

THE ROLE OF THE GASTROINTESTINAL TRACT IN  
AUTISM SPECTRUM DISORDER

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A Thesis Submitted to the Faculty of the University of Bridgeport College of  
Naturopathic Medicine in Partial Fulfillment of the requirements for the Degree of  
Doctor of Naturopathy  
and accepted this \_\_\_\_\_ day of \_\_\_\_\_, 20\_\_\_\_\_

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## ABSTRACT

Objective- The purpose of this literature review was to determine if there was an component of gastrointestinal involvement in children with autism spectrum disorder. This study reviewed the correlation of gastrointestinal issues in ASD. Additionally specific areas of study that correlate to ASD and GI issues were explored. They included dysbiosis, constipation, neuroinflammation, GI immunity, GFCF diet, and sensory/feeding behaviors

Basic Procedures- The primary search engine used for research was Eureka. Key word phrases searched were “ autism and gastrointestinal”, “autism and immune system”, “autism and neuroinflammation”, “autism and dysbiosis”, “autism and sensory processing”, “autism and constipation”, “autism and holistic healthcare”, “GFCF diet”, “autism, gut, brain connection”. Papers were chosen that were free whole articles and written within the last 10-15 years.

Main Finding- Children with ASD suffer from gastrointestinal illnesses that typically go undiagnosed and undertreated.

Principle Conclusions- Children with ASD present with challenging behaviors and limited ability to communicate that inhibit the process of assessing, diagnosing and treating their medical conditions. They present with GI compromises that most likely are contributing to their behavioral challenges. The relationship between the compromised gut, immune system and neuroinflammation need to be better

understood and treated in order to help restore homeobalance and improved health. As Naturopathic Doctors we are well prepared to address these medical conditions that are the root of autism.

## Chapter 1

### Introduction

According to the CDC (Center for Disease Control) about 1% of the world population has an ASD (autism spectrum disorder).<sup>(1)</sup> That percentage correlates to 3.5 million Americans living with an autism spectrum disorder.<sup>(2)</sup> The prevalence of autism in US children increased by 119.4% from the year 2000 when 1 in 150 children were diagnosed with autism, to 2010 when 1 in 68 children were diagnosed.<sup>(1)</sup> The prevalence of autism has increased by 6-15% annually from 2002 to 2010.<sup>(3)</sup> These statistics suggest that autism is the fastest growing developmental disability.<sup>(4)</sup> Dr. Robert Melillo describes the rise in ASD as “meteoric” and goes on to say it may be the most pressing social issue of our time. Melillo speculates that We are facing the largest childhood epidemic in history.<sup>(5)</sup>

The diagnosis of autism comes with a sizable price tag. The average cost of educating a student in the US is \$12,000.00 annually.<sup>(6)</sup> It costs an estimated \$20,600 to educate a child diagnosed with autism.<sup>(7)</sup> The 58% in educational costs per autistic student places an increased financial hardship on parents, family, schools, communities and taxpayers in general.<sup>(2)</sup>

Approximately 35% of young adults with ASD aged 19-23 leaving their high school setting remain unemployed, and typically do not receive post graduation education.<sup>(8)</sup> The average estimated cost of autism over the life of the individual ranges from 1.4 million dollars to 2.4 million dollars.<sup>(2)</sup> According to the Autism Society of

America the costs of lifetime care can be reduced by as much as 2/3 with early diagnosis and intervention. <sup>(9)</sup>

Families of children with a diagnosis of ASD frequently turn to complementary and alternative medicine (CAM). <sup>(10)</sup> The American Academy of Pediatrics recommends discussion of CAM with the family of all patients with ASD. <sup>(11)</sup> Complementary and alternative medicine includes the following: 1) Mind-body therapies, including meditation, prayer and mental healing 2) Biologically based practices, including the use of herbs, vitamins, and dietary supplements 3) Manipulation and body-based practices that include chiropractic and massage 4) Energy medicine such as Reiki, qigong and therapeutic touch 5) Whole medical systems that include 1-4 from above, such as naturopathic medicine. <sup>(12)</sup>

According to the Centers for Disease Control and Prevention, approximately 11.8% of U.S. children had utilized some type of CAM therapy in the preceding 12 months. <sup>(13)</sup>

In contrast, families of children with ASD are among the highest population with reported use of CAM being between 52% and 95%. <sup>(14)</sup> These families utilize a number of different CAM treatments with 50%-70% receiving biologically based interventions.

The scope of this thesis will review current literature regarding the clinical presentation of ASD. Specifically, the gastrointestinal symptoms that frequently

present with ASD will be reviewed (abdominal pain, constipation, dysbiosis, eating behaviors, sensory considerations in the diet, special diets, the GI immune connection and the GI brain connection, as well as a few treatment approaches).<sup>(15)</sup>

Given the naturopathic heuristic of “ First Treat the Gut” it would seem that the Naturopathic Physician could play a key role in treating individuals with ASD.

