The Association Between Children with Autism and Gastrointestinal Symptoms

Yasmeen Prince
yprince@emich.edu

The Association Between Children With Autism and Gastrointestinal Symptoms

Yasmeen Prince
Dr. Janet Okagbue-Reaves, Mentor

ABSTRACT

Every day many thousands of children face the complications of Autism. According to Geraghty, Depasquale, and Lane (2010), Autism has become one of the most frequently diagnosed developmental disabilities, with one in one hundred children diagnosed with Autism in the United States every day. The etiology of Autism Spectrum Disorder (ASD) has not been determined. One of many questions researchers are asking is whether an association exists between gastrointestinal disorders and Autism. This literature review examines the relationship between GI symptoms and eating patterns in children with Autism, and assesses whether special diets reduce symptoms of Autism Spectrum Disorder.

INTRODUCTION

Ito (2004) defines Autism Spectrum Disorder as "development disorders characterized by cognitive peculiarities such as social abnormalities, communication impairment, and restricted and/or repetitive behaviors" (p.430). According to Mouridsen, Rich and Isager (2009), Autism is classified as a group of neuro-developmental disorders commonly called the Autism Spectrum Disorders (ASD). ASD is also called Pervasive Developmental Disorders (PDDS), and includes five sub categories: Autistic Disorder (classic autism), Asperger's Syndrome, Pervasive Developmental Disorder Not Otherwise Specified (PDD-NOS), Rett's Disorder (Rett Syndrome), and Childhood Disintegrative Disorder (CDD). Autism is three to four times more common in males than females (Yates and Couteur, 2008).

Studies have suggested that children with Autism have higher rates of gastrointestinal symptoms than children who are not under the Autism Spectrum. Chandler et al. (2013) compared gastrointestinal symptoms in children with ASD compared to children with special educational needs and typically developing children. This study found that children with ASD displayed significantly higher rates of gastrointestinal symptoms (diarrhea and constipation) than children with special educational needs and other typically developing children. The Chandler et al. (2013) study also confirmed that the parents of children with ASD reported their children had bowel movements no more than three times per week. The study noted that the parents of children with ASD frequently reported abdominal pain more than children with special educational needs. Children with ASD also reported increased vomiting and diarrhea, compared to typically developing children (Chandler et al., 2013).

Adams, Johansen, Powell, Quig, and Rubin (2011) found that children with more severe Autism are likely to have more severe GI symptoms. Children with ASD are often unable to communicate their discomfort, and the pain caused by a GI disorder may cause them to experience aggression and self-abuse. Therefore, many researchers have suggested that gastrointestinal disorders may be linked to Autism. If this holds true, there will be more research needed to explore the reasons for the increased reporting of GI symptoms in children with ASD.

GI Symptoms and Eating Behaviors

Smith, FranWorth, Wright and Allgar (2009) developed a questionnaire that evaluated bowel symptoms by examining 51 children with ASD, with control groups of 35 children from special education and 112 from mainstream schools. Smith et al. (2009) noticed a noteworthy difference in the reporting of constipation, diarrhea, and flatulence between the two groups. Smith et al. (2009) stated that "of the children with ASD, 35 percent of parents had concerns about their child's bowels, compared with 4 percent of parents of mainstream children, and that this difference is statistically significant" (p. 347).

Smith et al. (2009) determined that there was a marked difference in concerns about gastrointestinal disorders in children with ASD, compared to the children in control groups. Smith et al. (2009) found that the parents of children with ASD (27%) expressed concerns to doctors that their child may have a bowel disorder at far higher rates than parents in control groups (4%). Parents (35%) also expressed concerns about the variety of food that their children consumed, compared to the control groups (4%). It is important to note that Smith et al. (2009) determined that more parents of children with ASD (18%) reported having their children on a specialized diet and had visited a dietician, as compared to the mainstream control group (4%). The study concluded that children with ASD exhibited the following GI symptoms: diarrhea (27%), constipation (25%) and excessive flatulence (24%), compared to children from special education and mainstream schools (Smith et al., p. 347-350).

