

Dear Doctor,

In October 2006, the organization “Autism Speaks” convened a group of pediatric gastroenterologists and autism specialists to review the available evidence relative to diagnosis and treatment of gastrointestinal (GI) disorders in children with autism spectrum disorders (ASD) and to propose future research initiatives. A goal of this meeting was to reach a consensus of this group on appropriate diagnostic evaluation and treatment of GI symptoms in children with ASD. Pediatricians and pediatric gastroenterologists see many children with ASD and GI symptoms. While the current literature does not contain any randomized controlled trials from which clinical recommendations can be generated, the following consensus represents a combination of expert opinion and data from the published literature.

The prevalence of GI symptoms among children with ASD is not known. (1-3). Reports of GI symptoms range from 9 to 70% of children with ASD depending on the population surveyed and how the history was elicited (4,5,6). The higher estimate included lifetime prevalence of GI symptoms (6). However, no epidemiologic studies have been published to date that specifically address the prevalence of GI symptoms in children with ASD (7). Among the most common presenting GI symptoms reported in children with ASD are constipation, diarrhea, reflux, vomiting, and abdominal discomfort (6). Diarrhea typically consists of the passage of 2-5 soft large stools per day that may contain undigested food. Constipation is defined as hard stools daily or less frequently. The child may present with loose stools signifying overflow diarrhea around an impaction. GI symptoms may be more common in younger children with ASD. Behaviors such as posturing, self injury and outbursts without obvious cause may occur secondary to many medical conditions that result in discomfort in children with ASD (8). Abdominal pain may be one common cause of behavioral exacerbation that should be considered especially in children who have limited language. At this time the precise causes of GI symptoms in children with ASD remain unknown. Both inflammatory and motility factors may be involved.

If a child with ASD presents with chronic or recurring GI symptoms, the following initial evaluation should be considered:

	Diarrhea	Constipation	Bloating
History			
# bowel movements per day	x	x	x
Size and consistency of bowel movement	x	x	x
Presence of blood in stool	x	x	x
History of abdominal pain	x	x	x
History of rectal bleeding	x	x	x
Appearance of stool	x	x	x
	x	x	x
Sudden unexplained temper tantrums or self-injury, aggression or sleep disturbances (Note: may have causes other than GI pain)	x	x	x
History of infectious exposures (e.g. Travel, well water, relatives with diarrhea)	x	x	x
History of food allergies or intolerances	x	x	x
History of diet and supplements	x	x	x
Family history of celiac disease and ulcerative colitis	x	x	x
Medication history for prior six months	x	x	x
Physical Examination			
Weight, height, and percentiles	x	x	x
General physical examination	x	x	x
Abdominal examination	x	x	x
Perianal inspection	x	x	x
Rectal examination is not mandatory, as some children with ASD may not tolerate this.	x	x	
Laboratory Evaluation			
Stool for occult blood	x	x	x
Complete blood count	x	x	x

Serum electrolytes	x		
BUN and Creatinine	x		
TSH		x	
Albumin and Total Protein	x		
Serum immunoglobulin A level	x	x	x
Tissue transglutaminase or antiendomysial antibody (Celiac testing)	x	x	x
Vitamin A, D, and E levels	x		
Inflammatory bowel disease serology (ASCA/pANCA antibodies)- refer to Peds GI	x	x	x
Bacterial studies (Salmonella, Shigella, Yersinia, campylobacter)	x		
Parasite analysis (giardia and amoeba)	x		
Clostridium difficile	x		
Spot fecal fat and reducing substances	x		
X rays			
Plain abdominal film should be considered to rule out impaction and/or overflow diarrhea	x	x	

Referral to a pediatric gastroenterologist should be considered if recurrent or chronic diarrhea, constipation, bloating or abdominal discomfort is not responsive to initial management by the primary care provider. The gastroenterologist should obtain a detailed clinical history, perform a physical examination, and order appropriate laboratory studies. Additional studies, such as testing for intestinal permeability with lactulose/mannose challenges, may be indicated based on review of this information. The consultant and family should discuss the potential benefits, risks, and controversies relative to potential investigation and interventions. Three possible approaches include endoscopy/colonoscopy, empirical treatment, and dietary intervention.