## Chapter 2

### Review of Literature

#### **History of Autism:**

Autism was first described in 1943 by child psychiatrist, Leo Kanner, at Johns Hopkins. Kanner described his observations of these unique children in the textbook, *Nervous Child*, under the title “Autistic Disturbances of Affective Contact”<sup>(16)</sup> In the first twenty years of Dr. Kanner’s practice he had never seen a case of autism. He first began observing the unique cluster of behaviors he later described as autism in 1938. Dr. Kanner opened the first child psychiatric unit in a hospital in the United States. He never described seeing these “fascinating” and “peculiar” childhood presentations until eight years after the establishment of his specialty. He described the unique characteristics of the syndrome as including: the inability to relate themselves to people and situations, poor (or absent) language skills, echolalia (repetitive verbal echoing), excellent rote memory, sensory sensitivity, perseverative and stereotypic behavior (stereotypy); an anxious obsessive desire for the maintenance of sameness; good cognitive potentialities; and general normal appearance.

In addition to describing the unusual behaviors of the first eleven cases observed, Dr. Kanner astutely made additional observations regarding the gastrointestinal and immunological health of these eleven children. Observations that were noted as significant included; “Eating has always been a problem for him”, “large and ragged tonsils”, “ Following the smallpox vaccination at twelve months, he had an attack of



diarrhea and fever, from which he recovered in somewhat less than a week”, “ Found to be healthy except for large tonsils and adenoids”, “ He vomited a great deal during the first year, and feeding formulas were changed frequently without success”, “ His tonsils were removed at three years old”, “ She nursed poorly”, “She quit taking nourishment at three months”, “ She was tube fed five times a day until one year of age”, “ He vomited all food from birth through the third month”, “ For the first two months feeding formulas caused considerable concern”, “He had been kept in bed often because of colds, bronchitis, streptococcus infection and impetigo”, “ There were frequent hospitalization due to feeding problems”, “ He suffered from repeated colds and otitis media which necessitated bilateral myringotomy”, and “febrile illness at eighteen months”. Being a psychiatrist, Dr. Kanner’s interpretations of these gastrointestinal and immunological health issues were viewed through the Freudian bias of the 1930s. He believed that these physiologic presentations were actually of psychogenic origin.

Dr Kanner’s early reports included his observations of the parents of these unusual children. Kanner’s observations included that these children were born to highly intelligent families. Additionally, in his opinion there were very few really warmhearted fathers and mothers. “For the most part, the parents, the grandparents, and collaterals are persons strongly preoccupied with abstractions of scientific, literary, or artistic nature, and limited in genuine interests in people. The question arises whether or to what extent this fact has contributed to the condition of the children”. As a result of Dr. Kanner’s work autism became categorized with

other strange and unusual psychiatric illnesses. The observations of Dr. Kanner, a Freudian influenced child psychiatrist, provided the foundation for the inception of the Refrigerator Mother Theory. <sup>(17)</sup>

In the 1950s Dr. Bruno Bettelheim, Ph.D. (philosophy) popularized the Refrigerator Mother Theory. He postulated that children were not born with autism, but they sensed from a very early age, sometimes only days after birth, that their mother's were withholding love from them. He further theorized that these children dealt with their lack of intimacy with their mothers by withdrawing from society and putting up a wall of defense and eventually regressing into autistic behaviors. Unfortunately, his treatment approach was to remove these children from their home and parents, the very environment that supposedly created the condition. These ill-fated parents suffered the loss of their children as they were not allowed contact with them during the residential therapeutic intervention. The Refrigerator Theory and the work of Dr. Bettelheim were the predominant approaches throughout the 1950s and 1960s.

In the early 1960s Dr. Bernard Rimland, an experimental psychologist and father of a child with autism, challenged the theories and treatment of the Refrigerator Theory. In 1964 his book, *Infantile Autism: The Syndrome and its Implications for a Neural Theory of Behavior*, suggested that autism was actually the result of genetic factors that were deeply embedded in human biology and not psychology. He is considered a founder in the biological approach to autism which is currently

embraced by numerous medical professionals and parents. The biological approach to autism is briefly described below by Dr. Nancy O'Hara and represents the thinking of professional and parents who embrace this medical model and approach to autism. <sup>(18)</sup>

### **ASD: Behavior, GI, Immune Connection**

Nancy H. O'Hara, MD, FAAP, MPH, is a board certified pediatrician and served as an assistant director for Defeat Autism Now. She describes that although children with a diagnosis of autism present with numerous behavioral, communicative, social and cognitive issues, these problems are frequently the manifestations of underlying gastrointestinal and immunologic metabolic medical issues. The awareness that medical conditions are an integral part of autism changes the ways in which autism is approached and demands a new paradigm that more effectively addresses the needs of the child with autism. The scope of this literature investigation will examine the numerous biological factors that are currently being considered in the diagnosis of autism. In an attempt to be thorough, priority will be given to the role of the gastrointestinal tract within the biomedical approach to autism.

