dear Colleagues,

In the November issue of the Journal of Pediatric Surgery, an article was announced by Peña et al. "Enema-Induced Spastic Left Colon Syndrome: An Unintended Consequence of chronic Enema Use" [1], which raised a very important problem arising in the treatment of patients with severe chronic constipation and fecal incontinence. The authors describe 22 patients complaining of increasing time to evacuate the enema fluid along with enemainduced colicky abdominal pain. Unfortunately, in the study, numerous mistakes were made that distorted the essence of the problem. Alerting the scientific community about serious complications that are allegedly caused by enemas can cause restrictions on the use of enemas (antegrade and retrograde), which, according to numerous authors, have shown a sustained improvement in bowel management and quality of life without serious complications.

1. X-ray analysis

The authors report that "Contrast studies in these patients have shown a startling picture of severe dilatation of the right colon, followed distally by a very impressive, narrow, left portion of the transverse colon, as well as descending and rectosigmoid colon" (see Figs. 1 and 2)". In signatures to radiographs lack important data: age, diagnosis, surgery, duration, and dose of treatment with Senna drugs, results of histological and manometric studies. Below is an analysis of these radiographs (**Figure 1**).

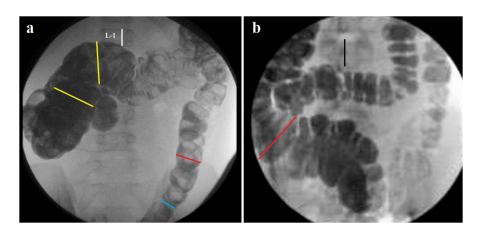


Figure 1. Radiographs from the peer-reviewed article. (a) (Figure 1) with the caption "Contrast enema shows dilated right and narrow left colon". The patient's age is not known. His sigmoid colon was removed, but the diagnosis is not specified in the article. The cecum is superimposed on the ascending and right side of the transverse colon. Knowing that in children 15 years of age, the L-1 body height is 2.2 cm, we calculated the approximate width of the ascending intestine (yellow line - 6 cm). The descending colon without gaustrations looks like a rosary. It consists of successive segments 3.3 cm wide (red line) with gaps between them 2.2 cm wide (blue line) (norm 2.5-3.2 cm). (b) In Figure 2, with the caption "Five representative contrast enemas showing dilated right and narrow, spastic left", the right half of the colon is visible in only one X-ray (b). Its width is 4.6 cm (norm 5.28 ± 0.32 cm). The descending colon contracted after partial emptying. In the remaining 4 cases, the right half of the large intestine is not visible. They have obvious symptoms of colitis.

The authors assessed the width of the colon lumen by comparing the right half with the left as if they must be equal. However, the width of different departments is equal only in children of the first year of life. In the process of ontogenesis, the width of the lumen of all departments increases, but not evenly. So, for example, already in adolescence, the width of the ascending colon is almost 3 times wider than that of the descending colon (**Figure 2**) [2].

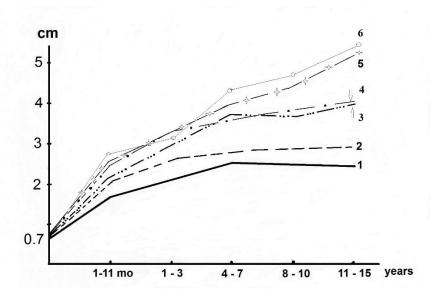


Figure 2. Scheme of expansion of the different parts of the colon and rectum in different age groups: 1-sigmoid colon; 2-descending colon; 3- rectum; 4 - transverse colon; 5 - cecum; 6 - ascending colon.

Since the average patient age was 19.6 years (range, 8–54), we accepted both patients as adults. Comparing the measurement results in Figure 1.a with the standards in Table 1 [2], we are convinced that these sizes do not go beyond the age limit. Nevertheless, in Figure 1a, the X-ray picture indicates a high tone of the descending colon, where fecal lumps are compressed in the intestine in the form of a rosary. Stretching of the intestine with water causes severe pain, which is characteristic of irritable bowel syndrome [3]. Figure 1.b shows a moderately dilated and elongated sigmoid colon and an almost empty descending colon after emptying. Feces in the rectum prevent complete emptying.

