abstract

OBJECTIVES: To develop a practical, readily applied algorithm for primary health care providers to identify, evaluate, and manage constipation in children with autism spectrum disorders (ASDs).

METHODS: The Gastroenterology Committee of the Autism Speaks Autism Treatment Network (ATN), a multisite consortium of centers dedicated to improving standards of medical care for children with ASDs, guided the development of the constipation algorithm through expert opinion and literature review. The algorithm was finalized based on results of field testing by nongastrointestinal, ATN autism medical specialists at 4 ATN sites. A systematic review and grading of the literature pertaining to constipation and children with ASDs was also performed.

RESULTS: Consensus among the ATN Gastroenterology Committee identified that in children with ASDs, (1) subtle or atypical symptoms might indicate the presence of constipation; (2) screening, identification, and treatment through a deliberate approach for underlying causes of constipation is appropriate; (3) diagnostic-therapeutic intervention can be provided when constipation is documented; and (4) careful follow-up after any intervention be performed to evaluate effectiveness and tolerance of the therapy. Literature review revealed limited evidence for the clinical evaluation or treatment strategies of children with ASD and constipation.

CONCLUSIONS: Constipation and its underlying etiology have the potential to be effectively identified and managed using a systematic approach. Lack of evidence on this topic in the literature emphasizes the need for research. Pediatrics 2012;130:S98–S105

AUTHORS: Glenn T. Furuta, MD,a Kent Williams, MD,b Koorosh Kooros, MD,c Ajay Kaul, MD,d Rebecca Panzer, MA, RD, LD,d Daniel L. Coury, MD,e and George Fuchs, MDg

aDigestive Health Institute, Section of Pediatric Gastroenterology, Hepatology and Nutrition, Children’s Hospital Colorado, University of Colorado Denver School of Medicine, Aurora, Colorado; bPediatrics, Division of Gastroenterology, Vanderbilt University Medical Center, Nashville, Tennessee; cChildren’s Medical Center, Dallas, University of Texas Southwestern Medical Center, Dallas, Texas; dCincinnati Children’s Hospital Medical Center, Cincinnati, Ohio; eCenter for Child and Adolescent Health Policy, Massachusetts General Hospital for Children, Boston, Massachusetts; fNationwide Children’s Hospital, Columbus, Ohio; and gPediatric Gastroenterology, Hepatology, and Nutrition, University of Arkansas for Medical Sciences and Arkansas Children’s Hospital, Little Rock, Arkansas

KEY WORDS
autism, constipation, gastrointestinal disease

ABBREVIATIONS
ASD—autism spectrum disorder
ATN—Autism Treatment Network
GI—gastrointestinal
NASPGHAN—North American Society of Pediatric Gastroenterology, Hepatology and Nutrition

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Address correspondence to George Fuchs, MD, Arkansas Children’s Hospital, One Children’s Way, Slot #512–7, Little Rock, AR 72202. E-mail: fuchsgeorgej@uams.edu

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Thus presenting a significant challenge to both parents and health care providers. Over the past quarter century there has been an increased recognition of medical comorbidities among children and adolescents with ASDs, including unre- solved and troubling gastrointestinal (GI) concerns, such as diarrhea, gastro-esophageal reflux–like symptoms, and constipation, among others. GI symptoms in children with ASD can be atypical and manifest merely as a change in behavior, as used in social communication, and/or restricted repetitive and stereotyped patterns of behavior, interests, and activities. Over the past quarter century there has been an increased recognition of medical comorbidities among children and adolescents with ASDs, including unresolved and troubling gastrointestinal (GI) concerns, such as diarrhea, gastroesophageal reflux–like symptoms, and constipation, among others. GI symptoms in children with ASD can be atypical and manifest merely as a change in behavior, thus presenting a significant challenge to both parents and health care providers.

Within this context, recognition and treatment of these disorders in children with ASDs are generally accepted to be relatively understudied and ill defined. A previous report provided review of the literature and consensus recommenda- tions related to children with ASDs suspected of having a GI disorder, including constipation. In addition, a comprehensive, evidence-based evaluation and treatment algorithm for children aged 1 year and older with constipation was developed by the Constipation Guideline Committee of the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN). Although these documents are of significant importance, the previous re- ports do not provide a clinical pathway for the treatment of constipation in ASD or other neurodevelopmental abnormalities. Additionally, the usefulness of the NASPGHAN guideline in children with ASD has not been evaluated.

