Hope
Health & Wellness

I dedicate this to my wife, children, patients, and clients who have taught me so much on how to persevere with seeking answers to heal our children and to never give up on this healing journey.

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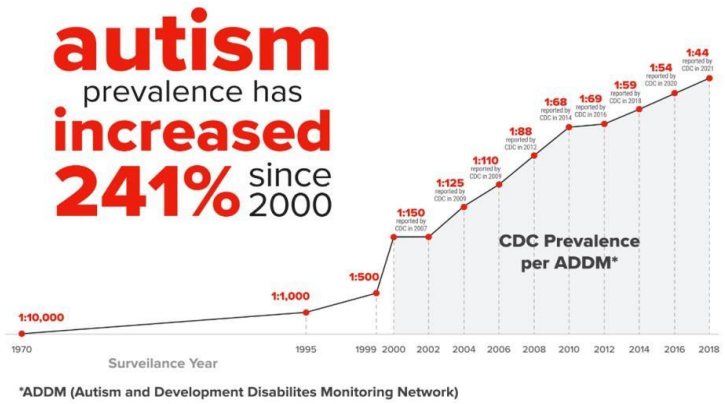
Introduction



In September 2021, the Centers for Disease Control (CDC) reported the incidence of autism spectrum disorder (ASD) at 1 in 44, otherwise being 2.27% of all children. There has been an exponential rise from 1 in 10,000 back in the 1970s to 1 in 44 now, indicating a 241% increase since 2000! We must ask ourselves, why is there such a drastic increase in autism diagnosis? Is there more awareness? These could be contributing factors, but they do not fully explain the drastic spike in incidence.

In 2001, my oldest child was diagnosed with autism. As first-time parents, we were thrilled with his development as he met all milestones on or ahead of schedule. At 15 months old, he developed an ear infection. He was treated with antibiotics and received a couple of his routine vaccinations. Shortly after, we noticed he was losing previously acquired skills. Not only did he stop acquiring new words, but his language disappeared, his hearing appeared impaired, eye contact diminished, and repetitive self-stimulatory behaviors began. We did not know it at the time, but he was regressing, and so began our family's journey of living with autism.

It now seems absurd to me, but during my training as a family medicine physician, I received no education about any aspects of autism throughout my training. When our son first began to regress, I recall listening to a radio show where NFL quarterback Doug Flutie talked about his son with ASD. While listening to Flutie describe his son's symptoms, the feeling of numbness began to consume me as it paralleled my own son's symptoms! Rather than my years of medical training, a radio show was the education that led me to

my son's autism diagnosis. Of course, we proceeded with evaluations by a developmental pediatrician, where at 2 years old he received his formal diagnosis.

We were in utter shock with his diagnosis but we knew we had to act immediately. My wife and I started researching feverishly and were determined to support him anyway we could – via education, behavioral support, therapies, biomedical, and nutrition. Within days of the diagnosis, I was on a plane flying across the country to attend a conference with scientists and physicians who were trying to heal children with autism. At the same time, we started behavioral therapy, speech therapy, and occupational therapy through early intervention. At this point, we were sad, but hopeful.

It was heartbreaking to see our once thriving little boy now struggling. Emotionally, he went from a happy, healthy child to one who was in distress and at times sad. Physically, he began having uncontrollable, horrific smelling diarrhea. His struggles motivated us to work even harder to find ways to help him feel better.

Our research led us to a local group of parents who were meeting to provide mutual support. It was extremely helpful to be with parents that were experiencing similar challenges as well as share ideas. We were in full action mode. My wife focused on education and therapies while I dove into anything biomedical. We had no idea what lay ahead and what a long, emotional, and arduous path it would be.

The conference I attended shortly after the diagnosis was organized by a group called Defeat Autism Now (DAN). At that time, DAN was a grassroots movement of practitioners working on addressing root causes and treating autism. The conference was enlightening, energizing and informative. There were myriad other practitioners attending who were eager to learn about autism in ways we were never taught in medical school. It was encouraging to hear that there were underlying issues that needed to be addressed and children were improving with treatment. There were so many relevant topics discussed that gave us hope which was not given to us by the doctor who diagnosed him. Like most families, when you are given the diagnosis, the prognosis is often grim. You're simply told to get him some therapy, don't bother with dietary changes, there are no cures, he won't recover, and prepare for the worst for his future. At the conference, I was grateful to be surrounded by families, professionals, scientists, and doctors who were all dedicated to improving the lives of children with autism. Like us, they were not giving up.

As with many conditions, there is a genetic predisposition with various environmental triggers. Genes load the gun and the environmental factors pull the trigger. This was the

case for our son and many (not all) children diagnosed with autism. His genetic predisposition, in combination with illness, antibiotics, Tylenol, and vaccines appeared to have impacted his immune system leading to neuroinflammation causing his regression into ASD.

Armed with more knowledge, we protected our next child from as many environmental triggers as possible and he developed typically with no regression. He is now a sophomore in college and healthy. While we took the same precautions with our youngest, to our dismay, she was also diagnosed with ASD. Unlike our eldest, she did not regress but failed to progress in many areas. Unfortunately, there were some environmental insults that she encountered that we could not control. My wife had a couple of mild viruses during her pregnancy- one of which required weekly ultrasounds to make sure there were not any fatal complications. Sadly, the viruses and frequent ultrasounds may have been the triggers for our daughter. However, had we not had the knowledge to protect her from other environmental factors that we could control, she probably would be more severely affected and facing even more health challenges.

I believe it is important to share my children's stories because history is important in helping the future. Finding the root cause(s) plays a significant role in reversing the disease. My children are just two examples of what could go metabolically awry leading to the manifestations of ASD. Autism has historically been viewed as a primary neuropsychiatric condition and classified as a mental health disorder. The paradigm is beginning to shift where ASD is being treated as a metabolic disorder causing secondary neuropsychiatric manifestations. Many practitioners are seeking root causes of ASD and treating the metabolic derangements with good results- in some cases, full recovery.

I have observed many children improve through various forms of intervention. Some from somewhat simple changes such as a gluten free casein free diet and others from a more complex combination of therapies such as supplements for mitochondrial, gut, and immune system support, hyperbaric oxygen therapy, and ionic foot baths. In some cases, the noticeable improvements happen quickly, and others take years. Some of the children respond to therapies and become indistinguishable from their neurotypical peers, while others improve but remain with some challenges. In about half of the cases, we see mild improvement. While parents hope for full recovery, we are thrilled with any positive gains to reduce our children's struggles.

Each individual with symptoms of autism has unique underlying causes that must be identified and addressed. The challenge is to uncover all the possibilities that could be contributing to their symptoms. The aim is to educate families by providing information

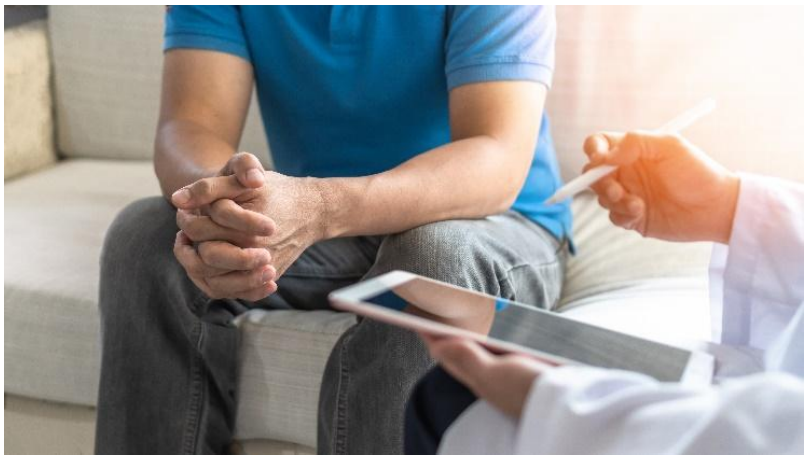
on potential underlying causes and available treatment options related to autism, with the goal of empowering families to aid in the healing of their children.

The information provided here will educate parents by addressing the pathogenesis of ASD utilizing the "**DAMN BIG HATS**" mnemonic as defined below. In the biomedical treatment model, many Medical Academy of Pediatric Special Needs (MAPS)- formerly Defeat Autism Now (DAN)-and functional practitioners will address these areas to improve the health of our children:

1. **D- Diet**
2. **A- Allergy**
3. **M- Mitochondrial Dysfunction**
4. **N- Nutrient deficiency, Neuroinflammation**
5. **B- Brain chemistry imbalances**
6. **I- Infections, Inflammation**
7. **G- Genetics, GI dysfunction**
8. **H- Hormonal abnormalities**
9. **A- Autoimmunity**
10. **T- Toxins**
11. **S- Sleep, Stress**

My objective is to empower you with my knowledge gained through education and experience as a father, family physician, and health coach.

Health Coach



After 20 years of practicing medicine, during which I treated a considerable number of children and adults with neurodiversity- including autism, Asperger's, ADHD, and PANS/PANDAS- I transitioned to health and wellness coaching. While practicing as a physician, I noticed that many patients would leave their office visits with information and strategies but often felt overwhelmed. With the daunting task of trying to heal their child, many families struggled to implement the plan provided and had difficulty making progress between visits. As much as I tried to help with extended visits, there still was a deluge of information for parents to manage and the follow-up was often a couple of months later due to how busy the schedule had become with treating new patients with ASD. Families may understand what needs to be done but not have a plan to implement. As a health coach, I can provide the necessary ongoing support and create successful outcomes with prioritization and execution.

As both a practitioner and parent, I have always felt that families need more support. Many parents are spending endless hours researching on their own and going to great lengths to help their children; however, there are still many children who are extremely ill and suffering. To support families, I have developed a program that educates parents on the functional approach to autism, provides insight into their child's health, empowers them with knowledge and guides them through the steps towards healing. Together, we will work towards reversing the metabolic dysfunction that can lead to the manifestations of autism.

Our modern lifestyle is out of alignment with our genes and biology. Our current conventional paradigm does not equip us with the right tools to prevent or reverse chronic disease, instead we are just managing it. It is geared toward treating acute problems. We need a new model that will support nutrition, lifestyle and behavioral

changes that will help turn the tide on autism. A collaborative relationship between clinicians, coaches, patients, and their families will help transform lives.