### **Theories of ASD**

According to naturopathic physician, Dr. Jared Skowron, the pathophysiology of autism isn't agreed upon at this time. <sup>(19)</sup> Current theories include: 1) Inflammation of the nervous system as the core of the syndrome, 2) Nutrient deficiencies that include minerals, vitamins, protein and fatty acids are present in all cases of autism,

3) The majority of children with autism present with some level of toxicity be it heavy metals, dioxins or other non metal toxins 4) Immune system imbalances that result from the inflammatory reaction create an imbalance that presents with low IgA and elevated IgE reactions, along with TH1/TH2 imbalances. As a result the child is increasingly vulnerable to intestinal infections. Most commonly these infections include yeast or *C. difficile*, as well as increased food antibody reactions that are most typically IgG in nature.

### **Immune Imbalances**

According to Samsan et.al. both GI abnormalities and immune system imbalances have been implicated in the pathogenesis of ASD. <sup>(20)</sup> The research suggests that both the quantity and function of immune cells are abnormal in children with autism. <sup>(17)</sup> Reported abnormalities include: decreased lymphocytes (including naïve T-cells, T-helper cells, cytotoxic T-cells, B cells), abnormal patterns of monocytes and eosinophils, skewing of serum immunoglobulin subtypes (with low total IgM, IgG and IgA, and elevated total IgE and IgG subtypes IgG2 & IgG4), elevated platelets, imbalance TH1/TH2 ( increased Th2), and an imbalance of cytokines toward proinflammatory with a reduction in regulatory cytokines. Additional research suggests that there is a subset of children with ASD who present with frequent infections followed by a decline in previously acquired cognitive skills and a worsening in behavioral symptoms. <sup>(21)</sup>

## **Neuroinflammation**

Although inflammation in the GI tract has become well documented in the scientific literature, MRIs of the brain and standard analysis of cerebrospinal fluid (CSF) have not typically confirmed neuroinflammation in the ASD population.<sup>(17)</sup> In analysis of brain samples from individuals with ASD having died from causes such as drowning, in comparison with controls, significant activation of the innate immune system was found in specific areas of the ASD brains. Activation of astroglial cells, macrophages and monocytes, all part of the nonspecific immune response, in the cerebellum were increased. These cells respond to signaling through the cytokine system and in fact increased quantities of proinflammatory cytokines were reported. This type of reaction is typical to what happens in Alzheimers, Parkinson's, ALS and HIV-related dementia. No evidence was found to support activation of the adaptive immune system. These findings would suggest that the target of the immune activation may not be the brain at all. Rather it is likely that a source outside the brain is causing systemic activation of the innate immune system via the circulating cytokine system. This neuroimmune, neuroinflammatory response may be genetically based or in response to environmental factors.

According to de Theije et.al., immune cells produce all kinds of substances such as cytokines and chemokines upon gastrointestinal inflammation.<sup>(22)</sup> The immune cells and substances are not limited to the gut. They enter the circulatory system and will pass to all organs of the body including the brain. These cytokines are able to pass the blood brain barrier (BBB) via active transport. Even immune cells can pass the

BBB via diapedesis. The gastrointestinal inflammation in individuals with ASD may influence the brain and subsequently behavior. The cerebellum is reported to be the area of abnormality in the ASD brain most commonly noted in neuroimaging. Specifically the Purkinje cells and granular cells of the cerebellum appear to be damaged in the ASD population.<sup>(17)</sup> The cerebellum is thought to be responsible for affect, motivation, social interaction, learning, and processing sensory and motor information, frequent areas of deficit in the ASD population.

It would appear that the GI abnormalities that have been established to correlate with ASD and its behavioral severity may in fact be a gut-brain interaction that contribute to the pathogenesis of ASD.<sup>(20)</sup> The imbalanced immune system in the ASD population may well be the bridge between the compromised GI integrity and the resulting neuroinflammation.

### **GI Disturbances in ASD**

A current working hypothesis into one of the potential underlying pathophysiologies in ASD has to do with intestinal permeability. Numerous reports of increased GI permeability exist in the ASD literature.<sup>(23,24)</sup> Additionally, numerous accounts of GI infection in the ASD population and its correlation to immune system imbalances are found in the ASD literature.<sup>(20) (25)</sup> The GI tract works in close relationship to the immune system with the goal of maintaining homeostasis and protecting our body from microorganisms and foreign antigens. The GI tract breaks down the structure of food particles via our digestion and

transforms them to small molecules. Utilizing a variety of transport mechanisms, the intestinal epithelium will absorb these small molecules and transport them via the blood or lymph to the other side of the intestinal mucosa cells, allowing them to enter systemic circulation. Mucosal immune functioning is maintained via the organized regulation of the intestinal barrier.