Gastrointestinal disorders have long been a concern in the ASD population. Pang and Croaker's (2011) study confirmed that children with autism spectrum deficits display more GI symptoms such as constipation, than the general population. Pang and Croaker (2011) conducted a study on children who attended the Pediatric Surgical Constipation Clinic. These children had autism with or without Neuro-Developmental Psychiatric (NDP) diagnoses. Pang and Croaker discovered that "up to 25% of patients who attended the clinic had autism with or without NDP deficits. These children have an earlier onset of symptoms, a longer history of GI disorders and experience symptoms suggestive of slow transit constipation" (p. 357). The children with ASD with or without NDP exhibited symptoms such as rocklike stools, straining, diarrhea, rectal bleeding, pain on defecation, stomach discomfort and bloating (2011).

Ibrahim, Voigt, Katusic, Weaver and Barbaresi (2009) reported that children with ASD were more likely to manifest constipation and feeding problems. The need for constant daily routines leads children with ASD to choose diets that may result in an inadequate intake of fiber, fluid and other important nutrients, thus leading to constipation (Ibrahim et al., 2009). Valicenti-

McDermott et al. (2006) confirmed that abnormal stool patterns and food selectivity were more common in children with ASD than in children with typical development, and children with other developmental disabilities. Valicenti-McDermott et al. (2006) also studied the relationship between gastrointestinal symptoms and the family history of those with autoimmune diseases. They found "no association between a family history of autoimmune disease and GI symptoms in children with ASD" (p. 128).

Children with ASD frequently have significant eating problems, due to their limited range of food choices. Their eating patterns and behaviors are often unsual and have an effect on family life. According to Gail et al. (2000), children with ASD often have difficulty developing verbal and nonverbal communication skills. Some children with ASD also have difficulty initiating and sustaining conversation. Communication problems and social behaviors seem to be presenting problems in children with ASD. It is also important to note that children with ASD engage in repetitive and restrictive behaviors and have difficulty interacting with their peers and expressing themselves.

Williams, Dalrymple, and Neal (2000) stated that children with ASD "demonstrate limited functional play and may interact with toys in an atypical fashion, thus having unusual preoccupations and sensory interests with objects, or extremely intense interests" (p. 259).

This is important to understand, because it explains why children with ASD desire certain foods of a particular color or texture, and "sameness." Due to their inability to communicate properly, children with ASD may not be able to express discomfort associated with GI symptoms. Aggressive behavior during meals could be caused by GI symptoms and the children's inability to express themselves verbally.

Nutritional Challenges

Wood, Wolery, & Kaiser (2009) found that "children with autism have an increased risk for food selectivity" (p. 169). Selective eating can be described as "consuming a limited number of foods, unwillingness to try new foods, totally avoiding some food groups, and having a strong preference about how food is prepared and presented" (Williams et al., 2005, p. 300).

The Williams et al. (2001) study stated that the families of children with ASD reported that their children were selective eaters. The reported problems included "reluctance to try new foods, mouthing objects, licking and eating objects, smelling and throwing food" (p. 264). In this study, the families of children with ASD reported health concerns such as gastro-esophageal reflux and GI symptoms. Rogers, Magill-Evans and Rempel (2012) completed a study on the processes involved in addressing the feeding challenges of children with ASD; they found that mothers reported "sensory aversions relating to the sight, smell and texture of foods, and sensitivities to seemingly small alterations to taste" (p. 25).

Rogers et al. (2012) reported that one mother was unable to cook meat when her child was home because the child was extremely sensitive to the smell. Another mother reported that her child would vomit at the sight of certain food (Rogers et al. 2012). The need for a diet consisting of the same food for children with ASD was very common. Some children required certain brands of foods, displayed sensitivity to changes in food preparation, and refused food altogether if their parents attempted to sneak food they didn't like onto their plates. Often the children refused to eat that particular food again.

Rogers et al. (2012) also discussed food jags and behaviorial challenges in children with ASD. A food jag is "when a food is accepted well for a time, sometimes to the exclusion of other foods, and then suddenly the child no longer accepts it" (p. 25). The parents of children with ASD described behavioral problems, including "difficulty sitting at the table to eat, throwing food, grazing, not having a feeding routine, and taking food from others' plates" (p. 25).

