

UNDERSTANDING AUTISM

The Physiological Basis and Biomedical Intervention Options of Autism Spectrum Disorders



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Forward

This document is copyrighted © 2003 by Bryan Jepson MD, PC. Dr. Jepson developed this document as the basis for the treatment offered by the Children's Biomedical Center of Utah. The information protocol contained in this document is based on Dr. Jepson's effort to compile information available from varied credible sources on the topic of Autism and reports published by the Autism Research Institute and the Defeat Autism Now! (DAN!) Association as well as personal experience in treating autistic children.

Disclaimer

This document is not a recommendation for diagnosis or treatment of Autism Spectrum Disorder independent of the supervision of a qualified physician. The intent of this document is to inform and provide treatment options to those families attending the Children's Biomedical Center of Utah.

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I. INTRODUCTION

Autism Spectrum Disorder (ASD) is a group of diseases that is characterized by a delay in language development, impairment of social interaction, and the use of restrictive, stereotyped behavior patterns. It was first described in 1944, but great strides in research and understanding of the disorder have been made only recently. It was initially felt to be a fairly rare illness (less than 5 in 10,000) but over the last twenty years there has been an explosive increase in incidence, growing on average around 25% per year and up to 100% per year in some areas. In the United States, it is currently believed to affect 1 out of every 250 individuals on average (up to 1 in 150 in some areas) with a 4 to 1 male predominance. Thanks to the dedication of many researchers, physicians and parents, we are rapidly learning much more about the biochemistry and origins of this illness. Concurrently, many treatments are being developed and are in use across the country with promising results. Many children who are receiving these treatments are improving, some to the point of total or, at least, functional recovery. It must be accepted, however, that the clinical research behind these treatments is in the early stages and as time goes on and our understanding is improved, the treatment protocols are likely to be modified. The treatment protocol that your child will be receiving is currently recognized as consensus among a group of physicians who refer to themselves as DAN! (Defeat Autism Now!) practitioners and has been implemented in thousands of children without significant danger or adverse effects. The DAN! movement arose out of an organization called the Autism Research Institute, which has been in the forefront of autism research for the last 40 years. The DAN! philosophy is that we can no longer afford to wait for all of the research to be completed and mainstreamed before we start trying things that have biological plausibility, are safe and may help. We understand the motivation of parents to do all that they can to help their own children with autism. In fact, many of us are parents of autistic children ourselves. Our goal is to help as many children as possible by aggressive early intervention.

We believe that autism is caused when a child with the appropriate genetic susceptibility is exposed to a number of environmental insults resulting in a complex series of interactions in several body systems, primarily the central nervous system (brain), the gastrointestinal system (the gut), and the immunological system (body defense). Understanding the biomedical model of autism requires recognizing that your child's body functions as a unit and that treatment requires an integrated approach. Treatments are based on priorities and should progress in a fairly logical and step-wise fashion. I will try to explain things with sufficient detail to help you understand the reasoning behind the intervention but without requiring you to have a degree in biochemistry. Try not to be overwhelmed by the amount of information contained in this packet. It is intended for reference. You certainly will not be asked to begin these treatments all at once or continue them all indefinitely. This is merely an explanation of the currently available treatments and the reasoning behind them. Remember that each child with autism is a unique individual and has unique biochemistry that has somehow become disordered. Our job is to help you find which treatments are most effective for your child. The treatments can be time consuming, expensive and may require a dramatic change in lifestyle but I believe you will find that it is all worth it when you see the strides that your child is making!

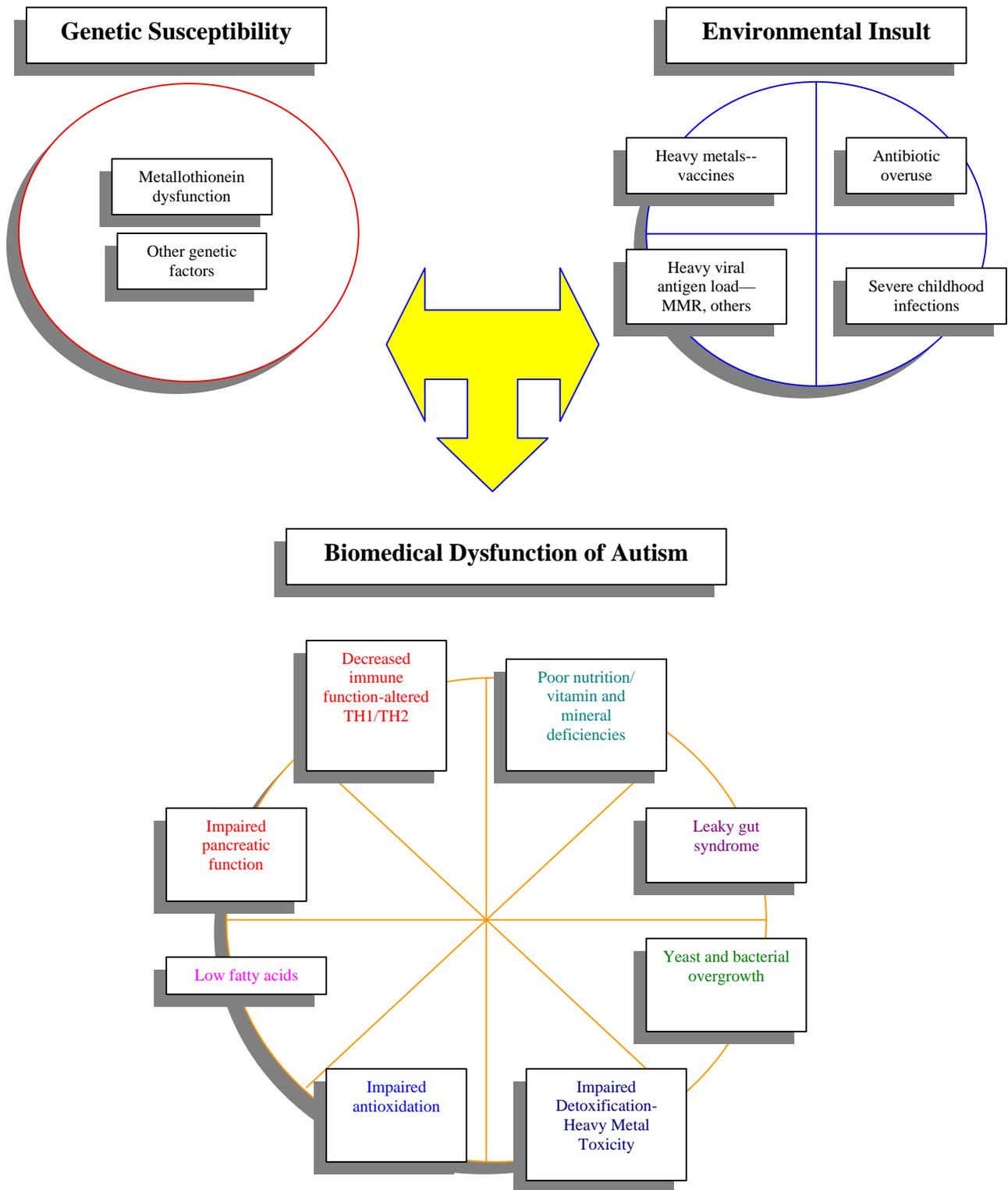


Figure 1. The size of each piece of the pie differs according to individual variability and may change over time.

II. GENETIC SUSCEPTIBILITY

A. Metallothionein dysfunction

This hypothesis was proposed by William Walsh, PhD, who heads the Pfeiffer Research Center in Illinois. He took extensive biochemical analyses of over 500 autistic patients that are treated at his clinic and discovered that almost universally, these children have abnormal copper/zinc ratios with high body copper and low body zinc. Extrapolating backwards, he discovered that the body's control mechanism for copper and zinc is a function of a family of proteins called metallothionein (MT). Other functions of MT in the body include development of brain neurons, detoxification of heavy metals, maturation of the GI tract, anti-oxidation, boosting immune function and delivery of zinc to cells. MT dysfunction would result, then, in many of the issues that we see with autistic children such as the leaky gut syndrome, incomplete breakdown of casein/gluten protein by zinc dependent enzymes, disrupted ability to combat yeast, reduced production of stomach acid and impaired stimulation of the pancreas by secretin. It would also lead to inability to clear the body of heavy metals, a disordered immune system and ultimately to the neurological changes seen in autism. It would also explain the male sex predominance (4:1) seen in autism because MT synthesis is enhanced by estrogen and progesterone. MT dysfunction could be caused by a genetic MT defect, a genetic disorder that disables MT, or an environmental insult that disables MT. Theoretically, if we could find a way to detect the MT abnormality early on, autism could be prevented through avoiding environmental insults and supplementing with MT promotional agents (zinc, glutathione, N-acetyl cysteine, selenium, pyridoxal-5-phosphate, vitamins A,C,D,E, others.)

