Management of Functional Constipation in Children with Lower Urinary Tract Symptoms: Report from the Standardization Committee of the International Children's Continence Society

Rosa E. Burgers, Suzanne M. Mugie, Janet Chase, Christopher S. Cooper, Alexander von Gontard, Charlotte Siggaard Rittig, Yves Homsy, Stuart B. Bauer and Marc A. Benninga*

From the Department of Pediatric Gastroenterology, Emma Children's Hospital/AMC, Amsterdam, The Netherlands (REB, SMM, MAB), The Children's Surgery, Cabrini Hospital, Melbourne, Australia (JC), Pediatric Urology, Department of Urology, University of Iowa, Iowa City, Iowa (CSC), Department of Child and Adolescent Psychiatry, Saarland University Hospital, Homburg, Germany (AVG), Department of Pediatrics, Aarhus University Hospital, Skejby Sygehus, Aarhus, Denmark (CSR), Children's Urology Group, Department of Pediatrics, Children's Urology Group, University of South Florida, Tampa, Florida (YH), and Pediatric Urology, Children's Hospital, Boston, Massachusetts (SBB)

Purpose: We present a consensus view of members of the International Children's Continence Society (ICCS) together with pediatric gastroenterologists, experts in the field of functional gastrointestinal disorders, on the management of functional constipation in children with lower urinary tract symptoms.

Materials and Methods: Discussions were held by the board of the ICCS and a multidisciplinary core group of authors was appointed. The draft document review process was open to all ICCS members via the website. Feedback was considered by the core authors and, by agreement, amendments were made as necessary.

Results: Guidelines on the assessment, and pharmacological and nonpharmacological management of functional constipation in children with lower urinary tract symptoms are outlined.

Conclusions: The final document is not a systematic literature review. It includes relevant research when available, as well as expert opinion on the current understanding of functional constipation in children with lower urinary tract symptoms. The document is intended to be clinically useful in primary, secondary and tertiary care settings.

Key Words: child; constipation; lower urinary tract symptoms; societies, medical; review

Functional constipation and lower urinary tract symptoms are common problems in children. The reported prevalence of childhood constipation varies from 0.7% to 29.6%. Similarly, pediatric urologists frequently report symptoms of constipation in up to 50% of children seen for lower urinary tract dysfunction. FC and LUTS have a significant impact on quality of life, affecting physical and emotional well-being of the child and family.

Childhood constipation is characterized by an infrequent, hard, often pain-

ful defecation and the involuntary loss of feces in the underwear.^{5,8} Fecal incontinence is also present as a single symptom without any symptoms or signs of constipation, known as FNRFI,⁹ or as a symptom in organic malfunction. These clinical conditions will not be discussed in this review.

DEFINITION OF CONSTIPATION

For many years physicians, patients and parents have used different definitions for constipation. The ICCS

Abbreviations and Acronyms

FC = functional constipation

FNRFI = functional nonretentive fecal incontinence

LUTD = lower urinary tract dysfunction

LUTS = lower urinary tract symptoms

MRI = magnetic resonance imaging

PEG = polyethylene glycol

RCT = randomized controlled trial

UTI = urinary tract infection

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* Correspondence and requests for reprints:
Meibergdreef 9 1105 AZ Amsterdam, The Netherlands (telephone: +31 20 566 30 53; FAX: +31 20 566 91 81; e-mail: m.a.benninga@amc.nl).

recommends the use of the Rome III criteria for diagnosing functional defecation disorders in children (Appendix 1).⁸

PATHOPHYSIOLOGY

The pathophysiology of childhood constipation is multifactorial and remains incompletely understood. In only a small minority of patients, constipation is secondary to an organic disorder, such as anorectal malformation, Hirschsprung's disease, neurological abnormality or an endocrine or metabolic disorder. In more than 90% of children presenting with constipation no organic cause is found and a diagnosis of FC is made. 5 The most common etiology of FC is withholding of stools that may begin after experiencing a hard, painful or frightening bowel movement. Changes in routine or diet, stressful events, ie birth of a sibling, parental divorce, entering kindergarten and school,⁵ intercurrent illness, perianal irritation, unavailability/dislike of toilets or postponement of defecation due to lack of interest or attention, contribute to the problem as well. As a consequence of withholding stools, the rectal mucosa absorbs water from the fecal mass, and the retained stools become progressively harder and more difficult to evacuate. This leads to a vicious circle of stool retention in which the rectum is increasingly distended (megarectum), resulting in overflow fecal incontinence, loss of rectal sensation and, in the end, loss of normal urge to defecate.^{5,10}

Slow Transit Constipation

A delay in total and segmental colonic transit time has been described in a subgroup of children with chronic constipation. Referred to as slow transit constipation, this might be due to dysfunction of the muscles of the colonic wall (resulting in nonpowerful contractions) or to dysfunction of the enteric nervous system (resulting in less coordinated motor activity). A delay in colonic transit time might also be secondary to massive chronic fecal retention in the rectum.