Children with ASD exhibited other mealtime challenges such as "oral motor problems, chewing difficulties and mouth stuffing, and feeling and responding to hunger cues" (Rogers at el 2012, p. 26). Rogers at al. (2012) also identified "Co-morbidities affecting feeding, included generalized anxieties, food sensitivities, lactose intolerance, and gut issues such as pain, diarrhea, and constipation" (p. 26). Geraghy at al. (2010) also note that children with ASD who are picky eaters can severely compromise their nutrient intake, and these eating behaviors may contribute to GI discomfort, among many other

factors. It is important to note that eating behaviors in children with ASD are likely to persist throughout childhood.

Children with ASD demonstrate more problematic eating patterns than the general population. Emond, Emmett, Steer, & Golding, (2010) indicated that in infancy, children with ASD have late acceptance of solid food, and were often described by their mothers as "slow feeders." Between 15 to 54 months of age, children with ASD were reported as difficult to feed, and were very picky eaters. By 24 months of age, children with ASD had a different diet from the rest of their family. The children with ASD ate fewer fresh fruits, salad, vegetables, and consumed fewer sweets and carbonated drinks. Their energy intake and growth, however, were not impaired (Edmond et al., 2010).

Herdon et al. (2008) compared the consumption of nutrients in children with ASD and children with typical developmental disorders. The research found that children with ASD consumed "significantly more vitamin B6, vitamin E and non-dairy protein servings, less calcium, and fewer dairy servings that could not be explained by differences in parental dietary restrictions, age, or sex" (Herdon et al., 2008, p. 220).

Zimmer et al. (2012) completed a study that matched twenty-two children with ASD with a typically developing control group. The children with ASD were more selective during mealtime than the typically developing children. The study concluded that children with ASD "had a higher average intake of magnesium, and lower average intake of protein, calcium, vitamin B12, and vitamin D. Selective eaters were significantly more likely than typical controls to be at risk for at least one serious nutrient deficiency" (Zimmer et al., 2012, p. 549).

William, Gibbons, and Scheck (2005) found that children with ASD and other developmental disabilities exhibited more chronic forms of selective eating than children without ASD, and that these children had one or more medical problems; the most common was constipation. Williams et al. (2005) discovered that when children with ASD were referred to a feeding program for evaluation and treatment of their food selectivity, many insisted on using the same utensils and having food prepared in a certain way at significantly higher rates than the control group.

William et al. reported (2005) that these feeding problems began early and continued for more than two years, and "the older children were just as selective as the younger children, and did not appear to be outgrowing their pattern of selective eating" (p. 308). They found that children with ASD gagged when new food was introduced, and insisted that particular foods were prepared a particular way (2005).

Martin, Young, and Robson (2008) asked mothers of children with ASD to complete a questionnaire measuring and evaluating their children's eating behaviors. The mothers were also asked to report the eating patterns of their typically developing children. The data was divided into three subgroups: children with ASD, typically developing siblings of children with ASD (SIB), and typically developing children (TD) with no sibling with a disability (2008). Marin et al. (2008) found that "children with ASD had marginally poorer self-feeding skills than either the TD or SIB children, and were slightly more likely to avoid foods and exhibit neophobic (fear of trying unfamiliar foods) eating behaviors (FNS) than either the TD or SIB children" (p. 1883).

Nadon, Feldman, Dunn, and Gisel (2011) compared children with ASD eating patterns to SIB children. Nadon et al. (2001) found that that "children with ASD were more selective with respect to food texture, temperature, and types of recipes, and it was more difficult to introduce unfamiliar food items to them" (p. 107). These findings are similar to the Martin et al. study. It is important to note that compared to their siblings, children with ASD did not allow foods they disliked on their plate, and some even rejected foods they had once eaten in the past. Nadon et al. (2011) also noted that children with ASD displayed behavior, such as "drooling, gagging, vomiting, coughing, or choking during mealtimes statistically more often than their siblings, and children with ASD ate fewer than 20 different food items and did not stay seated during meals, compared to their siblings. The children with ASD went through 'phases' such as wanting the same foods for a prolonged period of time" (pp. 105-106).