A. Endoscopy of the upper GI tract and colonoscopy of the lower GI tract may identify disorders that are medically treatable such as inflammation

associated with gastroesophageal reflux, H Pylori induced gastritis, focal enhanced gastritis apparently unrelated to H Pylori or Crohn's disease (9); lactase deficiency,; or celiac disease. Lymphoid nodular hyperplasia (LNH) and microscopic enterocolitis (10, 11, 12) have been reported in the terminal ileum and colon of children with ASD. The clinical significance of LNH in children with autism is unclear given that similar findings have also been reported in children with typical development as well as children with food allergies and immune deficiencies. Inflammatory and immune markers have been reported in intestinal biopsies of children with ASD (13-16). A second research group was unable to identify evidence of abnormal immune markers in intestinal biopsies in a small heterogeneous sample using a less sensitive method (17). Studies to date have been in children with ASD selected for evaluation because of recognized GI symptoms. It is unknown how many children with ASD without classic GI symptoms may have behavioral symptoms secondary to underlying GI disease. The clinical significance and therapeutic implications of inflammatory changes in the intestine, requires further investigation . Needless to say, identification of a disorder of the GI tract such as gastroesophageal reflux or celiac disease should lead to specific and appropriate treatment in children with or without ASD.

- B. Empirical medical therapy for children with diarrhea or constipation assumes that the underlying problem is related to disordered motility (similar to “toddler’s diarrhea” or irritable bowel syndrome). This hypothesis is yet to be evaluated. Inflammatory and motility causes can co-exist, however (18).
1. Initial conservative treatment of diarrhea may include:
 - a. The addition of a fiber supplement (e.g. psyllium) to the diet.
 - b. The cautious and temporary use of an anticholinergic agent (eg. Loperamide, hyoscyamine) to slow diarrhea.
 - c. The use of a brief course of antibiotic therapy or probiotics to treat presumptive “bacterial overgrowth” of documented enteric pathogens.
 - d. Dietary modifications e.g. milk elimination trial.
 2. Empiric treatment of constipation might include:
 - a c. A good clinical review of specific history to evaluate fluid intake, dietary fiber and behavior around stooling to guide treatment options
 - b. Stool softeners including polyethylene glycol (PEG) or lactulose
 - c. Short term use of stimulant agents such as milk of magnesia or senna agents
 - d. Enemas may be necessary if impaction is documented.

C. Dietary Interventions: There is no single dietary intervention that has been systematically evaluated for treatment of GI symptoms in patients with ASD. General recommendations to reduce diarrhea may include reduction in the amount of juice a child drinks to 12 ounces or less a day. A popular dietary intervention includes elimination of dairy and gluten containing foods. Although anecdotal reports have resulted in much popularity of dietary treatment, the few studies to date have not demonstrated the successes that are subjectively described (19). Other dietary interventions that families may use based on anecdotal reports are restriction of all carbohydrates and restriction of sugars and carbohydrates alleged to increase yeast growth in the colon. Allergy testing with skin or blood tests cannot reliably predict if a specific dietary intervention will result in improvement in a child's GI symptoms. Children whose parents pursue dietary interventions should have their overall nutritional status monitored by a health care provider with expertise in nutrition. Given that children with ASD may have limited diets on the basis of self selection as well, dietary interventions should ideally be performed with input from a nutritionist.

Summary:

Autism Speaks is a nonprofit, disorder-specific organization that seeks to advance scientific inquiry into the causes and treatments of Autism Spectrum Disorders. While many families identify GI symptoms in their children with ASD, few studies have addressed the epidemiology, presentation, evaluation or treatment of GI symptoms in this population. Autism Speaks is committed to facilitating additional research to characterize the pathophysiology and identify effective therapies for children with ASD and GI disturbances. Until such high quality studies can be completed, physicians caring for children with ASDs should remain alert to the possibility of disorders of the GI tract in their patients with ASDs. Physicians need to be aware that the communication difficulties of children with ASD may make it difficult to isolate the causes of discomfort. The clinician must consider GI causes for distress and discomfort in children with ASD. The above suggestions are being distributed to help pediatricians provide a medical home to children with ASD and GI complaints.

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