Physicians receive minimal training in nutrition and lifestyle medicine. Most of our training revolves around pharmaceuticals. As you may know, the only pharmaceuticals approved to treat the behaviors associated with autism and not the root cause(s) are antipsychotics which have many potential side effects. I have worked with numerous families on the complexity of autism and know how overwhelming it can be, not only for families but practitioners as well. There are so many pieces of the puzzle that could be affected and putting it together is complicated, especially with all the nuances occurring metabolically and behaviorally.

I want to educate and empower families of children with ASD on this journey of healing. My approach is client-centered where the families take charge with my support and guidance. It is collaborative and provides families with the capacity to meet their challenges and be in control. As a team, we tackle any obstacles that could be impeding progress and create a successful path towards healing autism.

Let's now dig into the areas of concern for our children and what we can do!

Neuroinflammation

One of the most critical processes affecting our children is neuroinflammation.

What is happening inside the brains of our children with ASD? Are their brains on fire?

Neuroinflammation is involved in the etiology of autism. Neuroinflammation, an inflammatory response within the brain, can come from infections, toxins, autoimmunity, poor diet, stress, allergens, nutrient deficiencies, sleep deprivation, gut microbiome imbalances, oxidative stress, and mitochondrial dysfunction. In essence, the immune system has become dysregulated by one or multiple factors leading to this pathological inflammatory response. Each case of neuroinflammation manifests differently with a variety of symptoms such as seizures, self-stimulatory behaviors, apraxia, muscle weakness, social and language impairments, sleep disturbances, and agitation.

Finding the root cause of neuroinflammation can ameliorate the behaviors and symptoms associated with ASD. For example, with my daughter, we noticed that she was missing important milestones from infancy. In her case, my wife contracted parvovirus during the pregnancy. This mild childhood disease during pregnancy can lead to miscarriage, stillbirth, or a condition known as fetal hydrops which is fatal in more than 50% of babies. As a result, we were recommended to have weekly ultrasounds to screen for any of these complications. There are studies showing maternal viral infections and prenatal ultrasounds may be linked to ASD. Fortunately, the ultrasounds came back negative; however, could the parvovirus and ultrasounds have been a trigger for the neuroinflammation during the pregnancy? Our daughter had no evidence of Parvovirus when she was born and had no further testing for it, however, is it possible that antibodies

were transferred from mother to fetus? Did these antibodies cross the blood brain barrier to attack neurons in her brain?

We know that there are white blood cells known as microglia that are active in the brains of children with ASD. There is a dysregulated immune response with an increase in pro-inflammatory chemicals called cytokines seen on autopsies of children with autism.

Neuroinflammation associated with ASD may stem from mast cell production as well. Indirect evidence of the role of mast cells in ASD comes from large epidemiological studies showing that ASD is associated with atopic diseases such as allergies, asthma, and eczema, all of which involve mast cells. Studies show how brain **mast cell activation** due to allergic, environmental or stress triggers could lead to focal disruption of the blood-brain barrier and neuroinflammation contributing to development of seizures with increased levels of mast cell neurotensin.

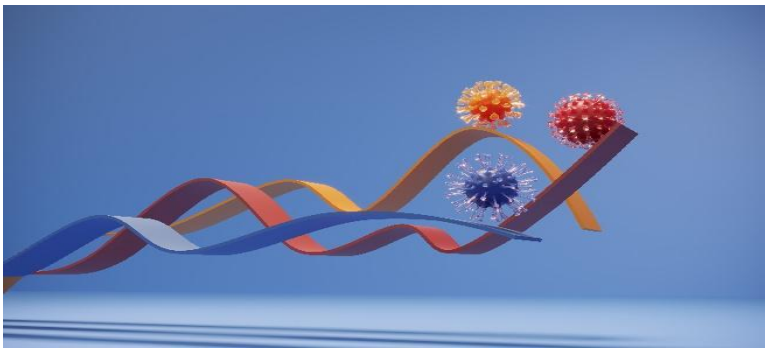
The neuroinflammation can be the etiology of the much higher prevalence of seizures (about 30%) in autism compared to their neurotypical peers (less than 1%). This inflammatory response can be a trigger for an epileptic focus of electrical discharge. A 24–48-hour EEG would help confirm any abnormal electrical activity to diagnose seizure disorder.

Autoimmunity can also lead to neuroinflammation and ASD. Regression that is often seen with ASD is similar to what is seen in autoimmune encephalitis which can occur after an infection attacks the brain or a person's own immune system attacks the brain in error. Numerous researchers have found maternal autoantibodies reactive to fetal brain tissue in a subset of mothers to children with ASD with an abundance of evidence showing their deleterious role in neurodevelopment. We can also see comorbid PANDAS/PANS from infections or environmental triggers that can provoke an autoimmune attack on the brain.

In some cases, researchers found an immune molecule, IL-17, is released suppressing a small region of the brain's cortex linked to social behavioral deficits. This confirms that the immune system is sending messages to directly influence the brain.

How can we address this neuroinflammation? Finding and treating the root cause(s) is paramount. The potential causes of a chronic inflammatory response are an inflammatory diet, allergies, autoimmunity, toxins, trauma, a leaky brain from a leaky gut, or infections.

Infections



Maternal infections during pregnancy have been studied and show that there is an increased risk with certain types of viruses such as Herpes Simplex Virus-2 (HSV-2). The mother's immune system activation could disrupt development of the fetus' central nervous system raising the risk of autism. This goes back to neuroinflammation. Women with elevated antibodies of HSV-2 were twice as likely to have a baby with ASD. Herpes is a latent infection that can be reactivated when the body is under stress. One study showed that pregnant women with flu were twice as likely to have a child with autism and those that had a fever lasting for longer than a week were three times as likely to have a child with autism. Another study revealed that there was a 79% increase in ASD diagnosis in children born to mothers with an infection during pregnancy.

Maternal immune activation sets off a cascade that produces inflammatory cytokines. When these cytokines are passed from mom to fetus through the placenta, they could have downstream effects on fetal development and have been found in the brains of adults with autism. Other studies showed that mothers that were hospitalized at any time during their pregnancy (any trimester) or had any type of infection (bacterial, viral, fungal) were at greater risk for having a child with ASD.

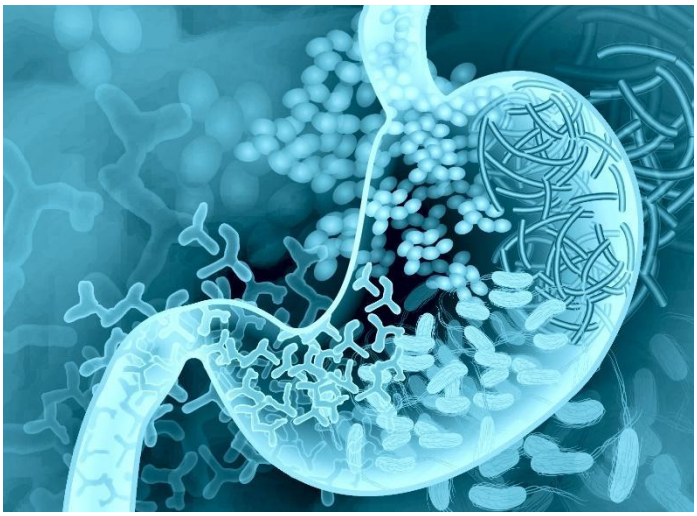
How about children that have infections when a pregnant mom does not? There are studies revealing that children who contract severe infections are at increased risk of developing ASD. Children with ASD were more likely to have an infection before the age of three compared to children with typical development. In addition, If the infection was bacterial, the child could have been treated with an antibiotic which could alter gut the microbiome leading to a leaky gut affecting child neurological development.

There is evidence that chronic infections and the immune system reactions associated with them can lead to autism. These infections include Bartonella, Babesia, Herpesviruses, Mycoplasma, Chlamydia, and Lyme. Extensive alterations in immune

system function in children and adults with ASD lead to increased vulnerability to these infections.

Pregnant moms and children should be evaluated immediately when there is the possibility of an infection. Evaluating a source of infection is critical. Supporting the immune system with supplements like vitamin C, vitamin D, and Zinc is often beneficial. If an antibiotic is necessary, consuming probiotics and probiotic rich foods will replete any healthy bacteria eradicated to prevent significant alteration of the microbiome and adverse consequences.

Gut and The Microbiome



The gut is frequently affected in our kids. They can exhibit symptoms of diarrhea, constipation, abdominal pain, vomiting or reflux. Many children have increased intestinal permeability better known as **leaky gut**. The mucosal layer between the intestines and the immune system of our circulation is protected by a barrier that contains tight junctions. These tight junctions should not allow any undigested food to escape into the bloodstream where the immune system will recognize it as foreign and create a host of problems including autoimmune disorders, pathogenic bacteria leaving the intestines and entering the circulation, and malabsorption of food leading to nutrient deficiencies. When altered metabolites enter the bloodstream through this leaky gut, they can get transported to the brain causing neuroinflammation leading to the ASD symptomatology our kids exhibit.

Dr. Fasano out of Harvard did a fascinating study on how zonulin production is caused by gluten and impairs the tight junctions of the intestines in people with celiac disease.

His discovery of zonular proteins has led to the discovery of other chronic disorders such as autism being caused by this. An abnormal inflammatory response with increased pro-inflammatory and fewer ant-inflammatory cytokines occurs leading to further breakdown of the mucosal barrier inducing a chronic inflammatory state.

With the immune system disrupted, overgrowth of opportunistic bacteria, fungi, and parasites can occur. When these pathogenic bacteria are "leaking" from our gut into our blood stream, it creates what is known as endotoxemia where the toxins released from these infections create a robust inflammatory response that can be delivered to every organ in the body through our systemic circulation. This perpetuates a vicious persistent inflammatory state where the body is constantly fighting these pathogens leaking from the gut circulating to the brain. We need to plug up and repair these leaks to prevent this state of endotoxemia.

