationship to Autism and ADD: Alternative Treatments

Chapter 1

Dr. William Shaw

Is There an Autism Epidemic?

The late Bernard Rimland Ph.D., at the Autism Research Institute ⁽¹⁾, asked the question “Is there an autism epidemic?” His data in Table 1 shows that, between 1965 and 1969, only 1% of parents who contacted him were inquiring on behalf of a child with autism less than 3 years old. However, between 1994 and 1995, 17 % of the parents who called him were inquiring on behalf of a child under the age of 3. Presumably, the higher percentage of inquiries on behalf of children under three could be attributed to two factors: ⁽¹⁾ a greater knowledge about autism on the part of physicians and parents, leading to an earlier diagnosis and/or ⁽²⁾ a higher incidence of autism in the younger age group. Furthermore, a large number of professionals, including pediatricians and physicians with large practices in the field of autism, have noticed an increase in the incidence of autism. William Crook M.D., a pediatrician who started his practice in the 1950's, although being aware of the symptoms of autism, says that he did not see a case of autism until 1973, 24 years later. From that point on, it seemed to him that the incidence of autism accelerated. Acknowledging this increase is critical for determining whether autism is mostly caused by genetic or environmental factors. If autism is mainly due to genetic factors, the incidence of autism would be constant. Furthermore, the percentage of individuals with autism in a particular age group would be the same. Thus, if the incidence of autism in three year olds is one in a thousand, the incidence of autism in fifty year olds should also be one in a thousand.

Table 1

Is there an autism epidemic?		
Year	% under 3 years	Number
1965-69	1	919
1970-79	5	4,184
1980-89	5	4,018
1990-93	8	6,785
1994-95	17	3,916

Fortunately, similar data has been reported in Iceland ⁽²⁾. Iceland is an ideal country for this evaluation since a single institution confirmed all cases of autism in the entire country and since the investigators personally reviewed all the diagnosed cases, data variability was minimized. These investigators found that the incidence

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of autism had doubled over the last 20 years. Furthermore, the male to female ratio had increased significantly over the same time period. This study is extremely important since it shows that factors other than genetics may be causing autism. What could some of these nongenetic factors be?

Data in Table 2 shows the extraordinary incident of cases of Autism in the United States.

Table 2

STATES	1992-1993	2001-2002	Percentage of Increase	STATES	1992-1993	2001-2002	Percentage of Increase
Alabama	68	904	1,229	Montana	20	197	885
Alaska	8	223	2688	Nebraska	4	415	10,275
Arizona	199	348	1,229	Nevada	5	518	10,260
Arkansas	30	774	577	New Hampshire	0	404	infinite
California	1,605	13,257	577	New Jersey	446	3,526	691
Colorado	14	538	3,743	New Mexico	16	265	1,556
Connecticut	164	1,470	796	New York	1,648	7,023	326
Delaware	15	294	186	North Carolina	786	3,095	294
District of Columbia	0	144	infinite	North Dakota	9	144	1,500
Florida	582	4,328	644	Ohio	22	3,057	13,795
Georgia	262	2,462	840	Oklahoma	31	785	2,432
Hawaii	52	380	631	Oregon	37	2,847	7,595
Idaho	39	356	813	Pennsylvania	346	3,969	1,047
Illinois	5	3,802	75,940	Puerto Rico	266	518	95
Indiana	273	3,262	1,095	Rhode Island	19	384	1,921
Iowa	67	554	727	South Carolina	141	1,012	618
Kansas	74	743	904	South Dakota	36	1,103	263
Kentucky	38	1,022	2,589	Texas	1,444	7,099	392
Louisiana	409	1,297	217	Utah	105	723	589
Maine	37	552	1,392	Vermont	6	248	4,033
Maryland	28	2,396	8,457	Virginia	539	2,365	339
Massachusetts	493	2,681	444	Washington	476	1,972	314
Michigan	288	4,719	1,539	West Virginia	101	374	270
Minnesota	296	3,270	1,005	Wisconsin	18	2,247	12,383
Mississippi	0	461	infinite	Wyoming	15	117	680
Missouri	336	1,953	481				
				50 States, DC, PR	12,222	97,847	701

Kontstantareas and Homatidis ⁽³⁾ at the University of Guelph in Ontario, Canada found a high correlation between the prevalence of ear infections and the incidence of autism. They found that the earlier a child with autism had an ear infection, the more likely that child had a more severe form of autism. They also found that the increased incidence of ear infections was also associated with the more severe rather than mild form of autism. Many similar studies have been conducted in the field of attention deficit hyperactivity (ADHD). These studies also indicate that increased ear infection early on in life results in much greater incidents of hyperactivity ⁽⁴⁻⁸⁾. Roberts and his colleagues ⁽⁴⁾ reported that recurrent otitis media during infancy was correlated with increased distractibility of the students later in life. Other studies ⁽⁵⁻⁸⁾ correlated recurrent otitis media in infancy with later low IQ scores, poor performance on reading, spelling, and math tests, increased retention in grade levels, increased attention deficits, and increased behavior problems in school.

Both the autism and ADHD research groups have assumed that this abnormal development is caused by hearing impairment brought on by the ear infection. My own interpretation of this data is that the abnormal development is instead caused by abnormal byproducts of yeast and drug-resistant bacteria being absorbed

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into the body from the intestines following the excessive use of antibiotics. Later chapters will deal with the mechanism of this problem in great detail.

The Antibiotic Revolution

Antibiotics were first produced on a commercial scale around the end of World War II. In 1949, the amount of antibiotic production was very low, about 80 tons per year ⁽⁹⁾. In addition to this low production, the kind of antibiotic used was mostly of the injectable type. But by the 1950's, the use of oral antibiotics became more predominant. As a child in grammar school in the 1950's, I got most of my antibiotics injected into the buttocks. By 1954, 250 tons of antibiotics per year were being produced. By 1990, 20,000 tons (40 million pounds) of antibiotics per year were being produced ⁽⁹⁾. I believe that this explosive growth in the use of antibiotics is a major factor for the increased incidence of autism, developmental disorders such as ADD, as well as a number of adult disorders such as fibromyalgia. In the United States, one of the main reasons for antibiotic use in children is to treat the condition called otitis media or ear infection.

Ear Infections

According to a publication ⁽¹⁰⁾ by The Panel for Otitis Media, a group of prominent pediatricians and scientists from throughout the United States concluded that:

- Ear infections account for one-third of all visits to the pediatrician and 75% of all follow-up visits.
- Between 1975 and 1990, office visits for otitis media increased by 150% to 24.5 million visits per year.
- Children under age two had the highest rate per year of office visits to the doctor for evaluation of otitis media and also the greatest increase in visits per year between 1975 and 1990: 224%!
- A two year study of children between the ages of 2 and 6 years in day-care showed that 53% had at least one episode of otitis media during their first year and 61% during their second year. Thirty percent of the children had recurrent bouts of otitis media.
- A cost analysis in 1991 estimated that the cost *per episode*, including direct and indirect costs, prescription drugs, and parents' time lost from work at \$406 for a total yearly cost in 1991 of about ten billion dollars.

Otitis media has proven to be a cash cow to both primary care physicians and the drug industry. Now consider another 30 billion dollars a year spent on specialized speech and developmental therapy ⁽¹¹⁾ and billions of dollars more spent to treat ADD, PDD, autism, and other disorders. If, in fact, the overuse of antibiotics is related to the increase in these disorders, then the financial impact of otitis media is very large indeed.

Nonhuman Use of Antibiotics and the Rise of Antibiotic-Resistant Bacteria

In addition to the marked increase in antibiotic use in humans, the use of antibiotics in food animals has also sky-rocketed, not because the animals are sicker than usual, but because they gain weight much faster when antibiotics are given with their feed. According to regulations, the animals are supposed to be withdrawn from antibiotic use prior to slaughter so that most of the antibiotics they are exposed to will have been eliminated by

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the time of their death. However, the abnormal microbial ecology in the intestines of these animals caused by the use of antibiotics persists. It seems likely that chemical byproducts (such as gliotoxins) produced in the intestines of these animals by yeast, fungi, and antibiotic-resistant bacteria may be absorbed into their bloodstream and are likely to be present in their meat as well. It is difficult to know how much of a problem this is for humans who eat this meat. Pamela Scott, who has written a later chapter in this book, was so concerned about this problem that she only fed her son meat from range animals not exposed to antibiotics in feedlots.

According to Stuart Levy M.D. a professor at Tuft's University School of Medicine in his book *The Antibiotic Paradox: How Miracle Drugs Are Destroying the Miracle* ⁽⁹⁾, the use of antibiotics for fattening animals and other agricultural uses also selects for more drug-resistant bacteria. These bacteria then enter the ecosystem through the meat and feces of these animals and, in turn, may infect humans. Dr. Levy found that six months after the use of antibiotics in feed for chickens, stool samples from humans in the surrounding community contained the same drug-resistant bacteria that had developed in the chickens. The use of human antibiotics in animal feed has been banned in Great Britain but is still allowed and is widely used in the United States. Antibiotics have even been added to the water in which salmon and catfish are raised, and as a result, antibiotic-resistant bacteria have been found in the flesh of these fish. In addition, antibiotics such as Streptomycin and oxytetracycline have been sprayed from airplanes to control diseases in fruit trees and potatoes, allowing the development of drug-resistant bacteria in soils over a wide geographic area. Some pathogenic bacteria may now be resistant to as many as 10 different antibiotics.

Bacteria That Causes Ear Infections

The three most common bacteria causing ear infection are *Streptococcus pneumoniae*, *Haemophilus influenza*, and *Moraxella catarrhalis*. These organisms account for 70-90% of all ear infections ⁽¹²⁾. These organisms commonly inhabit the nose and throat of children and can easily move into the ear via the Eustachian tube. *Streptococcus pneumoniae* accounts for 30-40% of all cases. As many as 28% of strains of this organism have been found to be penicillin resistant. *Haemophilus influenza* is responsible for about 21% of otitis media cases; 15-30% of strains of this bacteria are resistant to several types of penicillin. *Moraxella catarrhalis* accounts for 12 % of all cases. As many as 96% of strains of this organism may be resistant to penicillin such as amoxicillin ⁽¹²⁾. *Moraxella catarrhalis* is present at some time in the nose or mouth of 75% of infants before the age of two years.

The Panel for Otitis Media ⁽¹⁰⁾ stated:

"It is characteristic of health care providers in the United States to intervene for otitis media with effusion, but the panel was impressed by data suggesting that otitis media usually follows a benign course without treatment. Thus, although such a study might be difficult to implement because it runs counter to prevailing attitudes, research to document the natural course of otitis media with effusion is essential."

Translated into simple English, this means that doctors and parents are used to using antibiotics for ear infections. The proof that they work over the long run is shaky. However, it is going to be extremely hard to change the way things are done because habits are difficult to change.

A large Dutch study was done using 1,439 children, divided into two groups with one of the groups receiving no treatment and the other receiving antibiotics and antihistamines. In the untreated children, 60% of the children recovered without medical intervention within three months. This kind of treatment would almost never be done in the United States. To understand the cultural differences between the two countries for treating ear

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infections, only about 30% of physicians in Holland prescribe antibiotics compared to the United States, where close to 99% of physicians prescribe antibiotics on a regular basis. Parents and employers must also share in the blame for this antibiotic overuse because with so many two-income families, mothers are under pressure to be at work rather than stay home with a sick child. The parents put pressure on the physicians to use antibiotics even when inappropriate. The physician knows he may lose the patient unless he complies.

In another study of 518 children with ear infection, Cantekin ⁽¹³⁾ found that six weeks after stopping the antibiotic amoxicillin, the recurrence was 2-6 times higher in the antibiotic-treated children than those in the placebo group. Van Buchem ⁽¹⁴⁾ treated one group of otitis media patients with antibiotics, one with tubes in the ears, and a third with neither. The outcome in the three groups was essentially the same.

After examining the medical histories of many children with autism, I became very interested in otitis media due to the fact that a very high percentage of these children had a history of frequent ear infections or other infections treated by antibiotics. In hundreds of medical charts I examined at a hospital, children with seizures, autism, and even psychosis had a history of antibiotic use prior to the development of these conditions. The urine organic acid testing of these children frequently revealed high concentrations of compounds derived from yeast and/or bacteria that are commonly resistant to broad-spectrum antibiotics. The pattern was so prevalent and so striking that there is little doubt in my mind that there is a relationship between the high concentrations of yeast and bacteria byproducts and the resulting disorders.

Exposure to cigarette smoke is also a significant risk factor for otitis media. In a study of seven year old British children, the authors found cotinine, a metabolite of nicotine was present in the saliva of children exposed to secondhand smoke and that the level of cotinine increased with the number of smokers in the household. The authors ⁽¹⁵⁾ found that one-third of the cases of otitis media could be attributed to exposure to secondhand smoke.

In addition, allergies can frequently be the major underlying cause of ear infection because an allergic reaction can cause swelling of the tissues in the ears which interferes with proper drainage enabling bacteria to grow more readily. McMahan ⁽¹⁶⁾ and Nsouli ⁽¹⁷⁾ both found that treatment of underlying allergies greatly diminished the recurrence of otitis media. Because ear infections are such a difficult medical problem for both parents and children, I have compiled a list of different approaches for treating these ear infections, which is given at the end of the chapter.

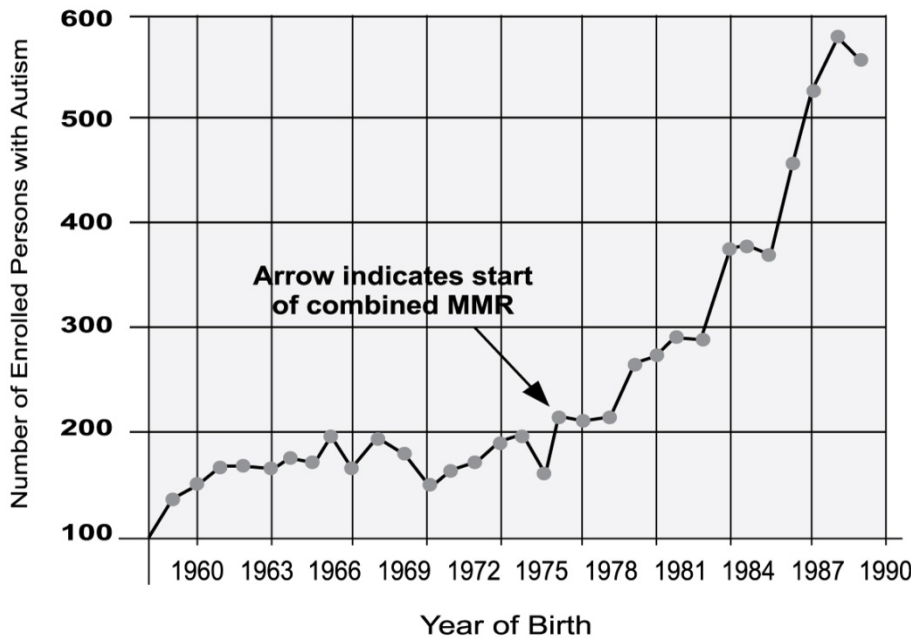
Vaccines

Numerous parents have reported the regression of their normally developing child within hours or days of vaccination with the MMR, DPT, or hepatitis B vaccines. The most serious research linking the vaccination to autism and PDD can be seen in the work of Andrew Wakefield, a British gastroenterologist. Dr. Wakefield perceived a significant increase in the incidence of Crohn's disease, an inflammatory bowel disease that he believes is related to the MMR (measles, mumps, rubella, vaccine). After parents of children with autism begged him to examine the gastrointestinal tracts of their children, Wakefield found that lymphoid hyperplasia was prevalent in children with autism who had been vaccinated with the MMR vaccine. Some of the children had severe fecal impaction with stool masses as large as a grapefruit. Many of the parents mistakenly thought that their children had diarrhea because much of the time, a limited amount of liquid stool would ooze around the fecal impaction. In some cases, the lymphoid hyperplasia was so severe that the intestinal lumen was nearly closed off. Wakefield describes the lymphoid hyperplasia as being similar in appearance to pus-filled

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tonsils. Data gathered in California indicates an increased incidence of autism that correlates with the introduction of the combined MMR vaccine (Figure 1). A significant increase in the incidence of autism appears to occur about three years after the MMR introduction. The vaccine issue is covered in greater detail in a separate chapter on vaccinations.

Figure 1
Distribution of Birth Dates of Regional Center Eligible Persons with Autism



Ear Infections and Other Recurrent Infections: How to Break the Cycle or At Least Reduce the Damage

The following are different techniques that will help break the cycle and minimize the damage. Remember that there are exceptions to every rule and antibiotics may sometimes be needed.

1. Tough it out or employ watchful waiting. Use ear drops containing benzocaine and a decongestant to stop the pain. A large study conducted in Holland showed no difference in outcome when children receiving antibiotics were compared to a placebo group. Antibiotics are not used nearly as much in Europe as in the United States. Only 31% of general practitioners in Holland use antibiotics to treat ear infections. By not treating the infection immediately, your child's immune system is allowed to react and build up a defense against future infections. If infections are treated immediately, the immune system will not have a chance to strengthen itself.
2. Eliminate milk, wheat, and other allergy causing foods from the diet. Milk is one of the most common food allergies, often causing sinus infections, leading to blockages of the Eustachian tubes, and resulting in ear infections. If milk and dairy elimination does not clear up the infections, get a comprehensive IgG food allergy test to determine if other foods are a problem.

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3. Stop any cigarette or other smoking inside the house.
4. Never use antibiotics for colds or flu since antibiotics kill only bacteria, not cold or flu viruses.
5. If you have to use antibiotics for your child, have your doctor prescribe the antifungal drug nystatin along with the antibiotic. There are no adverse reactions between nystatin and antibiotics because nystatin is only minimally absorbed into the bloodstream from the intestine. If your doctor won't prescribe nystatin, give one of the natural antifungal products such as garlic, caprylic acid, or grapefruit seed extract along with the antibiotic. Giving the beneficial bacteria *Lactobacillus acidophilus* while taking antibiotics may not help since the antibiotics may kill the acidophilus bacteria as well. Penicillin, chloramphenicol, erythromycin, tetracycline, oxacillin, vancomycin, and ceftriaxone all will kill the acidophilus bacteria. After antibiotics are completed, give supplements of *Lactobacillus acidophilus* for at least 30 days. Actually, giving acidophilus supplements regularly, on a daily basis, will help maintain a healthy intestine.
6. Get a throat culture done if your child has frequent infections. The most common organisms causing ear infection commonly inhabit the nose and throat. There is a vaccine available for *Streptococcus pneumoniae*, which is the most common cause of ear infections. If your child has a positive throat culture for *Streptococcus pneumoniae*, ask your pediatrician about getting vaccinated against this organism. The vaccine is termed the 23-type pneumococcal polysaccharide vaccine.
7. Consider having one parent stay home with your child until he is at least two years old and avoid preschool and day care centers. Day care is a breeding ground for germs.
8. Breast-feed your child for as long as possible since breast-milk contains antibodies against the bacteria that cause ear infections and other infections as well. Children who are breast-fed are much less likely to get frequent infections during the first six months of life ^(18,19).
9. Echinacea, the coneflower, was used extensively by the Plains Indians of the United States to treat infections and this knowledge was transferred to the settlers. Echinacea is a stimulant of the immune system and is available in pediatric doses in many health food stores such as Wild Oats. It can also be ordered over the phone (800-494-WILD) if a store is not nearby. This therapy is even more effective if drops of garlic and mull (also called mullein) oil are placed in the ears while giving the Echinacea. (My son used this method and resolved his earache overnight.) Three days of this therapy will clear up most ear infections. If this doesn't work, there is still always the option of using antibiotics. Echinacea will help to decrease the incidence and severity of colds and flu because of its stimulating effect on the immune system. This product has been used extensively in Germany for many kinds of illnesses. Although much of the literature documenting its use is written in German, some of the articles in English are listed in the references ⁽²⁰⁻²³⁾. Echinacea works best if it is given for 10 days and then discontinued for two weeks before starting again.
10. Ask your doctor to give your child a "shot" of rocephin in the buttocks instead of oral penicillin. As a child in the 1950's, I regularly received shots of penicillin as did millions of other people. The main benefit of the injection over oral antibiotics is that it will not kill the beneficial bacteria in the intestinal tract. Killing the beneficial bacteria often leads to an overgrowth of the intestinal tract with yeast and harmful bacteria like *Clostridia*. Therefore, the antibiotic "shot" will reach the human cells in the intestine, but will not reach the bacteria inside the intestinal cavity.

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11. If your child has four or more infections in one year, consider an evaluation of their immune system. Many children with autism have an inborn weakness of the immune system called an immunodeficiency. It is best to consult with a clinical immunologist, a physician (M.D. or D.O.) who specializes in these diseases. Usually these physicians are also part-time researchers and are associated with a medical school. If your child has a significant immunodeficiency, ask your physician about the possibility of using antibody infusions (called IVIG or intravenous immunoglobulin) to help your child's immune system fight off new infections. Sudhir Gupta M.D. at the University of California at Irvine has obtained complete remissions of some cases of autism ⁽²⁴⁾ using IVIG therapy. See the chapter on the immune system for more detailed information.
12. Consult a health practitioner trained in homeopathy. The technique called homeopathy was shown to be more effective ⁽²⁵⁾ than conventional antibiotic treatment in a German study of 103 children between 1 and 11 years. Homeopathy drops are also available at most health food stores. After one year, 70.7% of the children treated with homeopathy had no relapses compared to 56.5% of children treated with antibiotics. The average number of relapses was also much higher in the children treated with antibiotics than in those treated with homeopathy.
13. Consider tubes in the ear (tympanotomy tubes) if all else fails.

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The Microorganisms in the Gastrointestinal Tract

Chapter 2

Dr. William Shaw

Bacteria in the Intestinal Tract

In order to understand the devastating effects that may be caused by the widespread use of antibiotics, it is necessary to understand the role of microorganisms in the intestinal tract.

There are two main kinds of bacteria in the intestinal tract: aerobic and anaerobic. The aerobic bacteria need oxygen while the anaerobic bacteria don't need oxygen to live and even may be killed if oxygen is present. Some bacteria grow faster with oxygen but can adapt to a low oxygen environment. Another major group of organisms in the intestine are the yeast and fungi. In the intestinal tracts of some individuals, there may be single-celled animals called protozoa as well. These organisms, in a normal intestinal tract, are usually found in a natural balance that is healthy. It is estimated that there are 500 or more different species of bacteria in the average human intestinal tract ⁽¹⁾. Because there is limited oxygen in the intestinal tract, the anaerobic bacteria that don't require oxygen predominate. Of the 500 species, there are perhaps 30 or 40 species that constitute the majority of the bacteria present. It's estimated that there are about 10-100 trillion cells of bacteria in the intestinal tract at any one time ⁽¹⁾. To give you an idea of the size of that number, there are about a 100 trillion human cells in the entire human body. Thus, in a normal individual who is not on antibiotics, 10-50 % of their total cell volume is composed of bacteria.

There are very few bacteria in the stomach because the stomach acid kills them. In comparison, the colon harbors a million times more bacteria than the stomach. In the normal individual, this acid is neutralized with bicarbonate from the pancreas as food passes into the small intestine, allowing greater microbial overgrowth. Bacteria constitute about 50% of the content of feces. These residents of the intestinal tract are always in a state of flux with new bacteria continuously being produced and old bacteria continuously being flushed out in the moving intestinal contents and later in feces.

A study that was reported in the Journal of Infection and Immunology ⁽²⁾ found that when oral penicillin was administered to experimental animals, the total population of anaerobic bacteria, including the beneficial bacteria, was reduced by a factor of 1,000. These bacteria, which are called Lactobacilli, are also present in yogurt. As the good bacteria are killed off, the potentially harmful bacteria increase rapidly. This study reported translocation of the harmful bacteria out of the intestinal tract and into the lymph nodes surrounding the intestinal tract. From these lymph nodes, these bacteria were then strategically placed to cause new infections throughout the body.

Yeast Overgrowth in the Intestinal Tract

Another harmful effect of antibiotics is that killing off all the normal bacteria results in the proliferation of yeast. There are hundreds of articles in the scientific and medical literature indicating that yeast over-growth is associated with antibiotic use. Some of the most important are included in the references at the end of this chapter (3-13). There are two reasons for this. First, when the normal bacteria in the intestine are killed off, the yeast have no competition so they are able to get the lion's share of all the food that passes through the intestinal tract after a meal. Second, the yeast may actually be stimulated by many of the antibiotics (12, 13).

Scientific work on animals is relevant to yeast infection in humans. Infant mice were much more susceptible to *Candida* infection than older mice and, once exposed to *Candida* at an early age, developed persistent candidiasis (3). If these mice were given antibiotics at an early age, the *Candida* in the intestinal tract increased an average 130-fold. Exposure of infant mice to the hormone cortisone increased *Candida* in the intestine 8-fold. Similar results with antibiotics and cortisone are found in humans (5-11). Largely because of the overuse of antibiotics, the incidence of disseminated candidiasis has changed from a rare occurrence prior to 1960, to the fifth most common organism encountered in infections acquired at a hospital in Southern California (14). It is important to know that bacteria and yeast produce chemical byproducts in the body that are normally only present in very low concentrations. When yeast and bacteria, normally only present in small quantities in the intestinal tract, reach extremely high numbers, they produce these byproducts in much higher concentrations which are then absorbed from the intestinal tract into the blood. From there, they circulate throughout the body to all the tissues and are eventually filtered out of the body into the urine.

In addition to the production of these byproducts, the yeast cells may convert to their more invasive colony form. The yeast in this hypha form imbed themselves into the lining of the intestinal tract like ivy climbing a brick wall. This attachment is facilitated by the secretion of yeast digestive enzymes at the point of attachment. The intestinal lining is thus digested by a variety of yeast enzymes including phospholipase A2, catalase, acid and alkaline phosphatases, coagulase, keratinase, and secretory aspartate protease (15-17). The secretory aspartate protease is of special importance because it may destroy the lining of the intestinal tract and may also digest the IgA and IgM antibodies produced by the body to attack the yeast (15). The destruction of this gastrointestinal lining may be the reason for the abnormal secretin response discussed in the chapter on the digestive system.

As a result of multiple yeast attaching to the intestinal lining, some of the intestinal cells may die and the lining may appear like Swiss cheese on a microscopic level. Ordinarily, undigested food molecules would not be able to pass through this intestinal lining. However, because of the holes in the intestinal lining, undigested food molecules can pass through. This phenomenon is called the leaky gut syndrome. A major consequence of the leaky gut syndrome is a much greater susceptibility to food allergies. The undigested food is recognized as an invader by the immune system and as a consequence, antibodies of both the IgE and IgG types may start to be produced. After a while, both behavioral and allergic reactions may occur after eating these foods. Many times, patients with multiple allergies will be retested after anti-yeast therapy and find that their allergies have disappeared. When the yeast overgrowth has been eliminated, the intestinal lining heals, the intestine is no longer leaky, and the immune system may diminish its attacks against the offending foods.

Evidence for Abnormal Bacterial Byproducts in Autism

As discussed in the first edition of my book, one of the chemical compounds in urine that I initially suspected was due to intestinal yeast overgrowth was called dihydroxyphenylpropionic, acid-like compound (DHPPA). Several years ago, I began a collaborative study with Dr. Walter Gattaz, a research psychiatrist at the Central Mental Health Institute of Germany in Mannheim to evaluate urine samples of patients with schizophrenia. These samples were very valuable since they were obtained from patients who were drug-free. Thus, any biochemical abnormalities would be due to their disease and not a drug effect. Five of the twelve samples contained a very high concentration of a compound identified by gas chromatograph-mass spectrometer (GC/MS) as a derivative of the amino acid tyrosine, which is very similar to, but not identical to 3,4-dihydroxyphenylpropionic acid. I have since then identified this compound as 3-(3-hydroxyphenyl)-3-hydroxypropionic acid or HPPHA (Figure 1).

Newborn infants tested at approximately one month of age had extremely low values of this compound in urine since newborns are not colonized with intestinal germs (Figure 2). In older children, the values are much higher. In children with autism, values may be extremely high. There is some degree of overlap in the normal and autism population but the median and the mean values are significantly higher in the children with autism. (The median is the middle value of a group of numbers while the mean is the average value of the group.) The mean value for all infants is 3.7 mmol/mol creatinine with a standard deviation of 3.6 mmol/mol creatinine and a range from 0.3 - 12.7 mmol/mol creatinine. In normal male control children, the mean value is 91.5-mmol/mol creatinine with a standard deviation of 90.4; the median value in this group is 51.1 mmol/mol creatinine. In autistic male children, the mean value is double that of the controls: 192.4 mmol/mol creatinine with a standard deviation of 90.4; the median value in this group is 143.5 mmol/mol creatinine, nearly triple the value of the control group. In normal female control children, the mean value is 85.5-mmol/mol creatinine with a standard deviation of 55.9; the median value in this group is 74.5-mmol/mol creatinine. In autistic female children, the mean value is double that of the controls: 182.4 mmol/mol creatinine with a standard deviation of 200.6; the median value in this group is 111 mmol/mol creatinine, a value 49% greater than the control females. In all groups the median values are smaller than the corresponding mean values indicating that the values are not normally distributed and that the populations are skewed by some samples with very high concentrations of HPPHA.

What was surprising to me was that there was not a significant decrease in HPPHA after antifungal drug therapy. The mean value for the HPPHA actually increased a little. This increase indicated to me that this compound could not be due to the yeast, but was probably due to a different microorganism. Several children and adults with *Clostridium difficile* infection of the intestinal tract had high values of HPPHA in their urine and also a similar compound, called monohydroxyphenylpropionic ^(18, 19), which I suspected was being produced by one or more species of the bacteria genus *Clostridium*.

There are many different species of *Clostridium*. Some of the common species are *Clostridium tetani* which causes tetanus; *Clostridium botulinum* which causes food poisoning (botulism); *Clostridium perfringens* and *Clostridium difficile* which cause diarrhea; *Clostridium perfringens*, *Clostridium novyi*, *Clostridium bifermentans*, *Clostridium histolyticum*, *Clostridium septicum*, and *Clostridium fallax* which may all cause gangrene ⁽²⁰⁾. Many other species of *Clostridium* are normal inhabitants of the intestinal tract but may not even be scientifically described or named as a species. The major reason for a lack of knowledge about these organisms is that they are strict anaerobes that cannot tolerate oxygen. Since they must be processed in an oxygen free environment, many hospital laboratories do not have the capability to identify these organisms.

Chapter 2

Figure 1

Normal Catecholamine Metabolism and Its Altered Metabolism Due to Clostridia Bacteria

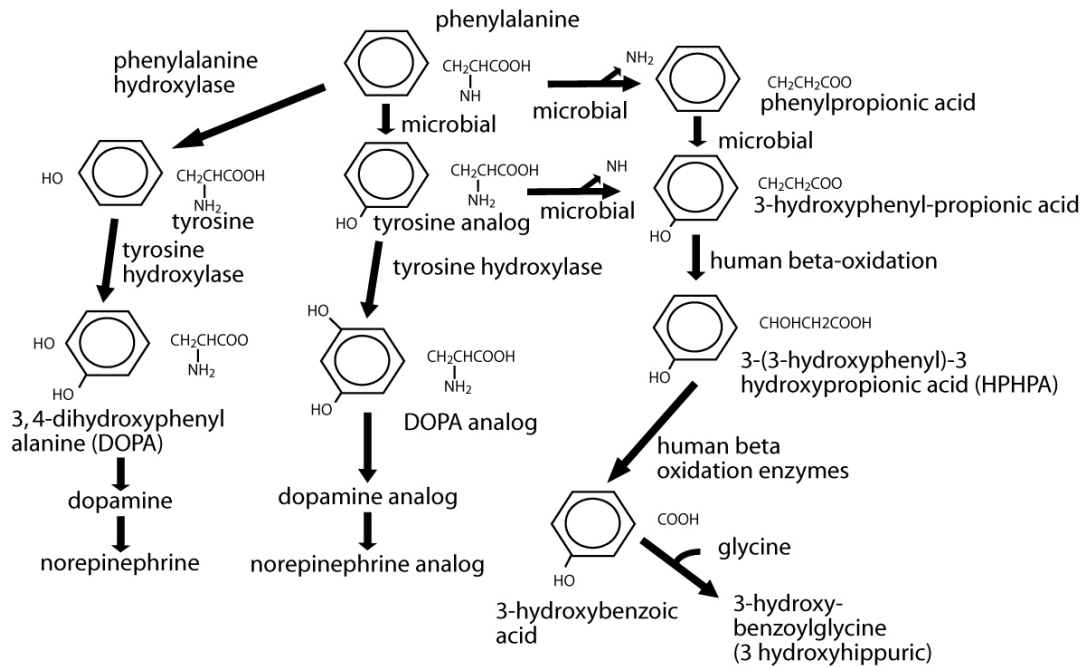
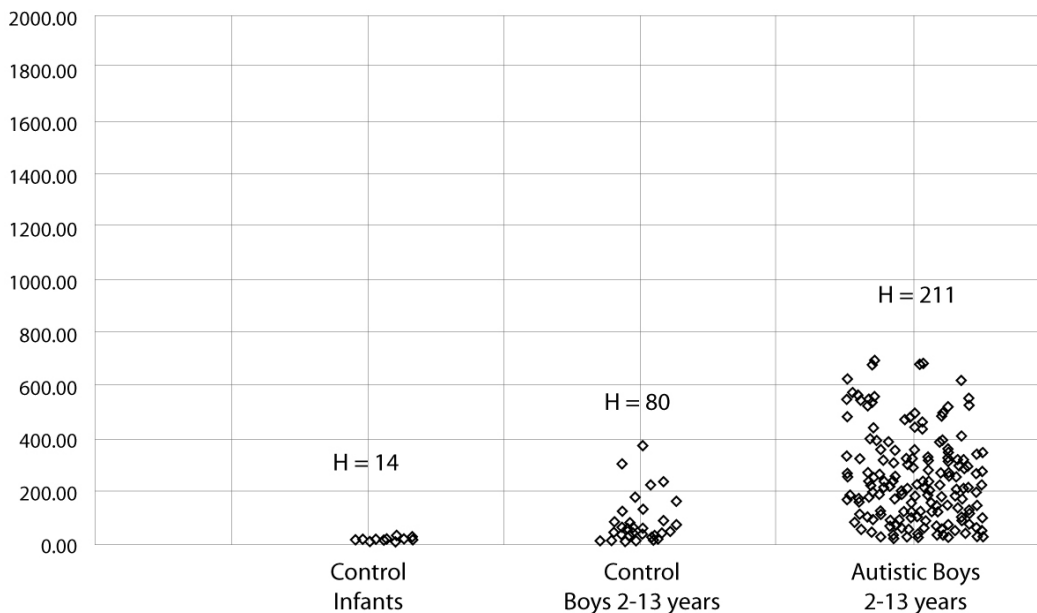


Figure 2

Distribution of Values for Clostridia Metabolite in Urine Samples of Male Infants, Control Boys, and Boys with Autism. The Creatinine Ratio Corrects for Differences in Fluid Intake.

3-(3-Hydroxyphenyl)-3-Hydroxypropionic Acid mmol/mol Creatinine



The exception is *Clostridium difficile*, which is identified by the toxin it produces in the stool rather than by the isolation of the organism itself. *Clostridium difficile* overgrowth of the intestinal tract causes a severe and potentially fatal disorder called pseudomembranous colitis ⁽²¹⁾. This overgrowth is frequently associated with the use of oral antibiotics, indicating that this organism is resistant to many of the common antibiotics such as penicillin, ampicillin, tetracyclines, cephalosporins, chloramphenicol, and others ⁽²²⁾. This organism is usually treated with either metronidazole (Flagyl) or vancomycin followed by a replenishment of the intestine with *Lactobacillus acidophilus* ⁽²³⁾. Since many bacteria can genetically transfer drug resistance to other similar species and even unrelated species, it is likely that multiple species of *Clostridia* may now be resistant to the most common drugs.

Another reason that I became interested in clostridia was due to the theory of Ellen Bolte ⁽²³⁾ that the tetanus bacteria (*Clostridium tetani*) might be responsible for some cases of autism. Her child developed autism after a DPT (diphtheria, pertussis, and tetanus) immunization, which includes a tetanus toxoid. She was concerned that her child may actually have contracted tetanus from a contaminated vaccine. When the antibodies to tetanus were checked several years after this vaccination, the antibodies to tetanus were very high. Her child was extremely developmentally delayed and also had a high value of HPHA in the urine. There are some interesting parallels between autism and tetanus. Individuals with tetanus, like many with autism, have extreme sensory sensitivity and often need to be placed in dimly lit rooms ⁽²⁴⁻²⁵⁾ and avoid loud noises. In addition, patients with this disorder, which is also known as lockjaw, might have difficulty chewing and swallowing. Likewise, children with autism frequently have difficulties eating foods with certain textures. Thus, Ellen's idea was that perhaps her child had instead contracted "subacute" tetanus causing many of the sensory related symptoms of autism, but in a non-lethal form because of the immunization. Such cases of subacute tetanus have been reported even in individuals who had been immunized and had high levels of antibodies to the tetanus toxin ^(24, 25). I thought it was highly unlikely that her child contracted tetanus from the tetanus vaccine. However, I thought it possible that he might have a *Clostridium tetani* overgrowth of the intestinal tract or an overgrowth of another species of *Clostridium* that might also be producing toxins similar to that of tetanus. As a result, these toxins might have caused the high antibody levels in her child or it is possible that one or more of the toxins in the vaccine was much more toxic to her child than to the average child immunized.

Clostridium tetani overgrowth of the intestinal tract has been demonstrated in rats ⁽²⁶⁾. The toxins produced by several different species of *Clostridia* (*tetani*, *botulinum*, *barati*, and *butyricum*) are very similar biochemically ⁽²⁷⁾ and therefore antibodies produced against one *Clostridium* toxin would also probably react against the tetanus toxin. Also the gene for the tetanus neurotoxin is located on a plasmid ⁽²⁸⁾, a piece of "naked" DNA that can be easily passed on to different species of *Clostridia* and perhaps even other species of bacteria which would confer on the new species the ability to make tetanus toxin.

Several of the patients with high urine concentrations of HPHA had positive stool immunoassay tests for *Clostridium difficile*, leading me to suspect that *Clostridia* species were responsible for the production of this compound. Treatment of a number of patients with elevations of this compound with drugs that kill *Clostridia* such as vancomycin and Flagyl resulted in nearly complete elimination of this compound in urine samples. There is a marked decrease in the urinary concentration of HPHA following the administration of standard age-appropriate doses of the antibiotic Flagyl (metronidazole). In all four patients, the concentrations of HPHA decreased 99% or more after two to three weeks on this drug (Table 1). In the first patient in the above series, HPHA rapidly increased following the cessation of metronidazole treatment. I suspect that this increase after stopping the drug was due to the fact that *Clostridia* are spore-forming organisms. Spores are extremely resistant forms of the bacteria that are difficult to kill and they "hatch out" when drug therapy ends and repopulates the intestinal tract. The first patient improved after Flagyl treatment but then regressed when the drug was discontinued. The same child was retreated with a six-week course of vancomycin. A

developmental specialist estimated that the child had gained six months of development after the six weeks of drug therapy. Again, the child regressed after discontinuation of therapy.

In a clinical study ⁽²⁹⁾, Dr. Richard H. Sandler from Rush Children's Hospital in Chicago, Illinois, along with a multi-center team recruited 11 children with regressive-onset autism who had a history of antimicrobial therapy. The children were given 500 mg of vancomycin per day for 8 weeks. Based on the Wilcoxon Signed Rank Z-scores and other measures during treatment with vancomycin, Dr. Sandler's group noted improvement in communication and behavior for the group as a whole. Their report indicated that "Although improvement was clear by several measures, unfortunately these gains did not endure." When the parents of the children were telephoned 2 weeks after the end of the trial, most reported "substantial behavioral deterioration." When the children were seen after 2 to 8 months, all but one had returned to baseline analog ratings.

Elevated levels of HPHPA is not only found in individuals with autism. Patients with values of HPHPA greater than 500 mmol/mol creatinine in the urine almost always have severe neurological, psychiatric, or gastrointestinal disorders. These types of disorders are often seen in autism, severe depression, chronic fatigue syndrome, tic disorders, psychotic behavior or schizophrenia, partial muscle paralysis, severe colitis, or sometimes a combination of these disorders. One young woman with an acute psychosis had the highest value I had ever seen, nearly 7500 mmol/mol creatinine, a value approximately 300 times the normal median value for adults! According to the patients' physicians, treating psychotic individuals with vancomycin, who have elevated HPHPA in the urine, resulted in remission of symptoms without the use of neuroleptic drugs.

How important is this compound in autism? A number of children with very high values (greater than 400 mmol/mol creatinine) of HPHPA have responded favorably to treatment with Flagyl or vancomycin. I would estimate that perhaps 20% of children with autism might have these very high values. However, in most cases Flagyl or vancomycin therapy might not even be needed. Instead, supplementation with a probiotic called *Lactobacillus acidophilus* GG may control this abnormality even in extreme cases. In *The Lancet* medical journal, Gorbach et al ⁽³⁰⁾ reported that this particular strain of *Lactobacillus acidophilus* was extremely effective in controlling recurrent *Clostridia* colonization of the gastrointestinal tract. Other strains of *Lactobacillus* have not been successful in the treatment of *Clostridia*. *Lactobacillus acidophilus* GG is available as the product Culturelle, which can be ordered from New Beginnings Nutritionals (www.nbnus.com) at (913) 754-0458. Culturelle may contain a minute amount of casein, although most children tolerate it with no problems.

In his evaluation of vancomycin for the treatment of autism, Dr. Sandler did not use *Lactobacillus acidophilus* GG after the children were treated with vancomycin. Therefore, the *Clostridia* most likely returned after the spores hatched or perhaps more drug resistant forms of *Clostridia* were produced after this relatively intense drug therapy. The results of Dr. Sandler are very similar to those of the child in Table 1 whose urine HPHPA cleared up after metronidazole (Flagyl) but became abnormal again after metronidazole was stopped. In addition to an inability to kill spores of *Clostridia* by his treatment protocol, Dr. Sandler also failed to control the *Candida* overgrowth, which is extremely common following the use of all antibiotics. *Candida* overgrowth would, of course, eventually eliminate many of the gains made by the elimination of *Clostridia*.

Chapter 2

Table 1

Effect of Flagyl Therapy on Urinary Excretion of HPHPA

Diagnosis Age (yr.) and sex	Length of Time (Days) from start of Flagyl Therapy	Urinary HPHPA Mmol/mol creatinine
Autism, male, 4 yr	0	435
	6	184
	16	1
	21(Stop Flagyl)	5
	24	2
	43	236
	93	274
Female, 54 yr C.difficile infection and uncontrolled diarrhea	0	396
	13	1
Autism, male, 3 yr	0	549
	19	1
	30	3
Autism, male, 4 yr	0	1362
	11	28
	15	3

Table 2

A Result Obtained in a Child with Autism After Treatment with Lactobacillus Acidophilus GG Treatment

Status	Lactobacillus in stool	Clostridia HPHPA in urine mmol/mol creatinine
Before treatment	0	3265
After treatment for 2 months with 1 capsule daily of Lactobacillus acidophilus GG	4+	174
Normal range	3+ - 4+	0-150

An examination of how HPHPA fits into normal human metabolism helps to give an insight into how this metabolic route may be involved in autistic behaviors.

HPHPA as a Possible Indicator of Abnormal Neurotransmitter Formation

There are two possible sources of HPHPA: phenylpropionic acid and 3-hydroxytyrosine (Figure 1). Both of these compounds have significant neurochemical effects that may produce abnormal behaviors in both animals and humans. As shown in Figure 1, HPHPA is produced from the amino acid phenylalanine in the diet. Phenylalanine is a constituent of almost all proteins, which are broken down to amino acids by digestive enzymes in the intestinal tract. Phenylalanine is an essential amino acid that cannot be restricted from the diet without causing serious health problems. Phenylalanine is important because it is the raw material from which the neurotransmitters dopamine and norepinephrine are formed.

When certain bacteria of the Clostridium family (genus) are present in high numbers, phenylpropionic acid or 3-hydroxytyrosine may be formed from phenylalanine in the intestinal tract (Figure 1). Either of these compounds may then be further converted to 3-hydroxyphenylpropionic acid which, in turn, is converted to HPHPA by the enzymes in the human mitochondria that break down fatty acids. Occasionally, fatty acids such as adipic, suberic, methylsuccinic, and ethylmalonic are elevated when 3-hydroxyphenylpropionic acid is elevated. Presumably, these fatty acids may not be burned up efficiently by the body and become elevated when the mitochondrial enzymes are swamped by excessive 3-hydroxyphenylpropionic acid.

Phenylpropionic acid is important because it is an inhibitor of the enzymes in the brain that break down enkephalins ^(31,32) and administration of phenylpropionic acid to mice raises brain enkephalin concentrations ⁽³²⁾ and causes analgesia (pain relief) when injected intraperitoneally (into the abdominal cavity) into mice. Enkephalins and endorphins are opioid peptides that are produced in the brain and adrenal gland. The enkephalins exert a whole range of biological effects including analgesia, regulation of the hypothalamus in the brain, modulation of emotions, stimulation of sexual and feeding behavior, and regulation of blood pressure, temperature, and intestinal function ⁽³³⁾. These compounds also profoundly alter many functions of the immune system ⁽³⁴⁾. Thus, the buildup of enkephalins after increased phenylpropionic acid in the blood might have extremely important effects on human physiology. I have found that phenylpropionic acid is frequently elevated when HPHPA is elevated in the urine. In the organic acid test done at The Great Plains Laboratory, measurements of Phenylpropionic acid in addition to HPHPA are included together with the metabolites of dopamine (HVA) and norepinephrine (VMA) which are discussed below.

3-Hydroxytyrosine (Figure 1), the other possible source of HPHPA, is important because it induces a characteristic behavioral syndrome in rats consisting of forepaw padding, head weaving, backward walking, splayed hind limbs, wet dog shakes, hyperactivity and hyper-reactivity in addition to depleting the brain of catecholamines ⁽³⁵⁾. Thus, this compound might play a direct role in causing abnormal behaviors in autism, schizophrenia, and other disorders. We have noticed that the molar ratio of the urinary concentration of the dopamine metabolite homovanillic acid (HVA) to that of the epinephrine/ norepinephrine metabolite vanillylmandelic acid (VMA) in urine (tested by mass spectrometry) is commonly elevated when HPHPA is elevated. This elevation appears to indicate that a byproduct involved in the formation of HPHPA likely inhibits the conversion of dopamine to norepinephrine, leading to relative dopamine excess. Animal studies have indicated that dopamine neurons mediate behaviors such as hyperactivity and stereotypical behaviors common in autism. Of course, the drugs such as the phenothiazines and haloperidol, commonly used to treat autism and schizophrenia, are well known to block the action of excessive dopamine at the receptor level ⁽³⁶⁾.

The following clinical implications result from this newly discovered metabolic pathway.

(1) **Supplementation with phenylalanine** has been recommended for the treatment of pain, depression, PMS, anxiety, and poor concentration ⁽³⁷⁾. However, supplementation with phenylalanine might lead to an overproduction of abnormal byproducts such as phenylpropionic acid and 3-hydroxytyrosine, perhaps leading to worsening of behavioral symptoms especially if the normal dopamine/norepinephrine ratio is further altered by a preferential oversynthesis of dopamine.

(2) **The use of organic acid testing** can provide a valuable tool in guiding therapy so that harmful microorganisms may be eliminated before treatment with amino acids like phenylalanine that might actually cause neuropsychiatric symptoms to worsen.

Control of Clostridia Overgrowth

I want to emphasize that the **die-off reaction** with Flagyl or vancomycin therapies may be **very severe**. The die-off reaction appears to be a release of toxins by the Clostridia as they die that may last 3-7 days after drug therapy. A child getting this particular therapy should be under very close medical supervision because the side effects may be much more severe than those associated with the yeast die-off reaction and can include symptoms such as heart palpitations, fever, and extreme tiredness: (some children may not even move during the first several days of therapy). The severity of the die-off reaction indicates to me the potency of the toxins produced by these organisms. However, the die-off reaction may be minimized by the concomitant use of materials such as bentonite or powdered charcoal, which are available in health food stores to absorb the toxins. In addition to the use of Culturelle, *Sacharomyces boulardii*, a non pathogenic yeast, has also been proven clinically effective at controlling and preventing recurrent Clostridia. **Probiotic control of Clostridia has been the most successful therapy to date.**

Clostridium difficile appears to be one of the organisms that produce the HPHPA. According to Sidney Finegold MD, one of the world's leading experts on anaerobic bacteria (Personal Communication), there are as many as 100 different species of *Clostridium* that may inhabit the intestinal tract. There is an immunological test for the toxin produced by *Clostridium difficile* that can be done on stool to confirm this organism. **A negative test for *Clostridium difficile* does not rule out all species of *Clostridium*, only *Clostridium difficile*.** There is no convenient method to confirm the identity of the other 99 species of *Clostridium* in the intestinal tract that may also produce this compound.

Relationship Between the Immune System, Early Use of Antibiotics, and the Microorganisms in the Gastrointestinal Tract

It has been found that injecting an animal with its own fecal matter, which consists of 50% bacteria by weight, only causes a mild immune response ⁽¹⁾. This indicates that the normal flora (germs) of the intestine are given tolerance by the immune system or that the immune system does not mount an attack against these organisms. The immune system takes an "inventory" of all the cells present in the body during fetal development and shortly after birth. (I have relied on material by Teresa Binstock Ph.D. ⁽³⁸⁾ at the University Of Colorado School Of Medicine as the primary source of this information.) In addition to the immune system taking inventory of its own cells, it seems increasingly likely that the immune system also takes an inventory of bacteria and yeast cells present in the intestinal tract. This inventory is performed by a group of cells called the

CD5+ B-cells, which are among the very first immunological cells to appear in the developing embryo and appear to play a role in tolerance to intestinal microorganisms in postnatal life. These cells may also play a role in regulating the secretion of IgA, the antibody class that is secreted into the intestinal tract and may be involved in selecting which microorganisms are tolerated there. Furthermore, the eradication of normal flora by repetitive antibiotic use during infancy may cause the CD5+ B-cells to reject normal organisms as foreign invaders at a later age. Any cells that are on this early inventory may be given immune tolerance and as a result, will not be attacked later on by the immune system.

This Secretory IgA antibody, which is produced by the immune system to fight intestinal germs, was found to react with harmful organisms but not with those of the normal flora. The secretory IgA coats the harmful bacteria and seems to prevent them from binding to the mucosa cells. Bacteria that cannot implant are more quickly flushed out of the intestine. Since a high percentage of children with autism are deficient in the production of IgA, their immune systems may have more difficulty in excluding overgrowths of harmful yeast and bacteria.

I have been impressed by numerous reports from parents of children with autism who indicate that their children used antibiotics at a very young age. I suspect that yeast and undesirable bacteria resulting from antibiotic therapy during early infancy have been “granted” immune tolerance; this immune tolerance may be one of the reasons why the yeast overgrowth in autism is so difficult to control and tends to recur even after months of antifungal therapy. Such an immune tolerance to yeast in the developing fetus may also occur if the mother has yeast infections during pregnancy. A woman, who had severe vaginal yeast infections during pregnancy, gave birth to a daughter with a severe yeast infection of the mouth called thrush. This daughter was later diagnosed with autism. Such cases may explain children who appear to behave abnormally even as young infants. Thus, a new direction for future research might be to find a way to reprogram CD5+ B-cells or to replace them with more suitable cells from a donor.

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Organic Acid Testing, Byproducts of Yeast and their Relationship to Autism

Chapter 3

Dr. William Shaw

Metabolic Disease Testing: The History of Organic Acid Testing

My discovery about abnormal organic acids in autism began as many discoveries do, as an accident. In the 1960's, a great deal of progress had been made in discovering the biochemical abnormalities that caused a number of diseases called inborn errors of metabolism using a technology called gas chromatography-mass spectrometry. It seemed possible that this new technology might be applied to any disease. However, thirty years later, very little progress had been made in solving the mystery of a number of diseases like autism, schizophrenia, and Alzheimer's disease.

In 1991, I had accepted the job as Director of Clinical Chemistry, Endocrinology, and Toxicology at a children's hospital because I wanted to improve upon what had been done previously in the field of metabolic diseases. I was also hoping to extend the existing technology to other diseases with unknown causes.

In the field of metabolic diseases, urine samples are analyzed for their chemical constituents after extracting the chemical compounds from the urine using organic solvents such as ether and ethyl acetate. It is preferable to test urine over blood because urine is a filtrate of blood in which much of the water has been removed, so that the concentration of a compound in urine might be 100 times more concentrated than it was in blood. A very high concentration of characteristically abnormal chemical compounds would indicate the likely presence of a genetic disease. For example, when a child has PKU (or phenylketonuria), which is a genetic disease where a genetic mutation is present, very high concentrations of chemical compounds called phenylketones will appear in the urine. This mutant gene codes for an abnormal form of the enzyme phenylalanine hydroxylase that converts phenylalanine to tyrosine. Since the enzyme is defective, phenylalanine is not converted to tyrosine and phenylalanine builds up in the blood just as a logjam begins in a narrow part of a stream. If a child with PKU is treated with a diet low in phenylalanine as an infant, the child will develop normally. However, if the diagnosis of PKU is not made until the child is much older; the child may be significantly impaired and suffer mental retardation ⁽¹⁾.

As a biochemist, I believed that any diseases which had caused devastating effects on an individual were bound to change their biochemistry. The presumption was that, if a person had a severe disease like autism, seizures, or cerebral palsy, there would have to be some change in one or more of the chemicals processed in the body. All of the body's chemical processes proceed by particular metabolic routes or pathways. Allow me to use an analogy to the Los Angeles freeway system. If an accident happens in Anaheim (a suburb of Los Angeles), traffic may back up in downtown Los Angeles. After a while, alternate roads begin to be utilized and the traffic begins to move again but at a much slower rate. If you measured the number of cars taking different alternate routes, you could pinpoint exactly where the accident had occurred. Using this analogy, the

chemicals we eat as food are the traffic, which proceeds along well-marked major highways called metabolic pathways until an accident occurs. The accident might be a mutation, an infectious disease, or a vitamin deficiency. As a result of the accident, the traffic flow of molecules is diverted onto the slow alternate routes instead of the twelve-lane expressway. The person with the slow traffic of molecules is alive but may not be functioning as well as individuals in which all the metabolic highways are open. The problem I was faced with, using the highway analogy, was "What if certain highways were not even listed on the highway map because the people who compiled them either didn't know about them, or knew about them but didn't include them on the map?"

In laboratories using the old organic acid technology, certain abnormal compounds in urine samples might be noted but the amount of the chemical compound would not usually be quantitated. In essence, the record of the analysis called a chromatogram would be visually examined or eyeballed to determine if a markedly abnormal substance was present. Although this method of examination may have been adequate 20-30 years ago, it was not up to date with the best and current technology.

Let me give another analogy: You go into a bank, open an account and make deposits for several weeks. After about a month you go back into the bank and you say, "I'd like to know my account balance." The teller looks at you and says with a straight face, "A lot". You feel concerned about this lack of information and press her for more information, and she says, "You really have more than most people do". That is still not satisfactory but there is no manager available so you walk away feeling confused and decide to go back later when a different teller is on duty. The next time you come in, you request the manager, asking again for your balance and this time the manager says, "Not much." Although this type of accounting may be adequate for comparing the assets of Bill Gates and a street person, it is not much help for those in the middle class. In essence, the majority of metabolic disease testing that was performed ten years ago was the "a lot" or "not much" variety, and this still exists in as much as 50% of the testing done today.



I suspected that many subtle changes in the body's metabolism were being overlooked in using this kind of technology as a result of the "not much" and "a lot" kind of interpretations. What I set out to do was to quantitate the changes in the different molecules in the urine just as the bank accountants in a bank balance the money transactions. I was successful because of new computer software that allowed for the rapid quantitation of very complex data. If it were not for this particular software, my work would not have been possible.

This computer software had originally been designed for the environmental field. Our drinking water, sewage and ground water can contain many kinds of pesticides, herbicides, and industrial chemicals. Testing for all of these chemicals requires very sophisticated computer software and this software was ideally suited for doing metabolic disease testing. The goals I set out to achieve were (1) to identify every chemical that I could, and (2) to quantitate everything I possibly could and do it as accurately as possible.

If we could know everything possible about people, including what kinds of chemical compounds were normal for them, then it would be easier to identify what was going on in the metabolism of a patient with a particular disease. Prior to beginning testing, we sent samples out to another laboratory performing the "a lot, not so much" kind of testing and I was very surprised to see that about 98% of the samples came back with an interpretation of normal. It does not seem possible, in my opinion, that someone could have a devastating disease, and not have it alter their metabolism in some way.

I continued to work on developing a more elaborate system of testing of my own. As a result, I found that, indeed, there was some increased detection (perhaps 5-10%) of certain known genetic diseases. However, this was a smaller increase than I had anticipated. I also noticed that in many different diseases, there were abnormal elevations of certain compounds that nobody seemed to know or care much about. When I discussed these findings with colleagues in the field of metabolic disease all over the world, they responded that these particular chemical compounds are not important because they are most likely a result of microorganisms in the intestinal tract.

After receiving this information and filing it away in my mind, I continued to remain skeptical of this common perception that microbial products were unimportant. The body did not have a metabolic segregation system in which human metabolites were allowed into certain areas of the body, while microbial products were separated into other compartments. All of these products were intermixed throughout the body. Several months after initiating my new laboratory service, Enrique Chaves, MD., a colleague of mine from the University of Kansas Medical School, and a pediatric neurologist who was also interested in biochemistry (a rather rare occurrence in physicians as a group) referred a woman to me who had two children with severe muscle weakness. Dr. Chaves, who had also been using the old technology in his laboratory, could find nothing unusual in the two brothers. The muscle weakness was so severe that sometimes, for several hours, these children could not even stand up. There had been an intensive search for the cause of this muscle weakness. When Dr. Chaves analyzed the lab results, he found no evidence of any genetic disease. Since I had this new technology, I was very interested in trying to find out what was going on. I told the mom that we would test samples of her children's urine and see if we could figure out what was happening to them.

Evaluation of Two Brothers with Autism

In the field of metabolic diseases, it is well known that some disease abnormalities only show up at the time the child is severely ill, i.e., if the child has a severe cold, flu or chicken pox. The biochemical pattern may be close to normal while the child is well. So when I spoke to the mom, I emphasized that we should get multiple

samples rather than just a single one. Several months later, the mom came back with a whole armful of samples saved in her freezer, which were actually more samples than we usually tested in an entire month. I talked to my technologist Ellen Kassen and told her we would have to bite the bullet and get these tests under way as best we could. We began to test the samples. In each sample, I would see that there was no chemical compounds characteristic of any of the known genetic diseases, which are called inborn errors in metabolism. My overall impression however, was that these samples were still abnormal because there was a marked difference in the kinds of chemical compounds found in the urine samples of the two brothers compared to those found in the urine of normal children.

These compounds were the same ones that my colleagues said were not important because they were from microorganisms in the intestinal tract. I was now very curious about what was going on. By this time, my colleague Dr. Chaves had moved from across town to the same institution where I was located. I was able to walk across the hall and further discuss with him any possible explanation as to why these brothers had these abnormal concentrations of chemicals resulting from microorganisms. At that time, he also mentioned that, in addition to the profound muscle weakness, the brothers also had autism. When I looked at their medical charts, I saw that they also had a history of frequent ear infections which is similar to many children with autism. A brief description of the technology used for testing the samples is appropriate at this point.

Urine samples are extracted to obtain a purified extract for analysis by a gas chromatograph-mass spectrometer (GC/MS). Samples are loaded onto a sampler tray of the GC/MS. The sample is then injected into a hollow tube in the oven of this instrument called a column. The different molecules in the sample go around and around in coils of this column just like a group of horses going around a racetrack and then come out at the finish line. At the finish line the sample is bombarded by a beam of electrons that break the molecules into pieces of different sizes and shapes. The molecules can be identified because each molecule has a characteristic way of breaking up or fingerprint. The data from this fingerprint is then transferred into a computer. Then the computer analyzes all that data, makes sense out of it, identifies it and quantifies how much of each kind of molecule is in the urine sample. The increase in the capability of this technology has been phenomenal. When I first started in this field, the analysis of a single chemical compound would have taken most of the day. Now we can identify a thousand different compounds in a single afternoon.

Figure 1 shows a typical chromatogram for the analysis of the urine sample of a normal child. This profile is called a total ion chromatogram. People who work in the field call each one of these blips that you see a peak. A peak is detected when identical molecules in the sample are swept by the pressure of an inert gas around the circular column and finish at a particular time. The size of this peak is proportional to how much of a particular kind of molecule there is. Small fast molecules cross the finish line faster than big slow molecules just as fast horses have the fastest race times. Fast molecules have the smallest transit time, which is called a retention time. The bigger the peak, the more of a compound is there. Conversely, the smaller the peak, the smaller the amount of compound.

A urine chromatogram of a normal child has many peaks, some of which are small and some of which are large. Contrast this chromatogram of a normal child with the child that has autism (Figure 2). An examination of this figure reveals that there are many more chemical products present in the urine sample of the child with autism. In retrospect, it was fortunate that the children I initially tested were more abnormal than the average child with autism since it helped me to notice the marked differences. There is both more of certain molecules (higher concentrations) indicated by larger peaks as well as more peaks (more compounds). In addition, some of the peaks found in the urine sample of the child with autism are nearly absent in the normal child.

What I found is that there was a consistent pattern of abnormally elevated chemicals in the urine samples of the two brothers with autism that were known to be derived from the intestinal microorganisms. So virtually all of the big changes that you see in the chromatogram of the child with autism (Figure 2) were due to the fact that they had much higher concentrations of the chemicals that were produced by microorganisms residing in their intestinal tracts.