Ideally inflammation is prevented via the organization of the intestinal barrier and mucosal immune surveillance. When antigens from undigested foods and/or pathogenic microorganisms challenge the intestinal epithelial mucosa, an innate immune system response can be triggered resulting in an abnormal inflammatory response of the intestines and an innate immune response. It is possible that the innate immune response that is initiated in the GI system is the trigger for the neuroinflammation that has been cited as a pathophysiology in ASD, as well as the innate immune imbalances observed in the cadaver brains of individuals with ASD.

Arthur Krigman, MD, has worked for years specializing in working with children with ASD and GI disturbances.<sup>(26)</sup> He has observed and described numerous lesions in the posterior pharynx, esophagus, stomach, small intestine and colon of these children. He has observed chronic clusters of enlarged lymphoid nodules in the posterior pharynx that may have been the result of exposure to food allergies, bacteria, viruses or protozoa. He described these observed lesions as “an exuberant immunological response”.

Krigman went on to observe and report on pathological changes in the esophagus. Typically he observed what he described as “eosinophil-laden” esophagitis. Biopsies that were done to the tissue confirmed immune response but were not able to discern if it was of IgE or non IgE mediated response. He also observed erosive esophagitis, GERD, and an unprecedented number of cases of Barrett’s esophagus. All of which were observed to suggest excessive immunological triggers resulting in inflammatory conditions.

Lesions that were observed in the stomach of 80-90% of the children with ASD in which gastroscopy was performed by Dr. Krigsman were described as reactive gastropathy. These microscopic observations were initially thought to be a reaction to some type of treatment the children were on. However, the identical lesions were present in children who were not on any medications nor supplements for their ASD. Additional pathologies observed upon scoping the stomachs of children with ASD included hypomotility, acid peptic ulcer, inflammatory polyp, gastric ulcerations, and nodular gastritis.

Upon observation of the tissue of the small intestine (duodenum, jejunum, ileum) Dr. Krigsman found duodenal acid-peptic ulcers, duodenal aphthous ulcers, lymphoid hyperplasia of the duodenum, non-specified duodenitis, IgE mediated allergic duodenitis, inflammation of the ileum and granulomas ( as in Crohn’s disease) of the ileum. Given the small intestine’s role in absorbing nutrients and calories it is understandable that the symptoms of these small intestine pathologies



included: diarrhea, food avoidance, self-injurious behaviors, poor sleep, stool incontinence, vomiting, constipation, mucus in the stool, malabsorption, poor growth and low blood serum albumin.

Finally, the colon of children with ASD was observed to present with colitis ulcerations, inflammatory polyps, ulcerative colitis, Crohn's disease and marked lymphonodular hyperplasia. Based upon his observation of immune over activation in the GI tracts of children with ASD from the posterior pharynx to the colon, Dr. Krigsman proposes that if a child in the spectrum presents with self injurious behaviors it should be assumed the child is in pain until proven otherwise. The child with ASD needs a full evaluation that includes history, physical evaluation and Testing. It may be important to examine the mucosa of the GI tract. He goes so far as to say that if the symptoms of the ASD child are dismissed as being "behavioral" the parents need to find another practitioner to work with. According to Dr Kingsman the lesions he observed were not curable, but were treatable. In his experience these children responded well to changes in diet, anti-inflammatory agents, probiotocs, antibiotics, antifungals and digestive enzymes. Interestingly these treatments designed to ameliorate the GI symptoms frequently result in improvements in behavior and cognitive functioning.

### **Cytokines**

Dr. Andrew Wakefield reports similar findings.<sup>(24)</sup> His clinical findings suggest that

lymphoid nodular hyperplasia is greater in children with ASD when compared with a control group (even if the control group had coexisting colonic inflammation). Additionally, analysis of the immune cells from the lining of the colon, small, intestines, and blood of children with ASD suggests a strong proinflammatory response. Proinflammatory cytokines (TNF- $\alpha$ ) were elevated while antiinflammatory cytokines (IL-10) were diminished. As a result the immune imbalance of a child with ASD with GI inflammation appears to be more profound than a patient with Crohn's disease. This imbalance in cytokines appears to be emerging as one of the more consistent immunological findings in the ASD population and a means of helping to better understand and address the pathophysiology of ASD.

