Candidiasis and Dysbiosis in children with Autistic Spectrum Disorders

Assessment and Treatment Strategies

By Scott Clack BSc, ND

Gastrointestinal complaints in ASD children are known and documented. Diarrhea or constipation are the common symptoms, as are abdominal pain, bloating and nighttime awakening. Several studies have been published in recent years confirming autistic children with GI complaints were found to have ileal lymphoid nodular hyperplasia (LNH). In one study (Wakefield 2000), 93% of the 37 ASD children studied had ileal LNH compared to 14% of controls. The authors described their observations as "a subtle new variant of inflammatory bowel disease that lacks the specific diagnostic features of either Crohn's disease or ulcerative colitis." An earlier study (Horvath 1999) using endoscopy and biopsy in 36 ASD children showed reflux esophagitis in 25 children, chronic gastritis in 15, chronic duodenitis in 24, and low intestinal carbohydrate enzyme activity in 21.

Many factors can contribute to these gastrointestinal conditions. Use, or abuse, of antibiotics to treat upper respiratory or ear infections is frequently reported in ASD cases. High prevalence of IgG sensitivities to gluten and casein-containing foods as well as high-sugar diets may cause inflammation of the intestines, leading to leaky gut and a myriad of common gastrointestinal complaints. Intestinal infections by yeast and bacteria are frequently reported among children with ASD, and will be the focus of this paper.

Dysbiosis in ASD: Assessment

The common pathogenic organisms in the intestinal tract include yeast (e.g. Candida albicans and parapsilosis) and Clostridia species. Several other bacterial species that are cultured from stool samples include Streptococcus (α and β hemolytic species), Staphylococcus aureus, Citrobacter freundii (also younaa and braakii species), Enterobacter aerogenes, Klebsiella pneumoniae, and Pseudomonas aeruginosa.

Parents of ASD children often report that treatment of yeast (Candida) overgrowth reduces autistic behaviours. Yet Candida overgrowth can be difficult to diagnose. Consensus on symptoms associated with yeast overgrowth is lacking in different fields of health care. Skin afflictions, painful swallowing, substernal chest pain, and urinary tract infections are the only symptoms noted in Sherris' Medical Microbiology (Ryan 1994) and Pediatric textbooks (Wehrle 1991). Candidiasis or the Candida Syndrome has been disputed over the years because the breadth of possible symptoms exceeds these criteria established in mainstream medical literature (Edwards 1988).

A proposed list of yeast-related symptoms in ASD patients includes "stimming" (repetitious actions or gestures), toe-walking, silly or goofy behaviour, echolalia, cravings for sugary or carbohydrate-rich foods, and abnormally formed stools (diarrhea or constipation). Signs of nutritional deficiencies from physical examination could also be indicative of yeast overgrowth since these pathogens will absorb nutrients for their own needs. Inflammation in the intestines also contributes to malabsorption.

Assessment and diagnostic options include patient history (i.e. gastrointestinal symptoms, antibiotic/medication use, allergic susceptibilities) and diagnostic tests including stool cultures, microscopy (observing hyphal forms), DNA analysis of stool samples, PCR-Elisa antibodies or urine Organic Acid Tests. Parent and physician reports (Autism Research Institute 2008, Baker 2005) of improvements in behavioural and gastrointestinal symptoms after administering antifungal medicines may be the only confirmation of yeast overgrowth. Parents often prefer to have diagnostic test results to confirm the need for antifungal treatments and diets. Clinical experience at *Touchstone Naturopathic Centre* (see Table 1) shows that while 63% of stool tests found yeast through microscopic examination, it was successfully grown in culture in only 11%. Therefore, yeast culture and sensitivity tests are unreliable. Arabinose and Tartaric acid (Shaw 1995) are two organic acids found in urine that may confirm yeast overgrowth. Arabinose was positive in 83% of the cases studied at TNC. PCR-Elisa testing showed sensitivity rating of 85% and specificity at 93% in one study (Badiee 2008). However, Elisa testing requires a blood draw, a step that is very stressful for the children and their families. Urine sampling for organic acids provides an easier option.

Clostridia species are a second virulent organism causing significant effects in ASD children. Symptoms presenting in an ASD child that could be associated with Clostridia infection include irritability, agitation, biting/kicking/screaming, head banging, not being engaged, abdominal cramping (which they may be unable to communicate) and loose stools (watery or bloody in extreme cases).