Environmental and Behavioral Factors

Various environmental and social circumstances are associated with a higher prevalence of FC in children, including low consumption of fiber, low physical activity level, living in a highly densely populated community and low parental education level. The relation between behavioral problems and constipation is complex, in part because constipation can be a cause and a consequence of behavioral issues. Constipation and/or fecal incontinence has been reported more frequently in children with specific behavioral phenotypes such as attention deficit hyperactivity disorder, autism spectrum disorders and anxiety and depressive symptoms. In a large epidemiological study of 8,242 children age 7

to 8 years, those with fecal incontinence had significantly increased rates of separation anxiety (4.3%), specific phobias (4.3%), generalized anxiety (3.4%), attention deficit hyperactivity disorder (9.2%) and oppositional defiant disorder (11.9%). Many more children are distressed by their incontinence and show subclinical symptoms. Unrecognized psychological issues will interfere with treatment of incontinence and result in less favorable outcomes. Therefore, all children with urinary and/or fecal incontinence should be screened for psychological and psychiatric issues.

Children with mental retardation and/or other developmental delay and constipation require a treatment approach with attention to individual needs. ¹⁸ A description of therapy in this group of children is beyond the scope of this report.

Constipation and Lower Urinary Tract Dysfunction

The coexistence of functional constipation and urinary tract disorders, including urinary incontinence, LUTD and recurrent UTI is well established. 19,20 The term bowel bladder dysfunction can be used instead of the term dysfunctional elimination syndrome, 21 and describes children with a combination of functional bladder and bowel disturbances, including bladder overactivity (urge), increased or decreased voiding frequency, bladder underactivity or constipation. The close anatomical proximity of the bladder and urethra to the rectum makes it likely that abnormalities within one system will affect the other. Relaxation of the pelvic floor muscles and striated sphincters is necessary for normal micturition and defecation. There are several complementary theories for the coexistence of bladder and bowel disorders. One hypothesis proposes that rectal distention in the constipated child puts direct pressure on the posterior bladder wall. This pressure is thought to lead to bladder overactivity or mechanical compression of the bladder with trigonal irritation, posterior bladder wall invagination, bladder neck and urethral obstruction or distention. 6,19,22 The effects of rectal distention were reversed in half of the children after rectal balloon deflation, which is compatible with a mechanical etiology, but persisted and progressed in the remainder, suggesting a neurological mechanism. This is in line with a second theory that suggests urethral and anal sphincter neural input is one functional unit with shared input to sacral reflexes from the bowel, bladder and proximal urethra. 19 A third hypothesis promulgates that prolonged external anal sphincter contraction in the presence of a large amount of stool leads to inappropriate pelvic floor muscle contractility and consequently concomitant urethral sphincter nonrelaxation. The detrusor-sphincter dyscoordination subse-

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Medical history and physical examination
 Criteria functional constipation (Rome III-criteria
Bowel diary for 7 days (including Bristol stool score) If + Treat accordingly
Urine analysis (Culture &Sensitivity: If + Treat accordingly
Ultrasound to measure:- Postvoid residual: If τ Treat FC first, then try urotherapy then try α-blockers
                          - Rectal diameter: If > 30mm then treat FC
                          - Bladder wall thickness: If Rectal diameter >6mm (empty rectum) and >3mm
                           (full rectum) then treat FC
LUTS and FC improve → Maintenance Rx for at least 3-6 months
FC improves but persistent LUTS→ Flow/EMG + treat accordingly: urotherapy then try anticholinergics
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LUTS improves but persistent FC→ ensure compliance and/or intensify toilet training and Rx: (PEG ± enemas), then try transcutaneous electrical neuromodulation then try biofeedback training

No improvement FC justifies thorough workup by a pediatric gastroenterologist (colonic transit measurement, spinal MRI, defecography, anorectal/colonmanometry)