A study by Sharp and Jaquess (2009) showed that children with ASD who have severe food selectivity also display higher rates of disruptive behaviors when larger bite sizes were introduced to

them. Once the bite sizes decreased in volume, their behavior improved. According to the 2009 study, "in the bite size assessments, larger volumes were associated with higher rates of disruptive behaviors, such as head turns and batting at the spoon (p. 168).

Schreck et al. (2004) suggested that "children with autism exhibited more general feeding problems, including refusing foods, requiring specific presentations of foods and specific utensils, eating only low texture foods, and eating a narrower variety of foods than children without autism" (p. 437).

Ashwood, Anthony, Torrente, and Wakefield (2004) examined 86 children displaying GI symptoms. All patients were required to undergo a diagnostic intestinal endoscopy and biopsy. According to the 2004 study, lymphocytic enterocolitis is often reported in children with ASD who had GI symptoms. Ashwood et al. (2004) wanted to know if "dysregulated intestinal mucosal immunity with enhanced pro-inflammatory cytokine production is present in these ASD children" (p. 664).

This study compared developmentally normal children both with, and without, mucosal inflammation. Colonic and duodenal and biopsies were carried out on 21 children with ASD, and 65 from a developmentally normal control group, of which 38 had symptoms of histological inflammation. According to Ashwood et al. (2004)

> Duodenal and colonic mucosal $CD3^+$ lymphocyte counts are higher in children with ASD compared to the non-inflamed controls. The lamina propria (LP) and epithelial $CD3^+IL\text{-}2^+$ and $CD3^+IFN\gamma^+$, and epithelial $CD3^+IL\text{-}4^+$ cells were more frequent in ASD children than in non-inflamed controls (p. 664).

In the colon, LP $CD3^+TNF\alpha^+$ and $CD3^+IFN\gamma^+$ were more common in ASD children than in non-inflamed controls. Also, there was a considerably greater proportion of $CD3^+TNF\alpha^+$ cells in colonic mucosa in those ASD children who were not on a special diet, compared to those on a special gluten-free, casein-free diet. Data showed a steady profile of $CD3^+$ lymphocyte cytokines

in the small and large intestinal mucosa of the ASD children, resulting in pro-inflammatory and decreased regulatory activities (Ashwood et al., 2004).

Food Allergies

Many people are concerned that GI symptoms in children with ASD are linked to food allergies. According to Jyonouchi (2009), "young children are more vulnerable to sensitization to common food proteins because of an immature gut mucosal immune system. Because of the high frequency of GI symptoms in children with ASD, the presence of food allergies has been widely speculated" (p. 197).

The Jyonouchi (2009) study included 325 children with ASD, using a standard diagnostic measure for atopy, which is an allergen skin prick test, and found no higher prevalence in children with ASD, compared to the typical population. Jyonouchi (2009) determined that in children with Aspersger's Syndrome, the prevalence of atopy was ten percent, confirming that atopy is not associated with GI symptoms in children with ASD. The reason for GI symptoms in children continues to be a puzzle for researchers, families, and medical professionals treating children with ASD.

The Gluten-Free Casein-Free Diet

Ibrahim et al. (2009) study shows that "many children with ASD are treated with restrictive diets, vitamin, mineral, and other dietary supplements aimed at putative gastrointestinal deficits" (p. 684). According to Elder (2008), there is no known cure for ASD. The parents of children with Autism often try alternative treatments to reduce their children's symptoms, and one of the alternatives is a specialized diet. This diet is called the gluten-free/casein free (GFCF) diet. This diet has grown popular over the years. There is no scientific proof that this special diet makes a difference in the symptoms of children with ASD.

The GFCF diet includes the elimination of all foods containing gluten (found in wheat, rye, and barley) and casein (found primarily in milk and dairy products). The GFCF diet is based on the theory that children with ASD may have an allergy or high

sensitivity to foods that contain gluten or casein. Children with ASD exhibit an inability to break down the proteins and peptides in food containing gluten and casein. Elder (2008) found that the "increased intestinal permeability, referred to as the "leaky gut syndrome," allows these peptides to cross the intestinal membrane, enter the bloodstream, and cross the blood-brain barrier, affecting the endogenous opiate system and neurotransmission within the central nervous system" (p. 584).