The effects of Clostridia on the intestines are well known. Clostridia difficile can cause pseudomembranous colitis in 0.2-10% of infants treated with antibiotics, especially clindamycin, cephalosporins and amoxicillin (Ryan 1994, Wehrle 1991). C. difficile produces two toxins: one known as Toxin A is an enterotoxin that stimulates infiltration of

neutrophils plus release of inflammatory mediators causing fluid secretion and changes intestinal membrane permeability. Neurotoxins from various Clostridia species (e.g. C. butyricum, C. baratti) are known to cause necrotizing enterocolitis.

Recent studies have provided support to the concept of "gut-brain" connection in Autism. Bolte (Bolte 1998) proposed that C. tetani produces a neurotoxin (TeNT) that ascends from the intestines to the brain via the vagus nerve. She reported, "some children with autism have shown a significant reduction in stereotyped behaviours when treated with antimicrobials (Vancomycin, Metronidazole) effective against intestinal clostridia. When viewed as sequelae to a subacute chronic tetanus infection, many of the puzzling abnormalities of autism have a logical basis." A recent study by Finegold (Finegold 2008) recommends further research to confirm that Clostridia infection is an etiologic factor of autism. He notes that autistic behaviours return after oral Vancomycin is discontinued, and stresses that safe and effective treatments and control of clostridia spores is needed. A new factor to consider in ASD is Propionic acid (PPA). Derrick MacFabe (MacFabe 2008) has shown in an animal study that PPA injected into the brain can produce brain and behavioural changes that resemble Autism. While the primary source of PPA is food or food additives, Clostridia bacteria also produce PPA (Thompson 1990).

Results of Organic Acid Test and Stool Analysis results of ASD children tested at Touchstone Naturopathic Centre (Nov. 2007 to Aug. 2008)

Organic Acids Test	Range	N	Positive	%
Arabinose	0-47	26	21	81%
Tartaric	0-16	26	2	8%
HPHPA	0-150	26	10	38%
Oxalic Acid	0-37	26	16	62%
Stool Analysis				
Yeast - microscopic	Present?	19	12	63%
Yeast – cultured	Present?	19	2	11%
Bacteria	Present?	19	9	47%
Parasites	Present?	19	1	5%
Reduced probiotic counts/ species	Deficient?	19	16	84%

This finding adds further support to the gut-brain connection theory for ASD. Patients may improve with treatment of Clostridia, as well as eliminating food sources of Propionic acid.

Detection of clostridia species can be difficult. Special anaerobic stool collection containers are required when attempting to diagnose with stool cultures. Urine organic acid testing has proven to be a reliable diagnostic. As shown in Table 1 on the previous page 38% of tested children were positive for HPHPA (3-(3-hydroxyphenyl)-3-hydroxyproprionic acid, a metabolite produced by enteric Clostridia bacteria and subsequently excreted through urine.

Dysbiosis in ASD: Treatment

Once deciding to treat yeast overgrowth, the next challenge is finding effective antifungal medicines that the child will take. Conventional prescription treatments include Nystatin, Diflucan (fluconazole) and Amphotericin-B. Several botanical medicines have been used with the most common being garlic (Allium sativum) (Lemar 2007), goldenseal (Hydrastis Canadensis) and Caprylic acid. Grapefruit Seed Extracts and oregano oil are mentioned in many references. Recent studies show Melaleuca, Artemesia (Valdez 2008), Mentha piperita (Yigit 2008), and Hypericum (Fidan 2008) may be effective antifungal agents as well.

Probiotics are the primary non-prescription treatment for Clostridia. The benefits of Lactobacillus species and Saccharomyces boulardii have been reported in several studies. Based on clinical experience, Lactobacillus (rhamnosus) GG and Lactobacillus plantarum should be administered at the beginning of Clostridia treatment, and replaced with Saccharomyces for maintenance. Practitioners should consider allergies and intolerances of their patients when choosing specific probiotic supplements. Many popular brands contain traces of casein that is contraindicated for some children. As well, children who are allergic/intolerant to yeast may not tolerate Saccharomyces boulardii.