Algorithm for management of LUTS/FC. Rx, medication. EMG, electromyography.

quently promotes bladder overactivity, urinary incontinence, urinary tract infection and/or vesicoureteral reflux. 19,23

EVALUATION

The evaluation and management of the child with lower urinary tract symptoms are depicted in an algorithm (see figure). Previously reviewed in detail, this entails a 3-day voiding diary and a 14-day bowel evacuation diary for this helps denote how the natural elimination habits of the child including how often and when the child is incontinent, and what is the relationship between urinary and fecal incontinence.20,24 A flow rate and post-void residual at the immediate end of voiding will determine the characteristics of the actual flow and the ability to empty. In addition it is important to look for bowel dysfunction in children with LUTS and to look for LUTS in children with bowel dysfunction. The evaluation of bowel dysfunction in children requires a thorough medical history and a complete physical examination. The rectal examination may help rule out most organic causes of constipation. If any parameters listed are abnormal, then referral to a specialist in urological or gastroenterological care is necessary.

Medical History

It should be emphasized that the history needs to be obtained by questioning the child and parents, as parents often under-recognize constipation symptoms.²⁵ A comprehensive history should include questions about defecation frequency, stool characteristics (consistency, caliber and size), whether the child experiences pain during defecation, the presence of episodes and timing of fecal incontinence, and stool withholding behavior. Importantly, talking to the child often reveals information that parents cannot provide.

The Bristol Stool Form Scale can help patients and physicians to classify the stool form using different images and descriptions in everyday language.²⁶ The accuracy of the defecation history in children as provided by the child and/or parents can be improved with use of a bowel diary. 5 Accompanying symptoms, including abdominal pain, loss of appetite, nausea, vomiting, weight loss or poor weight gain, neuromuscular development and psychological or behavioral problems should be assessed. Knowledge of the time of the first bowel movement is essential to discriminate functional constipation from Hirschsprung's disease. Dietary history and a history of previous treatment strategies for constipation should be investigated. Finally, it is important to ask for life altering events, such as death in the family, birth of a sibling, school problems and sexual abuse which might contribute to the development of retentive behavior.

Physical Examination

Complete physical examination should be performed in all children with defecation disorders. Abdominal examination is useful to assess generalized low to intermediate grade tenderness, often due to gaseous distention of the colon, secondary to fecal impaction. A fecal mass can sometimes be detected on left lower quadrant palpation related to a loaded sigmoid colon. Perianal inspection provides information about the position of the anus, the presence of gluteal cleft deviation, dermatitis, perianal feces, fissures, hemorrhoids and scars as sequelae of sexual abuse. Inspection of the lower back can give valuable information to exclude a spinal dysraphism, a lumbosacral spine abnormality or sacral agenesis.²⁷ Lower extremity evaluation, including strength, length, mass and sensation may also uncover an occult spinal dysraphism. Anorectal digital examination provides useful information regarding perianal sensation, anal tone, size of the rectum, the amount and consistency of feces in the rectal ampulla and function of the sphincter (ability to contract and relax the anal sphincter).⁵ It has been recommended to perform at least 1 rectal examination in children presenting with symptoms of constipation.8 However, we recommend performing a digital rectal examination in children only fulfilling 1 of 6 Rome III criteria for childhood constipation to confirm the diagnosis.

Laboratory

In general, laboratory investigation of constipated children rarely uncovers an underlying disease such as hypothyroidism or celiac disease. In children with a defecation disorder and LUTS, urinalysis should be performed to evaluate for urinary tract infection as well as for microscopic hematuria or proteinuria.²⁸

Radiology

Diagnostic tests are frequently used to diagnose childhood constipation. Nevertheless, a systematic review evaluating the additional value of diagnostic tools in the diagnosis of functional constipation in children found insufficient evidence for abdominal radiography, colonic transit time and transabdominal ultrasound.²⁹

Abdominal radiography. A plain abdominal x-ray with and without radioopaque markers to determine segmental and total colonic transit time is of limited clinical value in diagnosing pediatric constipation because of a poor diagnostic accuracy of fecal loading assessment. Radiography is only useful to determine the presence of fecal retention when there is uncertainty as to whether the patient is constipated and rectal examination is not possible because of obesity, refusal or psychological factors (sexual abuse) that make a rectal examination too traumatic. In approximately 50% of constipated children colonic transit is delayed with the majority of the delay in the rectosigmoid area.