### **Digestive Enzymes**

One possible explanation for the significant increase in the GI inflammation in the ASD population may be deficiencies with their digestive enzymes.<sup>(24)</sup> The small intestine is lined with highly specialized cells that aid in the degradation of carbohydrates, proteins and fats to facilitate their absorption into the body. Deficiencies in these enzymes may result in intestinal dysfunction that manifests as symptoms that include diarrhea, gaseousness, pain, failure to thrive, and pale bulky stools with undigested fats. Patients who present with diseases of the small intestines frequently have a deficiency in their digestive enzymes. Low levels of digestive enzymes have been reported in the ASD population.<sup>(27)</sup> Specific deficiencies included low activities of brush border disaccharidase enzymes

(lactase, maltase, sucrase, palatinase, and glucoamylase). Most frequently low lactase levels were found.

Studies that were done at Massachusetts General Hospital support this finding.<sup>(28)</sup> Individuals with ASD under went duodenal biopsies that were microscopically evaluated and then assayed for lactase, sucrase, and maltase activity. The frequency of lactase deficiency was greater than 50% in the individuals studied. The study also found that some individuals with ASD presented with enzyme deficiency without accompanying intestinal inflammation. The authors suggest that the association between GI symptoms and functional GI abnormalities offers valuable information in providing novel treatment options that may reduce the GI symptoms associated with ASD, as well as the behavioral and neurological symptoms associated with the diagnosis.

Low enzyme production is associated with devastating effects on overall health.<sup>(29)</sup> The use of digestive enzymes helps to facilitate the breakdown of foods limiting the components that may enter the bloodstream. Additionally they enable the basic components from the food to be more bioavailable, providing for the nutritive needs of the individual. Digestive enzymes decrease the strain on the immune system and help to provide homeostasis. Most individuals (50%) report positive results from supplementing with digestive enzymes within the first week. The percentage reporting benefits increases to 80% by the third week of supplementation. For some the necessary next step may be addressing dysbiosis and/or food allergies/food

sensitivities. Given that enzymes are reported to improve digestion and overall gut health they will most likely enhance whatever dietary interventions are chosen as well as supplements or medications. <sup>(30)</sup>

### **Food Allergies/Food Sensitivites**

In general, young children are vulnerable to food sensitization to common food proteins due to their immature gut mucosal lining immune system. For individuals with ASD the gut mucosal immune system appears to be compromised beyond early life. Parents commonly report improved behavior in response to the elimination of gluten and casein from their child's diet. <sup>(21)</sup> These behavioral changes subsequent to dietary modifications have lead to speculations that there may be a high prevalence of food allergies in the ASD population. Parents report frequent food allergies that are often multiple and most frequently to gluten, milk or peanuts. <sup>(31)</sup> Given the communication limitations and behavioral challenges presenting with children with ASD, the diagnosis of a food allergy can be increasingly difficult for the allergist or immunologist. According to research done by Dr. Harumi Jyonouchi on 325 children with a diagnosis of ASD, investigation did not find a high correlation of IgE mediated food allergies but rather the presence of cellular immune reactivity to common dietary proteins (mainly milk).

Although there are countless parental reports of their child's behavior improving on a gluten free casein free diet, the research is inconclusive. It would appear that allergies and or sensitivities to foods, especially gluten and casein, are not

universally a component of ASD. However, there appears to be a subset of children with ASD for whom these proteins are problematic. For this subset an elimination of gluten and/or casein results in improved behavior.<sup>(32)</sup>

### **GFCF Diet**

In 2010 a review of 14 studies regarding the use of a gluten free casein free (GFCF) diet for children with ASD was completed by Mulloy et. al.<sup>(33)</sup> They described the existing literature base on the subject as being “very limited” in regard to the overall scope and quality of the research in 2010 when the review was completed. It was the opinion of the authors that there was no conclusive evidence favoring the benefits of the GFCF diet for children with ASD. They go so far as to suggest that GFCF diets should only be implemented in the event of a food allergy or intolerance if detected.

In a subsequent study of 72 children diagnosed with ASD and divided into a GFCF diet group or a nondiet group, Whiteley et.al. found that the GFCF diet had a positive effect on developmental outcomes of some children with ASD.<sup>(34)</sup> Mulloy et.al. went so far as to write an addendum to their original literature review in order to address the Whiteley study that was published on the heels of their original publication.<sup>(35)</sup> They site numerous weaknesses in the Whiteley study regarding data analysis, participant attrition, discrepancy across comparable measures, as well as potential bias in parent ratings. They suggest that the results of the study must be interpreted with caution and that they retain their initial position that GFCF diets

are not effective treatments for the core symptoms of ASD. Although the literature is nonconclusive regarding the benefits of a GFCF diet for children with ASD, numerous parental accounts tout the amazing benefits their children with autism experience on the GFCF diet.<sup>(36)</sup>