Evaluation of a Third Child with Autism

Based on all the information that I had gathered, I reasoned that if the abnormal compounds from the intestinal tract had something to do with causing autism, then treatment of the microorganisms that produced these byproducts should improve the behavior of the child. I only had to wait a short time before I got the opportunity to test out my hypothesis. A child had been referred to the Neurology Department of the hospital to confirm a case of autism and organic acid testing had been requested. This child had the kind of history that is very frequent in autism.

The child was developing completely normally when the child began to have ear infections. The ear infections continued, and they came one after another. The child developed a thrush or yeast infection of the mouth that occurs because antibiotics have killed off the normal bacteria that keep the yeast population in check. Prior to the recurrent ear infections, the child had a vocabulary of about 150 to 200 words. Following the antibiotics and the yeast infection, the child's development began to slow and then regressed. The child no longer spoke any words. The child became extremely hyperactive, was no longer social, no longer made eye contact, and had a very disruptive sleep pattern. I have seen this particular pattern in many children with autism, but not in all. In some cases, the child may have been treated with antibiotics for recurrent streptococcal throat infections, urinary tract infections, sinusitis, or recurrent bronchitis.

I explained my theory to the mother of the child whom I'll call Bruce. The mother was a nurse at another nearby hospital and understood about thrush and antibiotics and was willing to give the antifungal drugs a try. The patient "belonged to" the chief of neurology and his approval would be necessary to get a prescription for the drug, which he declined. Being a nurse and knowing that the antifungal drug nystatin had no serious side-effects, she decided to obtain a prescription for nystatin from her family doctor, who was in private practice and not associated with the hospital. Within a couple of days of starting nystatin, Bruce, who had lost most of his normal development, began to improve. His eye contact came back, his extreme hyperactivity began to dissipate and he began to have a greater amount of focus. The sleep pattern improved as well and Bruce slept through the night for the first time in months.

At day zero, the day that Bruce first came in and had the organic acid test done, the tartaric acid value in urine was 300 mmol/mol creatinine, a very abnormal value that was about twenty times the median normal value. (Most chemicals measured in urine are divided by the urine creatinine concentration to compensate for different amounts of fluid intake in different individuals.) Following the treatment with the nystatin, the level of the tartaric acid, which was one of the compounds that I suspected was derived from the microorganisms, decreased considerably and continued to decrease as the nystatin was continued (Figure 3). Since nystatin is an antifungal drug, this indicated to me that a yeast or fungus (these terms are somewhat interchangeable in that they are biologically very closely related) was causing the secretion of this compound in the intestinal tract.

TIC of ctrl062794.d
Run at 10:42 AM CDT on Mon Jun 27, 1994

Abundance

TOTAL ION CHROMATOGRAM
NORMAL URINE

lactic

oxaloacetic

4-OH-phenylacetic

acetic

hippuric

citric

di-OH-phenylpropionic

VMA

galactonic

4-OH-hippuric

succinic

Time (min.)

Compound	Approximate Retention Time (min)
lactic	2.5
oxaloacetic	11.5
4-OH-phenylacetic	12.5
acetic	14.5
hippuric	15.5
citric	16.5
di-OH-phenylpropionic	17.5
VMA	18.5
galactonic	19.5
4-OH-hippuric	20.5
succinic	21.5

Abundance

TOTAL ION CHROMATOGRAM
Urine from autistic child

3.0e+07

2.0e+07

1.0e+07

0.0e+00

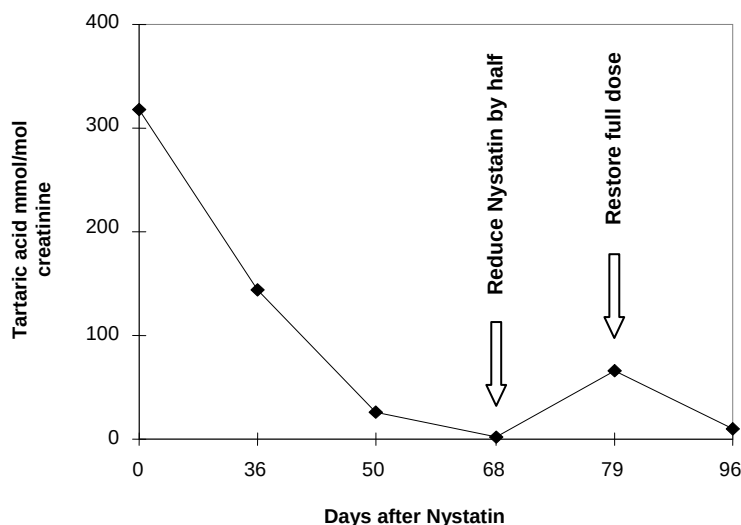
2 4 6 8 10 12 14 16 18 20

Time (min.)

glycolic
oxalic
3-OH-isobutyric
urea
phosphoric
succinic
3-deoxyketonic
citramalic
malonic
3-OH-phenylacetic
2-ketoglutaric
phenylacetic
phenylpyruvic
lactic
glutamic
glutamine
glutathione
hippuric
citric
3-OH-phenylpyruvic
urea
3-indoleacetic
phenolic
citric analog
uric
indole
3-OH-phenylpyruvic

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Figure 3
Effect of Nystatin on Urine Tartaric Acid



After 68 days Bruce's mother started running out of nystatin and began giving only 1/2 doses so that she didn't run out of it completely. During that time the tartaric acid started going back up and when she got the nystatin prescription refilled, the tartaric acid went back down. What this indicated to me was the fact that the nystatin was causing a marked reduction in this urinary tartaric acid. The other significant finding was that even after two months of nystatin, the biochemical abnormality would reappear within a short time of stopping the antifungal drug. In some cases, reports have been received of this same phenomenon in hundreds of other cases. Even after six months and after two or three years of antifungal treatment, there is often a biochemical "rebound" and loss of improvements after discontinuing the antifungal therapy. Several explanations are possible for this phenomenon:

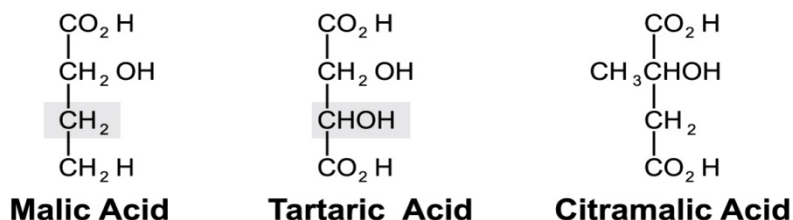
- As a result of one or more defects in the immune system (see chapter on the immune system), the yeast that are everywhere in our environment including the food we eat repopulate the intestinal tract very rapidly. Early antibiotic use may alter the normal microorganisms in the intestinal tract into an abnormal pattern that the immune system recognizes as normal and will not attack these organisms. (See chapter on gastrointestinal microorganisms.)
- The yeast are very resistant and have not been completely eliminated even after six months of antifungal therapy. Some of this resistant yeast might be the cell-wall deficient yeast described in the chapter on yeast.
- The yeast have genetically transformed some of the human cells that line the intestinal tract so that some of the human cells now contain yeast DNA. These genetically transformed human cells produce both yeast and human products and are somewhat sensitive to antifungal drugs but are not killed by them and produce yeast products whenever antifungal drugs are absent.
- Some of the yeast is hidden in recesses of the intestinal tract or in the deeper layers of the mucosa that lines the intestine where they are relatively safe from the drug. Although their numbers are small, they readily repopulate the intestine after antifungals are stopped.

Properties of Tartaric Acid

What is tartaric acid and what is known about this product? A toxicology manual ⁽³⁾ indicates that tartaric acid is a highly toxic substance. As little as 12g has caused human fatality with death occurring within 12 hours to nine days after ingestion. Since this compound especially damages the muscles and the kidney ^(4,5) and may even cause fatal human nephropathy (kidney damage)⁽⁶⁾, it was of particular interest to me since the two brothers with autism's initial symptoms were extreme muscle weakness as well as evidence of impaired renal function. Gastrointestinal symptoms were marked (violent vomiting and diarrhea, abdominal pain, thirst) and followed by cardiovascular collapse and/or acute renal failure ⁽³⁾. (A gram is approximately the weight of a cigarette.)

Interestingly, I have found that tartaric acid is also elevated in urine samples of adults with the disorder fibromyalgia, a debilitating disease associated with muscle and joint pain, depression, foggy thinking, and chronic fatigue. (Dr Kevorkian has assisted in the suicide of two people with this disorder, which is tragic since a simple antiyeast treatment ^(7, 8) may help relieve the symptoms of this disorder.) Values for tartaric acid in urine may be extremely elevated in autism. A young Korean child with autism had a value of 6000 mmol/mol creatinine, a value that is about 600 times the median normal value. (The child's value returned to normal after a few weeks of antifungal treatment.) Assuming that the yeast in the intestine of the child were producing tartaric acid at a constant rate, this child would be exposed to 4.5 grams per day of tartaric acid, over one-third of the reported lethal dose! Proponents of the theory that wheat gluten sensitivity is the main biochemical abnormality in autism would have difficulty in explaining this case, since rice was the only grain in this child's diet. (Gluten and casein restriction is a very important therapy in most cases of autism and is dealt with in the chapters by Lisa Lewis, Pamela Scott, and Karyn Seroussi, as well as in the chapter on the digestive system).

Figure 4



Surprisingly, the Food and Drug Administration lists tartaric acid in the Generally Recognized As Safe or GRAS category ⁽⁹⁾, which means this product, can be freely used as an additive in processed foods. Unless a food additive is put on the GRAS list, the food company using the product may have to spend thousands or even millions of dollars to prove its safety. Therefore, the political pressure to get a product on this GRAS list is intense. Tartaric acid is a byproduct of the wine industry and a tremendous amount of tartaric acid sludge has to be removed from the wine after the grape juice yeast fermentation. This sludge is the primary source of tartaric acid used as a food additive.

I have not yet found tartaric acid in Candida culture media but individuals with high amounts of tartaric acid in the urine also have high Candida counts in the stool. Tartaric acid is most likely a product of the breakdown of arabinose that may form in the body and/or during sample transport. In the example below, the normalization of tartaric acid in the urine after antifungal treatment was associated with a reduced Candida yeast count in the stool. The antifungal treatment used was nystatin and Lactobacillus acidophilus for two months.

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Status	Candida Krusei stool	Yeast tartaric urine*	Lactobacillus stool
<u>Before</u> antifungal treatment	4+	993	0
<u>After</u> antifungal treatment	0	1	4+
Normal range	0-1+	0-15	3+ - 4+

*mmol/mol creatinine

Tartaric acid is available as a food additive in baking powder, grape and lime flavored beverages, and poultry. It may also be found in grapes and grape products. Cream of tartar, which may be used for baking, is nearly pure tartaric acid. It is used in the food industry as a firming agent, flavor enhancer, flavoring agent, humectant, acidity control agent, and sequestant (9). There is no evidence that any mammals can produce it, so it is most likely, purely a yeast by-product. Tartaric acid may only be formed in the absence of oxygen and it is an analog of the Krebs cycle compound malic acid (Figure 4). An analog is a chemical compound that closely resembles but is not identical to another chemical compound. The atoms that differ in the two molecules are shaded in gray. The reason an analog is important is that the analog may prevent the normal biochemical from completing its normal biochemical function.

I would use this analogy to explain the analogs. You live in a neighborhood in which the same builder used the same locksmith who put a lock in each house that is just a little different. There have been a few burglaries in your neighborhood recently, so when you go to visit your neighbor next door, you decide to lock your door before going to your neighbor's house. When you arrive at your neighbor's house, your neighbor hands you a cup of coffee and you put your key on the kitchen counter right next to your neighbor's key. You drink the cup of coffee, chat for a while and when you decide to go home, you unknowingly reach down and pick up your neighbor's key. Then you take your neighbor's key, which looks almost exactly like yours, go back to your house and put it into the lock. It goes in but when you start to turn it, nothing happens.

On a molecular level, the same kind of thing happens. Probably in some of the cases, the analog or false copy of the molecule breaks off and is stuck in the biological keyhole, which may be the critical part of an enzyme or cell receptor. These analogs then prevent the biochemical functioning from occurring. In some cases, the key eventually comes out and the right one is able to perform its biochemical function, however, your metabolism has experienced some degree of delay and lacks efficiency. This lack of efficiency can have a big impact if a high percentage of your metabolic processes are being affected simultaneously. Organs like the brain with a high rate of metabolism may be affected more than other organs. Think of how your TV set runs during a brownout when the supply of electricity is too low. If your metabolic processes are not efficient and are not producing sufficient energy, the brain may not process information efficiently.

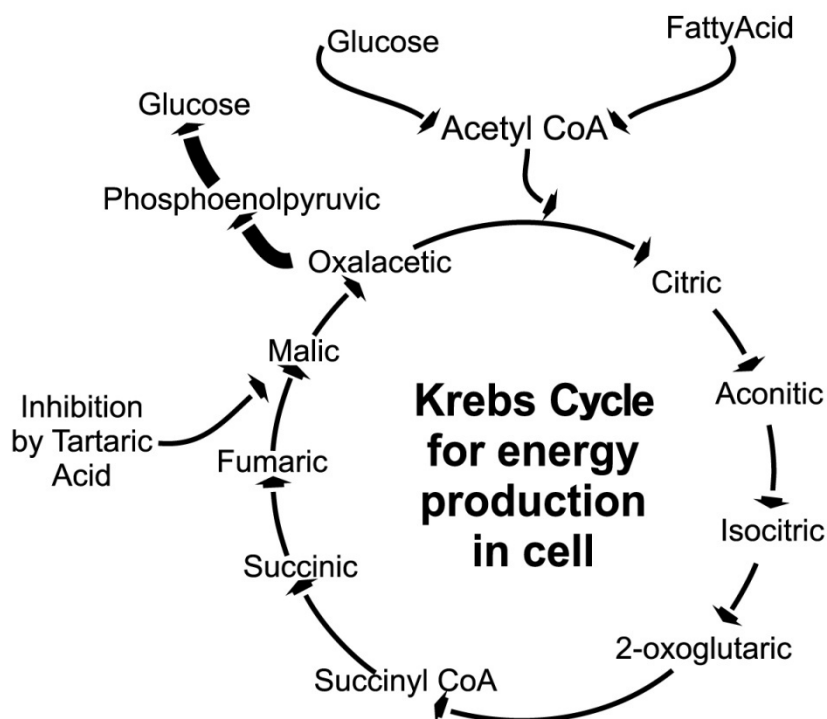
Let's return to tartaric acid and its specific role as an analog. Tartaric acid inhibits the enzyme fumarase (10), which is important in the function of the Krebs cycle, the biochemical process that produces most of the body's energy. In addition, the inhibition of fumarase also decreases the supply of malic acid for other functions of the cell. The proper function of the Krebs cycle depends on a continuing supply of malic acid. If malic acid is not provided in sufficient quantities, the Krebs cycle is short-circuited.

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A large percentage of patients with the disorder fibromyalgia, who have high amounts of tartaric acid in the urine, respond favorably to treatment with malic acid ⁽¹¹⁻¹³⁾. I presume that supplements of malic acid are able to overcome the toxic effects of tartaric acid by increasing deficient malic acid. Fifty percent of the patients with fibromyalgia, who also have elevated yeast metabolites, also suffer from hypoglycemia (low blood sugar) even though their diet may have adequate or even excessive sugar ⁽¹⁴⁾. The reason for this may be due to the inhibition of the Krebs cycle by tartaric acid. The Krebs cycle is the main provider of raw materials such as malic acid that can be converted to blood sugar (Figure 5) when the body uses up its supply. (The technical name for this process is gluconeogenesis or “new formation of glucose”.) If sufficient malic acid cannot be produced, the body cannot produce the sugar glucose which is the main fuel for the brain. Therefore, the person with hypoglycemia feels weak and their thinking is foggy because there is insufficient fuel for their brain. If adults with elevated values of tartaric acid in the urine have foggy thinking, little energy, and are so depressed that they may seek out Dr. Kevorkian, imagine what a similarly affected young child, who has yet to form a clear concept of the world, must feel like.

Citramalic acid, like tartaric acid, is another analog of the normal compound malic acid. Citramalic acid is exactly the same (Figure 4) as malic acid except it has an extra CH_3 group (called a methyl group) on it. Presumably, citramalic acid acts like tartaric acid in inhibiting the production of malic acid. There are two different types of citramalic acid called isomers. Both types of citramalic acid are probably in the urine of children with autism (2).

Figure 5
Krebs Cycle for Energy Production in Cell

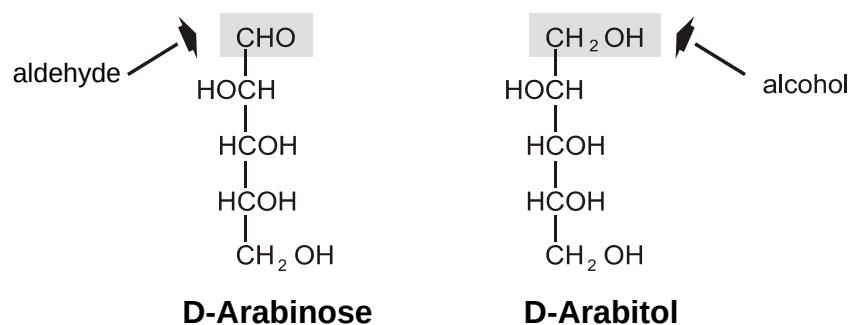


Arabinose and Candida

Figure 6 shows the chemical structure of a compound called arabinose, which is a sugar. (Arabinose is not an organic acid but is a chemical that we detect with our test.) This is not the same kind of sugar as kitchen table sugar but it is chemically very closely related. Like all sugars, it is sweet, which is what makes it a sugar. I found that, in the two brothers with autism, some of the values were much higher than in normal children.

Figure 6

Sugars Related to Yeast Overgrowth



In a study that was reported in the journal *Science* (a magazine in which experts report their findings to one another in highly technical language), Kiehn ⁽¹⁵⁾ reported information about a very closely related sugar called arabitol. Normal individuals have very low values of arabitol in the blood serum, but as people got sicker (or colonized) with the yeast, the values of arabitol increased. As the colonization worsened to a state called invasive candidiasis, the arabitol values could get extremely high: over a 1000 times the values found in the normal or control individuals. Many other papers have confirmed that high levels of this compound in both humans and animals were associated with *Candida* overload ⁽¹⁶⁻¹⁸⁾.

Figure 7 shows the distribution of arabinose values among two different groups. Each dot represents a different individual value for the urine concentration of this product. In children with autism, the values can be extremely high. Although there is some degree of overlap between the children with autism and the control group (normal children of the same age range), the mean and median values of urine arabinose for children with autism are much higher than those of normal children. The mean arabinose concentration in the urine samples of males with autism was over five times that of the normal male controls and the median value was six times that of the normal male controls. In infants (data not shown), arabinose values are extremely low, presumably because the intestinal tracts of newborn babies are nearly free of yeast.

Arabinose is a type of yeast sugar called an aldose that it is not known to be produced by humans. Arabitol (the alternative name for it is arabinitol) is a closely related yeast carbohydrate that is produced by *Candida*. I suspect that humans may possess the ability to convert arabitol to arabinose. Bacteria in the intestine may also convert arabitol to arabinose. We find a compound that is identified as arabinose in very high levels in urine of children with autism. A child with autism with the highest level of urine arabinose (over 40 times the upper limit of normal) had chronic hypoglycemia following antibiotic treatment for a throat infection as an infant (see chapter on gastrointestinal tract). Below is a comparison of the amount of arabinose in the urine of a child with autism with the amount of yeast in the stool taken at the same time. After four months of treatment with the antifungal drugs fluconazole and nystatin, both the arabinose in the urine and the *Candida* in the stool significantly decreased. This child had a severe *Candida* problem due to a complete deficiency of the antibody IgA that normally protects the intestine from *Candida* infections. This child had only two uses of antibiotics in

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his life, which was apparently sufficient to set up the yeast overgrowth. After treatment with antifungal drugs, the child had a marked reduction in autistic symptoms with a CARS (Childhood Autism Rating Scale) score in the normal range. Previous CARS scores indicated moderate to severe autism.

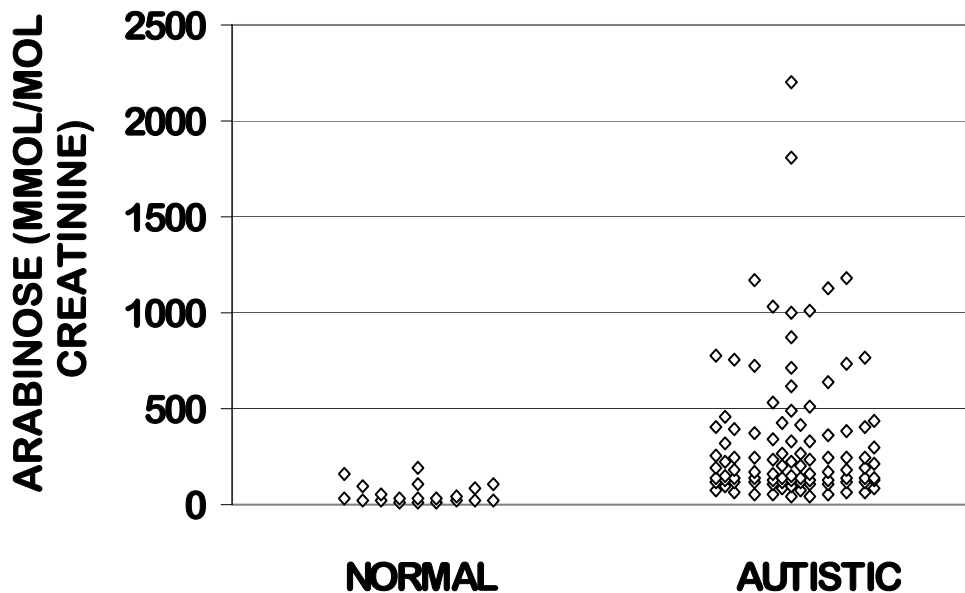
	Arabinose* in urine	Candida parapsilosis in stool
<u>Before</u> therapy	341	4+
<u>After</u> antifungal therapy	51	0
Normal range	0-47	0-1+

*mmol/mol creatinine

Women with vulvovaginitis due to *Candida* were found to have elevated arabinose in the urine ⁽²⁰⁾ and restriction of dietary sugar brought about a dramatic reduction in the incidence and severity of the vulvovaginitis. Thus, antifungal drug therapy for children with autism could be useful to reduce the concentration of a yeast produced abnormal carbohydrate that cannot be tolerated by the child with defective pentose metabolism. Arabinose tolerance tests should be able to rapidly determine if such biochemical defects are present in children with autism.

Elevated protein-bound arabinose has been found in the serum proteins of schizophrenics ⁽²¹⁾ and in children with conduct disorders ⁽²²⁾ and arabinose's ability to alter protein function might be another mechanism by which arabinose might affect biochemical processes in autism and other diseases.

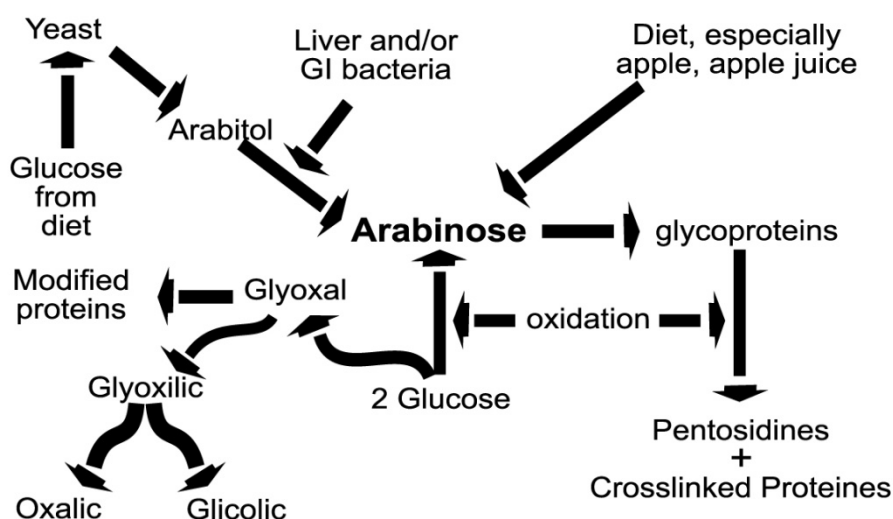
Figure 7



Other Sources of Arabinose

Arabinose may be found in some other foods in small quantities but the most significant source of dietary arabinose appears to be apples and pears. Arabinose values may be very elevated after drinking apple or pear juice or products such as applesauce or pear sauce (Figure 8). Therefore, apple and pear products should be restricted for a couple of days prior to testing. Several parents have reported severe worsening of autistic symptoms within a short time after their children ate apples. It is likely that the arabinose from apple products is responsible for this reaction.

Figure 8
Sources of Arabinose



Arabinose may also be formed from the breakdown of the sugar glucose ⁽²³⁾ and antioxidants such as glutathione may inhibit this conversion ⁽²⁴⁾. The breakdown of glucose also results in the formation of an aldehyde called glyoxal, which can also react with and modify protein structure and function. Glyoxal may be converted in the body to glycolic acid, glyoxylic acid, or oxalic acid. (Figure 8)

Arabinose, Pentosidine, and Protein Crosslinks

The aldehyde group of arabinose can react with the extra amino chemical group (called an epsilon amino group) of an amino acid called lysine that is present in a wide variety of proteins. This combined arabinose-lysine molecule may then form cross-links with an amino acid called arginine in an adjoining protein ⁽²⁵⁾, forming a compound called a pentosidine (Figures 9 A, B). The formation of a pentosidine may cross-link different proteins (Figure 10) and may alter both the biological structure and function of a wide variety of proteins ⁽²⁵⁾. The effect on all of the body's functions may be devastating.

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Figure 9A

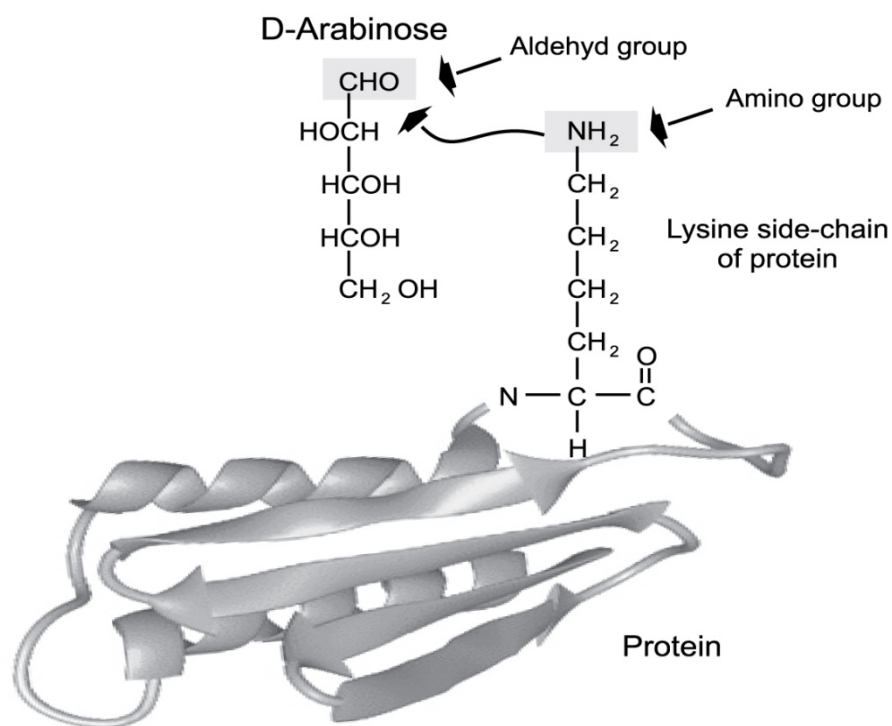
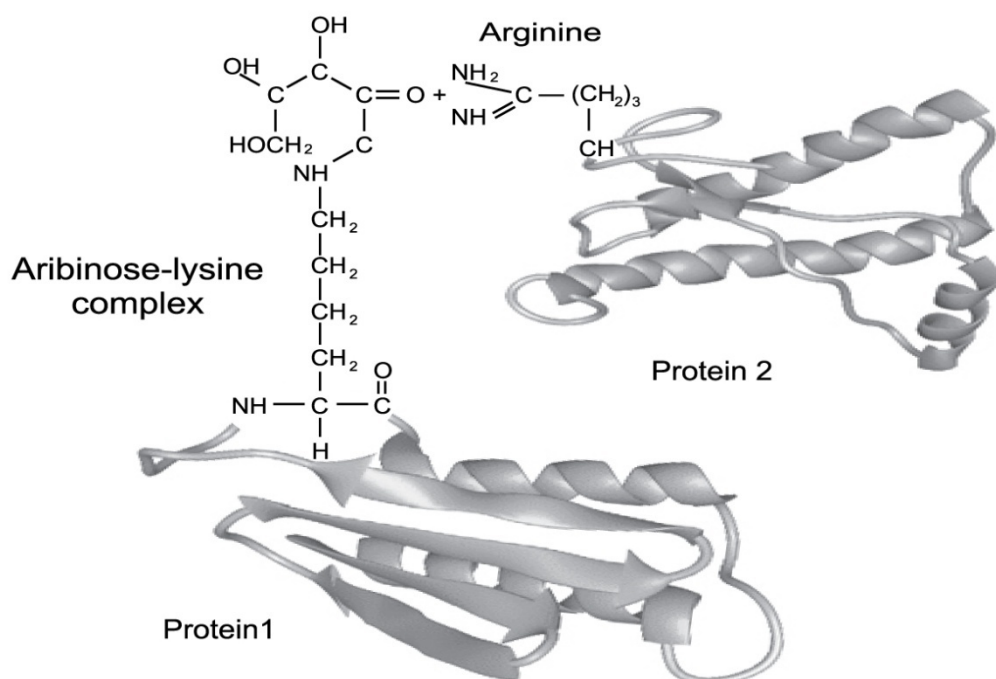


Figure 9B



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Figure 9C

Proteins crosslinked by pentosidine formation

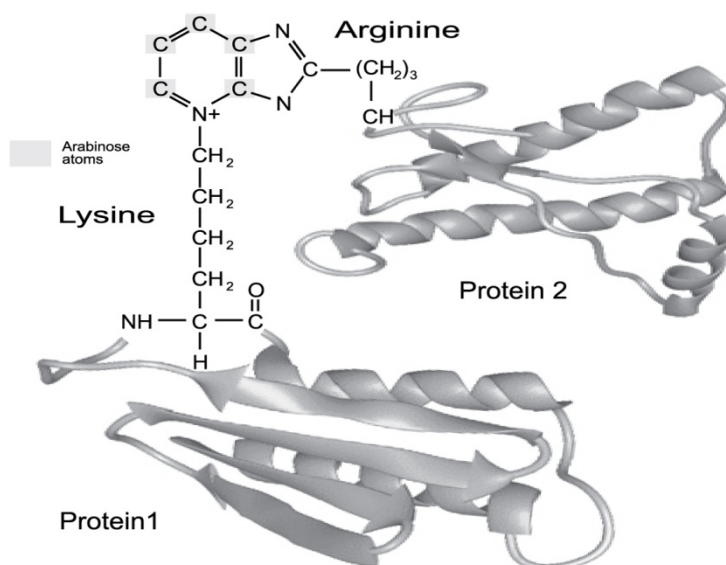
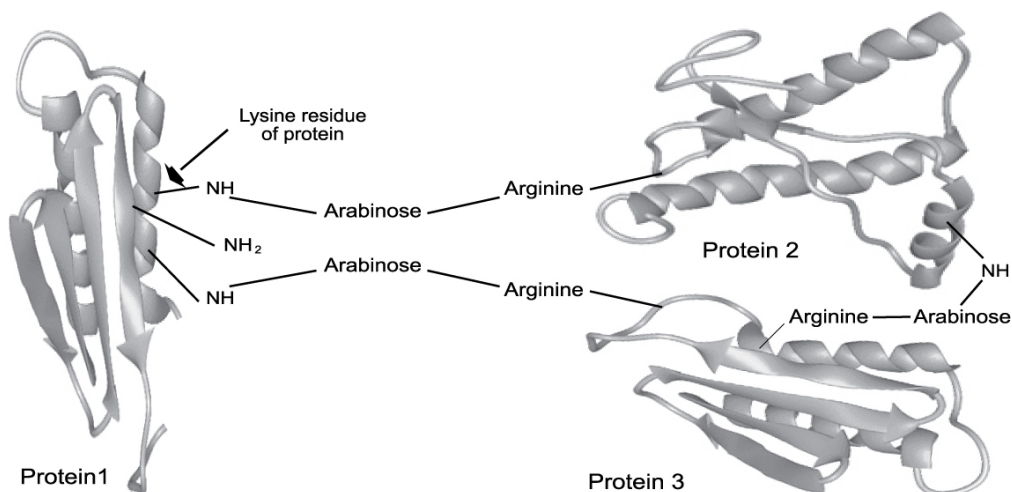


Figure 10



Let's use the LA freeway analogy again to understand. Suppose that on a very foggy day during rush hour, gremlins hiding under your moving car and those of your neighbors took strong steel bars and welded them to the frames of the moving cars. The steel bars stick out at a perpendicular angle for about three feet from the side of your car without you or any other driver noticing, because of the fog. Arabinose would be like the steel bar and the proteins would be like the cars. Next, the gremlins welded the other end of the steel bars to the frames of neighboring cars and they welded a bar between that neighboring car and a third car and so forth. Furthermore, some cars might be welded to each other by their bumpers in addition to their sides. Now imagine what will happen when one or more of the drivers wanted to exit or change lanes. Chaos and carnage would ensue. The combined molecule of arabinose, lysine, and arginine is called a pentosidine and is like the

two cars welded together. The undoing of these cross-links will become a major challenge in the future for treating older individuals with autism in which many of these cross-links have already been established.

I suspect that autism was reversed in the children of Pam Scott and Karyn Seroussi because they started therapy at a very young age. However, there have been many reports of improvements in people with autism in their twenties after antifungal therapy. Antifungal therapy cannot undo any of the existing cross-links, but can only prevent the formation of new cross-links by reducing the production of yeast arabinose. The tissue concentration of this combined molecule is almost linearly related to age ⁽²⁵⁾; the increase in crosslinks (steel bars) in this molecule is one of the main reasons we lose flexibility as we age.

One child with autism with a very high urine arabinose (1144 mmol/mol creatinine) was examined by MRI (a type of brain scan) and found to have diffuse demyelination (loss of myelin) of the white matter of the brain. (Values as high as 4000 mmol/mol creatinine have been found in children with autism who have not been eating apple products.) It is possible that pentosidine formation could account for this demyelination. Myelin is the material that covers the axons of the brain in much the same way that plastic insulating material is wrapped around copper electrical wire. Without an intact myelin cover, the nerve impulses in the brain are short-circuited just like an electrical wire with torn insulation. Most children with autism are not examined by their physicians with MRI but, on a research basis such an examination of children with high urine arabinose values might be helpful to prove a link between high arabinose and demyelination. A summary of the possible adverse effects of pentosidine is given in Table 1.

Table 1

Effects of Pentosidine Crosslinks
Decreased solubility-neurofibrillary tangles
Increased resistance to proteases
Decreased enzyme activity
Decreased access to coenzymes requiring free amino: B-6, lipoic acid, biotin
Crosslinks decrease flexibility of structural proteins in collagen and muscles
Stimulation of autoimmune disease by crosslink and glycosylated proteins

Arabinose and Impaired Vitamin Function

The epsilon amino group of lysine is a critical functional group of many enzymes to which the vitamins pyridoxal (vitamin B-6), biotin, and lipoic acid are covalently bonded during coenzymatic reactions ⁽²⁶⁾; the blockage of these active lysine sites by pentosidine formation may cause functional vitamin deficiencies (Figure 11) even when nutritional intake is adequate. In addition, the epsilon amino groups of lysine may also be important in the active catalytic site of many enzymes.

Pentosidines, Tangled Nerves, Alzheimer's Disease, and Autism

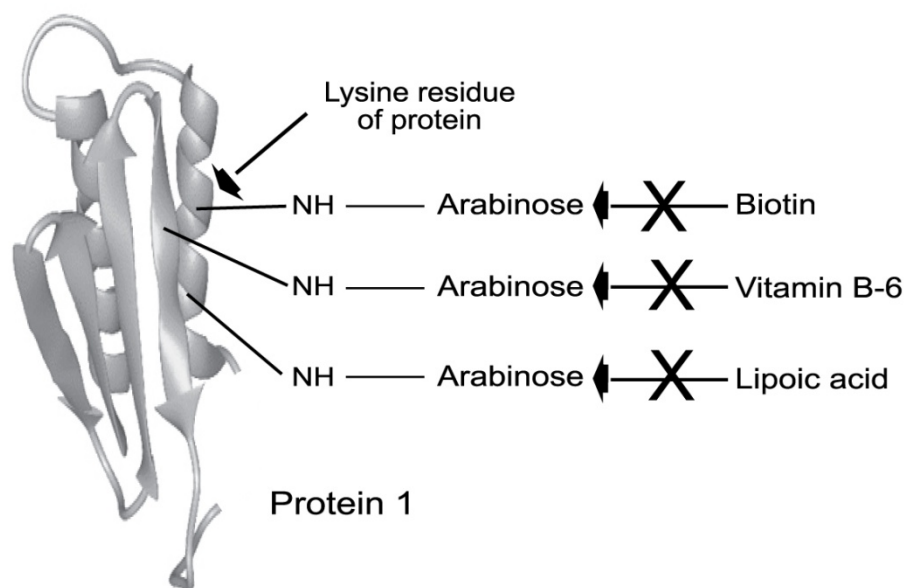
Protein modification caused by pentosidine formation is associated with crosslink formation, decreased protein solubility, and increased protease resistance. The characteristic pathological structures called neurofibrillary tangles associated with Alzheimer disease contain modifications typical of pentosidine formation. Specifically, antibodies against pentosidine react strongly to neurofibrillary tangles and senile plaques in brain tissue from patients with Alzheimer disease ⁽²⁷⁾. In contrast, little or no reaction is observed in apparently healthy neurons of the same brain. Thus, it appears that the neurofibrillary tangles of Alzheimer's disease may be caused by the pentosidines. The modification of protein structure and function caused by arabinose could account for the biochemical and insolubility properties of the lesions of Alzheimer disease through the formation of protein crosslinks. Similar damage to the brains of children with autism might also be due to the pentosidines and neurofibrillary tangles have also been reported in the brain tissue of an individual with autism ⁽²⁸⁾. It has been reported that frequent urinary tract infections are associated with more severe Alzheimer's disease ⁽²⁹⁾. The use of antibiotics to treat urinary tract infections would of course lead to yeast overgrowth. I have found that urine arabinose is elevated in some cases of Alzheimer's disease and have received a report of a favorable response from antifungal therapy to treat Alzheimer's disease from a woman with a child with autism and a father with Alzheimer's disease.

Prevention of Pentosidine Formation with High Doses of Vitamin B-6 and Other Vitamins?

Glutathione has been reported to inhibit pentosidine formation ⁽²⁴⁾. Supplementation with the vitamins biotin, pyridoxal (B-6), and lipoic acid (whose function at protein epsilon amino groups may be blocked by pentosidines derived from arabinose) might also be beneficial. Addition of vitamin B-6 derivatives or vitamin C to proteins helps to prevent pentosidine formation ⁽³⁰⁾. In fact, I suspect that the beneficial effects of vitamin B-6 in autism reported in multiple studies ⁽³¹⁾ may be mediated by prevention of pentosidine formation. Pamela Scott used high amounts of vitamin B-6, for her child who recovered from autism prior to starting antifungal therapy. I suspect that this reduced somewhat the effects of the yeast die-off reaction. One way to test this idea would be to do a formal study to see if vitamin B-6 supplementation was less effective in treating autistic symptoms after antifungal therapy compared to supplementation before antifungal therapy.

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Figure 11



Other compounds called furans that are occasionally elevated in the urine of children with autism are probably derived from fungus such as *Aspergillus* ⁽³²⁻³⁴⁾ rather than yeast although it is possible they may be produced by yeast as well. The names of these compounds are called 5-hydroxymethyl-2-furoic acid, furan-2, 5-carboxylic acid, and furancarboxylglycine. The concentration of furan compounds in the urine also dropped markedly in children with elevated values after nystatin therapy, indicating to me a probable yeast and/or fungal origin of these compounds. Other investigators ^(35, 36) noted that these compounds increased after sugar consumption and assumed that these compounds were sugar products of human metabolism but neglected to take into account the Japanese work and the role of gastrointestinal microorganisms in modification of sugars in the food. My interpretation is that these compounds may be derived from sugar but that they are converted to these furan products by the metabolism of yeast and/or fungi in the intestinal tract.

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Yeasts and Fungi: How to Control Them

Chapter 4

Dr. William Shaw

Since byproducts of yeast and fungi are frequently elevated in urine samples of people with autism, knowledge of the biology of these organisms and the therapies to control them are essential.

Fungi is a biological group of organisms that include yeasts, molds, and mushrooms. Thus, all yeast are fungi but many fungi are not yeast. One of the most common diseases causing species of yeast is *Candida albicans*. Other species of *Candida* include *Candida tropicalis*, *Candida glabrata*, *Candida pseudotropicalis*, *Candida guilliermondii*, and *Candida parapsolis*. Probably all of these species can cause disease especially if the immune system is weak ⁽¹⁾. *Candida albicans* can exist in four forms: yeast or single cell form, a colony of cells or mycelium, a chlamydospore or cyst-like form, and a cell-wall deficient form ⁽²⁾. Both the mycelium type and the chlamydospore are capable of tissue invasion ⁽²⁾. The vitamin biotin is thought to prevent the transformation of *Candida* from the yeast to the mycelium form and is sometimes included in nonprescription antifungal medications such as Candicyn ⁽³⁾.

The cell-wall deficient *Candida* may even be able to conceal itself inside of cells and may be the reason that complete elimination of *Candida* is difficult ⁽²⁾. These cell-wall deficient forms are extremely small—0.15 millionths of a meter. These cell-wall deficient organisms are extremely difficult to identify and would probably not be detected in the vast majority of hospital laboratories but only by advanced research laboratories. Certain yeast may actually grow faster when antibiotics are included in the growth media ^(4, 5). *Aspergillus* is a common food-borne mold, which is capable of living and reproducing in the gastrointestinal tract ⁽⁶⁾. The furan compounds, 5-hydroxymethylfuroic and furan-2, 5-dicarboxylic, which are frequently elevated in urine samples of children with autism, (see chapter on organic acids) are known products of *Aspergillus* species ⁽⁷⁻⁹⁾. The closely related compound furancarboxylglycine is probably a detoxification product of the other furan compounds, which is combined with glycine in the liver. The fact that antifungal drugs decrease the concentration of these products in the urine samples of children with autism, leads me to suspect that *Aspergillus* or similar species of mold are producing these compounds in their gastrointestinal tract.

Even ordinary household yeast, which is called *Saccharomyces cerevisiae*, might cause disease in susceptible individuals. Different strains of this same species are used in both the baking and brewing (alcoholic beverage) industries. *Saccharomyces cerevisiae* can also exist in the yeast or mycelium form and, like *Candida*, can cause vaginal yeast infections ⁽¹⁰⁾. This type of yeast is being investigated for its role in the intestinal disorder called Crohn's disease ⁽¹¹⁾, and it can cause systemic infection in individuals with impaired immune systems ⁽¹²⁾. The finding of high concentrations of tartaric acid, a product of *Saccharomyces cerevisiae*, in the urine samples of many children with autism indicates a strong possibility that *Saccharomyces cerevisiae*, or a closely related organism, may play a role in autism.

Since yeast have the ability to ferment sugar into alcohol, an increase in blood alcohol after intake of sugar can be used as an indicator of yeast overgrowth of the intestine. Dr. Eaton and his colleagues ^(13, 14) at The London Medical Centre in England found that blood alcohol concentrations in patients with suspected yeast overgrowth increased one hour after ingestion of glucose. Furthermore, they found that after dietary restriction of carbohydrates, 42% (27 of 64) of patients were negative on re-test ⁽¹³⁾. When these patients used both dietary restriction and antifungals, 78% (116 of 149) of the patients were negative on re-test, indicating that this therapy was highly successful in the treatment of intestinal yeast overgrowth.

Yeast is more complex than bacteria on the evolutionary scale. They are eukaryotic organisms that have cells with defined structures like mitochondria, nuclei, and chromosomes. Many yeast biochemicals are exactly the same as those produced by humans. In many children with autism, there is increased excretion of the compound called 3-hydroxy-3-methylglutaric acid in the urine. Increased 3-hydroxy-3-methylglutaric acid in the urine may be due to a genetic disease called 3-hydroxy-3-methylglutaric acidemia ⁽¹⁵⁾. However, the elevated values of urinary 3-hydroxy-3-methylglutaric acid in children with autism are much lower than the values in children with the genetic disease. Both humans and yeast use this chemical compound to make steroids. I suspect that high values in children with autism are due to yeast overgrowth of the gastrointestinal tract and that it is unlikely (but still possible) that some children with autism have a mild form of the genetic disease 3-hydroxy-3-methylglutaric acidemia.

Diagnosis of Yeast Disorders

Why is *Candida* such a problem to diagnose? The condition that occurs in most children with autism is not technically an infection; it is really an overgrowth of the intestinal tract. Furthermore, the yeast do not colonize the intestinal tract in an uniform fashion, but instead, usually form clusters or nests. Sometimes, they settle in the crypts of the intestine, which are small out of the way “side pockets”. Therefore, failure to detect these organisms by endoscopy examination (examination with a long tube) of the intestinal tract does not rule out their presence ⁽¹⁶⁾. There are several ways of diagnosing such a condition including the stool culture, the organic acid test, and the blood test.

Stool Testing

The problem with stool cultures is that many people have a small number of *Candida* present in their stool at any given time ⁽¹⁷⁾. Furthermore, if the yeast are in their hyphal or colony form, most of the cells are physically attached to the intestinal lining and the stool culture can only detect the cells that have broken off. If you get a positive test result on a stool culture for yeast, it really doesn't convey much information unless it is a quantitative one. The real question is not whether or an individual has *Candida*, but rather how much *Candida* is there? Even though the stool culture is not perfect, I have examined a large number of reports in which both the organic acid and stool culture tests were done and two techniques compliment each other. The Great Plains Laboratory now offers a combination test profile (Combo test) that includes a stool test for yeast as well as the urine organic acid test for yeast and bacteria metabolites. The stool test includes testing to determine which antifungal drugs are most effective for the particular yeast strain in stool.

Organic Acid Test for Yeast and Bacterial Byproducts

The organic acid test is valuable because it detects byproducts of yeast and fungi produced in the intestinal tract. These byproducts are then absorbed into the blood stream from the intestinal tract and are eventually filtered into the urine. The sample is easy to collect and only a small amount of first morning urine is required. The organic acid test screens for many genetic diseases such as PKU and nutritional deficiencies as well. In addition, the organic acid test will also detect byproducts of bacteria that may also be important in a subgroup of children with autism.

This testing is available from:

The Great Plains Laboratory

11813 W. 77th St.

Lenexa, KS 66214

E-mail: GPL4U@aol.com

Website: www.greatplainslaboratory.com

Phone: 913 341-8949

Fax: 913 341-6207

Blood tests for Candida

Severe Candida infection, called systemic Candidiasis, is a serious illness with severe symptoms like high fever, which can even be fatal in individuals with weakened immune systems. Candida infection of the brain, called Candida meningitis, can also be fatal ⁽¹⁸⁾ but this is a very rare condition that sometimes occurs in HIV-positive individuals or infants with extreme immune deficiency. Finding Candida by blood culture is considered the definitive test for systemic yeast infection; however, in one of the most intensive studies done ⁽¹⁸⁾, there was a very high incidence of false negatives using blood cultures for Candida. In children who really did have yeast invasion of their organs including brain, liver, or heart (and this was confirmed by autopsy), only 17% of the children's blood samples tested positive for yeast even though they had been tested repeatedly (an average of ten times) for Candida.

What is the reason for the failure of these blood tests in detecting systemic candidiasis? It is possible that Candida is a fastidious organism that doesn't grow if it doesn't "like" the particular culture of the media in which it is placed or perhaps the antibiotics given to the patients may have induced the development of cell-wall deficient forms that could not be detected by ordinary culture methods. Another explanation may be that yeast implanted in the tissues are not shedding very many cells into the blood where they can be detected. Antibodies can be used to detect Candida but such antibodies measure old infections. Even with Candida IgM antibodies, that measure recent infections, it is not clear whether this antibody test can pick up the intestinal yeast overgrowth because most of the time, the yeast are not in the blood stream.

However, with yeast overgrowth in the intestinal tract, fever rarely occurs. Symptoms of intestinal yeast may include behavioral changes such as hyperactivity, psychosis, depression and non-specific complaints such as fatigue, achy joints and muscles, sleep disturbance, increased allergies, chemical sensitivity, and increased incidence of vaginal yeast infections in women and "jock itch" in males ^(3, 19, 20).

There are several places that fungal infections can exist. There can be external or superficial infections, which involve the mouth, skin or vagina. Athlete's foot is one of the common kinds of fungal infections. Some people get fungal infections under the nails called onychomycosis. Internal or systemic yeast infection can be life threatening. In this type, the yeast has escaped from the intestinal tract, into the body, and can invade the

organs. It can invade virtually any organ of the body including the blood, the lungs, the bones, the kidneys, the liver, the heart, the eyes, and the brain ⁽¹⁸⁾.

Interactions of Yeast and Other Bacteria

Yeast and bacteria live together in the intestinal tract and it is not surprising that sometimes there is both synergy or cooperation and competition between the species. For example, studies have shown that *Candida albicans* has supported the establishment of *Staphylococcus aureus* infection in mice, ⁽²¹⁾. In addition, the treatment of yeast overgrowth with antifungals leads to bacterial overgrowth if beneficial bacteria are not used at the same time. Furthermore, it has been shown that *E. coli*, a common intestinal bacteria and *Saccharomyces* can exchange genetic information through a piece of DNA called a plasmid ⁽²²⁾, leading to the possibility that the genetic makeup of common yeast might eventually be contaminated by the genes of intestinal bacteria. An inhibitory effect of *Pseudomonas* bacteria on *Candida* growth has been reported ⁽²¹⁾ and might be evaluated as a potential therapy, if a suitable safe species of this bacterium could be developed.

Antifungal Therapies

The major therapies for treating yeast overgrowth in autism include probiotics, anti-yeast diet and non-prescription and prescription anti-fungal products.

Probiotics

Probiotics (pro=for + biotic=life) are microorganisms that are used therapeutically to control abnormal overgrowth of yeasts, fungi, and bacteria in the intestinal tract. Probiotics were first recommended by the Russian immunologist Metchnikoff, who received the Nobel Prize in Medicine for his discovery of the role of the white blood cells in fighting infection. In the early 1900's, Metchnikoff proposed that many human diseases were caused by abnormal overgrowth of harmful bacteria in the intestinal tract. He noted the good health of a European community that included large amounts of yogurt in the diet. Yogurt contains bacteria of the *Lactobacillus* family and Metchnikoff concluded that the *Lactobacillus* family was controlling the harmful bacteria that produced harmful "ptomaines". Metchnikoff's observations probably were a major impetus to the development of the health food industry.

There are now over a hundred different brands of beneficial bacteria that are available in mail order supply houses, pharmacies, and health food stores. Some of the common species of bacteria are *Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus bulgaricus*, *Lactobacillus salivarius*, *Lactobacillus thermophilus*, and *Lactobacillus plantarum*. Other beneficial species include *Bifidobacterium bifidum* and *Streptococcus faecium*, (not to be confused with *Streptococcus faecalis*, a pathogen.) In addition to these different species, these bacteria are found in many different formulations including suspensions, loose powder, capsules, and flavored chewable tablets. Some of these organisms are grown on dairy products as a source of nutrition while others are dairy-free. Because most children with autism are sensitive to the peptides derived from milk, it may be wise to choose a dairy-free brand.

I generally recommend *Lactobacillus acidophilus* GG, a special strain of *Lactobacillus acidophilus* that was formulated and patented specifically for controlling *Clostridia* overgrowth of the gastrointestinal tract. I generally recommend a dose of at least 10 billion cells per day for any child over three and half that amount for younger children. These products may help to control both yeast ⁽²³⁾ and abnormal bacteria such as *Clostridia* ⁽²⁴⁾ in the intestinal tract. In addition to probiotics, which are good bacteria, there is increasing interest in a beneficial yeast called *Saccharomyces boulardi* ⁽²⁵⁾ to control both yeast and *Clostridia* overgrowth of the intestinal tract. However, I would advise caution since there have been some reports of hypoglycemia with this agent. I recommend the simultaneous use of a probiotic product any time an antifungal drug is used. Yeast are part of the intestinal ecosystem and hold other organisms in check. Overgrowth of harmful bacteria may occur unless probiotics are taken simultaneously with prescription or nonprescription antifungal products.

Diet to Control Yeast Overgrowth

Numerous popular books by William Crook M.D. ⁽¹⁸⁾, John Trowbridge M.D. ⁽¹⁹⁾, and others have addressed the importance of sugar elimination to control intestinal yeast overgrowth because of the stimulatory effect of simple sugars on yeast. Vargas and his colleagues found that mice given sugar water had 200 times the amount of *Candida* yeast in the intestine compared to mice given plain water ⁽²⁶⁾. Similar results have also been reported in the treatment of humans for yeast related illnesses ⁽²⁷⁻²⁹⁾. The rule of thumb for sugar elimination is simple: If it's sweet, don't eat. The list of restricted foods includes candy, ice cream, cake, pie, soda pop, Kool-Aid, and even fruit juices. Since your child may be on a dairy-free diet as well, water may become your child's main drink. To ease the transition, you might want to dilute fruit juice ten-fold with water during the transition.

All types of sugar, both "natural" and refined, should be eliminated including honey, syrup, fruit sugar, and refined sugars. You will find some difference of opinion on sugar elimination. Some authorities recommend complete elimination while others allow occasional sugar in the diet. A vitamin C supplement may be needed if your child gets a lot of his daily vitamin C from orange juice. Fruits may have to be eliminated from the diet for a period of about a month to accelerate the yeast elimination. The high-sugar dessert foods may have to be eliminated indefinitely.

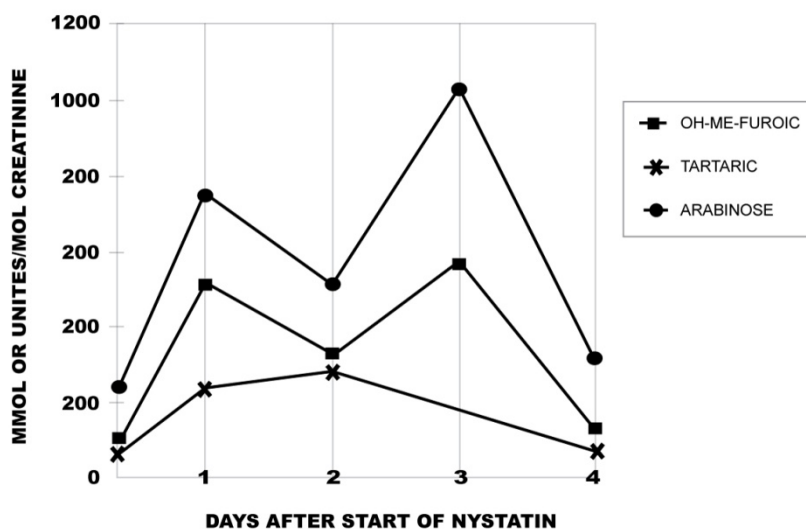
What is left to eat since wheat and dairy products may have also been eliminated for the casein and gluten-free diet? Major sources of carbohydrates may include potatoes, corn, rice, yams, and other vegetables such as beans, peas, broccoli, etc. All meat and fish are acceptable although both Pam Scott and Dr. Semon are concerned about antibiotic residues and fungal byproducts in commercial meat. Pam Scott went the extra mile to obtain antibiotic-free sources of these meats, which may or may not be essential but who can argue with success. It is true that complex carbohydrates are broken down to simple sugars in the intestinal tract, which then "feeds" the yeast. Therefore, diet alone may be insufficient to control a significant yeast overgrowth and it may be necessary to also use some kind of antifungal therapy. Eaton's data (mentioned earlier in the chapter) indicates that combining diet and antifungals is nearly double the effectiveness of diet alone in eliminating intestinal yeast overgrowth. I always recommend combining the two therapies. No formal assessment of these combined therapies is available but the experience of many physicians who treat for yeast-related illnesses indicates better response when both diet and antifungal products are used simultaneously.

The Yeast Die-off or Herxheimer Reaction

The Herxheimer reaction is also called the yeast die-off reaction ^(3,19). Usually for about 3 or 4 days after starting antifungal drugs the person may feel a little bit worse during that time. There may be symptoms of extreme tiredness and even fever. The Herxheimer reaction is probably due to the abnormal release of abnormal organic acids or other toxic byproducts during the yeast die off phase. The yeast is like water balloons filled with toxins. When you give the antifungal drugs, the water balloons burst and the contents of the water balloons are then absorbed into your body and are eventually excreted into the urine. Therefore, the concentration of abnormal urine organic acids increases when antifungals are first given (Figure 1) and then begin to drop as the yeast are all killed and the toxic organic acids are no longer released. My research is the first to document a marked increase in certain organic acids for several days after beginning an antifungal drug. The Herxheimer reaction is not limited to yeast and it also occurs when certain bacteria overgrowths of the intestinal tract are treated as well.

In cases of severe yeast overgrowth, Herxheimer or yeast die-off reaction can last as long as a week, though normally lasting 3 to 4 days. Some of the affects can be lethargy, fever, and an increase in stereotypical behaviors. Symptoms may also include bloating, nausea, vomiting, eczema, aching, headache, and stuffiness. In addition, children with autism or PDD may experience an intensification of symptoms such as craving sweets, self-stimulation, arm flapping, and hyperactivity. For example, if a child with autism normally does a lot of hand flapping, there may be an intensification of this behavior during this yeast die-off period. Some of the parents of children with autism tried nystatin years ago for their children and gave up on it because of adverse effects during the die-off reaction.

Figure 1
Biochemical Basis of Herxheimer Reaction



Four approaches can be taken to reduce the intensity of the yeast die-off reaction:

- Use nutritional approaches to cut down on yeast burden prior to using an antifungal drug. Eliminate sugar containing foods from the diet for two weeks prior to the use of an antifungal drug. Even this dietary change alone may cause a slight to moderate yeast die-off reaction. It doesn't matter whether or not a

sugar is natural or artificial. Any simple sugar (glucose, fructose, sucrose, or galactose) will serve as yeast food. In addition, sugared drinks and fruit juices may have more sugar than foods. It is important to give your child vitamin C during this period (500-1000 mg per day is recommended). Sugar substitutes include stevia, xylitol, fructooligosaccharides and FOS. FOS is not digested until it is acted on by gas forming anaerobic bacteria in the lower gastrointestinal tract. A lot of parents noticed excessive gas and abdominal pain in their children after ingesting FOS so it may not be the ideal sugar substitute. Aspartame can cause headaches and other symptoms. It appears stevia and xylitol may be the best choices for sugar substitutes.

- Since many of the yeast products are acids, release of these acids, which are absorbed into the body, may cause a condition called metabolic acidosis. An extremely simple therapy used by physicians who treat autism is to supply a mild antidote that neutralizes the excess acids. The most convenient product is a nonprescription drug called AlkaSeltzer Gold. Do not use any other kind of Alka-Seltzer. Alka-Seltzer Gold is simply a very safe product called bicarbonate that helps to neutralize excess acids of any kind. The dose for children is on the label. Do not exceed the number of recommended doses.
- If the organic acid test indicates your child has high concentrations of tartaric acid, the tartaric acid may be inhibiting the production of malic acid. Malic acid is essential for the efficient operation of the Krebs cycle and for providing raw material that the body can use to produce its own sugar between meals. The use of malic acid supplements will probably help during the yeast die-off reaction and may also be useful until the tartaric acid from the yeast is eliminated through a combination of a low sugar diet and antifungal therapy. The use of malic acid supplements must be under the close supervision of a dietitian and/or physician because malic acid supplements frequently contain magnesium. Some multi-vitamins have high amounts of magnesium and other supplements may also contain magnesium. It is possible to ingest too much magnesium if combining different magnesium containing supplements leading to magnesium toxicity, which can be fatal. Since vitamin B-6 has the ability to prevent the formation of the harmful pentosidines, I would strongly urge the use of Vitamin B-6 prior to starting antifungal therapy.

Nonprescription Antifungal Products

Antifungal supplements that are available without a prescription from health food stores and New Beginnings Nutritionals (www.nbnus.com) include garlic or garlic extract, grapefruit seed extract, oregano, caprylic acid and its oil form MCT oil, Samento, goldenseal, monolaurin, and lactoferrin. These products are also combined into different formulations. Even though these supplements do not require a prescription for their use and common experience indicates they are safe, they are best used under the supervision of a health care professional who is familiar with their side effects. All of these supplements can cause the yeast die-off reaction that is just as severe as the one caused by prescription drugs. There have been many positive reports from parents of children with autism who have successfully treated with all of these supplements. Some of these people undertook therapy on their own because they lived in a remote area where alternative health professionals were not available and their family doctor would not prescribe antifungal drugs. Others used these supplements in the belief that they were safer than prescription drugs because they were "natural". I would like to emphasize that nystatin is a very safe prescription drug and that it is probably just as safe as any of these natural supplements.