B. Other genetic factors

Much research is currently being done in an effort to discover the genetic basis of autism. It is beyond the scope of this document to describe in detail the genetic research in this area. As yet, no single gene has been isolated as the culprit and in fact, autism, with its wide spectrum of presentations and severity is unlikely to be caused by a single gene defect. Clearly, autism and autism-related illnesses tends to have a higher incidence in some families. There is also an increased incidence of other auto-immune diseases such as rheumatoid arthritis, diabetes and inflammatory bowel disease in the families of autistic children. I think that this indicates an underlying weakness in the immune system in these families. However, the overall rate of rise in the incidence of autism cannot be completely explained by genetics alone. Autism has risen over 1000% in the last 20 years which is not possible if genetic mutation is the only cause. There must be an environmental component that is inducing these susceptible children to become autistic.

III. ENVIRONMENTAL INSULTS

I have included below several environmental factors that I believe are playing a role in the rising incidence of autism. It is important to note that it is unlikely that any of these factors cause autism in isolation. I believe that it is a combination of these factors and probably many others that is creating a toxic overload in these children who have abnormal metabolism probably based on their genetic make-up. The worse their genetics, the fewer environmental insults it will take to induce the abnormalities and the severity of their deficits will likely be worse and evident at an earlier age. It is interesting to note that the regressive forms of autism (where the children seem to regress after a period of normal development) is rising at a much higher rate than the classic forms of autism which are evident from birth. This makes sense to me since these children are those whom I believe have less severe deficits genetically and so the rise in environmental exposure is starting the autism cascade, where 20 years ago, they may have avoided it.

A. Mercury Toxicity

In April 2000, Sally Bernard, a parent of an autistic child, and several other investigators published an article suggesting that autism is a form of mercury poisoning. They meticulously compared signs and symptoms of mercury poisoning with those of autism and found that there is striking similarity in almost every aspect. They cited examples of other historically-significant disease epidemics as evidence of autism-like illnesses created by environmental exposure to mercury. These diseases also presented with large range of variability and susceptibility among individuals in the population and were eradicated when the source of the exposure was eliminated. These illnesses are acrodynia or Pink's disease (teething powders), Mad Hatter's disease (occupational exposure) and Minamata's disease (consumption of contaminated fish.)

Physiologically, mercury has been shown to have many harmful effects. It can bind to sulfhydryl groups on many proteins resulting in decreased enzyme function and loss of structural integrity. This may be contributing to or causing a "leaky gut" by damaging intestinal lining (mucosa). Mercury can impair cell-mediated immunity resulting in decreased ability to clear viral and yeast infections. It induces autoimmunity (the body attacks itself) resulting in the production of anti-brain antibodies. It can cause or worsen zinc deficiency and inactivate DPPIV (the enzyme that breaks down casein and gluten.) It alters the brain's ability to clear unwanted brain cells or neurons (apoptosis), a process that is a normal and integral part of brain development. It affects the body's anti-oxidation ability by depleting intracellular glutathione (a protein important in clearing toxins from the body.) The clinical effect on the CNS includes impaired motor planning, decreased facial recognition, blurred vision and constricted visual fields, insomnia, irritability, tantrums, excitability, social withdrawal, anxiety, difficulty verbalizing, altered taste, impaired short-term memory, slowed reaction time and difficulty with concentration. It has been shown to be the most toxic to infants and males.

So how are our kids being poisoned by mercury? Mercury is not uncommon in our environment. Fish in our diet and dental amalgams in our mouths are common sources, but by far the largest exposure to our infants are from vaccinations! Thimerosal is a preservative that is included in many vaccines to prevent bacterial contamination and thus, prolonging shelf-life and facilitating multi-use vials. It consists of approximately 50% ethylmercury. As noted above, mercury can be highly toxic, even in small doses. Some infants receive up to 100 times the EPA recommended safe level of oral exposure to mercury based on adult weights, in one day. Injecting it into their muscle also bypasses one of the main first-line defense mechanisms, the GI tract. We now begin immunizing newborns with hepatitis B vaccines as early as the day of birth. It doesn't seem like much of a stretch in logic to think that these infants' immune systems and neurological systems are too immature to handle such a toxic load. Fact is, most children seem to be able to tolerate it just fine, but we believe that many children, who are genetically predisposed, are being adversely affected. Several databases have reported an alarming increase in the incidence of autism in the last 20-year period (over 1000% increase was reported in California.) It is also interesting to note that in that same period, the number of immunizations that a child receives before the age of two has increased from 8 in 1980 up to 33 in the year 2001, and more are being developed. When the Hepatitis B and the HIB vaccine were added to the schedule in the early 1990s the load of mercury to our children more than doubled. Largely as a result of the effort of many DAN!-affiliated practitioners and parents in 1998, the FDA has required that vaccine manufacturers remove thimerosal from their vaccines, but fell short of demanding a recall of the existing thimerosal-containing product. This remains a hotly debated issue among the medical and parent community. The Institute of Medicine convened in 2001 to research this issue in more detail and concluded that there is not enough evidence currently to prove or disprove the association between vaccines and autism but conceded that there is biological plausibility for the interaction. They called for more research into this issue.

Thimerosal has also been present in other commercial products such as contact lens solution (removed in 1998), eardrops and various nasal preparations. It is interesting that thimerosal was taken out of animal vaccines a decade ago because it was felt to be unsafe. There is ample evidence that manufacturers of vaccines new about the dangers of thimerosal as early as 30 years ago.

B. Heavy viral antigen loading

Mercury may not be the only way that vaccines may be harming some children. A British researcher, Andy Wakefield, has studied the relationship between autism and enterocolitis (an inflammatory bowel disorder). As will be discussed later, the majority of children with autism have some abnormalities of their gastrointestinal functioning. He did colonoscopies on a group of autistic children with gastrointestinal problems and found a significant degree of lymph node hyperplasia (enlargement) in the mucosa of the ileum (the last portion of the small bowel). On biopsy, he discovered that these nodules were full of vaccine-strain measles virus. He hypothesizes that the combination MMR vaccine overloads the autistic immune

system with too extensive of a viral load at one time. These children are unable to clear the virus resulting in a chronic sub-clinical infection. These initial findings have recently been replicated in other labs. Others have found evidence of measles virus in the cerebral spinal fluid of autistic children at rates that are significantly higher than normal children. It may be that combination vaccinations such as the MMR and the DPaT may also overstimulate these children's immune systems. Many autistic children show a hyperactive response when vaccine titers (especially measles) are tested. Whether this reaction to viruses is a cause or merely a reflection of the underlying immune system abnormalities is uncertain. Many epidemiological studies have been done that have looked at this connection without finding an association. However, these types of studies are unable to answer the question conclusively because they cannot limit the variables that may be involved. Clinical research on autistic children themselves is much more likely to resolve this issue. It certainly is plausible that the MMR and exposure to other viruses (including native infections) can be contributing to the severity of their symptoms but it is unlikely to be the sole causative factor.

Among the problems with the autistic child's immune system is an imbalance between the TH1 (responsible for viral and fungal infections) and the TH2 (responsible for antibody formation and allergies) subtype lymphocytes. Autistic children are shifted towards TH2 and away from TH1 making them less able to defend against and rid their system of viral and fungal infections. This shift also makes them more likely to form antibodies (resulting in multiple allergies) and autoimmune reactions. These persistent infections and antigens result in chronic inflammation that can lead to increased gut permeability and abnormal bowel flora. Many autistic children also have recurrent and prolonged viral infections (upper respiratory infections, gastroenteritis, bronchitis, etc.)

C. Antibiotic overuse

The over-prescription of antibiotics is a problem not isolated to autism and has led to the emergence of many antibiotic-resistant organisms that have become very difficult to eradicate. Autistic children have a particular problem with this because of the above discussion about their low TH1 lymphocyte activity. Antibiotics are generally broad-spectrum, meaning they wipe out all the bacteria that they come in contact with. Our bodies harbor a microscopic ecosystem of bacteria and fungi, some beneficial and some harmful. When we take an antibiotic, it clears our system of both kinds, good and bad, and provides the harmful resistant organisms an opportunity to take over. This is referred to as intestinal dysbiosis. Because autistic children have depressed TH1 function, they have less ability to clear these harmful organisms and to restore the normal balance of intestinal flora. This can result in yeast overgrowth and persistent bacterial and parasitic infections of their gut. These organisms can interfere with normal digestion and can emit harmful metabolites (break-down products) that can affect autistic behavior.

D. Other infections

Because of their diminished immune function and poor nutritional status, many autistic children are prone to other infections such as recurrent ear infections, reactive airway disease, eczema and sinusitis. This certainly exacerbates the problem with antibiotic overuse, as described above, since much of the time, antibiotics are prescribed to treat these illnesses. At times, other children, who seem to be developing normally, seem to regress after a more serious infection and develop symptoms of autism. This suggests that this infection may have been the triggering event that started their autistic biomedical cascade.