Table 1 Normal size of the anal canal, rectum and colon in children of different ages (modified from
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Age	Statistical indicators	Anal canal length	Widths of different parts of the intestine (cm)						Height of	Volume of
			Rectum	Sigmoid colon	Descending colon	Transverse colon	Ascending colon	Cecum	the cecum dome	the colon (mL)
1–11 months	n	7	12	12	11	10	10	10	9	9
	Fluctuations	1.7–2.5	1.3-3.0	1.4–2.0	1.7-2.4	2.3–2.7	2.4-3.4	2.4-3.0	1.4–2.7	350–800
	Mean (M±m)	2.2±0.15	2.24±0.09	1.73±0.06	2.05±0.06	2.51±0.07	2.71±0.13	2.62 ±0.10	2.13±0.12	562±38
1-3 years	n	7	9	9	8	7	6	6	6	6
	Fluctuations	2.3–2.8	3.0-3.7	1.8–2.4	2.3–2.5	2.4–3.8	2.5-3.6	2.5–3.6	2.4–3.5	600-800
	Mean (M±m)	2.55±0.10	3.21±0.11	2.11±0.08	2.54±0.08	3.02±0.23	3.09±0.27	3.26±0.21	2.95±0.13	675±12
4–7 years	n	9	9	8	9	8	7	6	7	8
	Fluctuations	2.5–3.6	3.0-3.9	2.4–2.6	2.6–2.9	2.9-4.2	3.2-5.4	3.2–4.6	3.5–4.2	650-1,100
	Mean (M±m)	3.17±0.14	3.43±0.14	2.52±0.03	2.76±0.07	3.75±0.15	4.24±0.35	3.95±0.26	3.72±0.10	910±16
8-10 years	n	18	19	19	19	18	18	15	13	17
	Fluctuations	2.6-3.7	3.2-4.1	2.1-2.6	2.5-3.2	3.0-4.3	3.6-5.7	3.6-5.4	3.5–4.9	750-1,200
	Mean (M±m)	3.11±0.10	3.72±0.05	2.41±0.03	2.81±0.06	3.56±0.09	4.62±0.17	4.35±0.16	4.02±0.24	1,000±21
11-15 years	n Fluctuations Mean (M±m)	13 3.1–3.9 3.43±0.10	15 3.6–4.6 3.95±0.07	13 2.2–2.6 2.36±0.03	15 2.5–3.2 2.82±0.05	14 3.6–4.4 3.89±0.15	11 3.9-6.4 5.28±0.32	13 3.9-6.0 5.10±0.21	11 3.8–5.2 4.46±0.19	15 900-1,200 1,050±32

Figure 3. Table of the normal size of the anal canal, rectum, and all parts of the colon in children of different ages [2].

Thus, firstly, none of the 7 presented radiographs showed the expansion of the right colon. Second, in six cases, the tone of the descending intestine was clearly increased, there was no haustration, its lumen was narrowed in five of them. This picture could be interpreted as evidence of colitis, but given the severe pain during the enema, the likelihood of a severe form of irritable bowel syndrome (IBS) is high. We observed an elderly patient with this form of IBS in whom, after many years of using laxatives, including Senna's preparations, the left half of the colon had difficulty passing fecal stones, despite many hours of trying to remove them

with an enema. Relief came after performing a colostomy on the right the colon (**Figure 4**) [4].

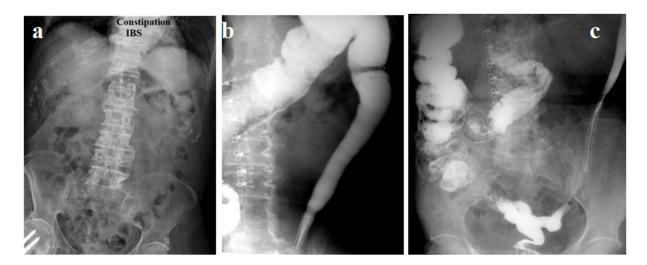


Figure 4. Radiographs of a 62-year-old woman with severe IBS, taken prior to a right-sided colostomy. (a) A frontal radiograph shows a symptom of a rosary in the descending colon. The right half of the colon is also narrowed. (b) During a barium enema, a sharply narrowed descending bowel is visible. (c) After emptying, a narrowed sigmoid colon, a spastic descending colon, and a narrowed right half of the colon are seen.

II. Analysis of literary sources (References)

To find out if this condition had been reported before, authors selected the papers specifically describing the antegrade or retrograde use of enemas for the treatment of fecal incontinence, severe intractable constipation. In analyzing the articles cited by the authors, only two of the 36 articles mention pain during an enema. In children with slow-transit constipation, "abdominal pains were relieved significantly (P <.05), and appetite and mood improved. Slow evacuation (12 of 29) and pain with an enema (17 of 20) were also common" [5]. However, the pain during the enema did not appear after numerous procedures, but at the beginning of treatment. Therefore, enemas were not the cause of this condition. In another study, the reasons for refusing enemas were catheter expulsion, rectal balloon bursting, instilled water leakage or retention, pain during irrigation, anal bleeding, anal fissure. However, even in these observations, we are talking about refusal in the first days and weeks of treatment [6]. In the systematic review and meta-

analysis by Emmett et al, it is emphasized: "Adverse events were inconsistently reported but were commonplace and minor"[7]. The most common reason for discontinuing enemas is disappointment with treatment results [5-7].