Garlic

Garlic is a potent antifungal product that also leaves a strong odor on the breath. Fortunately, it has been found that deodorized garlic has essentially the same antifungal activity as fresh garlic. Of course, fresh garlic is cheap and effective if you don't mind the smell. Allylsulfinyl alanine is a major constituent ⁽³⁾ of garlic that is converted to a compound called allicin when the garlic is crushed or eaten. Allicin and some of its byproducts contain sulfur its characteristic odor. When garlic is allowed to age for an extended time period, the odor dissipates. At lower doses, allicin is fungistatic meaning that it slows the growth of yeast or fungus. At higher doses, the allicin actually will kill *Candida albicans* ⁽³⁰⁾. The recommended dosage of Kyolic brand garlic for antifungal therapy for adults is three capsules per day. A child's dose would be proportionally less on a weight basis. Assume an average adult weight of 150 lbs. If your child weighs 50 lbs., the garlic dosage would be 50 lb/150 lb. or one-third the adult dosage.

Oregano

Oregano oil inhibited the growth of *Candida albicans* in vitro ⁽³¹⁾. The minimum inhibitory concentration (MIC) was less than 0.1mcg/ml when tested with 3 different strains of *Candida*; 0.1% survival occurred at a concentration of 45 mg/ml. Carvacrol, a major phenolic constituent of oregano oil, inhibited *Candida* as effectively as did the oil itself. Parents have indicated to me that oregano was sometimes helpful in their child with autism when nystatin was ineffective in killing the yeast. This killing of yeast by oregano was confirmed by stool yeast evaluation.

Caprylic Acid and MCT Oil

Caprylic acid is a fatty acid and is present in a wide variety of foods. Fatty acids have different numbers of carbon atoms ranging from two in acetic acid to twenty-four or more. Caprylic acid has six carbon atoms and thus is considered to be a medium chain length fatty acid. Caprylic acid eventually is just burned up by the body for fuel or may be stored as fat. Caprylic acid was found to have antifungal activity over 40 years ago ⁽³²⁻³⁴⁾. When three molecules of caprylic acid are combined with one molecule of glycerol, the compound is called a triglyceride. Triglycerides are also called fats or oils. Solid triglycerides are frequently called fats while liquid triglycerides are called oils. Triglycerides containing predominantly the medium chain length fatty acids are called medium chain triglycerides or MCT oil.

Caprylic acid is the predominant fatty acid in most commercially available MCT oil. MCT oil is a liquid at room temperature and thus can be administered to a child who cannot or will not take capsules or tablets of caprylic acid. The taste of MCT oil is fairly bland and it tastes very much like corn oil or other vegetable oils. When MCT oil reaches the intestine, it is broken down by lipases to form caprylic acid and glycerol. Since many children with autism have defective production of pancreatic enzymes, another positive benefit of MCT oil is in the fact that it is a medium chain triglycerides. Medium chain triglycerides are broken down to form caprylic acid at a much more rapid rate than long chain triglycerides ⁽³⁵⁾ so this compound can be broken down effectively when the pancreas is producing low levels of lipase (a digestive enzyme). Coconut oil also contains caprylic acid in a lesser concentration.

Caprylic acid is safe with the following exception. Children with the rare genetic disorder called medium chain acyl dehydrogenase (MCAD) deficiency cannot biochemically process caprylic acid ⁽³⁶⁾. Theoretically, caprylic acid could be harmful to these children. The organic acid screen performed in the Great Plains Laboratory checks for MCAD but it is possible that it might not be detected in its dormant form by the organic acid screen. The probability of a child having MCAD is low; probably less than one in six thousand. However, Duran and colleagues ⁽³⁷⁾ reported that no harmful effects were caused when a patient with MCAD was given a high dose of MCT oil. MCT oil is found in a variety of foods and infant formulas. A dose of up to one teaspoon twice a day for children over two years old and half that amount for infants would most likely be completely safe (even for a child with MCAD). However, if your child has MCAD or has ever had a lapse into a coma-like state, it is not recommended to use products containing MCT oil or caprylic acid since other effective antifungal agents are available.

Colloidal Silver

Silver is a metal that is used for jewelry and dinnerware. Solutions of silver have been used as a germicide since the early 1900's. In the Old West, prior to refrigeration, a silver dollar would be put in the milk container to prevent spoilage by microorganisms. Colloidal silver is a suspension of silver that kills almost all intestinal microorganisms including yeast, bacteria, protozoa, viruses, and parasites. My major concerns with this product are: (1) It essentially kills every living thing in the intestine including any beneficial bacteria. (2) It is a heavy metal and if the size of the silver particles is too large, the absorbed silver particles may lodge in the body causing a graying of the skin which is a condition called argyria ⁽³⁸⁾. Most heavy metals that kill microorganisms indiscriminately like mercury and arsenic are also toxic to humans. Although the claim is made that certain products are safe because the particles of silver are too small to be lodged in the capillaries of the skin and organs ⁽³⁸⁾, I would be *extremely* cautious about these products and would not use them except under close medical supervision of a physician who has used these products for a long time and is certain of the product's safety.

Lactoferrin

Lactoferrin is a protein found in many mammals including humans which possesses the ability to bind iron. Studies have shown that both human and cow lactoferrin kills *Candida albicans* and *Candida krusei* ^(39, 40). Lactoferrin is only active against *Candida* when it is free of iron since its mechanism of killing *Candida* is most likely by starving it from iron. Lactoferrin is available as a supplement but because of the iron inactivation and digestion by the body's enzymes, it is difficult to determine an appropriate dosing. A piece of the lactoferrin molecule called lactoferricin B can also kill *Candida*. Interestingly, this molecule also possesses potent antiviral activity as well ⁽⁴¹⁾. Since this product controls yeast by removing iron, an evaluation of your child's iron intake might be important. If a blood test shows that your child has high iron and high iron binding capacity, it might be beneficial to use vitamins that do not have additional iron when using lactoferrin for yeast control.

Combination Products

A large number of different combinations of antifungal products are available. There may be differences in the potency of each of these products as antifungals but there are few large studies with these products since the

small profits generated by these products cannot support expensive clinical trials. One product called Candida Defense Formula contains Pau D'Arco extract, oregano, gentian extract, caprylic acid, grapefruit seed extract, berberine, ginger, cinnamon, chamomile, and biotin.

Biotin

Biotin is one of the essential vitamins (termed vitamin H. Biotin) and it is commonly found in most multivitamin supplements but is usually present in doses well below the recommended daily allowance (RDA). In addition, biotin is one of the vitamins that is produced by good bacteria in the intestinal tract ⁽⁴²⁾. The use of antibiotics can eliminate this bacterial production of biotin leading to biotin deficiency.

I had a personal experience in my own family with this vitamin. When one of my sons was small, he was on antibiotics for an ear infection. He lost his appetite, began to lose weight, developed red eczema on the cheeks, became withdrawn, and then his hair began to fall out in large clumps. He began to look like a starved concentration-camp victim. Unfortunately, the role of yeast in such cases was unknown at that time. However, I knew that biotin deficiency could cause hair loss probably due to killing off the beneficial germs in the intestine, which produce it there. Supplementation with biotin started his hair growing back within a couple of days and he began to look better overall. This was the first episode that focused my attention on the negative side effects of the “miracle” antibiotic drugs and stimulated my interest in the role microorganisms play in our human biochemistry.

In addition to its nutritional role in humans, biotin is also needed by most other creatures including yeast. However, when yeast are exposed to biotin, they are stimulated to grow but are less likely to convert to their mycelium form, which is the form in which they invade the tissues ⁽¹⁹⁾. My recommendation is a supplement of 800-1000 micrograms per day for any person with a yeast-related condition. Biotin is a water-soluble vitamin and is completely safe at this dose. To minimize yeast overgrowth, it might be best to introduce biotin and other vitamins a week after beginning antifungal therapy.

Biotinidase Deficiency

Biotinidase deficiency is a genetic inborn error of metabolism that has been found both in autism ⁽⁴³⁾ and in Rett's syndrome ⁽⁴⁴⁾, a disorder in girls in which many autistic traits are present. Biotinidase deficiency is frequently associated with yeast and fungal infection ⁽⁴²⁾. Biotin from the diet becomes chemically bonded to many of the body's enzymes that require it. Biotin is attached to enzymes by combining specifically with the free amino group of the amino acid lysine ⁽⁴²⁾. If acetaldehyde or arabinose produced by yeast has previously reacted with these lysine sites, as discussed in other chapters, biotin will not be able to attach to these critical sites and cannot function properly. When the body eventually breaks down these enzymes, biotinidase is needed to chemically release biotin from its degraded enzyme.

When biotinidase is deficient, this bound biotin cannot be recycled in the body and, as a consequence, biotin is lost rapidly from the body. The symptoms of biotinidase deficiency are very similar to those in biotin deficiency. The therapy for this disorder is to give large doses of biotin daily: 5000-20,000 micrograms (mcg) per day. Defective regulation of the immune system has been reported in several patients with biotinidase deficiency ⁽⁴²⁾. Some of the patients had Candida dermatitis and some showed defective cellular immunity against Candida. One patient had reduced white blood cell killing against Candida and myeloperoxidase deficiency

(see chapter on immune system) that were normalized by biotin supplementation. Developmental delay is also common in biotinidase deficiency ⁽⁴²⁾.

Biotinidase may be especially important in autism because it has been found that the biotinidase enzyme also helps to break down peptides including those with opiate-type activity ^(45, 46). Therefore, patients with a biotinidase deficiency may be over-stimulated by endorphins and other peptides. It is also possible that the conversion of biocytin to free biotin by biotinidase might be inhibited by the high amount of undigested peptides from wheat and milk so that biotin might not be properly recycled even when biotinidase is present at normal values. Therefore, people with autism who are not on a gluten and casein free diet may need additional amounts of biotin in their diet. This enzyme is zinc dependent so it is possible that this enzyme may not function well if zinc is deficient, which is often the case in many children with autism.

Biotinidase deficiency is tested in only a handful of laboratories in the world and requires a blood test. This test is performed in the laboratory of Dr. Barry Wolf at the Genetics Dept at the Medical University of Virginia in Richmond, Virginia. The phone number is 804-828-9632. The easiest way to arrange for this test is to have your doctor request the test and then have a local pediatric hospital skilled in drawing blood from children take the blood sample and ship it to Dr. Wolf's lab.

Prescription Antifungal Products

Nystatin is one of the oldest and safest antifungal drugs. Its safety is largely due to the fact that it's not absorbed into the blood stream at the doses most commonly prescribed. Your entire intestinal tract is a long tube with your mouth at one end of the tube and your anus at the other end of the tube. Virtually 100% of nystatin is eliminated in the feces. Since nystatin does not enter the blood stream to any appreciable extent, it's very safe and can't cause any serious side effects. Nystatin is so safe that it is available in Germany without a prescription. Nystatin was named after the New York (NY) research laboratory in which it was discovered in the 1940's (NY=New York; *stat* = state; *in*). I know of no serious side effects that have ever been documented with the use of nystatin.

Most children with autism cannot swallow capsules so that the liquid suspensions of nystatin are sometimes the best options. The two brand names of nystatin suspensions are Mycostatin made by Squibb and Nilstat made by Lederle. William Crook M.D. advises against the use of these products because they contain both food dyes and sugar ⁽¹⁸⁾. However, most children with autism will not take capsules or plain nystatin powder that is measured out in scoops because of its bitterness. A good option is to find a compounding pharmacist who will mix it with stevia (a natural sweetener that can be bought at health food stores) and dye-free flavorings. All antifungal drugs cause the Herxheimer reaction or yeast die-off reaction.

Amphotericin B, which may be very toxic when given intravenously, is **very safe given orally**. When it is given orally, its safety is comparable to that of nystatin because like nystatin it is poorly absorbed from the GI tract. But to get this in a prescription in the United States that is suitable for oral use, you have to contact one of the special pharmacies that dispense this product including Wellness Health and Pharmaceuticals (1-800-227-2627) or College Pharmacy (1-800 855-9538). This drug is widely available for oral use in European pharmacies. The other prescription antifungal drugs are different from amphotericin and nystatin in that they are appreciably or completely absorbed from the intestinal tract into the bloodstream. There is a slight incidence of liver toxicity with all of these drugs that is not a factor with oral nystatin or amphotericin B. When these absorbed antifungal drugs are used, it is necessary to do a liver function test to make sure that the liver is not damaged. These absorbed antifungal drugs include Diflucan (fluconazole), Nizoral (ketoconazole),

Sporanox (itraconazole), and Lamisil (terbinafine). Even though these drugs can be considered safe for the most part, they are not as safe as nystatin or amphotericin B.

An increase in the activity of liver enzymes due to leakage from a damaged liver is usually an indicator of liver toxicity. However, a moderate increase in the activity of these enzymes after vitamin B-6 supplementation is not an indicator of liver toxicity. Vitamin B-6 increases the activity of certain of the transaminases or liver function enzymes called AST (SGOT) and ALT (SGPT). Vitamin B-6 is an essential cofactor for these enzymes and simply activates these enzymes. You need to be aware of this effect since you might be using these tests to monitor liver function when using systemic antifungal drugs. If B-6 supplementation was started at the same time as the drug, a moderate liver enzyme increase may be due to the B-6 activation of the enzymes rather than the release of these enzymes by a damaged liver.

When these absorbed drugs are used, it is necessary to check other medications that may be processed by similar liver detoxification mechanisms. Such drugs include anti-seizure medications, neuroleptics like phenothiazines and haloperidol, and antidepressants like amitriptyline. Other drug metabolism may also be affected and you should check with both your physician and pharmacist before using these drugs for your child. When these drugs are used with the absorbed antifungal drugs, the metabolism of both drugs may be slowed and the systemic amounts of these drugs may increase. Therefore, dosages for both drugs may have to be adjusted downwards. Sporanox has another undesirable side effect in that it inhibits testosterone production at higher doses and might affect a male's sexual development. The reason is that this antifungal drug works by preventing the synthesis of the fungal steroid ergosterol by yeast and fungus. Unfortunately, this drug also inhibits the human system that produces the human steroid testosterone. Diflucan does not have this effect at normal doses.

If there are so many concerns with these absorbed antifungals, why use them at all? The simple answer is that some of the yeasts and fungi are resistant to nystatin or oral amphotericin B or the yeast may be inside the deeper layers of the lining of the intestinal tract where nystatin cannot act. Nystatin and oral amphotericin B, which act mainly on intestinal yeast, may also be ineffective in treating persons with more severe fungal infections of the skin and nails.

How to Administer Nystatin

I am including more detail about nystatin because it is the most commonly used drug and it is one of the safest and most effective. The most common suspensions of nystatin are formulated to have 100,000 units per cc or ml. (1 cc equals 1 ml for water-based drugs.) Five cc or five ml is the amount in a teaspoon. In administering the doses, it is advisable to use a medicine dropper. There is too much variation in using a plain spoon.

The main consideration in using nystatin is how to avoid the side-effects of the yeast die-off reaction. This can be accomplished by increasing the dosage of nystatin gradually so that the severity of the yeast die-off is minimized. When this approach is used, the yeast are killed over a longer time period instead of during a very short time period. A typical dosing for 2-8 year olds is given in Table 1. If the symptoms of the die-off reaction are too severe, the dose may be held at the lower level for a day or two before going up to the next dose. If the concentrations of yeast metabolites are predominantly in the normal range when re-tested at 30 days, this dosage is continued. If the yeast metabolites are significantly elevated after 30 days of therapy, the dose of nystatin could be increased by 50-100 % or other antifungal drugs might be added. The die-off reaction may occur again when the medication is increased. Doses for children 8-12 years would be about 50% higher than those in Table 1 and for adults and children older than 13, the dose would be double the above schedule.

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These doses are my own suggestions. Your physician may want to prescribe a somewhat different regimen and Dr. Semon has suggested a somewhat different dosage schedule in Chapter 12.

Although there is no reason that the higher doses of nystatin might cause increased aggression, reports of such aggression have been fairly common when 4-8 times the dosages recommended above are given. I suspect that nystatin at high doses causes this side-effect although it is possible that the food colors or contaminants in the medication may be responsible. Nystatin is a biological product derived from a mold.

Table 1
Typical Dosage of Nystatin to Minimize Yeast Die-Off Reaction

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6 on
Total daily dose (Units)	50,000	100,000	200,000	300,000	400,00	400,000
Divided daily into	1 dose	2 doses	2 doses	3 doses	4 doses	4 doses

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Immune Deficiency, Food Allergies, and Yeast Suppression of the Immune System in Autism

Chapter 5

Dr. William Shaw

Overview of the Immune System

The critically important job of fighting off infections falls to our immune system. As you might expect, the immune system is complex because the human body must defend itself against diverse infectious agents including bacteria, viruses, fungi, etc.

Recent research by several scientists has shown that children with autism have serious abnormalities in this all-important system. In order to understand these abnormalities, and to show what effect they might have for the child with autism, it is essential to have a basic understanding of the immune system.

The immune system is made up of several different parts:

- B-cells that produce antibodies or immunoglobulins.
- T-cells (so named because they are derived from the organ called the thymus) are the cells involved in what is called cellular immunity. The functions of the T-cells are to kill foreign tissue or tissues infected and to produce lymphokines, which are large proteins that regulate other cells of the immune system and to help enhance the immune response.
- The complement system is a group of proteins involved as a nonspecific helper to the immune system.
- The phagocytic cells include cells called macrophages and neutrophils that engulf bacteria and yeast and digest them.

A large part of the immune system is located in or near the intestinal tract and helps to prevent germs from the intestine from entering into the rest of the body. Defects in the immune system may therefore lead to overgrowth of organisms like yeast in the intestinal tract. A defect in any of these systems may lead to increased incidence of infection. Defects in all parts of the immune system have been documented in children with autism. Studies done by the late Reed Warren Ph.D., Sudhir Gupta M.D., Ph.D., a clinical immunologist at the University of California at Irvine Medical School, and others, indicate that most children with autism have a substantial immune abnormality of some type ⁽¹⁻²⁰⁾. This probably explains why frequent infections are a common feature of the child with autism's medical history. In our society, frequent infections lead to frequent use of antibiotics. Some parents of children with autism have reported to me over 50 consecutive ear infections in their children. The antibiotics prescribed for ear infections also kill many of the normal organisms in the intestinal tract, and allow abnormal organisms such as yeast and bacteria (such as Clostridia) to proliferate in the intestinal tract.

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Antibodies or Immunoglobulins

The B-lymphocyte cells of the immune system produce antibodies called immunoglobulins. These antibodies are designed to react against specific antigens—foreign molecules introduced into the system by germs of various types. Antibodies react against viruses, yeast, and bacteria and allow them to be killed by the white blood cells. Composed mostly of amino acids, antibodies are proteins that can be divided into five major antibody classes called IgA, IgG, IgM, IgD, and IgE. Each has a unique chemical structure and a specific function. IgG stands for immunoglobulin G or antibody G and so forth.

- IgM is usually the first antibody produced by the immune system when a new germ is encountered and it is the body's early defense system. The presence of high amounts of specific IgM antibodies indicates a recent infection. Thus, high levels of IgM antibodies against *Candida* would indicate a recent *Candida* infection of the bloodstream. IgM antibodies diminish a few months after infection.
- IgG antibodies are produced by the B-lymphocyte cells when a germ attacks in a subsequent invasion. These antibodies may also be involved in causing food allergies.
- IgE is the antibody most widely known for its involvement in all types of allergies and may also be involved in protecting the body from parasites. Elevated IgE in blood is associated with a history of excessive allergies.
- IgA is the antibody that is involved with protection of the lining of the nasal passages and intestinal lining from germs. Secretory IgA or sIgA is a special form of the IgA antibody that is secreted to protect the mucosa, which is the lining of the intestinal tract. Secretory IgA is apparently secreted by the gall bladder and then trickles down the bile ducts into the small intestine. Some children with autism have very low or even completely absent levels of IgA ^(1,2); in such cases there is probably also a deficiency of a secretory IgA since secretory IgA is derived from IgA.
- IgD is an antibody that is usually present in very small amounts in the bloodstream and is probably involved as a receptor antibody on certain of the white blood cells and may help to regulate antibody production.

One of the conditions that lead to recurrent otitis media or other recurrent infections is called immunodeficiency, meaning the presence of a weak or deficient immune system. Immunodeficiency can be caused by a deficiency of antibodies such as IgG, IgA, and IgM. Children with autism have a high frequency of abnormalities of these different kinds of antibodies ⁽²⁰⁾. Deficiencies of any of the total antibodies indicate a probable immunodeficiency. In addition, the total amount of a particular antibody could be normal but the amount of a specific antibody might be deficient. For example, I suspect that many children with autism and PDD may be deficient in producing antibodies against yeast. An immune deficiency panel that tests for all of these types of antibody deficiencies is available from:

The Great Plains Laboratory, Inc
 11813 W. 77th St.
 Lenexa, KS 66214
 Phone: 913 341-8949
 Fax: 913 341-6207
 E-mail: GPL4U@aol.com
 Website: www.greatplainslaboratory.com

Cellular Immunity

The T-cells are the cells involved in what is called cellular immunity. T-cells kill foreign tissue or tissues infected with virus, and produce lymphokines. Lymphokines are large proteins that regulate other cells of the immune system, and help to enhance the immune response. Some of these proteins are called interleukins (IL). Eighteen different interleukins have been identified. Other proteins produced by the white blood cells include interferon, granulocyte-macrophage colony stimulating factor (GC-CSF), and tumor necrosis factor. Concentrations of IL-12 and interferon gamma are much higher in the blood of children with autism than in normal children, indicating an immune activation, possibly due to adverse vaccine reactions. In addition to T-cells, another type of lymphocyte (a white blood cell type) called natural killer (NK) cells is also important in the immune system. The data from Warren and Gupta indicates that 38-45% of children with autism have low NK cell numbers as well as significant T-cell abnormalities. The decrease of CD4 cells, a T-cell subtype, in children with autism may be another cause of increased colonization with *Candida albicans*. As mentioned in the chapter on the digestive tract, a deficiency of dipeptidyl peptidase IV may be one of the significant causes of immune abnormalities in autism.

TYPES OF IMMUNE DEFICIENCY THAT OCCUR IN AUTISM

Myeloperoxidase Deficiency

Myeloperoxidase is an enzyme present in the white blood cells (neutrophils) that combines hydrogen peroxide and chloride ions to form hypochlorite ion, the same active ingredient present in household bleach ⁽²¹⁾. The hypochlorite ion kills yeast just like household bleach does. If this enzyme is deficient, the white blood cells cannot produce sufficient hypochlorite to kill the yeast and the affected person cannot fight off yeast infection satisfactorily. This disorder can be detected by the use of automated flow cytochemistry instruments that can detect an absence of peroxidase in the neutrophils and monocytes. Certain children with autism should be tested for this disorder, but because the disorder is quite rare, most physicians are not aware of this test. It is important to be assertive and make sure that the right type of blood test is used. Because these cells look completely normal under the microscope, a routine blood examination is not a satisfactory test for this disorder. Most patients with this disorder have frequent yeast and fungal infections and often have fungal infections of the nails or even systemic yeast infections. Myeloperoxidase deficiency can be genetic or acquired. The genetic type is due to a mutation on chromosome pair 17 or to biotinidase deficiency ^(21,22). Acquired causes include lead poisoning, folic acid or vitamin B-12 deficiency, severe infection, and leukemias ⁽²¹⁾.

One particular child with autism whose parents consulted with me had severe external manifestations of yeast from a very early age. This child had fungal infection of the skin and nails and had been on antifungal drugs for years. The child was ultimately diagnosed with myeloperoxidase deficiency and she responded well to intravenous gamma globulin therapy, which is described later in the chapter. Every child with external manifestations of yeast or fungal infections should be tested for possible myeloperoxidase deficiency. Myeloperoxidase deficiency can be tested at the Mayo Clinic Laboratories in Rochester, MN. The phone number is (507)266-5700. Most myeloperoxidase tests are done for cancer so that you need to include a note indicating that you are interested in genetic myeloperoxidase deficiency as the cause of immunodeficiency.

Chapter 5

Severe Combined Immunodeficiency Disease (SCID)

Severe combined immunodeficiency disease is a defect in both the T and B-lymphocytes so that both antibody production and cellular immunity are impaired ^(23,24). This disease can be due to a genetic deficiency on the X chromosome or on one of the other chromosomes. Genetic deficiencies of the enzymes purine nucleoside phosphorylase or adenosine deaminase also cause SCID. Candida infections as well as other infections are common in this disorder. (Although not published in the medical literature, I have had personal communication with parents of children with autism with this SCID disorder.)

Selective IgA Deficiency

This extremely common immunodeficiency occurs in 1 in 600-1000 persons of European ancestry ⁽²³⁾. The causes of IgA deficiency are not completely known. There are some cases in which the deficiency runs in families while in other cases it does not. It has been reported in association with abnormalities of chromosome 18, but most individuals with IgA deficiency have no detectable chromosomal abnormalities. Drugs or viral infection may also cause IgA deficiency. Patients with IgA deficiency are usually deficient in both subtypes of IgA, IgA1 and IgA2.

A number of patients with IgA deficiency are also sensitive to gluten. In Gupta's study ⁽²⁰⁾, 20% of the children with autism had a deficiency of IgA and 8% lacked it completely. Reed Warren and his colleagues ⁽²⁾ also found that 20% of individuals with autism had low serum IgA compared with none of the normal controls. Thus, IgA deficiency is somewhere between 100 and 200 times higher in the autism population compared to the normal Caucasian population.

IgA replacement therapy cannot be used currently because the short half-life of IgA would make it an extremely expensive therapy.¹ IgG therapy can be used with patients with low IgA values. If the IgA values are so low that they cannot even be detected, giving IgG therapy would be too risky. It is possible that the immunodeficient person's body would produce antibodies against IgA, causing potentially fatal anaphylactic shock.

IgG Subclass Deficiency

Sometimes, the total IgG in the blood may be normal but the concentration of one or more subtypes of IgG may be low. There are four subtypes of IgG: IgG1, IgG2, IgG3, and IgG4. Antibodies against proteins are mainly of the IgG1 and IgG3 subtypes while antibodies against carbohydrates (sugars) are of the IgG2 subtype ⁽²³⁾. In Gupta's study ⁽²⁰⁾, 20% of the children with autism had an IgG subclass deficiency (Table 1). There are hundreds of different kinds of antibodies within each antibody type so that there could be an IgG antibody against rubella, another against smallpox, and another against whooping cough and so on. When all the different types of IgG are measured simultaneously, the total IgG is measured.

¹ A half-life is the length of time required for half of a substance to disappear from the bloodstream. When a medicine or chemical has an extremely short half life, it must be administered very frequently.

Complement C4b Deficiency

The complement system is a complex group of 20 proteins that assist or “complement” the work of the immune system by destroying invading yeast, viruses, and bacteria. The complement system can disintegrate the cell membranes of many species of bacteria and complement byproducts attract scavenger white blood cells to the site of the bacteria destruction. These scavengers then clean up the dead bacteria debris.

Some of the complement components also coat the bacteria, which allow the bacteria to be more easily digested by the scavenger white blood cells. Reed Warren and his colleagues found that the average concentration of one of the proteins in the complement system (termed C4b) was significantly lower than normal in individuals with autism ⁽¹⁵⁾. Complement C4b deficiency is also increased in schizophrenia ⁽²⁵⁾. Individuals with low amounts of this protein are more susceptible to infection from yeast and bacteria such as *Streptococcus pneumoniae* and *Haemophilus influenza*, two of the bacteria most commonly responsible for ear infections ⁽¹⁵⁾.

Table 1

Types of immune abnormalities in Dr. Gupta's study of 20 children with autism disorder

Immune disorder	Number of cases*
Common variable immunodeficiency	2
IgG1 deficiency	1
IgG2 deficiency	4
IgG4 deficiency	2
IgG3 and myeloperoxidase deficiency	1
Low IgG	1
Increased IgE	7
Increased antibodies to myelin basic protein	6
Specific antibody deficiency with normal IgG and IgG subclasses	1
IgA deficiency	4

* The number of types of immune deficiency is greater than 20 because some children had more than one immune abnormality

Gliotoxins and Other Immunotoxins Produced by Yeast and Fungi

Another cause of the recurrent infections associated with yeast overgrowth is chemical compounds called gliotoxins. Gliotoxins are immunotoxic, meaning they are toxic to the immune system. They are compounds that are produced by both yeast ^(28, 29) and fungi such as *Aspergillus* ⁽³⁰⁾. (Gliotoxins have no relationship to the glial cells of the brain and were named after the species of fungus *Gliocladium* in which they were first discovered.) Most strains of *Candida* that were isolated from humans have the ability to produce gliotoxins ⁽²⁸⁾. Gliotoxins are important because they selectively fragment the DNA of white blood cells called T-lymphocytes and macrophages so that they are ineffective in fighting off infections ^(31, 32). This is probably why the gliotoxins

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are so important and why *Candida* often causes recurrent infections. I suspect that exposure to gliotoxins may be a major cause of the frequent immune deficiencies in autism.

A second toxic effect of gliotoxins is probably due to their action on the sulfhydryl group of proteins, which they inactivate. These sulfhydryl groups are necessary for the functioning of a wide variety of enzymes ⁽³³⁾. Supplements of glutathione, N-acetyl cysteine, and lipoic acid might be useful to prevent this toxic action of gliotoxins since they help to regenerate free sulfhydryl groups.

A third way that gliotoxins may be causing their damage is by the generation of compounds called free radicals ⁽³³⁾. Free radicals are highly reactive chemicals that can cause many harmful effects to the body such as damaging our genetic material DNA. Many of these harmful reactions can be counteracted by compounds called antioxidants such as vitamin C, vitamin E, lipoic acid, glutathione, or N-acetyl cysteine. Several physicians who treat large numbers of children with autism have indicated to me significant improvement of symptoms in some children with autism after treatment with the nutritional supplements glutathione or N-acetylcysteine. It seems likely that prevention of free-radical damage induced by gliotoxins may be one of the reasons these supplements are effective.

Mannan is another yeast product that comes from both *Candida* and *Saccharomyces cerevisiae* (baking yeast) ⁽³⁵⁾. Other compounds produced by yeast also have a significant immunosuppressant effect on the immune system ⁽³⁶⁻³⁹⁾. The fact that *Saccharomyces cerevisiae* produces immune suppressants is one of the reasons that I recommend a yeast-free diet in addition to sugar restriction to control a yeast overgrowth of the intestinal tract. Even if the yeast cells are completely killed by baking (and some people think they may survive in the center of baked goods where the temperature may be lower), these immunosuppressant mannan compounds may not be destroyed by heating.

Other Toxic Byproducts of *Candida*

According to Orion Truss M.D., the pioneer in the treatment of yeast-related illnesses, acetaldehyde is one of the most important toxic yeast byproducts ⁽⁴⁰⁾. Vitamin B-6 is an aldehyde that must react with amino groups on many different enzymes throughout the body in order for them to function. If these amino groups have been used up by reacting with acetaldehyde, then other biochemical reactions mediated by vitamin B-6 cannot take place. Even though there may be an average intake of this vitamin, it is subjected to an increased rate of elimination, resulting in low blood and tissue levels ⁽⁴¹⁾. It is likely that high doses of vitamin B-6 may overcome the competition with acetaldehyde caused by the yeast and may be one of the main reasons that this vitamin is effective for the treatment of autism. I also suspect that high doses of vitamin B-6 may not be needed if the yeast are controlled (see chapters on organic acids and vitamin therapy). A controlled study needs to be done to prove this idea.

Acetaldehyde may also react with neurotransmitters such as dopamine and serotonin to form opiate-like compounds called tetrahydroisoquinolines ⁽⁴²⁾, which have been isolated from the urine of alcoholics. This is another way that an intestinal yeast overgrowth may affect brain function. Acetaldehyde also decreases the flexibility of the red blood cells ⁽⁴³⁾ so that they are less able to deliver oxygen to the tissues. In addition, acetaldehyde decreases the ability of the protein tubulin to assemble into microtubules, which may interfere with transfer of essential biochemicals into the dendrites, the fibers that are used for nerve cell communication in the brain ⁽⁴⁴⁾. In a study on rats given lethal doses of acetaldehyde ⁽³⁴⁾, administration of lipoic acid or N-acetyl cysteine was able to keep the rats from dying. This animal study indicates that humans, when exposed

to this same byproduct due to yeast overgrowth, might also benefit from increased intake of these same nutritional products.

Autoimmunity, Molecular Mimicry, and Candida: The Wheat and Yeast Connection

Singh has found that a high percentage of children with autism possess antibodies against their own tissues called autoantibodies ⁽¹⁸⁾. One of these autoantibodies is directed against myelin, a fatty sheath that insulates the axons of nerve cells like the plastic insulator on electrical wire. Why would the body produce antibodies against its own tissue? Sometimes the body mounts an attack against an invading germ and produces antibodies against it. If one of the germs possesses proteins on its surface that resemble human tissue, then the antibodies may be “fooled” to react against its own human tissue. The best-known example of this molecular mimicry is rheumatic fever, in which antibodies produced against a Streptococcal or “Strep” infection later react against the heart valve tissue ^(45, 46). The main reason that untreated strep throat is regarded as a serious medical condition, is to prevent this potential autoimmune reaction from occurring.

Vojdani has found that individuals with Candida infections often produce antibodies against Candida that also react against various tissues of the human body including brain, kidney, pancreas, spleen, thymus, and liver ⁽⁴⁶⁾. Furthermore, these same anti-yeast antibodies also reacted against wheat protein that may explain why so many children with autism have high titers of wheat antibodies and are sensitive to wheat. A portion of one of the major wheat proteins called alpha-gliadin is very similar to a portion of one of the yeast proteins that is involved in yeast reproduction ⁽⁴⁷⁾. Antibodies produced against yeast may be “tricked” into reacting against wheat because of the great similarity of portions of the two different proteins. This protein could be an important link between wheat and yeast sensitivity in autism.

If Orion Truss's acetaldehyde hypothesis is correct, the high reactivity of acetaldehyde may also provide an explanation for the high percentage of children with autoantibodies as well as the severe reactions some children experience after vaccination. Acetaldehyde reacts with virtually any free amino group on both proteins and amino acids. The amino acid lysine is one of the 20 amino acids found in most proteins. It is unusual in that it possesses two amino groups instead of one. This extra amino group on lysine is the target for acetaldehyde when it reacts with proteins. (This amino group is also the site at which arabinose reacts; see chapter on organic acids.)

It has been found that alcoholics, who form greater than usual amounts of acetaldehyde, possess antibodies against acetaldehyde-altered proteins ⁽⁴⁸⁾. Furthermore, it has been found that antibodies against acetaldehyde-altered proteins may cross react against formaldehyde-altered proteins ⁽⁴⁹⁾. The toxins from diphtheria and tetanus bacteria are treated with formaldehyde to prepare the DPT vaccine ⁽⁵⁰⁾. It is possible that if a child possesses antibodies against acetaldehyde-modified proteins due to yeast overgrowth, the vaccine may stimulate a marked increase in the autoimmune reaction, perhaps leading to a severe adverse immune reaction. According to Ellen Bolte of Cure Autism Now, her child's autism began a few days after her child was injected with the DPT vaccine. He was on antibiotics for ear infection at the time of the immunization and it is possible that a yeast overgrowth may have predisposed him to the adverse immune reaction.

I think that a possible role of human antibodies to Candida in reacting against myelin and other brain structures should be thoroughly investigated. In the future, it may be possible to deactivate or remove these autoantibodies that are causing harm to the body's own tissues and I believe that existing technology could be adapted for this purpose. As a matter of fact, the success that Gupta's has had in treating autism with gamma globulin could be related to these autoantibodies being deactivated ⁽²⁰⁾.

Chapter 5

THERAPIES

Gamma Globulin Therapy

Dr. Gupta has used intravenous immunoglobulin (IVIG) successfully to treat a small number of children with autism ⁽²⁰⁾. IVIG therapy is also called gamma globulin therapy. This product of human plasma has been used to treat immunodeficiency since 1952. Gamma globulin is purified from human blood components and then treated to remove harmful germs such as the HIV virus. Varying degrees of improvement after this therapy reported by Gupta included improved eye contact, calmer and improved social behavior, reduced echolalia, and improved speech in terms of better articulation and improved vocabulary. Speech improvement took the longest time to improve. Several patients regressed when the infusions stopped and then improved again when they were restarted. One child had a nearly complete reversal of the autism after about a year of therapy.

What is the mechanism of this improvement? No one knows for sure. I suspect that the immune system has a better ability to fight yeast and that the reduction of yeast byproducts allows the brain and the body to function better. It may have the effect of suppressing the production of antibodies against myelin, the covering of the nerve fibers in the brain. Elevated levels of this antibody have been reported in this illness. It may be that a specific component of the gamma globulin is responsible for the effects.

Intravenous IgG is usually given once a month due to the 28-day half-life of IgG. After administration of IgG, a child with low IgG values may have values in the normal range. An intravenous infusion takes about 2 hours. A sedative may be given the child to keep the child from being frightened during the procedure.

There are occasional mild and self-limiting reactions to IVIG including fever, muscle aches and pains, headache, nausea and vomiting, dizziness, and tachycardia that occur in less than 5% of all cases. The gamma globulin is derived from human blood so there is also a risk that unknown viruses might be present in the gamma globulin. The gamma globulin is checked for any known viruses such as HIV and hepatitis. Rarely, there are severe allergic reactions (less than 0.1%). This is a very expensive therapy that may cost as much as \$1500-\$2500 per month.

Insurance Coverage for Immune Therapies

Because immunological therapy for the treatment of autism is considered experimental, most insurance companies and HMO's will not cover these (substantial) medical expenses. Since virtually every company *will* cover expenses due to immune deficiencies, it is essential that the physician document the fact that the child has a significant immune deficiency. Because some insurance companies may not even cover the laboratory tests for the diagnosis of immunodeficiency, the wisest course is to contact a clinical immunologist.

Clinical immunologists are physicians, often associated with a large medical center or medical school, who are working part-time in the treatment of patients and part-time in research activities. These physicians may be of assistance in getting insurance coverage for therapies that are based on an immune deficiency diagnosis—such therapies might not be covered with an autism or PDD diagnosis.

When medical plans and HMOs are reluctant to even provide testing, it may be necessary to begin a letter writing campaign that includes scientific books (such as this one) and articles (referenced herein). If educating them is not persuasive enough, it is sometimes necessary to send letters from an attorney to show that you are very serious about pursuing testing and treatment. You may even want to consider contacting the news media about your dilemma.

Cimetidine

Cimetidine (Tagamet) is a drug that is primarily used to treat ulcers and is now available as an over the counter (nonprescription) drug. In a review article on candidiasis, Dupont ⁽⁵¹⁾ states that this drug is relatively safe and well-tolerated and recommends that this drug be used more frequently to treat patients who have Candidiasis but do not respond adequately to antifungal drugs. Cimetidine has been used at a dose of 30 mg/kg body weight/day to stimulate in the immune system in patients with chronic mucocutaneous Candidiasis ^(52, 53). This drug stimulates the white blood cells to kill the Candida. Cimetidine may reduce the rate of metabolism of many other drugs such as the antifungals, antidepressants and antiseizure medications that are absorbed into the bloodstream. Combining zinc supplementation with cimetidine has proven to be very successful in the treatment of recurrent infections in patients with immune deficiency (Int J Clin Lab Research 27:79-80, 1997). Check with your physician and pharmacist before using this drug about an appropriate pediatric dose and any drug interactions that might be associated with the use of this drug.

Transfer Factor Therapy

Transfer factors are molecules that may contain both protein and nucleic acids ⁽⁵³⁾ produced by the white blood cells. These molecules can transfer immunity from a healthy donor to a recipient who has impaired immune function. Dr. Masi found that severe Candidiasis could be effectively treated by Candida-specific transfer factor ⁽⁵⁴⁾. The results of recent studies show that transfer factor can be given orally, which was surprising since many proteins are destroyed by digestive enzymes when taken orally ⁽⁵⁵⁾. Dr. Hugh Fudenberg, a clinical immunologist from the Neuroimmuno-Therapeutics Foundation, found that 21 of 22 children with autism treated with transfer factor from parental cells responded favorably to transfer factor therapy. Ten improved enough to be mainstreamed into regular school classrooms. ⁽²⁶⁾ Dr. Fudenberg believes that either a live virus from one of the vaccines or an adverse reaction between the mother's antibodies and the vaccine are responsible for impairing the immune system. Transfer factor from bovine colostrum is also available as a food supplement from the 4Life Company. This transfer factor is nonspecific but reports from parents have indicated significant improvements in their children with autism after use. This product is quite expensive (\$400 per month).

Bovine Colostrums

Colostrum from cows has been used to treat a wide range of diseases including a variety of microbial (bacterial) overgrowths of the gastro-intestinal tract. A major problem with these products is that they contain an appreciable quantity of casein and ninety percent of children with autism are sensitive to casein. Two casein-free colostrums products that are available on the market is *Prime Colostrum* from Alt Med available at New Beginnings Nutritionals (www.nbnus.com) and *Colostrum Gold* from Kirkman. It is important to remember that some children with autism may be allergic to other milk proteins in addition to casein. Consequently, children should be given a very small dose at first to determine if there may be an allergic reaction. If allergic reactions occur, the colostrums should be discontinued immediately. This product is pasteurized in the same way as milk and should be considered safe from bacteria. It has been reported that after a relatively short treatment period with casein-free colostrums, some have seen decrease in autistic symptoms and reduced frequency of infections.

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Pentoxifylline

Pentoxifylline is a drug that is a purine derivative and is an inhibitor of an enzyme called phosphodiesterase. Purines are one of the components of DNA, which is the genetic material for most living creatures. Pentoxifylline was given to a child with autism in Japan to treat suspected brain damage from an accident ^(56, 57). After this treatment, the boy showed marked improvement of his autistic symptoms. When 23 children with autism were treated with pentoxifylline (150-600 mg/day), the drug was reported to be remarkably effective in 10 of the children with some of the group no longer considered to be autistic. The drug was also very effective in treating seizures. Side effects included nausea, vomiting, low blood pressure, and headache. Since the primary use of this drug is to improve blood circulation, you may find it difficult for a physician to prescribe it to treat autism.

IL-2

Interleukin-2 (IL-2) is a protein called a cytokine that stimulates the proliferation and activation of T-cells, B-cells, granular lymphocytes, and macrophages. When T-helper cells are stimulated by antigens from the Candida, white blood cells called T-helper cells produce IL-2 and activate other resting T-cells. IL-2 also stimulates natural killer cells to produce gamma interferon, granulocyte macrophage stimulating factor and other factors that help to fight Candida. Gupta's work shows that natural killer cells are deficient in children with autism. Although IL-2 is toxic at high doses, low doses of IL-2 are relatively safe. The use of low doses for several weeks would result in selective expansion of natural killer cells that will kill yeast ⁽⁵¹⁾. IL-2 is available as a pharmaceutical agent prepared using recombinant DNA. Most family doctors or pediatricians will probably be reluctant to use this product but a clinical immunologist might be willing to discuss the possible use of low dose IL-2 therapy.

Allergic Phenomena, Food Sensitivity, and Altered Behavior

A number of reports and books have documented the fact that allergies to foods, molds, and other allergens as well as the direct toxic effects of certain foods can markedly alter behavior. When the foods and allergens are removed or enzyme-potentiated desensitization (EPD) treatment is pursued, normal behavior can be restored ⁽⁵⁸⁻⁷¹⁾. Doris Rapp M.D. has written several books including *Is This Your Child?* ⁽⁵⁸⁾ in which she documents behavioral disorders in children caused by allergic reactions. She also has several videotapes available that dramatically demonstrate bizarre behavior after the introduction of an extract of an allergenic substance. In the book *Solving the Puzzle of Your Hard-To-Raise Child* by William Crook M.D. ⁽⁷¹⁾, many details are given on how to identify and eliminate food allergies and sensitivities. A physician named Dr. Jaekle, trained as both a psychiatrist and allergist, has recorded individuals on videotape suffering severe psychotic reactions following exposure to mold ⁽⁷²⁾. Dr. Jaekle concludes that many cases of schizophrenia may have a significant yeast involvement. The Feingold Association, started by the late allergist Ben Feingold M.D., can provide a list of foods that commonly cause hyperactivity, which is a common problem in autism and PDD.

Tests of Allergies

There are numerous allergy tests that are available including those that introduce the allergenic substance into the skin (prick test) as well as many other tests that are done on blood. Many laboratories perform the blood tests for IgE and IgG antibodies against specific allergens. These tests should not be confused with tests of total IgG and total IgE that are done to assess a possible immune deficiency. It is possible for an individual to be deficient in total IgG and yet still have high levels of IgG against a specific food.

IgG and IgE Allergy Tests

The Great Plains Laboratory, Inc
11813 W. 77th St.
Lenexa, KS 66214
913 341-8949
E-mail: GPL4U@aol.com
Website: www.greatplainslaboratory.com

Immunotherapy with Enzyme-Potentiated Desensitization (EPD)

In autism and PDD, allergies to foods, molds, pollen and other materials may lead to behavioral disturbances in addition to the usual allergic phenomena such as sneezing, asthma, and skin rashes. EPD is a method of immunotherapy developed by Dr. Leonard McEwen ⁽⁷³⁻⁷⁷⁾. The method involves desensitization with a combination of very low dose mixed allergens with the enzyme, beta-glucuronidase. The beta-glucuronidase increases the immunizing effects of the allergens and acts directly on T-suppressor cells, apparently inducing a longer lasting desensitization than does any type of previously known immunotherapy. This therapy involves receiving injections every 2 to 3 months at first, and then decreasing over time. The frequency of injections varies with the condition being treated and the patient response, but once maintenance is reached, average patients seem to require treatment 2 to 3 times yearly. Furthermore, McEwen's experience has been that at least 50% of patients can discontinue EPD between the 8th and 20th injection. Patients have remained in remission without immunotherapy for over 20 years. EPD also appears useful in the treatment of a large variety of conditions not previously considered responsive to immunotherapy of any kind ⁽⁷⁷⁾.

Numerous parents of children with autism and other behavioral disorders (see chapter by Pamela Scott) have reported beneficial results with this therapy. They also report that their children often don't do as well when the effects of the EPD begin to wear off just before the next series of EPD injections. As with every therapy, some children respond much more dramatically than others. Unfortunately, the U.S. Food and Drug Administration now limits this therapy to compassionate use only.

Homeopathy

Homeopathy is a technique employed by both physicians and non-physicians called homeopaths and its theoretical basis is unknown. This technique involves the preparation of dilutions with the allergy causing substances which a person takes orally to achieve desensitization in a way that is not completely understood.

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It appears that a small amount of a harmful substance is able to mobilize the body's own defenses against the substance. Although not generally approved of by mainstream medicine in this country, many alternative medicine physicians use this technique in their medical practices. This technique is recognized as valid by the World Health Organization and is part of mainstream medicine in France. When trying any new therapy, the best approach is to talk to the physician and with other's who have experienced the particular therapy and find out how helpful the medical practitioner was. One physician, who employs homeopathy, reported that homeopathic dilutions of arabinose, the sugar derived from *Candida*, favorably improved behavior in children with autism but that the response only lasted a few days. For the treatment of ear infections (otitis media), homeopathic treatment also appears to be more effective than antibiotic therapy ⁽⁷⁸⁾.

Treatment for Allergic Symptoms of Wheat and Dairy Products

In addition to EPD, other methods that have been used for the treatment of food allergies are provocation/neutralization (P/N), and NAET. Laboratory testing such as urinary peptides and IgG antibodies to gluten and casein as well as behavioral response should be used to document the degree of effectiveness of these other non-dietary therapies. Some children seem to lose their sensitivity to these foods after extensive dietary restriction, a phenomenon common in food allergies. Many people may become sensitive to these foods again once these foods are re-introduced, especially if they are ingested on a frequent basis.

NAET

Nambudripad's allergy elimination technique or NAET was developed by a nurse/chiropractor; Devi Nambudripad, Ph.D. Practitioners of this technique include physicians, chiropractors, and nurses. Allergies are detected by a technique called applied kinesiology (also called muscle testing) in which the person holds a vial of a substance (to which they may be allergic) and the practitioner assesses their muscle weakness. The validity of this technique, which is difficult to understand because there is no direct physical contact between the allergic substance and the patient, has been documented with conventional blood tests for IgG and IgE food allergies ⁽³⁰⁾. After determination of which foods are problematic, the practitioner treats the allergic reaction by the application of acupressure to a "meridian" or "energy field" of the body that is associated with a specific gastrointestinal function in Eastern medicine ⁽³¹⁾. Another interpretation is that NAET treatment stimulates the autonomic nervous system that regulates the gastrointestinal tract in such a way that the food allergens are more effectively processed by the digestive and immune systems. Usually the sensitivity to a particular food can be eliminated in a single treatment session but occasionally several treatments are necessary. One of the NAET practitioners (a chiropractor) successfully treated her child with autism who had an extreme gluten sensitivity with this technique. Prior to treatment, gluten caused extremely abnormal behaviors and severe head banging. After treatment, the child was able to eat wheat with no significant behavioral effects. A child with attention deficit hyperactivity (ADHD) was found to have an extremely abnormal brain electroencephalogram or EEG (a tracing of brain electrical activity), but after NAET treatment of food allergies, the EEG was completely normal.

Concerns have been raised that the NAET treatment may clear up allergic responses to wheat and dairy but not the abnormal peptides from wheat and dairy. This is a legitimate concern. I would recommend NAET treatment and/or digestive enzymes to parents who gave up on the gluten and/or casein free diet because their child has become malnourished or ill. Measurement of urine peptides and food allergies in blood samples should be done to confirm the effectiveness of this therapy since it is still unproven. NAET practitioners can be

located on the Internet at www.naet.com. It is advisable to obtain recommendations before choosing a practitioner. Success with this technique varies with the experience of the practitioner.

NAET therapy may cause significant side-effects during and after the clearing process. One parent who used NAET to clear food allergies from her highly allergic child with autism found that it took three treatments to clear her child's food allergy to sugar. The day after being treated for sugar, her child broke out in hives over his entire body. NAET practitioners consider such reactions as a normal part of the clearing process. Following this severe reaction, the child was no longer sensitive to sugar. When the same child was being treated for wheat, the vial containing wheat caused a welt to develop on the child's leg where it was touching. The same mother reports that extremely abnormal behavior occurred shortly after the NAET treatments including tantrums, lethargy, and extreme self-stimulatory behaviors and continued for nearly 24 hours. Blood allergy tests done before and after revealed a marked reduction in food allergies after NAET treatments. NAET treatment has also been used to reverse vaccine reactions. No scientific documentation of the success of this therapy for the treatment of vaccine reactions has been reported.

I have used this treatment for my own child who has attention deficit and impulsive behaviors. He had allergies tested by blood and skin prick methods to milk, cheeses, wheat, barley, yeast, peanut, tomato, corn, cats, and pollen. The allergies measured by muscle testing corresponded very closely to the conventional allergy tests. His milk allergy was extremely high by both muscle testing and by the blood allergy tests. He also had high levels of casomorphin and gliadorphin in his urine. His milk allergy could not be eliminated by the standard NAET treatment. The therapist then tested the various digestive organs by palpation with applied kinesiology and found that the bile duct was "sluggish." An electrode was then applied to the area of the abdomen near the bile duct and a small electrical current was applied for about 45 minutes after which the milk allergy finally "cleared". Unfortunately NAET therapy appears to only temporarily clear some food allergies, for example, after only a few weeks of being "cleared" of wheat, the wheat sensitivity was again detected using applied kinesiology. My son realized that he felt much better on the diet and decided to continue on the gluten and casein free diet. Other parents and physicians have also reported to me that NAET was ineffective for wheat and dairy allergies for long-term treatment.

A variety of natural antifungal products as well as many other high quality nutritional supplements can be found at New Beginnings Nutritionals, www.nbnus.com 1-877-575-2467.

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Abnormalities of the Digestive System: Gluten and Casein, Peptides, Secretin, CCK, and Pancreatic Atrophy

Chapter 6

Dr. William Shaw

Gluten and Casein Sensitivity

Numerous studies by Dohan, Reichelt, Shattock, Cade and others have established that children with autism and adults with schizophrenia have elevated levels of peptides in their urine resulting from the incomplete breakdown of certain proteins in milk and wheat ⁽¹⁻¹⁷⁾. Removal of these proteins either through diet or dialysis causes improvement in the symptoms of these diseases. The major protein in milk is called casein while the major protein in wheat is called gluten and each of these proteins is made of a combination of amino acids. There are 20 amino acids that are commonly found in proteins. A protein can be thought of as analogous to a string of pearls each with as many as 20 different colors. The amino acids would be individual pearls on the string. The protein's DNA or genetic code selects which particular amino acid (or which color of pearls) is present in each protein (string of pearls). When proteins are eaten, enzymes in the gastrointestinal tract first break them down to smaller pieces called peptides and then the smaller pieces are further broken down into individual amino acids. The individual amino acids are then absorbed through the intestinal lining into the bloodstream.

Historical Perspective

Both cow's milk and wheat are fairly new on the evolutionary scale to human beings and were probably first used as foods by many of our ancestors in the Mideast approximately 10,000 years ago, when the first sickles in Turkey were used to harvest cereals ⁽¹⁸⁾. Up until this time, our ancestors ate a varied diet of wild plants, fish, animals, and insects. Civilization from the Mideast spread throughout Europe as these new farmers moved into lands just vacated by retreating glaciers that covered northern Europe, Asia, and North America. The milk cow and domesticated grain seeds moved in with these invaders. Many of the native people in Europe, including children, were not biochemically adapted to eating these foods, and as a result, they did not do well on such diets and many died. Consequently, the genes associated with gluten sensitivity became reduced in the population. In countries such as Ireland, which were invaded more recently (about 3000 years ago) by people subsisting on high wheat and milk diets, the incidence of sensitivity to these foods is higher than in any other country. Because the toxic effects of milk and wheat have not had very long to kill off the sensitive individuals in the population, western Ireland has the highest incidence of schizophrenia ⁽¹⁹⁾ and celiac disease (1 in 300) in the world (and the two are probably related). Dohan found that schizophrenia was essentially absent from primitive people in the East Indies until they adopted a Westernized diet with increased grains ⁽²⁾.

Antibodies to Transglutaminase Cause Celiac Disease

What are the effects of gluten sensitivity? In the medical disorder called celiac disease, there is a reduced ability to digest wheat and there is often a direct toxic effect of gluten on the lining of the intestine called the intestinal mucosa. Symptoms may include diarrhea, failure to thrive, short stature, discolored dental enamel, depression, premature degeneration of the nervous system, seizures, arthritis, nutritional deficiencies due to malabsorption, and abdominal distension (20-23). Long eyelashes, premature balding and clubbing of the fingers are also commonly reported in this disease. In celiac disease, there is also an increase in the blood of antibodies to wheat, and also a marked increase in antibodies called endomysial antibodies. The exact nature of the endomysial antigen has recently been identified as the tissue transglutaminase enzyme (24, 25). Researchers in Norway (24) think that transglutaminase facilitates the physical linkage of the carboxamide group of an amino acid called glutamine in gluten to an epsilon-amino group of a lysine residue in transglutaminase in the intestinal tract. (The normal physiological function of transglutaminase is probably the repair of injured or inflamed tissue by cross-linking extracellular matrix proteins in the tissue, thus stabilizing the damaged tissue and protecting the surrounding tissue from further damage.) Since gluten has an abundance of the amino acid glutamine, it is especially vulnerable to this reaction with transglutaminase. This abnormally linked molecule is then perceived as a foreign antigen by the immune system and antibodies to transglutaminase begin to be produced, inhibiting the normal function of transglutaminase in repairing damaged intestinal mucosa. The test for antibodies to transglutaminase is now considered the most specific test for celiac disease with near perfect specificities and sensitivities for celiac disease and is now being offered by The Great Plains Laboratory. This test is invalid if the patient has been off wheat for several months.

I suspect that wheat and Candida sensitivity may be linked because of the pentosidine linkages discussed in the "Organic Acids" chapter in this book. I suspect that in autism, the arabinose from Candida, instead of transglutaminase, crosslinks the gluten molecule to other tissue proteins, leading to a different autoimmune reaction and gluten sensitivity.

In celiac disease, there is an increased incidence of certain antigens on the white blood cells called HLA (human leukocyte antigen). These HLA types are most commonly used to determine suitability for tissue transplants and for paternity testing. Patients with celiac disease have an increased frequency of the HLA-B8 and HLA-Dw3 types compared to the population as a whole (26). The HLA-B8 antigen is present on the white blood cells of about 85-90% of celiac patients compared to only 20% of the general population.

Differences Between Wheat Sensitivity in Autism and Celiac Disease

In celiac disease, the cells of the mucosa (the lining of the intestinal tract) lose their characteristic features, do not function as well, and may have impaired ability to produce hormones like secretin that stimulate the pancreas to function properly. As a consequence, the absorption of food from the intestine is impaired and there may be severe diarrhea due to this malabsorption. Severe nutritional deficiencies may also occur due to this defective absorption of nutrients in damaged individuals with autism and schizophrenia. The intestinal cells do not appear to be as bad as in celiac disease and if a small piece of the intestinal lining is removed in a biopsy, the microscopic pattern of the tissue is not usually the same as in celiac disease.

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Autism is also different from celiac disease in that patients with autism frequently have elevated antibodies against both wheat and milk. A major difficulty in both autism and schizophrenia appears to be the absorption of the incompletely digested pieces of the gluten and casein proteins called peptides. One of the reasons for the incomplete digestion may be a deficiency of enzymes that break down these small peptides. I have talked with numerous parents who had the biopsy done to test for celiac disease, and none of the tests indicated the microscopic pattern of classic celiac disease even though the child improved on a gluten-restricted diet. Most children with autism will be negative for the test for antibodies to transglutaminase but since celiac disease is such a serious condition, it may be worthwhile to test any child with autism positive for wheat allergy. Such testing must be done before wheat is restricted.

Peptides from gluten and casein are important because they react with opiate receptors in the brain, thus mimicking the effects of opiate drugs like heroin and morphine. The peptide from wheat is called gluteomorphin (gluten + morphine) and the peptide from milk is called caseomorphin (casein + morphine). Gluteomorphin (also termed gliadorphin) has been verified by mass spectrometry techniques to be present in urine samples of children with autism by Alan Friedman, Ph.D. in work done at Johnson and Johnson. Both casomorphin and gluteomorphin are composed of seven amino acids, which are abbreviated below. Both casomorphin and gluteomorphin start with the beginning N-terminal sequence tyr-pro (for tyrosine and proline) with additional pro residues (proline) in positions 4 and 6 of both peptides as indicated below. Similarities are indicated by bold print.

	1	2	3	4	5	6	7
Casomorphin:	tyr	pro	phe	pro	gly	pro	ile
Gliadorphin:	tyr	pro	gln	pro	gln	pro	phe

The inability to breakdown these peptides could indicate a possible genetic deficiency of dipeptidyl peptidase IV in children with autism according to Dr. Alan Friedman. Dipeptidyl peptidase IV is an enzyme that is also present on cells of the immune system called lymphocytes ⁽²⁷⁾. The particular cells are termed CD4+ helper cells. It has been found that this particular enzyme is identical to a cell surface marker called CD26. (Proteins on the surface of cells are given the designation CD or cluster domain. Dipeptidyl peptidase IV has the job of breaking down peptides in which the amino acid proline (abbreviation pro) is in the second position of the peptide as it is in both casomorphin and gliadorphin shown above. Dipeptidyl peptidase IV is found in the immune system cells and in the linings of the intestine, kidney, and blood vessels ⁽²⁷⁾.

Gliadorphin and casomorphin are important substrates for the enzyme DPP IV. Each molecule of casomorphin and gliadorphin is processed twice by DPP IV (Figures 1a and 1b). After two dipeptides are removed from gliadorphin and casomorphin, tripeptides with proline in the middle position remain. One might expect that DPP IV would then remove another dipeptide from these molecules; however, this is not the case. Instead tripeptides with proline in the center position are potent inhibitors of DPP IV that essentially inactivate DPP IV ⁽²⁷⁾. By breaking down casomorphin and gliadorphin, DPP IV essentially embarks on a course of self-destruction. As a result, many of the other functions of DPP IV may be impaired. As a matter of fact, the inhibition of DPP IV breakdown of other important regulatory peptides (Table 1) by casomorphin and gliadorphin may be much more important than the opiate effects of these molecules.