Transabdominal/pelvic ultrasound. Transabdominal ultrasound may show an impression of the rectum behind the bladder and is considered to be a simple and reliable technique to measure the transverse rectal diameter and demonstrate fecal loading in children.³⁰ A significantly larger diameter of the rectum was found in patients with LUTD and constipation compared to those with a normal defecation pattern. The However, there is insufficient evidence that the transverse diameter can be used solely as a predictor of constipation and fecal impaction.²⁹ In nonconstipated and constipated children a diameter greater than 30 mm correlated with a positive finding of rectal impaction on a digital rectal examination,30 implying that ultrasound can give information regarding rectal impaction as 1 of the 6 Rome III criteria. Furthermore, as with the plain abdominal x-ray, the acquired images may be of great help to convince parents and children of the need for constipation therapy.³⁰

MAGNETIC RESONANCE IMAGING

MRI of the spine is indicated in children with intractable defecation disorders presenting with neurological complaints and/or physical symptoms such as a shortened gluteal cleft (sacral agenesis) or deviation, a cutaneous manifestation (hair patch, dimple, subcutaneous mass), or lower extremity weakness or asymmetry, suggestive for spinal cord abnormalities. Tarcan et al studied the correlation of sacral skin lesions with occult spinal dysraphism on MRI in children with resistant LUTS. A spinal abnormality was found with MRI in 2 of 42 (5%) children

with a normal sacral examination compared to 7 of 19 (37%) children with an abnormal sacral finding. This implies that abnormal sacral findings are strong predictors of occult spinal dysraphism in children with resistant LUTS.

TREATMENT

Initial treatment should be directed at constipation and/or fecal incontinence in children with combined bowel bladder dysfunction. The most successful treatment includes a 4-step approach of education, disimpaction, prevention of reaccumulation and followup.⁵ Treatment is often of prolonged duration, which usually requires at least 3 to 6 months with frequent relapses.³² Several studies show a decrease in the occurrence of UTIs, 4,33,34 decrease in urinary incontinence episodes, 4,34 resolved intermittent/staccato flow patterns 33 and improvement of detrusor overactivity, ^{33,34} after successful treatment of constipation. ^{6,19,21,35} By evacuating the colon and rectum it has been suggested that the pressure on the bladder is relieved³⁴ and/or a more coordinated neural input into the area is reestablished.³⁵

Education, Demystification and Behavior Modifications

The first step of treatment consists of education and demystification.⁵ Simple explanations about bowel function, bowel problems and the physiology of the anorectum are valuable. Information concerning prevalence aims to remove blame, as many children are often teased before medical attention is sought.⁵ It is important to describe the coexistence of bowel and bladder problems in children, especially because questions regarding bowel habits are frequently not expected when the child is referred for urinary tract symptoms.

Disimpaction

Approximately 30% of children with long lasting functional constipation present with abdominal and/or rectal fecal impaction, with overflow incontinence in 90%. Maintenance treatment is more likely to be successful after fecal disimpaction, which can be accomplished by oral, nasogastric or rectal agents. The efficacy and safety of orally administered polyethylene glycol during disimpaction have been studied in several trials. Successful disimpaction occurred in 75% to 92% of the patients after 3 to 6 consecutive days, with a most effective dose of 1.0 to 1.5 gm/kg PEG per day. According to 6 days surprisingly well without any side effects.

Maintenance Treatment

Regularity for a longer period of time is important to prevent recurrent impaction and recurrence of stool withholding behavior. This usually requires maintenance laxatives in combination with behavioral therapy over a period, which may last for months or years. ^{5,38} Even after intensive medical and behavioral treatment only 60% of all children referred to a tertiary medical center for chronic constipation were treated successfully at 1 year of followup. A third of the children followed beyond puberty continued to have severe complaints of constipation and a fourth continued to experience symptoms as adults. ³⁷

Dietary Interventions

The role of dietary fiber in the etiology and treatment of childhood constipation remains unclear, with conflicting evidence in the literature. More data from high quality RCTs are required before the true efficacy of either fiber type in the treatment of chronic idiopathic constipation is known. The use of probiotics is increasingly evaluated as a treatment option in the management of childhood constipation. However, a recent systematic review revealed that there is inconclusive evidence that probiotics are effective in the treatment of pediatric FC.