IV. BIOMEDICAL DYSFUNCTIONS OF AUTISM

A. Poor nutrition/vitamin and mineral deficiencies

Autistic children are known to be very picky eaters. For reasons that we will discuss as part of the casein/gluten diet section, they tend to crave carbohydrates and become addicted to certain foods, and thus, narrowly self-limit their diet. This diet typically does not provide them with the essential vitamins and minerals that they need for healthy body functioning. Couple this with the fact that they have abnormal gastrointestinal systems that prevent absorption and proper utilization of the nutrients that are taken in. And, as mentioned in previous discussions, their body's system to regulate these essential nutrients is dysfunctional. For all of these reasons, children with autism almost universally are deficient in certain vitamins and minerals. These nutrients act as anti-oxidants and cofactors for many enzymatic pathways and are needed in the development of healthy gastrointestinal, immunological and neurological systems. They are also critical in detoxification. Common mineral deficiencies include zinc, selenium, magnesium, molybdenum, manganese, vanadium and chromium. They are deficient in vitamin C, vitamin B6 (pyridoxine or pyridoxal-5-phosphate), vitamin B12, vitamin A, vitamin E, folate and niacin.

B. The Leaky Gut Syndrome

As mentioned earlier, autistic children have abnormal gastrointestinal systems. The reasons for this are varied but include abnormal mucosal barriers from dysfunctional intestinal metallothionein, depleted sulfate which prevents normal healing of the mucosal layer, chronic inflammation from persistent viral infections and autoimmune reactions, injury to the mucosa from abnormal bowel flora and abnormal pancreatic digestive function. This leads to incomplete breakdown of proteins resulting in partially undigested chains of amino acids called peptides, which are usually several amino acids in length. These peptides, which would normally be broken down further or passed through the stool, are absorbed through the damaged and overly-porous mucosal lining. It has been shown that the peptides that most often are at fault are from casein (milk) and gluten (wheat, barley, oats, rye). These children have diminished functioning of an enzyme called DDPIV that is responsible for breaking down these particular peptides. The peptides are absorbed through the intestinal tract

into the blood stream and from there are carried to the various body tissues including the brain. These peptides have basically the same structure of a group of hormones called opiates. There are opiate receptors throughout the body but a particularly high concentration exists in the brain. When activated they cause euphoria and decreased pain response. These are the same receptors that bind opioid-like drugs including morphine and heroin. It is hypothesized that the gluten and casein proteins are binding to these receptors and effectively causing an opioid intoxication. That may be why these autistic children seem to crave foods rich in gluten and casein. They frequently will have severe tantrums when these foods are first eliminated or become unavailable. They are potentially going through an opiate withdrawal that often results in and is relieved by binging on these foods. All they know is that eating these foods seem to make them feel much better, which in turn causes them to limit their diet to these specific foods. Unfortunately, chronic opioid toxicity affects learning, social interaction and motor/sensory neurological function. Most autistic children have also shown to have an abnormal immune system response to gluten, casein and soy.

C. Yeast and bacterial overgrowth

Several reasons exist for the intestinal dysbiosis (abnormal imbalance of pathogenic gut flora) that is so common in children with autism, including low TH1 lymphocyte functioning in the immune system, antibiotic overuse, impaired metallothionein function and chronic inflammation with intestinal mucosal damage and altered pH. We have discussed details about these previously. Suffice it to say that the problem exists and can be difficult to eradicate, requiring consistent attention. Intestinal dysbiosis can cause symptoms including diarrhea and/or constipation, gas, bloating, abdominal pain and acid reflux. The organisms can also produce toxic metabolites that enter the bloodstream and affect immunological and neurological function. Yeast can also contribute to the leaky gut problem by forming spores that further damage the intestinal lining.

D. Impaired detoxification/heavy metal toxicity

Because of low levels of antioxidants, an overly permeable gut, and impaired metallothionein function, autistic children have a decreased ability to clear their body of unwanted toxins. These children are also very commonly deficient in a molecule called glutathione which is one of the key elements to the liver's ability to protect the body against harmful substances. This impaired detoxification ability has clearly been shown with the mercury issue. Other metals are found in autistic children at above normal levels including aluminum, arsenic, antimony, tin, and lead. The children are exposed to these metals from a variety of sources including food, water, soil, paint, medications and other commercial products. These metals can also create problems and sometimes the combination of these metals acting together are much worse than what they can do individually and thus, it is important that we assist their bodies with removal of these harmful materials.

E. Impaired anti-oxidation

Oxidation is a biochemical process that generates free radicals (containing an extra oxygen molecule). These free radicals can be quite damaging to body tissues especially the gut and the brain. Fortunately, the body has an anti-oxidation system in place to combat this damage. For a number of reasons, children with autism have an impaired anti-oxidation system. This relates to their poor nutrition since many of the vitamins and minerals, such as vitamin C, vitamin B6 and zinc are powerful antioxidants. Weak hepatic (liver) detoxification and greater toxic burdens also contribute to oxidative stress. These children are also measurably low in enzymes that normally counter oxidative stress including glutathione, GSH-reductase, lipoic acid, and uric acid.

F. Low Fatty Acids

Omega-3 fatty acids are naturally-occurring molecules that are highly concentrated in fish oils and other sources such as flax seed oil and wild game. The western diet has seen a significant decline in the intake of these oils as we have become less dependent on fish and wild game for food. Researchers have found a strong link between depletion of these acids and some psychiatric illnesses such as bipolar disorder and major depression. Supplementation of these oils has made profound differences in many people with these diseases. These researchers hypothesize that people with autism could also be helped with these supplements. There has been some anecdotal evidence that this may be the case. Other suggestive evidence of a relationship includes the high rate of inflammatory bowel disease present with autism that also correlates to low omega-3 fatty acids. Unfortunately, at this point, no quality research studies exist concerning this issue. These studies are currently being designed.

G. Impaired pancreatic function

We have previously discussed how many autistic children have impaired ability to break down certain proteins completely during digestion. There are many enzymes and hormones that participate in normal digestive function, many of these either secreted by or stimulate the pancreas. One of these stimulatory hormones is called secretin. Secretin is often injected during certain gastrointestinal procedures to stimulate the pancreas. It was discovered during one of these examinations in a child with autism that shortly after this test, his diarrhea resolved, he had improved task focus and he could imitate simple words. It has subsequently been used in many other autistic children with similar results. It is believed that not only does secretin stimulate proper digestion but works as a neurotransmitter directly on the brain. Secretin receptors have been found in an area of the brain called the amygdala. Functions of the amygdala include face recognition, emotion, fear, anxiety and stress response. It also controls the autonomic nervous system, which regulates body temperature, digestion, GI function, sensory input including taste and pressure, and cardiac and pulmonary function. Secretin use in autism has been studied with several placebo-controlled trials most of which have reported negative findings (i.e. it made no significant difference in the improvement of the children with autism.) The problem with these studies is that they had flaws in their designs and outcome

measures that may have skewed the results or at least, made it difficult to detect improvement. When measured by parental observation (also placebo-controlled) and after giving a series of 3 injections, significant improvement was demonstrated in younger children (ages less than 5). So, the findings in the research are still in debate but in the meantime, some autistic children are receiving secretin injections and seem to be getting better.

H. Decreased immune function/ altered TH1/TH2

Lymphocytes are cells within the body that are responsible for fighting infection. There are many subtypes, each of which has different responsibilities. Among these are TH1 lymphocytes that are responsible for combating viruses and fungal infections and TH2 lymphocytes that are responsible for producing immunoglobulins (antibodies) and responding to allergies. These are normally controlled and balanced very closely by a complex network of messengers called cytokines. Autistic children have an imbalance of these two types of T-lymphocytes with a predominance of TH2 and a deficit of TH1 functioning. This predisposes them to increased amount of allergic and autoimmune disorders and a decreased ability to fight off viral and fungal infections. For example, IgG food allergy tests show a significantly increased amount of food sensitivities in autistic children. They are also more prone to seasonal allergies, hay fever, asthma and allergic rhinitis. Autoimmune disorders such as inflammatory bowel disease, rheumatoid arthritis and lupus are much more prevalent in families of autistic children. Autoimmunity means that the body has an inappropriate reaction towards itself. In other words, the body misinterprets part of itself as foreign and attacks. In particular, Dr. Vijendra Singh as done extensive research in this area and found that a majority of the autistic children that he has tested have antibodies directed against the myelin sheath in their own brain cells. The myelin sheath acts as an insulator on the neuron that increases the processing time of the signals along this brain cell. If this sheath is destroyed, it would slow down brain processing time. This happens commonly in multiple sclerosis, another autoimmune disorder, but affects more of the peripheral nerves resulting in muscle weakness. As mentioned in other sections, autistic children also have impaired ability to clear common viruses and can have persistent yeast overgrowth in their bowels.