This could explain why children with ASD display Autistic behavior: because the brain treats these chemicals like false opiate-like chemicals, the reaction to these chemicals causes the children to behave a particular way (Elder, 2008). As noted earlier, children with ASD display GI abnormalities, and this could be the result of ASD sensitivity to gluten and casein.

Harris and Card (2012) investigated the relationship between the GFCF diet and gastrointestinal symptoms in children with ASD. They write that GI symptoms in children with ASD may be due to

> Intestinal dysbiosis, characterized by a disruption of endogenous gut microflora promoting overgrowth of pathogenic microorganisms suspected to produce neurotoxins. GI symptoms might also be related to a disruption in the mucosal lining of the gut, causing malabsorption of large proteins such as gliadin and casein, which can cause inflammation and are precursors to neuropeptides that alter neurologic function (Harris & Card, 2012, p. 438).

This study also examined the effectiveness of the GFCF diet on the behavior of children diagnosed with ASD (Harris & Card 2012).

Harris and Card (2012) completed a cross-sectional study in which 13 parents of children with ASD completed an online survey concerning their children's GI symptoms, diet, behavioral patterns and general health. GI symptoms were assessed using the

Gastrointestinal Symptoms Rating Scale (GSRS), which rates the severity of symptoms including abdominal pain, heartburn, nausea, flatus, and stools patterns. The children with ASD behavioral patterns were evaluated using the Childhood Autism Rating Scale (CARS), which consisted of fifteen questions relating to behaviors such as "imitation, emotional response, body use, object use, adaptation to change, visual response, listening response, taste, smell, and touch response and use, fear or nervousness, verbal communication, nonverbal communication, activity level, level and consistency of intellectual response, and general impressions" (Harris and Card, 2012 p. 438).

According to the study, there were no significant differences in demographics or type of ASD. Harris and Card (2012) reported that of the 13 children with ASD diets, 4 children tested positive for antibodies to casein or gluten. More than half were on the GFCF diet, in which they consumed 8.7 gluten and casein containing foods. The children not on the GFCF diet ate an average of 53 gluten and casein containing foods per week. The results suggested that the GFCF alleviated not only GI symptoms in children with ASD, but also promoted positive behavioral changes. One-hundred percent of the parents of children on the GFCF diet stated that both GI symptoms and behavioral patterns improved (Harris and Card, 2012).

Researchers have suggested that GI symptoms are related to behavioral patterns in children with ASD. Elder et al. (2006) tested the placebo effectiveness of the GFCF diet in treating children with ASD by using a double-blind controlled clinical trial. The Elder et al. study (2006) included 15 ASD children between the ages of 2 and 16. The children were selected from the Center for Autism and Related Disabilities, and the University of Florida's Department of Child Psychiatry Services. The study's goals were to "evaluate the efficacy of the GFCF on the severity of autistic symptoms, as measured by the Childhood Autism Rating Scale (CARS), and the Ecological Communication Orientation Scale (ECOS), and direct behavioral observation frequencies" (p. 415). The CARS used a point system to assess Autistic behaviors, and the ECOS documented child behavior and collect interactive

samples. The study also tested the effects of the GFCF diet on urinary peptide levels. The children with ASD were on the GFCF diet for 12 weeks.

Elder et al. (2006) found no significant changes in the behavioral data on children with ASD, and no significant differences in urinary peptide levels of gluten and casein. However, some parents and teachers of the children with ASD reported positive changes in behavior and language. The parents reported noticeable improvements in language, decreased hyperactivity and tantrums. It is also important to note that 9 of the parents decided to keep their children on the GFCF diet (Elder et al., 2006).