So, how can we help begin the gut healing process? One way is to investigate the microbiome of our children. The microbiome is throughout our body with the majority in our intestines. There are over one hundred trillion bacteria in our microbiome that play a key role in regulating our metabolism. These bacteria talk to our cells through postbiotic chemicals they secrete such as butyrate and acetate. One of the most important jobs of these butyrate producing bacteria is to preserve the integrity of the mucosal barrier of the intestines to prevent leaky gut. Our children have less diversity in their microbiome and altered gut microbes. There is an increase in pathogenic Clostridia and Candida species and a reduced level of beneficial Lactobacillus and Bifidobacterium species. Toxic metabolites are produced by pathogenic bacteria and travel to the brain through circulation and nerve pathways which can cause neuroinflammation with the development of autistic features.

There is "cross talk" between the brain and the gut through the bacteria and cells via the metabolites that these bacteria produce. While the pathogenic bacteria produce toxins, the beneficial bacteria produce short chain fatty acids that positive influence metabolism by promoting a healthy gut lining and producing vitamins, hormones, and neurotransmitters that are essential for creating health. We can compare our microbiome to a garden that you want to feed and fertilize with healthy nontoxic fertilizers and prevent and remove the weeds. We want to feed our microbiome prebiotic fiber and phytochemicals from fruits, vegetables, nuts, and seeds so our beneficial bacteria thrive and protect us. We want to remove foods such as sugar, refined carbohydrates, seed oils, and ultra-processed foods that the pathogenic germs feed off.

There are many other possibilities that could lead to an unhealthy microbiome in a child with ASD. One of the most common is when a child is treated with antibiotics for an ear infection or strep throat. Antibiotics like penicillin cannot discern the pathogen from the beneficial bacteria, so they eradicate everything. When the pathogenic bacteria outnumber the beneficial bacteria, there will be more of a potential for toxic effects from the detrimental bacteria outweighing the favorable effects of the healthy bacteria known as dysbiosis. Another common disruptor of the microbiome is toxic exposure to glyphosate from genetically modified organism (GMO) crops. Glyphosate, among other herbicides and pesticides, directly kills bacteria and increases gut permeability.

It is essential to know the history from the time mom conceived up until the present. If mom had a c-section, received antibiotics during pregnancy, or did not breast feed, these can have a significant impact on the baby's microbiome which can increase the risk for ASD. Other medications that commonly affect the microbiome are proton pump inhibitors like Prilosec used for acid reflux and SSRIs like Prozac used for depression and anxiety. Therefore, drugs moms ingest during pregnancy could negatively affect the microbiome of the fetus. Moms that deliver babies by C-section are not passing off their microbiome to their babies, since the babies are not passing through the vaginal canal to ingest these protective bacteria. In addition, babies that are not breast fed are not receiving a specific strain of probiotic, B. Infantis, which reduces intestinal inflammation.

Other common factors that could affect the microbiome are lack of exercise, an ultra-processed diet, poor sleep, and stress. Keeping our kids physically active will increase microbiome diversity. Maintaining a healthy organic diet low in sugar, refined carbs, and seed oils, but high in fiber, polyphenols, protein, and healthy fats will support a diverse gut ecosystem. Stress reduction will lower the body's cortisol release which will help promote a healthy gut. Avoiding chemicals in household products such as BPA in plastics, phthalates in personal care products, and heavy metals such as mercury in fish and lead in children's toys will reduce the toxic burden on the microbiome.

One study revealed that 84% of children with ASD have some GI disturbance. In many cases, our kids cannot express if they are constipated, have reflux or abdominal pain. If the leaky gut or a disrupted microbiome is causing GI symptoms which may be exacerbating ASD behaviors, addressing these problems can lead to significant improvement.

When there's a leaky gut with microbiome disruption, there is a "4R" method that many functional practitioners use to heal the intestines: remove, replace, reinoculate, and repair:

- **Remove**- this involves removing any problematic foods through one of the elimination diets or with food intolerance testing. You also want to remove any pathogens such as bacteria, parasites, and fungi, toxins such as heavy metals, pesticides, herbicides, and other toxic chemicals in the household; and medications that could be harming the gut such as antibiotics, anti-inflammatory medicine like Advil or Aleve, and PPI antacids like Prilosec or Prevacid.
- **Replace**- After removing the insulting factors, replacing molecules that could have been affected by damage to the gut lining is important. Stomach acid could be low from antacids, other medications, or an altered microbiome. Replacing stomach acid may be necessary to kill off pathogens and provide a nurturing environment for healthy bacteria. Digestive enzymes may be needed to digest food since a leaky gut may not be able to secrete the enzymes necessary to break down food to absorb nutrients.
- **Reinoculate**- During this phase, you want to put in beneficial bacteria that were either wiped out or initially missing. There are many probiotics to pick from, so how do you choose? You want a probiotic that is not going to be degraded by stomach acid once it reaches there. High quality spore-based probiotics are coated to help protect against degradation. Fermented foods can provide some healthy bacteria from foods like sauerkraut, kimchi, kefir, and yogurt. You then want to feed these probiotics with prebiotic fiber through fruits, veggies, nuts, and seeds.
- **Repair**- The last phase of the 4R program involves repairing the damage that has previously affected the gut lining and maintaining healing. Supplements such as L-glutamate, slippery elm, and marshmallow root can help coat the intestinal lining.

Given the high prevalence of gastrointestinal disturbances in children with autism spectrum disorder, it is important to investigate the gut as a potential contributor or cause of their symptoms. Over 70% of our immune system is in our gut, so if we are not treating the bacteria in our intestines well, the immune system will get activated leading to a persistent neuroinflammatory response. Studies have been done on the gut-immune-brain link.

Amino acids levels have been assessed in children with ASD for evaluating targeted amino acid therapy toward the microbiome to try and modulate the aberrant neuroinflammatory response. Dr. Adams at ASU did a remarkable study where he replaced the microbiome of children with ASD with healthy microbiomes by fecal transplant and observed an 80% reduction in GI symptoms and 25% improvement in

autism symptoms. Each microbiome is unique like each case of ASD and requires an individualized approach to ascertain the problem(s) to address.

The microbiome plays an integral role in supporting our metabolism and requires a healthy diet to establish and maintain a nurturing environment for beneficial flora to thrive.

Diet

Food is medicine! The food we eat has a wide range of effects on our metabolism- both beneficial and detrimental. In general, most practitioners would agree upon eating a whole foods-based diet that is organic, avoiding any GMOs and pesticides. A diet that consists of organic sources of protein- either animal or plant based, healthy fats with omega-3's, and low glycemic unrefined carbohydrates is often the healthiest approach. Shopping around the perimeter of the supermarket will provide you with the most wholesome healthy foods. Avoiding ultra-processed foods that contain highly inflammatory ingredients such as sugar, high fructose corn syrup, trans-fats, refined vegetable (seed) oils, food coloring, additives like MSG, artificial and natural flavors, and many preservatives is advisable. If you are purchasing anything in a box or bag, make sure to examine the ingredient list. In general, the fewer ingredients listed, the better. If you do not recognize an ingredient or cannot pronounce it, it is unlikely to be healthy. These harmful ingredients are used to preserve a food's shelf life. An unhealthy highly processed diet with inflammatory ingredients can exacerbate ASD.

I am often asked which diet to choose for their child with ASD- GAPS, Paleo, Keto, SCD, GFCF- sounds like alphabet soup. When our son was first diagnosed, many families tried a **Gluten Free Casein Free diet (GFCF)**. For many children, the gluten and casein were causing a "leaky gut." These proteins were crossing the blood brain barrier and binding

to opioid receptors in the brain causing behaviors and elevated levels of pain tolerance that are often seen with many children with ASD. Even though science has not corroborated the efficacy of the gluten free casein free (GFCF) diet; anecdotally, many families have seen improvement in their children with restricting these foods. Gluten and casein compounds can be found in urine testing in some children. In addition, food IgG panels looking at gluten and casein antibodies can reveal elevated levels which may be indicative of gluten or casein sensitivity or intolerance. This can help guide you on whether to introduce this diet. Often, the best approach is a trial of removing gluten and casein for at least a couple of weeks and assessing the response.

The **Gut and Psychology Syndrome (GAPS)** diet is another anecdotally effective diet for children with ASD. Dr. Campbell-McBride invented this diet after her son was diagnosed with a learning disability. She believed that a leaky gut and poor nutrition affected the brain. Many children exhibit gastrointestinal symptoms such as bloating, gas, constipation, diarrhea, and abdominal pain- signaling an unhealthy gut. The GAPS diet was developed to restore a healthy immune system which is dependent upon a healthy gut microbiome. The principles of the diet are to heal the gut lining, restore microbiome germ balance, and strengthen the immune system. Dr. Campbell-McBride uses nutrient dense food that consists of organic meat and poultry, certain types of fish, organic vegetables, limited organic fruits, organic eggs, fermented foods, bone broth, nuts, and seeds. No grains, processed carbohydrates, or refined sugars are allowed. Dr. Campbell-McBride authored a book to help guide parents through the various stages of the diet to help heal the gut, immune system, and brain.

The **Specific Carbohydrate Diet (SCD)** is like the GAPS diet in that it allows some carbohydrates from fruits and vegetables but eliminates sugar, grains, and milk products. It allows fresh unprocessed meat, poultry, fish, and eggs. Dr. Sydney Haas had pioneered SCD to treat Celiac Disease. His theory was that certain carbohydrates were not fully digested and must be broken down by bacteria in the gut. This can lead to overgrowth of harmful bacteria which can cause irritation and inflammation of the gut lining inducing a leaky gut. Since many children with autism have gastrointestinal symptoms and an imbalance of bacteria in their intestinal tract, it was thought that SCD could heal the gut, balance the microbiome, and improve the symptoms of ASD. Since often when there is leaky gut, there can be a leaky brain with subsequent neuroinflammation.