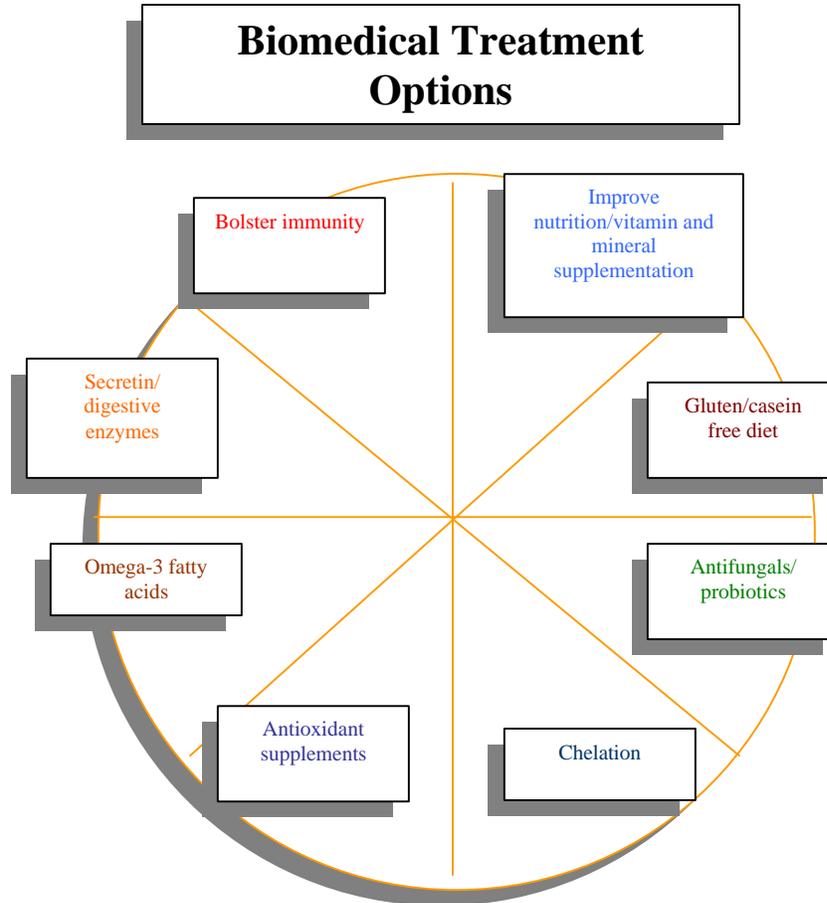


Figure 2. Biomedical Treatment Options

V. BIOMEDICAL TREATMENT OPTIONS

A. Improve nutrition/vitamin and mineral supplementation.

1. Decrease Additives

a) Rationale

Artificial colors and preservatives can cause various reactions in many “sensitive” people and it seems to affect behavior in many autistic children. Eliminating these from the diet is a good first step.

b) Which additives are safe/which to avoid

Please refer to the diet and nutritional supplement handout for a list. Special Diets for Special Kids by Lisa Lewis is also a good source for information in this area.

2. Sugar and artificial sweeteners

a) Rationale

Excessive amounts can cause disturbances in sleep, mood, behavior, cognitive functioning and general appearance. It also worsens yeast overgrowth.

b) Try an "elimination test"

5 days usual amount of sugar, 3-week slow taper off sugar, then a 5-day binge and see what happens. This will probably convince you about how sugar affects behavior.

3. Increase fiber

a) Rationale

Many autistic children have trouble with constipation alternating with diarrhea. Keeping the stools soft decreases gastrointestinal discomfort and improves digestion.

b) Recommendation

Keep stools soft with a goal of at least one good bowel movement each day.

c) Sources of fiber

(1) whole grains (careful about gluten), veggies, fruit, nuts, seeds, etc.

(2) commercial fiber supplements.

(3) herbal supplements

(a) Use 1-2 tablespoons daily of ground flax seed, psillium seed powder or food grade cellulose which is available as Cellulose Powder from Allergy Research Group at www.emersonecologics.com or 800-654-4432.

d) Laxatives

(1) You may need to use these occasionally to treat constipation, but you should avoid these on a regular basis so that your child does not become laxative-dependent. Oral magnesium is a very good laxative and most autistic children are deficient in magnesium anyway.

(2) Examples

(a) Smooth Move Tea (Traditional Medicinals),

(b) Herb-lax (Shaklee)

(c) Karo syrup

(i) 1 tsp per ounce of liquid

(d) Prune Juice

(e) Miralax

4. Increase water intake

a) Rationale

Decreases constipation, improves digestion and prevents dehydration which can aggravate side effects of certain medications

b) Source

Filtered or bottled water would be ideal. It is less contaminated with heavy metals and other toxins

5. Increase protein

a) Rationale

Processed carbohydrates can cause wide fluctuations in blood sugar resulting in difficulties with behavior and attention. Protein has more of a stabilizing affect on the blood sugar by less immediate stimulation of body insulin.

b) Source

(1) meats, eggs, protein powders, nuts, seeds

(2) commercially available protein powder (use soy or rice based if on gluten-free diet)

c) Amount

A good estimate of protein need would be the child's weight multiplied by 0.8 grams per day divided into 3-4 servings. Providing relatively more protein in the morning will often improve concentration throughout the day.

6. Organic foods

a) Rationale

Changing to foods that are free from artificial chemicals, hormones and antibiotics would decrease the toxic and allergic burden on your child.

b) Source

Many supermarkets provide organic foods. Wild Oats Market or Good Earth are examples of local grocery stores with a good selection of naturally-grown and organic foods.

7. Vitamin/Mineral supplements

a) Multivitamin/mineral supplements—some have been specially formulated for children with autism or PDD

(1) Nu Thera

(a) Kirkman Labs 503-682-5678

(2) DAN PLEX

(a) Hopewell Pharmacy 800-792-6670

(3) Brainchild

(a) www.brainchildnutritionals.com

b) Vitamin C

(1) Benefits

(a) an important antioxidant

(2) Dose/formulation

(a) Start at 5-10 mg/kg/day and gradually increase to tolerance up to around 50 mg/kg/day in divided doses (average around 8,000 mg/day)

(b) Use the buffered preparation of vitamin C esters

(3) Side effects

(a) gastrointestinal distress and diarrhea, usually in higher doses

(b) potential for kidney stones at high doses.

c) Vitamin E

(1) Benefits

(a) an important antioxidant

(2) Dose/formulation

(a) 2-4 mg/kg/day (3-6 IU/kg/day)

(b) Mixed tocopherols is preferred preparation

(c) Many are prepared from soybeans and may be a problem if your child is allergic to soy.

d) Vitamin B6

(1) Benefits

(a) another antioxidant

(b) has shown to be effective in about 50% of patients in multiple well-controlled studies

(c) improvement is seen in language function, eye contact, self-stimulatory behavior, interest in surroundings, tantrums

(2) Dose/formulation

(a) Can be found as B6 (pyridoxine), pyridoxal-5-phosphate (P5P) or a mixture of the two (rare).

(i) Super-Nu-Thera from Kirkman's labs is a multivitamin/mineral supplement with extra B6

(b) Dose up to 17 mg/kg/day of B6 or 3 mg/kg/day of P5P (maximum of 500 mg B6 although some have suggested that 1000 mg is better or 100 mg P5P).

(c) Start at about 25% of target dose and increase slowly over 10-14 days.

(d) Keep in mind that there is not a correct "dose" and to look for the most effective amount for the individual.

(e) Even very high doses have been safe.

(f) Many of the P5P preparations contain supplemental copper so use a copper-free preparation.

(3) Duration of treatment

Do a 6-8 week trial and discontinue if no positive effect. Benefits often start within a few days

(4) Side effects

(a) Magnesium deficiency

(i) Add magnesium supplement

(b) Peripheral neuropathy (numbness in hands and feet)

(i) Rare

(ii) improves with magnesium supplements or discontinuing B6.

e) Vitamin A

(1) Benefits

(a) supports gastrointestinal membranes

(b) improves vision

(c) bolsters immune function.

(2) Source

(a) cod liver oil - This is the best from as many of the synthetic forms found in vitamin supplements have limited absorption and a structure that prevents them from attaching to the appropriate receptors

(b) vitamin supplements

(3) Cautions

(a) can cause fetal defects so avoid during pregnancy

(b) can develop toxicity if given in too high of doses

(i) Signs of excess include nausea, headache, dry "dirty-skin" rash around neck.

(ii) These symptoms should go away if vitamin A is discontinued

f) Vitamin B12

(1) Benefits

Mechanism not well understood but many autistic children show improved behaviors with supplements. Vitamin B12 deficiency in other forms can present with a combination of muscular, neurologic and even psychiatric symptoms. Vitamin B12 deficiency can also result in anemia. It is also felt that Vitamin B12 helps to build and repair the myelin sheath that is often damaged in autistic children.

(2) Tests

(a) Serum B12

(i) level reads false B12 and may be elevated, even if low functionally

(b) Urine or blood methylmalonic acid (MMA)

(i) better test

(ii) accumulates when Vit B12 not functioning well

(c) Tests may not be the best indicator of response—trial of therapy is better

(3) Route

(a) Give as IM (intramuscular) injection initially

(i) It works better. Some individuals are unable to absorb the oral form and require injections.

(ii) Helps you to assess best response of child

(b) May substitute high oral dose if you can duplicate child's best response with it, indicating that they are absorbing it orally. Theoretically, oral dose should work as well since most of these children do not have an intrinsic factor deficiency which creates the inability to absorb Vit B12 orally.