Johnson, Handen, Zimmer, Sacco, Turner (2011) conducted a three month study evaluating the effectiveness of the GFCF diet. Johnson et al. (2011) compared the GFCF diet to a healthy, low sugar diet. The study involved 22 preschool children with ASD. Eight of the children with ASD were randomly assigned to the GFCF diet, and while fourteen were assigned to the controlled diet. Results showed no noteworthy differences in terms of age, gender, or IQ between the two groups. The parents of the children in the control group received counseling and materials on healthy eating. The healthy, low sugar diet focused on fruits, vegetables, whole grains, fish, and lean meats. The parents of the children with ASD in the GFCF diet group were told to eliminate all gluten and casein products, and offer their children more fruits and vegetables. Data was collected on both groups, and there was no statistically significant difference in the behavior of children with ASD.

According to Gereaghty, Bates-Wall, Ratliff-Schaub, and Lane (2010) the specific carbohydrate diet (SCD) was originally developed by Dr. Sydney Haas for adults with Inflammatory Bowel Disease (IBD). Although not as popular as the GFCF diet, this diet works by removing all carbohydrates that are difficult to be absorbed into the bloodstream. Eliminating these carbohydrates from the diet decreases harmful bacteria in the intestines and may help improve symptoms of GI. When undigested complex carbohydrates reach the large intestine, they ferment, resulting in diarrhea, constipation, gas, and bloating. Monosaccharides such as

glucose and fructose are more easily digested than disaccharides (sucrose, lactose, and maltose) and polysaccharides (starches). Children with ASD and GI symptoms may benefit from a mono-saccharide-only diet. This diet is important to consider because it offers a different perspective on GI symptoms and ASD (Gere-aghty et al. 2010).

Some researchers have linked the GFCF diet to health risks. Arnold, Hyman, Mooney, and Kirby (2003) studied the influence of the diet on amino acid patterns in 36 children with ASD. Ten of the children were on the GFCF-restricted diet, and 26 had an unrestricted diet. The children in both groups exhibited amino acid deficiencies, suggesting a lack of protein in their diet. The children with ASD on the GFCF diet had an increased prevalence of essential amino acid deficiencies. The children with ASD that were on the unrestricted diets were more likely to have a deficiency of valine, leucine, phenylalanine and lysine, while children with ASD on the GFCF diets were more likely to have deficiencies of valine, isoleucine, leucine, phenylalanine, and lysine (Arnold et al., 2003). ASD children on the GFCF diet were found to have a lower plasma level of essential acids, including the neurotransmitter precursor's tyrosine and tryptophan, than both control groups and children with autism on unrestricted diets (Arnold et al., 2003).

Hediger et al. (2008) assessed bone development in 75 boys with ASD on the GFCF diet. The boys on the GFCF diet exhibited signs of suboptimal bone development and reduced bone cortical thickness. Two nutrients, calcium and vitamin D, are critical for bones to development optimally. Hediger et al. (2008) stated that "longitudinal studies or supplementation trials will be necessary to determine whether bone growth is slowed because of the casein-free diets and may improve with supplementation, or whether children with GI symptoms and poor calcium absorption show slow bone development and respond better to gluten- and/or casein-free diets" (p. 855). If families of children with ASD decide to implement the GFCF diet, their children's nutritional status should be carefully monitored.

Children with ASD have restricted food repertoires that make it difficult for them to be on a GFCF diet. Elder (2008) rec-

ommended that before families decide to put their children on the GFCF diet, they should take into consideration that this diet is very expensive, for foods containing no casein and gluten are hard to find. Preparing these specialized diets is time consuming. Families should always keep a journal or food log to measure food intake and behavioral changes. This information must be accurate and precise.

Families must also work to ensure dietary compliance at home, in school, and other settings. For example, school parties should be planned in advance, so that GFCF food substitutes can be put in place for the child. Parents should communicate closely with schoolteachers and other caregivers so that dietary restrictions are followed. The families of the children with ASD should know if the GFCF diet will further limit food repertoire, causing other deficiencies in the child's diet. Families of children with ASD should consult professionals who can offer practical advice, and continue to seek understanding and clarity of their children's behavioral and medical problems (Elder, 2008).