How about the **Paleo** diet? This is how our hunter gatherers ate over 10,000 years ago before farming emerged. It focuses on anti-inflammatory whole foods such as lean meats, poultry, eggs, fish, fruits, vegetables, nuts, seeds along with healthy fats and oils. Organic

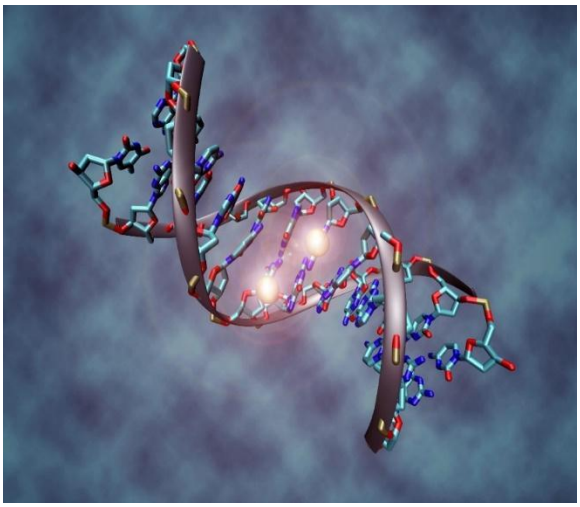
products are integral along with grass fed meats and pasture raised poultry. It eliminates grains, sugar, high fructose corn syrup, processed foods, refined oils, legumes such as beans, most dairy products, and trans-fats. Like the other diets, it helps reduce inflammation in the gut which affects the brain.

The gut's ecosystem is balanced when many problematic additives like MSG are removed. As mentioned earlier, eating organic will help prevent exposure to toxic chemicals like glyphosate (Roundup) that is used in conventional GMO agriculture. By eliminating toxins and foods that irritate the gut and the microbiome, our children can heal, and symptoms of ASD will improve.

The **Ketogenic** diet (Keto) has been studied for many inflammatory conditions including autism. Keto reduces the amount of total carbohydrates ingested daily to less than 50 grams. This was first studied in children with epilepsy. Since many children with ASD have seizures related to neuroinflammation, this has been helpful for a subset of children. Some of the challenges could be restrictiveness, compliance, and sustainability. A ketogenic diet can promote metabolic flexibility and increase energy production which supports many low tone, low energy kids.

The common link of these dietary interventions is elimination of a certain food(s) - an elimination diet. There are clues in a child's history that can help determine which diet can be implemented successfully. A food IgG panel or evaluating urine for peptides of gluten and casein can help provide guidance. You must take into consideration sensory issues such as taste, texture, smell, and any oral motor difficulty. Eating a healthy diet will help reduce neuroinflammation, mitigate oxidative stress, improve mitochondrial function, help with gut healing and support methylation.

Methylation



You may be thinking what methylation is and what it has to do with autism. DNA methylation is a process where a methyl group is added to DNA to suppress abnormal gene expression leading to disease. DNA methylation has been found to be abnormal in many children with ASD. Methylation has control over numerous processes in the body and is essential for our overall well-being: DNA production, neurotransmitter production, detoxification, fat metabolism, hormone metabolism, and cellular energy production. It has a significant impact on pathways that regulate cardiovascular, neurological, reproductive and detoxification systems. SAMe is a compound that is the universal donor of this methyl group. SAMe is dependent on a critical B vitamin, 5-methylhydrofolate (5-MTF), to allow the methylation process to work effectively.

Unfortunately, approximately 60% of people in America have a genetic mutation that causes a lack of production of enough 5-MTHF. There are many critical molecules such as melatonin, CoQ10, serotonin, l-carnitine, and nitric oxide that are not efficiently made when the DNA methylation switch is turned off.

There is a growing body of research showing that methylation influences the development of ASD. An insufficiency of 5-MTHF impairs methylation and adversely impacts brain function. Variants in the MTHFR gene and folate receptor antibodies are two factors that can have an impact on autism. When there's a genetic variation in the MTHFR gene, specifically the C677T allele, there's reduced activity of the MTHFR enzyme resulting in lower levels of 5-MTF.

Genetic variants like MTHFR load the gun and the environment pulls the trigger. Diet, toxins, microbiome imbalances, leaky gut, and maternal/childhood infections can be triggers for ASD with this genetic predisposition. Genetic panels like 23andMe and

methylation lab testing can help guide treatment. Nutrients like 5-MTF, folinic acid, methyl B12, B6, glycine, choline, creatine, and magnesium are essential for methylation.

Cerebral folate receptor antibodies can also impair methylation by not allowing transport of folate from the blood to the brain. There is a reduced amount of methyl folate binding to receptors in the brains which could induce neurological abnormalities seen in ASD. In one study, 75% of folate receptor antibodies were found in patients with ASD.

Lab testing for cerebral folate antibodies will help determine if this may be a causative factor. Treatment with leucovorin calcium (folinic acid) has demonstrated significant improvement in verbal communication, expressive and receptive language, attention, and stereotypical behaviors.

One of the major roles of methylation is to support detoxification. When methylation is abnormal, a buildup of toxins can harm all our organs, especially the brain.

Toxins

Environmental toxins such as heavy metals, plastics, and pesticides can affect DNA methylation which inhibit detoxification pathways associated with an increase in ASD. We want to reduce our children's exposure to environmental toxins starting when mom is pregnant.

Studies have confirmed the implication of heavy metal accumulation because of impaired detoxification in autism. Exposure to lead, mercury, aluminum, arsenic and other heavy metals during pregnancy and early childhood can cause developmental delays and impair brain function due to the toxin's ability to be transferred through the placenta and cross the blood-brain barrier.

One study showed how elevated levels of mercury and lead along with low levels of Glutathione-S-Transferase and Vitamin E correlated with an increase in severity of ASD. An NIH study linked the toxic load of lead seen in baby's teeth to autism. The study showed how toxic metals like lead and mineral deficiencies like zinc may harm brain development in the womb or early childhood. The concern is there could be irreversible neurological damage caused by these heavy metals even after removing the offending metal and bringing their levels down to a normal range.

How are we exposed to these heavy metals?

Lead can be found in the water supply, crystal glassware, pottery and ceramics, cosmetics, home remedies, and painted toys and furniture. Kids will either put their hands on lead containing products and put them in their mouths or drink contaminated water without knowing it. Avoidance of any lead containing products will reduce exposure and having your water tested will determine if there is any lead. Lead attaches to red blood cells and circulates throughout the body. It can be absorbed into bones and remain there for years.

Mercury has been studied extensively in ASD, and the preponderance of evidence reveals that mercury is either a causal or contributing factor. Due to impairment in their detoxification pathways, children with ASD have difficulty excreting mercury which continues to accumulate and may lead to symptoms seen with ASD.

How are we exposed to mercury? Thimerosal, a mercury containing compound (ethyl mercury), has been used as a preservative in vaccines and other pharmaceutical products since the 1930's to prevent contamination with harmful pathogens. In 2001, most of the thimerosal in vaccines for children was removed except for certain vaccines such as DTaP, DTaP-Hib, and the multidose inactivated flu vaccine containing thimerosal due to concerns about the additional mercury burden on the body in conjunction with other environmental sources. Science has repudiated the link between ASD and thimerosal claiming that ethyl mercury does not accumulate in the body and is metabolized much faster than methylmercury which comes from dental amalgams and fish.

Methylmercury is often a by-product of industrial processes such as burning coal for power. Vaporized mercury makes its way into rain, soil, and water where it can pose a risk to plants, soil, and humans. When levels rise in pregnant moms or children, it could cause neurological damage affecting a child's early development. You can lower mercury exposure by avoiding fish high on the food chain such as tuna, swordfish, shark, and bass. Avoiding amalgam fillings since they are composed of approximately 50% mercury

will reduce any toxic burden. Mining for gold, certain types of jewelry, contact with a broken thermometer, and exposure to toxic air near factories that are emitting mercury such as coal plants will increase mercury exposure.

Another heavy metal, **aluminum**, at toxic levels, has been linked to ASD. Aluminum is found in the air, water, medications, foods, vaccines, cosmetics, baking tools, cans, and aluminum foil. It is one of the most widely distributed elements in the environment. Eliminating products such as aluminum foil, aluminum coated dishes or pots, and cosmetic products with aluminum such as deodorants and toothpastes mitigates exposure. The most aluminum is found in antacids or anti-perspirants. Aluminum is used as an adjuvant in many vaccines such as Hepatitis A, Hepatitis B, DTaP, and HiB to help build stronger immunity against the germs being vaccinated against.

One study has shown that the amount of aluminum in brain tissue with ASD is extraordinarily high and that it is associated with inflammatory cells. Limiting exposure to aluminum containing products in pregnant women and children will reduce toxic exposure to aluminum to help reduce the rising incidence of ASD.

Arsenic is another heavy metal that is widely distributed in air, water, and land and present in baby food and rice. Arsenic can cause severe brain damage and is responsible for cognitive deficits in children in many countries. It alters nitric oxide signaling pathways similar to autism associated mutations. There is oxidative stress on the neurons from free radical formation which leads to mitochondrial dysfunction. A study on mice showed exposing pregnant and lactating mice to arsenic in drinking water induced autistic-like behaviors of repetitive behaviors, abnormal social behaviors, language and memory impairment, and anxiety. Avoiding rice and baby foods containing arsenic will reduce the toxic burden of arsenic. **Cadmium** is also found in about 65% of baby food, is neurotoxic, and is another heavy metal that could be contributing to the rise in ASD.

Another major toxicant implicated in autism is **glyphosate,** better known as Roundup. Glyphosate is the most widely used herbicide in the world. Farmers in conventional farming are using it on GMO crops such as soy, corn, and wheat to control and kill weeds. In addition, it desiccates the crops to expedite harvesting. There has been a reported rise in ASD cases with its increased usage on soy and corn crops between 1995-2010. Glyphosate alters the composition of the gut microbiome leading to an increase in pathogenic bacteria such as Clostridia which can secrete metabolites that cause ASD-like behaviors. In addition, there is an increase in gut permeability, just like with gluten. where tight junctions are broken leading to endotoxemia impairing brain development

in children causing ASD. It also can break down the blood brain barrier allowing toxins and pathogens to enter the brain.

Glyphosate causes mineral depletion in our food supply, lowers our sulfur supply which is vital for detoxification, inhibits enzyme function for thousands of biological processes in all organ systems, affects mood regulating hormones such as serotonin and dopamine, and inserts itself in protein chains substituting for an important amino acid, glycine, disrupting a vital pathway involved in the assembly of amino acids known as the shikimate pathway.

The most important ways of reducing glyphosate exposure are to eliminate household use of Roundup and eat organic products, since glyphosate cannot be used on USDA certified organic grown crops.