Oral Laxatives

Available oral laxatives consist of osmotic and stimulant laxatives.⁵ Although oral laxatives are widely used in the pediatric population, to date, only 2 randomized controlled trials have compared the effectiveness of oral laxatives vs the use of a placebo.⁴¹ Both studies concluded that PEG was more effective than placebo in increasing frequency of bowel movements, reduction of hard stools, pain and straining during defecation. A recent Cochrane review concluded that the use of PEG is superior to lactulose for the outcomes of stool frequency per week, form of stool, relief of abdominal pain and the need for additional products.⁴¹ Frequently used oral laxative agents for maintenance therapy are listed in Appendix 2.

Enemas

The role of retrograde enemas in the maintenance treatment of children with a neurological disorder as an underlying cause of their symptoms is well established and proven to be therapeutically effective. ⁴² Although, little is known about the role of retrograde enemas in the maintenance treatment of children with chronic functional constipation. A recent RCT showed that application of enemas on a regular basis is well tolerated, but had no additional benefit over conventional treatment with oral laxatives in the maintenance phase of treatment. ³⁷

Antibiotic Therapy

Children who present with constipation and are susceptible to chronic or recurrent UTI may benefit from antibiotic prophylaxis. Although there are no specific studies to document the benefits of maintaining constipated children with LUTS on prophylactic antibiotics, the relationship of constipation and UTI is sufficiently well documented to support the rationale for this option. Antibiotic prophylaxis is often maintained, along with treatment of constipation, until the child demonstrates improvement in symptoms of constipation and LUTS.

Behavioral Therapy and Biofeedback Training

Behavioral interventions (toilet training, incentive and reward schemes, desensitization of toilet avoidance and environmental management) are used to reduce the level of distress and to restore normal bowel habits by positive reinforcement. 43 Behavioral modification or habit training involves teaching a child to defecate regularly and is effective in 15% of children even without starting other therapeutic interventions. A recent RCT showed no advantage of teaching parents behavioral procedures and behavioral play therapy with a child in the presence of his or her parents over conventional treatment consisting of behavior interventions in combination with laxatives. 44 This latter study clearly showed that psychological referral is only indicated in constipated children with severe existing emotional problems, scored upon validated child behavioral checklists.44

Paradoxical external anal sphincter/pelvic floor muscle contraction or partial or nonrelaxation during attempted defecation is present in approximately 50% of children with FC.⁵ Biofeedback training aims to eliminate this by visually and aurally reinforcing repeated external anal sphincter relaxation until a recognizable sensation is achieved without the need for feedback. However, the clinical relevance of biofeedback training in the treatment of childhood constipation is doubtful since it has been shown that normalization of defecation pattern with biofeedback training does not correlate with successful treatment outcome.^{5,43}

Surgery

The majority of children with FC are successfully treated with conventional medical therapy. However, a small group of patients has severe, refractory symptoms, unresponsive to intensive medical management. This minority may benefit from surgical interventions. The antegrade delivery of enemas enables the patient to evacuate the colon at regular intervals, avoiding impaction of feces and reducing fecal incontinence. Antegrade enemas can be delivered through an appendicostomy or a cecostomy button with both techniques providing a high success rate varying between 52% and 92% among the different studies. 45 The occurrence of complications varies, and include development of granulation tissue, leakage around the tube, tube dislodgment, skin infection, fecal incontinence, channel stricture or perforation, stoma stenosis and luminal obliteration if the channel is not catheterized regularly.

Neuromodulation

During neuromodulation the sacral nerves are stimulated per or transcutaneously and is used in children with refractory constipation. The mechanism of action is modulation rather than stimulation and, therefore, it is called sacral neuromodulation. Sacral neuromodulation has been successfully applied in adult patients with combined fecal incontinence and urological symptoms as well as in those with functional constipation only. 46

Interferential therapy is another technique wherein the proposed mechanism of action is via neuromodulation. This technique uses transcutaneous electrical stimulation with 4 surface electrodes that produce 2 sinusoidal currents that cross within the body. This approach is considered less invasive and less expensive compared to the percutaneous approach. A RCT showed that transcutaneous electrical stimulation was effective in improving colonic activity, fecal incontinence, and quality of life in children with slow transit constipation.