CONCLUSIONS

Based on my research, there is a measurable connection between ASD and GI symptoms. Children with ASD exhibited GI Symptoms such as constipation, diarrhea, stomach pain, and other symptoms associated with GI disorders. Children with ASD also exhibited adverse eating patterns, and lacked the recommended nutrients important for growth and development. The cause of GI symptoms in children with ASD are not clearly understood. There is a strong possibility that GI symptoms are related to aggressive behavioral patterns in children with ASD. Along with other treatments, specialized diets such as the GFCF diet are popular among parents of children with ASD. There is no scientific proof that such diets alleviate Autistic symptoms, but many parents have chosen to implement them. It is important for parents to carefully weigh the pros and cons of the GFCF diet. More extensive research needs to be conducted to explore the relationship between the GFCF diet and GI symptoms. Also, additional research needs to be conducted to clearly determine the cause of GI symptoms in children with ASD in order to discover successful treatments in treating symptoms of ASD.

REFERENCES

Adams, J. B., Johansen, L. J., Powell, L. D., Quig, D., & Rubin, R. A. (2011). Gastrointestinal flora and gastrointestinal status in children with autism—comparisons to typical children and correlation with autism severity. *BMC Gastroenterology, 11*(1), 22-22. doi:10.1186/1471-230X-11-22.

Ashwood P, Anthony A, Torrente F, Wakefield AJ. (2004) Spontaneous mucosal lymphocyte cytokine profiles in children with autism and gastrointestinal symptoms: mucosal immune activation and reduced counter regulatory interleukin-10. *Journal of Clinical Immunology.* 24(6), 664-673.

Chandler, S., Carcani-Rathwell, I., Charman, T., Pickles, P., Loucas, T., Meldrum, D., Simonoff, E., Sullivan, P., & Braid, G. (2013). Parent –reported gastrointestinal symptoms in children with autism spectrum disorders. *Journal of Autism and* Developmental Disorders, 1 February 2013 (on-line). doi: 10.1007/s10803-013-1768-0.

Clark, J. H., Rhoden, D. K., & Turner, D. (1993). Symptomatic vitamin A and D deficiencies in an eight-year-old with autism, *Journal of Parenteral and Enteral Nutrition*, 17(3), 284-286.

Darvill, L., McCaughey, E., & Wootton, S. (2010). Quality of diet and eating behaviours in children with autism. *Proceedings of the Nutrition Society, 69*(OCE1) doi:10.1017/S0029665109991911.

Elder, H. J., (2008). The gluten-free, casein-free diet in autism: an overview with Clinical implications. *Nutrition in Clinical Practice.* 23(6) 583-588. doi: 10.1177/0884533608326061.

Emond, A., Emmet, C. S., & Golding, J. (2010). Feeding symptoms, dietary patterns in young children with autism spectrum disorders. *American Academy Pediatrics*, 126(2), 337-342. DOI: 10.154?peds.2009-2391.

Geraghty, M. E., Depasquale, G. M., & Lane, A. E. (2010). Nutritional intake and therapies in autism: A spectrum of what we know: Part 1. *ICAN: Infant, Child, & Adolescent Nutrition*, *2*(1), 62-69.

Harris, C., & Card, B. (2012). A pilot study to evaluate nutritional influences on gastrointestinal symptoms and behavior patterns in children with autism spectrum disorder. *Complementary Therapies in Medicine, 20*(6), 437-40. doi:http://dx.doi.org/10.1016/j.ctim.2012.08.004 .

Hediger, M. L., England, L. J., Molloy, C. A., Yu, K. F., Manning-courtney, P., & Mills, J. L. (2008). Reduced bone cortical thickness in boys with autism or autism spectrum disorder. *Journal of Autism and Developmental Disorders, 38*(5), 848- 56. doi:http://dx.doi.org/10.1007/s10803-007-0453-6.

Herndon, A. C., DiGuiseppi, C., Johnson, S. L., Leiferman, J., & Reynolds, A. (2009). Does nutritional intake differ between children with autism spectrum and children with typical development. *Springer*, 39, 212-222. DOI: 10.1007/s1083-008-0606-2.