## **Microbiome**

It is possible that the GI vulnerabilities and food sensitivities reported by many families and practitioners of children with ASD are the reflection of significant differences that have been reported in the GI microorganisms between children with ASD and controls.<sup>(37)</sup> According to Tomova et.al. there is considerable evidence that the numerous GI disorders experienced by individuals with ASD are linked to dysbiosis.<sup>(38)</sup> The development of our immune system is modulated by gut microbiota. The content of the microflora may contribute to, or even determine the health status of children with ASD. The theories of the pathogenesis of ASD are being expanded to include the etiopathogenic role of specific bacteria. The manifestation of ASD frequently is associated with Lactobacillus, Bifidobacterium, Clostridia, and Desulfovibrio. The following trends were found in the stool of children with ASD compared to their typically developing peers: the Bacteroidetes/Firmicutes ratio was decreased, Lactobacillus was elevated, as was Clostridia and Desulfovibrio. Post supplementation with probiotics, the subjects had a normalized Bacteroidetes/Firmicutes ratio, and a decrease in both Bifidobacterium and Desulfovibrio.

Disturbances of the homeostasis of the microbiota may have a negative impact on host health resulting in gastrointestinal, immunological and even neurological disorders.<sup>(39)</sup> Host health can be positively impacted via the use of prebiotics, probiotics and diets rich in both fatty acids and proteins to facilitate the health and balance of the microbiota. Research suggests that probiotics promote generalize immune function of the gut by strengthening immunological barriers and stimulating immune functioning.<sup>(40)</sup> Additionally, the use of probiotics can help control yeast and fungi by direct competition or by directly attacking it with *Saccharomyces boulardii*.

Probiotics also help to promote Th-1 immunity and help to rebalance the skewed Th-2 immune system.<sup>(41)</sup> More research to better understand and design optimal treatment for the interactions between the probiotics and microbiota for generalized health, GI disturbances, immune system dysregulations and brain balancing are called for. We need to better understand these complex biological mechanisms that may well be contributing to the epidemic of ASD.

Additional observations regarding trends in microbiota and ASD were made by Kang et. al., who found the microflora of this population tends to be of reduced richness and diversity.<sup>(42)</sup> They observed a significant reduction of Prevotella, Coprococcus and unclassified Veillonellaceae. These patterns of decreased diversity in the microbes were more closely linked to ASD symptoms than they were to the severity of GI symptoms and/or specific diets or supplement regimes. Hsiao et.al., go

so far as to propose that ASD, and likely other behavioral conditions, are potentially diseases involving the gut that ultimately impact the immune, metabolic and nervous systems.<sup>(43)</sup> Better understanding of the crosstalk between gut microbiota and immune and neurologic systems may provide targets for treatment.

Certain gut bacteria associated with ASD produce fermented metabolites called propionic acid.<sup>(44)</sup> When mice are fed the byproduct of carbohydrate metabolism under the influence of these “bad bugs” they present with behavior and brain changes such as repetitive behaviors, decrease social interaction and seizures. The byproducts of our microbiota circulate through the human blood system and influence our bodies in numerous ways. Dr. Stanley Hazen likens this to our endocrine system. It is as if our gut microbiome is our largest endocrine organ. What we feed it can influence these messages and our overall health. Fecal transplant is becoming more widely accepted as a means of addressing conditions such as C. diff, severe inflammatory bowel disease, and ulcerative colitis. Perhaps fecal transplants will provide a means of restoring health to the dysbiosis of children with ASD in the future.

Dr. Sydney Finegold has studied children with regressive autism and the importance their microflora play in the manifestation of their symptoms.<sup>(45)</sup> The abnormal gut flora most typically observed was an overgrowth of *Desulfovibrio* which responded well to oral treatment of vancomycin. Finegold et. al., speculate that improvement with oral vancomycin suggests the altered microflora may lead to the symptoms of



ASD. <sup>(46)</sup> In subsequent work Finegold goes on to speculate that the key factor in the virulence of the *Desulfovibrio* has to do with its lipopolysaccharides which cause sulfate reduction. <sup>(47)</sup> As a result the organism depletes the host (and other bacteria) of sulfur which is essential to numerous physiologic reactions in the body.

*Clostridium difficile* is another specific intestinal bacteria that causes harm. <sup>(48)</sup>

*C. diff* secretes neurotoxins and toxins that irritate the gut. It can contribute significantly to the severity of behavioral and neurological symptoms of ASD. It is typically present secondary to antibacterial overuse. Dr. Sears typically prescribes metronidazole for a *c. diff* infection. Vancomycin is also commonly used, followed by a replenishment of *Lactobacillus acidophilus*. <sup>(25)</sup> Numerous findings suggest significant improvements in the behavior of children with ASD when treated with vancomycin, only to see symptoms return when the medication is discontinued. This is speculated to be the result of the *c. diff* spores that remain after treatment.