The Autism Treatment Network (ATN) was founded in 2005 with a goal to in- crease understanding and improve care of children with ASDs. With the marked increase in the incidence of ASDs combined with lack of published data on the management of GI disorders in this subset of children, the need to develop guidance for the primary care practitioner has become even more pressing. In the absence of relevant data to develop evidence-based guidelines, it was determined that expert opinion would be a helpful initial endeavor.

In response to this concern, the ATN convened a committee of pediatric gas- troenterologists and developmental pediatri- cians to develop evaluation and management recommendations for children with ASD and constipation. Given that GI disorders are a major comorbidity of ASD, the ATN GI committee identified recognition, accurate diagnosis, and management of constipation as a priority issue for parents of children with ASDs and challenge to health care providers. To prospectively study GI problems in children with ASDs, the ATN field tested a symptom questionnaire that identified constipation as a major problem.

METHODS
The ATN Gastroenterology Committee, consisting of pediatric GI specialists representing 14 sites as well as 2 de- velopmental pediatrician representa- tives, gathered to address the challenge of constipation in children with ASD. Because of a paucity of data focusing on constipation in children with ASD or with other neurodevelopmental disorders, the ATN Gastroenterology Committee used the NASPGHAN evidence-based guideline and algorithm for constipation as an initial template. The algorithm was modified to meet the needs of clinicians serving children with autism. In addition to development of an ASD-specific algorithm and accompanying text, a complementary “checklist” was developed as a practical tool. A checklist, unlike the more comprehensive algorithm and text, was designed specifically for practicality and application during clinic visits with the child with ASD.

Algorithm Development
The adaptation of the NASPGHAN guidelines for this algorithm was completed in 2 stages. First, the ATN Gastroenterology Committee members modified the original guidelines by consensus, expert opinion through a series of teleconferences, and face-to-face meetings. The draft documents were reviewed by ATN developmental pediatricians and subsequently revised. Second, the ATN selected 4 pilot sites (University of Arkansas for Medical Sciences and Arkansas Children’s Hospital, Cincinnati Children’s Hospital Medical Center, University of Colorado Denver School of Medicine, and the University of Rochester Medical Center) consisting of autism health care providers (not GI special- ists) who tested the feasibility of the algorithm over a 6-month period in an effort to identify points of concern; the intent was not to validate the algorithm. The pilot sites participated in monthly conference calls to provide updates, understand variance, and recommend changes to the algorithm. Working with the National Initiative for Children’s Health Care Quality, the GI specialists refined and finalized the algorithm based on the feedback from the pilot sites and developed a 1-page checklist designed to guide care providers through the algorithm.

Literature Review
To ensure that relevant evidence was not omitted from the algorithm, an ex post facto systematic literature review system was used to identify evidence with regard to the treatment of constipation in children with autism. The OVID, CINAHL, Embase, Database of Abstracts and Re- view, and the Cochrane Database of Systematic reviews databases were searched for applicable materials. The
<table>
<thead>
<tr>
<th>Study &amp; Grade</th>
<th>Sample</th>
<th>Intervention &amp; Duration</th>
<th>Measures Used to Arrive at Conclusion</th>
<th>Results</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>A clinical study of secretin in autism and pervasive developmental delay</td>
<td>Included: 48 pts of 64 eligible completed the study. All dx with ASD or DD from a recognized specialist (39 male, 9 female, ages 2–32; 5 were adults.</td>
<td>Pts received 1 vial of secretin at baseline. Evaluated for 8 wk after. No new tx conducted in concurrence.</td>
<td>• At baseline, completed form of sx ranking from 0 sx absent to 12 sx severe. Parents completed form weekly during study. Included bowel function: diarrhea, constipation, poor appetite, bloating, and abdominal pain.</td>
<td>• 11 = moderate (score 1–5). After tx, 2 with moderate constipation ceased, 2 improved, 7 did not change.</td>
<td>Secretin may improve sx of constipation in some children with ASD but evidence is limited to support a correlation between secretion and sx of constipation.</td>
</tr>
<tr>
<td>Lonsdale et al (2000)</td>
<td>Control group of 5 girls and 28 boys; aged 2–15 y. Control group not used to compare GI sx.</td>
<td>Hair analysis conducted pre and post for Al, As, Cd, Ca, Cu, Pb, Mg, Hg, K, Na.</td>
<td></td>
<td>• 15 = severe constipation (6–12). After tx, 5 with severe constipation ceased, 5 improved, and 6 had no change.</td>
<td></td>
</tr>
<tr>
<td>Dietary fiber intake and constipation in children with severe developmental disabilities</td>
<td>Included: 27 severe DD children aged 3–17 y living in institutional setting. Able to take food po and medically stable.</td>
<td>Assess dietary fiber over 3 consecutive days. Food/menu was managed by staff. Fiber supplement (wheat bran cereal at breakfast) given over 4-mo period in stages:</td>
<td>Bowel motions and no. of laxatives for each child recorded throughout study period.</td>
<td>Baseline fiber 2 g/d</td>
<td>Fiber supplementation may improve constipation in children with ASD.</td>
</tr>
<tr>
<td>Tse et al</td>
<td></td>
<td>• Stage 1 (20 d): added 17 g fiber</td>
<td></td>
<td>No. of laxatives decreased significantly from baseline and stage 1 (1.22 ± 0.36 vs 0.9 ± 0.79) than to stage 2 (0.7 ± 0.40). Difference in laxative significant when comparing baseline significant (stage 1 P &lt; .05; stage 2 P &lt; .01). No significant difference between stages 1 and 2.</td>
<td></td>
</tr>
</tbody>
</table>