Ibrahim, S. H., Voigt, R. G., Katusic, S. K., Weaver, A. L., & Barbaresi, W. J. (2009). Incidence of gastrointestinal symptoms in children with autism: a population-based study. *Pediatrics*, *124*(2), 680-686.

Ito, M. (2004). Nurturing the brain as an emerging research filed involving child neurology. *Brain and Development*, 26, 429-433. DOI: 10.1016/j.brandev.2003.02.001

Lane, A. E., Depasquale, G. M., & Geraghty, M. E. (2010). Nutritional intake and therapies in autism: A spectrum of what we know: Part 1. *ICAN: Infant, Child, & Adolescent Nutrition, 2*(1), 62-69. doi:10.1177/1941406409358437.

103

Martins, Y., Young, R. L., & Robson, D. C. (2008). Feeding and eating behaviors in children with autism and typically developing children. *Journal of Autism and Developmental Disorders, 38*(10), 1878-1887. doi:10.1007/s10803-008-0583-5.

Mouridsen, S. E., Rich, B., & Isager, T. (2010). A longitudinal study of gastrointestinal disease in individuals diagnosed with infantile autism as children. *The Authors Journal Compliation*, 36(3), 437-443. DOI: 10.111/j.1365-2214.2009.01021.x.

Nadon, G., Feldman, D. E., Dunn, W., & Gisel, E. (2011). Mealtime problems in children with autism spectrum disorder and their typically developing siblings: A comparison study. *Autism, 15*(1), 98-113. doi:10.1177/1362361309348943 .

Pang, K. H., & Croaker, G. D. H. (2011). Constipation in children with autism and autistic spectrum disorder. *Pediatric Surgery International, 27*(4), 353-358. doi:10.1007/s00383-010-2680-8 .

Rogers, L. G., Magill-Evans, J., & Rempel, G. R. (2012). Mothers' challenges in Feeding their children with autism spectrum disorder—Managing more than just picky eating. *Journal of Developmental and Physical Disabilities*, *24*(1), 19-33.

Schreck, K. A., Williams, K., & Smith, A. F. (2004). A comparison of eating behavior between children with and without autism. Journal of Autism and Developmental disorders. 34(4) 433-438.

Sharp, G. W., & Jaquess D. L. (2009). Bite size and texture assessment to prescribe treatment for severe food selectivity in autism. Behavioral Interventions, 24, 157-170. DOI: 10.1002/bin282.

Smith R. A., FranWorth, H., Wright, B., & Allgar, V. (2009). Are there more bowel symptoms in children with autism compared to normal children with other developmental and neurological disorders. *The National Autistic Society*, 13(4) 343- 355. DOI: 10.117/1362361309106418.

Valicenti-McDermott, M., McVicar, K., Rapin, I., Wershil, B. K., Cohen, H., & Shinnar, S. (2006). Frequency of gastrointestinal symptoms in children with autistic spectrum disorders and association with family history of autoimmune disease. *Journal of Developmental and Behavioral Pediatrics,* 27(2), 128–136.

Williams, P. G., Dalrymple, N., & Neal, J. (2000). Eating habits of children with autism *Pediatric Nursing*, *26*(3), 259.

Williams, K. E., Gibbons, B. G., & Schreck, K. A., (2005). Comparing selective eaters with and without development disabilities*. Journal of Development and Physical Disabilities*, 17(3), 229-309. DOI: 10.1007/s10882-005-4387-7.

Wood, B. K., Wolery, M., & Kasier, A. P. (2009). Treatment of food selectivity in young children with autism*. Focus Autism and other developmental Disabilities*, 24(3), 169-177. DOI: 10.1177/1088357609338381.

Yates, K., & Le Couteur, A. (2009). Diagnosing autism. *Paediatrics and Child Health, 19*(2), 55-59. doi:10.1016/j.paed.2008.10.010.

Zimmer, M. H., Hart, L. C., Manning-Courtney, P., Murray, D. S., Bing, N. M., & Summer, S. (2012). Food variety as a predictor of nutritional status among children with autism. *Journal of Autism and Developmental Disorders,* 42(4), 549-556. doi:10.1007/s10803-011-1268-z.