Summary

ASD children frequently suffer from intestinal infections caused by yeast (Candida) and bacteria such as Clostridia. Research and clinical observation indicates that these infections can contribute to behaviour and other stereotyped deficits associated with ASD. Treatment of these infections is necessary and possible with natural medicines, including botanical medicines and probiotics. To detect these infections, especially in cases where gastrointestinal symptoms are not obvious, urine organic acid tests can be one of the most effective options. ■

References

Autism Research Institute. Parent Ratings of Behavioral Effects of Biomedical Interventions. www.autismwebsite.com/ari/treatment/form34q.htm. Accessed October 2008.

Badiee P, Kordbacheh P, Alborzi A, Malekhoeseini S, Ramzi M, Mirheni H, Mahmooki M, Shakiba E. Study on invasive fungal infections in immunocompromised patients to present a suitable early diagnostic procedure. Int J Infect Dis 2008.

Baker S, Pangborn J. Autism: Effective Biomedical Treatments (Have We Done Everything We Can For This Child? Individuality In An Epidemic). San Diego: Autism Research Institute; 2nd Edition Sept. 2005.

Bolte ER. Autism and Clostridium tetani. Med Hypotheses. 1998; 51(21): 133-144.

Edwards JE. Systemic Symptoms From Candida In The Gut: Real Or Imaginary? Bull. N.Y. Acad. Med. 1988; 64(6): 544-549..

Fidan I, Ozkan S, Gurbuz I, Yesilyurt E, Erdal B, Ylkbakan S, Imir T. the efficiency of Viscum albus ssp. album and Hypericum perforatum on human immune cells in vitro. Immunopharmacol Immunotoxicol. 2008; 30(3): 519-528.

Finegold SM. Therapy and epidemiology of autism-clostridial spores as key elements. Med Hypotheses. 2008; 70(3): 508-511.

Horvath K, Papadimitriou JC, Rabsztyn A, Drachenberg C, Tildon JT. Gastrointestinal abnormalities in children with autistic disorder. J Pediat. 1999; 135:559-563.

Lemar KM, Aon MA, Cortassa S, O'rourke B, Muller CT, Lloyd D. Diallyl Disulphide depletes glutathione in Candida albicans: oxidative stress-medicated cell death studied by two-photon microscopy. Yeast. 2007; 24(8): 695-706.

MacFabe DF, Rodriguez-Capote K, Hoffman JE, Franklin AE, Mohammad-Aset Y, Taylor AR, Boon F, Cain DP, Kavaliers M, Possmayer F, Ossenkpp KP. A Novel Rodent Model of Autism: Intraventricular Infusions of Propionic Acid Increase Locomotor Activity and Induce Neuroinflammation and Oxidative Stress in Discrete Regions of Adult Rat Brain. Am J Biochem and Biotech. 2008; 4(2): 146-166.

Ryan KJ, Ray CG. Sherris Medical Microbiology, 3rd ed., Appleton & Lange, 1994 pp 303-304.

Shaw W, Kassen E, Chaves E. Increased Urinary Excretion of Analogs of Krebs Cycle Metabolites and Arabinose in Two Brothers with Autistic Features. Clin. Chem. 1995; 41(8): 1094-1104.

Thompson GN, Walter JH, Bresson JL, Ford GC, Lyonnet SL, Chalmers RA, Saudubray JM, Leonard JV, Halliday D. Sources of propionate in inborns errors of propionate metabolism. Metabolism. 1990; 39; 1133-1137.

Valdez AF, Martinez JM, Lizama RS, Vermeersch M, Cos P, Maes L. In vitro anti-microbial activity of the Cuban medicinal plants Simarouba glauca DC, Melaleuca leucadendron L and Artemisia absinthium L. Mem Inst Oswaldo Cruz. 2008;103(6):615-618.

Wakefield AJ, Anthony A, Murch SH, Thomson M, Montgomery SM, Davies S, O'Leary JJ, Berelowitz M, Waker-Smith JA. Enterocolitis in children with developmental disorders. Am J Gastroenterol. 2000; 95:2285-2295.

Wehrle PF. Current Pediatric Diagnosis & Treatment (3rd ed.), Appleton & Lange, 1991 pp 627-628.

Yigit D, Igit N, Ozgen U. An investigation on the anticandidal activity of some traditional medicinal plants in Turkey. Mycoses. 2008.