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Figure 1a
Breakdown of Casomorphin By DPP IV

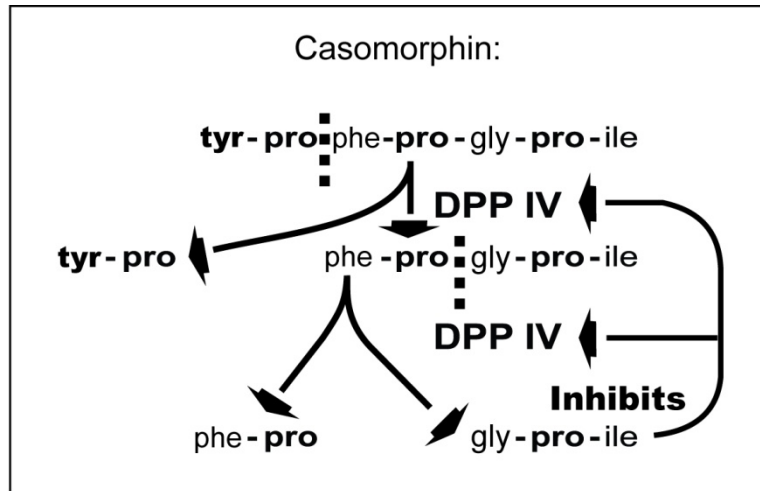
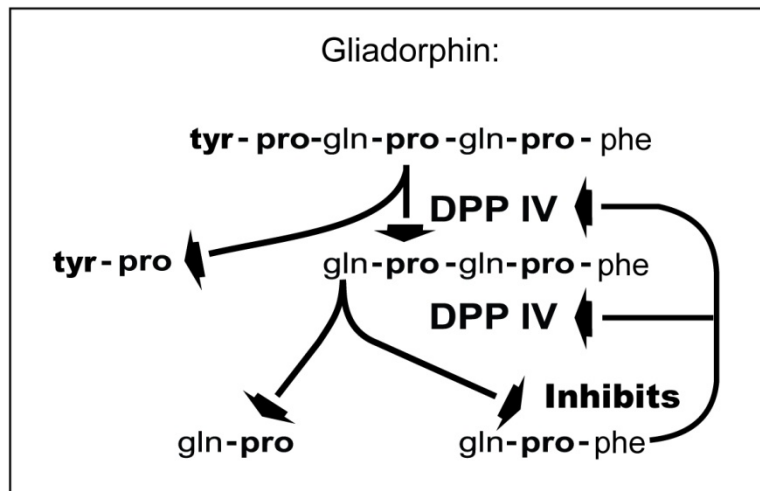


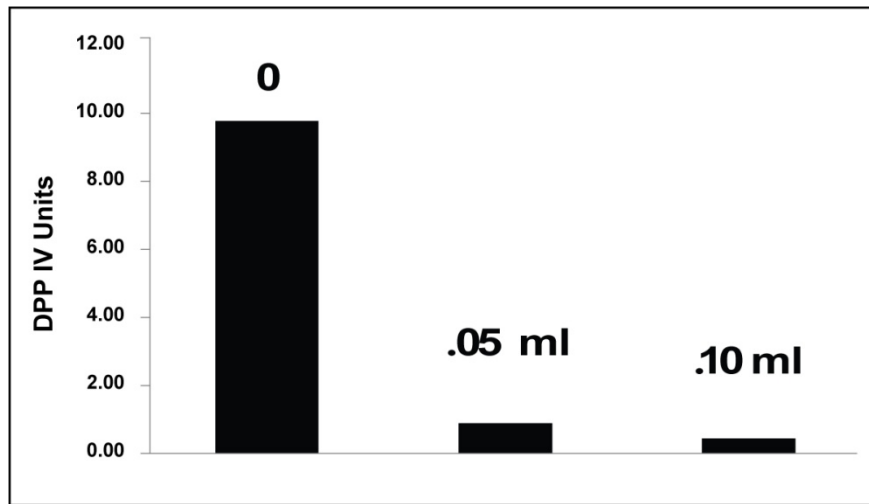
Figure 1b
Breakdown of Gliadorphin By DPP IV



At The Great Plains Laboratory, we found that the MMR vaccine is a potent in vitro inhibitor of DPP IV, presumably due to its hydrolyzed gelatin content (Figure 2). Gelatin is a byproduct of collagen from bones, tendons, and hooves obtained from animals at slaughterhouses. Whether this additive could be a factor in adverse vaccine reactions deserves further investigation. Gelatin is the major ingredient of Jell-O and Knox and gelatin is also the major ingredient of capsules for food supplements and drugs. Whether or not the small amount of gelatin in capsules, the gelatin in vaccines, or the large amounts of gelatin in Jell-O are significant in autism is unknown. The simplest way of finding out whether gelatin is a factor in causing autistic symptoms is to try a dietary challenge with a serving of unflavored Knox gelatin after restriction of all gelatin products for a week or more.

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Figure 2
Effect of MMR Vaccine on DPP IV Enzyme Activity In Vitro



Hydrolyzed gelatin is even a more potent inhibitor of DPP IV probably because hydrolysis releases peptides with proline in the third position of the peptides or tripeptides with proline in the second position (like the residual tripeptides from casomorphin and gliadorphin after DPP IV action). Such peptides are potent inhibitors of DPP IV ⁽²⁷⁾. Hydrolyzed gelatin is a component of the combined current MMR and DPT vaccines as well as the single component vaccines at a concentration of 0.2 g per 100 ml ⁽²⁸⁾.

One parent reported that her child did poorly in his ABA class consistently after he was given marshmallows as a treat in the afternoon. Suspecting gluten or casein contamination, she contacted the manufacturer who reported that the marshmallows did not contain any gluten or casein. Marshmallows do, however, contain gelatin. NAET testing indicated gelatin sensitivity. The day after NAET treatment for gelatin allergy, her child began to converse for the first time. Much more research needs to be done to determine if dietary gelatin is a problem for most children with autism or PDD.

I was especially interested in the possibility that the gelatin in the vaccines might cause an abnormal immune reaction in autism since numerous reports ⁽²⁸⁻³²⁾ have implicated gelatin as a major risk factor in children with severe immediate vaccine reactions to MMR, DPT, Varicella, and to vaccinations with single components of the MMR and DPT vaccines. Most of the children with these reactions had elevated IgG and IgE antibodies in serum to gelatin. At The Great Plains Laboratory, we tested the blood of 25 children with autism for the presence of IgG and IgE antibodies to intact gelatin using a commercial enzyme immunoassay and no abnormal results were found, indicating that the vaccine reaction in autism is different than the previously reported vaccine reactions involving gelatin. However, it is still possible that there may be antibodies produced against gelatin peptides (present in the hydrolyzed gelatin of many vaccines) in individuals with vaccine reactions and this should be separately tested. Investigators evaluating the autism vaccine connection should carefully scrutinize the dates that the hydrolyzed gelatin was first employed and see if the increased autism incidence occurs at the same time.

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Table 1
Gastrointestinal and other peptides that are activated or inactivated by DPP IV

Peptide	# of amino acids	Location	Function
Peptide YY	36	Small and large intestine	Causes intestinal constriction, inhibits motility of gastrointestinal tract, inhibits pancreatic secretion of enzymes and bicarbonate.
Neuropeptide Y	36	Sympathetic nervous system, gut, brain (hypothalamus and limbic system)	Kills Candida when N-terminal dipeptide removed by DPP IV. Inhibits effect of CCK. Inhibits glucagon and insulin secretion and renin release. Regulates hypothalamus in the brain. Increases blood pressure. Structure similar to Peptide YY. Increases thirst, drinking, eating. Facilitates memory.
Pancreatic polypeptide	36	Pancreas	Increases pancreatic secretion when stimulated by secretin.
Enterostatin	5	Brain, intestine	Inhibits food intake.
Substance P	11	Brain, peripheral nerves, intestine, skin, sensory organs, lungs, urinary tract	Suppresses bile production and release and reduces pancreatic response to secretin. Causes flushing and diarrhea. Mediates pain, touch, and temperature perception and acts as a neurotransmitter. Releases histamine. Causes diuresis (increased urination).
Growth hormone releasing factor	44	Hypothalamus, pancreas, spleen, thymus	Releases growth hormone from pituitary gland. Increases feeding. Stimulates the immune system overall.
Procalcitonin	116	Para follicular cells of the thyroid gland	Storage form of calcitonin, a major hormone regulating calcium. Calcitonin lowers calcium in blood and is an antagonist of parathyroid hormone.
Glucose dependent insulinotropic polypeptide	42	Duodenal mucosa	Stimulates beta cells of pancreas to release insulin.
Glucagon-like peptide-1 (GLP-1)	30	Small and large intestine, brain	Part of proglucagon, which contains GLP-1 and GLP-2. Inhibits food and water intake. Decreases blood glucose.
Glucagon-like peptide-2 (GLP-2)	33	Small and large intestine	Part of proglucagon, which contains GLP-1 and GLP-2. Increases intestinal growth.
Peptide histidine methionine (PHM)	27	Intestine, brain, nasal mucosa, stomach, genitals. Highest in colon.	13 amino acids of PHM are similar to vasoactive intestinal peptide (VIP). Relaxes smooth muscle in lungs, gall bladder, and stomach. PHM is encoded in VIP gene and is secreted as part of ProVIP hormone.
Interleukins 1 β , 2, 3,5,8,10,11,13	varied	Cells of the immune system	Interleukins are potent regulators of the immune system
Bradykinin	9	Pancreas, sweat glands	Activates pain receptors and causes smooth muscle contraction

It is significant that substance P, a peptide hormone that regulates the intestinal tract and many other polypeptide hormones, also have a proline in the second position of the peptide and are broken down by DPP IV. If DPP IV were inhibited by gliadorphin or casomorphin tripeptides, then substance P might accumulate to abnormally high levels if the enzyme is defective. Substance P is a neurotransmitter in the brain and nervous system ⁽²⁸⁾ and it is also a mediator for the transmission of pain signals. The inability to break down substance P might cause prolonged painful stimuli that might account for the extreme sensitivity of children with autism to certain sounds as well as the gastrointestinal pain reported by Wakefield. Substance P is also a regulator of the immune system besides regulating pain, touch, and temperature ⁽²⁸⁾. Several other proteins that regulate the red blood cells and immune system including IL-1 β , IL-2, granulocyte-macrophage-colony stimulating factor, and erythropoietin also have the proline in the second position and could accumulate if dipeptidyl peptidase is defective ⁽²⁹⁾. Table 1 lists a number of peptides that are acted on by DPP IV. Thus, DPP IV regulates peptides that influence many types of behavior and physiological functions including hunger, thirst,

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digestive function, food intake, growth, pain and touch perception, control of Candida, overall immune function, and calcium metabolism.

Low values for DPP IV in blood serum are found in patients with major depression ⁽³³⁾ and in alcoholics ⁽³⁴⁾, even when abstinent. In depression, the severity of depression is proportional to how depressed DPP IV is in the blood serum ⁽³³⁾. High values are found in patients with schizophrenia ⁽³⁵⁾ and low amounts of DPP IV are present in the intestinal cells of people with celiac disease ⁽³⁶⁾. Low values have also been reported in people with rheumatoid arthritis ⁽³⁷⁾ and anorexia nervosa ⁽³⁸⁾. The Great Plains Laboratory has measured and analyzed DPP IV in blood serum of both children with autism and in normal control children and no significant differences were found. However, DPP IV levels in the intestine might still be decreased in autism and this should be evaluated because it is in the intestines and kidneys that amounts of DPP IV is present in the highest quantities.

Casomorphin and gliadorphin have been shown to react with areas of the brain such as the temporal lobes ⁽³⁹⁻⁴¹⁾, which are involved in speech and auditory integration. Furthermore, the administrations of drugs like naltrexone (see chapter by Bruce Semon M.D. Ph.D.), that block the effects of opiate drugs, can lessen the symptoms of autism ⁽⁴²⁾. Children with autism frequently improve overall after restriction of these foods and slip-ups can be catastrophic. One mother reported to me that her teenage son with autism, who was doing very well on a gluten-restricted diet, severely damaged her house in a rage after eating a few wheat crackers. I have personally been informed of so many cases of improvement after gluten and casein restriction that there is no doubt in my mind that this dietary restriction should be considered for every child with autism. I would be very cautious in changing the diet if it has been successful. Because the milk and wheat peptides function as opiates, a withdrawal reaction similar to that of a drug addict may occur when these foods are removed from the diet.

The withdrawal reaction from gluten and casein can sometimes be severe. Some parents have reported seizures and hallucinations during the withdrawal period. Sidney Baker M.D. describes the reaction of one child with autism to the removal of gluten and casein in his book *Detoxification and Healing* ⁽⁴³⁾. The child refused to eat, lost 15 pounds, was extremely hyperactive, barely slept, increased biting and hitting behaviors, and had to have liquids forced on him to prevent dehydration. Repeated doses of Alka-Seltzer Gold provided temporary relief from the symptoms. At the end of the six weeks, the withdrawal ended and the child was significantly improved. Alka-Seltzer Gold is a bicarbonate that helps to neutralize stomach acid.

Warning! Other types of Alka-Seltzer are not the same as Alka-Seltzer Gold and could cause serious side effects if given excessively.

Chapter 6**Testing for Wheat and Dairy Sensitivity**

Several different laboratory tests are available to evaluate gluten and casein sensitivity including tests for IgG antibodies to gluten and casein as well as antibodies to related grains such as rye, barley and oats; testing for the presence of antibodies to transglutaminase to confirm celiac disease, and testing for the presence of the peptides casomorphin and gluteomorphin in urine. Peptides in the urine may become normal within a week of dietary restriction of wheat and/or dairy products. Antibody tests will usually remain abnormal for three to twelve months after the start of dietary restriction of the specific food. Anyone in the world can obtain all of these tests from:

The Great Plains Laboratory
11813 W. 77th St.
Lenexa, KS 66214
Phone: 913 341-8949
Fax: 913 341-6207
E-mail: GPL4U@aol.com
Website: www.greatplainslaboratory.com

Restriction of Gluten and Casein from the Diet

Lisa Lewis, Pamela Scott, and Karyn Seroussi, and Bruce Semon deal extensively with dietary therapies and I will not cover them here except for two important topics: calcium deficiency due to milk and dairy restriction and soy sensitivity.

Prevention of Calcium Deficiency on the Casein Free Diet

Calcium deficiency can be a severe problem in normal children on a milk free diet since milk is a significant source of protein, vitamin D, and calcium. Some physicians have reported rickets, a bone deformity in children with autism on the gluten and casein free diet. Calcium and vitamin D supplementation is essential to children on a casein free diet since most children with autism do not eat substantial amounts of other calcium rich foods.

Children with autism may have an even more severe problem with calcium deficiency. Mary Coleman, M.D. reported that children with autism who are calcium deficient are much more likely to poke out their eyes and a substantial number of children with autism have done so (44). This abnormal behavior is associated with low urine calcium because blood calcium levels were usually normal. Treatment with calcium supplementation prevents this behavior. This behavior may be due to increased eye pain resulting from high substance P in the eye and low calcium may act to intensify this pain. Subsequently, the child pokes at the eye in an attempt to relieve the pain. Dr. Coleman also found that speech developed very quickly after calcium supplementation in a portion of mute children with autism who had low urine calcium. Parathyroid hormone, calcitonin, and vitamin D were all normal in patients with low urine calcium. In one case, according to a parent who contacted me, her child with autism persisted in poking at the eyes even after one eye had been poked out and surgically replaced. Calcium supplementation stopped this behavior immediately.

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I have talked to several parents of children with autism that began to touch their eyes after starting the casein-free diet. Calcium supplementation quickly eliminated this behavior. Calcium, magnesium, and zinc need to be balanced for optimal nutrition. Vitamin D supplementation may also be needed when milk is eliminated unless other sources of vitamin D are included in the diet. Recommended calcium and magnesium supplementation amounts are given below:

Age in yrs	Amount of calcium	Amount of magnesium	Amount of zinc
1-2	600 mg	100 mg	2.5 mg
3-4	800 mg	200 mg	5 mg
5-10	1000 mg	250 mg	15 mg
>10	1000-1200 mg	350 mg	25 mg

Do not exceed dosage recommendations because excessive magnesium can be fatal!

Soy Sensitivity

A review of IgG food allergy tests at The Great Plains Laboratory indicated that almost every child with autism or PDD who had been switched to soymilk or other soy products as a part of their gluten and casein restricted diet had extremely high allergies to soy. Frequently, the parent would indicate that the child had not responded well to the diet or responded favorably for a few weeks and then regressed. Restriction of soy in such individuals usually results in improvements in the behavior of the children according to the parents. The adverse reaction to soy is so common that I would advise against the use of this food. Soy has been shown to produce biologically active peptides ⁽⁴⁵⁾. Furthermore, Dr. Lori White of the Pacific Health Institute in Hawaii found disturbing effects of soy. She found that Japanese-American men who ate tofu (soy sprouts) at least twice a week had a more rapid decline in mental abilities with age than those who did not eat tofu and that they also had significant brain shrinkage ⁽⁴⁶⁾. A group of scientists has recommended that soy not be used in baby formulas because it inhibits mineral absorption and might cause fertility problems or alter sexual development due the high content of estrogen-like molecules called isoflavones. In addition, soy can cause abnormalities of the thyroid gland, and might be a factor in breast and pancreatic cancers ⁽⁴⁶⁾.

Use of Other Therapies to Control Gluten and Casein Sensitivity

Several other approaches have been evaluated to reduce sensitivity to gluten and casein. None of these approaches has been as extensively evaluated as dietary restriction of gluten and casein, which remains the "Gold Standard" for treatment. Nevertheless, all possible therapies should be investigated. Laboratory testing such as urinary peptides and IgG antibodies to gluten and casein should be able to document the degree of effectiveness of other non-dietary therapies.

Other New Peptides That May Be Important in Autism

A chemist, Alan Friedman, Ph.D. has reported at several autism conferences the presence of increased amounts of other opiate peptides using mass spectrometry. Two of these opiates, deltorphin and dermorphin, are extremely potent and can bind to human granulocytes, a type of white blood cell. As a result, these opiates might alter the response of the immune system. Deltorphin has been isolated from the skin of frog species and Dr. Friedman believes that this compound is not being produced by the frogs themselves, but instead by bacteria or fungus on the skin. He suspects that the deltorphin, found in humans, has a microbial origin because of the presence of D-amino acids, which are not characteristic of human metabolism. However, recent information indicates that the frog genome does indeed code for these peptides and that the amino acids are modified to the D-form after the protein has been formed. Thus, it is possible that humans may also produce these peptides.

High-Protease/Peptidase Enzyme Products Enhance Protein Digestion

In 1999, the first plant-based enzyme product targeted for children with autism was introduced. Since then, other enzyme products with better specificities and higher potencies have made their way into dietary protocols. Most physicians now agree on the use of digestive enzymes as a means of enriching the gut environment. Dipeptidyl Peptidase IV (DPP IV), an enzyme found in the lining of the gut wall, is also found in certain protease blends. This enzyme is responsible for degrading the exorphin peptides produced from certain proteins found in wheat, dairy, soy and many other foods. Just as important is the use of other proteases that actually alter the manner in which these proteins are broken down, such that exorphin peptides are not produced. This two-pronged approach of diminishing production of exorphins while also targeting the direct breakdown of any exorphins produced in the gut is the forefront of products such as Houston Enzymes' AFP Peptizyde. Many parents report that their child was able to use this product as an alternative to the GFCF diet. Others found they could add back foods previously not tolerated, or found additional benefits beyond what the GFCF diet provided alone. As every child presents differently with their particular digestive problems, care should be taken when using these products as a GFCF alternative. These enzymes are highly purified proteins from *Aspergillus oryzae*, a non-pathogenic fungus, which is not related to yeast mold (*Candida albicans*). Unless a specific allergy to *Aspergillus* exists, the enzymes should not be a factor even in those with mold allergies.

Alpha-1-Antitrypsin Deficiency

Alpha-1-antitrypsin is a protein produced by the liver. Deficiency of this protein is associated with chronic obstructive lung disease (or emphysema), cirrhosis of the liver, and respiratory distress of the newborn. Alpha-1-antitrypsin is an inhibitor of enzymes that break down proteins (proteases). It inhibits the action of a number of naturally occurring proteases including trypsin, chymotrypsin, collagenase, white blood cell proteases, and plasmin and thrombin, which are released in inflammatory reactions of the lung. In the absence of sufficient alpha-1-antitrypsin, plasmin and thrombin may begin to digest the lung itself. Elevated values for this protein are found in patients who are genetically heterozygous deficient for alpha-1-antitrypsin, during infection, during pregnancy, in bacteria infection, following estrogen or steroid therapy, and in rheumatoid arthritis. In the gastroenterology department of a children's hospital in Australia, it was discovered ⁽⁴⁷⁾ that 8 of 15 children with autism had abnormally low values of alpha-1-antitrypsin. In children with celiac disease, there was also an

increased incidence of low values of alpha-1-antitrypsin. The authors think that the low level of alpha-1-antitrypsin might predispose children to wheat sensitivity. The Great Plains laboratory now offers testing for alpha-1-antitrypsin activity.

Pancreatic Atrophy, Hypoglycemia, and Antibiotics

I reviewed the results of a very interesting case, which illustrates the possible damage of yeast byproducts. (I encountered many similar cases but this child, who was tested over an extended time period and extensively evaluated by many different medical specialists, had his biochemistry analyzed exhaustively.) At about 10 months of age, this normal child whom I'll call Ralph, developed a Strep throat and was given antibiotics. The Strep throat cleared up but the conscientious parents were advised to be sure to finish giving the entire 14-day supply of antibiotics. When Ralph's mom went to check on him, she found that he was having convulsive seizures. She rushed Ralph to the emergency room at the hospital where his blood glucose (blood sugar) was near zero. Ralph would have died if his mother had brought him in any later. Ralph was given an infusion of glucose into his vein and began to recover.

Because of Ralph's extremely low blood sugar, the attending physician sent a urine sample to my organic acid laboratory to see if Ralph had one of the genetic disorders that caused low blood sugar. When I examined Ralph's urine organic acid profile, he had none of the abnormalities associated with any of the genetic diseases that cause hypoglycemia (low blood glucose) such as fatty acid oxidation disorders. Ralph did have, however, very high levels of the sugar arabinose, which indicated a severe yeast overgrowth resulting from his antibiotic treatment for Strep. I reported my findings. A new physician at the hospital was sure Ralph had one of the genetic disorders and ordered a retest. Again, the only significant abnormality was the elevation of the same yeast-related compounds that I had found in children with autism.

When Ralph returned home, his parents became concerned because he began to stagger at certain times of the day. When tested repeatedly, his blood glucose was low again, testing between 30-50 mg per dl. Normal is about 100 mg per dl. Many other endocrine tests revealed no cause for Ralph's hypoglycemia. Ralph was referred to another specialist who suspected that Ralph might have a tumor of the pancreas, which would oversecrete insulin, therefore lowering blood sugar. However, repeated testing revealed only a slight increase in insulin at most and not a value high enough to indicate a tumor.

His parents were taught how to perform a blood sugar test and tested Ralph's blood sugar several times a day. The child's pancreas, where the insulin-secreting cells are found was examined by an imaging technique called MRI and it was found that there was a severe atrophy of the pancreas. In addition, the tail of the pancreas was completely missing, but a tumor secreting insulin was not found. Additional organic acid tests at later times revealed the same elevation of - byproducts. Several times I recommended the use of an antifungal drug but my suggestions were ignored.

Instead, the parents of the child were instructed to give the child multiple doses a day of a food called cornstarch, which is broken down into sugar in the intestine. The idea here was that sugar derived from cornstarch would increase the child's blood sugar. However, the child's blood glucose continued to be abnormal and the parents were reprimanded for not being diligent enough in giving enough cornstarches throughout the day. More than likely, the excessive cornstarch was feeding Ralph's untreated yeast overgrowth and just made his hypoglycemia worse. Low blood sugar is prevalent in fibromyalgia ⁽⁴⁸⁾, a disorder in which yeast overgrowth is common ^(49, 50). Finally, at about the age of two and a half years, I learned that Ralph was being referred to a developmental pediatrics department with the diagnosis of a probable autistic-

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spectrum disorder. At this time, a trial of nystatin was introduced. Ralph's blood sugar returned to normal in about a week and his organic acids were normal for the first time since he had started antibiotics as an infant. There is no doubt in my mind that I had witnessed and documented over a span of about two years, the transformation of a normal infant into a child with autism.

I have lost contact with the child's parents and do not know what happened to him later on. Ralph's story indicated to me that yeast overgrowth could cause severe hypoglycemia and that it might also severely damage the pancreas. Another parent of a child with autism reported to me similar hypoglycemia and even more pancreatic damage in her son. The hypoglycemia could be due to the yeast byproducts. I suspect that the damage to the pancreas was due to antibodies against the yeast that cross-reacted with the pancreas in an autoimmune reaction. (See the chapter on the immune system.) It is possible that protein crosslinks of pentosidines caused by abnormally high arabinose might also be responsible for some of the damage. (See the chapter on organic acids.) The pancreatic damage probably resulted in deficient production of digestive enzymes by the pancreas. This deficiency of digestive enzymes would also result in the incomplete digestion of wheat and milk proteins that would then be absorbed and cause their opiate effects on the brain.

Secretin

Secretin is a small protein called a polypeptide produced by the cells of the small intestine and is made up of 27 amino acids ⁽⁵¹⁾. The function of secretin is to cause the pancreas to release bicarbonate after a meal. After a meal, the stomach secretes acid and the food passing through the stomach is very acidic. Next, the pancreas secretes digestive enzymes to digest the food arriving into the small intestine from the stomach. These enzymes will not be able to properly digest the food if the acid from the stomach is not neutralized by bicarbonate from the pancreas. Thus, if secretin secretion is deficient, no bicarbonate will be formed and foods will not be digested properly. Secretin is produced by certain cells in the intestine and is stimulated by the presence of stomach acid. Secretin has been used to assess the function of the pancreas and is derived from pig intestine. Synthetic human secretin is now available.

Human and pig secretin are very similar (Table 2) and the molecules differ in only 2 of the 27 amino acids ⁽⁵²⁾. Furthermore, these amino acids, that are different in human and porcine secretin, are considered to be conservative replacements. Amino acids, which make up secretin, belong to certain families based on their chemical characteristics. These families are aromatic, aliphatic, acidic, basic, hydroxyl containing, and sulfur containing. The two amino acids that are different in porcine and human secretin belong to the same families. These similarities decrease the likelihood of an autoimmune response in a human using porcine secretin. However, elevated antibodies to secretin have been reported in children with autism treated with pig secretin.

In order to assess pancreatic function, secretin is injected into the vein and is transported by the bloodstream to the pancreas. If the pancreas is functioning properly, then the pancreas will produce bicarbonate. The production of bicarbonate can be monitored through a tube down the esophagus and stomach while the patient is sedated.

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Figure 3

Comparison of Amino Acid Sequence in Pig and Human Secretin.

** Amino Acids That are Different in the Two Types of Secretin are Indicated with Bold Type.

Pig secretin –

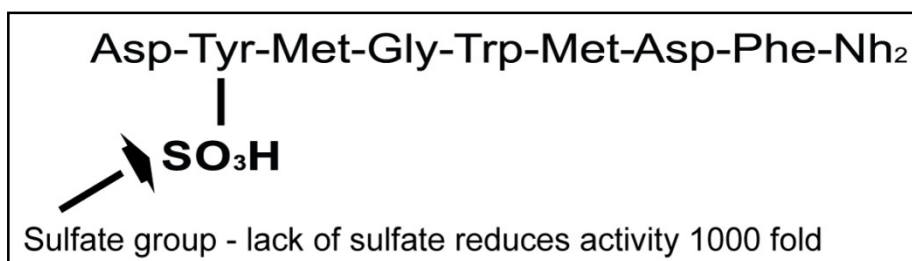
27 amino acidsH-His-Ser-Asp-Gly-Thr-Phe-Thr-Ser-Glu-Leu-Ser-Arg-Leu-Arg-
Asp-Ser-Ala-Arg-Leu-Gln-Arg-Leu-Leu-Gln-Gly-Leu-Val-NH₂

Human secretin –

27 amino acidsH-His-Ser-Asp-Gly-Thr-Phe-Thr-Ser-Glu-Leu-Ser-Arg-Leu-Arg-
Glu-Gly-Ala-Arg-Leu-Gln-Arg-Leu-Leu-Gln-Gly-Leu-Val-NH₂

Figure 4

Cholecystokinin (CCK 8)



Why are these children reacting to these infusions so dramatically? Several explanations are possible:

(1) Children with autism are not producing secretin in sufficient amounts and their digestive process is impaired as a result. The gush of bicarbonate after secretin might be due to the fact that the pancreas has not been stimulated adequately with the body's own secretin and therefore it overacted to the external secretin administered intravenously. This is the most likely explanation. Reduced secretin production may be related to gluten sensitivity, Candida damage, or viral damage to the intestinal mucosa caused by the live virus vaccines such as the MMR. In celiac disease, the gluten damages the intestinal cells that produce secretin ⁽⁵¹⁾ and presumably, a similar mechanism is operating in autism. (2) Children with autism are producing a defective type of secretin that is not capable of stimulating the pancreas (3) It is also possible that secretin has some direct beneficial effect on brain functioning (4) And lastly, the autoantibodies against the pancreas, induced by Candida, may be preventing the pancreas from responding to the normal amount of secretin produced by the child's own body.

Dr. Horvath and his colleagues recently reported on additional gastrointestinal abnormalities in children with autism ⁽⁵⁴⁾. It was found that 58% of children with autism had low intestinal carbohydrate digestive enzymes (lactase) and 75% had increased pancreatic fluid after secretin. Lactase deficiency was found to be the most common enzyme deficiency in these children. Nineteen of the 21 patients with diarrhea had significantly higher fluid output than those without diarrhea. Reflux esophagitis was found in 69% and inflammation of the duodenum was found in 67%. A particular type of duodenal cell called a Paneth cell was found to be present in much higher numbers than in control samples. Dr. Horvath's work seems back up the work of Dr. Wakefield in confirming that there is a physiological basis for the stomach pain and abdominal distress commonly reported by parents of children with autism.

Routes of Administration and Forms of Secretin

The most significant difference among secretin suppliers is whether the secretin is of human or porcine (of pig) origin. The routes of administration are oral (by mouth), intravenous, intramuscular, and transdermal (through the skin). Each of these routes may have certain advantages and disadvantages. Human synthetic secretin, which is identical to human secretin and is less likely to cause autoimmune reactions, can be obtained from Bachem, AG, CH-4416 Bubendorf, Switzerland. Repligen Corporation (<http://www.repligen.com>), a biopharmaceutical firm, based in Massachusetts, has been awarded a U.S. patent for the use of secretin in treating autism and is also developing synthetic human secretin. Most of the secretin used in the United States to date has been administered by the intravenous route using porcine secretin. Porcine secretin is produced in the United States by Ferring Pharmaceuticals. At this time, it appears that Ferring has discontinued the production of secretin because they did not find it sufficiently profitable. The Japanese drug company Eisai also used to produce porcine secretin under the trade name, Secrepan®. In Japan, secretin has been widely used to treat ulcers. The route of administration of secretin in Japan is the intramuscular route. There have been no significant reports of toxicity of secretin from Japan, but only adults have been treated with Secrepan® until recently.

In Taiwan, Dr. Shin-siung Jung, a neurologist at the Springtide Foundation of Taipei City reported the results of the first double blind study of secretin on the Internet. They concluded Secrepan® is a mild to moderately effective treatment of autistic symptoms in 75% of children with autism. The main improved symptoms included improved vocalization, stabilized emotion, improved socialization, decreased sleep disturbance, and improved eye contact. No improvement or worsening was found in 25% of the treated children. Adverse side effects included irritability, sleep disturbance, hyperactivity, and poor appetite and these were observed in both placebo and Secrepan® treatment groups. It was very difficult to differentiate adverse side effects of Secrepan® from day-to-day fluctuation of autistic symptoms. No significant allergic effects were noted in the study. The Secrepan® product has been reported to have significantly less secretin than the Ferring product. Ironically, it is possible that the lower purity of Secrepan® may be one of the reasons this product was more effective in treating autism. Other hormones in the product may have produced additional benefits not produced by more highly purified secretin.

A trial of synthetic secretin done on a large group of children with PDD or autism was published in December 1999 ⁽⁵⁵⁾. The trial was a single dose and no differences in improvement were found between the secretin and placebo groups. Another unpublished study also found no difference between placebo and synthetic secretin. In both studies of synthetic secretin and the Taiwan study, there was a significant placebo effect of around 50%, indicating to me that there is a critical need to develop better means of objectively assessing behavioral changes in autism in such trials.

The difference in results between the Taiwan studies and the studies using synthetic secretin may mean that other impurities in the pork secretin are causing the beneficial effects. It is possible that the impurities enhance the effect of the secretin, or that the route of administration for secretin is critical for success. An alternate explanation is that the synthetic human secretin did not work because it was not dissolved in the optimum solution. The three-dimensional structures of peptides are highly dependent on the ionic strength, pH, and other factors in the solution. An anticancer peptide called endostatin that prevents angiogenesis, the development of a tumor blood supply, only was effective under certain stringent conditions and was ineffective under other conditions. I think it is premature to give up on synthetic secretin trials until many other factors are investigated. The use of insulin for treating diabetes would have been discontinued if the results of a single insulin injection were the only factor used to assess treatment effectiveness.

Adverse Reactions to Secretin

Common side effects associated with secretin infusions include increased stimming and hyperactivity for up to two weeks after the infusion. More serious side effects have occasionally been reported. Some children have contracted childhood diseases to which they had been immunized, possibly due to the effects of secretin on the immune system. One child developed sores that covered the inside of the mouth shortly after the first infusion of secretin, making it difficult to eat. A seven-year-old girl began to develop breast buds after several secretin infusions. It is impossible to know if these side effects were due to the secretin treatment, or were simply coincidental. However, there are secretin receptors on the ovaries and it is possible that secretin may have stimulated these.

I personally talked to a parent whose child had The Great Plains Laboratory organic acids urine test a few days before his first secretin infusion. The test revealed an extremely high arabinose value (1600 mmol/mol creatinine), indicating a severe intestinal yeast overgrowth. The child was put on antifungals shortly before a scheduled secretin infusion, but antifungal treatment was stopped due to “Internet wisdom,” that anything taken by mouth might prevent secretin success. A few days after the secretin infusion, the child had grand mal seizures. This child had no previous history of seizures. Thus, it is possible that the seizures may have due to the severe yeast problem or may have been due to a yeast secretin interaction.

Side effects were even more severe in a second child. This child was a seven-year-old male with a normal EEG, no history of seizures or allergies, and he was not on any medications. Three prior infusions of Ferring Secretin had been well tolerated at 6-week to one-month intervals, and anti-secretin antibodies had remained consistently negative. Small test doses were given prior to each infusion to test for allergic reactions. Shortly after the infusion, the child began having generalized motor seizures and stopped breathing. The child eventually responded to treatment with Valium and oxygen and resumed breathing spontaneously. No further seizures occurred. This case indicates that parents should be sure that their physician is prepared to treat serious life-threatening reactions that might occur.

Cholecystokinin (CCK)

Cholecystokinin (CCK) is another hormone produced by the cells of the small intestine. CCK has a 32 amino acid structure that is similar to the hormone gastrin. CCK is produced initially as a prohormone with 58 amino acids and then is broken down into peptides with 33, 22, 12, or 8 amino acids. The 8 amino acid peptide, CCK₈, is as biologically active as the 33 amino acid peptide. CCK stimulates the release of pancreatic enzymes, like secretin does, and also stimulates the release of bile from the gall bladder. As shown in Figure 4, a sulfate group is attached to the tyrosine in CCK. If sulfation is defective, as has been reported in autism, CCK may not be adequately sulfated. CCK, without the sulfate, loses almost all of its hormone function. The defective sulfation in autism would likely lead to defective sulfation of CCK, resulting in defective gastrointestinal regulation. Parents using over-the-counter CCK as an oral dietary supplement for their children with autism or PDD have reported beneficial effects similar to those of secretin. High doses suppress the appetite and the product is marketed as a weight loss treatment under the name Bodyonics®. CCK is available from GNC stores (800) 797-8828. For use in children, 1/8 to 1/4 of a 100 mg capsule of the CCK product is given exactly one hour after the first bite of food with each meal. The dosing and timing of administration are critical and should only be used under a physician's supervision. Overdosage has caused panic attacks and appetite suppression. When given at the beginning of the meal, pancreatic enzyme

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secretion begins **before** the food reaches the small intestine and may cause rectal burning. This product is a beef extract so food allergy to beef could cause severe reactions.

Abnormal Bile Secretion

Parents of children with autism often report abnormal color of their children's stool. The stool is frequently described as clay colored, white or lightly colored. The brown color in normal stool is due to bile pigments. Light or uncolored stools probably indicate an inadequate flow of bile possibly due to inadequate stimulation of bile release from the gall bladder due to deficient CCK. Many parents report the presence of "sand" in their child's stool. This "sand" is probably due to the presence of insoluble bile salts. The amount of "sand" is reported to increase dramatically after secretin infusions probably because secretin stimulates bile release. Bile salts containing taurine do not form this "sand" because they are more soluble. Supplementation with taurine might be useful since taurine is frequently low in the urine amino acid profiles of children with autism. The Great Plains Laboratory measures taurine and many other amino acids in its urine amino acid profile. Children with light colored stools may be significantly deficient in vitamin A, vitamin D, vitamin E, and vitamin K due to inadequate amounts of bile salts which aid in their absorption. Vitamin A palmitate, the prevalent form of vitamin A, may be especially difficult to absorb since bile salts are needed to remove the palmitate group before it is absorbed. A bile salt deficiency may be the reason that free vitamin A is needed for many children with autism. The organic acid test gives some clue as to which children may have this problem. Reduced bile salts cause increased absorption of oxalic acid, which is frequently elevated in children with autism. The reason for this abnormality is that if taurine containing bile salts are not present, free fatty acids remaining in the intestinal lumen compete with oxalic acid in combining with calcium to form insoluble soaps that are eliminated in the stool. Free oxalic acid is absorbed from the intestine more readily than the oxalic acid salt combined with calcium, which is insoluble and is not absorbed from the gastrointestinal tract. Testing for vitamins A, D, E, and K may be useful in children with high urine oxalic acid or with light colored stools.

Tests of Pancreatic Function

A common way to evaluate pancreatic function is to measure the concentration of pancreatic enzymes in the stool or blood and is included in the comprehensive stool test performed by The Great Plains Laboratory.

Other Digestive Enzyme Supplements

While enhanced protein digestion through the use of high-protease enzyme supplements can produce significant benefits in addressing gut health, other areas of digestion are also of concern. The function of different digestive enzymes is listed in Table 1.

AFP Peptizyde, previously mentioned in another section, addresses only protein digestion. But many children also have problems with carbohydrates, fats, and certain fruits and vegetables high in polyphenolic compounds. Enzyme supplements may help in these areas as well.

Many children suffer from gas, bloating, and loose stools. Carbohydrase enzymes, which degrade complex carbohydrates such as starch to simple sugars, can provide help by reducing the tendency of large

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carbohydrate molecules to draw water into the gut. Undigested carbohydrates are also a source of food for “bad” bacteria and yeast. Once sugars are produced from the carbs, they are rapidly removed from the gut, taking water out as well. This results in a drier, more formed stool, as well as a more hospitable environment for probiotics and other “good” bacteria. Houston Enzymes carries a formula known as Zyme Prime, a combination of many carbohydrase enzymes. Many parents have noted better bowel movements and less “carb craving” when given on a consistent basis to their children. Certain highly-colored fruits and vegetables cause behavioral and digestive problems in a subset of spectrum children. These foods can be addressed in certain xylanase-containing enzyme products, such as No-Fenol from Houston Enzymes. While the mechanism of action is still not fully understood, it is thought that the enzymes may remove certain types of sugar groups attached to polyphenols. This removal may then allow the phenolic compound to be processed without the subsequent red cheeks and ears that are characteristic of such food intolerances.

Behavior, Food Dyes, and Inactivation of Digestive Enzymes

Several studies have documented adverse effects of food colors on behavior ⁽⁵⁶⁻⁵⁸⁾. One possible mechanism for the negative effects of food dyes may be an inhibition of digestive enzymes by the food colors. In a study done in Germany ⁽⁵⁹⁾, it was found that the biochemical function of the digestive enzymes amylase and trypsin were significantly inhibited by many common food colors. Thus, one of the best things you might do for your child is to remove food dyes from his diet. Children who may have pancreatic damage due to autoantibodies or intestinal damage due to toxic peptides do not need the additional burden of food colors to inhibit any functional enzymes that remain active. The Feingold organization can be reached at www.feingold.org.

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Table 2
Human Digestive Enzymes

Human digestive enzyme	Function
Amylase	Converts starches to sugar
Sucrase	Converts sucrose to simple sugars
Lactase	Converts milk sugar (lactose) to glucose and galactose
Nucleases	Convert nucleic acids (DNA and RNA) to nucleotides
Lipase	Converts fats (triglycerides) to fatty acids and glycerol
Phospholipase	Converts phospholipids to fatty acids and glycerophosphate
Trypsin	Converts proteins to peptides
Chymotrypsin	Converts proteins to peptides
Carboxypeptidase	Converts peptides to amino acids
Aminopeptidase	Converts peptides to amino acids
Cholesterol esterase	Converts cholesterol esters to free cholesterol
Nucleosidase	Converts nucleosides to nucleic acid bases
Phosphatase	Converts organic phosphates to free phosphates

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Immunizations and Autism

Chapter 7

Dr. William Shaw

Congressional Investigation of Vaccine Safety

Representative Dan Burton, the Chairman of the United States House of Representatives committee on government reform, said at a hearing in 1999 ⁽¹⁾ that his grandchildren are among those who have suffered from immunization damage. He said there were reports last year of more than 11,000 cases of children getting sick after inoculations. Many of their ailments were minor, yet some required hospitalization, he said. Burton said most American children are required to get 22 shots by the time they start school (the actual recommended number is 33 or more agents if, for example, the MMR is counted as 3 agents ⁽²⁾; see Table 1) and "some have described the current mandating of an increasing number of vaccines to children to be a good intention gone too far." By comparison, an elderly person in the United States received a single immunization, the one for smallpox. Plans are underway for "super vaccines" containing 100 or more agents.

Burton said his granddaughter had to be hospitalized within hours of receiving a Hepatitis B vaccine, and his grandson became autistic after getting the shots. "You can call that a coincidence, but I think it is more," said Burton.

A Brief History of Vaccines

The word vaccine comes from the Latin word for cow, vacca. An English physician, Jenner, made the observation that milkmaids who were exposed to cows infected with cowpox did not become infected with the closely related human disease smallpox that was the most serious illness in the 1700's. When material from the lesions of cows was scratched into the skin, the recipient of the treatment did not get smallpox. Jenner then proposed the first vaccination program but was widely ridiculed in articles with cartoons showing him growing horns and cow udders. Jenner's vaccination proposal caught on nevertheless. When Lewis and Clark departed on their exploration of the American West, they carried pox scabs to vaccinate the Indians they would encounter as ordered by United States President Thomas Jefferson. Well into the twentieth century, smallpox vaccination was the only vaccine used in the United States and many other countries.

A Parent Speaks Out On Vaccines

"Doctors say to me, 'Who are you? Are you a physician?' I say no, I'm just a mother and I saw the change in my son," says Shelley Reynolds ⁽³⁾ of Baton Rouge, Louisiana, who was instrumental in helping introduce the Louisiana bill to allow children to receive separate instead of combined vaccines.

"It was right after his shot, and it was pretty dramatic. I've talked with many, many parents -- at conferences, over the Internet -- who also believe that their children were affected after the MMR (measles, mumps, rubella) vaccine.

"Liam was developing fine and normal. He made every milestone. But he'd been on tons of antibiotics because of ear infections. He'd just finished a six-week round of antibiotics, and when we went to get his ears rechecked, the doctor said, 'We've been putting this immunization off for a month, it's time to give it to him.' Within a few days, he started having strange behaviors. And the final straw was at 22 months, when he got his DPT shot (diphtheria, pertussis, tetanus). Three days later, he totally stopped talking."

Table 1

Immunizations Recommended by Kaiser Permanente, a
Leading Health Maintenance Organization (HMO) in the USA

Age	Recommended immunization	Number of agents
Birth	Hepatitis B	1
1 month	Hepatitis B	1
2 months	DaPT, HIB, polio	5
4 months	DaPT, HIB, polio	5
6 months	DaPT, HIB	4
6 to 18 mo	Hepatitis B, polio	2
12 to 15 mo	HIB, MMR	4
12 to 18 mo	VAR	1
15 to 18 mo	DaPT	3
4 to 6 years	DaPT, polio, MMR	7

** Abbreviations

DaPT-Diphtheria, tetanus, acellular pertussis.....MMR-Measles, mumps, rubella

HIB-Haemophilus influenza type b.....VAR-Varicella (chicken pox)

MMR Vaccination and Autism

In England, Andrew Wakefield, M.D., a gastroenterologist and his colleagues at the Royal Free Hospital examined with electron microscopy intestinal biopsy samples from children with autism. Their examination revealed the presence of virus particles similar to those from measles virus, raising the possibility that live measles virus from the MMR vaccine may actually be responsible for some of the gastrointestinal abnormalities common in children with autism. Wakefield's original article ⁽⁴⁾ reported:

"Onset of behavioral symptoms was associated, by the parents, with measles, mumps, and rubella vaccination in eight of the 12 children, with measles infection in one child, and otitis media in another. All 12 children had intestinal abnormalities, ranging from lymphoid nodular hyperplasia to aphthoid ulceration. Histology showed patchy chronic inflammation in the colon in 11 children and reactive ileal lymphoid hyperplasia in seven, but no granulomas. Behavioural disorders included autism (nine), disintegrative psychosis (one), and possible post viral or vaccinal encephalitis (two)."

A follow-up study by Wakefield ⁽⁵⁾ on 30 children with autism reported similar results and again reported onset of autistic symptoms following vaccination in a substantial number of the children. Parents of children with abnormalities of the gastrointestinal tract virtually all reported that onset of autistic symptoms almost always occurred **after** vaccination with MMR rather than **before** vaccination. In parents of children who were revaccinated with MMR, additional regression was always **after** rather than **before** the injection.

Wakefield's latest data ⁽⁶⁾ indicates that the nucleic acids of the measles virus are present in biopsies of the lesions from children with autism but not in those of controls. The ultimate proof of Wakefield's hypothesis would be to reverse the gastrointestinal lesions and autism by elimination of the measles virus. Wakefield also states that combining the mumps virus in the MMR greatly increases the probability of adverse reaction to the measles virus in the vaccine.

Based on Wakefield's work, it is reasonable to conclude that any child with autism who complains of gastrointestinal pain, chronic diarrhea, or and/constipation or who reacted adversely to the MMR or other vaccine should receive an endoscopic examination of the intestinal tract to detect damage to the intestinal lining. Similar damage to the intestinal tract has been reported in children with attention deficit hyperactivity ⁽⁷⁾, raising the possibility that an adverse vaccine reaction may be implicated in the cause of attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD).

Dr. Singh at the University of Michigan found that high titers of measles antibodies or antibodies to human herpesvirus-6 in children with autism were associated with high levels of autoantibodies to myelin basic protein and neuron-axon filament protein ⁽⁸⁾. Such autoantibodies might be directly related to the cause of autism since these proteins are involved in the function of nerve cells in the brain. Interferon-gamma is the principal cytokine produced after primary measles immunization ⁽⁹⁾. Furthermore, the results of animal studies ⁽¹⁰⁾ strongly support the hypothesis that IFN-gamma is a key effector molecule in immune-mediated demyelinating disorders and indicate that the presence of this cytokine in the CNS may also disrupt the developing nervous system. Interferon gamma is one of the cytokines present in very high levels in blood serum samples of children with autism ⁽¹¹⁾. The mean value in the group with autism was 30 times that of the control group.

Increased mortality in children in developing nations receiving measles vaccine has been reported to occur six to twelve months after immunization probably due to immune suppression ^(12, 13). The main factor that decreases mortality due to measles infection is not immunization but nutritional status. Death rates due to measles infection in non-immunized middle class children were extremely low in the United States prior to

availability of measles vaccines due to good nutrition ⁽¹⁴⁾. Measles, however, is a significant cause of child death in third world countries with poor nutrition ⁽¹⁴⁾. Vitamin A supplementation markedly reduces the severity of measles infection ⁽¹⁴⁾. Another factor that is able to predict adverse reaction to the MMR vaccine is low titers to the tetanus vaccine ⁽¹⁵⁾. It seems possible that low vitamin A might be one of the reasons for adverse reactions to the measles vaccine in children who later develop autism. Mary Megson M.D. presented data at the 1999 Defeat Autism Now Conference that indicates that children with autism may not be able to absorb the type of vitamin A commonly found in supplements called vitamin A esters (retinyl palmitate and retinyl acetate).

Gupta found high amounts of antibodies to rubella (German measles) in mothers of children with autism ⁽¹⁶⁾. Gupta states that these high amounts of antibodies would be transferred across the placenta and may also persist for a prolonged period in the child. If the infant receives the rubella immunization while antibodies from the mother are still present (which is now more likely because of earlier immunization schedules), the antibodies may react with the rubella virus in the vaccine forming immune complexes that “confuse” the immune system ⁽¹⁶⁾. Dr. Hugh Fudenberg ⁽¹⁷⁾, a clinical immunologist reported that some patients with autism “developed symptoms (of autism) within a week after immunization with the measles, mumps, and rubella (MMR) vaccine.” Dr. Fudenberg also found that some of these children also had extremely high fever or seizures within one day of the vaccine. Reed Warren and his colleagues ⁽¹⁸⁾ think that children with this immune deficiency “may not be able to clear certain viruses completely or before the viruses affect the central nervous system.”

Another mother whose child reacted unfavorably after the MMR writes ⁽¹⁹⁾: “Nicholas has severe mental impairment after having the MMR injection. He has no speech, no understanding of language at all, no concentration, bizarre behavioral problems, and rarely acknowledges anyone. He has become very strong and aggressive. He is having constant tantrums, screaming and flinging himself to the ground and biting anyone who tries to restrain him. He is very frustrated and agitated most of the time... Our son was once a bright, happy, normal child who could speak and love everyone.”

Thus, it is possible that a viral infection (derived from a live vaccine) of the intestine has caused certain of the intestinal cells to malfunction in the production of secretin or peptidases needed to prevent the toxic effects of wheat or milk peptides. Based on many similar case reports, parents who already have a child with autism who reacted adversely to an immunization might wish to consider delaying immunizations for subsequent children to two years or later. Another option would be to consider giving the vaccines separately rather than in the combined form like the MMR. The diseases prevented by these immunizations might also increase the risk of harm to a growing child but this risk is decreased when most other children in the community are immunized. In Japan, the use of the combined MMR has been prohibited since 1993 because of harmful side effects such as meningitis. Children may receive the measles and the rubella vaccine once separately between the age of 1-7 years but must receive the measles vaccine first ⁽²⁰⁾. If the MMR is so safe, why is it not used in Japan? Are the Japanese ignorant and backward people who do not care about their children's health?

Credibility Gap of Health Care Officials on Vaccine Reactions

An article from the Orlando Sentinel ⁽²¹⁾ summarizes the skepticism of parents toward the medical establishment.

“The pertinent characteristic of a bureaucrat, even one with a medical degree, is that his focus is on programs and budgets, not on individuals. Like the good soldier, the bureaucrats have a tendency to defend the program, to minimize or dismiss critics or dissenters. In the case of grant-making, they tend to finance their own prejudices and to deny money to people, no matter how well qualified, who have different ideas. That is

probably why federal medical research, despite billions of dollars spent, has not found a cure for corns or colds, much less for cancer or acquired immune deficiency syndrome. Once the government decides to mandate vaccinations, the bureaucrats will justify it. But you should ask yourself: If the vaccines are so safe, why did the manufacturers seek from Congress a grant of immunity from liability suits?"

Positive Aspects Of Childhood Diseases

Philip Incao M.D., a Denver physician, argues ⁽²²⁾ that the positive benefits of childhood diseases like measles, German measles, mumps, and chicken pox are overlooked. He argues that these childhood diseases have a greater effect in the stimulation of cell-mediated immunity than exposures to the corresponding vaccines. The enhanced immunity from getting these diseases protects the child from serious diseases like asthma, degenerative diseases of the bone and cartilage, and cancer. Dr. Incao implicates the recent asthma epidemic with the increased vaccination for common childhood illnesses; DPT-vaccinated children had five times the risk of asthma as nonvaccinated children. In March of 1995, the Developmental Delay Registry reported that developmentally delayed children were four times more likely to have had an adverse vaccine reaction than normal children ⁽²³⁾.

Hepatitis B Vaccine and Autism

A health official from Missouri, noticing the increase in developmental disorders in the state commented ⁽²¹⁾: "There is only one common thread we can identify with all these children: They are the children who received the first trial of hepatitis B injections as newborns in the early 1990s. Hepatitis B is a viral infection of the liver that is a danger mainly to health care workers who accidentally expose themselves to blood or needles or to drug abusers. The wisdom of requiring all children to be vaccinated prior to school entry has been challenged ⁽²⁴⁾ by the National Vaccine Information Center (NVIC): According to the NVIC, there were 872 serious hepatitis B vaccine-associated adverse events reported to the Vaccine Adverse Event Reporting System in children less than 14 years of age in 1996. In comparison, there were 279 cases of hepatitis B infection in children under the age of 14 in 1996. Thus, the number of vaccine adverse events reported were three times the incidence of hepatitis B in the population that is supposed to be protected. The group calls the government-mandated policy of vaccination of all children against hepatitis B a "dangerous and scientifically unsubstantiated policy."

The case of Jeana Smith ⁽²⁵⁾ is a very revealing one. Jeana is the mother of identical twin boys, Jacob and Jesse. They are alike in every way except that Jacob is autistic while Jesse is completely normal. Jesse is above average in school and has a very engaging personality. They were treated alike in every way except that Jacob, unfortunately, took the hepatitis B vaccine at one month of age while Jesse did not. Shortly after the vaccine Jesse began to develop the frequent ear infections common in the history of children with autism. If autism is purely a genetic disease, then Jacob should have had autism as well. I am convinced that the early hepatitis vaccine altered the normal function of the immune system and triggered the susceptibility to later ear infections.

According to Michael Belkin ⁽²⁶⁾ whose child died 15 hours after receiving the hepatitis vaccine, "almost every newborn US baby is now greeted on its entry into the world by a vaccine injection against a sexually transmitted disease for which the baby is not at risk – because they couldn't get the junkies, prostitutes, homosexuals and promiscuous heterosexuals to take the vaccine. That is the essence of the hepatitis B

universal vaccination program.” Furthermore, Belkin is strongly suspicious of the power of money to corrupt medical policy: “Selling vaccines is extremely profitable and the process of mandating vaccines is fraught with conflicts of interest between vaccine manufacturers, the Advisory Committee on Immunization Practices (an adjunct of the Centers for Disease Control and Prevention) and the American Academy of Pediatrics. The business model of having the government mandate everyone must buy your product is a monopolist’s delight.”

One concern about many vaccines, including the one for hepatitis B ⁽²⁷⁾ is that they are preserved with Thimerosal, a preservative that contains 50% ethyl mercury which is extremely toxic. Thimerosal is effective at preventing bacterial contamination of certain vaccines. It isn’t needed in all vaccines, including those made of live viruses, but it is present in vaccines against hepatitis B, whooping cough, diphtheria, tetanus and bacterial meningitis.

In June 1999, the government notified vaccine experts that if infants younger than 6 months receive a number of thimerosal-containing vaccines during the same doctor’s visit, the thimerosal levels could give small infants a dose of mercury over the limit set by the Environmental Protection Agency. Most vaccines are now available without mercury but many of the same vaccines containing mercury are still available. A website listing the mercury status of vaccines is available at <http://www.immunize.org/news.d/thimtabl.htm>. Recently, the Association of American Physicians and Surgeons urged a moratorium on hepatitis B vaccinations in infants because of studies linking the hepatitis vaccine and 25,000 adverse reactions, including death and neurological diseases such as multiple sclerosis and autism. Bart Classen, a Maryland physician published data showing that diabetes rates rose significantly in New Zealand following a massive hepatitis B vaccine campaign in young children, and that diabetes rates also went up sharply in Finland after three new childhood vaccines were introduced ⁽²⁸⁻³¹⁾. Data from France ⁽³²⁾ links immunization against hepatitis B to the development of autoimmune rheumatoid diseases such as systemic lupus erythematosus and rheumatoid arthritis as well.

DPT Vaccine and Autism

The DPT (Diphtheria, Tetanus, Pertussis) is also one of the vaccines linked with numerous adverse reactions. The book “A Shot in the Dark” ⁽³³⁾ by Harris Coulter and Barbara Fisher documents numerous adverse reactions, particularly with the Pertussis component of the vaccine. The DPT is one of the vaccines commonly reported to me by parents as a trigger in the development of autism. The pertussis part of the vaccine is perceived as the one with greatest potential harm. The following account ⁽³⁴⁾ is from a mother whose child had two adverse reactions to the DPT.

“In late February 96 (at the age of 22 months) Tyler received the first DPT immunization. He began having a reaction within one hour, which included the following symptoms: a high fever, uncontrollable crying for more than 3 hours, limping, and extended episodes of staring. The adverse effects of this vaccine were quite apparent, especially because Tyler was a mobile toddler who had reached many significant developmental milestones (i.e. walking, talking in simple sentences, etc.), whereas an infant may have many of these symptoms go without recognition. It was obvious Tyler’s muscle tone and disposition were strongly influenced in this reaction, and the doctors agreed he should receive no further pertussis vaccinations.

(Four months later), I scheduled well care appointments for both of my children; Tyler was scheduled to receive a DT (Diphtheria and Pertussis), and Katrina a tetramune (Diphtheria, Tetanus, Pertussis and

Hemophilus influenza b (HIB)). An error occurred, and Tyler received a tetramune containing both components (HIB and Pertussis) to which he had a documented history of reactions. Upon realizing the error, the nurse summoned the doctor, who claimed a repeated reaction was highly unlikely. As a preventive measure, they treated him with an anti-allergenic medication and sent us home.

Within one hour Tyler began crying in a high pitch, lost all muscle tone in his lower extremities, experienced labored breathing, episodes of staring, was unable to recognize familiar objects/people, and suffered a grand mal seizure. I immediately phoned Children's Hospital's Emergency Department, which instructed us to call the doctor's office and follow their directions. The pediatrician's office insisted we bring Tyler back into their office for examination; we did. They administered additional anti-allergenic medications and informed us that even though Tyler was having a significant reaction it was not life-threatening.

Later that night he developed a high fever and allergic type rash. Again we phoned the pediatrician's office and they insisted we had no reason for concern. At this point, our only medical knowledge about vaccines was that being provided by the pediatrician's office. Within 48 hours the fever dissipated and Tyler's muscle tone had returned to a somewhat normal level. Tyler had again developed notable facial, eye and hand swelling and was placed on antibiotics.

Tyler was far from the same normal child he was prior to the vaccine. Immediately following the vaccine reaction Tyler developed multiple severe allergies (to foods, chemicals, and environmental factors), autistic behaviors, behavioral problems, dramatic changes in sleeping patterns (from the time of the reaction to present his average daily amount of sleep is 6-7 hours), allergy induced seizures and loss of developmental milestones."

Tyler's symptoms now included hyperactivity, aggressiveness, self-injurious behaviors, repetitive running in place or spinning, rolling repetitively, lethargic appearance, and allergic rashes. When the parents asked the physician for the child's medical records to document their child's reaction to the vaccine, the office staff was unable to locate them. (In Pam Scott's chapter of this book, she documents similar errors in vaccination protocols. Her physician actually altered her child's medical record to cover up the error.)

The Acellular Pertussis Vaccine

Some of the side effects of the pertussis vaccine could be eliminated if a newly developed purified vaccine called the acellular pertussis vaccine was used instead of the ordinary pertussis vaccine ⁽³³⁾. The whole cell or standard pertussis vaccine is produced today in a manner very similar to that of the inventors in 1912. The vaccine consists of pertussis bacteria grown on casein and yeast supplements and preserved with Thimerosal, a mercury derivative. (The use of casein in the preparation of the vaccine might be one reason so many children with autism are sensitive to casein and/or might be responsible for adverse reactions to this vaccine.) The bacteria mixture is washed and the bacteria are killed with heat and formaldehyde. Then this "toxoid" is bottled by itself or with other agents such as tetanus and diphtheria. The effectiveness and toxicity are based on mice testing. The clinical trials upon which the safety of the pertussis vaccine is based were performed mainly on infants older than 14 months. Very few infants in the human safety trial were the age at which this agent is now administered: two months.

Based on a number of adverse reactions, the Japanese developed and tested a cleaner vaccine called the acellular vaccine, which is used throughout Japan beginning in 1981 ⁽³³⁾. The acellular vaccine was much more

effective than the cellular vaccine in inducing immunity and had a much better safety record than the cellular vaccine. Despite these advantages, the United States Food and Drug Administration did not approve the acellular vaccine until 1996. Today, the more toxic cellular vaccine is still widely available in the United States. The acellular combined vaccine is termed DaPT while the older more toxic vaccine is termed DPT. The older more toxic DPT vaccine is cheaper to make and is more profitable than the DaPT. To get the safer, acellular vaccine you simply have to ask for it.

Reporting Vaccine Damage

The National Vaccine Information Center founded in 1982, is the oldest and largest vaccine safety and informed consent rights advocacy organization representing health care consumers and the vaccine injured (33). This organization collects information about harmful effects of vaccines and collects lists of “hot” lots that have been associated with greater damage to children. This center does not administer the vaccine damage fund but can provide you with information about it. Contact the National Vaccine Information Center at (703) 938-0342 or <http://www.909shot.com> if you suspect that your child has had a behavioral change, processing problems, or acquired autistic behaviors after any of their routine vaccinations.

Vaccine Damage Fund in the United States

The vaccine damage fund in the United States that compensates families for harm caused by vaccines has not usually awarded compensation for autism caused by vaccination. The legislation establishing the compensation fund should be amended to include vaccine damage causing autism and other severe diseases. The amendment of this legislation should be a top political priority of the Autism Society of America. By law, people injured by vaccines must apply for compensation before suing drug companies or physicians who administered the shots. Those who lose can sue, but few do. A tax on vaccines, paid by consumers, goes into an award fund, which has grown to a record \$1.3 billion. The fund took in \$160 million last year and paid \$43 million in benefits. Awards average around \$600,000 to \$700,000. Since the vaccine injury compensation program began 10 years ago, about 5,300 claims have been filed and more than 3,200 (or 60 percent), have been rejected. The program has awarded \$900 million to 1,300 families.

Many other cases remain unresolved. Parents, applicants' lawyers and activists who lobbied for compensation say the program, which pits government lawyers against claimants, has turned unnecessarily adversarial and even stingy. They blame poor administration, lack of congressional oversight and modifications that make it harder to win aid. The government is well-armed to argue against parental claims with 17 lawyers and 100 expert witness physicians. The average time for applicants who prevail is three and half years, and newer cases take a year less. Yet nearly 400 applicants have been waiting over seven years for a decision, according to program figures. The Autism Society of America needs to become involved in lobbying to change the way this program is administered so that parents of affected children have a more significant role in making appropriate decisions.