(4) Indications

- (a) Macrocytic anemia
- (b) High methylmalonic acid
- (c) Positive anti-myelin basic protein antibodies

(5) Dosing

(a) Methylcobalamin is the most effective form and you will probably need to have this done at a compounding pharmacy.

(i) Coastal Compounding in Georgia is a good source, but there are some local pharmacies like University Pharmacy in Salt Lake who are now providing this for us.

(b) Initial loading is 1250 mcg injections twice a week for 2 weeks, followed by once a week for an additional four weeks. This should give you your best response at which point you can substitute oral forms of it. It is not uncommon, however, to use the injections twice a week indefinitely until the labs reverse or you are no longer seeing positive effects.

g) Folic acid

(1) Benefits

- (a) Helps to quench hyperactivity seen when DMG supplement is used.
- (b) Helps prevent birth defects.
- (c) Helps to correct certain types of anemia related to a deficiency in folic acid and B12.

(2) Tests

(a) Usually measures high in serum or red blood cells but functional form of folic acid is often low.

(3) Dose

- (a) 800-2400 mcg

h) Zinc

(1) Benefits

- (a) An antioxidant,
- (b) couples with DMSA and is more readily absorbed during chelation.
- (c) decreases intestinal permeability.
- (d) increases immune function
- (e) induces many digestive enzymes

(2) Dose

- (a) 1-2 mg/kg/day (maximum of 50 mg/day unless lab evidence supports marked deficiency)
- (b) I frequently use the formula of the child's weight in pounds plus 15 mg in zinc as a daily supplement especially in those children who are chelating because they have a hard time maintaining adequate zinc levels.
- (c) use plasma, erythrocyte or platelet zinc levels as guide to higher dosing. RBC levels are most accurate in reflecting total body deficit. I usually check minerals levels every 6 months to ensure that it is in the right range.

i) Calcium

(1) Benefits

- (a) Component of bone growth
- (b) Important for proper skeletal and heart muscle function

(2) Signs of deficiency

- (a) Muscle cramps, irritability, insomnia, weakness

(3) Dose

- (a) At least 1 gram/daily
- (b) This is especially important to supplement in those children on a casein-free diet since they will not be getting calcium from milk.
- (c) There are many calcium fortified casein substitutes and even orange juice is calcium-fortified, but I usually add a calcium powder to ensure proper daily doses.

j) Selenium

(1) Benefits

- (a) Selenium is an important mineral in that it assists mercury detoxification in particular.

(2) Dose

(a) Limit to 1-4 mcg/kg/day

(b) Can be toxic in excess doses, however, it has been rare to see elevated RBC selenium levels in any autistic child that I have tested at doses up to 200mcg a day.

k) Magnesium

(1) Benefits

(a) Important for proper muscle function and is one of the major intracellular electrolytes that maintains our cell membrane activity throughout the body.

(2) Signs of deficiency

(a) Muscle twitch, headache, hyperactivity, constipation, muscle weakness, heart palpitations and arrhythmias with severe deficiency.

(3) Dose/Formulation

(a) Used as magnesium sulfate cream or Epsom salts to improve sulfation as well as boosting magnesium levels

(i) Epsom salt bath once a day or magnesium sulfate cream 1 gram twice a day. Available from Kirkman Labs

(b) 3-4 mg/body pound up to 400 mg per day in adults as oral supplement. You can use lab values to guide treatment but needs to be from an RBC minerals test since a serum level is maintained strictly within a narrow range by the body and can be misleading about total body stores.

(4) Also needed in conjunction with high dose B6 to prevent depletion

l) Other minerals

(1) Molybdenum, manganese, vanadium, chromium should also be supplied as part of multi-mineral supplement

(a) Everyday Companion powder from Kirkman's labs is a good multi-mineral.

(2) Copper

(a) Most autistic children have an elevated copper level

(b) Avoid copper—use copper free supplements.

8. Avoid allergenic foods

Using IgG and IgE antibodies food sensitivity testing, you can learn which foods your child may be sensitive to. IgG is a marker for delayed hypersensitivities and can produce more behavior-related and subtle physical symptoms (red ears, red cheeks, bowel pattern changes) whereas IgE are more likely to have immediate allergic symptoms including hives, swelling, and trouble breathing. Most people have some food sensitivities but autistic children tend to have more than usual. A trial of strict avoidance of allergenic foods will help you to know which foods your child is particularly sensitive to (the antibodies test is not a perfect indicator.) Do a 2-week trial of strict avoidance followed by reintroduction of the food and see what happens. I typically do not order this test until several months of vitamin therapy, gluten-free/casein free diet and antifungal therapy because I believe that many of the food allergies are related to leaky gut syndrome and may correct themselves with these interventions. It has been found as well that many autistic children are allergic to soy and so I would avoid soy-based substitutes to casein as much as possible.

B. Gluten/Casein Free Diet

1. Casein Free

- a) Casein is a milk protein—refer to diet handout.
- b) no test exist that definitively detects need for diet
 - (1) trial is the best test
- c) a 3-week trial of removal of all milk and casein should be enough to detect benefit. If it helps, keep doing it.

2. Gluten Free

- a) Gluten is a wheat protein but exists in many foods and commercial preparations
- b) Diet information/gluten-containing foods
 - (1) Please refer to diet handout for more information about which foods contain gluten
 - (2) Special Diets for Special Kids, by Lisa Lewis
 - (3) The Cheerful Chemist's No Casein, No Gluten, Sugar Optional Cookbook by Sally Ramsey.
- c) Tests exist but are not definitive, just suggestive
 - (1) Urine test for intestinal permeability
 - (2) IgG antibodies to wheat, rye, oats, barley

(3) Antibodies to transglutaminase, endomysium, reticulin, and gliadin (these are tests for celiac disease which occurs in a minority of autistic children and if negative, do not rule out gluten sensitivity.)

(4) Elevated IgA antibodies strongly correlate with celiac disease

(5) Small bowel biopsy—more specific for celiac disease, can be negative for gluten sensitivity.

d) Gluten-free diet trial

(1) It is difficult and life-style changing but gets easier over time.

(2) Get help from other parents on the diet

(3) Be ready before you start

(4) 4-month trial

(a) takes longer to see effects than with casein

(5) Every autistic child should have a trial, regardless of test results

e) Duration

(1) If it helps, keep going as long as possible

(2) It is difficult to know when to stop the diet. Hopefully, once the other GI system problems are fixed and they can tolerate gluten and casein. Some children have done well coming off the diet and substituting digestive enzymes in its place but others have regressed when this was tried. I think this will be an individual decision but at this point, I would recommend continuing the diet as long as possible.

3. Enzyme Supplements

There are commercially-available enzyme supplements of DDPIV that seem to help to some extent but should not be used as a replacement for the diet at least initially. These may help for preventing problems with food “accidents”. They are available through Kirkman’s labs and Houston neutraceuticals.

a) Kirkman’s Enzyme Complete with DPPIV or Houston’s Peptizyde.

b) Work best if given just before every meal.

C. Antifungals/Probiotics

1. Antifungals

a) Tests

(1) Stool culture

It is good for detecting aerobic yeast but cannot rule out presence of anaerobic yeast if negative. A sensitivities test would aid in choice of antifungal by determining drug resistance.

(2) Urine organic acids

(a) indirect evidence of fungal overgrowth by measuring fungal metabolites. This will detect anaerobic yeast.

(b) Elevated citramalate, B-ketoglutarate and tartaric acid are markers for yeast overgrowth.

b) *Saccharomyces boulardii*

(1) It is a natural grown yeast that kills other yeasts and then clears out of your gut when you stop taking it

(2) Can get without a prescription and works similar to antifungal medications.

c) Medications

(1) Nystatin

(a) Dose/formulation

(i) Use powder form or have it compounded in a stevia base

(ii) Frequent dosing (4-6 times a day)

(iii) Unfortunately, many of the yeast are resistant to nystatin, so it usually requires stronger antifungals to kill them.

(b) Side effects

(i) No toxicity because it is not systemically absorbed (it stays in the bowel).

(ii) Die-off reactions

(a) along with *saccharomyces boulardii*, it produces the most profound die-off reactions of all the antifungals.

(b) transient worsening of diarrhea and behavior after initiating therapy as all the yeast is being killed (more of the yeast metabolites are being released into the blood).

(c) Activated Charcoal

- (i) May help minimize die off reaction by absorbing toxins
- (ii) dose is 4 capsules a day
- (iii)do not give with food or other medication

(2) Systemic antifungals

- (a) Must monitor liver function tests every 3 months for toxicity—has always been reversible when you stop the medication
- (b) Should also monitor kidney function tests with Lamisil
- (c) Examples include Nizoral (ketoconazole), Diflucan (fluconazole), Sporanox (itraconazole) and Lamisil (terbinafine).
- (d) I typically prescribe 3 week treatment regimens most commonly which avoids liver toxicity.

d) Duration of therapy

Yeast can be very difficult to eradicate. It may take prolonged duration of antifungal use, higher than usual doses, or trial of multiple agents. It is best to monitor for yeast frequently if your child is one of those with problems. DMSA/lipoic acid is also likely to create yeast overgrowth, even in children who did not have problems previously.