There are certain methods available to help rid the body of glyphosate. Besides eating organic foods rich in sulfur and manganese along with fermented foods, detoxification of glyphosate can be enhanced through using infrared saunas, ionic foot baths, taking pre and probiotics to repopulate the microbiome destroyed by it, and by using binders such as bentonite clay or activated charcoal to promote excretion. There are some medicinal plant extracts like dandelion, burdock root and barberry that can protect cells against this toxin.

There are many other toxins that have been associated with autism. **Phthalates** are common environmental chemicals found in cosmetics, food packaging, medical devices, and toys. They have endocrine disrupting properties and have been linked to autism in children when moms were exposed to them during pregnancy and when young children were in contact with them.

To know which products to avoid that are high in phthalates, use the Environmental Working Group (EWG) database or app to find household and personal care products. Also, do not use plastic wrap and plastic food containers made from PVC- a better choice is to use glass or stainless-steel containers instead. Avoid fast food because of the extensive use of plastics to produce and serve these foods. The best treatment is avoidance. It is helpful to eat a diet high in fiber and use supplements that are either antioxidants or support detox pathways such as milk thistle, resveratrol, curcumin, and dandelion root which can expedite the removal of any phthalates in the body.

There are studies showing **polychlorinated biphenyls** (PCBs) being implicated in contributing to ASD by modulating signaling pathways altering neurodevelopment. PCBs are found in many industrial products like transformers, capacitors, and oil

plasticizers. Even though they were banned from use in 1977, they are still showing up in the environment, since they don't readily break down and are still being released by old devices such as transformers, electrical devices and appliances that were made before the ban on PCBs was instituted. We are exposed to PCBs by breathing air or drinking water contaminated with them. PCBs can be released into the air from improper handling. The major dietary sources of PCBs are fish, meat, and dairy products from water and soil that remain contaminated with PCBs. Fluorescent light fixtures and caulking material have been found in schools and have been addressed with the EPA to reduce children's exposure to this neurotoxin. There are studies showing PCBs contributing to ASD by aberrantly modulating signaling pathways.

Like phthalates and other toxins, the best treatment is avoidance of exposure and supporting the detoxification pathways of the body with a diet high in antioxidants and supplements with antioxidants such as resveratrol, N-Acetyl Cysteine (NAC), curcumin, quercetin, and CoQ10.

Bisphenol-A is another toxic plasticizer linked to ASD. BPA, like PCBs, is in many plastics like water bottles and other beverage containers, automobile parts, plastic dinnerware, toys, and dental sealants. BPA is an endocrine disruptor and several studies have investigated exposure during pregnancy and its effect on neurodevelopment. Avoidance of products containing BPA such as plastic bottles or cans and use of glass or stainless steel is recommended instead. Paper receipts contain BPA, so have your receipts emailed instead of touching them. As with other toxins, supporting the detox pathways with a healthy organic diet rich in antioxidants such as cruciferous vegetables will assist in excretion of BPA. Binders such as bentonite clay, chlorella, spirulina and activated charcoal can also be helpful.

Mycotoxins have emerged as playing a role in the pathobiology of autism. They can impact the nervous system through immune system activation contributing to ASD. Mycotoxins are produced by fungi/mold and affect a wide range of plant products such as corn, wheat, nuts, dried fruits, spices, and rice. They proliferate in warm humid conditions. The most common mycotoxins that pose a concern to us are aflatoxins, ochratoxin A, patulin, nivalenol, zearalenone and fumonisins. How can you detect dangerous mycotoxins? They can be found in discolored food with a fuzzy texture that tastes off, water damage in house with water spots where mold can be growing, and areas where there is a musty unidentified smell that can't be eliminated. Elimination of any source of mold in your house through remediation and proper storage of food to prevent

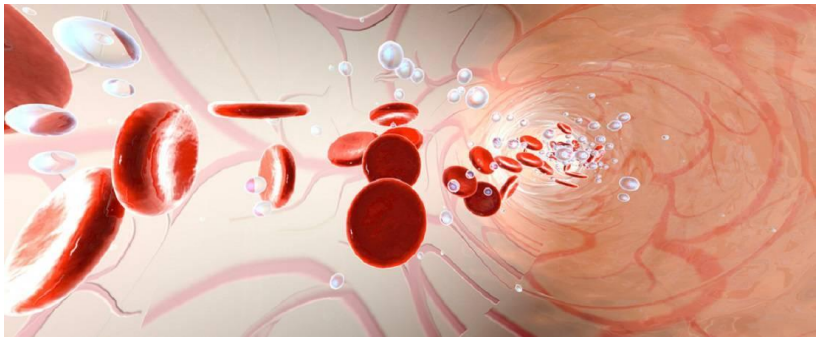
mold formation are imperative. If mold is detected, there are binders like activated charcoal that can help remove mycotoxins.

There are many other hidden toxins in household products, cosmetics, foods, medications, dental products. Take it one step at a time when researching products and you can use guides like the EWG to find which products are safest to use to avoid any bodily insults to pregnant moms and children that can trigger or exacerbate ASD.

Tylenol (Acetaminophen) has received a lot of press recently regarding women taking it during pregnancy. There is an increased risk for ASD and ADHD due to its toxic effects on neurodevelopment including the endocannabinoid system, changes in brain derived neurotrophic factor (BDNF), oxidative stress due to immune system activation, and changes in neurotransmission and endocrine disruption. Studies have reported that even small doses of Acetaminophen may affect neurodevelopment and this effect is sometimes apparent years after exposure.

There is emerging research establishing a link between **electromagnetic field (EMF)** exposure and autism. Dr. Paul has found that voltage-gated calcium channels are impacted by EMFs increasing the amount of calcium inside the cells which is connected to autism. Too much calcium affects synapses in the brain causing neurological dysfunction. Steps that could be taken to mitigate our children's exposure to EMFS are limiting screen time, enabling Airplane mode when not using a device, using an EMF radiation protection shield, placing a Wi-Fi router away from an area in the house where you normally spend time, and turning off the Wi-Fi when you're not using it. In one study among boys, longer screen time at 1 year of age was significantly associated with autism at 3 years old. Overexposure to EMFs can cause oxidative stress which is linked to autism.

Oxidative Stress



What exactly is this? The body's mitochondria are the power producing organelles in cells throughout our body. They use food and oxygen to produce ATP which is our gasoline or energy currency. During this process, there are byproducts known as free radicals or reactive oxygen species that are produced. When these free radicals outweigh our body's antioxidant capacity and cause deleterious effects, oxidative stress occurs. This causes damage to the mitochondria which leads to abnormal function, "rusting" and disease. In children with ASD, there are higher free radical levels leading to mitochondrial dysfunction. The brain is sensitive to a large accumulation of these free radicals. Diminished levels of glutathione, the master antioxidant, have been found in children with ASD and contribute to deficiency in detoxifying this harmful debris. This will induce neuroinflammation causing damage to cells and a decline in brain function. This is associated with a loss of connections or underconnectivity in the brain. Oxidative stress and neuroinflammation often go hand in hand.

The key is to find out what is causing or contributing to the oxidative stress: infections, allergies, autoimmunity, leaky gut/imbalanced microbiome, vitamin/mineral deficiencies, mitochondrial dysfunction, toxins, diet, lack of exercise and sleep, stress, etc. There are many antioxidant supplements that have been studied and are beneficial such as glutathione, N-Acetyl Cysteine (NAC), CoQ10, sulforaphanes, and omega-3's.

Oxidative stress often leads to mitochondrial dysfunction.

Mitochondrial Dysfunction

Mitochondrial dysfunction is the most common metabolic abnormality associated with ASD with a study showing it may be present in up to 80% of cases. Brain cells have approximately two million mitochondria in each individual cell. When these mitochondria are not producing energy effectively, free radicals are overwhelming the antioxidant system leading to oxidative stress and neuroinflammation. When the brain is

inflamed, developmental delays can occur with subsequent ASD symptoms and behaviors.

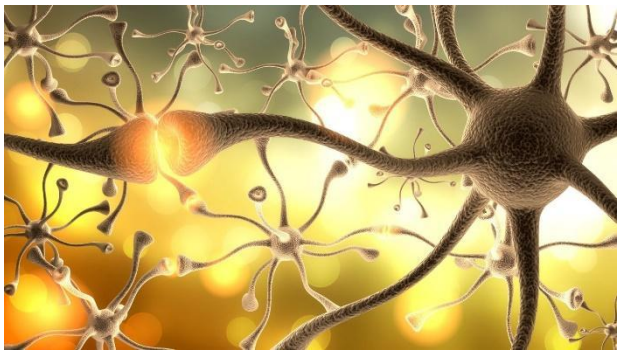
A study using magnetic resonance spectroscopy revealed evidence of mitochondrial brain energy metabolic abnormalities showing a correlation between these metabolites and low intelligence and language scores seen in kids with ASD. It is difficult to tell whether mitochondrial dysfunction is a feature of all people with ASD, whether it is a cause or effect of ASD, and whether the dysfunctions are localized to specific regions of the brain.

Like oxidative stress, mitochondrial dysfunction can be linked to a poor diet, lack of exercise and sleep, stress, infections, autoimmunity, leaky gut/microbiome imbalances, medications, toxins, genetic mutations, and vitamin or mineral deficiencies.

There are many supplements that support mitochondrial function including CoQ10, amino acids, creatine, alpha lipoic acid, omega-3 fatty acids, l-carnitine, thiamine, niacin, riboflavin, vitamin B6, vitamin B12, folate, vitamin C, and vitamin E. The influence of these supplements on mitochondria is important. There have been some randomized trials, such as with l-carnitine, where there was improvement seen in ASD symptoms.

One study concluded that ASD may be caused by a defect in mitochondrial bioenergetics. If there's mild mitochondrial inhibition which impairs nerve function, it is possible for metabolic therapies to provide therapeutic intervention. You can see how the brain, which has the highest concentration of mitochondria in the body, can be impacted by mitochondrial dysfunction. If the brain's mitochondria cannot produce enough energy, it can affect a child's ability to walk, talk, socialize, behave, learn, interpret environmental stimuli, and perform executive functions. When the mitochondria are affected throughout the body, the symptoms can be multisystemic. Brain cells have a signaling system known as neurotransmitters.

Neurotransmitters



Neurotransmitters are vital for conducting messages from nerves to target cells in the body. They play a crucial role in neurodevelopment, and when there is an imbalance in these molecules, bodily dysfunction can occur.