When to Think About Refusing Vaccination

In “A Shot in the Dark”, Coulter and Fisher ⁽³³⁾ argue that the health of the population overall does not suffer if a small percentage of highly vulnerable children are not immunized. They list the following situations in which children are much more likely to have adverse immunization reactions:

- History of seizures or other neurological diseases in the child or other member of the immediate family
- History of severe allergies in the child or immediate family member
- History of allergy to components used in the vaccines such as eggs, gelatin, casein, or thimerosal
- Prematurity or low birth weight
- Chronic illness or a recent severe illness
- A parent or sibling with a vaccine reaction
- Previous severe reaction to a vaccination

Based on reports of parents of children with autism, I would also suggest that children on long-term prophylactic antibiotics or who were recently treated with antibiotics are also at much greater risk of adverse immunization reactions. The role of vaccination in a set of identical twins helps to clarify this issue ⁽³⁶⁾. Mrs. Johnson had identical twin boys, John and Michael. The delivery was normal and both boys received perfect Apgar scores. Both children developed normally until they were 17 months old when they were administered the MMR vaccine. John was on Bactrim® (a sulfa antibiotic) for an ear infection at the time MMR was administered and Michael, who did not have an ear infection and was not on antibiotics. (The Physician Desk Reference ⁽³⁷⁾ states that there is limited data on the safety of Bactrim® in children under 2 years of age and that Bactrim® is not indicated for prophylactic administration in otitis media at any age.) Two hours after the MMR vaccination, John started a high-pitched scream, developed a wide range of gastrointestinal problems, regressed in development and later received the diagnosis of autism. Michael, on the other hand, developed normally.

What Factors to Consider in Delaying or Omitting Vaccination

If your child has any of the significant risk factors listed in the previous section, what are some of the alternatives?

- Consider delaying immunizations until the child is two years old or more. All infants are immunodeficient. In the womb, the mother passed antibodies to the infant through the placenta and at birth, this process ceases. The amounts of all types of antibodies decrease markedly after birth but are near adult values by the age of two years.
- Make sure your child has been on adequate vitamins, especially vitamins A and C before vaccinations of any type. Diphtheria toxin severely depletes vitamin C when injected into guinea pigs, mammals that, like humans, cannot make their own vitamin C ⁽³⁸⁾.
- Do not accept the “dirty” pertussis in the DPT vaccine for your child because the acellular pertussis in the DaPT vaccine is much safer. If your physician refuses to provide it, find another physician.
- If your child has not tolerated cow's milk well, he may be allergic to casein. Since casein is used in the preparation of the pertussis vaccine, he may be at greater risk for this agent. Consider blood tests for casein allergy prior to vaccination.
- Only use mercury-free vaccines for your children. Insist on reading the product insert. Check with your physician concerning which brands they use before your child's vaccine appointment, since mercury containing and mercury free versions of all vaccines are available. Due to parental influence,

children's vaccines in the United States are now supposed to be mercury free as of 2002. Other vaccines, such as flu vaccines, may still contain mercury.

- Prior to your child's vaccine appointment, ask to have your child immunized with single versus combined vaccines and space the vaccines several months apart. Be prepared that physicians may be resistant to this approach. In addition, drug companies are working overtime to discourage this as well because it is less profitable for them to have to produce, distribute, and store different kinds of vaccines.
- If your child has already had an adverse reaction or the number of risk factors is substantial, you may wish to file a religious or philosophical exemption if permitted in your state or to file a lawsuit to be exempt from one or all vaccinations. Only two states, West Virginia and Mississippi, allow no exemptions for vaccines.
- A decision to avoid vaccination of your child is not one to be taken lightly. Your child is more vulnerable to childhood infections such as measles, German measles, mumps, and chicken pox if not vaccinated. In most cases, the symptoms of these diseases are mild but in a minority of cases, they may be severe or even fatal. Diphtheria, pertussis and tetanus are serious life-threatening diseases in almost every case.
- The hepatitis B vaccine has been linked with numerous side-effects that far outnumber the incidence of disease. I would recommend this vaccine only for health care or child care workers exposed to blood or other body fluids, intravenous drug abusers, individuals who are sexually promiscuous people traveling in third world countries, and families of people with these risk factors or who have active hepatitis B. Meanwhile, work with your representatives to rescind state regulations mandating its use in children.
- Work to develop laws that would require long-term safety evaluations (ten years or longer) of all vaccines.
- Testing to determine antibody levels may indicate that the child has adequate immunity and does not need boosters.

Summing Up

Parents who demand that vaccines used for children be both completely safe and effective are not cranks or freaks. Imagine what would happen if the response by the airlines and the government to the TWA and Alaska airline flights that crashed into the ocean had been:

"Oh well! No activity is completely safe. People fall in the bathtub and break their neck every day. There is no evidence of terrorism or mechanical failure. Flying is, after all, a very safe activity in most instances. No further investigation is needed."

Instead the airline, the aircraft company, and the government expended thousands of man-hours, sent divers to the bottom of the ocean, and spent millions of dollars to investigate the crash. The press printed thousands of pages of analysis of the investigation of the causes of the crash.

Children with autism and other developmental disorders and adults with other chronic diseases in the thousands, have crashed in a vaccine program that may be safe for *most people*. It is important that neither bureaucracy, greed, apathy, or denial get in the way of a large-scale investigation into the reasons for this crash.

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Heavy Metals Toxicity

Chapter 8

Dr. William Shaw

Heavy Metals, Especially Mercury, Implicated in Autism and Learning Disabilities

There has been a marked interest in the role of toxic metals in autism and PDD. The potential role of mercury was of special concern because of evidence that the amount of mercury injected into infants and toddlers via childhood vaccinations has exceeded government safety guidelines on both individual and cumulative vaccine doses. Vaccines contain the preservative thimerosal, which is 50% ethyl mercury. Symptoms of mercury poisoning are very similar to those of autism and include stereotypical behaviors, delayed speech, sensory abnormalities, toe walking, self-injurious behaviors, gastrointestinal abnormalities, and cognitive impairments.

What is Mercury?

Mercury is a naturally occurring metal found throughout the environment. Mercury can enter the environment from deposits of ore containing mercury due to wind or rain or from the actions of humans. In addition to mercury from vaccines, other major sources of mercury that contaminate humans are dental fillings, which are about 50% mercury and large fish such as tuna and swordfish. Mercury exists in two major forms, inorganic and organic. Inorganic mercury consists of metallic mercury and inorganic mercury compounds called salts. Metallic mercury is a liquid at room temperature. It is the shiny silver material in thermometers and is commonly combined with silver as an alloy for dental fillings. Mercury is also used in alkaline batteries. Liquid mercury from thermometers can give off vapor if a thermometer breaks which could then be absorbed through the lungs. Organic mercury compounds include methylmercury, ethylmercury, and phenylmercury. Methylmercury is produced from inorganic mercury by microorganisms in the environment and perhaps by the microorganisms in the intestinal tract. Methylmercury is extremely toxic. Exposure to three drops of methylmercury to the gloved hands of a researcher was fatal. Parents of a child with developmental delays and a muscle disorder reported that their child ate salmon or tuna five or six times a week and was found to have high levels of mercury in the hair and blood. Although fish are an excellent source of essential fatty acids, most large fish have significant amounts of methylmercury and the FDA has recommended that women abstain from certain fish during pregnancy. Since methylmercury is fat soluble, it might also contaminate supplements derived from fish oils. In addition, mercury was used as an antifungal agent in paint prior to 1992. Therefore, anyone in an older house needs to be aware that peeling paint or sanding off existing paint could lead to mercury exposure. Mercury in the fillings of pregnant women may be a significant source of exposure to developing infants in utero. Ethyl mercury is the most common preservative found in vaccines, nasal sprays, and eye ointments, and up until ten years ago, has been the preservative agent in contact lens solutions.

Health Effects of Mercury and Recurrent Candida

Mercury is toxic to all tissues and organs. Documented toxicity includes significant effects of mercury on the lungs, heart, gastrointestinal symptoms, blood, muscles, liver, kidneys, skin, thyroid gland, immune system, nerves, and brain. Dental workers exposed to mercury had significantly more reproductive failure than controls including increased abortions, stillbirths, congenital malformations, and menstrual disorders; the extent of abnormalities correlated with mercury levels in the hair. A wide variety of neurological abnormalities are associated with mercury toxicity including muscle tremors, irritability, excessive shyness, nervousness, insomnia, hearing loss, hallucinations, headaches, memory loss, visual field defects, hostility, depression, anxiety, unsteady walking, decreased hand-eye coordination, abnormal reflexes, EEG changes, decreases in intelligence and memory tests, increased aggression, weakness, muscle cramps, and tingling of the hands and feet. The half-life of mercury in the body ranges from 40-80 days. The recurrent Candidiasis that is common in autism may be linked to mercury and/or lead exposure in some cases. Workers exposed to even “safe” levels of mercury were found to have white blood cells with impaired ability to kill Candida. The reason is that mercury and lead inhibit the key white blood cell enzyme myeloperoxidase, an enzyme that produces hypochlorite ion, which is the body’s main defense against Candida.

Other Heavy Metals

Heavy metals may often have combined effects so that exposure to multiple heavy metals at low levels might be just as toxic as exposure to one metal at a high level. Heavy metals found to be elevated in children and adults with autism and PDD include uranium, mercury, cadmium, arsenic, lead, aluminum, and antimony. Many children with autism and PDD have multiple toxic elements in hair or in urine after DMSA challenge. Arsenic is high in seafood such as shrimp and crabs, chicken feed as an additive, pressure treated wood (used in playground equipment and decks), and may be elevated in drinking water. Lead is found in paint in older houses and in soils near freeways exposed to leaded gasoline in the past. Antimony is found in some of the flame-retardants in children’s pajamas and in carpet. Aluminum is common in cookware, baking powder, drinking water, and cans. Cadmium is high in cigarette smoke and may also be released from particles of steel belted tires. Uranium may occur naturally in rock or may enter the environment as a contaminant from the arms industry, which uses uranium in bullets and shells because of its extreme hardness. (All forms of uranium are radioactive.)

Treatments of Mercury Toxicity

Chelation therapy is the preferred method for removal of mercury and many other heavy metals. Chelation agents bind to heavy metals in the blood or tissues. Then the metal-chelation agent complexes are eliminated in the urine or stool. Chelation agents which are prescription drugs include British Anti-Lewisite (BAL), D-penicillamine, dimercaptopropane-1-sulfonate (DMPS), ethylenediamine tetraacetic acid (EDTA) and CHEMET, a trade name for 2,3-dimercaptosuccinic acid (DMSA). DMSA appears to be the most effective agent of the group with the fewest side effects. Nutritional supplements that may aid in mercury elimination and/or reduce toxic effects include N-acetylcysteine, selenium, lipoic acid, vitamin E, cilantro, vitamin C, milk thistle, glycine, garlic, and peptidyl chelating products, among others. In addition, mercury and other heavy metals may be removed by sauna treatment, which increases the excretion of mercury in the sweat.

How to Decide Which Test is Most Appropriate for Metals Testing

Hair Analysis is considered by many to be the best, the easiest, and the most cost-effective way to screen for heavy metal toxicity. Heavy metals, such as mercury, may be 250 times higher in the hair than in the blood. It is important to note that mercury toxicity will only show up in the hair if the exposure has been recent.

Some individuals consider a DMSA (Chemet) challenge test to be an even more sensitive screen for metal toxicity than hair because the drug DMSA is able to bind heavy metals deposited in tissues in the body whereas such metals might not be detected by hair tests. (This is true with mercury, when the exposure has not been recent.) The difficulties associated with urine DMSA testing are:

- First, DMSA is a drug that must be prescribed by a physician. However, some nutritional supplement companies may also sell it as a nutritional supplement.
- Some physicians may be reluctant to prescribe it unless they have used DMSA previously.
- Second, numerous side effects can be caused by DMSA. Although the short exposure of the person being tested by DMSA is unlikely to cause significant long-term side effects, such side effects are still possible.

Urine metal testing without DMSA is generally considered less sensitive than hair metal testing or urine metal testing with a DMSA “challenge.” Since the metal issue may be very important, a person might want to get both a baseline and a post-challenge urine test done.

If the patient goes on DMSA therapy because of abnormal metal results, the patient should get a weekly complete blood count with white cell differential and platelet estimation. Many physicians, who follow a slower chelation protocol, prescribing lower doses spread over a longer period of time, recommend blood testing only every 2-3 months.

Blood testing is considered the least sensitive but most significant indicator of toxicity of metals. Low metal levels in blood do not rule out metal toxicity. High metal values in blood almost always indicate a clinically significant and often recent toxic exposure.

Side Effects of DMSA

The Physicians Desk Reference lists a number of side effects associated with DMSA usage. The side effects affect between 1-20% of the individuals. It might be expected that a single dose of DMSA would cause fewer side effects than a long-term treatment with DMSA. Common side effects include:

- Gastrointestinal side effects include nausea, vomiting, stomach pain, and abdominal pain and diarrhea.
- Hematological (blood) side effects include neutropenia, eosinophilia, and increased platelets.
- Temporary regression of autistic symptoms as the metals are being “stirred up.”
- Elevated liver enzymes and other side effects including drowsiness, dizziness, sleepiness, rash, decreased urination, cardiac arrhythmia, leg and knee pain, and flu-like symptoms.

Treatment for Heavy Metal Toxicity

If the challenge test or hair analysis shows toxicity, then a treatment plan needs to be implemented. The most important aspect of the treatment plan is the removal of any current source of heavy metal poisoning. If the child's house is contaminated with lead or mercury-based paint, the parents may have to move or have the lead removed from the house. If the child is chewing on pajamas containing antimony-containing flame-retardant, they may have to be replaced. If the child has significant mercury from vaccines containing the mercury compound thimerosal, non-mercury vaccines should be used in the future. Fish intake may have to be eliminated or reduced. If the water supply is high in uranium or arsenic, then bottled distilled, deionized, or reverse osmosis water should be used.

DMSA Treatment

The next step is the use of agents to remove toxic metals. The most commonly used agent is DMSA. Despite some side-effects, DMSA is considered the safest agent and is available without a prescription. Supplementation with beneficial minerals such as calcium, magnesium, selenium and zinc is very important since these minerals may compete with toxic metals being depleted during the chelation process. DMSA is effective in removing many heavy metals such as lead, mercury, cadmium, arsenic, and antimony but is not effective in the removal of aluminum. Chelation can take from 1 – 2 years, with younger children successfully chelating more quickly. In addition, certain nutritional supplements have also been used for the removal of heavy metals although safety and efficacy studies frequently are lacking. As with all treatments, it is advised to always proceed cautiously, do your research, and engage the help of a qualified and experienced physician.

Lipoic Acid

The vitamin lipoic acid (also referred to as alpha lipoic acid or ALA) has two sulfhydryl groups that readily bind to mercury and result in its elimination. However, concerns have been raised that lipoic acid might also transfer heavy metals from the peripheral tissues to the brain so it might be wise to limit lipoic acid until DMSA chelation has been completed and the bulk of toxic metals have been removed. Lipoic acid is available in any health food store.

Tests Available From The Great Plains Laboratory

- All tests are performed using ICP-mass spectrometry, the most advanced analytical method available
- Hair, blood, and urine tests are all available. Hair testing is prohibited in New York State probably because of excessive claims of promoters of such testing in claiming uses beyond determination of exposure to heavy metals.

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Inborn Errors of Metabolism as Causes of Autism

Chapter 9

Dr. William Shaw

Abnormal Purine and Pyrimidine Metabolism in Autism: New Tests and Treatments for People with Unique Subtypes of Autism and PDD

Ted Page Ph.D. and Mary Coleman M.D. have established that abnormalities of purine and pyrimidine metabolism are common in children with autism and PDD. Although these abnormalities began to be reported over 30 years ago, progress has been hampered because only a very small number of research laboratories performed this kind of testing and only on a very sporadic basis. The children with these genetic diseases have many or all of the classic diseases of autism and therefore cannot easily be distinguished from “typical” children with autism. A critical finding of Drs. Page and Coleman is that two major subtypes of this disorder can be distinguished by a simple clinical test of urine, which is the content of uric acid in the urine.

Purines and pyrimidines are the building blocks or bases of nucleic acids DNA and RNA, which carry the genetic code for all living creatures. Purines and pyrimidines can be attached to a sugar, forming compounds called nucleosides. Compounds called nucleosides can have one or more phosphate groups attached to them, making them compounds called nucleotides. The names of these different compounds are given below:

Base	Nucleoside	Nucleotide
Uracil	Uridine	Uridylic acid
Thymine	Thymidine	Thymidylic acid
Cytosine	Cytidine	Cytidylic acid
Adenine	Adenosine	Adenylic acid
Guanine	Guanosine	Guanylic acid

Dihydropyrimidine Dehydrogenase Deficiency

I became interested in the role of these compounds after noticing that a significant number of children with autism had high amounts of the compound uracil in the urine tested with the organic acid test in our laboratory. The upper limit of normal is 22 mmol/mol creatinine but we found that one child with autism had a value of 360 mmol/mol creatinine and perhaps 15% of all children with autism had elevated values to a lesser degree. This was a very interesting finding since there is an inborn error of metabolism called dihydropyrimidine dehydrogenase deficiency in which both uracil and thymine are elevated in the urine. Some of the individuals

with this disorder had autistic symptoms. However, the individuals tested by The Great Plains Laboratory, with the abnormal uracil levels, invariably had normal or very slightly elevated values for thymine in the urine. As a result, I assumed that they did not have dihydropyrimidine dehydrogenase deficiency. However, Ted Page suggested to me that these individuals might have a form of enzyme deficiency in which thymine could be processed by the enzyme but uracil could not.

Low Urine Uric Acid and Elevated Nucleotidase in Autism

A Subtype of Autism That Responds to Dietary Pyrimidine Supplementation

In the 1990's Ted Page and his associate reported a biochemical abnormality in a group of patients with low urine uric acid. The syndrome is also associated with elevated levels of an enzyme that breaks down nucleotides called nucleotidase in the cells of skin samples. The symptoms of the patients included developmental delay, seizures, impaired fine motor control, distractibility, hyperactivity, abnormal social interaction, speech deficit, immune deficiency, and frequent infections. Treatment with pyrimidine nucleotides or nucleosides resulted in a marked improvement in symptoms in a double-blind placebo trial. The sugar ribose which combines with pyrimidines to form nucleosides was also therapeutically beneficial but to a degree lesser than the nucleosides. The exact frequency of this disorder is unknown since only a small number of children with autism have been tested for this abnormality.

High Uric Acid and Autism

A Subtype of Autism That Responds to Dietary Restriction of Purines and/or Allopurinol

Ted Page and Mary Coleman reported that there is a group of patients with autism (perhaps as high as 20% of all people with autism) with high amounts of uric acid in the urine with symptoms including: lack of interest in social contact, impaired communication, stereotypical behavior consisting of repetitive motions, toe-walking, hand-flapping, increased auditory sensitivity, self-injurious behavior, and decreased sensitivity to pain. Of the 9 patients studied with this subtype, 6 of them had seizure activity as well. Treatment with the drug allopurinol or a diet low in purines (that form uric acid) reduces symptoms. Ted Page reported at an autism conference in St. Louis in 2001 that the use of the nucleotide uridine was also effective in this subtype of autism. The cause for this increase in uric acid is unknown but is probably due to a defect in the interconversion of purine compounds. The standard test for elevated uric acid in blood serum may not be abnormal in this disorder so the urine test is preferred.

Abnormal Succinylpurines and Autism

Researchers in Belgium first reported the presence of a genetic abnormality implicated as a probable cause of autism. Furthermore, they stated that this abnormality might not be rare (1). However, this abnormality is almost never tested in children with autism, even in those who undergo extensive biochemical testing at the time of initial evaluation. The biochemical reactions that result in the elevated succinylpurines (adenylosuccinate and succinylaminoimidazole carboxamide) are indicated on the next page.

The case reports indicate that these three children with autism are not significantly different than many other children with autism. A description of symptoms in the children is useful:

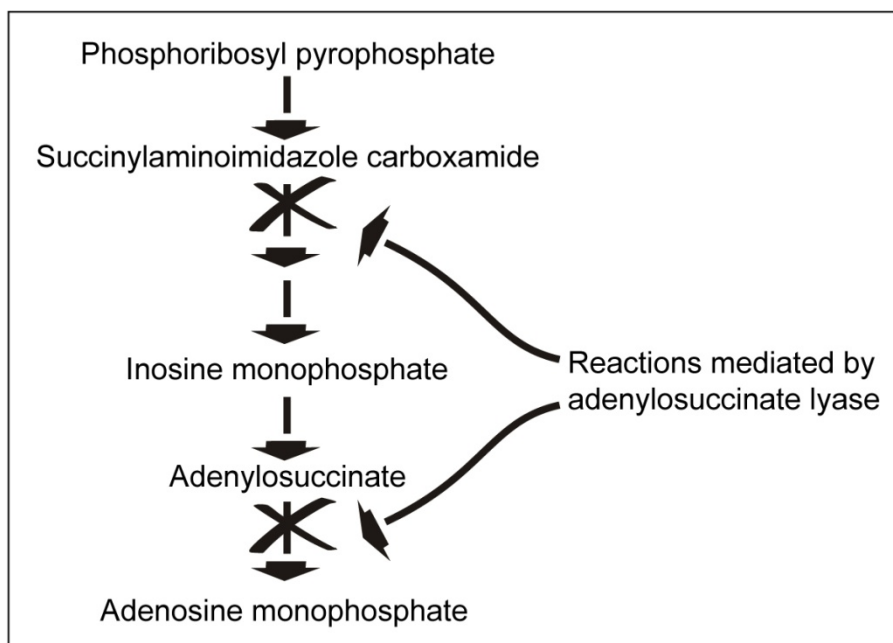
Child one: The first girl evaluated had low muscle tone, a symptom prevalent in almost all children with autism. She had impaired development and motor skills. She had no readily apparent physical abnormalities. She would not maintain eye contact and she spent hours repetitively manipulating toys and grimacing. She cried incessantly and ground her teeth and bit herself. She was found to have striking autistic symptoms. Interestingly, a brain scan (CT) detected an underdeveloped cerebellum, an abnormality that has been reported, by Eric Corchesne, to be present in many individuals with autism.

Child two: The second patient was a boy who had impaired development and motor skills and the parents both noticed autistic behaviors when the child was a few months old. The child still had no speech at 3 years 8 months, lacked eye contact, and spent hours handling the same object and laughing to himself. He had tantrums without cause and spent excessive time with eye stimming and hand clapping. Like the first child, he also had a significantly underdeveloped cerebellum determined by a brain scan.

Child three. The third child was the sister of child two. She had the same autistic features as her brother and a brain scan also detected an underdeveloped cerebellum.

All three of the children had markedly elevated amounts of incompletely made purine compounds called succinylpurines in their urine samples, which include adenylosuccinate and succinylaminoimidazole carboxamide. Children with this disorder have markedly low amounts of the enzyme adenylosuccinate lyase in certain tissues of the body but normal amounts in other tissues. Purines are necessary for virtually all living creatures from viruses to whales so an inability to produce purines is a significant biochemical abnormality. Ted Page reported at a conference in St Louis that supplementation with nucleosides or ribose appears to be effective in the treatment of this disorder as well. Such compounds are available throughout the world. Nucleotides are essential for the production of RNA, which is needed for the production of all proteins and they have many other functions as well.

Biochemical Pathways Blocked in Succinylpurine Excess Subtype of Autism



Testing

- The standard organic acid test from The Great Plains Laboratory includes testing for uracil and thymine. Although there is no current treatment, new DNA biotechnology might be available as a treatment in the future.
- Uric acid in urine will be available as a screening test at The Great Plains Laboratory using the enzymatic uricase method using first morning urine. To get the most accurate screening for high uric acid autism and low uric acid autism, a 24-hour urine collection is necessary.

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Frequently Asked Questions

Chapter 10

Dr. William Shaw

Do I have to get a physician's approval to get blood, urine, hair, or stool sample tested?

Yes. A medical practitioner who is licensed to order urine testing in your state must approve the test order. Regulations vary from state to state so an approved medical practitioner could be a medical doctor (M.D.), osteopath (D.O.), nurse practitioner, chiropractor (D.C.), or naturopath (N.D.).

How often should I get my child re-tested?

As a general rule, every three to six months may be satisfactory for organic acid testing. However, I recommend retesting be done sooner if the child does not respond favorably by the end of one month of antifungal therapy since the yeast or bacteria might be resistant to the drugs used for treatment.

Allergies might be checked every year or so since they may change with altered diets. The immune deficiency test probably does not need to be rechecked if normal. It might be useful to recheck in a year or so if there are significant abnormalities of the immune system.

Heavy metals should be rechecked during removal of metals to monitor therapy until normal values are obtained.

My physician says everyone has some yeast in his or her intestine. Why isn't everyone sick?

The most important question is not whether yeast are present or not. The critical factors are the **quantity** of yeast and the **kinds and amounts of toxic products** they produce. Everyone in this society has carbon monoxide in his or her blood from auto exhaust and secondhand cigarette smoke and can tolerate a **low** value. When the amount of carbon monoxide increases, some individuals feel depressed, some have headaches, some develop muscle weakness, some feel tightness in the chest or angina, some experience nausea and vomiting, some become dizzy, some develop dimming of vision. As values further increase, symptoms may include convulsions, coma, respiratory failure, and death. Some individuals who recover from severe carbon monoxide poisoning may suffer residual neurological damage. Different people will respond with different symptoms to the same concentration of carbon monoxide.

Why is it surprising that exposure to a wide range of toxic yeast products at different times and at different ages might produce different symptoms?

If I suggested that there were a carbon monoxide connection with all of the diverse symptoms associated with carbon monoxide exposure, no one would challenge me. The reason that the carbon monoxide connection is accepted is because carbon monoxide can be easily measured in blood. The toxic yeast byproducts were only recently discovered. As knowledge of them increases, acceptance of the yeast-related illnesses will increase.

My child is currently taking antibiotics now. Should I wait until after the antibiotics until I get the organic acid test or stool tests for yeast?

Many have assumed that if the child has a significant yeast overgrowth of the intestine while on antibiotics that the yeast overgrowth will disappear when the antibiotics are stopped. However, this is not necessarily the case and the yeast overgrowth may even become worse especially if the person is on a high sugar, high carbohydrate diet. There is no evidence that the yeast overgrowth will spontaneously disappear on its own. Furthermore, the yeast overgrowth may be suppressing the immune system, preventing your child from recovering from the infection. The sooner the yeast problem is controlled, the sooner the vicious cycle of antibiotics and frequent infections may be broken.

Why should I get the organic acid test? Why don't I just start the nystatin or other antifungal treatment?

Some children with autism don't have the yeast problem but may have an overgrowth of the Clostridia bacteria. Treating these children with an antifungal could make the bacteria problem even worse. Also, if your child has the yeast problem, he will likely require major changes in his diet (and that of your family) and drug therapy for six months or longer. I think that it will be very difficult to make a commitment to the diet and drug therapy if you are not even sure if your child has the yeast problem. Your child could have a yeast overgrowth with drug-resistant yeast and if you don't do the testing beforehand, it would be difficult to know what is happening. Also, if the problem is severe, the yeast die-off reaction may be more severe and you may want to take additional steps to control the yeast before using antifungals. And it may be very difficult to get your doctor's cooperation for the prescriptions and insurance reimbursement if there is no evidence that the yeast problem even exists.

Where can I get the organic acid test done?

The organic acid test is available from:

The Great Plains Laboratory
11813 W 77th St.
Lenexa, KS 66214

Phone: 913 341-8949
E-mail: GPL4U@aol.com

What other information will I get from the organic acid test?

The test evaluates all of the well-defined inborn errors of metabolism that can be detected with this technology called GC/MS such as PKU, maple-syrup urine disease, and many others. In addition, the organic acid test checks for many other abnormalities such as vitamin deficiencies and abnormal metabolism of catecholamines, dopamine, and serotonin. We currently quantitate 66 substances but also evaluate other substances that are not quantitated. Some of the other biochemical abnormalities common in autism include elevated uracil and elevated glutaric acid.

I already had the urine organic acids test done earlier by another lab. Can't I get the information from the earlier test?

No. No other laboratory routinely analyzes the same compounds as this laboratory. Most test for the inborn errors of metabolism and that's all.

I have an HMO and they have to send the organic acids test to a certain lab. Is that OK?

No. No other laboratory routinely analyzes the same compounds as this laboratory including Labcorp, SmithKline, or Mayo Medical laboratories. If you do not specify our laboratory, your child's urine will be sent to one of the large reference labs, which cannot accurately evaluate your child's condition. Most test for some of the inborn errors of metabolism and that's all.

Do most insurance companies reimburse for your tests?

Yes, but we cannot guarantee how much (if any) reimbursement will be given. Many health care plans also require a preauthorization. Most HMO's will pay but you may need some additional documentation to get payment. Use the information in this book to indicate to your HMO why no other labs are acceptable.

What about reimbursement for Medicaid and Medicare?

The Great Plains Laboratory is now set up for Medicare but does not accept Medicaid.

Can I test my infant who is having frequent ear infections or other frequent infections and who now seems "spacey" to see if they are developing the abnormal yeast byproducts?

Yes. The Great Plains Laboratory provides tape-on bags to collect the urine from infants or children who are not potty trained.

My child has a large number of food allergies. Could this be related to the yeast problem? When should I get food allergies tested?

Yeast can exist in two forms: a floating single cell form or a colony form. When yeast form colonies, they secrete enzymes such as phospholipase and proteases that break down the lining of the intestinal tract in order to attach the yeast colony to the intestinal wall. The holes made by the yeast produce a condition called leaky gut syndrome in which large undigested food molecules are absorbed into the bloodstream and elicit food allergies. Once the underlying yeast problem is controlled, the holes in the intestine will heal. Then less undigested food gets into the blood and the number of food allergies will decrease. I recommend that the allergy testing be done three months after the yeast problem is controlled so that you will have fewer allergies to deal with and therefore fewer foods to restrict from the diet. The yeast control diets are already complicated enough without further dietary restrictions and/or allergy desensitization shots.

Where can I get the food allergy test done?

The food allergy test, which is a blood test, is available from:

The Great Plains Laboratory
11813 W 77th St.
Lenexa, KS 66214
Phone: 913 341-8949
Fax: 913 341-6207
E-mail: GPL4U@aol.com
Website: www.greatplainslaboratory.com

Do the food allergy tests at The Great Plains Laboratory check for wheat and dairy sensitivity?

Yes, both the basic and comprehensive food allergy tests check for wheat and dairy sensitivity. We have found that children with autism have increased amounts of IgG antibodies to both wheat and dairy.

Do I need to do both food allergy tests on blood as well as the urine peptide test?

Most children with autism have both elevated IgG antibodies to gluten and casein as well as elevated peptides in the urine. If the allergy test is positive, it is not essential to do the peptide test also. However, if the allergy tests for wheat and dairy were negative, it would be a good idea to do the peptide test.

How does the gluten/casein sensitivity common in autism and other diseases relate to the yeast problem or are they separate issues?

There does appear to be some relationship between the two medical problems. Gluten and casein are proteins. Gluten is one of the major proteins in wheat. Casein is the major protein in milk and cheese but is an additive in a wide variety of other foods such as soup and TV dinners. If these proteins are absorbed before being completely digested, the undigested pieces of protein enter the brain and attach to opiate receptors in the areas of the brain controlling language and other areas of the brain and impair the brain function. These pieces of protein called peptides are eventually eliminated in the urine where they are measured.

The test is called the urinary peptide test. I suspect there would be less of a problem with these molecules if the yeast is controlled and am working to obtain a grant to test this hypothesis. In the meanwhile, I advise you to do the gluten/casein urinary peptide test three months after the yeast have been controlled. The elimination of these foods is a difficult process and I would advise doing the urinary peptide test before implementing the diet. I think that you will be more highly motivated to implement the diet if you know there is a definite problem that cannot be controlled by other means.

Where can I get the urinary peptide test done?

The Great Plains Laboratory
11813 W 77th St.
Lenexa, KS 66214
Phone: 913 341-8949
Fax: 913 341-6207
E-mail: GPL4U@aol.com
Website: www.greatplainslaboratory.com

Will drugs or any of these nutritional supplements interfere in the organic acid test?

No, there is no interference from any known drug or supplement since the technology of mass spectrometry is the most accurate technology available. If your child takes vitamin supplements like vitamin C, then high concentrations of vitamin C will be detected in the urine. However, if antifungal supplements or drugs are taken before the test, you will probably get a lower value for the yeast byproducts. I advise you to get the test first so that you will know what the starting point is.

Will the use of nystatin interact adversely with other medications the patient is taking?

Nystatin is not absorbed from the intestinal tract in any appreciable quantity unless extremely large doses are used. Therefore, there are no adverse reactions with drugs such as antiseizure medications, antidepressants such as Prozac or Elavil, or any other medications. If you use antifungals that are absorbed from the intestinal tract such as Lamisil, Sporanox, Diflucan, and Nizoral, then drug interactions must always be considered. Other drugs used simultaneously may be more potent or make the antifungal more potent when these latter drugs are used.

Could there be adverse reactions to the food colors and flavors in the nystatin?

Yes, that is a possibility. If that is the case, then you may have to use the pure nystatin powder and disguise it in food. One way to disguise it might be to combine it with the herbal sweetener Stevia. Stevia is available in most large health food stores. A good compounding pharmacy in your area is helpful since they can often mix Nystatin into a suspension using Stevia and hypoallergenic flavoring.

My child has a yeast infection in the genital or anal area. Does this indicate a yeast overgrowth of the intestinal tract?

Yes, but it is impossible to know for sure without testing to confirm it.

If my child has no external signs of yeast such as thrush, or anal or genital rashes, could he still have the yeast problem?

Yes, in many cases the behavioral abnormality is the only clue to the underlying yeast overgrowth of the intestinal tract.

Could intermittent low-grade fever be a symptom of yeast infection?

Fever often accompanies yeast infection of the blood stream, which is termed systemic yeast infection. To test for yeast in the blood, you need to have a yeast culture and/or yeast antibody tests on blood. Remember that these tests may give a high percentage of false negative results. Your child may also have an intestinal yeast overgrowth as well.

My insurance company won't reimburse for any lab test dealing with autism. What can I do?

Many different diagnoses that accurately describe the medical condition of your child can be used for insurance reimbursement and many times reimbursement can be obtained when an appropriate diagnosis is used.

My child has a white coating of the mouth. Could this be a yeast problem?

Yes. One of the most common yeasts in the intestine is *Candida albicans*. *Albicans* is a Latin word for white and a white coating of the tongue may very well be *Candida*.

What foods have *Lactobacillus acidophilus* in them?

Yogurt is high in *Lactobacillus acidophilus*. The unflavored kind or plain is more highly recommended than the flavored because yeast may grow in the kind with fruit on the bottom. Some milk now also has acidophilus added. Just read the labels. However, most children with autism are sensitive to casein so the use of these sources may not be wise.

What kind of changes might I expect with the antifungal drug therapy?

Results are highly variable but the most usual improvement noted is increased focus and concentration. Other improvements may include increased and clearer vocalization, less stimming, decrease in aggressive or self-abusive behavior like head-banging, better sleep pattern, increased socialization, and more eye contact. Antifungal therapy may help individuals with normal or marginally elevated yeast metabolites but the percentage of those benefiting is lower than in individuals with high concentrations of these metabolites. Antifungal therapy is not usually a cure for autism by itself but may significantly improve the life of the child and his family. Antifungal therapy combined with other measures such as gluten and casein restriction, elimination of food allergies, and behavioral therapies have been successful in reversing autism in two cases in which these therapies were started at a very young age. Their accounts are included later in this book. Both of these successful families adopted very similar therapies completely independently of one another and started treatment about two years of age. Only large long-term studies will determine if these successes can be translated into successful therapies for the majority of children with autism.

What side-effects may be associated with the use of Flagyl or oral Vancomycin to control the overgrowth of *Clostridia* in the intestinal tract?

The main side effects of this drug are probably due to the release of bacterial toxins as the *Clostridia* and other bacteria die. Side effects may be very severe and usually last from 2-10 days. *The child should be under close medical supervision while on this drug.* Side effects may include severe diarrhea, heart palpitations, extreme lethargy, and fever with drenching sweats. Talk to your physician about the use of adsorbent materials such as Bentonite or charcoal (available in pharmacies and health food stores) to adsorb the toxins since they may decrease the die-off reaction. The child should not start both the Flagyl/Vancomycin and antifungal therapy simultaneously because the combined die-off reaction may be too severe. Both Flagyl and Vancomycin will kill the friendly bacteria and it is very important to start *Lactobacillus acidophilus* as soon as the Flagyl/Vancomycin therapy stops or there may be a recurrence of the *Clostridia* or a yeast overgrowth. It is OK to continue nystatin during Flagyl/Vancomycin therapy. Just don't start the antifungal and antibacterial therapies simultaneously.

My child has urinary tract infections or a vaginal yeast infection. Could the microorganisms in the urinary tract affect the test results?

Microorganisms might contaminate the sample and lead to erroneous results if the urine stands too long at room temperature. We suggest that you freeze the sample right away to minimize any effects of such contamination since no new metabolites will form while frozen.

My child only eats bread, dairy products, cereal or pasta. How can I change his diet without starving my child?

Parents have reported to me that their children may refuse the altered diet for three or four days and then give in and eat the new foods. I think that it would be wise to consult your physician and/or a dietitian before starting the diet. I do not think a **short** time without eating is harmful to most children but might be significant if your child has special medical problems like diabetes. Some children have not adjusted well to the gluten/casein free diet and may have to go back to gluten or casein containing foods because of substantial weight loss on the restricted diets.

How long will my child need to be on the antifungal therapy?

This is a difficult question that will only be answered by future research. I have personal knowledge that many children helped by antifungal therapy regress following the discontinuation of therapy even after six months to five years of antifungal treatment. This regression is virtually always accompanied by an increase in abnormal yeast metabolites. Discovering a way to overcome this resistance should be a national priority for future research. I recommend a minimum of nine months of antifungal treatment for children with autism/PDD if the intestinal yeast overgrowth is significant.

The Use of Vitamin B6, Magnesium, and DMG in the Treatment of Children and Adults with Autism

Chapter 11

Dr. Bernard Rimland

The following information is condensed from articles appearing in the Autism Research Review International, the newsletter of the Autism Research Institute. The original articles, including summaries of and literature references to the 18 studies of vitamin B6 in autism, as well as to other studies referred to below, are available on request from the Autism Research Institute, 4182 Adams Avenue, San Diego, CA 92116.

Vitamin B6 (and Magnesium) in the Treatment of Autism

From the Autism Research Review International, Volume 1, No. 4:

All 18 studies known to me in which vitamin B6 has been evaluated as a treatment for autism have provided positive results, and no significant adverse effects have been reported in any of the studies. This is a rather remarkable record of efficacy and safety, since the many drugs that have been evaluated as treatments for autism have produced very inconsistent results; and all drugs pose a risk of serious side effects. If a drug shows positive results in about half of the evaluation studies, it is considered a success and the drug is then advocated for use with autistic patients. However, despite the remarkably consistent findings in the research on the use of vitamin B6 in the treatment of autism, and despite its being immeasurably safer than any of the drugs used for children with autism, there are at present few practitioners who use it or advocate its use in the treatment of autism. The reasons are obvious: most physicians know little about vitamins and have no economic incentive to recommend a substance that does not require a physician's prescription.

Research on the use of vitamin B6 with children with autism began in the 1960s. In 1966 two British neurologists, A. F. Heeley and G. E. Roberts, reported that 11 of 19 children with autism excreted abnormal metabolites in their urine when given a tryptophan load test. Giving these children a single 30 mg tablet of vitamin B6 normalized their urine; however, no behavioral studies were done. A German investigator, V. E. Bonisch, reported in 1968 that 12 of 16 children with autism had shown considerable behavioral improvement when given high dosage levels (100 mg to 600 mg per day) of vitamin B6. Three of Bonisch's patients spoke for the first time after the vitamin B6 was administered in this open clinical trial.

After my book *Infantile Autism* was published in 1964, I began receiving hundreds of letters from parents of children with autism throughout the United States, including a number who had tried the then-new idea of "megavitamin therapy" on their children with autism. Most had begun experimenting with various vitamins on their children with autism as a result of reading books by popular nutrition writers. I initially was quite skeptical about the remarkable improvement being reported by some of these parents, but as the evidence

accumulated, my interest was aroused. A questionnaire sent to the 1,000 parents then on my mailing list revealed that 57 had experimented with large doses of vitamins. Many of these had seen positive results in their children. Intensive study of the medical literature convinced me the vitamins were safe. As a result, I undertook a large-scale study, on over 200 children with autism, of megadose quantities of vitamin B6, niacinamide, pantothenic acid, and vitamin C, along with a multiple-vitamin tablet especially designed for the study. The children were living with their parents throughout the U.S. and Canada. We required that each child be medically supervised by the family's own physician. (Over 600 parents had volunteered for the study, but most could not overcome their physicians' skepticism.)

At the end of the four-month trial it was clear that vitamin B6 was the most important of the four vitamins we had investigated, and that in some cases it brought about remarkable improvement. Between 30% and 40% of the children showed significant improvement when the vitamin B6 was given to them. A few of the children showed minor side effects (irritability, sound sensitivity and bed-wetting), but these quickly cleared up when additional magnesium was supplied. The magnesium not only eliminated the side effects, it often brought about even more improvement in speech and behavior.

Two years later two colleagues and I initiated a second experimental study of the use of megavitamin therapy on children with autism, this time concentrating on vitamin B6 and magnesium. My co-investigators were Professors Enoch Callaway of the University of California Medical Center at San Francisco and Pierre Dreyfus of the University of California Medical Center at Davis. The double-blind placebo-controlled crossover experiment utilized 16 children with autism, and again produced statistically significant results. For most children dosage levels of B6 ranged between 300 mg and 500 mg per day. Several hundred mg/day of magnesium and a multiple-B tablet were also given, to guard against the possibility of B6-induced deficiencies of these other nutrients.

In both studies the children showed a remarkably wide range of benefits from the vitamin B6. There was better eye contact, less self-stimulatory behavior, more interest in the world around them, fewer tantrums, more speech, and in general the children became more normal, although they were not completely cured.

People vary enormously in their need for B6. The children who showed improvement under B6 improved because they needed extra B6. Autism is thus in many cases a vitamin B6 dependency syndrome.

After completing his participation in our study, Professor Callaway visited France, where he persuaded Professor Gilbert LeLord and his colleagues to undertake additional B6/magnesium research on children with autism. The French researchers, although skeptical that anything as innocuous as a vitamin could influence a disorder as profound as autism, became believers after their first, reluctantly undertaken, experiment on 44 hospitalized children. They have since published a number of additional studies evaluating the use of vitamin B6, with and without additional magnesium, on children with autism and adults. Their studies typically used as much as a gram a day of vitamin B6 and half a gram of magnesium.

LeLord and his colleagues measured not only the behavior of the children with autism, but also their excretion of homovanillic acid (HVA) and other metabolites in the urine. Additionally, they have done several studies in which the effects of the vitamin B6 and/or the magnesium on the brain electrical activity of the patients was analyzed. All of these studies have produced positive results.

LeLord et al. recently summarized their results on 91 patients: 14% improved markedly, 33% improved, 42% showed no improvement, and 11% worsened. They noted that "in all our studies, no side effects were observed." Presumably, no physical side effects were seen.

Several studies by two groups of U.S. investigators, Thomas Gualtieri et al., at the University of North Carolina, and George Ellman et al., at Sonoma State Hospital in California, have also shown positive results on autistic patients.

While no patient has been cured with the vitamin B6 and magnesium treatment, there have been many instances where remarkable improvement has been achieved. In one such case an 18-year-old autistic patient was about to be evicted from the third mental hospital in his city. Even massive amounts of drugs had no effect on him, and he was considered too violent and assaultative to be kept in the hospital. The psychiatrist tried the B6/magnesium approach as a last resort. The young man calmed down very quickly. The psychiatrist reported at a meeting that she had recently visited the family and had found the young man to now be a pleasant and easy-going young autistic person who sang and played his guitar for her.

Another example: a frantic mother phoned me to ask for information on sheltered workshops in her city, since her 25-year-old autistic son was about to be expelled for unmanageable behavior. I knew of no alternate placements for the son, but I suggested that the mother try Super Nu-Thera, a supplement containing B6, magnesium and other nutrients. Within a few weeks she called again to tell me excitedly that her son was doing very well now and his piecework pay had risen dramatically from the minimum pay of \$1.50 per week to \$25 per week.

In view of the consistent findings showing the safety and efficacy of the nutrients B6 and magnesium in treating autistic individuals, and in view of the inevitability of short and/or long-term side effects of drug use, it certainly seems that this safe and rational approach should be tried before drugs are employed.

Vitamin B6 in Autism: The Safety Issue

From the Autism Research Review International, Volume 10, No. 3:

There is no biological treatment for autism which is more strongly supported in the scientific literature than the use of high dosage vitamin B6 (preferably given along with normal supplements of magnesium). Eighteen studies have been published since 1965, showing conclusively that high dose vitamin B6 confers many benefits to about half of all the children with autism and adults on whom it has been tried. While B6/magnesium is not a cure, it has often made a big, worthwhile difference.

Included among the 18 studies are 11 double-blind, placebo-crossover experiments, 8 experiments in which abnormal substances appearing in the urine of children with autism have been normalized by the B6, other studies in which brain waves have been normalized, and a wide range of other improvements: 18 consecutive studies showing megadose B6 to be effective and no studies failing to show that megadose B6 is effective. No drug even comes close.

None of the studies of B6 in autism have reported any significant adverse effects, nor would any significant adverse effects be expected. I conducted an intensive analysis of the literature on B6 safety before embarking on my first study of B6 in the late 1960s. A review published in 1966 by the American Academy of Pediatrics confirmed my own conclusion: "To date there has been no report of deleterious effects associated with daily oral ingestion of large doses of vitamin B6 (0.2 to 1.0 grams per day)."

Tens of thousands of people, including thousands of children with autism and adults, took large doses throughout the '60s, '70s, and beginning '80s with no reported signs of any adverse effects. However, in 1983,

a paper by Schaumburg et al. reported significant, though not permanent or life-threatening side effects in 7 patients who had been taking 2,000 mg to 6,000 mg per day of B6. The side effects, peripheral neuropathy, were numbness and tingling in the hands and feet -the sensation one gets when one's hand or foot "falls asleep." The foot numbness in some cases interfered with walking. These patients were not taking magnesium, the other B vitamins, nor any of the other nutrients that should be taken if one is taking large amounts of B6. It is at least possible that the adverse reactions were due not to B6 "toxicity" but to deficiencies of magnesium and the other B vitamins induced by taking large amounts of B6. It is also possible that the problem was caused by a contaminant in the B6, rather than by the B6 itself.

It should be noted that the Schaumburg study covered only 7 patients and had 7 authors from several major medical centers throughout the United States. It would seem that a national search had been done to locate these patients, once the first case had been identified.

In the ensuing years, a few other patients have been reported in the literature who showed similar symptoms of peripheral neuropathy.

In my own experience, covering almost 30 years, and many thousands of children with autism and adults, I have, to the best of my knowledge, encountered only four cases of peripheral neuropathy. In these cases the numbness in the hands and feet was noticed by the parents, who reported that the child would: a) shake the hands as though to try to get the circulation back, b) have difficulty in picking up objects, such as bits of food, or c) have difficulty walking, because of numbness in the soles of the feet. When the B6 was discontinued, or the dosage was markedly reduced, these symptoms went away very quickly and completely.

Some individuals may be exceedingly sensitive to larger than normal amounts of B6. These cases are very few and far between, and discontinuing the B6 seems in all cases thus far to resolve the problem.

If you contrast these findings with the findings reported on a daily basis on the drugs that are used for autism, it becomes instantly clear that the B6 is immeasurably safer. There has never been a death or serious illness associated with ingestion of even very large amounts of B6. Deaths and permanent disability from prescription drugs are commonplace.

My own son, now 40, has been taking about 1 gram per day of B6 (along with 400 mg of magnesium, and other nutrients) for some 30 years. If there is a healthier person in North America, I would be surprised. Mark's only physical problem to date occurred in his early 20s, when a dentist found one small cavity in one tooth.

Despite the extraordinary safety of B6, I have been told, over the years, by thousands of parents, that their physicians have warned them against giving their children high doses of B6, because of the supposed risks involved. It is unfortunately very typical of most of the medical establishment (which of course makes its money by prescribing drugs) to denigrate and exaggerate the dangers of taking nutritional supplements.

A case in point: recently the national news media gave heavy coverage to a paper from the University of Michigan which warned the public against the dangers of taking vitamin B6. This report was given national television coverage, and we received a number of alarmed inquiries in our office from parents who were frightened by the warning, "B6 is toxic!"

When I read the study, I was truly appalled. The authors, from the University of Michigan Medical School, were supposedly investigating the value of vitamin B6 in the treatment of carpal tunnel syndrome (a painful malady of the wrists, which has become very common in recent years, and is usually considered a repetitive motion injury). The conventional treatment is surgery, which is often ineffective, as well as being disfiguring,

expensive, and painful. There are a number of well-documented reports that high doses of vitamin B6 successfully treat carpal tunnel syndrome, in the majority of cases, so that over a six-week period people who were scheduled for surgery no longer need such drastic treatment.

The Michigan researchers had not given even one milligram of B6 to even one of their subjects (not patients)! Their warning was based primarily on the 1983 Schaumburg report. Further, they had not included even a single subject who actually had carpal tunnel syndrome! They did blood and nerve conduction studies on people who were "potentially" at risk for carpal tunnel syndrome, but did not in fact have carpal tunnel syndrome. The anti-vitamin B6 bias in the report is very evident when you read, in their review of research, that "several" studies have reported B6 to be effective in treating carpal tunnel syndrome, while "numerous" reports have failed to confirm the finding. If you look at the actual references in their study, you will see that there are 12 favorable reports, and only 7 negative reports. So, to them, "several" equals 12 and "numerous" equals 7!

The University of Michigan study, with its highly publicized and totally irrelevant conclusions, is certainly one of the worst and most appalling studies I have ever read. Alan Gaby, M.D., author of *The Doctor's Guide to Vitamin B6*, referred to it as a "disgusting" display of bias, and I certainly agree with that assessment.

Nothing is perfectly safe, but B6 is exceptionally safe, particularly when compared to the alternative, drugs, which are infinitely more likely to cause severe illness, injury, and even death. An autistic person will improve on high dosage B6 only if that person's body requires extra B6. The benefits of B6 often start within a few days. If no benefits are seen in three to four weeks (in about 50 percent of cases), or if any signs of peripheral neuropathy appear (very rare), stop giving the B6.

A 1995 paper by Ellis and McCully reported that elderly patients who had been taking 100-300 mg per day of B6 for some years experienced only 27% the risk of heart disease, and among those who died of a heart attack, the average age at death was 84.5- eight years longer life than control group patients from the local area. In a 1993 study of epileptic newborns, Pietz found 300 mg of B6/kg/day-18 times the dosage used in autism-to be superior to seizure drugs. And B6, in amounts as high as 50 grams per day, is used as an antidote for victims of certain poisons. Is vitamin B6 toxic? Hardly!

Dimethylglycine (DMG), a Nontoxic Metabolite, and Autism

From the Autism Research Review International, Vol. 4, No. 2

DMG is a rather sweet-tasting substance that was described in a recent article in the *Journal of Laboratory and Clinical Medicine* (1990, 481-86) as a "natural, simple compound with no known undesirable side effects." The article did not pertain to the use of DMG in autism, but instead described an experiment in which DMG was used to try to enhance the function of the immune system of laboratory rabbits. It worked-the immune systems of the animals given DMG showed 300% to 1,000% better response to infection than the controls.

DMG is readily available in many health food stores. It is legally classified as a food. It does not require a prescription. It is manufactured by several companies, and comes in various forms, most commonly in tiny foil-wrapped tablets about 1/3 the size of an aspirin.

The taste is pleasant and children chew the tablets readily. At about 25 cents per tablet, the cost is minimal, since only one to eight tablets a day are usually taken (eight for adults). "So far so good," you may be saying, "but what does this have to do with autism?"

In 1965, two Russian investigators, M. G. Blumena and T. L. Belyakova, published a report showing considerable improvement in the speech of 12 of a group of 15 mentally handicapped children who had not been able to use speech to communicate. The children had been treated with a substance variously known as calcium pangamate, or pangamic acid, or "vitamin B15." In addition to enriched vocabulary, the children began to use simple sentences, their general mental state improved, and there was better concentration and interest in toys and games. Subsequent research has shown the essential factor in calcium pangamate to be DMG.

Soon afterward psychiatrist Allan Cott visited Moscow and brought back a small supply of pangamic acid, which he tried on a number of children in his practice, some of whom were autistic. Many of Cott's patients responded in the same way the Russian children had. One mother wrote, "It's the most exciting thing I've ever experienced. He was repeating words and he answers questions now!"

At about this time pangamic acid, or B15, entered the U.S. market. Chaos ensued. Every manufacturer touted his product as "the original Russian formula." There were at least four different formulas on the market, partly, it is believed, as a result of deliberate deception and obfuscation on the part of the Russians. DMG, in small amounts, was a component of some of the formulas. The FDA stepped in and lengthy legal battles ensued. One outcome is that the term B15 was outlawed. (Although DMG resembles the B vitamins in many ways-it is found in the same foods, for example--there are no known overt symptoms characteristic of a DMG deficiency.)

The significant outcome of the legal battles is that the sale of DMG is now permitted, as long as it is not referred to as a vitamin, and as long as it is sold as a food and not a drug.

I have been following the pangamic acid-DMG situation for almost 25 years. I have mentioned it in some of my lectures, and told parents and professionals about it in conversations and correspondence. Always I would ask, "If you try it, please let me know what results you see, even if no improvement is found."

I am now so firmly convinced that DMG is helpful to a substantial proportion of children with autism and adults that I have decided to "go public" in the Autism Research Review International -to tell people about it freely and openly, so they may try it if they wish.

Some who hear of this boldness may be aghast: "Where are the double blind placebo-controlled scientific studies showing it to be effective in autism?" they will ask. My reply is simple. "There aren't any, and none are needed." There are, of course, numerous double blind non-autism studies of DMG in the scientific and medical literature, using not only humans, but many kinds of laboratory animals, often given very large amounts of DMG. As noted earlier, no adverse side effects have been found with even massive intakes of DMG. (I say "intakes" rather than "dosages" because "dosage" implies that DMG is a drug, which it is not.)

Since no company has the exclusive right to make DMG, competition keeps the price-and profits-down. Thus there is almost no chance that anyone will sponsor a \$200,000 double blind study of DMG on children with autism. A parent can buy 30 tablets for about \$8.00. That is a sufficient supply, even for an adult given five or more tablets a day, to determine, in most cases, if it will be helpful. If it is felt to be helpful, fine. If not, you have wasted \$8.00 (except for the boost given to the immune system).

To help the parents receive unbiased input, I usually tell them to refrain from mentioning to teachers, grandparents and others in the child's environment that DMG is being tried. I have numerous letters in my files saying, "Johnny's speech therapist says he has made more progress in the last two weeks than in the last six months. As you suggested, we had told no one at his school that we were trying DMG."

I am 100% in favor of double blind studies on drugs with considerable potential for harm, such as fenfluramine, Haldol, or the like. However, it doesn't make sense to insist on such refinements before trying a perfectly safe substance such as DMG, apple pie, or chicken soup.

If DMG is going to work, its effects will usually be seen within a week or so, though it should be tried for a few weeks or a month before giving up. In some cases dramatic results have been seen within 24 hours: A Los Angeles mother was driving on the freeway, three-year-old Kathy in the back seat, five-year-old mute autistic son Sammy in the front. DMG had been started the day before. Kathy began to cry. Sammy turned and spoke his first words: "Don't cry, Kathy." The mother, stunned, almost crashed the car.

A similar case: A Texas mother secured her six-year-old mute autistic daughter in the front seat, then, before driving off, turned to tell her husband, "I'll drop Mary at the babysitter's house first." Mary, on DMG for two days, startled her parents with her first words: "No! No babysitter!"

Although speech is the most notable positive change in those children helped by DMG, behavioral improvement is also often reported. One father gave his son one DMG tablet per day without mentioning it to the school. He later requested a copy of the school's detailed record of his son's day-by-day behavioral transgressions. The correlation between outburst-free days and the use of DMG was unmistakable.

An article in the New England Journal of Medicine (October 1982) reported that a 22-year-old mentally retarded man who had 16 to 18 seizures per week on standard anticonvulsants, experienced only three seizures per week while on DMG. Two attempts to remove the DMG dramatically increased seizure frequency.

Last year I sent information on DMG to Lee Dae Kun, Director of the Pusan (Korea) Research Center on Child Problems. He tried the DMG on 39 children with autism, ages three to seven, for three months, with the following (summarized) results:

Benefits seen:

Yes: 31 (80%) No: 8 (20%)

(Improved speech, eating, excretion, willingness, etc.)

8 children had difficulty sleeping for weeks 1 and 2.

6 children became more active for weeks 1 and 2.

Lee Dae Kun wrote that the parents, usually skeptical, saw the improvements clearly. He concluded that DMG is very beneficial for children with autism, even if it is not a cure.

Information about the use of DMG with older persons is also encouraging. One mother of a 26-year-old who squeezed things (people, TV sets, etc.) very hard when frustrated, tried DMG, quite skeptically, to see if it would stimulate his very sparse speech. It didn't, but brought remarkable improvement in his frustration tolerance. "Even my husband, who was even more skeptical than me, now is a believer," she wrote.

DMG certainly doesn't always help, and it certainly is not a cure, but it is certainly worth trying, in my humble opinion. If you try it, let me hear from you.

Treating Yeast in Children with Autism: Typical Results of Anti-Yeast Therapy

Chapter 12

Dr. Bruce Semon

Introduction

I am a child psychiatrist and nutritionist who has been treating children with autism using anti-yeast therapy for the past six years. What follows are some representative cases based on my clinical experience. The cases I have selected involve children ranging in age from 20 months old to eight years old, all of whom showed significant improvement in the first few weeks and months following anti-yeast therapy. Their names have been changed to protect their identities. As you will see, these cases (except in the case of the 20 month old) are not "cures," but they do show the possibility for improvement in children with autism. Nor is the anti-yeast therapy intended to be the only therapy that a child receives. I firmly believe, however, that use of the diet and nystatin treatment vastly improves the child's baseline physical functioning, eliminating headaches, stomach and gut pain, and for some children, pain in hands and feet. By using the anti-yeast therapy, these children have the potential to achieve more in their lives and profit more from the other therapies and education that their parents offer to them.

CASE HISTORIES

Jon

Jon is a 6-year-old boy who had been diagnosed as autistic at age 3. He presented for aggressive behavior toward teachers and parents. Mother stated (on a follow-up visit) that he was hitting her so much that she was black and blue. He also hit his teachers regularly. He was kicking, biting and head butting, more so when tired or at transitions. He had lost language at age 18 months but some language had come back and he could use about 50 words. Jon had a history of head banging but this symptom had improved after a second set of ear tubes were placed.

Jon had had ear infections since age 1 with four sets of ear tubes being placed. He had chronic loose stools, eczema on his back and he was not toilet trained.

He had been placed on Mellaril before coming to see me due to violence against teachers. The Mellaril did little at low doses (10 mg). Higher doses were too sedating. He was off all dairy.

At the initial visit, Jon did not answer any questions and made little eye contact.

Chapter 12

Jon was started on the anti-yeast diet and nystatin. Jon returned six weeks later. His mother reported that his language had blossomed and his aggression had diminished from being constant to being only at transition times and at these times, the aggression was less. His sleep was improved and mother had stopped his Mellaril.

Jon returned three and a half months later. He was continuing to improve. He was now toilet trained for urine during the day. He was not hitting anyone in the family and he was interacting with his brother.

Jon has been treated for about nine months now and he has continued to improve. At each visit he has more speech and language. He also benefited from the addition of a low dose of naltrexone (explained below) daily.

Andrew

Andrew is a 2 and a half-year-old boy who presented with autism. He had stopped responding to his name at 15 months and had stopped playing with toys. His hearing was tested at 18 months and was fine. At 20 months he was referred by a child development specialist to a "birth to three program" for occupational and speech therapies. He was over active. He also had rashes, eczema and loose stools. At the first visit, he ran throughout the room and did not speak. Parents stated that he could vocalize at the 12-month level. Andrew was started on the anti-yeast diet and nystatin.

He returned four weeks later and his mother reported he was "more with it". School people told mother that Andrew was sitting longer with better attention. His bowel movements had firmed up. On exam, Andrew was vocalizing more and he sat in one spot on the floor with a pen and paper. He was no longer overactive.

Joshua

Joshua is a 20 month old boy who presented for being "crazy" the last few months, ripping things apart and being destructive. He was up four times per night screaming and yelling. His mother noted that he had a high tolerance for pain. He had had frequent antibiotics for ear infections which had sometimes caused diarrhea and he was plagued by frequent hives. His mother reported that he could understand speech but his expressive speech was behind and that he had lost some words. He had been an easy infant. On exam he was unhappy and unsmiling.

Joshua was started on diet and nystatin (but continued on milk). Two weeks later, his mother noted a huge improvement in how he felt. He no longer screamed at night. His activity level was lower. I noted that in my office he was smiling and playing with toys. A month later his mother reported that his speech had improved, that more words were coming and he was putting two words together.

Barbara

Barbara is a three-year-old girl who presented for speech delay. She had seemed normal until about 18 months when she had a severe vaginal yeast infection. This infection continued for six months. At that time her speech stopped developing. At the interview her parents reported she could say a few words. I could not discern any intelligible speech. She was unhappy and screamed occasionally and ran around.

She was started on diet and nystatin. She came back three weeks later. Her parents reported that she was attending better at school and could sit for longer periods of time. She was having fewer temper tantrums and was saying 4 to 5 words per day. In my office she said "mama" and smiled. She played with a toy and was not hyperactive.

Steven

Steven is a three-year-old boy who was reported to be normal until age 2. At 25 months he began screaming and arching his back. Speech was noted to be delayed. Before his third birthday, he was diagnosed as autistic. He had constant loose stools. He had skin rashes until his parents took milk away a few weeks before the interview. He had a history of milk intolerance with vomiting and diarrhea.