2. Antibacterials

a) Rationale

- (1) The bowel may also be colonized by an overabundance of bad bacteria and eliminating these can make it easier to reestablish normal flora.
- (2) Those at risk often have a history of frequent or recent antibiotic use, or complex chronic illness

b) Testing

(1) Urine organic acids

- (a) Clostridia species overgrowth is suggested by high levels of dihydroxyphenylpropionic acid (DHPPA)
- (b) There are about 7 or 8 other markers that are commonly elevated with abnormal bacteria or parasite presence in the bowel.

c) Medications

(1) Biocidin

A natural supplement that fights clostridia

(2) Flagyl

(a) I usually prescribe this for about 14 days.

(3) Oral gentamycin

(a) 160 mg five times a day for 3 days

(b) not systemically absorbed so complications are limited.

(4) Oral vancomycin

(a) 250 mg five times a day for 3 days

(b) not systemically absorbed so complications are limited

(5) Oral IG

(a) Some doctors have successfully treated more severe or resistant gut bugs with immunoglobulins given orally. There has been some recent research that suggests that this can be helpful. The main disadvantages of this therapy is the cost and the small risk of contracting blood-borne infectious illness since IG is a blood product.

(6) TOUFF

This is a new transfer factor that is specific to *Clostridium* and shows promise in treating these organisms without the risk of antibiotic use. It is made from eggs, though, and so children who have egg sensitivities should not use it.

3. Anti-parasitics

a) Rationale

There is some controversy about the need to rid the gut of some of these parasites—many are common in normal stool samples (*Dientamoeba fragilis*, *Entamoeba hartmanni*, *Entamoeba coli*, *Endolimax nana*, and *Balantidium coli*), others are more virulent (*Entamoeba histolytica* and *Giardia lamblia*). Value of removing them is felt mostly to be due to the fact that they evoke an immune response to their presence and potentially could be causing symptoms such as fatigue, malaise, rashes, night sweats, headaches and a long list of other vague complaints. Some people have found that these symptoms went away after they were treated

b) Treatment

(1) Bactrim or Septra (trimethoprim/sulfamethoxazole) DS one pill twice a day plus Humatin (paromycin) 250 mg four times a day for 14 days.

(2) Metronidazole for 14 days (dose dependent on weight)

(3) Yodoxin (diiodihydroxyquin) 650 mg three times a day for 14 days.

4. Probiotics

a) Rationale

Help to promote re-colonization with normal bowel flora

b) Sources

(1) Lactobacillus

(a) found in yogurt (not recommended on casein-free diet) but also comes in commercial preparations (e.g. Kirkman labs).

(i) ProCulture Gold

(ii) Culturelle

(2) Bifidobacter

(a) commercially available (eg. Kirkman labs)

(i) ProBioGold

5. Yeast-free diet

a) Rationale

Although yeast that comes from diet does not cause yeast infection, it is felt to contribute to the immune response of the individual who is already sensitized. High sugar and carbohydrates provide nutrients to yeast that are already colonized.

b) Diet

Avoid leavened foods, fermented and aged products, juices, dried fruits, condiments and sauces, mushrooms, B vitamins, sugar and carbohydrates

c) Trial of avoidance

(1) 5-14 days then a binge and see what happens.

d) Duration

If your child has a dramatic change in behavior, it is best to try to maintain diet as yeast-free as possible.

D. Heavy metal chelation

1. Rationale

a) Chelation is the binding of heavy metals to medications that are subsequently eliminated from the body naturally.

b) The obvious effect is the removal of heavy metals but it is possible that this is a coincidental rather than treatment effect, meaning that this may not be why the children are improving. Perhaps the effect of chelation is to improve sulfation leading to better sulfur amino acid balance (autistic children have elevated cysteine/sulfate ratios and other indications of disordered sulfur amino-acid chemistry.)

c) DMSA is a strong antioxidant so that may also be why it helps.

2. Preparatory treatment

It is imperative that the intestinal dysbiosis, abnormal intestinal permeability and nutritional derangements be corrected as much as possible before starting chelation. Many of the drugs and supplements used in chelation can cause an explosion of an existing yeast problem masking the treatment effect and in fact, making the child seem worse.

3. Lab testing

Many of these are unnecessary in making decision whether to treat; a clinical trial may still be warranted.

a) urine, blood and hair mercury

(1) typically normal or negative unless the exposure has been fairly recent (within a few months). In fact, a low hair mercury level (especially if from a sample from child's first haircut) indicates an abnormal excretion of mercury from the body and may give indirect evidence of an abnormally high body mercury load. Autistic children's hair mercury level is usually much lower than neurotypical children.

(2) Unprovoked mercury levels in the urine and blood are usually extremely low or zero. This is because the mercury moves quickly out of the blood and binds to body tissues.

b) Provoked excretion of mercury and heavy metals

(1) the only accurate way to estimate the total body burden of heavy metals. Unfortunately, this can be misleading as well with a single sample because even with chelators, individuals can metabolize the metals and different rates.

(2) Give DMSA 10 mg/kg and collect the next six to twelve hours of urine produced for a heavy metal analysis.

(3) No reference range exists for provoked metals so any level over the unprovoked reference range is sufficient to warrant treatment.

c) Glucose-6 phosphodiesterase (G-6PD) levels

(1) usually between normal and deficient in heavy metal poisoning

- d) Urine organic acids and amino acid test
 - (1) Uncoupling of oxidative phosphorylation
 - (a) elevated fatty acid metabolites
 - (b) elevated lactate
 - (c) elevated hydroxymethylglutarate
 - (2) Partial blocks of several Krebs cycle enzymes
 - (3) Elevated dopamine
 - (a) Indicated by elevated homovanillate
 - (4) Impaired detoxification markers (usually several abnormalities)
 - (a) Classic is glutathione depletion—indicated by elevated pyroglutamate
 - (5) Dysbiosis markers
 - (a) Classic mercury picture is elevated yeast metabolites, but pathogenic bacteria, including Clostridium, can also be present.
- e) Glutathione reductase
 - (1) reduced in heavy metal poisoning
- f) elevated blood or urine pyruvic acid level
- g) fractionated urine porphyrins—
 - (1) uroporphyrin, coproporphyrin (elevated) and pre-coproporphyrin (most specific but not commercially available) analysis
- h) myelin basic protein and glial fibrillary acidic protein antibodies
- i) low erythrocyte glutathione level
- j) low plasma essential amino acids
 - (1) almost universal, not correlated with diet
 - (2) Two known effects of mercury are inhibition of synthesis/release of hydrochloric acid in stomach and inhibition of various proteases and peptidases making it harder for amino acids to be absorbed.
- k) Elevated urine D-glucaric acid
 - (1) Doctor's Data lab on first morning urine
- l) Immune system Tests

- (1) Elevated CD4 cells, low CD8 cells, elevated CD4/CD8 ratio (opposite of AIDS)
- (2) Low NK (natural killer) cells
- m) CBC with differential
 - (1) High MCV (can also be from Vitamin B12 or folate deficiency), high monocytes, high eosinophils
- n) Serum electrolytes
 - (1) Low CO₂
- o) Liver function test are elevated
- p) RBC intracellular trace minerals (metamatrix)
 - (1) Classic pattern is normal calcium, potassium, and copper with low to borderline-low values of everything else.
- q) Hair elements
 - (1) Scattered pattern—at least 2 less than 2 standard deviation below mean, plus at least 2 more than 2 standard deviations above mean—usually see many more than 2 both high and low.
 - (2) High hair calcium
- 4. Physical exam findings
 - a) Dilated pupils (secondary to mercury inhibiting synthesis/release of acetylcholine)
 - b) Sweaty hands and feet
 - c) Pathologic reflexes—babinski most common
 - d) Very brisk knee jerk reflexes
 - e) Slight esotropia
 - f) Rashes, eczema
 - g) Elevated heart rate
- 5. Concurrent testing
 - a) CBC, ALT, AST
 - (1) Test after first or second cycle then every 3 months after that if initially normal

(2) If abnormal, stop treatment and follow labs until returned to baseline

(3) If abnormalities are not too severe, continue DMSA at lower dose with careful monitoring

b) Urine metal analysis

(1) Do after 2nd cycle and about every 4-6 cycles after that

(2) Collect after the second dose and within six hours of the last dose of the cycle (morning urine on the 3rd day of the cycle is best)

(3) Timed specimens are best if able (24 hr, 12 hr or 6 hr) or first morning urine if child continent at night (represents an 8 hr specimen)

(4) Random or spot urines

(a) May miss peak excretion

(b) Acceptable if you collect two or more specimens and combine them.

(c) Best time for a spot urine sample is two or four hours after a dose.

c) Stool mercury analysis

(1) Route to measure mercury after you add lipoic acid as this is major route of excretion, but more difficult to gauge peak excretion in the stool. Results can also vary depending on your child's natural gut motility. If it is difficult to get a good specimen, hair mercury may be the next best alternative.