GABA is the main inhibitory neurotransmitter in the brain. In autism spectrum disorder, scientists at Harvard found that autistic behavior is associated with a breakdown in the GABA signaling pathway with a deficit in GABA. This same pathway is implicated in seizures, so this may be why seizures are seen in up to 25% of children with ASD. Some children take GABA as a supplement to calm the nervous system to help increase socialization and school performance.

Glutamate is the main excitatory neurotransmitter and counteracts the effects of GABA. Further research needs to be done on the glutamate/GABA imbalance in ASD. Excitatory/Inhibitory imbalance can affect the sensory, emotional and memory system requiring the need for intervention in ASD. Measuring the GABA/Glutamate ratio by magnetic resonance spectroscopy is a useful biomarker and finding treatments to increase this ratio are being investigated. NMDA receptors bind to glutamate which acts as an excitotoxin to cause neuronal death. NMDA receptor antagonists like L-theanine reduce glutamate levels to mitigate excitotoxicity, reducing aggression and irritability. There are other glutamate receptor antagonists that have been used for Alzheimer's Disease being investigated for use in ASD.

Serotonin, known for its role in anxiety, depression, and social phobia, is another neurotransmitter that has been linked to autism. Children with ASD have been found to have low levels of serotonin in the brain on imaging studies or that serotonin is not binding to receptors to take effect. This can account for social difficulties, repetitive behaviors, and anxiety. Selective serotonin reuptake inhibitors (SSRI) medications like Prozac and Zoloft have not yet been shown to universally benefit children with ASD.

Increasing tryptophan levels through supplements like 5-Hydrotryptophan (5-HTP) is inhibitory and can improve sleep, mood, behavior, self-stimulatory behaviors, and language.

Dopamine is a neurotransmitter that regulates movement and feelings of pleasure and motivation. Dopamine dysfunction may explain why some kids with ASD have hyperactivity, tremors, and motor deficits. Abnormal levels of dopamine have been detected on radiology scans and through lab biomarkers. Increased seizure rates, motor abnormalities, stereotypical and repetitive behaviors, executive dysfunction, abnormal gaits, problems following eye gaze, and attention abnormalities are all components of ASD and linked tightly to the midbrain dopamine systems. Dopamine acts like an accelerator which is great for focus and concentration but can lead to aggressive behaviors when it's out of balance.

Dopamine is converted to **noradrenaline** and then **adrenaline** which triggers the body's fight or flight response. When there is too much adrenaline, aggressive and hyperactive behaviors can ensue. Balancing dopamine, serotonin, adrenaline, and noradrenaline levels can help improve language, behaviors, focus, mood, and sleep in our children.

Histamine is a central nervous system neurotransmitter released by mast cells that promotes wakefulness. This is why antihistamines like Benadryl that work on histamine receptors in the brain can cause drowsiness. We are most familiar with histamine released during an allergic reaction and take antihistamines to combat the response. It is not uncommon for children with autism to have elevated histamine levels due to a leaky gut, infections, chronic stress and insufficient methylation impairing enzymes COMT and HNMT which detoxify histamine from the body. Elevated levels of histamine can be a problem for children with autism and it is important to ensure that underlying allergies and infections are addressed and measures are taken to manage the symptoms that elevated histamine can cause. Some of these symptoms include anxiety, headaches, food intolerances, behaviors, rashes, and digestive problems. Removing foods that are cured, smoked, and fermented can help lower histamine levels.

Acetylcholine is a neurotransmitter essential in evaluating the stimuli and changes in the environment; therefore, it has a role in regulating behaviors relevant to autism including attention, cognitive flexibility, social interactions, and stereotypical behaviors. Neurons in the nucleus of the brain in ASD patients are unusual in size, shape, and number and decreased levels of choline, a precursor of acetylcholine, were found and correlated with

the level of severity of autism. Alterations in cholesterol metabolism can have an impact on acetylcholine signaling affecting the glutamate/GABA excitatory-inhibitory balance in the brain.

The neurochemistry of the brain can be affected and regulated by various hormones.

Hormones

Hormones are the body's chemical messengers that target different tissues and organs. Our kids can experience various hormonal imbalances.

Hypothyroidism has been linked to autism. The thyroid gland is a master regulator and catalyst for brain development. Thyroid hormone deficiency in early development can cause central nervous system damage leading to autism. Folate receptor antibodies could affect the developing thyroid contributing to the pathology of ASD.

Cortisol is a hormone produced by our adrenal glands in response to stress. Children with ASD have been found to have significantly higher cortisol levels with a prolonged duration and recovery of a cortisol elevation after a stressor. Lower functioning children with ASD exhibit higher levels of cortisol. Increased levels of cortisol will induce chronic inflammation causing oxidative stress and mitochondrial dysfunction impacting ASD. Cortisol levels can ultimately diminish due to chronic adrenal stress which can elicit hyperactivity and aggressive behaviors similar to having excessive dopamine, adrenaline, and glutamate.

Oxytocin is a hormone produced by the hypothalamus in the brain that has been found to be low in some children with ASD. This has been considered the "social hormone" and regulates social-reward learning. Oxytocin has been used intranasally with inconsistent results with a recent trial showing it to be ineffective. Some patients have shown improvement in social abilities after treatment.

Melatonin is a hormone produced primarily in the pineal gland of the brain and by the gut microbiome. It helps regulate the sleep-wake cycle and has been found to be abnormal in some children with ASD. Multiple studies have shown improvement in autistic behaviors and sleep with administration of melatonin. Melatonin is also a potent mitochondrial antioxidant and helps protect against cell death and inflammation.

Another important hormone, also a vitamin, which is deficient in many children with ASD is **Vitamin D**. Vitamin D plays a role in reducing neuroinflammation and regulates GABA, glutamate, dopamine, and serotonin. Administration of vitamin D can provide improvement in signs and symptoms of ASD. An increasing amount of evidence is showing that gestational and early childhood vitamin D deficiency causes some cases of autism.

Neurotransmitters and hormone levels can be affected by neuroinflammation which is influenced by diet, toxins, infections, autoimmunity, and leaky gut. Searching for the root cause of any imbalance is paramount since all these systems are interacting. Treating one neurotransmitter imbalance may suppress symptoms but will not treat the primary abnormality that is driving this inflammatory response in the brain leading to ASD symptomatology.

Neurotransmitters, hormones, vitamins, and minerals work like a symphony in the body to provide the messaging and energy that is needed to fuel the body.

Vitamin and Mineral Deficiencies

Studies have reported low levels of vitamins and minerals in numerous cases of ASD. These are essential for development and normal body functioning. Vitamins A, B1, B6,

B12, and D have been found to be deficient. These deficiencies led to worsening of ASD symptoms, however once treated, improvement was observed.

Vitamin D is not only a hormone but also the most studied nutrient deficiency associated with ASD. Most studies show that pregnant women with a low vitamin D level have a higher risk of having preeclampsia and preterm births placing them at greater risk for having a child with autism. Children born with low levels of vitamin D have a 33% increased risk of ASD compared with high vitamin D levels.

Vitamin D is important in brain development and has been shown to completely prevent ASD traits in their offspring when given to mice during pregnancy. When vitamin D is deficient, it prevents testosterone from being broken down leading to higher testosterone in the brain which could explain the higher prevalence of ASD in boys. Two open label trials found that high dose vitamin D improved the core symptoms in 75% of children with ASD.

Folic acid (vitamin B9) has not only been associated with fewer neural tube defects in pregnant women but also autism. As mentioned earlier, it has an impact upon the MTHFR SNP which has an associated risk with autism. It has been identified to be integral to fetal development and plays a role as a modifiable risk factor in ASD. Improvement in verbal communication, motor skills, and plasma levels of folic acid, homocysteine, B12, and glutathione have been seen with supplementation of folinic acid. Giving methyl folate can also be beneficial since many children with ASD have abnormal methylation preventing the brain from utilizing the folate effectively.

Thiamine (vitamin B1) may play a role in autism by regulating cell death, neurotransmitter modulation, oxidative stress, and multiple enzymatic pathways. Supplementing with thiamine revealed benefit in people with ASD. In one study where children with ASD were administered a thiamine derivative for 2 months, there was improvement in social skills, communication, sensory integration, and behaviors as well as a reduction in heavy metals.

Pyridoxine (vitamin B6) is involved in over one hundred enzymatic reactions in the body and is a cofactor in the production of serotonin and GABA to help stabilize mood, sensory processing, and reduce anxiety, impulsivity, and stress. In addition, it plays a key role in methylation and detoxification. Magnesium has been used with B6 to help absorb the B6 better and reduce side effects such as neuropathy, depression, and headache. This aims to improve communication, behavior, and social interaction.

Cyanocobalamin (vitamin B12) deficiency can cause significant problems with methylation, nerve and red blood cell production, and brain development. In one study, it was found that B12 levels in children with ASD were three times lower than neurotypical children. Preliminary evidence shows that B12, particularly injected methylB12, improves metabolic abnormalities in ASD along with clinical symptoms.

Vitamin A is essential for behavioral development and cognitive function. In a study, Vitamin A was found to be deficient in almost 78% of children with ASD and it was suggested that supplementation with vitamin A may improve symptoms in a subset of children. Children with ASD have elevated serotonin levels compared to typically developing children which appears to be related to vitamin A deficiency.

Magnesium deficiency has been linked with the rise in ASD and prevents against encephalopathy and developmental delays. Magnesium is an essential mineral involved in over seven hundred enzymatic processes in the body. Magnesium is needed to make glutathione, our master antioxidant. Without glutathione, our kids have trouble with detoxifying chemicals, heavy metals, and other toxins. Other symptoms that could be associated with magnesium deficiency are irritability, insomnia, anxiety, constipation, hyperactivity, muscle spasm, and weakness.

A study showed that 82% of children with ASD were **Zinc** deficient. Zinc deficiency can affect immune function, neurological function, and the gut microbiome. Like magnesium, zinc deficiency can affect glutathione metabolism leading to vulnerability to environmental insults and oxidative stress. Zinc also plays a key role as a cofactor in over three hundred enzymatic pathways and levels were found to be abnormal in hair, plasma, and nails in children with ASD. In another study, increased dietary zinc induced changes in nerve synapse function and plasticity that occur with reversal of ASD related behaviors.