At his first appointment, Steven had no meaningful speech and he would not sit down. He moved all over the room.

He was started on the anti-yeast diet and nystatin. He returned four weeks later and his parents reported that he was more verbal and was showing some control. He was having normal bowel movements. I observed Steven walk around the room, rather than run. He was responsive to his parents and he smiled and talked appropriately several times with his parents.

Ann

Ann is a two and a half year old girl who had not developed much speech. She was making little eye contact and was screaming regularly. She had already been diagnosed as autistic by the time she was first seen. At the time of the first interview, she had no meaningful speech, although she occasionally said single words spontaneously.

She was started on the anti-yeast diet. Her mother noticed an improvement in speech after only four days on the diet. She asked for juice, using the word. She was put on nystatin at this time. Within a few days, she was putting two words together meaningfully. By six weeks she appeared at my office naming body parts and saying "I want ..." on a regular basis. She had been involved in intensive in-home applied behavior analysis therapy for several months preceding the anti-yeast therapy. Her therapists expressed amazement at her progress once she started the diet and nystatin.

David

David is an eight year old boy who had not developed language by age 3. He received a diagnosis of autism at age 6. He had been in an applied behavioral analysis discrete trial program for a year when first seen. He had made some progress in the behavioral program but his speech was unclear and he would only occasionally speak spontaneously. At the time he was seen, he responded to "What is your name?" in a whisper, which I could not understand. He otherwise was non-responsive and made little eye contact.

He was seen six weeks later after being put on diet and nystatin and his mother reported that there was more spontaneous speech. He could name things more completely. Before, if a request was made to touch his father, he would touch anyone. Now he would respond by touching his father. At this visit, he talked with his mother about going to eat. His mother told me that he had been taught such phrases in behavioral therapy. What struck me was that I could understand this time what he was saying. His speech was much more intelligible.

Diet and Antifungal Treatment

I use a combination of a special diet and the anti-yeast drug nystatin to treat children with autism. Dr. Shaw describes nystatin elsewhere in the book, but I will review it briefly. Nystatin is a non-absorbed chemical compound which kills the yeast *Candida albicans*. There are no toxic side effects from nystatin and nystatin can be taken for long periods of time. Although nystatin is a potent anti-fungal medication, it only reaches its maximum effectiveness when combined with a special diet. Before describing the specific treatment, including the steps to achieving the diet and directions for using nystatin, I will describe how I arrived at the diet.

Origin of the Treatment

I began treating children with autism in 1991. My first patient was my son. He had developed normally until age two and a half and from age two and a half to age four his development slowed. From age four to four and a half, he lost most of the function he had. He lost most of his speech and he lost his fine motor skills. He also began screaming much of the day and he was awake for three to five hours every night. No doctor had helped us. We had taken him to some of the best in the Washington, D.C. area.

But, on this early morning day in January 1991, there was to be an insight. My wife was sitting up with our son, as she had been each night for the previous month, during his waking hours of two to seven AM. He was staring at something, saying "the lights, the lights." All of a sudden, it hit her: our son was experiencing a migraine. He had had a peanut butter sandwich for bedtime snack, a food known to cause migraines, and this was it.

I grew up with a strong family history of migraines, and my wife Lori suffered from them occasionally. Both of us experience what is called an "aura" before the pounding pain of the headache: flashing lights, dizzying patterns dancing before their eyes. My father had had several migraines a week when he was in college, until he read an article in a magazine, stating that if one avoided certain foods, the migraines would decrease in frequency. My father avoided these foods and his migraines diminished considerably. The list included such foods as chocolate, pickles, salad dressing, bacon, alcoholic beverages, nuts, and aged cheese. I have since

seen from other headache clinics similar lists of foods to avoid. We decided to take away from our son a small list of foods known to cause migraines.

We took away chocolate, peanut butter, orange juice, aged cheeses, and some other foods. The improvement was immediate. Our son looked and acted as if a weight had been lifted from his head. Two years later, at the age of six, his headaches completely disappeared unless, by mistake, he ate something we knew was bad for him. His tactile defensiveness completely disappeared, too. At the beginning, however, we did not know how far we had to go.

After taking away several foods, we began to see the onset of separate headaches, when we would make a mistake and give him foods we should not have, or when he would eat something that we learned later caused problems. We saw the headaches set in about three times a week instead of being chronic. This change only took a few days to see.

Our son's symptoms of what we now know to be autism also began to diminish. He no longer screamed all the time. His behavior improved. He seemed more with us, more engagable. If he accidentally got into the wrong foods, the screaming began again.

In the first few weeks, we noted that not all the screaming went away. We tried to determine what foods were still causing problems. At the time, I was a research fellow at the National Cancer Institute, in a laboratory concerned with nutrition and cancer. Using the vast resources of the National Institutes of Health, I began researching what might be causing our son's problems. Based on my research, we decided to eliminate vinegar, a staple of our lives. Our son was a kid who ate ketchup (a significant source of vinegar) on everything, including popcorn, and loved Asian food, sprinkled with rice vinegar. Again, we saw immediate improvement, but knew that we were still missing something. I had no idea what the relationship was among the foods on the original list. Around this time, we also found that something in children's pain relievers were causing the headaches to last longer than necessary. We do not know exactly what that substance is, suspecting many of the additives, including aspartame (NutraSweet) but we do know that switching to pure acetaminophen, and later to pure ibuprofen, considerably shortened the life of the headaches. Life for our son improved considerably, but he still suffered considerable pain and still continued to lose his speech. We heard his last real word for five years in March, 1991.

We got our next break about eight weeks later with the Jewish holiday of Passover. For this holiday, all food containing yeast, leavening and fermented foods are eliminated. This holiday lasts eight days. By about three days into Passover, our son was clearly improving again. He appeared much more comfortable. By this time his speech was gone, so we were dependent on how he looked and behaved. His behavior had improved to the point that he was accepted into a special education speech and language summer program.

After those eight days, though, our son deteriorated. The screaming intensified. We had no idea what had happened. What was in the food that we were now giving again? We had many snack foods from the health food store, all supposedly healthy. I read the labels and the one ingredient that I did not recognize was "barley malt." What was barley malt?"

Barley malt is a byproduct of beer manufacturing. Yeast is mixed with barley to split the barley. Anytime that yeast is allowed to degrade a food, the process is called fermentation. The liquid part of this fermentation mixture goes off to be made into beer and the solid part is a nice sweet mash, which is then called barley malt or malt extract or simply malt. Malt is a fermented product.

What was the relationship among items on the list? Vinegar is literally spoiled wine, so it comes from fermentation. Barley malt is clearly a product of fermentation. But what was chocolate and what about nuts? I went back to my research to find out. I knew about certain cancer causing chemicals in food. One is called aflatoxin, a potent cancer causing chemical found in small amounts in peanuts. Aflatoxin comes from a fungus, called *Aspergillus*, which contaminates the peanut plant. Chocolate beans are dried with a fungus. Now the relationship among the items on the migraine headache list became clear. They are all products of yeast fermentation or of fungus contamination. Yeast and fungus contain many similar biochemical pathways, although in general, fungus produce poisons much more potent than yeast can produce.

Something produced by yeast and fungus was wreaking havoc on our son. We needed to know what it was. My lab happened to be at the same site where the US Army has its germ warfare labs and there are several people there who work in specialized fermentation. One research group was right down the hall. They got me started. The first chemical I found that I thought might be causing a problem is called acetol. Acetol is a skin irritant and an eye irritant (probably known from research to see if it could be used in cosmetics). Acetol is in vinegar. Acetol is also found in maple syrup and in cheese. I thought I was making progress. I had found something toxic in vinegar which may be causing problems. The identification of what foods could cause problems for our son was becoming easier. As I identified what foods contain which chemicals and we took these foods away, our son improved, albeit slowly.

Once we eliminated barley malt, vinegar, and yeast, the improvement was dramatic. We began to see the light at the end of the tunnel, but little did we know how long that tunnel was. At the time, simply decreasing his headaches to once a week or once every two weeks, and seeing his behavior improve and his autistic symptoms decrease were major victories. We had turned the tide before we lost our son Avi altogether. He was coming back to us, very, very slowly.

We found, though, that foods were not the only key to our son's puzzle. We were introduced to a book called The Yeast Connection by Dr. William Crook, about people who have problems with something called *Candida albicans*. We found a similar list of foods recommended for avoidance. Could it be that our son had a yeast problem? Certainly no professional had ever mentioned this, but certainly no professional had been able to help us to this point. We decided to try treating him with a non-toxic medication called nystatin. Nobody would prescribe it for us, but fortunately, I have a medical license.

Within a few days of starting on the nystatin, our son made a year's growth in playground development. He got off the swings and climbed jungle gyms, went down slides, and began to look like a four year old kid again. He still did not get his speech back, but he was better able to function.

Over the next few years, we were able to refine the diet, gradually eliminating all fermented foods, and, in addition, eliminating casein, gluten and eggs. He has remained on nystatin. He is a completely different child than he was in 1991, when he sat for hours screaming or spinning on a swing, making emotional contact with virtually nobody. He is a happy, healthy child, has been able to tolerate a regular classroom at school since first grade, and began to talk again with the help of significant intensive applied behavioral analysis therapy at home. Any deviations from the diet bring back autistic symptoms to some extent; some foods are worse than others. Screaming, aggression, including scratching, kicking, and biting; non-cooperation; lack of progress in school--all of these remind us what life would be like with untreated autism.

I have since treated several other children, only some of whose cases I noted above, with excellent results. My son, and these children, responded well to being treated with a combination of diet changes and the taking of nystatin. Why did this regimen help, and what is this regimen?

Although it seemed at first that the diet recommended in The Yeast Connection could have saved us a lot of work, and perhaps could have saved our son's speech had we discovered the book sooner, we found that it did not answer the questions that our son posed to us. Had we followed that diet, which at the time was the standard for anti-yeast diets, our son still would have been eating many of the foods that we know cause him, and many others, tremendous problems.

The main difference is that in diets based on The Yeast Connection recommend eating a great deal of meat and eliminating most carbohydrates. The reason for this is that Dr. Orion Truss, who first published the idea that *Candida albicans* can cause health problems in The Missing Diagnosis, observed that yeast grow well in carbohydrate and not particularly well in protein. Therefore, he reasoned, one should remove carbohydrate from the diet so the yeast doesn't grow as well. Subsequently, the standard anti-yeast diet recommends eliminating all sugar and yeast from bread and substitute more meat and fish. However, in my practice, I have found that this diet is not optimal. The human body is not as simple as a test tube nor is the human diet as simple as culture media for yeast in a Petri plate.

In my practice I have seen many frustrated patients with many symptoms, ranging from autism to chronic fatigue syndrome to arthritis and fibromyalgia to multiple sclerosis, who had followed these recommendations, eliminating sugar and bread from their diets, probably increased meat and fish, and enjoying few results. The reason for their lack of results is not their lack of effort, but the fact that the main dietary yeast offenders (vinegar and barley malt) had been left in their diets. In fact, most of the anti-yeast and allergy related cookbooks have vinegar as a staple food and recommend a diet high in animal protein, which is problematic, and nuts, which are thoroughly mold contaminated. Our experience with our son and with my other patients is that this recommendation of using meat and eliminating almost all carbohydrate is wrong.

When yeast spoils meat, the toxic chemicals formed are worse than those formed by yeast in carbohydrate. In addition, chicken and pigs are fed cottonseed meal which is contaminated with a fungus called *Aspergillus*. I speculate that the animals store in their fat the *Aspergillus* poisons. This technique is a common way for animals to handle poisons. It is possible that storing the fungus poisons is one reason why yeast sensitive patients should not eat large amounts of meat. Meat from the right sources and in small quantities is acceptable on the anti-yeast diet, however. We have found that the easiest meat to eat is veal. Cattle receive less or no cottonseed meal (other feeds are cheaper) and there is little time for any poisons to accumulate in the calf prior to slaughter. We found with our son and again with many patients since that a diet of complex carbohydrate is the best for yeast problems.

I left the National Cancer Institute in August of 1991. A month later I began treating patients for *Candida albicans* using the dietary principles I developed while working with our son and using the non-toxic anti-yeast drug nystatin. I found that I could treat supposedly untreatable conditions such as autism, psoriasis, eczema, chronic fatigue syndrome, multiple sclerosis, chronic vaginal yeast infections, attention deficit disorder and refractory depression. These conditions all respond to treatment of *Candida albicans*.

I also found that other children with autism responded well to the same treatment as I had given my son. I have never had a child not respond to the treatment for yeast, when the parents make an effort to follow the treatment. In fact, the improvement seen with this treatment regimen is often dramatic. The best explanation for the results for the children described above is that *Candida* produces compounds which affect the brain and reduction of *Candida* by diet and nystatin leads to fewer of these chemicals reaching the brain which leads to a reduction in autistic symptoms.

The Medical Regimen: Diet Plus Nystatin

An overview of the schedule for treatment is helpful to understand that this treatment is a long term process, and a long term treatment. The first three to four months are spent adjusting to the appropriate diet and level of nystatin. After that, other medications may be introduced, if appropriate.

Schedule for Treatment:

Preceding treatment, you may wish to have urine testing done using Dr. Shaw's testing. If so, first see the doctor; order testing, then at return visit, assuming yeast problem, start the following:

Week 1: Doctor's Appointment. Start diet, Stage I, for 3 days, on 4th day: start nystatin.

Week 2: Continue diet Stage I; continue nystatin up to the prescribed maximum dose.

Week 3: Doctor's Appointment to help with questions, assess progress. Continue diet Stage I. Continue on nystatin.

Weeks 4, 5: Continue diet Stage I; continue nystatin. By week 5 patient should be at full dose.

Week 6: Doctor's appointment. Start diet Stage II if appropriate.

Week 7-9: Continue diet Stage II; continue nystatin.

Week 10: Doctor's appointment; assess progress to determine whether to go to Stage III. Continue diet and nystatin per doctor's instructions.

Weeks 11, 12, 13: Continue following doctor's instructions.

Week 14: Doctor's appointment to assess progress; at this point, patient may consider retesting urine, and/or doing allergy testing for food allergies.

After this point, patient should return to the doctor to evaluate any testing results. Other medications such as naltrexone may be considered. Patient should continue on the prescribed treatment plan, returning in 4 weeks, then 6 weeks, then 8 weeks, then every 3 months for the first year.

The Diet

Changing diet is extremely difficult for everyone, including our family. As my wife often says, if she didn't live with the doctor, she would have a much harder time sticking with the program. Food has social and emotional contexts as well as nutritional value. To change diet, you need to have a good reason. A chance to allow someone with autism to live a "normal" life, to me, is the best reason. Autism is a lifelong condition that can cause tremendous suffering, not only to the person who has autism, but to the person's entire family. Recognizing these problems, I have tried to make dietary change simpler and more gradual by dividing it into stages. Some children respond so well to the first stage of the diet that further adjustments are unnecessary. Other children need more intervention.

STAGE I: Eliminate:

- **Barley malt**-a by-product of beer making found in many cereals, crackers, breads and bagels and in many health food snacks. **Substitute:** similar foods that do not contain barley malt. For example, many breakfast cereals contain barley malt, but others do not (most General Mills cereals, such as Cheerios and Kix, do not contain barley malt). Similarly, some brands of pretzels, graham crackers, etc., contain barley malt, but others do not. When shopping read labels carefully and avoid anything with malt in it.
- **Vinegar**- is literally spoiled wine and is very concentrated in toxic yeast products. Vinegar is found in virtually all condiments, including ketchup and mustard, sauces and salad dressings. **Substitute:** freshly squeezed lemon juice; tomato paste for ketchup
- **Chocolate** - Chocolate has two problems. Chocolate is dried with a fungus. Chocolate also contains a chemical compound which is similar to one of the yeast products. Unfortunately, there is no substitute for chocolate.
- **Pickles and pickled foods** such as herring, tomatoes, and pickled peppers (yes, there are such things)
- **Alcoholic beverages and non-alcoholic beer**
- **Aged cheese**
- **Soy sauce** (substitute: sea salt)
- **Worcestershire sauce**
- **Anything containing cottonseed oil** (The cottonseed plant is often mold contaminated and the products of the mold end up in the cottonseed oil.)
- **Nuts and peanuts**
- **Apples and apple products**
- **Grapes and grape products**
- **Coffee**
- **Hot dogs, salami, and other processed meats containing nitrates and/or nitrites.** "Natural" hot dogs can still be eaten at this point.

These foods must be eliminated for 3-4 days prior to starting nystatin according to the schedule listed below. Continue the diet and nystatin for 4-6 weeks, then consult the doctor to consider whether going to Stage II.

These foods are the most concentrated in toxic yeast and fungal chemicals. Without eliminating these foods, nystatin will not work well and children will not get much better, even if they are given nystatin. Apples and grapes contain yeast byproducts that Dr. Shaw has isolated, and in my clinical experience, wreak havoc in a child sensitive to yeast.

STAGE II: Eliminate all of the above, plus:

- **Baked goods containing yeast, including bread.** **Substitute:** non-yeast bread (Dr. Semon's recipe for Delicious and Nutritious Whole Wheat Bread), but not sourdough bread (this too is highly fermented)
- **Corn and rye** - corn and rye are both highly contaminated with mold
- **Vanilla extract** - highly fermented; contains alcohol
- **Dried fruits and raisins**
- **Concentrated fruit juice**
- **Monosodium glutamate (MSG) and aspartame (NutraSweet)**

Chapter 12

- Maple syrup
- Bananas
- Cut back on all meat and fish except veal
- Spices such as cinnamon, dried mustard, curry powder, chili powder, cayenne pepper. (All green herbs, fresh or dried, are acceptable.)
- Mushrooms
- Soda drinks
- Cooking oils except safflower oil, soy oil, and olive oil. Canola oil is acceptable unless a child reacts badly to it.
- Sugar, including both white and brown. Substitute: unprocessed honey
- Margarine - margarine has a host of problems. The human body does not metabolize it. Butter, a natural product, is much better for the body, even though it contains cholesterol. Substitute: butter
- Buttermilk

Patients should follow Stage II for a period of four to six weeks, continuing with the nystatin. After consultation with the doctor, they should consider moving on to Stage III, eliminating gluten and casein (dairy and all grains containing gluten, including wheat, barley, oats, rye, and others.) Note that there is little information on what is in eggs. However, they do seem to stimulate food allergies. Any child with a chronic skin problem should have eggs removed to see if this helps with the skin problem.

STAGE III: eliminating gluten and casein

ELIMINATE all of the above, plus:

- All foods containing milk protein--butter is acceptable. Butter in small amounts is acceptable because butter is a fat which does not contain the milk protein casein.
- All foods containing gluten, including wheat, oats, barley, rye

The transition to a casein/gluten free diet is described elsewhere in this book by Lisa Lewis Ph.D. The difference between her description and my description is that the diet I recommend also eliminates yeast products and fermented products, so some gluten-free grains, such as corn, which are acceptable on a gluten-free diet, are not acceptable on a yeast free diet.

Patients should follow Stage III for four to six weeks, continuing with the nystatin, then consult the doctor. At this time, they might move on to Stage IV. In my experience, only the most severe cases of sensitivity need to continue to Stage IV. At this point, patients might consider retesting urine by Dr. Shaw, and at this point, they could consider testing for food sensitivity using immunological testing.

STAGE IV. ELIMINATE all of the above, plus:

- Melons
- Grapefruit and oranges
- All meat except veal
- Yellow onions (leeks are acceptable)
- Fruits except very fresh fruit in season, such as berries
- Canned goods - canned goods often contain mold contaminated food, because the canning process does not allow for discrimination
- Fish

ALLOWABLE FOODS on Stage IV: WHAT CAN WE EAT?

In my practice, I have found that the basic diet, and the best foods to eat, which should form the staple part of your diet unless you have documented food allergies or sensitivities to them, are the following:

- Beans (kidney, black, garbanzo, Navy, etc.)
- Brown rice (long grain, short grain)
- Tomatoes
- Potatoes
- Herbs (marjoram, dill, basil, oregano, etc.), including seeds from herbs (dill seed, celery seed, etc.)
- Butter
- Safflower oil
- Green Vegetables (zucchini, broccoli, celery, spinach, kale, lettuce, etc.)
- Roots, such as parsnips
- Fresh fruit in season, especially berries (you can freeze berries in season for use later in the year)
- Unprocessed honey

Some people choose to stick with only these foods, rather than eliminating everything else slowly, but I do not advise this. Most children will not end up at Stage IV. You may be able to continue eating a variety of foods not on this list. You don't want to lose that opportunity!

Even if this restrictive list is where you ultimately will end up, and this is where we have ended up after several years, I do not recommend starting with it, because the change is too drastic for most families, including my own. You will end up failing your child because you simply cannot enforce the diet. It is much better to implement the diet over the course of several months in a way that enables you to stick with it. After all, you are the gatekeeper for your child's health and the role model for your children.

Is this Treatment Worth the Family's Aggravation for the Sake of My Child?

This diet is inconvenient. Remember, though, how inconvenient untreated autism is that led you to seek medical help: all of the nights of screaming, the extreme sensitivities to touch and chemical substances, and the behavioral issues, all of which I have seen improve more rapidly using the anti-yeast treatment than on any non-biological therapy. Changing diet is relatively easy compared with a life in agony. To my knowledge, I repeat, all children I have treated with the above diet (that is excluding foods containing toxic yeast chemicals) and nystatin have improved. I have never had a parent come back to me saying they followed the diet and the nystatin, and the child failed to respond. This response is totally different from the response to many of the medications I have prescribed for children with autism in my psychiatric practice.

The tragedy in waiting to decide about whether you are ready to tackle this diet is that children with autism respond best the earlier and sooner the intervention. The longer you wait the more function the children lose. All children I have treated who still have some speech left gain more speech with this treatment. Once children have lost their speech entirely, there is less hope that speech can come back.

Using Nystatin

I have heard often from people that they gave nystatin and it was not helpful. I have found nystatin to be of little benefit without the diet, so these stories do not surprise me. However, the dose of nystatin is also important.

Dr. Shaw writes elsewhere in this book about the problem of "die-off". That is when nystatin kills the yeast, it is similar to bursting a water balloon with a pin. The yeast are like the balloons: once pricked, they release all of their contents at once, which are these same toxic chemicals that make the patient feel bad to begin with. The person can feel worse temporarily. Nystatin can cause some temporary nausea when it is first started but this nausea is not "die-off". This nausea will go away. To avoid "die-off", Dr. Shaw suggests starting the nystatin dose very low and increasing the dose over a week. His final dose is much lower than I recommend to patients.

I also recommend starting with a small dose of nystatin, increasing gradually. Using this strategy combined with the diet, I have never seen this "die-off" with children with autism. When the diet is combined with nystatin, I believe that the yeast do not grow back. This problem of "die-off" and whether "die-off" can be prevented with the diet described here needs to be tested further.

Another possibility can be seen from some of Dr. Shaw's test results. He has shown that giving nystatin alone can result in an increase in bacterial byproducts found in the urine. He suggests that clearing out the yeast may leave room for bacteria to grow and make toxic byproducts. He suggests treatment for the bacteria also.

I suspect that my suggested nystatin dosages combined with my suggested diet may prevent the overgrowth of these harmful bacteria but further testing will be needed to confirm this idea.

I prescribe the nystatin powder, which is the most effective form of nystatin. I recommend mixing the powder with a small amount of unprocessed honey, enough to dissolve the nystatin (about 1/2 teaspoon). For convenience, you can mix one day's worth of doses at once in well washed film canisters, and store them in the refrigerator. These are hermetically sealed. You can send these premixed doses with your child to school. Use a chopstick to mix, and a baby spoon to scoop out the nystatin from the film canister.

The important thing is to get the nystatin down to your child's digestive tract, not have it all over their faces, shirts, and your floor. Especially for the first few days, use anything possible that is acceptable on Stage I of the diet to mix your nystatin, including ice-cream, orange juice, syrup, butter: that is, anything. Once your child begins to associate taking nystatin with feeling better, giving it will be easier for you, and you can switch to honey.

For those who cannot in any manner get a child to take the nystatin, it does come premixed in a sugar syrup. This is not optimal, as it is much more dilute than the powdered nystatin and is full of sugar.

The truly tough (adults) can put the powder on their tongue and wash it down. Nystatin powder can be pushed into capsules. Nystatin also comes in pill form.

Dosing Schedule:

Notes: An eighth teaspoon of nystatin is about 500,000 units. When "twice in the day" is recommended, that means spaced evenly--e.g., take one at breakfast and one at dinner. Three times a day might be breakfast, lunch and dinner. I recommend taking nystatin after you have eaten something, to avoid possible nausea.

******Week 1**

Day 1 1/16 teaspoon once in the day
 Day 2 1/16 teaspoon twice in the day
 Day 3 1/16 teaspoon three times in the day
 Day 4 1/16 teaspoon four times in the day
 Days 5, 6 and 7 1/16 teaspoon four times in the day

******Week 2**

Day 1 1/8 teaspoon once in the day, 1/16 three times
 Day 2 1/8 teaspoon twice in the day, 1/16 two times
 Day 3 1/8 teaspoon three times in the day, 1/16 1 time
 Day 4 1/8 teaspoon four times in the day
 Days 5, 6 and 7: 1/8 teaspoon four times in the day

*****Week 3 (First alternative)-**

Day 1 1/4 teaspoon once in the day, 1/8 three times
 Day 2 1/4 teaspoon twice in the day, 1/8 two times
 Day 3 1/4 teaspoon three times in the day, 1/8 one time
 Day 4 1/4 teaspoon four times in the day
 Days 5, 6 and 7 1/4 teaspoon four times in the day

******Week 3 (Second alternative)-**

Day 1 1/8 tsp. 5 times per day
 Day 2 1/8 tsp. 6 times per day
 Day 3 1/8 tsp. 7 times per day
 Day 4 1/8 tsp. 8 times per day
 Days 5, 6, 7 continue at 1/8 tsp. 8 times per day

********Two alternatives are listed for week 3 because many people have a hard time taking 1/4 tsp. at a time. Smaller amounts are easier to take.

Other Anti-Fungal Medications

There are both over-the-counter remedies and herbs and other prescription medications that kill yeast. Dr. Shaw has written about them in this book. In my experience, nystatin is the most effective and least toxic means to fight yeast. The problem with the other medicines is that they are absorbed and have toxic side effects. Both Diflucan and Nizoral can affect the liver. Thus they can only be given for a short period of time. Once they are stopped the yeast can grow back.

Nystatin is a totally natural substance that pharmaceutical companies have harnessed and made a prescription medication. Nystatin has been available longer than 35 years. According to all of the literature on it, including the standard PDR (Physicians Desk Reference), nystatin has no known toxic side effects. Apart from some possible nausea during the first few days, there really are no side effects from nystatin. It can be taken indefinitely because it is not absorbed into the blood stream. Nystatin acts only in the intestinal tract. Children with autism must be treated for a long time to allow their brains to recover and develop as much as possible. Treatment for a few weeks is not sufficient. The only drug which can be used for long periods of time is nystatin. My son, for example, has been on nystatin for more than six years, with no ill effects.

How Long Does Treatment Last?

Parents are accustomed to treating problems for a few days or weeks, then stopping treatment. Usually other people, including some doctors, encourage them to cease treatment to see what happens. This is unfortunate, because many people never resume treatment, even when they see their child's behavior deteriorate. They assume that the treatment did not work.

When treatment is stopped, so do the gains made while on the treatment, and, if you are unlucky, your child may lose all of the gains over time. Dr. Shaw has tested children for whom nystatin doses are simply reduced and he has shown that toxic yeast chemicals in the urine increase when the nystatin dose is reduced. Unfortunately, the yeast comes back when nystatin is stopped. Anti-yeast treatment is a long-term treatment, and it is effective in combating autism.

How Does the Anti-Yeast Treatment Compare with Standard Psychiatric Medication for Children with Autism?

I am a child psychiatrist and have prescribed many medications for children with autism, including Clonidine, Ritalin and others. Not one of the children on any of these medications has done as well as any of the children on the anti-yeast diet and nystatin.

One medication to consider adding to the diet and nystatin treatment is naltrexone. This is most effective when combined with the Stage III diet (anti-yeast and free of casein and gluten). Naltrexone blocks opioids in the brain. I said above, the opioids from milk and wheat may slow the brain down. At low doses, naltrexone may help clear the brain of opioids which have already gotten into the brain. Unfortunately, the doses of naltrexone which have been used in academic studies have been too high, and the studies show that sometimes naltrexone has the opposite effect of what is intended. These studies also have not combined use of naltrexone with elimination of dairy products and wheat. In my clinical experience, the best results are

obtained from naltrexone if dietary opioids are also eliminated (that is, dairy and wheat), and using a very low dose of 3 to 6 milligrams per day (the pills are 50 milligrams each). The doses used in studies have been 25 to 50 milligrams per day, and in my experience, those high doses can cause children to have increased pain and headaches.

Are There Any Other Natural Substances to Treat Autism?

First, remember that although nystatin is a prescription medication, it is a totally natural substance.

There are many other possible substances advanced to treat autism. Again, I do not recommend trying any until the Stage III diet, or the most restrictive diet prescribed for your child, has been in place for at least six months, and with the consultation of your supervising doctor. Eliminating toxic yeast chemicals from the diet, eliminating casein and gluten, and treating intestinal yeast are the first priorities. After six months of continuous treatment, parents may wish to experiment with substances.

One herb I have found helpful is called ginkgo biloba. This herb opens up blood vessels. There is evidence that blood flow is reduced in the brains of children with autism. Ginkgo may help reverse this lack of flow. I think ginkgo may be most helpful when combined with anti-yeast treatment. The brain may be closing down the blood flow to protect itself from toxic yeast chemicals. When these are removed, ginkgo may do more good.

Conclusion

I would advise any parent of a child with autism to try treating their child with diet and nystatin. The presence of yeast chemicals in the urine can be verified using Dr. Shaw's test. Symptoms such as skin problems, diarrhea, constipation, and behavioral problems following antibiotic use also strongly suggest an overgrowth of the intestine with the yeast *Candida albicans*. Following Stage I of the diet and using nystatin for two to four weeks will tell you if the treatment is beneficial to your child, with no adverse effects or risk to your child.

I have treated many children with autism who showed significant gains by following the diet prescribed along with the nystatin. I have designed the dietary regiment to allow for a gradual transition to the yeast-free level of least intervention necessary for your child. The nystatin-dosing schedule is similarly graduated to provide for the least die-off effect. Combining the two will yield gratifying results, for you, your child, and your family.

Dietary Intervention for the Treatment of Autism: Why Implement a Gluten and Casein Free Diet?

Chapter 13

Dr. Lisa S. Lewis

Introduction

When my son was first diagnosed with autism (in 1991) my husband and I were both stunned, and in an odd way, relieved. Relief may seem like a bizarre reaction, but for almost two years we had been dealing with the unknown. It was terribly frightening and we never really knew if we were on the right track. Professionals were of little help. At Sam's three-year checkup I asked our doctor point blank: "Could he be autistic?" At least he was honest. Shaking his head slowly, he replied, "I just don't know."

With a diagnosis, we had something to grab and run with. We both hold doctorate degrees in Anthropology, and as a result we were already trained to do research. Without discussing it, or formally dividing up what needed to be done, a division of labor seemed to occur naturally. As I look back on it now, I realize that doing research was our coping mechanism. We didn't have time to cry and ask "Why us?" We sprang into action, devoting ourselves to doing something positive for our son.

My husband, Serge, immediately called a wonderful local organization called COSAC (New Jersey Center Outreach and Support for the Autistic Community) and set up an appointment. There we got valuable information on services available to us, our legal rights, whom we should call and where we should start, as well as a copy of Ivar Lovass's *Me Book*. We signed up for a six-week parent training course due to start in a few weeks. Serge began looking into schools and other educational matters. (At that time Sam was in a half-day, "preschool handicapped" program that was not meeting his needs.) Armed with the information he had gathered, we were ready for our IEP (individualized educational plan) meeting, where we presented a case for moving Sam to a more specialized (and far more expensive!) school.

While Serge was looking into education and therapeutic interventions, I began an extensive search for anything I could find on autism—medical and other interventions, outcome and etiology. Fortunately for me, the World Wide Web was just then "taking off," and I was able to do much of my research without leaving my desk. As a (then) employee of Princeton University, I was able to access anything on-line quickly, and at no expense. I had already learned to use the basic tools of electronic research for my work at the university, but now I really honed these skills to find specific information. I found a lot, and I also found how many other people were out there "seeking." I began extensive correspondence with many other parents, and with some notable professionals too, including (the late) Roland Ciarnello who was running the Stanford University Genetics Research program on Autism. Dr. Ciarnello was a big help, and sent us several his articles when we were looking for specific information.

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We combined the results of our research to come up with a plan, which included where to have a good educational evaluation done on Sam, where to send him for speech and occupational therapy and what kind of school to put him in. Our school district was helpful and supportive, and gave us most of what we asked for. Still, we continued to search. At that time, there were few Internet news groups on the subject, and locally, we only found “support” groups that stressed coping with the diagnosis rather than research or treatment. After reading much of the literature on the subject we weren’t surprised by the focus of these groups. Autism was, after all, described a lifelong developmental disability, intractable to most medical treatment.

When Sam was three, he began having violent tantrums. I had read that many children who were allergic to milk behaved that way. He loved milk and any milk products and consumed lots of milk, yogurt, cottage cheese and ice cream. And why not? After all, I was raised to believe that milk was the perfect food! I never loved it but my mother insisted that a certain amount be consumed every day. But as Sam’s tantrums intensified I started reading about allergies, and found that children with food allergies generally craved most, those foods that they should not have.

I removed dairy from Sam’s diet, and while he did seem to settle down a bit, there wasn’t really a profound difference. I still suspected that something he ate was affecting him, and his pattern of recurrent ear and upper respiratory infections which eventually led to asthma, seemed to indicate an immune system gone awry. We took him to a highly recommended pediatric allergist in Philadelphia. Her tests confirmed that Sam was very allergic to pollens and molds, but she found no evidence of food allergy. That was the end of dietary intervention—for a while.

Two years later, when Sam was five, I saw Dr. Doris Rapp on a talk show. She spoke about environmental allergies and food allergies, which I found very interesting. But then she showed videotapes of children who were given concentrations of foods to which they were allergic. These nice children suddenly became wild animals! Screaming, attempting to hit or scratch, throwing tantrums and worse. Milk was said to be one of the main allergens that produced this response. Wheat was also named as a common cause culprit.

At this, a bell went off for me. In addition to his love of dairy, Sam loved crackers, bread, rolls, pretzels—anything starchy and most foods made of wheat. We had been calling him “Carbo-man” because he so loved these (mostly) *wheat-based* foods. I could not help noticing the resemblance between those videotapes, and the behavior I had been witnessing and dealing with in my own son. Though he had tested negative for a wheat allergy, I decided then and there to remove it from his diet.

Within three days, I began getting notes home from school, saying that Sam was doing beautifully and that his behavior was enormously improved. What had we done? I decided not to reveal the removal of wheat at this point. But two weeks later I was eating a slice of pizza. Sam came by and asked for some. I was watching something on television, and was preoccupied. I mindlessly handed him a slice and only after he was halfway through did I realize what I had done. Oh well, I thought, the damage (if any) was already done.

The next morning when Sam asked for a Pop-Tart® I went ahead and gave it to him. Then I waited. At 4:00 his bus pulled up and even before he was out his aide said, “I hear he had a pretty rough day.” I barely looked at Sam, instead grabbing his backpack to find his notebook. As I had suspected, the note was not good. During the course of the day, Sam had numerous tantrums, had been extremely aggressive and very unfocused. Only late in the day did he start to come around, telling his teacher “don’t write in the book” realizing that I would read of his many transgressions!

From that point on, I explained to his teachers and therapists what we were doing (no more pretzel reinforcers during speech therapy!) I began sending wheat free lunches and snacks, and wrote up a long list of what he should not be given at school.

Though I was completely convinced that Sam was greatly affected by what he ate, I was still puzzled over why he tested negative to wheat and milk allergies. I mentioned this to an “electronic friend” (someone I’d met on the Internet, and subsequently in person) named Jean Jasinski. She recalled reading an article about autism and gluten intolerance. I vaguely remembered something about it too, but couldn’t remember the authors or where I had seen them. Bless Jean—she searched until she came up with one article, which she mailed to me. I then was able to find other articles by the author, Paul Shattock of the University of Sunderland in Sunderland, England. Shattock’s articles in turn led me to the work of Dr. Karl Reichelt in Norway.

After reading about the research going on in England and Norway, I came to realize that I should have removed all gluten grains from Sam’s diet, rather than just wheat. I did this, as well as I could. It was very hard to manage since it was new to me, but I found information about celiac sprue and went from there (more on this below.) I did not see the huge change in Sam that I’d seen after first removing wheat, but this seemed natural to me. I had already removed the grain that had the highest concentration of gluten proteins; perhaps I had succeeding in weaning him from the offensive proteins.

Two years later I found Mr. Shattock “on-line.” I sent him e-mail immediately, and so began a correspondence which continues to this day. He and his colleagues have proved tremendously helpful to me.

So many people began asking me for information, that I wrote a twenty-page document on how and why to try this intervention. Before long, I was spending a lot of time and money duplicating the article and mailing it to people. There had to be a better way. At that point, many more people had Internet access from their offices or homes, and the World Wide Web was becoming widely available. Since nearly all requests for the article were coming to me via e-mail, I decided to put this document up on the web. I created a home page, and announced it to the autism world, and what a reaction it has had.

I began to receive phone calls, letters and e-mail from all over the world. From these contacts I met many more parents with whom I began exchanging information. It was from this and references from friends who had read my article, that I made contact with many of the “seeker parents” out in the world.

At first, when I began talking and writing on this topic, I was thought to be something of a “nut.” For the last year or so, however, the subject of diet is on “the net” constantly, and even doctors have begun taking it seriously. It may not cure, and it may not even help all that try it, but it will help many. I hope the information provided in this book and in this chapter will help you to decide whether or not to try new interventions for your child. I hope that I can provide you with information on why it might be a useful experiment. And if you do want to try it, some information is included that will help you get started.

What is Gluten? Why Eliminate it from the Diet?

Gluten is a protein found in the Plant Kingdom Subclass of *Monocotyledonae* (monocots.) These plants are members of the grass family of wheat, oats, barley, rye and their derivatives. Derivatives include: malt, grain starches, hydrolyzed vegetable/plant proteins, textured vegetable proteins, grain vinegar, soy sauce, grain alcohol, flavorings and the binders and fillers found in vitamins and medications. Casein is a phospho-protein of milk, which has a molecular structure that is extremely similar to that of gluten.

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In the early 1980's, two scientists noted that the behavior of animals, under the influence of opioid drugs such as morphine, was very similar to that of some people with autism. Dr. Jaak Panksepp proposed that people with autism *might* have elevated levels of naturally occurring opioids in their Central Nervous System. There are several such naturally occurring compounds. The best known of these are the beta-endorphins which produce the so-called "runner's high."

At about the same time, work by Swedish autism expert Christopher Gillberg showed elevated levels of "endorphin-like substances" in the cerebrospinal fluid of some people with autism. It is particularly interesting that levels are high in those children with autism who are insensitive to pain and those who engage in self-injurious behaviors. Dr. Karl Reichelt found abnormal peptides in the urine of people with autism; these peptides are apparently similar to those found by Gillberg. The Autism Research Unit later replicated Reichelt's findings at the University of Sunderland, under the direction of Paul Shattock.

According to Shattock, "In the urine of about 50% of people with autism there appear to be elevated levels of substances with properties similar to those expected from opioid peptides." Because the urinary compounds greatly exceed what could be possibly be of CNS origin, it is presumed that they result from the incomplete breakdown of certain foods.

Proteins consist of long chains of amino acids. Normally intestinal enzymes digest them, breaking the bonds that connect the protein's amino acids. Genetic mutations, caused by changes in the DNA, can mean that specific enzymes cannot do their work.

Enzymes are also proteins; they are long chains of amino acids that fold into specific three dimensional shapes. Each enzyme has an active site into which the protein it is designed to digest can fit. An alteration in the gene that codes for a particular enzyme can mean that it folds in new way, and the protein to be modified no longer fits into the active site. "Mutations...can change the chemistry of the body by preventing or altering the way certain enzymes and chemical reactions work" (Comings, 1990).

In this case, an incomplete digestive process would leave amino acids bound into short chains called peptides. If the peptides still have biological activity—that is, if they still function as opioids—they could result in symptoms we see in autism. Most of the peptides would be dumped harmlessly into the urine, but if a portion escapes the gut and enters the bloodstream, they could cross the blood-brain barrier and cause serious neurological problems.

Two commonly ingested proteins are known to break down into peptides that have opioid activity. *Casein*, a protein in cow's and goat's milk, breaks down to produce a peptide called *casomorphine*, and *gluten* from wheat breaks down to form gliadinomorphins. The amino acid sequences of these two molecules are extremely similar, which is why the elimination of both gluten and casein is usually recommended.

If one lacks the ability to break down these proteins appropriately, there must be a strategy for reducing the effects of the resulting opioids to minimize neurological effects. One approach would be the anti-opioid drug "naltrexone." Naltrexone has shown very mixed results, however, and there are some difficulties associated with its administration. (Dr. Shaw's note: See Dr. Semon's chapter for effective dosing of Naltrexone to supplement dietary changes.) Finding the optimal dose has proved difficult, and it is a very bitter pill, which most children will resist taking. A second approach is excluding casein and gluten from the diet.

Many parents have had traditional allergy tests run, and most report that their children are not allergic to wheat or milk. This is probably true. Children who are helped by this diet are generally not allergic in the traditional

sense; they are gluten or casein sensitive. According to Shattock, "The results are akin to poisoning rather than an extreme sensitivity such as occurs in coeliac disease or sensitivity to certain food colourings."

Many children suffer an initial bad reaction to the removal of their favorite foods. Often, these children seem nearly addicted to a specific type of food--often consuming large quantities of dairy or wheat products. Some children do very well for a few days, then suffer a regression. According to Reichelt, this bodes well for the success of the intervention. Once this period passes, it is generally followed by a good response. Younger children are more likely to benefit dramatically from this intervention, but adults have also been noted to have improved concentration and communication, as well as lessened sensory scrambling.

When I first learned of this research, Dr. Reichelt was working with many families in his native Norway. This work convinced him of the diet's efficacy. He was the only person that I knew of who had data from tests of these theories, and I wanted to know more. I tracked down a fax number for him and sent him a letter requesting more information. I included my e-mail address in my fax, and was delighted to receive a response via e-mail, in just two days. In this mail Dr. Reichelt said:

"In general we recommend a diet free of gluten and casein for autistic...patients. The reason for this is that opioid peptides from gliadin are almost of the same structure as casomorphins from casein. We also recommend addition of multivitamin with trace minerals and magnesium, cod liver oil and calcium. We usually remove both casein and gluten. Opioids from these proteins are very similar."

He ended with: "Effects of diet if useful, tends to be cumulative. Must be tried for 1 year."

Further Research

Mr. Shattock, along with colleague Dawn Savery, has recently written a paper that brings their work on this topic up to date. At the time of writing, Shattock and Savery had examined urine samples from nearly 1,000 subjects. While little other information about the subjects was collected initially, the study is now more formal and involves the collection of much more detailed behavioral and other information.

The theoretical model on which their study is based remains the same, relying heavily on work by Reichelt and colleagues (Knvisberg and Waring.) To summarize:

...autism could be the consequence of the action of peptides of exogenous origin effecting neurotransmission within the Central Nervous System (CNS.) We believe that these peptides result in effects which are basically opioid in nature....The CNS neuroregulatory role which is normally performed by the natural opioid peptides...would be intensified to such an extent that normal processes within the CNS would be severely disrupted.

The presence of this intense opioid activity would result in a large number of the systems of the CNS being disrupted....Perception; cognition; emotions; mood and behaviour would all be affected. ...Many and diverse symptoms by which autism is...defined would result. We believe that these peptides are derived from an incomplete breakdown of certain foods, and in particular, gluten....and from casein.

--"Autism as a Metabolic Disorder,"

Paul Shattock and Dawn Savery (1997)

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Any time proteins are broken down in the gut, peptides result; they are intermediate compounds which should then be broken down further into their amino acid components. In all individuals, a proportion of these may cross from the intestines into the bloodstream, and hence, cross the blood-brain barrier. However, if the gut is "leaky" then the proportion of improperly broken down peptides that cross this protective barrier will be far larger, with potentially devastating consequences. [See discussion on Phenol sulfur Transferase below.]

Sam's Story

I gave an overview of what we did when our son was diagnosed, but here is a little more background about him, and his family.

Sam is now nine years old, and was diagnosed as PDDNOS, pervasive developmental disorder-not otherwise specified, a form of autism at age three and a half. We believe that his development was normal for approximately the first 18 months of his life, but by the age of two and a half he was in an early intervention program. Country officials who ran this program never gave us a specific diagnosis, saying only that he had "sensory integration difficulties." This is certainly true—he was significantly delayed in motor planning, he had a poor sense of where he was in space he had "tactile defensiveness"—refusing to touch textures such as shaving cream, finger paint or sand. But as I read the little that was available about the subject, it seemed clear to me that sensory integration problems were likely a *symptom* of something else, rather than the cause of his many problems.

By age three Sam was in a multiply-handicapped half-day preschool, and was receiving private speech therapy. Though he had language from an appropriate age (13 months), by two it was far behind that of peers and was characterized by (appropriately placed) echolalic utterances. When Sam was three and a half, a neurologist at the University of Medicine & Dentistry of New Jersey (at Rutgers University) finally confirmed our suspicions that he might be autistic.

At this time we began doing the research outlined previously, and we sought an independent educational evaluation at the Eden Institute in Princeton, New Jersey. A placement more specific to autism was recommended, and Sam was accepted at the Douglass Developmental Disabilities Center (DDDC) for the next year.

Because DDDC is a data based program, we have hard data on what happened when wheat was removed from Sam's diet. After five days, Sam's aggressions had dropped dramatically, from double digits over the course of a five-hour day to an average of 6.1/day. During the month he was on vacation, Sam did not aggress at all. When he returned to school in September, his aggressions dropped further, averaging 2.47/day over the next seven months.

Reduced aggression was not the only change we noted when dairy, wheat and gluten were removed from Sam's diet. For two years we had struggled with Sam's reversed pronouns. We did drills at home; he worked on it at school and with his private speech therapist. Within one week of his dietary change, his use of pronouns was suddenly and completely correct. His attention span increased and he responded more quickly to lessons at school, home and in private speech and occupational therapies. His speech therapist referred to him as her "one-trial learner."

In the spring of 1994, we visited Dr. Sidney Baker of Westport, Connecticut. He placed Sam on a strict with *anti-yeast diet coupled with high doses of the anti-fungal drug Nystatin*. We were told that before seeing any

improvement we might first see a regression. Sam did have a regression that lasted for three weeks, with terrible behavior but no loss of previously attained skills. After a few weeks, Sam's behavior normalized and his aggressions gradually decreased to a level of 2.47 day during the remaining school year. I did not see a marked improvement as a result of this treatment, however, which was a disappointment. I later had the organic acids test performed by Dr. Shaw, which indicated that a new trial of anti-fungal medication might be in order. Since the test has been expanded and refined, we will likely do it again and try, if necessary, an antifungal other than Nystatin.

Dr. Baker also ordered extensive testing of blood, urine, saliva and stool. While most were normal, Sam was deficient in eight amino acids, and low in zinc. In order to put Sam's system into better balance, we added a vitamin compound, additional calcium and zinc to Sam's daily regimen.

I later added molybdenum and magnesium, as well as essential fatty acids (evening primrose oil.) At various times I have also experimented with DMG, L-Carnitine, a (milk-free) acidophilus powder, extra inositol, pycnogenol and octocosanol. Since I never saw any benefit from these additions, I have not continued to use them on a regular basis. I do know of many children who have responded very well to some of these compounds, and I retry them on a period basis just in case something has changed in his system that might make them helpful.

Sam's diet and nutritional supplements are certainly not the only things that have helped him. He spent four years at an excellent special school, and attended weekly speech and sensory integration therapy for five years. For two years he wore yoke prism glasses and did visual therapy prescribed by Dr. Melvin Kaplan of Tarrytown, New York. The prism glasses helped Sam to focus his visual attention for longer periods (though this remains a problem) and it also put an end to his habit of looking at the world using primarily peripheral vision (i.e. squinting his eyes and turning his head and looking from the side.)

However, the change after removing wheat was both remarkable and undeniable, as is what happened on the occasions that he accidentally ingested gluten. On several occasions Sam has eaten gluten without our knowledge, and the changes in him were fast and quite marked. In each case we were able to determine what had caused the sudden, and thankfully short-lived, regression.

While I cannot be sure what has helped Sam the most, I do have a daily record of his behavior and many of his utterances dating back to when he was three. I can therefore correlate changes with particular interventions. Because autism is likely a disorder with multiple etiologies, it is doubtful that every person with autism would benefit from this diet. I believe strongly, however, that the approach would help many children. Indeed, in the three years since I first began to write on this subject, I know the diet has helped thousands that I am aware of and no doubt countless others who have never contacted me. It is certainly worth trying.

For a child with a limited diet, I would start with lab tests to determine if he is likely to benefit from the diet (see below). All parents of children with very limited diets want to broaden the food choices the child accepts. However, if positive test results show that gluten and or casein could be causing damage to the CNS, changing the diet is critically important. NOTE: tests will not be valid once the child has had gluten and/or casein removed from his diet for any length of time.

Because Sam responded so well to a GF (and greatly reduced casein) diet, I feel frustration that more parents have not been willing to try this diet. However, I also know that I am lucky. My son is not a fussy eater, and accepts the various substitutes I provide for him. He can now monitor his own diet to a certain extent, refusing "regular" bread or cookies. He also eats a wide variety of foods, much of it healthful. He is now able to swallow pills, and can take the vitamin supplements I give him without trouble.

Jake's Story

Sam's brother Jacob was born when Sam was three, and we watched his development very carefully. He was only three months old when we had a definitive diagnosis for Sam. I tried to remain calm about his development, but when Jake was nine months old I began to worry in earnest.

Jake showed little pre-verbal development; he did not babble and he made very few sounds. While his pediatrician understood the source of my concern, he maintained that it was far too early to see anything, and that I should just keep a close eye on him. At this same visit, the pediatrician told me that Jake was ready for cow's milk. I was working full time and under a great deal of stress. My own milk supply had waned and to keep him happy I had added formula to his diet. I was thrilled to throw away the breast pump and the nasty smelling formula supplements. I bought some whole milk and Jake drank it with gusto.

Cow's milk, however, seemed to cause an immediate change in Jake. He got fussier and had more stomach upsets. Within a day I knew that this child was not ready for cow's milk. I immediately went back to the store to buy formula. Then, in a moment that in retrospect seems like an epiphany, I bought soy formula instead. Within two days Jake was happier than he had ever been. Within three days he was saying "mamamamam" and "dadadada".

On his first birthday Jake had about ten words; by 15 months he had 200; by 18 months he spoke in sentences. He has continued to develop into an incredibly imaginative, verbally precocious little boy. At five, Jake calls himself a scientist and is fascinated by all sea creatures (especially sharks.) He wants to be an underwater photographer and to make nature films, but agrees that perhaps kindergarten should come first. He was four before he had cow's milk products again, and by that time they had no effect on him so they are back in his diet to a limited extent. In addition to the joy he has brought to his parents, Jake is the best "therapist" Sam ever had!

Did I "save" Jacob from autism by removing a potentially harmful protein at a vulnerable age? Did I save him from some other developmental disability? Of course, I will never know.

Testing for Urinary Peptides

Because modification of the diet is far less invasive or harmful than most interventions, it would seem logical to try this method. Many children with autism, however, have such finicky eating habits that the idea of cutting anything they will actually eat out of their dietary repertoire, strikes fear the hearts of their parents. For this reason, some might prefer to test their child's urine for the presence of the urinary peptides found by Reichelt and others. If there are no peptides found, it is unlikely that the diet would help the child. However, if the peptides are present and are escaping from the gut into the bloodstream, it is believed that they can "mimic" neurotransmitters and thus result in the scrambling of sensory input.

If you have already tried the diet you will not learn anything meaningful from the urine test. By eliminating gluten and casein from the child's diet, you have removed the source of the peptides. It can take a long time to build them back up to pre-diet (baseline) levels, and this is not advisable, especially if the diet has proven helpful.

Dr. Cade, an autism researcher now deceased, has had some success with adding prescription strength digestive enzymes to the regimen of children with autism. These enzymes apparently help break down proteins in individuals whose digestive system is not functioning properly. While it may not mean that the child can start eating whatever he or she would like to, it can be one more weapon in our treatment arsenal.

Testing for Celiac Disease

What exactly IS Celiac Disease (CD)?

"Celiac disease (also known as Celiac Sprue or gluten-sensitive enteropathy) is a chronic disease in which malabsorption of nutrients is caused by a characteristic...lesion of the small intestine mucosa. The lesion is produced, through unclear mechanisms, by protein constituents of some cereal grains"(J.S. Trier, 1993). Traditionally, doctors have suspected celiac disease only when patients show poor growth, extreme gastrointestinal problems and fatty stools. It is now known, however, that many patients with sensitivity to gluten serious enough to damage the gut wall show no such symptoms!

In people who have celiac disease but continue to eat gluten, the intestinal wall is excessively porous; not only are nutrients improperly absorbed, but large molecules which should be contained by the gut wall are not. This could be the way in which improperly digested peptides pass into the bloodstream and then cross the blood-brain barrier. Thus, the speculation that celiac disease is present in some children with autism who would benefit from a gluten free diet is not inconsistent with the opioid excess theory of Reichelt and Shattock.

Various experts on autism long ago dismissed the idea that gluten could be a significant causal factor. However, gluten exists as a "hidden ingredient" in many foods, medicines and even in the envelope glue we lick. It is possible that children with autism children put on a so-called gluten free diet were inadvertently ingesting gluten in small amounts.

For those with full blown celiac disease, tiny amounts of gluten can be toxic; it is not so far fetched to imagine that in less severe forms of gluten intolerance, minute amounts could also cause harm. When full blown celiac disease is diagnosed, it can take more than a month on a gluten-free diet to see changes; again, it is not far fetched to assume that the same is true for people with gluten intolerance that have different outward symptoms.

It may be then, that early researchers and parents who tried this intervention in the past simply gave it up too soon. Patients with full-blown celiac disease often have terrible symptoms of gastrointestinal distress, fatigue, and failure to grow or gain weight. These kinds of symptoms cannot be ignored, and the diet is changed when the child is relatively young. But it is possible that far less severe forms of CD exist and are, in fact, quite common. If so, they could go undiagnosed for years. Undiagnosed, the toxic effects of the ingested gluten could prove extremely damaging and could cause what is likely to be permanent damage to the central nervous system.

According to an article by Dr. Alessio Fasano in a 1994 newsletter of the American Celiac Society:

In recent years there has been a noticeable change in the age of onset of symptoms and the clinical presentation of celiac disease. Because the typical symptoms of gastrointestinal dysfunction are frequently absent in older children, the diagnosis beyond the first two years of life is more difficult and often delayed. These cases are now regarded as having atypical or late onset forms of celiac disease.

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Rimland and Meyer noted as long ago as 1967 that children with the highest score on Rimland's E-2 Diagnostic Checklist also showed many gastrointestinal symptoms. It has also been suggested that celiac disease is an autoimmune disorder with gluten stimulating increased synthesis of some antibodies in celiac disease patients. Ruth Sullivan noted that "though few children with celiac disease have autism, it seems a disproportionate number of children with autism have celiac. Why?

Does malabsorption of the small intestine prohibit vital substances (like serotonin...) from reaching the brain? If so, why do not all classic cases have celiac? Or do they? ⁽¹⁹⁷⁵⁾

A disorder very closely related to celiac disease, and necessitating the same dietary intervention, is a skin disease known as dermatitis herpetiformis (DH). According to the newsletter of the American Celiac Society, "Dermatitis herpetiformis is the skin manifestation of gluten sensitivity and 70-80% of DH patients have coexisting damage in the intestine." In many cases DH sufferers have no outward signs of intestinal difficulty, and yet at least 70% actually do suffer from celiac disease! DH appears as a bumpy rash, usually on the arms, legs or buttocks. It is extremely itchy and may also burn.

Interestingly, Sam had such a rash on his arm and inner thigh. This rash first appeared at approximately age 2 (around the age his autistic symptoms also appeared) and was diagnosed by our pediatrician and two dermatologists as severe eczema. All prescribed cortisone creams but the rash did not improve. It was so itchy that my son would frequently scratch until he bled. We removed all synthetic fibers, dressing him in only 100% cotton washed in soap that had no colors or dyes. Nothing helped.

Then, as mysteriously as it appeared, the rash went away. Around the time that I changed Sam's diet I also began giving him evening primrose oil, which was said to help eczema. I credited the oil and bought several bottles. Then I stopped using it and the rash did not reappear. I now realize that the cause of the improvement was probably not the oil, but rather the removal of gluten from Sam's diet! Though I cannot have the tests run because he is been off gluten too long) I am convinced that he was likely showing signs of DH, which were unrecognized by the doctors who saw it. [Note: I later realized the importance of evening primrose oil for the essential fatty acids it provides, after reading Leo Galland's excellent book, *SuperImmunity For Kids*. I then reinstated the oil into Sam's daily regimen.]

New blood tests show latent and sub-clinical cases of celiac disease. Because even latent celiac disease will cause damage to the intestinal wall, it makes sense to have these tests run. The relevant tests involve screening the blood for celiac antibodies. The tests are called endomysial IgA, gliadin IgA and reticulin IgA. The blood test can rule out or suggest Celiac Disease. If celiac disease is not ruled out, a diagnosis still cannot be made. Celiac disease can only be positively identified via intestinal biopsy. If a gluten free diet has already been implemented, these tests will not be valid. While these tests will not reveal a possible sensitivity to casein, they should certainly be done on children who developed normally for up to two years (and who are thus more likely sensitive to gluten). Not all labs are equipped to run these tests. If a local lab cannot do it, you might want to contact Specialty Laboratories, Inc., in Santa Monica, CA at 310-828-6543.

Although no child will willingly donate blood, all four tests can be performed following a single draw. While it is doubtful that all people with autism will turn out to have celiac disease, these tests should be performed to rule it out.

Certainly celiac disease causes a leaky gut; if various proteins are being improperly metabolized, such a gut would provide a pathway into the bloodstream for these peptides. Clearly these tests should be added to the battery that children undergo when a diagnosis of autism, PDDNOS or atypical autism is made.

Intestinal Permeability tests also exist, and should be performed, if possible [see section on the DAN! protocol below.] This test requires a patient to ingest a sweet drink provided by the lab performing the test, then eat nothing for several hours. This is followed by a collection of all urine for the next 24 hours. This test must be ordered by a doctor, and will show whether or not the patient has a "leaky gut." If the child is not toilet trained, a bag (obtainable from your doctor) can be taped used to collect urine at each diaper change.

Phenol-Sulfur Transferase (PST) Deficiency

Preliminary studies by Rosemary Waring, of the University of Birmingham, UK, suggest a particular enzyme deficiency in many children with autism. This abnormality affects the sulfur-transferase system, which is one of the body's major means of detoxification. In a recently published book, Dr. Sidney Baker describes this system very succinctly:

This system helps us get rid of leftover hormones, neurotransmitters and a wide variety of other toxic molecules. Some such molecules come from our own metabolism, like leftover hormones and neurotransmitters, and some come into us with our food or are made by the germs that live in our intestines (*--Detoxification & Healing; The Key to Optimal Health, 1997*).

With insufficient PST, individuals have an extremely low capacity to oxidize sulfur compounds. Children with this enzyme deficiency are unable to fully metabolize certain foods and chemicals that contain phenols and amines.

As stated by Dr. Baker, PST is necessary to break down hormones, some food components and toxic chemicals. If the enzyme is deficient, the body cannot detoxify the system—that is, it will be unable to render these substances harmless. Harmful substances that should be metabolized would build up to abnormal levels, substances which include serotonin, dopamine and noradrenaline. Many metabolic processes can be disturbed by phenolic compounds and cause many physical problems that may not have been previously thought connected to autism (excessive thirst, night sweating, facial flushing, reddened ears etc.)

The children most likely to show this deficiency (based on Waring's small sample size) showed normal development for the first 18 months to two years of life, and also show family histories of asthma, skin problems and migraine, as well as sensitivity to foods (especially wheat, milk and salicylates.)

There are some tests that can identify whether an individual has a weak detoxification pathway, however, normal levels have not been established for children under the age of twelve. Dr. Waring has a working test for children, which uses acetaminophen (Tylenol®) as a "probe" for finding weakness in the PST system. Testing does require a 24-hour collection of urine, a nearly insurmountable difficulty if a child is not reliably toilet trained. For more information, Dr. Waring can be contacted at: The School of Biochemistry, University of Birmingham, Edgbaston, Birmingham, B15 2TT England. Dr. Waring does not currently have Internet access. Dr. Robert Sinaiko, a San Francisco specialist in Allergy and Immunology, is working on perfecting a test in this country. Hopefully, such a test will be available soon.

Unfortunately, there is no standardized, recommended treatment for PST deficiency. Two approaches may be taken—you can try to *increase* the body's ability to detoxify itself, or you can try to *decrease* the toxic load you subject it too. Neither approach is particularly easy or 100% effective. To quote Developmental Delay Registry Founder and nutritionist Kelly Dorfman:

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Some parents have used diets that remove all known phenol compounds (such as Sara's Diet) to take pressure off the PST...system. While sometimes helpful, these diets are extraordinarily difficult to implement long-term as naturally occurring phenols are in every food with color. Except in extreme cases, a diet reducing toxic load from the most concentrated sources...appears to be the best.

That is, reduce juices (or limit to pear juice) and eliminate all artificial colors and flavors.