(2) Obtain it once before lipoic acid is started to get a baseline of dietary mercury intake (which hopefully will be very low.) That way you can more accurately assess effect of the treatment and to know when to stop.

6. Detoxification

a) DMSA (succimer, Chemet)

(1) Benefits

(a) best combination of safety and efficacy of the standard chelators

(b) has been studied and used extensively for lead poisoning

(c) positive effects include rapid progression of language ability, improved social interaction, improved eye contact,

decreased self-stimulatory behavior, improved strength and coordination.

(d) Typically, behavior improvement is seen only after lipoic acid is added, since this is when mercury is actually being removed from the brain (see below).

(2) Dose

(a) No more than 10 mg/kg/dose and no more than 30 mg/kg/day (maximum of 500 mg/dose and 1500 mg/day)

(3) Dosing interval

(a) Any convenient period (no evidence that intervals shorter than every eight hours provide any inherent benefit). Most commonly, dose every 8 hours.

(b) Lower dose at shorter intervals may reduce side effects (i.e. every 4 hours)

(4) Route

(a) Orally although IV is possible

(i) Mix it with orange juice or other sweet beverage (acidic or neutral liquid)

(5) Duration/Treatment cycles

(a) Optimal is 3 days on , 11 days off (but can be anywhere from 3 to 5 days with an equally long rest.)

(b) It commonly takes 8-12 treatment cycles before the body tissue mercury has been eliminated and you can begin using lipoic acid. The older the child is when you begin, the longer it takes to remove the mercury.

(6) Side effects

(a) Common

(i) nausea, diarrhea, anorexia, flatulence, fatigue, rash

(b) serious

(i) rare

(ii) allergic reaction, neutropenia (low white blood cells), thrombocytopenia (low platelets), toxic epidermal necrolysis (TEN) and erythema multiforme (Stevens-Johnson syndrome).

(iii) TEN and Stevens-Johnson syndrome are illnesses presenting with severe rash, fever and

systemic toxicity and are absolute contraindications for restarting therapy.

(iv) The other side effects are more dose related and DMSA may be restarted at a lower dose when numbers return to normal with additional caution in monitoring labs.

b) Other supplements

(1) alpha-Lipoic Acid

(a) Benefits

(i) a native chelating agent, powerful antioxidant

(ii) it crosses blood-brain barrier and is responsible for removing mercury from the brain (DMSA does not cross blood-brain barrier)

(iii) minimal toxicity (it is a natural product of human cells)

(b) Dose

(i) 1-3 mg/kg/day and increased to 10 mg/kg/day as tolerated

(c) Precautions

(i) should be used in conjunction with DMSA to prevent it from facilitating movement of mercury out of some tissues and into others. The DMSA "grabs" the mercury and removes it from the body.

(ii) It can reduce copper excretion, but if used with DMSA should not be a problem

(d) Tests

(i) Stool mercury

Lipoic acid is excreted in the bile, so mercury levels in the stool should be elevated

(e) Begin after total body mercury from DMSA alone, drops to zero. This is referred to as Stage 2 of the chelation protocol.

(f) Improvement of symptoms from chelation will probably not be present until this step, since it is the brain mercury that really counts.

(2) Melatonin

(a) Benefits

(i) regulates sleep/wake cycle

(ii) powerful antioxidant

(b) Dose

(i) up to 0.1 mg/kg at bedtime should help with sleep disturbances, smaller doses may be as effective

(3) Taurine

(a) Benefits

(i) A sulfur-containing amino acid important in the production of bile salts and therefore, the native excretion of toxins and absorption of fats and fat-soluble substances.

(ii) It helps as a chelation support especially during stage 2.

(b) Deficient in many autistic children

(c) Dose

(i) 250-500 mg/day (maximum 2g/day in adults)

(4) Glutathione

(a) Benefits

(i) Keystone of cellular antioxidant system

(b) Often deficient in autistic children

(c) Systemic absorption may be zero when given orally but gut mucosal stores can be replenished so it may still have some benefit.

(d) Dose

(i) 250-500 mg/day orally

(ii) Transdermal 1-2 grams a day.

(iii) can give IV doses (usually 400-600 mg every 2-4 weeks)

(iv) I usually start low with each of these methods and work up slowly.

(v) Alternatives to giving glutathione directly include N-acetyl cysteine, IV cysteine, lipoic acid. In fact, this can be more effective in boosting levels. These have some side effects as well (see below), however and should be done under supervision.

(e) Side effects

(i) Some children do not tolerate glutathione supplementation and can exhibit temporary regressive behavior especially if you start at a high dose. In spite of this, I think glutathione supplementation is fairly critical to boost their ability to detoxify.

(5) Allithiamine

This is a fairly new addition to the armamentarium of autistic treatment. It is a combination of thiamine (vitamin B1) and a sulfur-based compound that binds effectively to heavy metals.

(a) Advantages

(i) Early experience with it suggests that it may be as effective, if not more so, as a chelator than DMSA.

(ii) It is not thought to have the same side-effect profile and shouldn't worsen intestinal dysbiosis since it is metabolized mostly through the kidneys rather than the liver.

(iii) It is also formulated as a cream which makes it much more convenient than oral dosing.

(b) Dose

(i) ½ ml (50 mg) of cream applied to skin twice a day.

(ii) Many people are using it in conjunction with DMSA or other chelators without adverse effects.

(c) Disadvantages

(i) It is still new and hasn't been extensively researched.

(ii) It has a sulfur (skunk-like) smell.

(iii) Just with any chelator, it can bind with minerals and the children who are nutritionally prepared do much better when it is started.

(d) Other advantages

(i) Good source of thiamine which is a neurologically critical vitamin and can help to repair the myelin sheath.

(ii) Good source of sulfate which most autistic children are significantly deficient in.

(6) MT Promoter

This is a supplement created by Pfeiffer institute which is the building blocks of the metallothionein (MT) protein. The idea is to boost MT function in a natural way and allow the body to chelate itself. Many autistic children are currently using this supplement with anecdotal evidence of positive effects. The research that is being done through Pfeiffer is not yet published.

(a) Advantages

- (i) Allows the body to detoxify itself naturally and may self-correct some of the other dysfunctions that are present based on MT abnormalities.
- (ii) Does not effect blood count or liver function and does not worsen gut bugs.

(b) Disadvantages

- (i) The metals do not come out in a bolus and so it is difficult to test for them and you have to take it on faith that it is actually chelating.
- (ii) Can also deplete minerals, especially zinc and so you must be strict about maintain adequate mineral supplementation.

c) Supplements to be wary of

(1) Cysteine/cystine

- (a) Can bind to and mobilize mercury and may worsen mercury intoxication by spreading it to other tissues.
- (b) Excellent culture medium for yeast
- (c) Blood levels may already be high in autistic children

(2) N-Acetyl-L-Cysteine (NAC)

- (a) Can bind with mercury and carry it across the cell membrane
- (b) Good culture medium for yeast
- (c) Can rapidly increase intracellular glutathione levels which is beneficial for treating antioxidant deficiency but use either in conjunction with DMSA or after mercury detox is well under way
- (d) Use with extreme caution in children with elevated cysteine levels

(3) Chlorella/other algae

- (a) Touted as herbal remedy for mercury poisoning.
 - (b) Does bind well to mercury but often is contaminated with mercury that it has absorbed from the water that it is grown in.
 - (c) Can also be contaminated with toxic dinoflagellates (parasites)
- d) End-of-treatment indications
- (1) When improvement ceases
You may want to continue a couple of months after the “plateau” to avoid misinterpretation of “false plateau” due to an illness or other reason.
 - (2) If there is no significant progress or a regression
 - (a) Some children show transient regression before significant improvement so give it some time
 - (b) If intestinal dysbiosis is not adequately treated before chelation, it may be worsened leading to regression of behavior that could be falsely interpreted as a chelation treatment failure.

E. Antioxidant supplementation

Vitamin C, vitamin B6, vitamin E, zinc, magnesium, selenium, melatonin, glutathione, NAC and lipoic acid have been addressed previously.

F. Omega-3 fatty acids

- 1. Precautions
 - a) Precede treatment with antioxidants
- 2. Sources
 - a) Fish oils
 - (1) Advantages
 - (a) well-tolerated
 - (b) good patient acceptance
 - (c) no weight gain
 - (d) highly concentrated forms available
 - (2) Disadvantages
 - (a) high dose required

- (b) most currently available preparations have inadequate potency
- (c) occasional fishy aftertaste
- (d) potential contamination with mercury
- (3) Dose
 - (a) 1.5-10g/day (3-5 g/day is typical) divided twice a day (once or three times ok)
 - (b) Get highest EPA concentration possible--work up to a dose of 200-500mg of EPA
- (4) Side effects
 - (a) GI distress at high doses
 - (i) divide dose
 - (ii) add ginger root and Daikon radish
 - (b) theoretic risk of increased bleeding
 - Avoid use with anticoagulants or high dose NSAIDS
- (5) Available as
 - (a) OmegaBrite
 - (i) www.omegabrite.com or 1-888-43-OMEGA
 - (b) Coromega
 - (i) Kirkman Laboratories (503) 694-1600
 - (c) Nordic Naturals Pro EFA
 - (i) Kirkman Laboratories (503) 694-1600
 - (d) Cod liver oil
 - (i) Kirkman Laboratories (503) 694-1600
- b) Flax seed oil (alpha-Linolenic acid)
 - (1) Advantages
 - (a) more palatable than fish oil
 - (b) more concentrated than native fish oil
 - (c) may be used in recipes
 - (2) Disadvantages
 - (a) not studied
 - (b) limited conversion to longer chain omega-3
- c) Primrose oil (gamma-linolenic acid)

(1) Rationale

Some individuals are deficient in delta 6-desaturase which causes problems in their fatty acid chemistry.