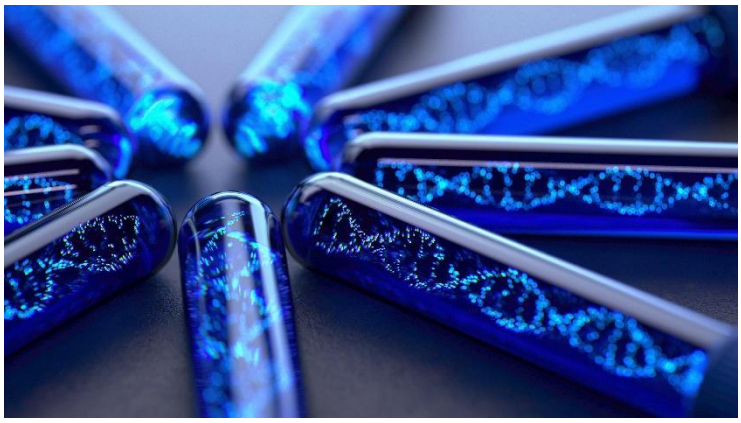
Copper competes against Zinc in the body, therefore an increase in copper levels can lead to zinc deficiency. Zinc/copper ratios have been evaluated and tend to be low in children with ASD. High copper may be associated with low GABA and high adrenaline levels which may manifest as hyperactivity and excitability associated with autism.

There is a high prevalence of **iron** deficiency in children with ASD. There is a study that showed a correlation between increased maternal iron intake during pregnancy and lower rates of ASD. Iron is critical to brain development and production of neurotransmitters. Deficits in iron lead to alterations in production and function of dopamine and other neurotransmitters.

Lower levels of **omega-3 fatty acids**, EPA and DHA, were found in children with ASD compared to typically developing peers and correlated with a greater severity in symptoms. Altered metabolism of omega 3's led to an increase in inflammation, oxidative stress and an imbalance in formation of neurotransmitters associated with ASD. Children that took omega 3 supplements saw improvement in spelling, social responsiveness, overall behavior and reading level.

We have focused on the environmental and metabolic factors thus far. Genetics play a role as well.

Genetics



Genetics may load the gun, but the environment pulls the trigger for disease. We know that autism is a combination of genetics with environmental influences, epigenetics. Most of the research originally focused on genetics due to the high rate of ASD being inherited- up to 80 %. A new study revealed that there are 185 genes associated with autism. Gene therapy has been studied to be effective in some children with genetic variations.

It may be beneficial to consider genetic testing for a child with developmental delays, especially if the child does not display the typical regressive symptoms, there is a history of autism in the family, or the child is not responding to biomedical treatments.

Some of the genetic disorders that are commonly associated with ASD are Fragile X, Rett Syndrome, Angelman Syndrome, Turner's Syndrome and Tuberous Sclerosis. In these syndromes, the disease can be attributed to one gene. Most cases have pathologic variants of multiple genes which have led to hundreds of risk genes being identified.

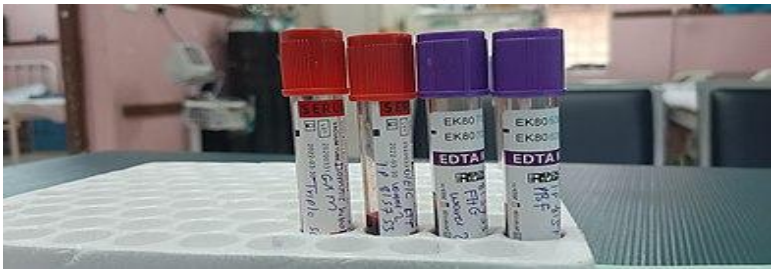
One of the genetic variations that has been remarkably linked with ASD is the single nucleotide polymorphism (SNP) MTHFR C677T. MTHFR regulates folate metabolism and methylation which have been found to be abnormal in many children with this SNP.

Approximately 10% of children with ASD have a genetic disorder where they are born with developmental delays with the other 90% having the regressive type which are often triggered by toxins or infections. For children that don't have genetic disorders like Fragile X, there could be an abnormal SNP like MTHFR or glutathione deficiency.

One study looked at 29 SNPs on different genes and was able to classify individuals with mild, moderate, or severe ASD by constructing SNP based diagnostic models. Some of the candidate genes associated with 90-95% of the cases of autism are AVPR1a, DISC1, DYX1C1, ITGB3, SLC6A4, RELN, RPL10, and SHANK3.

There are numerous companies that provide genetic testing to detect any SNP that could be linked to autism. There is also genetic testing such as whole exome sequencing and chromosome microarray that can evaluate for duplicated or missing chromosomal segments and mutations in children with ASD. Genetic testing can help identify a genetic link to autism, promote early detection and intervention, develop treatment plans to target ASD related conditions, and create risk evaluation information to help with counseling and education of families.

Testing



There are numerous tests available to evaluate root causes and links to ASD. It is important to document a thorough history from pregnancy until present to work on fitting the pieces of the puzzle together. Each case of autism is unique. One child's autism could be precipitated by mercury toxicity while another could be triggered by gluten intolerance. This is where history will yield an abundance of information to guide testing and treatment. In some cases, the answer might be known without testing but confirmation with objective evidence can be helpful. In other cases, the history will not

elicit enough information and testing is needed to determine what is happening "underneath the hood."

Here are some of the more commonly ordered tests used to assess for the potential causes or links to ASD broken down according to each potential root cause:

- **Neuroinflammation**: CBC, CMP, CRP, sed rate, ANA, vitamin B12, folate, vitamin D, iron, copper, zinc, magnesium, micronutrient panel, TSH, Lyme Antibodies, Omega-3 index, cerebral folate receptor antibody, homocysteine, ferritin, lipid panel, immunoglobulin panel, Food IgG and IgE panel, environmental IgE allergy panel (RAST), mycotoxin profile
  for molds, heavy metals panel, GI-MAP, urine organic acid test (OAT), MRI brain, SPECT scan, EEG

- **Infections**: CBC, Sed Rate, CRP, CDSA, GI-MAP, SIBO testing, urine culture, OAT, Strep antibodies, Mycoplasma Antibodies, Lyme and coinfection antibodies, HHV-6 antibodies, chlamydia antibodies, HSV-1 and 2 antibodies, Epstein-Barr Panel, Immunoglobulin panel

- **Allergies/Mast Cell Activation Syndrome**: CBC, Food IgE panel, Environmental IgE panel, serum tryptase, urine porphyrins, blood histamine

- **Autoimmune**: CBC, sed rate, CRP, ANA, cerebral folate receptor antibodies, Celiac panel

- **Diet**: Food IgE and IgG panel, Celiac panel, urine for gluteomorphins and casomorphins

- **GI/Microbiome**: CBC, CMP, GI-MAP, OAT, small intestinal bacterial overgrowth (SIBO) breath test, calprotectin, zonulin, celiac panel, food IgG panel, CRP, nutrient panel

- **Methylation**: Methylation panel, folate, B12, cerebral folate antibody, homocysteine, methylmalonic acid (MMA), Salivary DNA methylation pathway profile

- **Toxins**: metals testing through hair, urine, stool, or blood (heavy metals), mycotoxin panel (mold), GPL-TOX panel (non-metal environmental pollutants), glyphosate, OAT, urine porphyrins

- **Oxidative Stress**: Isoprostanes (IsoPs), malondialdehyde (MDA), Lipid Peroxides, Glutathione, Superoxide Dismutase, CoQ10, 3-Nitrotyrosine, homocysteine, cysteine, methionine, folate, vitamin B12, Oxidative Stress panel, OAT

- **Mitochondrial Dysfunction**: CBC, Comprehensive metabolic panel, magnesium, zinc, vitamin D, CRP, thyroid panel, heavy metal panel, MTHFR, Iron, Celiac panel, Lactate, Pyruvate, Carnitine, plasma amino acids, CoQ10, creatine kinase, plasma acylcarnitines, ammonia, creatine, OAT, CDSA, mitochondrial disorders panel, Mitoswab

- **Neurotransmitters and Hormones**: neurotransmitter test kit, sleep balance test kit (melatonin and cortisol), vitamin D, plasma oxytocin, salivary cortisol, urinary catecholamines, amino acids, magnesium, B12, folate, B6, homocysteine, methylmalonic acid, MTHFR, DUTCH

- **Vitamin and Mineral Deficiencies**: vitamins A, B1, B2, B6, D, B12, folate, homocysteine, methylmalonic acid (MMA), vitamin D, vitamin E, Iron, ferritin, zinc, copper, CMP, RBC magnesium, micronutrient panel, omega-3 index

- **Genetics**: whole exome sequencing, whole genome, chromosomal microarray, Autism panel, Fragile X, SNP testing

Supplements

There are only two medications, Risperdal and Abilify, classified as atypical antipsychotics, which are FDA approved for irritability, aggression, and self-injurious behaviors in autism. Other medications have been used to treat comorbidities associated with autism such as Depakote for seizures and Zoloft for anxiety and depression. Leucovorin has been used for cerebral folate deficiency. There are other drugs currently being studied in clinical trials such as Suramin that are not FDA approved for autism.

Many practitioners work with families using supplements to help with the imbalances and metabolic abnormalities associated with ASD to ameliorate the condition. Depending on the root cause and associated abnormalities, each child's regimen will be unique. What should be universally implemented are the foundations of health- an organic whole foods diet (whichever works best for your child), exercise/movement, abundant sleep, and stress mitigation.