AS, autistic subjects; DD, developmental disabilities; dx, diagnosis; Lvl, level; NAS, non-autistic subjects; po, orally; pts, patients; sx, symptom; tx, treatment. Grade Categories: Category I 80% to 100% of ideal methodology met; Category II 60% to 79.99% of ideal methodology met; Category III 40% to 59.99% of ideal methodology met; Category IV <39.99% of ideal methodology met.
searches were limited to primary and secondary research conducted in humans, published in the English language, involving children aged 0 to 18; published between January 1995 and July 2010. Individual studies were graded by using an adaptation of the GRADE system (Table 1) by 2 primary reviewers (K.K. and R.P.) and then reviewed by a content expert (A.K.) for consensus. Any discrepancies were resolved by an unaffiliated third party.
Results

Algorithm

The algorithm describes 10 steps in the evaluation and management of constipation in children with ASD (Fig 1). A smooth-edged box indicates a starting or ending point, a sharp-edged box indicates a predefined process or specific action, and a diamond shape indicates a point of decision. The items in the accompanying text are points of elaboration whose number corresponds to the algorithm item number (Table 2). To facilitate practical implementation of the algorithm during the patient–health care provider interaction, the Constipation Checklist summarizes key steps (Table 3) to be completed during the visit. Children with ASD often have unusual oral texture and/or taste (Table 2).
sensitivity. This sensitivity might adversely affect compliance with certain of the medications used in neurotypical children, requiring health care providers to try different medical regimens (Table 4).

**Literature Review**

A total of 1528 articles were located. After removing review articles, commentaries, case studies with an n of fewer than 10, nonintervention trials, and reports that did not address our target questions, 2 articles remained (see Table 1).

**Algorithm Testing Results and Discussion Points**

The algorithm was field tested at 4 ATN sites (University of Arkansas for Medical Sciences and Arkansas Children’s Hospital, Cincinnati Children’s Hospital Medical Center, University of Colorado Denver School of Medicine, and the University of Rochester Medical Center). The objective was to systematically document the feasibility of implementing the algorithm in children with ASD and constipation. The algorithm was completed on a total of 48 children. At the 4 sites, a total of 48 children completed the algorithm. Findings indicated that each ATN site differed in practice flow. New and previously seen patients entered the algorithm at the beginning when constipation was identified. For patients who responded to impaction treatment but were not symptom free at the time of follow-up, treatment medications were adjusted 69% (18/26) of the time. Long-term follow-up was arranged for 82% (28/34) of patients in whom treatment was found to be effective. Patients were effectively managed with parental education, dietary modification, behavioral strategies, and oral medications 51% (22/43) of the time. No children were referred to specialists other than pediatric gastroenterology. Additionally, the blood test step was used in only 1 patient of the 48.

The sites reported that the final algorithm was readily applied and did not interrupt the clinic flow of the autism specialist. When treatment was deemed effective, long-term follow-up was done by either the primary care provider or care continued to be provided by the autism specialist.

Most patients required medication adjustments in follow-up visits, which indicates the importance of follow-up, particularly because pharmaceutical and dietary management have such a central role in the treatment of chronic constipation. Not surprisingly, the only referrals deemed necessary were to a pediatric gastroenterologist.