(2) Dose

(a) Start at 50-100 mg and work up to 600 mg of GLA as tolerated

(b) available as evening primrose oil, borage oil

(3) Duration

(a) 3 week to 3 month trial

G. Improve pancreatic function/digestion

1. Secretin

a) Available forms

(1) Victoria Pharmacy – Switzerland
(www.access.ch/victoria_pharmacy/welcome.html)

(a) Gaspretin

(i) 1 vial/10kg body wt

(ii) cost approximately \$6.50/vial

(2) Secrelux (www.pharmaworld.com)

(a) IV infusion

(3) Repligen Corporation (www.repligen.com)

(a) Has available product

(b) Holds patent on uses of secretin in autism

b) Dose at 3-week intervals

2. Digestive enzymes

a) Rationale

(1) used to support peptidase, lipase, disaccharidases

(2) theoretically aids in breaking down peptides into component amino acids. Many autistic individuals have trouble digesting foods other than gluten and casein as well.

b) Use with meals, especially if dietary “accident” from gluten/casein

c) examples: Enzyme Complete with DPPIV (from Kirkman's) , HN Peptizide and HN Zyme Prime (from Houston Nutraceuticals)

H. Bolster Immunity/Treat autoimmunity

1. Tests

- a) Consider quantitative immunoglobulins (low), anti-MBP antibodies (high), total IgE (high), NK cells (low), anti-NAFP antibodies (high).

2. Intravenous immunoglobulin (IVIG)

a) Benefits

- (1) supplies deficient children with additional antibodies to fight infection
- (2) effective in children with anti-MBP antibodies, low levels of immunoglobulins
- (3) majority improve in at least one DSMIV category

b) Dose

- (1) 1-1.5 g/kg (max 2) every 4-6 week (Dr. Gupta currently using 800 mg/kg)

c) Precautions

- (1) Do not give if IgA deficient.
- (2) Risk of contracting blood-borne illnesses as IVIG is a blood product.

3. Oral steroids

a) Benefits

- (1) decreases inflammation and autoimmune response

b) Dose

- (1) pulse dosing (1 mg/kg for 5-7 days) decreases side effects

c) side effects

- (1) adrenal suppression, fat deposition, thin skin, ulcers, increase susceptibility to serious illnesses if used chronically

4. Colostrum

a) Benefits

- (1) provides immune factors from mother and bolsters immunity particularly in the gastrointestinal tract. Can help with yeast control.

b) get casein free product

(1) Kirkman Labs—Colostrum Gold

5. Transfer factor

a) Benefits

(1) It is an immune factor derived from colostrum that promotes production of TH1 lymphocytes and improves balance of the immune system.

I. Other supplements/treatments

1. Anti-virals

a) Valtrex

(1) anti-herpes virus medication but has some effect against other viruses.

(2) mechanism of action is not clear

(3) do not continue long-term unless clear effect demonstrated

b) Oral IFN-alpha

(1) proposed as an anti-measles agent, not much experience.

c) Echinacea

(1) An herbal supplement used as anti-viral agent

(2) dose

(a) Liquid, up to 10 drops in juice every 4 hours

(3) precautions

(a) Do not give if child has severe allergy to ragweed

2. Dimethylglycine (DMG)

a) Benefits

Significantly improves language and some other behaviors

b) Source

A naturally occurring product that can be purchased without a prescription at most health food stores

c) Dose

Average dose is 125 mg three times daily, but much larger doses have been used with efficacy and safety, in responders.

d) Duration

- (1) It is best to give it a therapeutic trial of about a month,
- (2) you should see effects within days to weeks.
- (3) If it is helping, then continue indefinitely.

e) Side effects

- (1) Hyperactivity, which can be treated with folic acid supplementation

3. Tryptophan

a) Benefits

(1) Improved sleep

It is an amino acid that is used in serotonin synthesis. Serotonin is a chemical that regulates our sleep cycle and tryptophan supplementation seems to help autistic children sleep better.

(2) Decreased repetitive behaviors

- (a) This is the rationale for including some during the day.

b) Dose

- (1) Start with 250 mg and gradually increase to max of 4000 mg/day divided 2/3 in p.m. and 1/3 in a.m. You may want to reverse the a.m./p.m. dose initially to see if it is effective in making your child sleepy.

4. Bethanacol

a) Benefits

(1) stimulates acid production by the stomach, tightens the gastroesophageal sphincter to stop reflux esophagitis, stimulates digestive enzymes, supports and builds up pancreas, stomach, small and large bowel mucosa.

(2) stimulates local immunity and ordered peristalsis (gut motility.)

(3) mimics acetylcholine which modulates language cross pathways in the brain.

b) Precautions

(1) It can lower the seizure threshold and increase airway secretion.

(2) The child should be monitored after the first dose in physician's office for one hour.

(3) Works best if preceded by a couple of months of Vitamin A supplementation via cod liver oil.

VI. IMMUNIZATION RECOMMENDATIONS

Please understand that DAN! Physicians are not against immunizations. They have been one of the major advances in public health and modern medicine and have led to the eradication of many infectious diseases resulting in countless lives saved. We do however suggest caution in the administering of immunizations with the following general guidelines (a more detailed description available on our website www.cbcutah.org):

- Use only thimerosal-free vaccines
- Avoid all unnecessary combination vaccines
 - Use monovalent measles, mumps and rubella in separate injections on different days as opposed to MMR. (Unfortunately, this is not currently available) DTaP is currently not available in monovalent form.
- Space immunizations by as much time as possible
 - 6 months for live vaccines (measles, mumps, rubella) is ideal, 3 months is reasonable
- Use single dose vials
 - Provides more uniform dosing, avoids preservatives
- Use inactivated polio (IM, not oral)
- Do not vaccinate your child if he/she is sick or still recovering from an illness
- Ensure RDA of Vitamin A (1250-5000IU based on age—1250IU equals ½ tsp of cod liver oil) for three days before and the day of a shot. Give vitamin C 150 mg twice daily for infants and 300 mg twice daily for toddlers for three days before and the day of the shot.
- Prioritize vaccines that will be of most value to your child when he/she is most likely to contract the illness. For example, hepatitis B is contracted through sexual activity and drug abuse or from maternal infection at birth. There is no need to vaccinate most infants for Hepatitis B unless mother falls into a high risk category. Hemophilus B (HiB) is probably highest priority because it causes meningitis and epiglottitis (a severe throat infection) often in the first year of life. Next is probably DTaP.
- Get immune titers if possible before repeating doses (these are fairly expensive blood tests). Many children are fully immunized after the first dose and may not require subsequent boosters.
- Avoid re-immunization with a vaccine if there is a negative reaction to it.
- Do not immunize newborns.

A. Vaccine schedule

Below is an example of an immunization schedule that provides the required vaccinations prior to entering school. Please understand that this is just an example and does not constitute an official recommendation. I think that there are many modifications that

could take place depending on the individual circumstances. Notice how difficult it is to follow the guidelines about limiting injections to two in one day if all of the currently recommended vaccinations are included. You could extend the schedule into to 10th, 11th or 12th month but this also decreases the chance that they will get all of the necessary immunizations when they are most risk for the illness, especially in the cases of Hib, DTaP and Prevnar.

- Birth—Hepatitis B, if mom Hep B positive. If unsure, check titer in mother. If mother involved in high risk behavior in last 6 months, give vaccine.
- 4 months—Hib, IPV
- 5 months—DtaP
- 6 months—Hib, Prevnar
- 7 months—DtaP
- 8 months—Hib, IPV, Prevnar
- 9 months—DtaP
- 15 months—measles
- 17 months—Hib, IPV, Prevnar
- 18 months—DtaP
- 27 months—Rubella
- 39 months—Mumps
- 4-5 years—Varicella (if not immune already)
- 4-5 years—Hepatitis B series (you may wish to delay this until age 10-12 since they are at low risk of contracting the disease before that)
- 4-5 years—DtaP, IPV boosters
- 4-5 years—test titers for MMR and do not give unless low
- 12 years—retest titers, boosters if needed.

Please note that as of this writing, there is a national shortage of MMR vaccinations and therefore, Merck is no longer making monovalent measles, mumps and rubella vaccines until the shortage is corrected. They estimated that it would take about a year.

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