Here is a list of some of the more common supplements that have been used for these ASD related concerns:

- **Neuroinflammation**: folinic acid, methyl folate, methylB12, vitamin B6, vitamin C, vitamin D, magnesium, zinc, curcumin, omega 3's, probiotics, phosphatidylcholine, phosphatidylserine, palmitoylethanolamide (PEA), Spirulina, CBD

- **GI/Microbiome**: prebiotics, probiotics, digestive enzymes, betaine, L-glutamate, slippery elm, marshmallow root, licorice root, collagen

- **Methylation**: methyl folate, folinic acid, methylB12, riboflavin, trimethyl glycine (TMG), dimethylglycine (DMG), magnesium, zinc, choline

- **Toxins**: vitamin C, vitamin E, B vitamins, magnesium, Epsom salts, calcium D glucarate, glutathione, NAC, milk thistle, dandelion root, chlorella, zeolite, bentonite clay, activated charcoal, humic acid, fulvic acid, taurine, sulforaphane, omega 3's

- **Infections**: vitamin C, vitamin D, zinc, quercetin, echinacea, caprylic acid, biocidin, goldenseal, berberine, grapefruit seed extract, uva ursi, olive leaf extract, oil of oregano, garlic, ginger, monolaurin, L-lysine, S. boulardi

- **Allergies**: quercetin, vitamin C, probiotics, stinging nettle, spirulina, luteolin, mangosteen, DAO

- **Autoimmune**: omega 3's, vitamin D, glutathione, curcumin, resveratrol, probiotics, adaptogens such as ashwagandha

- **Oxidative Stress**: vitamin A, vitamin C, vitamin E, vitamin K, zinc, magnesium, vitamin B6, methylB12, methyl folate, melatonin, NAC, glutathione, resveratrol, carnosine, NADH, CoQ10, alpha lipoic acid, spermidine, astaxanthin

- **Mitochondrial Dysfunction**: vitamins B1, B2, B5, B6, methylB12, Biotin, methyl folate, vitamin C, vitamin E, vitamin K, CoQ10, L-carnitine, alpha lipoic acid, L-creatine, L-arginine, selenium, magnesium, glutathione

- **Neurotransmitters**: GABA, 5-HTP, L-tyrosine, vitamin B6, magnesium, L-theanine, taurine, inositol, lithium orotate, Folinic Acid, methylB12, alpha-GPC, phenylalanine, DAO, vitamin C, quercetin, nettle, mangosteen, black seed oil

- **Hormones:** Selenium, Iodine, Zinc, thyroid, adaptogens, melatonin, vitamin D, adrenal support.

- **Vitamins and Mineral Deficiencies**: multivitamin, B-complex vitamin, folinic acid, methylb12, vitamin A, vitamin C, vitamin D, vitamin E, magnesium, zinc, iron, calcium, omega-3's

As you can see, there are some supplements that work through various mechanisms to ameliorate symptoms of autism. Working to find the underlying cause of what is triggering your child's autism is integral to healing. In many cases, changes in lifestyle accompanied with tailored supplements can make a world of difference. There are cases where treating the symptoms without being able to find an underlying root case can be helpful such as supplements to improve speech, behaviors, mood, and sleep.

Other Therapies

There is a high prevalence of **sleep** disturbances among children with ASD, many of which are unrecognized and can take a toll on the well-being of the child and family. Trying to find the root of the problem and working on sleep hygiene is critical. Some children require a sleep study to determine what may be disrupting their sleep. If no other treatable cause is found, there are supplements such as melatonin, magnesium, lemon balm, chamomile, passionflower, L-theanine, valerian and GABA that can help promote sleep.

Hyperbaric oxygen therapy (HBOT) has gained much attention in the autism community over the years. Several studies have shown improved cerebral perfusion and decreased markers of inflammation in children with ASD. Some families have anecdotally reported improvement in their children's symptoms, even though it is not FDA approved. One study showed statistically significant improvement in ATEC and CARS autism scales after undergoing forty HBOT sessions lasting 60 minutes. The current absence of conclusive evidence for treatment of ASD has not supported its endorsement by the FDA.

Infrared Sauna therapy has been another therapy used for children with ASD. Like HBOT, it reduces oxidative stress, improves mitochondrial function, reduces inflammation, and promotes detoxification. Increased levels of tetrahydrobiopterin (BH4) and heat shock protein 90 (HSP 90) have been seen with sauna therapy leading to improvement in neurotransmitter formation and maintaining intracellular health.

Ionic foot baths have been used for detoxification by creating a charge in water to draw toxins out of the soles of the feet. Many families have anecdotally reported improvement in their children after treatment. A company did a study on the efficacy of glyphosate being excreted through the urine using their footbath detox and saw significant improvement in symptoms and ATEC scores.

Medical Marijuana (THC) has been approved in certain states for the treatment of autism. Marijuana can help with social communication and cognition and reduce irritability, aggression, restlessness, agitation, and self-injury. Proposed mechanisms of action include immune system modulation, anti-convulsant effect, and reducing neuronal excitability and transmission. Cannabidiol (CBD) has also shown some promising results.

Stem cell therapy is being done at the Stem Cell Institute in Panama and in Mexico. This is not an FDA approved treatment for autism, therefore is unavailable in the US. They are using umbilical cord tissue derived mesenchymal stem cells that are donated by mothers after normal healthy births. Four consecutive daily intravenous infusions are administered. These stem cells modulate the immune system, mitigate inflammation, affect neurotransmitters, form new blood vessels, and reestablish new neural connections. Long-term safety and efficacy of stem cell therapy need to be further evaluated. Anecdotally, patients that claim it has been effective often say the effects are not long lasting and it is very expensive.

Homeopathy is individualized just like other autism treatments. The homeopathic approach essentially takes a very small dose of the offending agent to help treat the condition. Most studies support the use of homeopathy in the treatment of autism and found it to efficiently control ASD symptoms and supplement other therapies.

Treatments in Clinical Trials

The lack of diversity in the microbiome of children with ASD has been proposed as a mechanism for ASD. **Microbial Transfer Therapy** (MTT) has been studied with encouraging results. Children showed improvement in ASD behaviors and GI symptoms 2 years after MTT and showed improvement in maintenance of diversity and abundance of beneficial bacteria. There are current clinical trials evaluating MTT for future treatment.

Repeated Transmagnetic Stimulation (rTMS) is where an electrical current is generated through a magnetic field and applied to the scalp to modulate brain activity. TMS has shown promising results in specific behavioral deficits in some individuals with ASD. TMS has the capacity to modulate excitability, connectivity, and plasticity that are abnormal in ASD brains. Clinical trials are being performed to assess the efficacy and mechanism of action of rTMS in children with ASD.

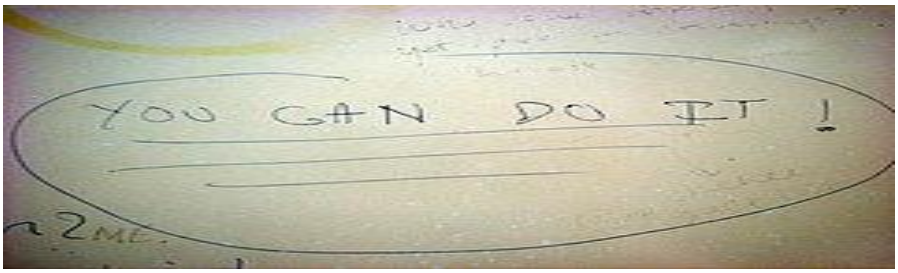
Transcranial Photobiomodulation (tPBM) is another neuromodulatory approach characterized by the delivery of low-level infrared light to the brain. In one study, there was a reduction in ASD severity shown by a decrease in CARS scores after the intervention with a reduction in cognitive and behavioral rigidity and improvement in sleep quality. Further research is being done to see if this will be an effective modality.

The autism drug pipeline consists of forty-seven drugs in different phases of development targeting carious pathways in the body. One promising drug is CM-AT, a digestive enzyme that aids in digesting protein since many children with ASD produce low amounts of the enzyme, chymotrypsin.

An investigational drug, **Suramin**, is being repurposed as a potential treatment for the core symptoms of ASD. It is a purinergic receptor blocker that is postulated to mitigate

neuroinflammation and reduce mitochondrial dysfunction. The drug is one hundred years old and has been used to treat river blindness and African sleeping sickness. Dr. Navieux's lab has been studying this and feels that Suramin's mechanism of action acts on the cell danger response (CDR), where the body can move out of defense mode because it is sensing danger and return to normal development, healing, and growth. The results thus far are encouraging.

Conclusion



There are various factors that can contribute to the symptoms of autism spectrum disorder (ASD). The prevalence of ASD has been increasing rapidly, with recent statistics indicating that 1 in 30 children are diagnosed with the condition. There are a variety of metabolic abnormalities that can contribute to autism, and it is important to identify your child's specific issues. Through functional evaluations, it is often possible to identify treatable abnormalities.

The paradigm is shifting. Autism is no longer viewed as a genetic neuropsychiatric condition that is irreversible. Autism is a systemic metabolic disorder that can be treated, and some children may show minimal improvement while others experience full recovery. Though every parent may hope for full recovery, any improvement is celebrated. With the right knowledge and resources, significant progress can be made in treating autism.

Continue to do your research as there is new information emerging about ASD daily. I am online daily researching the newest studies and findings in autism to incorporate into educating our families. Navigating the journey and addressing autism can be challenging, so it's important to take deep breaths and approach it with patience. As parents, it is important to maintain sound physical and mental health for us and our children. We can't help our children if we're not in good health.

My goal is to assist as many families as possible in improving the well-being and lives of their children. Together, we can take control of your family's health. By understanding the biochemical foundation of ASD, you will be able to collaborate with your team of professionals to get your child on a healing path. In the past, it was believed that there was a limited window of neuroplasticity for recovery of children with autism, and after that, it was considered hopeless. However, this is not the case. Adults who had not seen improvement with previous therapies may experience recovery once the underlying causes of their autism are addressed. There are some practitioners reporting up to 25% of children recovering from ASD with treatment where the kids are indistinguishable from neurotypical peers, another 50% responding to treatment, and the remaining 25% considered non-responders.

It is important to not let yourself feel overwhelmed. You've got this! Proceed methodically and always keep in mind that you have the best understanding of your child. If a particular practitioner is not a good fit, don't hesitate to look for someone else. Implementing the biomedical approach to autism can be challenging, but it can be broken down and addressed step by step. I am here to support you and guide you along your journey to healing your child from autism.

Having 20 years of experience as a physician and health coach, I provide guidance and support to families with autism throughout their journey. I hope that this eBook provides families with a foundation to assist them on their journey of healing their child. For families that need further assistance, I have created a 12-week program to dive deeper into various topics and provide you with the knowledge and support you need to heal your child. To learn more about the program, visit my website at https://www.myhopewellness.com/autism-healing.

Wishing you all the best on your healing journey!