**TABLE 3 Constipation Checklist for Children with ASD**

<table>
<thead>
<tr>
<th>Assess</th>
<th>Treat</th>
</tr>
</thead>
<tbody>
<tr>
<td>H+P include assessment for red flags and workup if needed (defined as fewer than 3 bowel movements per week or difficult defecation)</td>
<td>Impaction if needed</td>
</tr>
<tr>
<td>Red flags and workup if needed Interview parents</td>
<td>Educate family</td>
</tr>
<tr>
<td>Make a differential diagnosis Impaction: x-ray abdominal rectal</td>
<td>Counsel diet (eg, increase fiber, fluid intake) and Behavioral therapy (eg, scheduled sitting on the toilet every day)</td>
</tr>
<tr>
<td></td>
<td>Oral meds including PEG 3350, lactulose (note Kristalose is clear; tasteless), Senna</td>
</tr>
<tr>
<td></td>
<td>Manage meds</td>
</tr>
<tr>
<td></td>
<td>Arrange Follow-up Establish a consistent follow-up interval</td>
</tr>
<tr>
<td></td>
<td>Consider referral to pediatric gastroenterologist Consider ordering blood test (T4, TSH, Ca, Pb, Celiac) for children whose chronic constipation does not resolve</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Clinical experience and review of the literature indicate constipation to be a significant problem in children with ASD; however, data on the spectrum of clinical manifestations, prevalence, and best approach to evaluation and treatment are lacking. The goal of this group, including the ATN Gastroenterology Committee, the test sites, and members of the National Initiative for Children’s Health Care Quality, was to develop a practical and effective algorithm and checklist for the evaluation and management of constipation in children with ASD by the primary care practitioner. Within this context, any child with ASD and signs or symptoms (including atypical) consistent with the possibility of constipation should undergo an evaluation as defined in the algorithm and with the use of the checklist. Examples of atypical behaviors include self-abusive behavior (biting or hitting oneself, head banging) or posturing, such as bending over furniture, grimacing, holding the abdomen, squeezing the legs together, walking around with a narrow gait to hold stool in. Based on the outcome of the initial evaluation per the algorithm, referral to a GI specialist may or may not be indicated. Our experience from the field-testing component of the algorithm indicated that the algorithm is readily usable and did not interrupt the flow of the clinic.

The fact that most children responded to the modified algorithm suggests that they have “functional” constipation (not caused by an otherwise known pathologic reason) as is true in neurotypical children. Additionally, it was evident that most of the children, even some with encopresis, could be managed by non-GI specialist health care providers with the assistance of the presented paradigm. Regular follow-up (either by phone or clinic visit) to document continued response to the regimen was found to be critical for success. Identifying
TABLE 4 Constipation Algorithm Text: Medication Options

<table>
<thead>
<tr>
<th>Laxatives</th>
<th>Dosage</th>
<th>Side Effects</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmotic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lactulosea</td>
<td>1–3 mL/kg/d in divided doses; available as 70% solution.</td>
<td>Flatulence, abdominal cramps; hypernatremia has been reported when used in high dosage for hepatic encephalopathy; case reports of nontoxic megacolon in elderly.</td>
<td>Synthetic disaccharide. Well-tolerated long term.</td>
</tr>
<tr>
<td>Sorbitolb</td>
<td>1–3 mL/kg/d in divided doses; available as 70% solution.</td>
<td>Same as lactulose.</td>
<td>Less expensive than lactulose.</td>
</tr>
<tr>
<td>Magnesium hydroxidea</td>
<td>1–3 mL/kg/d of 400 mg/5 mL; available as liquid, 400 mg/5 mL and 800 mg/5mL, and tablets.</td>
<td>Infants are susceptible to magnesium poisoning. Overdose can lead to hypermagnesemia, hypophosphatemia, and secondary hypocalcemia.</td>
<td>Acts as an osmotic laxative. Releases cholecystokinin, which stimulates GI secretion and motility. Use with caution in renal impairment.</td>
</tr>
<tr>
<td>Magnesium citratea</td>
<td>&lt;6 y, 103 mL/kg/d; 6–12 y, 100–150 mL/kg/d; &gt;12 y, 150–300 mL/kg/d; in single or divided doses. Available as liquid, 16.17% magnesium.</td>
<td>Infants are susceptible to magnesium poisoning. Overdose can lead to hypermagnesemia, hypophosphatemia, and secondary hypocalcemia.</td>
<td>Effective if child will accept it; many children with ASD reject because of the flavor.</td>
</tr>
<tr>
<td>Magnesium oxided</td>
<td></td>
<td></td>
<td>Tasteless, or different flavors available (“Natural Calm”). Superior palatability and acceptable by children.</td>
</tr>
<tr>
<td>PEG 3350</td>
<td>Disimpaction: 1–1.5 g/kg/d for 3 d Maintenance 1 g/kg/d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osmotic enema</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Polyethylene glycol-</td>
<td>For disimpaction: 25 mL/kg/h to 1000 mL/h by nasogastric tube until clear or 20 mL/kg/h for 4 h/d. For maintenance: (older children): 5–10 mL/kg/d.</td>
<td>Difficult to take. Nausea, bloating, abdominal cramps, vomiting, and anal irritation. Aspiration, pneumonia, pulmonary edema, Mallory-Weiss tear. Safety of long-term maintenance not well established.</td>
<td>Information mostly obtained from use for total colonic irrigation. May require hospital admission and nasogastric tube.</td>
</tr>
<tr>
<td>Electrolyte solution</td>
<td></td>
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<td></td>
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<tr>
<td>Lubricant</td>
<td></td>
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<tr>
<td>Mineral oil enemaa</td>
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<tr>
<td>Saline enema</td>
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<tr>
<td>Stimulants</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Senna</td>
<td>2–6 y: 2.5 mL/d; 6–12 y: 5–15 mL/d; Available as syrup, 8.8 mg of sennosides/5 mL. Also available as granules and tablets.</td>
<td>Abdominal pain, cathartic colon (possibility of permanent gut, nerve, or muscle damage). Idiosyncratic hepatitis, Melanosis coli, hypertrophic osteoarthropathy, analgesic nephropathy.</td>
<td>Increased intestinal motility. Melanosis coli improves 4–12 mo after medications discontinued. Can be used in conjunction with Miralax. Once withholding behavior is overcome, Senna should be cut back.</td>
</tr>
<tr>
<td>Bisacodyl</td>
<td>≥ 2 y: 0.5–1.0 suppository. 1–3 tablets per dose. Available in 5-mg tablets and 10-mg suppositories.</td>
<td>Abdominal pain, diarrhea, and hypokalemia, abnormal rectal mucosa, and (rarely) proctitis. Case reports of urolithiasis.</td>
<td></td>
</tr>
</tbody>
</table>