Followup and Referral

Although most children with constipation will respond to conventional treatment, a minority of patients remains with symptoms of infrequent painful defecation and fecal incontinence.³⁷ Studies have estimated constipation remission rates to range between 60% and 90% after 6 months of treatment.³² Therefore, referral to a pediatric gastroenterologist is advised when 6

months of consistent and documented intervention of laxatives and a toileting program have not resulted in amelioration of symptoms.

CONCLUSIONS

Evaluation of bowel habits is recommended as an integral part of the initial assessment of a child presenting with lower urinary tract symptoms. Childhood constipation is a common, frustrating and long lasting disorder worldwide. A thorough medical history and a complete physical examination are necessary to rule out most organic causes of constipation. Only in atypical cases or when conventional treatment fails, additional diagnostic tools might be useful to exclude pathology. Adequate and prolonged treatment with behavioral interventions and medication is required to regain normal bowel habits since this condition is not self-limiting. This is even more vital since constipation can have a major role in the function and dysfunction of the lower urinary tract in children. Further research into the exact mechanisms of rectal-bladder interactions and the pathophysiological connections between fecal retention and lower urinary tract dysfunction in children is justified. Moreover, development of new treatment strategies involving the brain-bowel and brain bladder axes is necessary given the fact that a subgroup of children with constipation with or without fecal incontinence fails to achieve a successful clinical outcome even after intensive medical and behavioral treatment.

APPENDIX 1

The Rome III pediatric criteria for functional constipation and FNRFI

Functional constipation

Must include 2 or more of the following in a child with a developmental age of 4 years or older with insufficient criteria for a diagnosis of irritable bowel syndrome:

2 or fewer defecations per week

1 or more episodes of fecal incontinence per week

History of retentive posturing or excessive volitional stool retention

History of painful or hard bowel movements

Presence of a large fecal mass in the rectum

History of large diameter stools that obstruct the toilet

FNRFI (nonretentive fecal incontinence)

Must include all of the following in a child with a developmental age of at least 4 years:

Defecation in places inappropriate to the social context at least once per month

No evidence of an inflammatory, anatomical, metabolic or neoplastic process

No evidence of fecal retention

Adapted from Rasquin et al.8

APPENDIX 2

Oral laxative maintenance treatment

Osmotic Lactulose
Magnesium hydroxide
PEG 3350/4000

1-3 ml/kg 1 or 2 times daily 1-3 ml/kg of 400 mg/5 mL 0.26-0.84/gm/day Flatulence, abdominal discomfort Hypermagnesemia due to concurrent renal failure Loose stools, bad taste, abdominal distention, abdominal pain, nausea

APPENDIX 2 (continued)

Mineral oil (liquid paraffin) Lubricant Bisacodyl oral

Bisacodyl rectal

Less than 1 year; not recommended Older than 1 year: 1-3 ml/kg/day 5 mg every other day - 10 mg daily

5 mg every other day - daily (suppositories)

Senna 2-6 years old: 2.5Y7.5 mL/day 6-12 years old: 5Y15 mL/day

Available as syrup, 8.8 mg of sennosides/5 mL. Also available as granules and tablets

Bad taste, anal leakage, aspiration pneumonia (more than 12 months,

dysphagia)

Abdominal cramps, abdominal pain, diarrhea

Abdominal cramps, anal irritation Abdominal cramps, melanosis coli

Adapted from Mugie et al.5

Stimulants

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EDITORIAL COMMENT

We would like to provide additional insight regarding the undeniable relationship between constipation and pediatric urological conditions. Burgers et al claim, "urologists frequently report constipation in up to 50% of children seen for LUTS." We would hypothesize that this number is closer to 90% to 100%.

In addition, the authors state that parent reports of stool symptoms are not reliable, yet the offered Rome III criteria to diagnose constipation depend on an accurate history. According to the Rome III criteria, one must have more than 2 of 6 criteria. However, 5 of the 6 criteria are based on history alone. Therefore, using the Rome III criteria, constipation will be under diagnosed.

We propose that the voiding diary and ultrasound before treating constipation are unnecessary. Any abnormalities may simply be related to the constipation and not bladder dysfunction. Our recommendation is to merely assume that all patients who present with LUTS are constipated. This assumption obviates the need for inaccurate diaries and ultrasound, thereby decreasing cost and time.

In summary, should we consider the term stool retention instead of constipation in caring for children with LUTD? Stool retention speaks to the actual behavior that caused the problem and gets away from the taboo term of constipation.

Angelique Champeau and Laurence Baskin

UCSF Children's Hospital San Francisco, California