### **Constipation**

Parents of children with ASD often report that their child presents with frequent and significant constipation. <sup>(49)</sup> Some would suggest that constipation is the most commonly found symptom of all the GI disorders that children with ASD present with. <sup>(50)</sup> Unfortunately, it is frequently overlooked, unrecognized or untreated by the primary healthcare provider. The colonic and duodeal immunopathology in children with regressive autism may suggest a specific disturbance of gastrointestinal motility. It is not clear if the distal constipation that was observed

was immune mediated and antigen driven or caused by poor handling of dietary morphines.<sup>(49)</sup> An effective treatment of the constipation may improve behavioral difficulties.

Given the frequency with which children with ASD present with functional constipation it is important that screening questionnaires allow for parents to describe these symptoms. Requesting functional magnetic resonance imaging may contribute to more insight as to how best address the apparent joint pathophysiology of ASD and functional constipation.<sup>(51)</sup> Children with ASD and functional constipation present with unique and confounding behaviors of sensory processing deficits, motor planning difficulties and food selectivity and abnormal feeding habits, all of which contribute to and make treating the functional constipation more challenging. Additionally, they may ignore the need to defecate given a hyper focus on other events and/or, tend to withhold due to fears of association of prior pain upon defecation.

Fortunately, Autism Speaks in collaboration with Autism Intervention Research have created a resource for families entitled Guide for Managing Constipation in Children: A Tool Kit for Parents.<sup>(52)</sup> They recommend increasing fibers and liquids in the child's diet. Additionally, they suggest regular daily exercise and a bowel habit training program. Supplements and or medications may be required to improve peristalsis and the texture of the stool. Recommendations for each aspect of the

program are detailed specifically for the ASD population making this a valuable resource for parents of the numerous children with ASD and functional constipation.

### **Sensory Sensitivities**

Difficulties of elimination, as well as nutrition, for individuals with ASD are complicated by their frequent restrictions of foods. Sensory sensitivity may lead children with ASD to restrict their intake of food to preferred, tolerable, and manageable textures.<sup>(53)</sup> Meal time behavior problems frequently seen in children with ASD are commonly a reflection of difficulties with sensory sensitivities as well. Qigong massage has been demonstrated to improve both sensory impairment and elimination in children with ASD.<sup>(54)</sup> Studies suggest that children who participate in regular Qigong massage experienced strengthening of their GI systems, resolution of constipation and diarrhea, improved appetite, and an opening of their intellect.<sup>(55)</sup>

### **Castor Oil**

Another holistic therapy for improving the GI symptoms of ASD is the use of castor oil packs. This is an ancient folk remedy that is still widely used today.<sup>(56)</sup>

Castor oil packs can help to stimulate peristalsis, maintain mucus membranes, improve assimilation, stimulate bile secretions, liver, pancreas and gall bladder secretions, improve coordination of functioning organs and glands, stimulate the nervous system, regulate metabolism, improve lymphatic circulation, and draws infection from the body.<sup>(57)</sup> This one therapy can help to address a number of the GI and immune imbalances facing individuals with ASD.

## Chapter III

### Procedure

The search engines utilized to gather research included Google, Google Scholar, Pubmed, and Eureka Digital Library. On January 17, 2015, an Eureka Digital Library health sciences search entitled "*Autism and GI*" revealed 1,357 hits. On January 20, 2015 an Eureka Digital Library health sciences search entitled "*Autism and constipation*" revealed 1,819 hits. The same search was repeated on Pubmed and 79 hits were revealed. On February 1, 2015 an Eureka Digital Library health sciences search entitled "*Autism and bacterial overgrowth*" revealed 433 hits. The same key words were used on February 5, 2015 to complete a Google Scholar search and 2,810 hits were obtained. The key words "*Autism and holistic treatments*" were searched via Eureka Digital Library health sciences on February 12, 2015 and yielded 963 results.

On February 17, 2015 a Google search was completed using the words "*Incidence of Autism*" and 728,000 hits were obtained. On February 20, 2015 an Eureka Digital Library health sciences search entitled "*Autism and neuroinflammation*" revealed 21 hits. Finally, on February 25, 2015 an Eureka Digital Library health sciences search entitled "*Autism and the immune system*" revealed 6,573 hits.

A total of 47 full text articles were selected to review, with 96% of them having been published within the past ten years and 4% being published within the past fifteen years. An additional twelve texts, all published within the past eight years, on the subject of autism were utilized for the literature review as well.

## Chapter IV

### Discussion

We are experiencing an epidemic of autism. In spite of that, autism receives fewer research dollars than the majority of other diseases that impact the pediatric population. Autism is like a child snatcher that sneaks in during the night, wrapped in a black cloak and robs families of their precious children. Twenty years ago most had never heard of autism. Today the majority of us either have a child with ASD in our family or know someone who does.