Unfortunately, no amount of intervention...can totally unburden PST...enzymes....That is why it is critically important to improve the efficiency of the faulty enzyme system while attempting to lessen the load. Several nutrients may help. They include vitamin C, vitamin E, reduced L-glutathione and N-acetylcysteine. All of the antioxidants (including selenium and bioflavonoids) are valuable for detoxification in general.

-From *New Developments*, Winter 96-97, a DDR publication.

Autism researchers have been intrigued by the fact that the PST deficiency can cause the improper metabolism of some neurotransmitters (serotonin, dopamine and noradrenaline.) It has been known for years that people with autism often have abnormal levels of serotonin, as least as is measured in the blood. But the buildup of serotonin may be less significant than another outcome of a PST deficiency—namely, the effect this deficiency would have on the permeability of the intestinal lining.

One outcome of an improperly operating sulfur-transferase system is insufficient connective tissue in the gut wall. Thus, a PST deficiency could be yet another reason (besides Celiac Disease and other gastrointestinal ailments) that the gut wall would be "leaky." As stated above, when improperly metabolized proteins (such as gluten or casein) are able to escape the gut lining into the bloodstream, they can cross the protective blood-brain barrier.

I noted above that my son's urinary amino acids tests revealed a deficiency in eight amino acids. Five of these are sulfur-carrying amino acids. Dr. Baker informs me, that this is a pattern he sees very frequently in autistic patients. It will be interesting to follow Dr. Waring's research to determine whether or not there is a relationship between her theories and the deficiencies he finds. Because the sulfur-carrying amino acids are involved in the detoxification of the body of both exogenous and endogenous pollutants, disturbances in these systems indicate disturbed immune systems.

Considering how frequently these children suffer from numerous infections and allergies, this is not an unlikely assumption. In some parts of the country immunological approaches are being taken with some benefits to children with autism, and it is possible that for some the cause of autism may be an autoimmune disorder.

Though it cannot yet be proven, there is good evidence that a diet that eliminates gluten and or casein may indeed be beneficial. In an unpublished (1993) manuscript, Waring and Reichelt state "We think that the demonstrated peptides may be central to the aetiology of the disease. Exorphins not only increase social isolation in animal models, but may cause CNS inhibition of maturation." Another observation is equally intriguing: "...because most bioactive peptides are found in different chain lengths, but with very similar activity, different peptidase defects would cause similar but not identical symptom profiles and peptide profiles." They believe that this indicates that such "effector peptides" would be the "final common path of several clinical subtypes involving different lengths of peptides. It would also suggest that other diseases may show autistic symptoms if peptides are involved, as is seen for coeliac disease."

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If you are convinced (or become so after having tests run) that this dietary intervention is worth trying with your child, you have your work cut out for you. Even a very good cook must relearn how to shop, how to plan menus and how to cook.

For many of the children who respond positively to dietary intervention, gluten and casein are not the only problematic foods. Some children react to corn, soy and eggs, in addition to gluten and casein. Some can eat dairy but not gluten. Some can eat gluten, but no dairy or eggs. Dietary intervention is time-consuming and tedious because you must be systematic in determining which foods cause problems for a given child. But if your child responds, it is worth the trouble.

Where to Go for Help with a Gluten and Casein Free Diet

There is a large population of celiac sufferers in this country; they are experienced in food substitutions and can be a great source of information for people trying to avoid gluten. Five organizations that have newsletters containing lots of valuable information are:

American Celiac Society
201/325-8837 (New Jersey)

Celiac Sprue
Association, USA 402-
558-0600 (Omaha, Nebraska)

Gluten Intolerance Group of Florida
Orlando, Florida 32837
Internet: Celiac@ispace.com

Gluten Intolerance Group
P.O. Box 23053
Seattle, Washington
407-856- 3754

Celiac Disease Foundation
13251 Ventura Blvd. Suite #3
Studio City, CA 91604
818-990-2354

The Gluten-Free Baker Newsletter is published quarterly, and gives recipes for sweet and savory baked goods. 361 Cherrywood Drive, Fairborn, Ohio, 45324-4012

If you have Internet Access, there is a **Celiac List**, which has a great deal of useful information. For information on subscribing to this list, send e-mail to Celiac@ispace.com. You will also receive instructions on how to access the archived recipes posted over the last few years.

The Autism Network for Dietary Intervention (A.N.D.I.) publishes a quarter newsletter. For more information write to *The ANDI News*, PO Box 77111, Rochester, NY 14617-0711 or send e-mail to AutismNDI@aol.com.

Some Good Cookbooks

Because so many people have asked for more details on the information contained in this chapter, I have recently completed a book on the topic. Over half of the book is devoted to actually implementing the diet, and it contains over 100 gluten and casein recipes. See the end of this chapter for more information.

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The Gluten Free Gourmet, *More From the Gluten Free Gourmet* and *The Gluten Free Gourmet Cooks Fast and Healthy*, by undisputed GF Guru Bette Hagman, are all published by Holt. All are excellent. Each has over 200 gluten free recipes for bread, cookies, pizza, chicken pot pie, cakes etc. It's also full of advice about adapting regular recipes and what to use as substitutions. If you can buy only one cookbook, make it one of Bette Hagman's.

Other useful and excellent cookbooks include: *Allergy Cooking With Ease* by Nicolette Dumke and *The Allergy Self-Help Cookbook* by Marjorie Hurt Jones. For those who are limiting yeast, *The Candida Control Cookbook* by Gail Burton is a very good source of recipes.

Full of Beans by Kay Spicer and Violet Currie has recipes using beans and bean flour. These "odd" ingredients make wonderfully moist and delicious baked goods. *No-Gluten Children's Cookbook* by Pat Cassidy is available for \$25.50 from RAE Publications, PO Box 731, Brush Prairie, WA 98606. *The Practical Gluten-Free Cookbook* by Arlene Stetzer is available from Main Street Systems (608) 534-6730.

There are MANY others-check bookstores and libraries! For Web surfers, visit www.amazon.com.

Where Do We Go From Here?

Everyone agrees that autism is a puzzle. It seems at times, that all the pieces are black and we are trying to put it together in the dark! Everyone has to do what he or she thinks is best for his or her children, and for their families. For forty years parents have been given false hopes and empty promises. There are still few definitive answers, and there are still lots of promises being made.

I hope that the reader of this book does not believe that special diets fall into this category. I do not believe that dietary intervention will "cure" children with autism (or at least, not very many.) But it can help, and it can help a lot. For those children who respond to dietary changes, the ones who respond the most will likely be the very young ones. The few children who were cured by dietary interventions (i.e. they have been reclassified after an initial diagnosis of autism) were generally started prior to the age of three, and usually prior to the age of two. My son was five, and while he has made tremendous progress, he is still autistic. I have even heard from autistic adults, who started the diet in their twenties and beyond. They are still disabled, but it has alleviated symptoms that were always present and thus cleared up some of the "fog" these folks felt they were in.

This diet probably won't help everyone who tries it, but should you decide to try, you must be both serious and scrupulous about it the trial. You must also make sure that school staff, sitters and (especially) grandparents gets with the program. Many an effort has been scuttled by a grandma saying "but just a little couldn't hurt, could it?" Or by a disbelieving outsider betting you won't notice if they slip a cookie or a pretzel to your child. This cannot work unless everyone who comes near your child follows the strict guidelines that you provide.

But what else should you do? If we all now know (no thanks to the late Bruno Bettelheim) that this disorder is an organic rather than an emotional problem, why has so little been done to find a medical answer? Fortunately, things are changing somewhat. In January of 1995, Dr. Bernard Rimland convened the first Defeat Autism Now! (DAN!) Conference in Dallas, Texas. It was a gathering of serious researchers who want to find a way to help children with autism, now, not in twenty years. A major undertaking of the group was the writing of a medical protocol to be used by physicians who treat autistic patients.

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Called "Clinical Assessment Options for Children with Autism and Related Disorders: A Biomedical Approach," it represents a consensus report of the participants. The protocol was written by Drs. Sidney Baker and Jon Pangborn, and approved by all but one of the practitioner participants. It has recently been revised, and includes a list of doctors who are willing to use the protocol.

The Dan! Protocol, as it is called, is available from The Autism Research Institute. It is a somewhat daunting document, but it is very well worth the effort to buy the protocol and go through it with your child's doctor.

No one expects that every parent will do every test in the protocol. But when you study it, you will find those tests that seem most likely to give you important information for your child. It is a valuable document, and I highly recommend that you contact the Autism Research Institute at 4182 Adams Avenue, San Diego, CA 92116. The Autism Research Institute's phone number is 619 563-6840 and its website is www.autism.com/ari. In addition to the DAN! Protocol, The Autism Research Institute's newsletter will keep you up to date on everything going on in the autism world.

I was fortunate to have been one of four parents invited to join in the first meeting of Dan! Since that time, Dr. Rimland has convened another conference aimed at training doctors and informing parents (and more are planned.) One thing that came out of these meetings is the shameful lack of research money dedicated to autism. Another parent who attended the DAN! meetings decided to do something about this situation and along with her husband, started the Cure Autism Now Foundation. CAN is dedicated to raising money for research. Please contact CAN at 1-213-549-0500 or electronically at can@primenet.com for information on what you can do to help. If you have access to the Internet, visit the CAN web page at www.canfoundation.org. It is absolutely vital that we all join in this effort!

Sam's Story...Today

Many people write and call me to discuss the issues covered in my original paper on this topic. Without a doubt, the question I am asked most often is "How is Sam doing NOW?" There is no simple answer to this question. In general, we are very gratified at the progress Sam has made and continues to make. But there are always "glitches" along the way.

As of this writing, Sam is nine, and is attending third grade at a "regular" district school. He was transitioned into the district gradually when he was almost seven, with a great deal of support and instruction from the staff of his former school. He has a personal aide who was also trained by DDDC staff. Sam does his academic work in a self-contained classroom, and most of it is one-on-one with his teacher or aide. He attends morning meeting, art, music, gym, lunch, recess and other "specials" with his third grade peers.

Sam's attendance at this school requires a lot of patience on the part of school personnel, and a lot of adjustment on our parts. At times we miss the extra attention and support we got as a family from his former school. But Sam is so happy to have peers who respond to him! Though his behavior has been difficult at times (we still struggle with bouts of non-compliance and aggression) his attendance at this school is a great experience for everyone. He is well liked by staff and students. His peers try hard to help and understand him, and my husband worked with them at the start of the year so that they could understand Sam's struggles better. They are proud to help him when they can, and he greatly enjoys his social times. They have benefited from learning that not everyone faces the same challenges in life.

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Sam continues to have difficulty with visual processing, and reading remains a real challenge. It is a challenge he is meeting however, and I am encouraged that Sam will read fluently in the not too distant future.

Sam's language is excellent, and he shows that he is able to generalize ideas and skills quite well. He clearly has a "theory of mind" and is improving at abstract thinking. His school provides two sessions of speech therapy per week, and two of occupational therapy. Noting that Sam really needed and benefited from input to his vestibular system (the system controlling balance), his occupational therapist obtained a weighted vest for Sam. He wears it for much of each day, and teachers report it calms him down a great deal.

Now, about those "glitches"...Sam has shown, over the last four years, a troubling and completely predictable seasonal cycle. As late autumn approaches, life seems to become increasingly difficult. By mid-winter we are deep into a funk, which includes an increase in the number of tantrums and extremely difficult behavior. At this time of year, if he is not under medication, he will regress into terrible aggression and to a lesser degree, self-aggression. We have found that a small dose of Risperdal (Risperidone) is necessary to get through this portion of the year. As spring approaches, behavior improves as does Sam's attitude and mood. Last year, I removed the medication during his "up" period, but he really seemed to need it even then. As of now, he is taking this medication and doing very well on it. I doubt very much that we could get through a winter without this chemical help.

Sometimes being Sam's advocate is very hard work, but we are extremely proud of him. Getting along in the world is more challenging for him than I can even imagine. Despite the rough spots, however, he is in general sweet and friendly. He can (and does) charm the socks off most adults who meet him and work with him. To sum up: life goes on, and we all work hard to ensure that he will be the very best that he can be.

A final note: if you have found this chapter interesting and would like to pursue a dietary intervention, please contact The Great Plains Laboratory, Inc. to obtain a copy of my book on this subject, *Special Diets for Special Kids: Understanding and Implementing Special Diets to Aid in the Treatment of Autism and Related Developmental Disorders*. In addition to discussing the topics covered here, it contains many recipes and tricks to get you started.

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Managed Recovery from Autism and ADD: One Family's Journey

Chapter 14

Pamela Scott

Introduction

My husband and I were in our late twenties when we decided to start a family. Excited about the prospects of becoming parents for the first time, we were totally unprepared for the events that took place which would change our lives forever. We were certain of two things when we planned our new family: we were going to produce great children and they would be loved beyond belief.

Well, we did produce great children--two of them in fact. And they are certainly loved with all our hearts. What we had not planned on, not even thought about for more than a fleeting moment, was the possibility that something would be different about our babies; that they wouldn't develop like other "typical" children. And we certainly could not have predicted that not just one, but *both* of our children would have disabilities. This reality was never part of our dream, our vision, for our family.

Instead of experiencing the joy of watching a child grow and learn, we felt fear and anxiety as we agonized over every developmental milestone that our children did not meet.

As we compared our children to our friends' children, we became *angry*.

Angry that our lives were different.

Angry that physicians and therapists didn't have the answers to our questions.

Angry that the services and programs available did not meet our children's and family's needs.

Angry that we were supposed to just accept our children's disabilities and go on with our lives.

Just plain angry!

But out of that *anger* came the *energy* we needed to fight for our children. We decided to search for *our* own answers, to see what researchers were working on. We decided to find *our* own ways to help our children be the best that they could be. We decided to rely on *our* own judgement of what was right for our family. We decided to not accept the standard form of medical treatment for our children's disabilities. We took responsibility and control of our family's future.

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With this control and responsibility came extreme skepticism and lack of support from most physicians and therapists. What we proposed in the form of treatment for our children was considered by many to be alternative, extreme, and controversial. Nonetheless, we felt it was our best chance to enable our children to become independent, self-sufficient adults. We were willing to take the risk. It was a risk that would have huge pay-offs if it was successful. And it was for our family. We would have never forgiven ourselves if we hadn't at least tried these interventions: these controversial, alternative treatments. Yes, they took an extraordinary amount of time and effort. And yes, our lives were certainly anything but normal during the initial stages of implementation, but we managed. Sometimes we managed quite well and sometimes not, *but it wasn't impossible*.

I would like to share with you our family's journey. It wasn't easy and there were many times when we doubted our decisions. But our sons who had been diagnosed with autism and attention deficit disorder are entering kindergarten and second grade this year *without* an educational label. They will **both** be in a regular education classroom. They do not require an aide or for that matter an individualized education plan (IEP). My husband and I believe, beyond a shadow of a doubt, that this would not have been possible without all of the interventions we chose for our children.

I know all families will not make the same decisions that we did for our children; every family and child with a disability is unique. I also recognize the fact that not all children with autism and attention deficit disorder (ADD and ADHD) will benefit as significantly as ours did from these types of interventions. But I do want to encourage you to read carefully the information presented in this book and give it due consideration. *It changed my family's life*.

I would now like to discuss in detail our journey with our first child Alan who had attention deficit disorder and then our second child Taylor who was diagnosed with autism.

Alan

Alan was very blue at birth, which concerned us somewhat, but he recovered quickly once the nurse gave him oxygen. I was able to hold and nurse him shortly thereafter. He spent his first night curled up next to his father on a cot beside my hospital bed. All things considered, the whole experience went relatively smoothly. We were dismissed from the hospital ten hours after the birth of Alan, our beautiful, 8 pound baby boy, ready to embark on our new life as a family.

We knew to expect a lot of crying from the latest member of our family; newborns do that. And we knew that lack of sleep would now be a part of our lives; this was also part of caring for a new baby. What we didn't know, because this was our first child, is that babies typically sleep for more than an hour at a time, that they shouldn't throw up almost as much as they eat, that colic doesn't mean that they scream for hours on end every day, and that they typically don't need to be in constant motion to not cry, at least not for the majority of a twenty-four hour period.

Ten days after his birth, we took our son to the physician's office. We were reassured that all babies cry and were told that our son could possibly have colic. I barely touched on the fact that we were walking, rocking, or swinging our son in an effort to calm him almost all of his waking hours, which were plenty.

I decided not to go back to work at the end of my maternity leave and opted to stay home and care for Alan.

At six months of age, he still wasn't sleeping like we knew he should. He wasn't throwing up any more, but he was drooling excessively. The constant screaming and crying that resulted in us walking, rocking, swinging, and bouncing him many hours every day was replaced by loud vocalizations and constant motion on his part. By six months of age he could navigate a walker anywhere he wanted to go. We referred to him as a very "busy" child. He was never still!

While we knew Alan wasn't like any of our friend's children, we didn't really know how to articulate these differences to the professionals. He wasn't behind in his development, *just different*. We didn't know how to convey to them that there must be some unknown medical reason for Alan's peculiarities. Consequently, we were never referred to the services and supports we needed. We continued to attribute all of his "odd" behaviors and any developmental deviance to a visual impairment, which we were unclear about because our physicians did not give us good information. We allowed his vision to become the scapegoat. It would take the birth of our second son for us to start putting the developmental puzzle pieces together in order to get the intervention both of our children needed.

When Alan was eight months old, he was prematurely given his fourth DPT shot by the clinic nurse. It had only been five weeks since he had received his third DPT shot and there is supposed to be a minimum of eight weeks between vaccinations. I didn't realize at the time that this shot should not have been given. I vividly recall the nurse taking Alan's immunization card and "whiting out" the information that she had logged about this DPT vaccination. I thought she put the information in the wrong place and was making a correction.

One of the problems this *correction* caused was that our son received one too many DPT vaccinations. This fourth vaccination was never logged on his immunization card. It never occurred to us that the nurse had made a serious mistake. Not only did Alan receive a DPT vaccination three weeks prematurely, he also received an extra DPT vaccination eight weeks later because the nurse, covering up her mistake, falsified his immunization card! Quite frankly if I had known of the mistake at the time, I am confident I would not have understood the significance it would make in our son's health. We simply did what we were told and believed everything the medical professionals told us. That *in itself* is amazing given both my husband's and my own personality.

Prior to this, Alan had never run a fever or even been cranky after receiving a DPT shot. But it wasn't going to be so easy for him this time. He went to sleep very easily and early that night, which was highly unusual for him. Concerned because he hadn't put up his typical bedtime fight, I went to check on him after a half hour or so to make sure nothing was wrong. I found him arched back, shaking, and running a pretty good fever. Terrified, I screamed for my husband Bill to come and help me. We sponged him off to lower the fever and the convulsions stopped almost immediately. Alan was now awake, alert, and somewhat cranky.

We called the doctor's emergency number and were asked about Alan's current status. When the doctor learned that he now appeared to be fine and was only running a low-grade fever, he asked what fever reducing medication I had administered. I sheepishly told him none. While I certainly kept some on hand, Alan had never needed any due to a DPT vaccination or, for that matter, any illness. I was chastised and told that Alan's convulsions were due to the fever and to administer the fever reducing medication immediately and continue giving it for the next 24 hours. We were asked to bring him in the next day for a full checkup, which we did.

Feeling very guilty and responsible for his reaction, we stayed up for the remainder of the night to keep a close watch on him. We took him to the clinic first thing the next morning. During this visit, they made it *extremely* clear that Alan's reaction was due to the fact that we did not give him fever reducing medication. If we had understood the vaccine information we received, we would have known to administer the fever reducing

medication. We were never informed that they had incorrectly given our son a DPT vaccination three weeks prematurely. They never even reported Alan's reaction to the proper agencies. This "error" went undetected by us for over three years. I guess the hardest thing to deal with is the fact that the clinic made us feel responsible for Alan's fever and subsequent convulsions, when they were negligent.

In spite of receiving one too many DPT immunizations and one of those being given prematurely, Alan continued to grow and develop. His development had always been somewhat different and the truth of the matter is, the unfortunate vaccination mistake didn't change any of his *outward* behaviors. *(We now feel confident that these vaccination errors intensified his unusual immune system responses.)*

Alan never learned to crawl but was pulling up and "cruising" by the time he was seven months old. And by the time he was eight months old, he was walking very well and into everything. He had also mastered climbing out of his crib, so bedtime was literally a nightmare. When he did stay in the crib, it was to bounce it across the floor or bang it into the wall. I was going crazy!

The other moms I knew could place their child on a blanket on the floor with a few toys and actually get some things done around the house. But not me! These other moms also had children who took naps. I didn't dare let Alan sleep during the day or we would be up all night, instead of the luxurious three maybe four hours of uninterrupted sleep we were getting. Of course this sleep came after Alan had put up at least an hour and a half worth of protest. It wasn't that he wasn't tired or sleepy; but he just couldn't be still or relax long enough to allow himself to sleep. These horrific sleep patterns continued until Alan was 4 years old. This child had endless energy and we were exhausted.

If nothing else, Alan was consistent. His strong preferences about everyday routines were carried over into his eating habits as well. I had been making my own baby food for Alan, but he was very particular about what he would eat. His favorite food groups, after nursing, were dairy and grains. He enjoyed only a few other foods and this disturbed me somewhat because he was on the low end of all the growth charts every time we went to a well baby visit. I thought perhaps if he consumed a wider variety of foods it would help him to gain weight. How much he ate wasn't the problem, he had a sufficient appetite. But his strong attraction to certain foods bothered me.

Alan tolerated the rice and barley baby cereal I fed him, but he loved cottage cheese, American cheese, mashed macaroni and cheese, yogurt, scrambled eggs, applesauce, bananas, and almost any kind of bread or cracker. I had no way of knowing at the time that these very foods were responsible for a large portion of his hyperactivity and sleep disturbances (even though we didn't call it hyperactivity back then). We were unaware that Alan had been plagued with significant food allergies since birth and that a majority of his atypical behavior and development could be explained by these allergies.

I was having a difficult time keeping up with Alan as I entered into my second pregnancy. He seemed to be getting more restless and noncompliant. We attributed this to the terrible two's and the expectation of a new baby. I can remember when the new baby started moving. It was so different from Alan's movement in the womb. While the new baby was gently stirring, I would recall how Alan had *literally* almost broke my ribs a few weeks before delivery! In fact, he had been a very active baby even before he was born.

And so, five months into focusing on Alan's needs, I gave birth to our second son, Taylor.

(We would later learn that while Alan did not have elevated fungal metabolites due to yeast, he did have elevated levels of anaerobic bacteria products commonly found in children who have been diagnosed with Attention Deficit Disorder and Attention Deficit Disorder with Hyperactivity.)

Taylor

The first year of Taylor's life, we watched him experience a "typical" development. In doing so, we realized how atypical Alan's development had truly been. Taylor actually played with his baby toys and could entertain himself. He was so much calmer than Alan that when we looked back on Alan's first two years of life, it was hard to believe we had survived.

Taylor continued to grow and become his own little person. He was blossoming. He had a wonderful sense of humor, could follow simple instructions, and by one year of age was able to combine a few words, "mama up, want down, go bye-bye, I love you, want more." And he was proficient at making farm animal sounds upon our request! Like his brother, he was an early walker, mastering this feat at 10 months of age after a short stint of belly crawling.

When he was approximately 10 months old, I stopped breast-feeding him (actually he was just not interested in nursing anymore) and was having a difficult time finding a formula he would drink. Against the advice of our *new* family physician, I began to give Taylor whole milk. He just would NOT drink anything else (or so I was inclined to believe at the time).

Within a few weeks of adding whole milk instead of a formula to his diet, he needed a round of antibiotics to clear up an upper respiratory tract infection. This would be the first antibiotic in a long line of prescriptions that Taylor would receive for his **repeated** infections. Though the physician was aware that I was giving Taylor whole milk (occasionally Taylor would tolerate the Carnation Good Start formula), the correlation between the increase in milk products and subsequent infections was never made.

Over the course of the next year, Taylor was sick more often than he was well. We were told he had common upper respiratory tract infections. He looked and felt terrible most of the time. In fact he was sick so often, the physician began writing Taylor's prescriptions to be refilled without an office visit, for our convenience. In spite of feeling ill most of the time, Taylor continued to develop typically, *for a while*.

As you know, when a child doesn't feel well it can be a stressful event for the child *and* the family. It was very distressing to have a toddler who was constantly sick and it began to trouble me deeply that we could not find the cause of Taylor's ever increasing upper respiratory tract and occasional ear infections. The antibiotics being prescribed were becoming less effective, more potent, and quite expensive.

Between 10 months and 22 months of age, Taylor received 7 rounds of antibiotics. He began developing dark circles under his eyes and a constant wheezing sound in his chest. At diaper changes, we began noticing that his urine had an odd musty smell to it. He began to have consistent loose stools that often contained mucous, but it was not diarrhea. His genital area would be **VERY** red at times and as soon as his diaper was loosened at changes, he would grab his reddened genitalia. (Dr. Shaw's note: all of these symptoms are characteristic of intestinal yeast overgrowth.)

A significant sleep disturbance was emerging as well. He started having difficulty going to sleep and began waking up at least four times in the night shaking and crying pitifully. He would literally *gulp down* one or two glasses of water as fast as he could and then fall back asleep. He didn't seem to urinate sufficiently for the amount of fluid he took in either. He started to ignore our requests and stopped following simple commands. He became very cranky, tired, and agitated most of the time. We thought he was starting the terrible two's somewhat early when, in fact, *he was changing in a different way*.

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Between taking care of a sick toddler who was up several times a night and trying to keep up with a child who slept very little and was extremely energetic (*hyperactive*), I was beginning to feel overwhelmed again. I knew in my heart of hearts that something was going on with my children; I just couldn't put my finger on it.

While Alan was making definite progress in many areas of development, we still had areas of concern about other aspects of his personality. He just never sat still and played appropriately with toys. He was constantly in motion: running, rolling, and spinning. He was frequently making this odd "p-shoosking" sound. He had also begun to ask us questions repeatedly. (*We would answer his question and two to five seconds later he would ask it again. He would continue asking, sometimes to a point of breakdown, his and ours.*) He was grinding his teeth down to nothing and compulsively biting the skin around his nails. He was obsessive about insisting on sameness in household routines and he was becoming very disruptive. He felt the need to empty **everything** in a closet, toy box, drawer, cabinet, whatever, into a pile in the floor. It didn't matter if you were visiting someone else's home either; if the urge came over him, it was done.

In addition to this, he was becoming aggressive toward his brother. I couldn't leave Taylor unattended in the same room with Alan for fear he would hurt him. It wasn't that he didn't love his brother or get enough one-on-one attention from his father and I either. (This had been suggested to us several times when we would discuss our concerns with family, friends, and professionals.) Alan simply couldn't control himself. He was having trouble listening to us at home and his preschool teachers were having difficulties getting him to following directions at school as well, even though he was an incredibly bright little boy.

I recall visiting with a friend from church one day about Alan's behavior. It was immediately after he had consumed a cup of red fruit punch in Sunday school. I never purchased this brand of punch, preferring 100% juice. Alan was *literally* climbing the walls within 15 minutes of drinking it. Needless to say, we hurried home from church. By the time we got home, Alan was extremely agitated. He started rolling on the floor and making odd vocalizations. He was unable to focus and could not control his emotions. Fortunately, my friend had heard about the dyes and preservatives in foods causing these types of adverse reactions in some children and shared this information with me.

This was news to me and I was skeptical. I was also desperate to find answers about my son's behavior because I didn't feel like an effective parent. I decided to put this newfound knowledge to the test. Not believing food could actually cause this type of a reaction, I purchased the same brand of punch Alan had that day at church. I gave it to him for lunch. Our afternoon was not pleasant!

Once again, he exhibited the same type of reaction: rolling on the floor, odd vocalizations, agitation, and emotional distress. I was clearly shocked that food could cause my child to behave in such a fashion. With that seed being planted, I began to wonder about what else food could do to effect behavior and health. Could there be a connection between Alan's strange behavior and other foods? Could Taylor's chronic illnesses be allergy related?

I didn't have to wait long before I had my first opportunity to visit with our family physician on this topic. Taylor had developed yet another infection. This time when I went to the physician's office, I was armed with a list of questions regarding food allergies and illnesses. I was told Taylor's chronic infections had absolutely **nothing** to do with food allergies. All children catch several colds their first two years of life which easily lead to the secondary infections Taylor was experiencing. I was also told that food dyes were safe and did not in any way affect behavior in children. END OF CONVERSATION. At least with him anyway.

I didn't feel confident pursuing the matter any further and left with yet another prescription for antibiotics. I thought his response was a little too emotional and the finality with which he made his claim somewhat

disturbing. One thing was for sure, Alan would not be ingesting any fruit punch or other foods that contained colors or dyes even if the physician believed there was not a connection between food, allergies, and behavior!

Taylor's development was typical up until he was 15 months old, with the exception of the constant infections. Since his birth, we had the good fortune to participate in a Missouri Department of Education Program called "Parents as Teachers". The program assigned us a parent educator that came to our home for routine visits. The parent educator distributed parenting and educational materials, administered a developmental screening, and documented the findings. Taylor met or exceeded all expectations on each of these screenings until he was 17 months old.

During this particular home visit, the educator asked me about imitation, or the emergence of it, in Taylor's play. I really had to think hard to remember if I had seen him doing anything like that in awhile. I couldn't confidently answer her question. At 17 months of age, this type of play should be developing and she told me to watch for it over the coming summer. This was in May and her next scheduled visit would be in the fall, when the school year started. We would not have to wait that long to discover that Taylor was not on track.

My inability to confidently answer the educator's question tormented me. I began to mentally go over Taylor's development and note the changes in his behavior. Taylor had certainly started communicating early. He had begun using words and putting them together precociously. But he just didn't seem to have the desire to talk anymore or to participate in our family. When I would mention this to family members and friends, I was cautioned not to compare my children to one another. Meanwhile, Taylor continued to withdraw and I was scared.

By the time Taylor was 18 months old I was becoming increasingly alarmed. While I was watching for him to start imitating in his play, I noticed how differently he had started to interact with his toys. It wasn't the same type of play he had exhibited several months earlier and he would throw an absolute fit if you interrupted him or tried to play with him. By the time he was 21 months old, it appeared to me that Taylor was purposefully ignoring my simple requests to interact. Then I began to question his hearing.

I discussed this with my husband and we felt like it was certainly a possibility worth pursuing. We decided to ask babysitters, Sunday school teachers, friends, and relatives if they had noticed a difference in Taylor's personality. We asked if they thought he was fussy and cranky because he couldn't hear and was having a hard time understanding what was going on. They all agreed that he had become withdrawn, "spaced out", and difficult to manage. And then one of them said, *"Well, I have noticed he doesn't talk much anymore and he seems upset much of the time. He used to be so happy."*

We decided to test his hearing ourselves. We set up a variety of opportunities for Taylor to interact with his family and environment. For one of our tests, we quietly came into the room with a pot and spoon and began to loudly bang it, repeatedly, in close proximity to his head. He was sitting in the middle of the living room floor manipulating his toy cars (lining them up) and HE DIDN'T EVEN FLINCH. He was absolutely lost in his own world. We stood there watching him for a few seconds, waiting to see if he would acknowledge our presence. He did not. I can't begin to tell you how scared we both were. The remaining tests we devised proved to be just as disappointing. I immediately made an appointment for Taylor to see our family physician.

Because we had insisted on the first available appointment, we saw a new physician in the practice. He was a very good listener and legitimized our concerns. He called an ear, nose and throat clinic while I waited and scheduled an appointment with an audiologist for the following morning. He agreed that we needed to investigate a possible hearing loss.

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Surprisingly, Taylor cooperated nicely for the audiologists. They placed him in a high chair in the middle of the testing booth. He turned on cue every time he heard a sound. He “passed” all their tests. I was confused. I discussed, *in detail*, my concerns about his hearing. I was told he had scored within normal limits on all their tests and they hadn’t found anything out of the ordinary. They recommended I wait a month and discuss my concerns with our parent educator through the Parents as Teachers program. (I had filled out an extensive patient history.)

I boldly refused this advice and insisted on a visit with the ear, nose and throat (ENT) specialist (otolaryngologist). I needed a *physician’s* opinion on Taylor’s hearing. While I was scheduling this appointment, I learned that the clinic had a speech pathologist on staff and requested an appointment with her as well. If Taylor wasn’t communicating anymore, maybe she could help us figure out why. Fortunately, the ENT doctor and speech pathologist agreed to work us into their schedule that afternoon.

That afternoon my husband and I took Taylor to the clinic for his preliminary evaluation with the Speech Pathologist. As she observed Taylor and began to ask us questions, we had the realization that something very serious was going on. After she had gone over all the forms and questionnaire we had filled out, we were asked to wait in the reception area so she could consult with the ENT doctor.

The ENT doctor was a compassionate man who listened intently to our concerns and fears. He observed Taylor manipulating toys and tried to interact with him repeatedly. He looked at us with genuine anguish as he shared the speech pathologist’s findings and his own conclusion. Their findings indicated that something other than his hearing lay at the root of our concerns. They were both sensitive to our feelings and very understanding. (We weren’t accustomed to this.) He suggested that Taylor see a pediatric neurologist **immediately**. There was only one specialist of this nature in our area and because he was new, his schedule was full. Though the ENT had tried to get us in the following day, we had to wait a week for the appointment. Needless to say, it was an unpleasant week for our family.

Suspecting your child’s development is out of the ordinary and having those concerns validated by a specialist is terribly frightening. We had wholeheartedly anticipated that the ENT would find the cause of Taylor’s mysterious behavior to be linked to a hearing loss.

Since you don’t see neurologists for anything remotely routine, we were very nervous about the appointment. Because we were so afraid and didn’t have a clue what to expect, we filled our time by examining Taylor’s development. We began by polling all the people involved in his life. We talked about their answers and shared our own observations. Then we compiled a list of all the changes that had occurred in Taylor’s personality and development over the past few months. The list was quite extensive.

1. Lack of language or any verbalization
2. Loss of previously used words and phrases
3. Severe sleep disturbances
4. Constantly tired, cranky, and unhappy
5. Spaced out
6. Dark circles under his eyes
7. Spinning himself for an unusual amount of time per day
8. Chronic infections
9. Possible hearing loss
10. Unusual play with toys
11. Resistance to human interaction
12. Developing a weird gait while walking

13. Toe walking
14. Teeth grinding
15. Odd change in hair color and texture
16. Unaware of his environment and the people in it
17. Purposefully putting himself in tight places (i.e. between the wall and refrigerator, and under couch cushions)
18. Excessive thirst at night
19. Lining up his toys
20. Avoidance of eye contact
21. Putting his body at odd angles to look at things
22. Prolonged temper tantrums
23. Clumsiness (previously he had been very well coordinated)
24. Musty odor to urine
25. High tolerance for pain

Shocked by the number of items our list contained, we realized how serious Taylor's situation was. We had never sat down and analyzed his development before. It was clear he was regressing. Feeling intimidated, we asked Bill's mother to go with us to the neurologist for moral support. In the meantime, we began searching medical books and looking on the Internet for possible solutions to the symptoms Taylor was experiencing. Autism was the word that kept cropping up.

Our encounter with this particular neurologist was the best and worst thing that could have happened to our family. Despite his poor bedside manner, the visit started off typically enough with him looking over Taylor's file. He read our family doctor's report, the ENT doctor's report, and the speech pathologist's report. He asked a few questions (some of them we found quite odd) and made an inflammatory remark about the speech evaluation. We were then moved to an examination room where he tested Taylor's reflexes, tracked his eye movement, and watched him walk.

I cautiously brought up the subject of autism and asked if he felt this could be at the root of Taylor's regression. I was told (in a very condescending manner) that children who have autism were very different from our son and that autism was evident from birth. Because of our recent research into Taylor's regression, I knew this was not totally accurate, but I wasn't sure how to respond.

In a manner you would use to tell someone their child has a cold, he informed us of our son's suspected misfortune. *"It doesn't look good for Taylor,"* was his first statement. The three of us were dumbfounded. "What do you mean, it doesn't look good?" I asked.

He proceeded to tell us that Taylor had a neurodegenerative brain disease, that we would have to do extensive testing to determine which disease it was, and that these diseases were incurable.

I pressed on, "What do you mean incurable? Will he die from this disease?"

His response was even more shocking *"Yes. It could take 18 months or 18 years depending on which disease it is. But you better hope for 18 months, because the pain and suffering are unbearable."*

I was numb. I could clearly see that my husband and mother-in-law were as astonished at this remark as I was.

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We assumed he found something conclusive in his examination of Taylor that would give him the confidence to make a statement like this. "What causes this disease?" was our next question. Another offensive response: *"It's genetic. Let's just say that it is unfortunate that you and your husband met and had children."* Terrified, I asked the next question. "If it's genetic will it affect our other son?" His answer: *"Once we determine which disease Taylor has we will have to test Alan. Chances are he will acquire this disease as well."*

Feeling the crushing weight of the world, we sat in silence, in disbelief. He told us we would need to have blood tests done immediately to determine which neurodegenerative disease we were dealing with. It would take six to eight agonizing weeks before we could expect to have the test results back. Since these were rare diseases, not all labs were equipped to administer the tests. The blood would have been sent to laboratories in several states. Physician's orders in hand, we made our way to the hospital laboratory.

The two months of waiting were a nightmare. I remember thinking how nice a diagnosis of hearing impaired or autism would sound in comparison to being told you were going to lose one and quite possibly both of your children to a hideous disease. We stumbled through the days and cried through the nights as our lives came crashing down around us. We poured every ounce of energy into interacting with Taylor. We refused to watch him leave us without a fight.

Remembering the speech pathologist who had been so compassionate and understanding, we decided to give her a call, to take a chance. We knew full well that if Taylor had one of these neurodegenerative diseases, a speech therapist would be of no help. We asked her to start coming to our home twice a week. My husband and I wanted to know how to communicate with the son we were losing. With reservation, she accepted the challenge. It was one of the best decisions we ever made.

The day for answers finally arrived. We had prepared ourselves as much as we could for the news. When we entered the neurologist's office, it was evident that his tone and demeanor were somewhat different from our initial visit. He wasn't quite so abrasive and egotistical. Almost begrudgingly, he informed us that all of our son's tests were normal. (The urine organic acid test done initially was done at a laboratory that did not check for byproducts of microorganisms). He couldn't answer any of our questions except to say that if he were in medical school and Taylor's history was presented as a case study on an exam, he would have failed the exam had he not proceeded in EXACTLY the same manner in which he had.

The neurologist wanted us to see a child psychiatrist. He said he had spoken with her about Taylor and that she would be the appropriate professional to help us. When I called to make an appointment, I was told what the visit would entail, how long to expect to be there, and the cost. When I asked about the specific developmental tests mentioned, I was told that these were the standard tests administered when diagnosing autism or pervasive developmental disorder. I WAS FURIOUS! I thanked the receptionist for her time and promptly canceled the appointment.

I have since learned that the child psychiatrist is a competent, well-respected professional. But I wasn't about to see a professional recommended by the neurologist who so condescendingly informed my family that Taylor's regression had NOTHING to do with autism.

Diagnosis of Autism

Knowing that because of this misdiagnosis we would always and forever get a second medical opinion on anything remotely serious, we scheduled appointments for Taylor to be evaluated by our local regional center (the state agency responsible for diagnosing and providing services to individuals with developmental disabilities) and a team of neurologists at a University Autism Clinic. We went through all the testing and questions and watched with agony as Taylor failed to comply with their requests. They were all in agreement: late-onset infantile autism. It became Taylor's official diagnosis.

Intervention

The diagnosis of autism was easy to take after believing your son was going to suffer a slow, agonizing, painful death. So, while Bill focused on meeting our growing financial demands due to the necessary therapies (*by working three jobs*), I focused on educating myself about autism.

Taylor had been participating in speech therapy for over a month when he was officially diagnosed. Immediately after receiving a confirmed diagnosis, we added small group speech therapy (at a local university communications disorders lab), occupational therapy (with an emphasis on sensory integration), and in-home behavior management. Initially, the only one-on-one therapy Taylor received outside the home was occupational therapy and we changed this to in-home as soon as possible.

Though Taylor seemed to be benefiting from these interventions, we knew he was going to need something more if we wanted to get our happy little boy back. I was fortunate enough at this time to come across work by Dr. Bernard Rimland and Dr. Ivar Lovaas. I soon realized that we should consider a nutritional approach as well as an intensive one-on-one program.

The occupational therapist that did Taylor's initial evaluation was intrigued by my comments on a dietary approach. She shared with me information about a family she worked with whose child was diagnosed with autism. *Some* of this particular child's autistic behavior was directly related to the food allergies he struggled with. While a diet did not cure this child, the results were remarkable. The occupational therapist arranged for me to visit with this family who was willing to share their experiences with an elimination diet (which helps detect hidden food allergies) and other allergy interventions. I was grateful.

As a direct result of my conversation with this wonderful family and my own experience with foods causing adverse reactions (Alan and the red fruit punch), I decided to start with a dietary/nutritional approach. While I was reading one of Dr. Rimland's papers regarding the removal of certain foods from the diet and the positive effects it had on some children with autism, I noticed a one-line statement about Candida-related autism. My interest was piqued. I knew first hand that a round of antibiotics could cause a vaginal yeast infection and I decided to look into the matter since Taylor had certainly had more than his fair share of antibiotics.

I first learned everything I could about yeast and its possible effects on the body.

It seemed logical that Taylor's loose, mucous-containing stools were the direct result of a yeast overgrowth. It also seemed logical that the redness around his anus and in his genital area, which we thought was a diaper rash, was actually a yeast rash that was causing an intense itching feeling. It could also explain his urine's musty odor. I read that a yeast overgrowth could cause fatigue, which Taylor certainly suffered from.

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In one of Dr. William Crook's papers (author of *The Yeast Connection*, *Tracking Down Hidden Food Allergies*, and many other books and articles on allergies and yeast) he talked about ear infections, upper respiratory tract infections, antibiotics, and their relationship to allergies and childhood behavior. I became confident there was a correlation between Taylor's chronic infections, antibiotic use, and his subsequent regression.

During my quest to learn about yeast, I came across a book entitled "*Dr. McFarland's Anti-Candida Diet*". The book was actually a six-month program, divided into phases, to eradicate the overgrowth of yeast using a strict diet and a large number of nutritional supplements. Though the program was designed for adults with yeast related illnesses, it made sense to me and I decided to modify the supplement portion of the plan to accommodate a 24-month-old child.

(I would like to note that Taylor began taking Super-Nuthera powder approximately one month before we implemented an anti-Candida diet. His eye contact certainly increased with the addition of this supplement and he didn't have as many tantrums at transitions.)

As I began educating myself on diet and nutrition, it became very clear that Alan needed a diet overhaul as well. He had experienced hives on several occasions (*it wasn't always clear what brought on this reaction*) and he had also begun to have unexplained low-grade fevers, joint pain, muscle weakness in his legs, and migraine headaches. His hyperactivity and inability to concentrate were at an all time high. I didn't think he would benefit from the same anti-Candida diet I had planned for Taylor, (*I was mistaken*) but I certainly felt that he would benefit from having all colors, dyes, preservatives, sugar, and processed foods removed. I devised a separate diet and supplement program for him.

Initially, we were unable to find a physician who would listen to our concerns and help with the allergies we felt both of our sons were tormented by. (*In fact, it took us almost two years before we found such a physician*). Not only were physicians not helpful, but also we were told on more than one occasion that food or chemicals in the environment COULD NOT cause the type of reactions we were describing. We were bold enough on one occasion to bring copies of our programs for Alan and Taylor for their approval. What a mistake! We were told to not waste our time, that these alternative therapies were a hoax. Since these same physicians were unable to offer their own treatment plan (other than a pharmaceutical "fix" to help our children sleep), we decided to forge ahead with our plans and implement the necessary dietary and supplement changes.

Feeling extremely apprehensive about undertaking such an enormous task without a formal education in nutrition, I decided to consult with a pediatric dietician. The problem was, we couldn't get an appointment until well after the holidays. We decided to proceed on our own until our scheduled appointment. So approximately one month before Christmas, our family started on a journey that would lead to incredible successes for both our children.

We had developed a great relationship with Taylor's speech pathologist and she was very encouraging. We shared with her all of the information we had gathered and she felt it was certainly worth pursuing. Her encouragement meant everything. We also had the support of a family friend who had been fighting yeast-related illnesses for several years. She proved to be critical in helping us to modify recipes.

It is extremely intimidating to step outside the box of standard medical practice and it is so very critical that families receive the necessary supports when doing so. If our own family had not received support from a few key individuals, it would not have been possible for us to manage this type of intervention.

The following diet and nutritional supplement programs we implemented for our children were vital to the successes they achieved.

Anti-Candida Diet

- Hormone-free, free-range meats (*You will need to purchase free-range meat from a health food store or a natural food cooperative. Store-bought meat contains the hormones and antibiotics the animals have been administered.*)
- Fresh vegetables (*organic if possible*)
- Organic brown rice
- Filtered water
- Spices (*sea salt, pepper, and fresh garlic*)
- Expeller pressed canola oil (*Oils in the grocery store are derived through a process using petroleum-based chemicals.*)
- Now Brand Pure Vegetable Glycerin (*I used this to "sweeten" Taylor's rice and to add to his supplements so he would take them*)
- Hain Safflower Margarine (*DO NOT purchase the "no salt" formula as it contains a preservative that may or may not be from a natural source.*)
- Brown Rice Flour Brown Rice Pasta (*There are many brands available at health food stores that contain only filtered water, sea salt and brown rice.*)

This restrictive diet seemed to us to be the most natural approach to killing the yeast we felt was interfering with Taylor's development. Because Candida thrives in a sugary environment, we eliminated not only processed simple sugars, but all sugars (i.e. fruits and fruit juices, honey, maple syrup, brown rice syrup etc.) In our efforts to limit carbohydrates (which the yeast can convert to food to survive on), we had unknowingly removed gluten from Taylor's diet. We removed milk and dairy products because we felt confident they had played a role in Taylor's repeated infections. The diet portion of this program was relatively easy to follow since all processed foods were eliminated. Although it was not complicated, it took a little more time to plan ahead and prepare. Getting him to eat the foods was another matter.

Taylor's Supplements

- NON-DAIRY liquid calcium supplement *Since Taylor is now able to take his supplements in capsule form; I prefer to use calcium citrate capsules. I prefer to use calcium citrate capsules.*
- Magnesium *I now use magnesium citrate or magnesium glycinate in a capsule form that can be pulled apart and added to a food if the child cannot tolerate swallowing pills. Both our children now take their magnesium in a citrate and glycinate form.*
- Garlic Oil Extract (If your child can swallow pills, you may want to use the capsule form, but make sure it is the formula that does NOT contain whey, which is a form of dairy.) *I would get Taylor to take this by putting it on his pasta for flavoring. This product is an antifungal agent.*
- MCT Oil (medium chain triglycerides) (This product is broken down in the intestine to form the antifungal agent caprylic acid; see chapter on yeast and antifungal treatments.)
NOTE: If your child can swallow pills, caprylic acid supplements are very effective in killing yeast. *DO NOT attempt to pull caprylic acid capsules apart in order to add the powder to food, it is extremely bitter and causes a burning sensation on the mucous membranes in the mouth.*

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- Acidophilus (DAIRY FREE acidophilus in a powder, they also make a capsule form, it is to be given 30 minutes prior to meals in a small amount of filtered water) DDS now makes a powdered formula that contains FOS, (fructooligosaccharides). FOS is a natural carbohydrate that effectively promotes the growth of beneficial bacteria such as lactobacillus acidophilus and bifidobacteria in the lower intestine. (1)
- NOTE: When taking any form of acidophilus or FOS (fructo-oligosaccharides) it is important to gradually work up to the recommended dosage. Adding acidophilus too quickly can cause constipation OR diarrhea. FOS may initially cause gas and belching. (1)
- Zinc (chelated zinc gluconate and zinc picolinate, 30mg) *Taylor now takes zinc in the picolinate form only. If your child cannot swallow pills you can buy a capsule form, pull it apart and add it to food. You may also choose to purchase zinc in a liquid form.*
- Super Nuthera Multivitamin with high dose B-6 (powdered form) *Taylor still takes this supplement in the tablet form.*
- Choline/Inositol *At the time Taylor was taking SuperNuThera in the powdered form and it did not contain choline and inositol. I knew the tablet form did and decided to supplement these B vitamins. Choline is needed for nerve transmission and inositol is vital for hair growth. (1) Remember, Taylor's hair had changed colors and texture. It really didn't feel like hair at all, it was dry and brittle and when he was having a particularly bad day in regards to his behavior, his hair would literally be standing straight up. It was an unexplainable phenomenon.*
- (Multiple Mineral Supplement)
- (Evening Primrose Oil) Primrose oil contains essential fatty acids (EFAs) which aid transmission of nerve impulses and are needed for normal brain function. EFAs are also beneficial in the treatment of candidiasis. (1)
- CoQ10 (Coenzyme Q10) Is a vitamin like substance that resembles vitamin E, but which maybe an even more powerful antioxidant. It is also called ubiquinone. It plays a crucial role in the effectiveness of the immune system, it is beneficial in treating candidiasis, and it has the ability to counter histamine and therefore could be valuable to allergy and asthma sufferers.(1)

Getting Taylor to take all of his supplements was not an easy task. We developed a schedule and he took his supplements before and after every meal and at bedtime. It has been three years and nine months since we started using nutritional supplements and what he takes and the quantity has changed considerably. He is now able to take all of his necessary supplements with his breakfast and evening meal.

Alan's diet was not nearly as restrictive as Taylor's and was originally based on the *Feingold Diet*. The *Feingold Diet* addresses not only food allergies and sensitivities, but the relationship food additives play as well. We eliminated ALL preservatives, colors, dyes, and processed foods from Alan's diet. In addition, we had to eliminate many typically healthy fruits and vegetables. While this diet made a *marked* improvement in his behavior, we were still missing a critical piece of the puzzle. He took the following supplements while he was on this diet.

For more information about food-additive free diet contact:

The Feingold Association of the United States
 554 East Main Street, Suite 301
 Riverhead, New York 11901
 Phone: 800 321-3287
www.feingold.org

Alan's Supplements

- (Chewable Multiple Vitamin)
- MultiMin (Multiple Mineral Supplement)
- (Evening Primrose Oil)
- Citronex (Grapefruit Seed Extract)
- Pycnogenol (pinebark)
- CoQ10 (Coenzyme Q10) Is a vitamin like substance that resembles vitamin E, but which maybe an even more powerful antioxidant. It is also called ubiquinone. It plays a crucial role in the effectiveness of the immune system, it is beneficial in treating candidiasis, and it has the ability to counter histamine and therefore could be valuable to allergy and asthma sufferers. (1)
- (Multiple strains of probiotics, i.e. acidophilus)
- Zinc 30 mg(chelated zinc gluconate and zinc picolinate)

These diets will seem severe and too difficult for many families to adhere to. We decided on them for a variety of reasons.

In Taylor's case we had heard about using Nystatin to kill yeast overgrowths. We had even talked to a couple of families who had children with autism who had been using Nystatin successfully for several months. The problem was, when the child went off the Nystatin, the autistic symptoms returned. We didn't like the idea of a long-term use of any pharmaceutical agent and decided to try a "natural" approach with garlic oil, Lactobacillus acidophilus bacteria, and MCT oil first. Everything we read about yeast and Candida outside of "mainstream" medicine insisted on modifying the diet and using nutritional supplements.

In regards to Alan, we had learned that even fresh fruits and vegetables could cause adverse affects in individuals who are sensitive to salicylates. Salicylates occur naturally in many healthy foods and are found artificially in the colors, dyes, and preservatives used in so many of our processed foods. They can also be found in unsuspecting toiletries; mouthwash, toothpaste, etc. (2)

All things considered, we didn't feel like we had a lot of options. We were losing our youngest son to autism and our oldest son was beginning to experience unexplained physical illnesses. In the process of losing Taylor, Alan had begun to have migraine headaches. At first we thought it was due to the stress our family had been through as a direct result of Taylor's misdiagnosis. Then Alan began to experience low-grade fevers. Sometimes the fever was accompanied by muscle weakness in his legs and joint pain, other times not. At about this same time he also started to have hives. The diets just seemed like the right thing to try.

Implementing the Anti-Yeast Diet and Dealing with the Yeast Die-Off Reaction

Once we made the commitment, everything just seemed to fall into place. Researching and planning these interventions for our family was simple compared to the actual implementation! We had no idea how much skepticism and resistance we would encounter-- not from our children (*although they weren't too cooperative in the beginning*), but from family and well-meaning friends. We even had our own doubts and it was particularly difficult when Taylor experienced the die-off reaction (*Herxheimer reaction*) after only one day on the diet. We had read about this effect, but we were in no way, shape or form, ready to experience it.

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We had decided beforehand that NO MATTER WHAT, we would NOT go off the diet for at least ten days. By mid-afternoon the first day, I was ready to quit. Taylor had been extremely agitated and upset at his entrees for breakfast and lunch and Alan wasn't any too happy either. While the speech therapist was trying to interact with a very tired Taylor, I went to check on Alan. To my astonishment, he was sitting at his table coloring, inside the lines, something I had NEVER seen him be able to do. He was always either too busy to sit still or he would scribble wildly all over the paper. I decided to stick to my guns about the diet.

Taylor refused to eat ANYTHING the first day of the diet. We had anticipated he might be stubborn about some of the dietary changes, but we certainly didn't expect him to refuse everything. We made sure he drank an ample amount of filtered water, but that didn't alleviate our concerns about his well-being.

He actually went to bed early the first night of the diet, which frightened us considerably. For the past six months he had been fighting sleep horribly and at one point, he was sleeping one to three hours in a 24 hour period and *not all at one time*. The dark circles he had developed around his eyes were even more pronounced after only one day on the diet and he looked terribly pale. We were convinced we were somehow harming our little boy.

The following day didn't prove to be any better. Taylor was extremely lethargic and just lay on the couch for several hours, doing nothing. He had a thick greenish-yellow discharge in the corners of his eyes this day, and for several days thereafter. I prepared and offered him his "new" foods but he didn't have the energy to move, let alone eat. So another day went by and Taylor consumed NOTHING but filtered water.

By the end of the third day, I was in tears. Taylor was still experiencing flu-like symptoms and I was convinced we were killing him. When Bill came home (*working three jobs, we barely got to see him anymore*), he was able to coax Taylor into eating a few green beans and a couple of small pieces of meat. Taylor had NEVER eaten meat that wasn't processed (i.e. ham, meat sticks, lunch meat, and hot dogs) and I couldn't believe Bill had been able to get him to swallow it. Things were looking up.

By the fourth day, he started eating *some* of his new foods. He still wasn't thrilled with his options, but each day got easier as he slowly began to accept his new diet. The supplements were a little trickier. He soon realized, however, that we were just as stubborn as he was on this issue and he gave up fighting. (There were many days I spent the majority of my time getting him to swallow his supplements.) About ten days into the diet, Taylor's energy level returned.

The Tide Begins to Turn

Everyone who was involved in Taylor's therapy noticed a major difference IMMEDIATELY upon the implementation of the diet and antifungal supplements. We knew we had made the right decision. While the diet and antifungal therapy certainly did not cure our son's autism, it helped him in many significant ways. His eye contact was increasing and his tantrums were lessening in frequency and severity. He was certainly not as spaced out anymore, and he was able to pay attention and focus more on the *people* in his environment.

After only one month on the diet, his allergic symptoms were vanishing and he looked so much healthier. His dark eye circles were almost non-existent, he wasn't wheezing anymore, and he didn't have the chronic running nose. We decided it was time to forge ahead and add the next component: an intensive, one-on-one, 40-hour per week, home-based program.

Home-Based Program

It took us two months to devise a plan that would meet Taylor's needs and not totally disrupt our lives (our so we thought). We had already established a solid foundation of therapeutic intervention for Taylor. He was receiving speech therapy (both one-on-one and group), occupational therapy (with an emphasis on sensory integration), and Bill and I were working with a behavior management technician from a local agency in an effort to learn how to *consistently* and *effectively* handle Taylor's tantrums and non-compliant behavior.

I had the privilege of talking to Dr. Bernard Rimland about the incredible improvement Taylor was making simply by manipulating his diet and adding nutritional supplements. He suggested I talk with a colleague of his who had a child with autism. Through my discussion with her, I learned about the book *Let Me Hear Your Voice*, by Catherine Maurice. It is an incredible book that I used as my guide in setting up Taylor's program. I had already read *The Me Book*, by Dr. Ivar Lovaas, and was aware of the studies that had been conducted using a discreet trial method of teaching (ABA-- applied behavioral analysis). The results of the studies were impressive and we decided to implement this type of teaching technique into Taylor's program.

Because of Taylor's group therapy, I had the advantage of knowing a few professors and many graduate students at the university. It was relatively easy to convince them to participate in our program. Many of them had personally witnessed Taylor's improvement at the onset of the dietary intervention. The key component that was missing was someone who would commit to helping me write and implement a program specifically for Taylor.

We decided to ask the behavior management technician that we already had a relationship with. We fully expected to have to beg her; Alan and Taylor weren't the easiest children to work with! She gladly accepted the invitation and would later prove to be the cornerstone of Taylor's program. Without her loyalty, commitment and dedication, I am confident my children would NOT be where they are today.

The following program changed periodically over the 17 months of its existence. For the most part, we were able to keep the core group of therapists that initially began working with Taylor. Of course, college students graduated and moved on and a few needed to quit because Taylor was so difficult to work with, at least in the beginning.

Therapy Schedule

Occupational Therapy.....	2-3 hours per week
Speech Therapy (<i>one-on-one</i>).....	3-5 hours per week
Speech Therapy (<i>group</i>)	3 hours per week
Discreet Trial Training (<i>ABA</i>)	up to 10 hours per week
Community Integration	10 hours per week
<i>(We had serious problems with Taylor's behavior in public places)</i>	
Graduate Students	up to 12 hours per week
<i>(To insure Taylor was constructively involved in an appropriate activity at all times)</i>	

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Even though Taylor's behavior had greatly improved simply by modifying his diet, it was clear that he still needed to "catch up" in his development. He wasn't attempting to initiate communication and was content to be left alone for as long as we would allow (usually to line up his toy cars or blocks). At times he would still become extremely agitated if we tried to interact with him.

His resistance strengthened with the utilization of discreet trial training. He put up such a fight during these therapy sessions that we were questioning our decision to use this method of teaching. It took well over a month for him to settle down and start to make progress. At the time, his progress seemed painstakingly slow, but in reality it was quite fast. This portion of his program, which was initially very uncomfortable to witness, was an integral part of his success.

Six months into the anti-Candida diet and three into the home-based program, Taylor was doing so well that we began to add foods back into his diet. We chose not to give him dairy products (we suspected they were at the root of his repeated infections) and substituted soymilk and soy cheese. We didn't see any major changes. We then gradually added grains (i.e. wheat, cereal, pasta, etc.). Once again we didn't see any major changes. (*I want to note that Taylor had not been ill since the first few days of the anti-Candida diet!*)

With the exception of Alan drinking cow's milk, both boys were now on the same diet. Difficult as it was, we were very motivated to follow this diet to the letter, knowing how much it had improved our children's lives. Taylor was beginning to speak, his breakdowns at transitions were continuing to lessen, and his tantrums were becoming almost nonexistent. Alan was much more in control of himself. After being on the diet for a little less than two years, we were able to gradually discontinue Taylor's home program. He still received speech and occupational therapy but the emphasis was shifted to interacting with children his own age. He was still having difficulty with this.

Even though both boys had made remarkable improvements, they were far from having typical development. They both still had trouble focusing and paying attention to task. They could be extremely impulsive and emotional and at times they were very compulsive and obsessive.

And so we continued to plod along, pleased that the boys were doing better, but still feeling like there was something we were missing. It was about this time I read Lisa Lewis's article on *Understanding and Implementing Gluten and Casein Free Diet*.

I realized while reading Dr. Lewis's article that we had made a grave error when we added the soy products (they contained casein) and grains (they contained gluten) back into Taylor's diet. I also realized that this could be the missing ingredient in Alan's intervention as well. Determined to find answers, I called our family physician and asked him to order the blood and urine tests. (I had to argue with him over which laboratory we needed to send the specimens to.) A few weeks later we had our results.

The results were conclusive; not one, but *both* children had extremely elevated IgG antibodies to gluten, gliadin, and casein, and also to ovalbumin (egg). We swiftly removed all offending foods and basically went back to the anti-Candida diet with a few fruits added.

We expected to see the boys immediately improve with this removal of troublesome foods and were very disappointed when they didn't. They both developed skin rashes and Taylor even started getting hives that ranged from the size of peas to quarters on his scalp and forehead. (Note by Dr. Shaw: These rashes are extremely common when withdrawing from gluten- and casein-containing foods according to Dr. Karl Reichelt in Norway.) Their bowel movements changed to very loose stools and they complained of stomach

aches. These symptoms persisted for 6 weeks and were very intense. Agitated would best describe their disposition and aggressive their behavior during this period.

Since we knew without a doubt that the proteins in grains and dairy products were problematic for our children, we decided to stick it out. (I am not sure we would have had the fortitude to continue, if we hadn't had the test results to remind us why we were doing it.) It was one of the more difficult times we experienced. We had been accustomed to continual progress (even though it wasn't fast enough for us) and this seemed like such a setback. Taylor, who had never been hyperactive, was becoming so and Alan was out of control. We had read in Dr. Lewis's article that it could take as long as a year to see any positive results after removing gluten and casein from the diet and we hoped we wouldn't have to wait that long. While there wasn't ever a regression in any skills they had mastered, both boys got *much worse* behaviorally for several months. They became extremely agitated and cranky. We encountered quite a lot of skepticism from some family members about the effectiveness of this "crazy" diet.

While I was out in the community, I ran across another mother with a child who had autism. She knew about my children and I began sharing with her our latest experiences with gluten and casein removal. She told me about Dr. William Shaw, a researcher in Kansas City, who was doing urine organic acid testing to determine the levels of abnormal fungal metabolites in children with autism and attention deficit disorders. She had ordered the test for her daughter. Although her daughter had taken antibiotics on only one occasion, she had elevated levels of fungal metabolites. I knew we had to order the test for our boys. I began to wonder if Taylor might still have a yeast problem, even though he had made such incredible progress, and I wanted to assure myself that yeast wasn't the culprit in any of Alan's difficulties.