* Adjust dosage to induce a daily bowel movement for 1 to 2 mo.

nonresponders early and changing to an effective regimen in a timely manner also proved to be crucial for ongoing success.

There was, however, a definite subset of children, particularly those on the severe end of the ASD spectrum, who failed to respond to standard therapy. These children with lower cognitive abilities appeared to have difficulty correctly interpreting normal physiologic cues, such as rectal distension with stool, but this remains to be clarified. Some of these children displayed classic withholding behaviors, either from past unpleasant experience with defecation or true rectosphincteric dyssynergia from never having learned the correct defecation dynamics of abdominal muscle contraction and anal sphincter relaxation.

The process of developing this algorithm and checklist, as well as clinical experience of the ATN Gastroenterology Committee gastroenterologists, identified certain important challenges in assessment and management of children with ASD and constipation. Often the only presentation is a change in baseline behavior and not the typical straining, passing hard infrequent stools, and soiling. Evaluation of the child with ASD by routine abdominal and/or rectal examination can be difficult or not possible, leading to reliance on clinical history and characteristics of the child’s bowel pattern. Radiographic assessment is frequently obtained to determine whether a fecal mass in the rectum or excessive fecal load is present. The effectiveness of many standard medical therapies for constipation might be
severely constrained because of the volume, texture, or taste sensitivities in children with ASD. The available literature is small, and only 2 articles even reached the level to address the target concerns, indicating the need for high-quality research in this field. As a result, the health care provider, with input from parents, may need to be creative and try various therapeutic agents with the aim of identifying one to which the child will comply. There was consensus opinion that the child with ASD and constipation should initially undergo evaluation and management as per the algorithm presented. Those who do not respond to this should then be referred to a gastroenterologist.

CONCLUSIONS
As the literature on evaluation and management of constipation in children with ASD is quite scant, development of the algorithm was based largely on modification of the NASPGHAN Guidelines and expert opinion and further complemented by input after field testing. Until such time as evidence becomes available to further define the best approach, we recommend that the current algorithm with accompanying text and, as a practical, clinic-based tool, the checklist be incorporated into routine care of children with ASD and constipation.

ACKNOWLEDGMENTS
Special thanks to the National Initiative on Children’s Healthcare Quality for their guidance on the algorithm creation and testing. Review and comment on this clinical algorithm was provided by the following organizational liaisons: Paul Carbone, MD (American Association of Pediatrics Council on Children with Disabilities, Autism Sub-Committee); Ivor Hill, MD (American Association of Pediatrics Section on GI and Nutrition); George Fuchs, MD (NASPGHAN); Robin Hansen, MD (Society for Developmental and Behavioral Pediatrics). The valuable assistance of the members of the Autism Treatment Network Gastroenterology Committee in reviewing this document is gratefully acknowledged.

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