Ironically ASD is a DSM V psychiatric diagnosis. The majority of children suffer with behavioral, communicative and social delays that get labeled as the problem, when in fact they are symptoms of the underlying medical condition that is at the root of autism. Autism is not a disability but a disease. It is a disease of impaired immunity. It is a disease of gastrointestinal physiopathology. It is a disease of neuroinflammation. The majority of family physicians and pediatricians who should be active leaders, if not at least participants, in creating the road to health and wellness for these children, do not understand the diagnosis, nor how to support healing. As a result, parents of children with autism have become a self educated, empowered group of passionate parents unwilling to accept the status quo. Much of what we have learned about autism has been the result of dedicated parents in their desperate attempt to rescue their children.

Currently the majority of children with a diagnosis of ASD are educated in expensive special purpose programs designed to meet the unique behavioral, educational, social, sensory and communicative needs they present with. Few of them are fortunate enough to have a physician on the team facilitating the physical healing that needs to happen to restore their health.

In frustration and despair parents have turned to complimentary and alternative healing modalities to create alliances to promote the physical healing that needs to happen. Parents know that their children are sick, can't poop normally, get sick frequently, are super picky eaters, can't tolerate touch, have nutritional deficiencies and have numerous other physical maladies. The best educational programs in the country are not able to address these medical issues.

As naturopathic doctors we have a great deal to offer these children and their families. We need to take our place at the forefront of innovation in providing treatment for this complex, rapidly growing population of our children.

Thankfully, in spite of the limited funding available for research of autism, numerous scientific pioneers are putting together the pieces of the autism puzzle. Some of that literature was reviewed for the purpose of this paper. Findings consistently supported the correlation of an increase of gastrointestinal disorders with children with ASD. Although the symptoms may vary and some symptoms are more objectively measured than others, when compared to controls children with

ASD have an increase in gut issues. Many reported that constipation is the number one GI issue for these children.

Although it is speculated that GI symptoms may be improved by a GFCF diet, the research didn't support that finding. None the less researchers do not argue that consistently parents and numerous providers report improvement in a variety of symptoms with a GFCF diet. There is a need for more studies, with a larger number of subjects, and rigorous experimental design in order to demonstrate the improvements that many parents swear by. To this day numerous providers, MDs & NDs alike put children with ASD on a GFCF diet that yields favorable results.

Children with ASD appear to have dysbiosis that may explain or contribute to a number of the unique GI, immune and behavioral components of ASD. This has become a hot topic in the field of ASD. Studies are showing patterns of variation in the flora of children with ASD when compared to their peers. Researchers are working to determine what these patterns are, which of the patterns are most significant, the behavioral correlates of specific patterns of dysbiosis and implications for treatment.

Whether reviewing general studies on ASD and GI issues, or ASD, GI and immune issues, or ASD GI and neuroinflammation, or dysbiosis in the ASD population, or feeding behaviors in children with ASD there is one consistent finding, we need to

fund more research to help us understand and develop more effective medical interventions for children with ASD.

We know that in order to facilitate the healing processing for these children we need to be ready to identify and treat the underlying gastrointestinal issues they present with. We need to be ready to help support establishing health and balance in the immune system and decrease the inflammation that contributes to their ill working brains. We need to replenish their nutritive needs, rebuilding their physical, mental and emotional wellbeing. It is a daunting proposition yet no one is more prepared professionally than we are as naturopathic doctors. We are armed with potent knowledge and tools to facilitate health restoration. We can offer botanicals and supplements to soothe the gut, special diets to reduce inflammation, enzymes to facilitate absorption, probiotics to balance the flora, botanical antimicrobials if need be. We have numerous modalities that include but are not limited to energy work, hydrotherapy, massage, saunas, ozone therapy, homeopathy, botanicals, and nutrition. It is time to be reversing the trend in the ever climbing numbers of children diagnosed with autism and to be offering hope of restored health to these children and their families.



## Chapter V

### Summary and Conclusions

Children and individuals with ASD are identified in terms of their behavioral, social, communicative and sensory delays, disorders and needs. Their “treatments” are found in educational and therapeutic settings where amazing work is done and miracles happen. However, none of this is addressing the cause of autism, but rather treating symptoms of the disease of autism.

In this literature review a number of scientific research articles and books on autism were utilized. Specific focus was put on exploring ASD from within the gastrointestinal tract. The growing incidence of autism and growing evidence for GI issues as at least a contributing pathophysiology of ASD were investigated.

Additionally, specific topics that pertain to ASD and GI issues that include inflammation, allergies, GFCF diet, dysbiosis, constipation, sensory & feeding issues were explored in an attempt to understand the systemic impact the deregulated GI system has on the whole child with ASD.

The findings were consistent that GI issues are significant in the ASD population and contribute significantly to the challenging and complex behavioral issues in this population. Given our expertise at treating the gut we as Naturopathic Doctors need to step forward to facilitate healing and promote wellbeing for children with ASD.

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