We were excited to learn that we didn't need to make a doctor's appointment to order the test, (our doctor just needed to sign the release) and that the urine organic acid kit would come directly to our home. We sent for the kits, administered the tests, and waited anxiously for the results. We were very surprised to learn that the children's test results were so similar!

Taylor's urine organic acid results performed in Dr. Shaw's lab showed increased tartaric, possibly of a fungal origin and both Taylor and Alan had increased dihydroxyphenylpropionic-like compound of possible anaerobic bacterial origin in their urine. I didn't know what to make of the test and called Dr. Shaw to discuss the results. He was very helpful and after going over the boy's tests with him, I decided to make changes in their supplement program. The most significant finding this test revealed was that both children had high levels of byproducts probably derived from the Clostridia family of bacteria. *(I can only imagine what Taylor's test results would have been prior to the anti-Candida diet.)*

The following day we began increasing the number of probiotics (i.e. Lactobacillus acidophilus) the boys were taking. Gradually we worked up to 15-20 billion organisms a day, or 15 to 20 capsules, depending on which brand we were using. We were trying to replace the anaerobic bacteria, probably from Clostridia bacteria, with "good" bacteria. We continued using this high dosage for six months and then slowly backed down to 5 billion per day, which is the dosage both boys are currently taking.

Even with all the progress the children were making, we began to wonder how long we could continue to live on such a restricted diet. If you indeed call it living! We heard about an *immunotherapy with enzyme-potentiated desensitization* (EPD, see chapter on the immune system) and decided to pursue it. We found an environmental allergist in the Kansas City area who used this form of allergy treatment in his practice and we made an appointment.

Behavioral Effects of Food Allergies and EPD Therapy

After three days of testing to determine if the children qualified for the EPD allergy treatment, I was ready for the “nut” house. What we found was that both boys were not only allergic to ALL the foods we tested, but also to animals, molds, pollens and chemicals. Their reactions to the testing ranged from “passing” out, uncontrollable screaming and crying, hitting, spitting, licking other patients, and running wildly around the office, to falling asleep. If I had not been there, I never would have believed that corn, chocolate, apples, peanuts, wheat, molds, etc., could cause this type of reaction. In fact, I lived it and STILL find it hard to believe!

We decided to have a few more tests run to identify digestive abnormalities, possible PST enzyme dysfunction (see chapter by Lisa Lewis, *Understanding and implementing a gluten and casein free diet*) and vitamin and mineral deficiencies. What we learned was beneficial and it helped to explain why the diet and supplements were helping our children. Although we felt EPD might be advantageous for our children, we didn't look forward to any more restrictions being placed on the way we lived our lives.

After many discussions, we finally made up our minds to start EPD the following month. Preparing for the shot every eight weeks was (and is) a lot of work and the three-day diet you must adhere to is anything but tasty. We adjusted the children's supplements, because it is critical to follow the EPD supplement schedule in order to maximize the benefits of the shot. After six months of the EPD allergy treatments and nine months after the removal of gluten and casein from the diet, *both boys started making incredible progress.*

Alan began excelling in school. The learning difficulties he experienced (mainly, dyslexic tendencies and inability to retain information) had more to do with his allergies. Alan was finally able to pay attention and do age-appropriate work. His hyperactivity, unexplained fevers, migraine headaches, hives, joint pain, and muscle weakness have been almost totally alleviated. *He has been on EPD for 17 months now and has received 8 injections. He has had only two unexplained headaches and one instance of muscle weakness since starting EPD. Prior to EPD, he would miss three to five days of school a month because of these complaints.*

Recovery From Autism

Taylor stopped all formal therapies and was able to attend a typical preschool program, with minimal difficulties, 33 months after starting on the dietary and nutritional intervention program. They were NOT told of his “PREVIOUS” diagnosis of autism. He passed his kindergarten screening this past spring with flying colors and is excited about school. Dietary infractions can still cause him to have adverse reactions, but they are minimal and short-lived. He has friends he has made ON HIS OWN and they regularly call him and invite him to play. *Taylor has also been on EPD for 17 months and has received 8 injections.*

We are still gluten and casein free and we plan to continue the EPD treatment as long as necessary. *(Fourteen months into EPD, we decided to give the boys a shot of B-12 with their EPD shot to see if it would enhance its effects. It certainly seems to be making a difference.)* Currently, we can stretch the time between the children's shots to almost ten weeks without too many symptoms occurring. These symptoms can range from irritability to the inability to control emotions. It is our hope that through EPD, we may some day be able to add gluten and casein back into their diet, at least in limited amounts. But if not, their allergies caused by other foods and environmental factors *should* be eliminated. Only time will tell. While our diet is certainly

different from most and children shouldn't have to swallow umpteen supplements a day, it is worth the sacrifice. It is the reason our children have "recovered".

The Rest of Our Story

It has been a little over seven years now since my husband and I became parents. Most of those years we have spent trying to figure out a way to enable our children to lead healthy, productive lives. Many times, the very people who were supposed to provide us with support were the ones who put the biggest obstacles in our path. We learned to count on each other.

Researching and implementing the interventions we chose for our children took so much of our time and energy (not to mention money), that as I read our contribution to this book I am amazed we made it.

Alan and Taylor were certainly worth all our efforts. They started school a few days ago and as I watched them get on the school bus one morning and wave good-bye, I realized how fortunate our family was.

We were able to plan the strategies and interventions we chose for our children because we happened to come across the right information at the right time. It shouldn't be like this. All families should have access to the same information as we did, so that they may have the opportunity to choose interventions that could drastically affect the quality of their children's lives. All children with autism and related disorders deserve the chance to RECOVER. I hope that my contribution in this book will make the way easier for other families.

Chances are if you try any of these interventions, things may get worse before they get better. Don't give up. I remember wanting to quit hundreds of times. But every time I hear Taylor playing with a friend, or watch Alan draw one of his intricate pictures, I thank God I didn't.

(A videotape *Managed Recovery from Autism* is available from The Great Plains Laboratory. The tape documents Taylor's recovery from autism and includes footage before and after recovery.)

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Following a Different Path: A Child's Documented Recovery from Autism

Chapter 15

Karyn Seroussi

I wish that there was more public awareness about the early symptoms of autism. Too many of my sentences seem to begin with the words, "when I look back," or, "in retrospect...". I know this is all too common among parents of children with autism.

Even if I did know what I was seeing, even if a scarlet "A" had appeared on Miles' forehead, I still wouldn't have gotten any useful advice from my pediatrician. This is a disorder in transition, its etiology only beginning to be understood. No one walked up to me and announced that Miles' early developmental differences were treatable with changes in his diet. His diet, for heaven's sake! Who would have believed something like that?

When our son Miles was born, in December of 1993, he was a cranky baby. Not colicky, just crabby and unpredictable. He never settled into a routine, he spit up so much that I had to change my shirt after nursing him, and he didn't like to be held when he was tired; he preferred to cry himself to sleep. We never knew when he'd wake up again though; he could sleep for half an hour, two hours, four hours, or longer, if we were really lucky. This went on for months.

I endured the nursing for 12 weeks and then switched Miles to soy formula. My pediatrician seemed surprised that I chose soy. When I told her that there were a lot of allergies in my family she gave me one of those looks that clearly said, "if you say so." I remember feeling slightly embarrassed, but I knew that milk was a common allergen, so why take chances?

Miles did better on the soy formula, although his nights were still terrible. He was one of those children with autism whose social and language development was normal for the first year or so before they regressed, and we had no way of knowing that we would ever be facing a problem greater than our own sleep deprivation.

At eleven months old, our little boy was getting ready to walk. He said "cat" and "fish," and liked to play peek-a-boo. He smiled at us when we played with him, waved "bye-bye" and clapped hands.

When he was almost twelve months old, at his doctor's suggestion, we switched him to cows' milk and it seemed that nothing changed. Then the ear infections began, one after another. The first one was accompanied by a rash on the scalp, face, and neck. I went back to the doctor. Something viral? A case of Roseola? She gave him antibiotics and told me to stop using fabric softener. My faith in her began to ebb. The rash had coincided with the fever. It didn't occur to me at the time that the problem might be related to cow's milk, but I knew it wasn't a matter of laundry. The flushed cheeks persisted, on and off, for months, while Miles was put on a prophylactic dose of amoxicillin for his recurring ear infections.

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A parent knows when something is wrong, even when it can't be put into words. When a child learns language, his gains should be progressive. On the day that Miles had tubes inserted in his ears, at fifteen months old, he used the word "fish" for the last time at the aquarium in the doctor's waiting room. A month later, he no longer clapped hands or waved "bye-bye." Contrary to the otolaryngologist's assurance that Miles' language would now "explode," more than ever he appeared to be deaf.

One day, exhausted and late for work, I began to weep in the regular pediatrician's office. I told her that I didn't think she was taking my concerns seriously. I needed to know what *caused* this constant illness that was making our lives were so difficult. She told me, sarcastically, that "parenting can sometimes interfere with our work schedules." I then did the smartest thing I ever did as a parent. I scooped up my son and found a new doctor.

The new pediatrician didn't know much about developmental delays, but she agreed to help us find out what was going on. With the exception of something she called "chronic non-specific diarrhea," Miles was physically normal, but he was an odd kid. He had a very long attention span for certain activities, and resisted interaction. Ignorant of the symptoms of autism, I described him as "in his own world." I again expressed my concern that he didn't have any expressive or even receptive language. I had noticed that he didn't recognize the word "cup," which was his favorite thing in the world. In fact, he drank so much milk that for financial reasons we had to restrict him to about 70 oz. of milk per day - over half a gallon! The doctor was concerned that Miles had lost the few words he had learned. She gave us a referral to a speech pathologist and a child psychologist.

On July 12, 1995, I found myself in the emergency-room at midnight. Miles had a high fever and febrile seizures, only eighteen hours after his DPT inoculation. Were the two related? The doctors didn't know. As he lay limply in my arms, exhausted from two hours of screaming, Miles gazed into my eyes for a long, long time. I marveled at his gaze - he seemed to be recognizing me for the first time. How could that be? I realized how odd it was that I found his scrutiny to be unusual. When had he stopped making eye contact?

At nineteen months old, he was seen by a developmental pediatrician. There was a word for what Miles had: autism. We began to see the horrible truth of the diagnosis. Miles would sit in the sandbox for forty-five minutes pouring the same cup of sand, or putting together and taking apart the same two pieces of a toy. He never pointed to objects or brought us toys to look at.

Our lives began to seem as though they were spinning out of control. When my husband and I realized the implications of this diagnosis we could barely function.

Then I read somewhere that a child was misdiagnosed with autism because of a milk allergy. His mother, Mary Callahan, had written a book, describing this as a "cerebral allergy". I was skeptical, but I went to the library for a book about allergy and it mentioned the possible link between ear infections and milk. It also mentioned that children sometimes crave milk if they have an allergy to it. Then my mother-in-law reminded us that my husband had begun to talk at three after she took him off milk products.

One morning I put down my library book, Doris Rapp's "Is This Your Child," and called Alan, my husband, at work.

"Honey, do we still have any soy formula, or did we give the last few cans away?"

We removed dairy from Miles' diet when he was 20 months old.

Surprisingly, he accepted the soy formula and the rice milk I found at the supermarket. We didn't know what would happen but there was no mistaking his reaction to this change. On the first night, tired whining replaced the familiar sound of screaming. The next day, for the first time ever, we awoke to the sound of Miles playing in his

room. His crying was greatly reduced that day, and he made more eye contact than he had made in a month. The unfamiliar sound of babbling made us realize how little vocalizing Miles had done. Our babysitter was not immediately told about the reason for the change and she remarked emphatically about the differences in him.

When Alan came home from work on the third day and watched Miles reluctantly participate in a game of "Ring Around The Rosy," he made a pronouncement: Miles was to have no more dairy. No milk, no butter, no casein, no whey, no way.

The developmental pediatrician listened patiently while we raved about his improvement in the two weeks since he had stopped having milk. She agreed that he did seem to be doing well in some areas and suggested that we find an aggressive treatment program for him. However, her diagnosis was still autism. We later discovered that she had heard about this connection before, from "crackpot" parents and researchers, but said nothing to us at the time. She seemed to be taking us seriously, however, since my husband was a research scientist with a Ph.D. in chemistry. She simply agreed that if the diet seemed to be helping, it couldn't hurt to continue.

At 21 months, I noticed that when Miles had a cup of soy formula before his nap he woke up cranky and had small tremors for a few seconds. I restricted him to rice milk. We saw a neurologist at this time who listened attentively to my opinions and asked if I could give Miles some milk and soy, and then try to document any behavioral changes on videotape. Based on his observations he seemed amazed that Miles had been diagnosed with autism, and was skeptical about the original diagnosis. I could see why, since Miles had improved so much, especially in the area of social interaction. I could not bring myself to do what he had asked and give milk to Miles, however. We knew what we were seeing, and his progress was too important to us.

We had implemented a home-based behavioral program to which Miles was responding well, and he began attending a special nursery school four mornings per week. We agreed that these were a factor in his recovery but we knew they would not have been effective while Miles was drinking milk. In one month, Miles had gained over six months in his fine motor skill evaluation, and lost several points on our (his parents') application of the CARS test, indicating a reduction in autistic behaviors. He was rapidly gaining spontaneous appropriate language and social skills, his eye contact was now almost completely normal, he pointed to everything to learn its name, he brought us objects just to share them with us, and he watched his sister carefully for new cues about behavior.

We looked for a sympathetic allergist. Some other parents of children with autism recommended one who agreed that some foods can affect certain children even when they do not show a classic allergic immune system response. He was somewhat helpful. Miles had a reaction to some molds, but only a very minimal reaction to foods, among them egg, corn, wheat, soy, oats, and fish. There was no reaction to milk or rice. I was surprised - why would Miles have such a problem with milk if he did not have an allergy to it?

The doctor explained that he believed there were two types of allergy. In the primary type, symptoms such as hives, swelling, or difficulty breathing were common reactions. I remembered that my nephew had such a problem with peanuts - my sister had to keep an epi-pen(a source of the drug epinephrine to inject in the case of a severe allergic reaction) with him at all times. In the secondary type of allergy, a different part of the immune system seemed to be affected, and the response to such allergens could be headache, diarrhea, disorientation, irritability, or even depression or hyperactivity. He suggested a rotation diet.

A rotation diet is based on the principle that one can eat allergenic foods every four days or so with a lesser reaction than if one ate them every day. In addition, after three days without the food, one was more aware of allergic reactions when it was introduced.

I sat down at my computer and wrote up a weekly schedule of foods that Miles could eat - from a list that already seemed to be rather short.

During the rotation diet, we noticed that Miles definitely no longer tolerated soy. Chinese food gave him hives (soy sauce) and soy formula gave him a severe diaper rash. We also found that corn in any form made his diarrhea worse. We already knew that citrus, grapes, and most fruits gave him a rash, (which was true of our daughter at that age), so we were running out of food choices. To top it off, Miles was very picky about food tastes and textures.

Still, our biggest question was still unanswered: why was Miles getting better from autism after the removal of dairy from his diet?

In November we had a behavioral consultant from California take a look at Miles. He agreed that he had a lot of autistic characteristics and some autistic-like delays, but admitted to being baffled by his social behavior. When we explained about the dairy he said he was mystified, and suggested that we look into galactosemia and other metabolic disorders.

I bought a modem and got on the Internet, hoping to find more information. Within 48 hours I was bombarded with the news about casein/gluten intolerance and autism. I was overwhelmed.

To be taken seriously and to discover that Miles shared his case history with others was breathtaking. Parents like Lisa Lewis and researchers like Paul Shattock made it easier for me to understand that the problem might be caused by the improper breakdown of milk and wheat proteins into opiate-like neurotoxins. Paul suggested removing gluten from Miles' diet. Gluten is a protein found in wheat, oats, rye and barley. It was abundant in all of Miles' favorite foods, and I was horrified to discover that wheat is added to most packaged products as a filler, or to keep foods from sticking together. The prospect of starting a gluten-free diet seemed daunting, but it would be worth it if only to stop the diarrhea. I joked, via e-mail, that if Miles had a formed stool I would buy Paul a bottle of champagne.

We took Miles off gluten in November, when he was twenty-three months old, or so we thought. After a few days I realized that the Rice Krispies I had been giving him contained barley malt - a no-no. Then, within twenty-four hours of removing that food, we were amazed to see his bowel movements normalize.

Miles' gastroenterologist was mystified. He had been given the gluten/gliadin antibody tests and did not prove positive for celiac disease, and yet she saw him improve after the removal of gluten. She had even seen his diapers beforehand - an odious mass of sickly-smelling slush. I later found out that many children with autism seemed to have a form of celiac disease without testing positive to the gluten antibody test. When they were further tested with a small-bowel biopsy, they were usually diagnosed with celiac disease based on their flattened intestinal villi and gut permeability.

Shortly thereafter, without really understanding why, we started giving Miles low doses of nystatin. One of the parents we knew told us that it had helped her son, but was unsure about the reason. After ascertaining that the drug seemed safe, we asked our doctor for a prescription. During this time, his "postural insecurity" greatly improved. Later, after hearing Dr. Shaw speak at a conference and understanding about the Candida theory, I wondered about that. Was the lack of balance caused by the gluten or the yeast? I couldn't say, but Miles soon began to climb stairs on two feet and to try using a seesaw. He lost the drunken gait that had characterized his movement for so long. He remained on nystatin for over two years, and continued to take probiotics such as acidophilus and bifidus.

After a few weeks, we tried a "multiple food elimination diet." This meant that we cut Miles' diet down to the very few foods that seemed the least likely culprits: kosher chicken, potatoes fried in canola or safflower oil, white rice, and tapioca, and then added new things back, one at a time.

We soon discovered that other foods also gave him loose stools, such as eggs and pear juice. By the time we had tested every food at least twice for physical or behavioral reactions, Miles was reduced to the following diet: rice, potatoes, chicken, pork, sesame seeds, macadamia nuts, teff, arrowroot, and tapioca. Within a few months of his being on the diet we discovered that the removal of the other foods had made him even more sensitive to them. Corn was bad and soy was worse, but even the smallest trace of gluten would result in several days of marked regression and diarrhea.

At that point we became very careful, almost fanatical about Miles' diet. If we accidentally dipped a spoon from the pot of wheat pasta into the pot of rice pasta, we threw away the entire batch and started again. Everyone in the household, including our three-year-old daughter, learned to wash their hands after touching bread. Miles had a separate toaster, a separate shelf in the pantry, and sat at the end of the table where crumbs were less likely to fly from our hands.

Our friends and family might have thought us crazy, but we believed that the fact that we were doing the diet 100% was important to his success. We knew other children who responded to the diet whose parents weren't as careful, and their progress was often uneven. Miles' growth continued to soar.

Although we couldn't swear by it, three daily tablets of DMG seemed to improve his language function; he seemed somehow "clearer." At twenty-eight months, he began using three-word combinations. By two and a half, he had a mildly rote manner of speaking, but his sentences were longer and more meaningful, such as "look Mommy, I see a slide." His voice had a sing-song quality to it too, still residual from the autism, but he was highly motivated to communicate.

Miles had finally discovered his sister, only eighteen months older and eager for a playmate. They began to play games of imagination, such as "zoo," "dolls," and "dinosaurs." His imaginary play began as a replay of the same scene, usually involving a carnivorous dinosaur attacking everyone else. As the months went by, however, he took great pleasure in longer and more complex storylines which were always changing. There arrived a day when his sister began to let him take the lead in the play because his ideas were so exciting and different.

By the time Miles was three, his evaluation revealed that he no longer qualified for special education services. In fact, his language tested at a level over eight months above age level. Socially and developmentally, the teachers in his "integrated" classroom found him to be one of the most advanced in the class.

If his special-education teachers were skeptical about my use of the diet at the beginning of the year, they certainly were not by graduation. They had all seen the dramatic changes in Miles, as well as having seen the frightening deterioration that followed the rare occasions when they slipped up and let him get hold of a stray pretzel or cookie. One of them told me that she had never seen a child recover from autism before, and that she would always tell other parents of children with autism to try the intervention.

Another of his teachers told me that after twenty years of working with autistic students, she didn't want to work with any children whose parents refused to at least try the diet. On the days when Miles ate a problem food such as corn, she could always tell without being told, and would pronounce her session with Miles "an utter waste of time." Two of her students, Miles and a younger boy named Bobby who was following a similar path, had opened her eyes to a whole new avenue for recuperation.

The regular nursery school class that he attended twice a week was a good indication of Miles' functioning; he was very well-liked by the other children, who liked to do "whatever Miles was doing." These were "typical" children, and I was pleased to see how well he fit in on the days when it was my turn to assist in the classroom. His teacher assured me that he adapted very well to the rules and routine of the classroom, and was surprised by my anxious questions when I came to pick him up, such as "how did things go today?"

Because of the toileting delays typically associated with autism, potty training had seemed like such a long shot that we didn't push it. We were shocked to hear the toilet flush one day and see Miles walk out of the bathroom with a dry diaper in his hand. A few days later, after dragging me excitedly to the bathroom, Miles pointed out his first bowel movement. Afterwards, as we walked into the living room, Miles took my hand and said, "Mommy, I'm so proud of myself!"

At three and a half, Miles was so different from the child he had been that the past year seemed like a displaced memory, or a fragment of a movie about someone else's life. He was a charming, loving, intense child with an impish grin and a great imagination. He adored his family, readily made new friends, loved to swim and draw pictures, and insisted on picking out his clothes and dressing himself. He expressed himself well and even had a rather sophisticated sense of humor.

Our only reminder of what seemed like an impossible past was Miles' limited diet. He did not have potty accidents so we got a little bit adventurous with new foods, but Miles still had problems with the same list that he had reacted to as a baby. Stomach aches and diarrhea were the usual result, with occasional headaches or trouble sleeping. Although several people suggested EPD (Enzyme Potentiated Desensitization) injections to widen his diet, we decided to wait until Miles was older.

Miles is in a regular school now, with no problems whatsoever. He knows what he can eat, and is very cautious about touching other people's food. If I give him something unfamiliar, he asks, "Is this okay for me?" Miles is a good sport about it - he says "yay, French fries!" like a child who is not seeing them for the fourth time that week. We are resigned to the fact that he may never be able to eat casein or gluten, and that his diet may always be as limited as it is today. However, he gets enough protein and carbohydrate, he is supplemented with vitamins, minerals, calcium, essential fatty acids and amino acids, and the level of his functioning is so good that this seems a small price to pay.

I am one of the lucky parents, I know that. When I start my sentences with "when I look back," I can finish them with thoughts like, "it was a good thing we got such an early diagnosis," or "thank goodness for the Internet." Early intervention was the key for our little boy. Not just treatment of his symptoms, but the treatment of his immune system and the cause of his problems. Miles was young, and his nervous system had not sustained enough permanent damage to impair him for life.

Do I think that every child will respond as well as he did to the diet? Of course not. I have only seen three others in the past two years, all of them under three years old. But hey, that's four children in my city who do not have autism and that ain't bad. In addition, I have seen dozens of older children whose functioning improved well beyond their parents' expectations with the implementation of this diet, and that seems to me to be as good as a million dollars worth of special education.

My advice to parents is to look to the cause first, and treat the symptoms later. Find out as soon as possible if you can strengthen your child's immune system and improve his functioning. A gluten and casein-free diet, vitamin B6, MCT oil, DMG, and essential fatty acids are several safe things to try. Definitely test and treat for yeast and anaerobic bacteria, since it is so prevalent in children with autism and may be causative to the other problems. It

doesn't matter how old they are - Donna Williams didn't discover dietary intervention for her own autism until she was in her twenties, and it greatly reduced her anxiety and improved her ability to function and interact with others.

It used to break my heart when I saw a young child with autism, perhaps one that craved milk the way Miles did, and his parents told me that they did not want to try a dietary intervention. I would knock myself out pestering them and explaining it to them, but finally learned that people won't try new things unless they're ready. Unfortunately, a developing brain is not always that forgiving - certain behaviors are meant to be learned during certain stages of development.

For the sake of a child with autism who had terrible diarrhea, I once even found myself begging his mother to take gluten from his diet. I actually used the words, "please, I am begging you." It was very uncomfortable, and I felt embarrassed when she said no. Two years later I found out through a mutual acquaintance that he had been diagnosed as "failure to thrive," and she finally tried the diet with great success. I tried to imagine how awful she must have felt. It's one thing not to have the information, but another thing entirely to have it and not try it out because of intimidation or fear of the unknown.

Perhaps some of my frustration comes from my own fear of what might have happened if we had not pursued the course we did. I suspect that with my own arrogance and skepticism, if my doctor hadn't told me to, or if I hadn't discovered this for myself, I might not have tried the diet based on hearsay.

Another thing I've learned is that there is still a lot to know about the biological processes that lead to the symptoms of autism. I have spent a long time formulating theories which make a lot of sense to me until the next conference I attend, the next parent I speak with, or the next research paper I read. I suspect that Miles' vaccinations either introduced a virus that started the problem, or else aggravated his already unstable immune system. I strongly believe that the liberal amount of antibiotics he was given either triggered or contributed to the outcome. All I can say for certain is that a breakdown in the immune system certainly does seem to be involved, as well as the abnormal production of substances which are clearly not present in the urine of normal test subjects, and which can disappear after implementation of a gluten and casein-free diet.

Therefore, tempting though it is to assure parents of newly diagnosed children with autism that I have all of the answers, I usually just share Miles' story, or give them a copy of a paper I wrote, entitled "Frequently Asked Questions About Dietary Intervention For Autism and Other Developmental Disabilities" and lend them one piece of advice before stepping back: try whatever you have to try so that you won't spend the rest of your life wishing you had started sooner.

Frequently Asked Questions about Dietary Intervention for the Treatment of Autism and Other Developmental Disabilities

Disclaimer: The following is not medical advice. All changes to your child's diet should be supervised by a physician or a qualified nutritionist.

Q: I don't think my child has allergies, or that allergies could cause autism. Why should I try removing foods from his diet?

A: Although parents have been reporting a connection between autism and diet for decades, there is now a growing body of research that shows that certain foods seem to be affecting the developing brains of some children and causing autistic behaviors. This is not because of allergies, but because many of these children are unable to properly break down certain proteins.

Q: What happens when they get these proteins?

A: Researchers in England, Norway, and at the University of Florida have found peptides (breakdown products of proteins) with opiate activity in the urine of a high percentage of children with autism. Opiates are drugs, like morphine, which affect brain function.

Q: Which proteins are causing this problem?

A: The two main offenders seem to be gluten (the protein in wheat, oats, rye and barley) and casein (milk protein.)

Q: But milk and wheat are the only two foods my child will eat. His diet is completely comprised of milk, cheese, cereal, pasta, and bread. If I take these away, I'm afraid he'll starve.

A: There may be a good reason your child "self-limits" to these foods. Opiates, like opium, are highly addictive. If this "opiate excess" explanation applies to your child, then he is actually addicted to those foods containing the offending proteins. Although it seems as if your child will starve if you take those foods away, many parents report that after an initial "withdrawal" reaction, their children become more willing to eat other foods. After a few weeks, many children surprise their parents by further broadening their diets.

Q: But if I take away milk, what will my child do for calcium?

A: Children between the ages of one and ten require 800-1000 mg of calcium/day. If the child drinks three 8-oz glasses of fortified rice, almond or potato milk per day, he would meet that requirement. If he drank one cup per day, the remaining 500 mg of additional calcium could be supplied with one of the many supplements available.

Twin Labs makes a chewable calcium citrate wafer that contains no allergenic fillers and tastes like a "SweetTart" candy. Custom-made calcium liquids can be mixed up by compounding pharmacies (such as Pathway - 1-800-869-9160) using a maple, sucrose syrup, stevia or water base.

Editorial Note: High quality calcium supplements are also available in capsule, liquid, or chewable forms through New Beginnings Nutritionals (www.nbnus.com, 877-575-2467).

There are some very good calcium-enriched milk substitutes on the market. Rice Dream, in the white box, is usually available at the supermarket. Because this brand of rice milk is processed with barley enzymes, there is some concern over whether it will cause a reaction in individuals highly sensitive to gluten. If your child is also on a gluten-free diet, look for other brands of rice milk at your health food store. Darifree, a pleasant-tasting potato-based milk substitute, is available by mail-order (1-800-497-4834.)

Q: Is this diet expensive?

A: There is no denying that many of the gluten-free ingredients you will need to keep on hand are more costly than the staples you are used to buying. However, when you order by the case, the above milk substitutes cost about the same as cow's milk. Some parents report that their children with autism were drinking over a gallon of cow's milk per day (about \$60/month!) but these same parents were reluctant to switch to rice milk at \$1.30/quart.

As with all foods, convenience products such as frozen rice waffles are expensive, but making these from scratch is easy and inexpensive. Bulk rice flour is about 45c/pound, and there are several good gluten-free cookbooks. You'll find yourself making rice and potatoes more often, instead of ordering out. You might even save money.

Q: Isn't milk necessary for children's health?

A: Americans have been raised to believe that this is true, largely due to the efforts of the American Dairy Association, and many parents seem to believe that it is their duty to feed their children as much cow's milk as possible.

However, lots of perfectly healthy children do very well without it. Cow's milk has been called "the world's most overrated nutrient" and "fit only for baby cows." There is even evidence that the cow hormone present in dairy actually blocks the absorption of calcium in humans.

Be careful. Removing dairy means ALL milk, butter, cheese, cream cheese, sour cream, etc. It also includes product ingredients such as "casein" and "whey," or even words containing the word "casein." Read labels - items like bread and tuna fish often contain milk products. Even soy cheese usually contains caseinate.

For more information on dairy-free living, there's a very good book called "Raising Your Child Without Milk" by Jane Zuckin. This can be ordered at Barnes & Noble and at Waldenbooks. There is also a very good little book called "Don't Drink Your Milk" by Frank Oski (the head of Pediatrics at Johns Hopkins and author of "Essential Pediatrics.") This book cites the results of several research studies which conclude that milk is an inappropriate food for human children. It is available for \$4.95 from Park City Press, PO Box 25, Glenwood Landing, NY 11547, ISBN # 0671228048.

Q: I might be willing to try removing dairy products from his diet, but I don't think I could handle removing gluten. It seems like a lot of work, and I'm so busy already. Is this really necessary?

A: What you need to understand is that for certain children, these foods are toxic to their brains. For some, removing gluten may be far more important than removing dairy products. You would never knowingly feed your child poison, but if he fits into this category that is exactly what you could be doing. It is possible that for this subgroup of people with autism, eating these foods is actually damaging the developing brain.

Q: Removing both foods at once seems overwhelming, and I'm afraid of my child's reaction. Can I start slowly?

A: Many parents strongly suggest that you try removing dairy first, and then work on planning for a completely gluten-free diet. Gluten can take more effort and some education on your part, and preparation may take a bit longer. Some physicians recommend doing this diet one step at a time to accurately record the child's response, and to reduce withdrawal reactions. The experts seem to agree that the milk and wheat proteins are so similar to each other that if one is a problem, the other should be removed as soon as possible.

Q: How do I know if this applies to my child?

A: Although there is some peptide testing available, the waiting time for results can be long, and widespread use of a reliable test is not yet available. The researchers agree that this is a very common problem in the autistic population, so a trial period on the diet may be your child's best bet. Although a lab result is more convincing to a doctor, the noticeable improvement many children exhibit will usually persuade even a reluctant spouse to support the diet.

Many affected children who eat a great deal of dairy and/or wheat-based foods will show changes within a few days of their elimination. The diet must be strict.

Many parents have found that their child did not improve until they discovered and removed a hidden source of gluten or dairy. Noticeable changes in eye contact, sociability, and language are one sign that diet is an important issue. Another thing to look for are changes in the child's bowel movements or sleep patterns.

Q: When my child was taken just off dairy he improved greatly, but then he started eating a lot of wheat, perhaps to make up the opiates he was missing. Will I see the same kind of noticeable improvement when I remove gluten?

A: Children who eat a lot of gluten should show an improvement when it is removed. Some parents say that their child's response was more obvious with dairy, and some with gluten. Unfortunately, gluten seems to take longer to disappear from the system than casein does. Urine tests show that casein probably leaves the system in about three days, but it can take up to eight months on a gluten-free diet for all peptide levels to drop. If this intervention is followed by a deterioration or regression (a withdrawal-type response,) stay the course! It almost certainly means that your child will benefit. This may seem like a lot of work for an uncertain payoff, but in the lifetime of your child it may be the most important step you take.

Q: The only non-dairy, non-wheat foods my child will eat are French fries and chicken nuggets. Are these okay?

A: Chicken nuggets are coated with wheat. Some French fries are dusted with wheat flour to keep them from sticking together. It is a very good idea to get used to checking with your supplier or the manufacturer. Keeping a stack of blank, pre-stamped postcards in the kitchen is a handy way to check.

The biggest problem with French fries eaten out of the house is contamination of the frying oil with gluten from onion rings and other breaded products. Making fries homemade is a good option. If your child refuses them at first, it may be because of what they're missing! Some parents report that their kids have an uncanny ability to detect gluten in foods. Since many of the children enjoy salt, salting the fries might make them more acceptable.

Q: What else contains gluten?

A: Wheat, oats, rye, barley, kamut, spelt, semolina, malt, food starch, grain alcohol, and most packaged foods - even those that do not label as such. There is a lot of information on gluten intolerance because of a related disorder called Celiac Disease.

Q: After I removed gluten and casein, I discovered that other foods seemed to be causing a problem, like apples, soy, corn, tomatoes, and bananas. I see irritability, red cheeks and ears, and sometimes diarrhea or a diaper rash. I thought you said that these kids don't have allergies!

A: Many do have allergies, or allergy-related symptoms such as hay fever, asthma or eczema. Sometimes they have problems with foods which are not "classical" allergies, and which won't show up on skin tests. In this case, a different part of the immune system seems to be involved.

Q: So if these foods are not contributing to his autism, they're okay?

A: Not really. Current research indicates that in a great many cases, autism seems to be an immune system dysfunction. This not only leads to a problem breaking down casein & gluten, but it may also result in a problem breaking down foods which contain phenols (phenol sulfur transferase deficiency,) and an over-reactive response to other allergens.

Often, once gluten is removed, this effect becomes more noticeable, perhaps because the allergens were "masked" by the effect of the gluten. It is also possible that a "leaky gut syndrome," caused by the gluten intolerance, is now permitting other foods to pass through the intestinal screen and into the bloodstream.

For children who respond to this diet, allergens do seem to place further stress on the immune system, and have often been shown to worsen behavior and development.

Q: But my child's immune system seems to be working unusually well - he is rarely sick.

A: What we're describing is not an immune deficiency, but rather an immune dysfunction. Many (although not all) seem to share a history of ear infections and spitting up as babies (possibly milk-related,) or of chronic diarrhea, constipation, or loose stools (possibly wheat-related.)

Other parents note that their children with autism seem to be the healthiest members of the family. In this case, it has been hypothesized that the immune system is too aggressive and ends up turning on the nervous system. This may explain the presence of anti-myelin antibodies in some children, and may also explain why some have immune issues like multiple allergies but do not respond well to dietary intervention.

Q: What causes this problem? Autism seems to be so much more common than it used to be.

A: Researchers are not sure, but it seems likely at this time that many cases are caused by a genetic predisposition or by environmental toxicity, combined with some kind of triggering event that stresses the immune system, such as a vaccination or virus. In several cases, prolonged use of antibiotics seems to have contributed to the onset of the disorder.

Q: So, if I can't give him milk or wheat, and if he has some other food allergies, what do I feed my child?

A: Most kids are okay with chicken, lamb, pork, fish, potato, rice, and egg whites. Parsnips, tapioca, arrowroot, honey, and maple syrup are usually okay too. French fries from McDonalds are gluten free (but may contain soy or corn.) Certain white nuts, like macadamia and hazelnuts, are also usually tolerated. Others kids may be okay with white corn, bacon, fruits such as white grapes or pears, beans, sesame seeds, or grains such as amaranth and teff (available at natural foods stores.) There's always something to feed them - even the most finicky kids seem to like sticky white Chinese rice or French fries.

Q: How do I know which foods he's allergic to?

A: Try an allergy elimination diet. For example, keep tomato out of his diet for a few days and then re-introduce it. If you see symptoms, either physical or behavioral, try again in a few days. Try to be systematic, to be certain before ruling out a food. Two excellent resources, which are probably available at your library, are Doris Rapp's book, "Is This Your Child," and William Crook's "Solving the Puzzle of Your Hard to Raise Child."

Q: I'm already worried about my child's nutrition, and his "allergies" are causing me to further reduce his choices. If apple juice and bananas are the only fruits he will eat and he's reacting to them, how is he supposed to get by?

A: Fruit contains water, sugar, fiber, and vitamins. He needs to get these things from other sources.

Q: I thought the "five food groups" were so important!

A: They are, to an individual without food intolerances. But, just as a person who eats a balanced diet might not need to take vitamins, a person with poor nutrition can make up for a lot with a good vitamin and mineral supplement.

Q: So I should be giving my child a vitamin supplement?

A: Absolutely. Poly-vi-sol with Iron is probably okay, or order a gluten-free multi-vitamin & mineral formula from your natural foods store. Kal Dinosaur Chewables are tolerated by many food-sensitive children, and are available with or without minerals.

Because many children with autism have been reported to improve on a regimen of vitamin B6 and magnesium, you may want to order a supplement rich in these nutrients from a compounding pharmacy such as Pathway (1-800-869-9160.) For a 40 pound child, Dr. Bernard Rimland of the Autism Research Institute recommends 300 mg of B6 and 100 mg of magnesium per day. It is likely that in people with a leaky gut, absorption of B6 (which aids in nervous system function) is often greatly diminished.

Editorial Note: It is now understood that multivitamins supplements for children with autism should not contain iron or copper, unless these children have been tested to be low in these minerals. Since this chapter has been written, supplements are now easily available through companies such as New Beginnings Nutritionals (www.nbnus.com, 877-575-2467), which carries a wide range of vitamins, minerals and other nutritional supplements specifically formulated to meet the needs of children with autistic spectrum disorders.

Q: What else does my child need?

A: There are six basic things a person needs from food: water, protein (and amino acids,) carbohydrates, fats, vitamins, minerals (including iron & calcium.) In addition, food contains certain phytochemical substances which seem to help with functions like disease prevention. It is helpful to consult a nutritionist about the use of supplements such as pycnogenol for any child on a limited diet.

Children who have gone for one year eating only chicken, canola oil, potato, rice, calcium-enriched beverages, and a liquid multivitamin supplement with minerals have had excellent results on nutritional blood tests. You'd be surprised to learn just how unnecessarily varied an American diet is, compared with the diets of other cultures!

Q: So how do I know if my child will respond to this diet?

A: The biggest clue is when a child self-limits his diet - especially to milk and wheat. This is no longer seen as a "need for sameness" but as a biological addiction. Children who don't necessarily "self-limit" but who also respond are those who eat an unusually large or small amount of food. Although the former may not recognize the source of the opiates, he knows that eating makes him feel GOOD. The latter may realize that many foods make him feel ill, and tries to avoid eating whenever possible. These "failure to thrive" children with autism are very hard to put on this diet because of their parents' fears, but will usually respond when acceptable substitutes to the non-tolerated foods can be provided.

Other symptoms of food intolerance or vitamin deficiency are dermatitis or extremely dry skin, migraines, bouts of screaming, red cheeks, red ears, abnormal bowel movements, abnormal sleep patterns or seizures.

Q: What's all this I hear about yeast?

A: Candida is a yeast that lives in our bodies in small amounts. It was speculated that in individuals with improperly-functioning immune systems, it could flourish in the gut and lead to a host of problems, including fatigue, sugar cravings, headaches, and behavioral problems.

Q: How do we know if this is really true?

A: We didn't, until recently. Dr. William Shaw in Kansas found unusually high levels of "fungal metabolites" (yeast waste products) in the urine of several groups of abnormally functioning individuals (including people with autism.) His first paper describing this phenomenon was published in the Journal of Clinical Chemistry in 1995 (Vol. 41, No. 8.) He is currently conducting further studies on the effect of anti-fungal therapy on urinary organic acids from children with autism. His test is performed by the Great Plains Laboratory, at 913-341-8949.

Q: So does yeast cause autism?

A: This finding is likely to be just another consequence of the abnormally-functioning autistic immune system. However, it has also been hypothesized that the Candida might aggravate a condition of gut permeability (the "leaky gut" syndrome) which might let the gluten and casein proteins into the bloodstream before they are broken down, so it may in part be responsible for autistic behaviors. Many parents of children with ADD/ADHD as well as those with autism report that treatment for Candida does improve their children's behavior and concentration.

Q: How do I treat for Candida?

A: One approach is to ask your pediatrician for a course of nystatin, which is a non-systemic (not absorbed into the bloodstream) anti-fungal. Taken orally, it works locally in the gut to fight Candida. This medication is considered to be quite safe, even when taken for several months. For a 25-35 lb. child, ask the doctor for a prescription for nystatin powder (125,000 units per cc) in a stevia base, starting with 1 cc 4x/day. Your local pharmacy probably carries a commercial preparation in a sugar base - this feeds yeast! Again, try Pathway, at 1-800-869-9160.

"Probiotics" such as acidophilus, the natural bacteria found in yogurt, are other Candida-fighters, and are available at the natural foods store in powdered form in the refrigerated section. Some acidophilus preparations are milk-based - be sure to get one that is not! Bifidus works in the large intestine and can be of great benefit. "FOS" is desirable in these supplements, as it feeds the probiotics.

Q: Aren't probiotics the "healthy flora" I've heard about?

A: Yes, they compete with Candida for the sugars you eat. It's the "good bacteria." You may be aware that acidophilus is eradicated from your gut when you take antibiotics.

Q: That's why you're supposed to eat yogurt when you are on antibiotics!

A: Exactly. As a matter of fact, in the 1950's, when oral antibiotics were first prepared for general use, scientists knew about this Candida problem and coated the tablets with nystatin. After a few years, the FDA decided that the two drugs should be prescribed separately (which they never were) and made them stop.

Q: My friend's child tried nystatin and it made him vomit. If nystatin is so safe, why did he react to it?

A: The child may have experienced a "die-off reaction" to the Candida. As it dies, Candida releases toxins into the bloodstream and can cause nausea, vomiting, or diarrhea. It is likely that Candida was indeed a problem for this child. Your friend should discuss a dosage change (starting with a low dose and working up to a "normal dose") with the prescribing doctor.

Q: My doctor has never heard of any of this and she is extremely skeptical. I'm embarrassed to tell her I'm considering this approach.

A: Skepticism is a good thing in a medical doctor or scientist. However, since there is preliminary evidence to support this safe, non-invasive intervention, it is up to you to educate her, state your wishes, and ask for her support. For a doctor, it is better to wait until all of the data is published in peer-reviewed journals before advocating a treatment. For a parent, it is reasonable to want to help one's child without waiting for all of the results of the "double-blind placebo" studies. Because this approach does not include any unusual supplements, invasive drugs, or expensive treatments, your pediatrician should be supportive. Explain that you would like to try this for a few weeks, and agree that you will be objective about recording your child's progress while on the diet.

Q: Where can I find support?

A: It is likely that other parents in your area are already aware of this intervention. Forming a support group, or forming a local chapter of Parents of Allergic Children may be a good option. There are also several support groups for the biological treatment of autism on the Internet (search "Autism and Diet,") as well as support for a gluten free diet (search "Celiac Disease.")

Good luck!

For more information about the implementation of a gluten-free diet, visit the ANDI website at <http://members.aol.com/AutismNDI/PAGES/index.htm>.

For a free copy of the ANDI Newsletter, send mailing address to: Autism Network for Dietary Intervention, PO Box 17711, Rochester, NY 14617-0711, or by email to: AutismNDI@aol.com.

(An extremely popular new book by Karyn Seroussi, *Unraveling the Mystery of Autism and Pervasive Developmental Disorder, A Mother's Story of Research and Recovery* is available from The Great Plains Laboratory and can be ordered by fax, mail, phone, or from our website www.greatplainslaboratory.com.)

Summing Up

Chapter 16

Dr. William Shaw

How effective are the nutritional and antifungal therapies discussed in the previous chapters? According to parents of children with autism who were surveyed by Bernard Rimland Ph.D. of the Autism Research Institute, some of these therapies were much more effective than all of the commonly used psychoactive drugs including neuroleptics and stimulants which are commonly prescribed for autism. (These data in Tables 1 and 2 were adapted from Dr. Rimland's published study and are reprinted with permission on the following pages.) The better to worse ratio for antifungal drugs (nystatin and ketoconazole) in children with suspected yeast overgrowth of the intestinal tract is five times higher than the second most effective drug, the psychoactive agent Clonidine (Table 1). (The higher this ratio, the more effective the drug is rated.) I suspect that the effectiveness of the antifungal agents might be even higher if dietary restriction of simple sugars to reduce yeast overgrowth were employed. Several antiseizure medications were ranked poorly (ratios less than 1.0) based on behavioral response (not on antiseizure effectiveness). All of the stimulant drugs including Cylert, Ritalin, and amphetamine were also rated very poorly. With nutritional supplements (Table 2), high ratios, indicating high effectiveness, were reported for vitamin B-6, DMG, zinc, niacin, vitamin C, calcium, and folic acid.

The idea that autism is made worse or caused by abnormal byproducts of microorganisms and opiates from wheat and milk is not inconsistent with other research findings in autism such as abnormal neuroanatomical findings, abnormal EEG results, and abnormal brain scans. Similar abnormalities were found in the disease PKU even though the primary abnormality is a genetic defect in a single enzymatic reaction. There is no inherent reason that dramatic biochemical changes in multiple biochemical systems, caused by byproducts of microbes or abnormal peptides from wheat and milk, would not be expected to alter brain structure and function.

In PKU, correction of the metabolic defect by restriction of phenylalanine during infancy allows for normal development; retardation occurs if dietary intervention occurs too late. If abnormally elevated metabolites of yeast and bacteria cause autism, then it is reasonable to think that elevations of these compounds would have maximum negative impact during periods of critical brain growth and development. As in PKU, metabolic intervention in autism might only be possible in the early stages of the disorder before the brain has matured. The differences in severity of the disorder and individual differences in symptoms might be due to different combinations of metabolites, how elevated they are, the duration of the elevation, the age at which the metabolites become abnormally elevated, and the susceptibility of the individual developing nervous system to the different microbial metabolites. Indeed, these differences may even determine *which disease is manifested*. ***The concentrations of these microbial products are not trace amounts on the metabolic scale.*** One child with autism evaluated in my laboratory had a urine tartaric acid concentration (6000 mmol/mol creatinine) that was nearly 400 times the upper limit of normal (approaching a lethal dose) after the use of multiple oral antibiotics. Many of the concentrations of these microbial compounds found in the urine of children with autism frequently exceed even the concentrations of the predominant mammalian organic acids in urine.

Table 1
Parent ratings of behavioral results of drugs

Drug	Got Worse	No Effect	Got Better	Better: Worse	No. of Cases
Aderall	41%	25%	34%	0.8:1	475
Amphetamine	47%	28%	25%	0.5:1	1217
Anafranil	32%	38%	30%	1.0:1	381
Antibiotics	31%	57%	12%	0.4:1	1799
Antifungals ^C : Diflucan	5%	41%	55%	11:1	330
Antifungals ^C : Nystatin	5%	46%	49%	10:1	986
Atarax	25%	53%	22%	0.9:1	477
Benadryl	24%	51%	25%	1.0:1	2711
Beta Blocker	18%	50%	33%	1.9:1	256
Buspar	26%	44%	30%	1.1:1	328
Chloral Hydrate	41%	38%	21%	0.5:1	418
Clonidine	21%	31%	47%	2.2:1	1280
Clozapine	40%	42%	18%	0.4:1	102
Cogentin	19%	54%	27%	1.5:1	162
Cylert	45%	35%	20%	0.4:1	600
Deanol	15%	56%	30%	2.0:1	200
Depakene ^D : Behavior:	25%	43%	32%	1.2:1	957
Depakene ^D : Seizures	12%	32%	57%	4.8:1	627
Desipramine	34%	31%	34%	1.0:1	67
Dilantin ^D : Behavior	28%	49%	23%	0.8:1	1077
Dilantin ^D : Seizures	14%	36%	50%	3.5:1	400
Felbatol	21%	53%	26%	1.2:1	43
Fenfluramine	20%	52%	28%	1.4:1	459
Halcion	37%	37%	26%	0.7:1	54
Haldol	38%	28%	34%	0.9:1	1154
IVIG	7%	51%	42%	6.3:1	45
Klonopin ^D : Behavior	28%	38%	34%	1.2:1	192
Klonopin ^D : Seizures	31%	60%	10%	0.3:1	42
Lithium	26%	43%	31%	1.2:1	410
Luvox	29%	35%	35%	1.2:1	161
Mellaril	29%	38%	33%	1.2:1	2062
Mysoline ^D : Behavior	43%	43%	15%	0.3:1	136
Mysoline ^D : Seizures	19%	59%	22%	1.2:1	64
Naltrexone	20%	46%	34%	1.7:1	221
Paxil	29%	30%	41%	1.4:1	283
Phenergan	29%	46%	24%	0.8:1	266
Phenobarbital ^D : Behavior	47%	37%	16%	0.3:1	1076
Phenobarbital ^D : Seizures	17%	43%	40%	2.4:1	480
Prolixin	31%	40%	30%	1.0:1	91
Prozac	31%	32%	36%	1.2:1	1123
Risperidal	18%	28%	54%	3.0:1	616
Ritalin	45%	26%	29%	0.7:1	3813
Secretin: Intravenous	7%	44%	48%	6.7:1	333
Secretin: Transdermal	10%	49%	41%	4.2:1	132
Stelazine	28%	45%	27%	1.0:1	420
Tegretol ^D : Behavior	25%	45%	31%	1.2:1	1423
Tegretol ^D : Seizures	12%	33%	55%	4.6:1	762
Thorazine	36%	40%	24%	0.7:1	919
Tofranil	30%	38%	33%	1.1:1	713
Valium	35%	41%	24%	0.7:1	824
Zarontin ^D : Behavior	34%	45%	21%	0.6:1	136
Zarontin ^D : Seizures	19%	53%	28%	1.4:1	93
Zoloft	33%	33%	34%	1.0:1	321

Table 2
Parent ratings of behavioral results of nutrients

Nutrients	Got Worse	No Effect	Got Better	Better: Worse	No. of Cases
Vitamin A	2%	58%	41%	23:1	618
Calcium ^E :	2%	62%	36%	15:1	1378
Cod Liver Oil	3%	47%	50%	16:1	818
Cod Liver Oil with Bethanecol	16%	45%	39%	2.4:1	56
Colostrum	5%	58%	37%	8.1:1	345
Detox. (Chelation) ^C :	2%	22%	76%	35:1	324
Digestive Enzymes	3%	42%	56%	20:1	737
DMG	7%	51%	42%	5.6:1	5153
Fatty Acids	2%	42%	55%	23:1	626
5 HTP	10%	51%	39%	3.7:1	145
Folic Acid	3%	54%	42%	12:1	1437
Food Allergy Treatment	3%	37%	61%	21:1	560
Magnesium	6%	65%	29%	4.6:1	301
Melatonin	8%	30%	61%	7.3:1	573
P5P (Vit. B6)	13%	37%	51%	4.0:1	213
Pepcid	9%	63%	28%	3.2:1	93
SAMe	15%	66%	19%	1.3:1	62
St. Johns Wort	14%	64%	21%	1.5:1	84
TMG	14%	44%	42%	3.0:1	434
Transfer Factor	8%	53%	39%	4.8:1	98
Vitamin B3	4%	55%	41%	10:1	659
Vitamin B6 alone	8%	63%	30%	3.9:1	620
Vitamin B6 with Magnesium	4%	49%	47%	10:1	5780
Vitamin B12	4%	33%	63%	15:1	192
Vitamin C	2%	57%	41%	18:1	1706
Zinc	2%	51%	47%	20:1	1244

I think that the reason these abnormalities (some of which have been known for decades) have been ignored for so long, by almost all of the researchers in the field of metabolic diseases, is because the intense focus has been on finding new inborn errors of metabolism. By definition, abnormal microbial products are not due to a genetic defect in a human biochemical pathway. In addition, it is likely that most researchers in the field of metabolic disorders also made the unwarranted assumption that microbial metabolites are metabolically and physiologically inert. Instead, it appears to me that the human body and the microorganisms in the gastrointestinal tract are an integrated and interdependent biochemical system within the human body.

Early intervention is key to the treatment of PKU. Children with PKU who are put on the special diet low in phenylalanine have close to normal IQ's while those who are untreated until later in life are impaired. The children of Pamela Scott and Karyn Seroussi, both who recovered from autism, were started on their therapies at the age of two years. Even this age may be too old for some children. I think that any child, under two years old having frequent infections treated with antibiotics, is at risk for autism, seizures, and/or ADD and should be tested and treated if abnormal microbial overgrowth is present.

An extensive body of research by Bauman, Corchesne, and others has documented numerous abnormal structures in the brains of children with autism. Children with autism caused by a defect in succinyl purine metabolism have the same kind of brain abnormalities reported by this group (see chapter 9). However, I wish to emphasize that finding abnormal anatomical structures in the brain proves nothing about the cause of

these abnormalities. I suspect that some or all of these abnormalities may be due to the toxic effects of the microbial metabolites or the abnormal peptides from wheat and milk just as the drug thalidomide caused abnormal development of the limbs of children exposed to this drug in utero. Saying autism is a brain disease makes just as much sense as saying that the flippers in children exposed to thalidomide are due to an arm disorder; both statements have elements of truth but the oversimplification distorts the complexity of the truth. If autism is caused by microbial metabolites and peptides, then scientific studies, in which these compounds are given to animals, should be able to reproduce the symptoms of autism.

These abnormalities that I found in autism are not just specific for autism. I have found them elevated in Rett's Syndrome, which is a separate disorder seen primarily in girls in which some autistic-like behaviors are exhibited and in the genetic disease Smith-Magenis syndrome. Elevated values have also been found in urine samples of children who have autistic symptoms with Prader-Willi syndrome, Fragile-X syndrome, Tourette's syndrome, Williams disease, neurofibromatosis, and tuberous sclerosis. Autistic symptoms are common in all of these disorders. In addition, I have found the yeast byproducts to be elevated in the urine of children with Down's syndrome *who also* exhibited autistic symptoms. In addition, I have found elevated yeast and/or bacterial metabolites common, both in adults and children with seizures, psychosis in severe depression, and in perhaps 80-90 % of children with attention deficit hyperactivity. These metabolites are also found in some people with hypoglycemia or low blood sugar.

All of my work leads me to discard the prevailing dogma that microbial metabolites are inert in human metabolism.

Based on all of my work and the work of many other researchers, I have developed a theory for autism:

Factors that impair the immune system can lead to recurrent infections such as ear infections, strep throat or bronchitis. These factors can include genetic deficiencies of the immune system and inborn errors of metabolism. Other non-genetic factors include adverse reactions to immunizations such as gastrointestinal viral infection (from live vaccines) and metal and chemical toxicity (which can also be due to environmental factors). These infections are then treated with antibiotics.

A yeast overgrowth of the gastrointestinal (GI) tract occurs following the elimination of the normal flora of the gastrointestinal tract. The yeast produces abnormal compounds called gliotoxins and other immunotoxins such as mannan byproducts that are toxic to the immune system and make it weaker. Yeast overgrowth of the intestinal tract may persist in children who are exposed to any use of antibiotics as infants, especially if immune deficiencies are also present. Because of immunodeficiency, a child is more likely to be re-infected and be exposed to additional antibiotics until a vicious cycle has been established.

The yeast produces abnormal sugars which may interfere with carbohydrate metabolism or alter the structure and function of critical proteins through the formation of pentosidines. The yeast also produces analogs of the Krebs cycles that inhibit energy production and gluconeogenesis. The yeast also produces enzymes such as phospholipase, which break down phospholipids, and proteases such as secretory aspartate protease which break down proteins. These enzymes may partially digest the lining of the intestinal tract itself. This digestion of the intestinal tract takes place as the yeast cells attach to mucosa lining the intestinal tract. The digestion of the intestinal lining by the yeast and/or viral infection (perhaps from live virus vaccines) causes a leaky gut and may also limit the ability of intestinal cells to produce hormones such as secretin that is necessary for the production of sufficient pancreatic digestive enzymes. Undigested wheat products and other food molecules are more likely to be absorbed from the intestinal tract into the body and elicit an allergic response, a food allergy. Some of these food allergies may manifest as behavioral disorders.

Candida proliferation also elicits the production of antibodies that cross-react against many of the human tissues including the brain, pancreas and wheat proteins, perhaps leading to atrophy of the pancreas and disruption of key brain functions caused by myelin autoantibodies. Pancreatic atrophy may be associated with further impairment of digestive function with resulting malabsorption and malnutrition. In addition to the yeast overgrowth, there may also be an overgrowth of certain bacteria of the *Clostridia* family. The *Clostridia* share one common attribute with the yeast in that they are resistant to many of the common broad-spectrum antibiotics used to treat ear infections and Strep throat. *Clostridia* bacteria produce 3-(3-hydroxyphenyl)-3-hydroxypropionic acid and perhaps other neurotoxins that are absorbed into the body and which may also alter behavior.

The undigested peptides from wheat and milk, which react with opiate receptors in the temporal lobes of the brain that are responsible for auditory integration and language, disrupt the functions of this key area. Cade's work established significant improvements in almost every aspect of autism in a group of 70 children with autism after only one month on the gluten and casein free diet (1). Areas of improvement included social isolation, eye contact, mutism, learning skills, hyperactivity, stereotypical activity, hygiene, panic attacks, and self-mutilation. The behavioral aspects of autism can be reproduced in rats by intraperitoneal injection of bovine casomorphin (2). Within seven minutes of injection, the following behaviors were observed in the rats: running violently around the enclosure, jumping behavior, wet dog shakes, dilation of pupils, raised hair, salivation, rapid respiration, teeth chattering, vocalization, circling behavior, reduced sound response, decreased social interaction, and abnormal postures. In addition, the peptides from wheat and milk may profoundly alter the metabolism of a large number of important hormonal peptides hydrolyzed by DPP IV.

Implications for Gene-Searching

A large amount of money from the National Institutes of Health and other sources has been allocated to various academic centers throughout the country to discover the gene or genes that predispose to autism. If my theory is correct, there would not be a single gene but a whole host of genes, perhaps fifty or even a hundred or more that would lead to increased susceptibility to infection. The current approach is to extract DNA (the chemical basis for our genetic material) from the white blood cells of people with autism, break down the DNA to smaller pieces with enzymes called nucleases, and then separate the pieces by a process called gel electrophoresis. Computers are then used to determine if two siblings from the same family have an abnormal matching band of DNA that is not present in normal people. If my theory is correct, the matching band may very well be different in each family and could result in this information being misread by the researcher since they are looking for a small number of genes. The much higher incidence of autism in males compared to females naturally led geneticists to suspect that genetic factors influencing autism are linked to the X-chromosome. Since many of the genes for different immunodeficiencies are linked to the X-chromosome, it would seem worthwhile to focus DNA research on the well-documented phenomenon of immune deficiencies in autism.

Where Do We Go From Here?

Recently, a psychological test called the CHAT (3), used for early diagnosis of autism, was developed in England. This test is extremely accurate in predicting autism in children at 18 months of age. No children with a normal CHAT score developed autism while all of the children with two or more major abnormalities in the CHAT test developed autism by the time they were thirty months old. I propose a relatively simple study of the

effectiveness of the therapies in this book. Two hundred children with an abnormal CHAT test would be identified. With an incidence of autism at about one in a thousand, approximately 200,000 children would need to be screened. The test is relatively easy to administer, not very time consuming, and could easily be included in a routine well-baby examination with very little expense.

Half of the two hundred children identified as high risk by the CHAT test would receive the following as needed: a low sugar diet, antifungal therapy, therapy for Clostridia bacterial overgrowth, gluten and casein restriction, vitamin B6 and DMG supplementation, and food allergy desensitization. Children with immunodeficiency would be treated with gamma globulin and/or transfer factor.

The other 100 children would receive conventional medical treatment. Both groups would get any special services available such as Lovaas therapy, speech therapy, occupational therapy, etc., but the therapists would not be told which therapy group the child was in. At the end of one year, psychologists, who did not know which therapies the children had received, would evaluate all of the children. If early biochemical intervention in autism is most effective when started early (as in PKU), then the children with the "alternative" treatments would do much better than the children treated with conventional therapies. I propose that these younger children be tested because I suspect that autism is very much like PKU, in that the earlier a child is treated, the better the outcome. I have received many reports of benefits of these same therapies in adults and older children with autism and do not want to appear to "write-off" any group of people. But I believe our first priority should be an attempt to prevent of any new cases of autism.

There is obviously a tremendous amount of additional work that needs to be done to clarify the best dietary approach used with antifungal therapy; there is considerable disagreement about the best dietary approaches to autism, even among the contributors to this book.

The overuse of antibiotics, especially for recurrent otitis media, needs to be completely re-examined and a large epidemiological study should be undertaken by the Centers for Disease Control to determine how much damage has been caused to our children by antibiotic use. A tax on antibiotics could be used to pay for such a study and other experimental studies on the role of abnormal microbial byproducts in human disease. A large group of infants, perhaps 10,000 or more, should be monitored by stool cultures for yeast and bacteria. Urine organic acid testing should also be done, on perhaps a monthly basis, for several years to evaluate the association between a wide number of disorders such as ADD, autism, and seizures and abnormal yeast and bacteria overgrowth caused by oral antibiotics.

However, I think it would be a tragic mistake to wait until all the data are collected before taking additional action. It is better to act on preliminary findings, because the stakes are so high, especially when many safe alternatives are available.

Our children are our most precious resource.

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