Thus, the analysis of the literature does not give any reason to suspect that the long-term use of antegrade and retrograde enemas can lead to serious damage to the colon, such as colitis or irritable bowel syndrome.

III. Bowel management by Pena et al.

It is known from the literature that the bowel management program includes after amount of laxative that will empty their colon effectively, which usually is higher that what they previously received and is 2, 3, 4, 5 or 10 times more than what the books recommend. After that we determine the amount of laxative needed daily to empty the patient's colon. To achieve this, we increase the amount of laxative (usually a senna derivative) on a daily basis, taking daily abdominal films, until we find the dosage that provokes a complete emptying of the colon as radiologically demonstrated. It takes a certain amount of time and explanation to convince the patient that there is no sensation inside the rectum" [8]. It turned out that Senna causes severe abdominal pain. In the article of Bischoff et al a protocol to treat idiopathic constipation was presented. All patients are started on a Sennabased laxative. If the dose of the laxative provokes abdominal cramping, distension, and vomiting, without producing bowel movements, patients are considered nonmanageable [9]. Detailed protocol analysis is given in a letter to the editor [10].

Discussion and conclusion

It is known that saline solution has been used for cleansing enemas for many decades, and so far, no negative effect on the human body has been found. This solution is widely used for intravenous and interstitial administration. And this

review of several thousand patients who were treated with enemas for a long time did not find any negative effects of the saline solution on the colon.

In the systematic review for evaluating critically the evidence regarding the adverse effects of herbal medicines, serious adverse effects were noted only for four: Herbae pulvis standardisatus, Larrea tridentate, Piper methysticum and Cassia senna [11]. Senna preparations cause a strong contraction of the muscle layer of the colon. The use of this laxative causes abdominal pain because of severe muscle spasm. Long-term use of large doses of Senna causes irreversible damage to the motor function of the colon, which is more pronounced in the left half. The amount of enema fluid that normally causes only the sensation of movement causes, in patients with irritable bowel syndrome causes severe pain. Thus, Senna is a damaging factor, and an enema is a pain provocateur.

References

- 1. Peña A, de La Torre L, Belkind-Gerson J, Lovell M, Ketzer J, Bealer J, Bischoff A. Enema-Induced Spastic Left Colon Syndrome: An Unintended Consequence of chronic Enema Use. Pediatr Sugr. 2020 Nov doi.org/10.1016/j.jpedsurg.2020.10.027
- 2. Levin MD^{1,2}. Reaction to Koppen et al., 'Assessing colonic anatomy normal values based on air contrast enemas in children younger than 6 years'. Pediatr Radiol. 2018 Jun 30. doi: 10.1007/s00247-018-4181-1.
- 3. Ritchie J. Pain from distension of the pelvic colon by inflating a balloon in the irritable colon syndrome. Gut. 1973 Feb;14(2):125-32. doi: 10.1136/gut.14.2.125.
- 4. Levin MD, Korshun Z, Mendelson G. Rare case of surgical treatment of the irritable bowel syndrome. Novosti chirurgii. 2012; 20 (5):123-6.
- 5. Marshall L, Hutson JM, N Anticich N, Stanton MP. Antegrade continence enemas in the treatment of slow-transit constipation. J Pediatr Surg. 2001 Aug;36(8):1227-30. doi: 10.1053/jpsu.2001.25768.
- 6. Bildstein C, Melchior C, Gourcerol G, et al. Predictive factors for compliance with transanal irrigation for the treatment of defecation disorders. World J Gastroenterol. 2017 Mar 21;23(11):2029-2036. doi: 10.3748/wjg.v23.i11.2029.
- 7. Emmett CD, Close HJ, Yiannakou Y, Mason JM. Trans-anal irrigation therapy to treat adult chronic functional constipation: systematic review

- and meta-analysis. BMC Gastroenterol. 2015 Oct 16;15:139. doi: 10.1186/s12876-015-0354-7.
- 8. Bischoff A, Levitt MA, Peña A. Bowel management for the treatment of pediatric fecal incontinence. Pediatr Surg Int. 2009 Dec;25(12):1027-42. doi: 10.1007/s00383-009-2502-z. Epub 2009 Oct 15.
- 9. Bischoff A, Brisighelli G, Dickie B, Frischer J, Levitt MA, Peña A. Idiopathic constipation: A challenging but manageable problem. J Pediatr Surg. 2018 Sep;53(9):1742-1747. doi: 10.1016/j.jpedsurg.2017.09.022.
- 10. Levin MD. Letter to the editor ("Are Senna based laxatives safe when used as long treatment for constipation in children?"). J Pediatr Surg. 2018 Aug;53(8):1634-1635. doi: 10.1016/j.jpedsurg.2018.03.007. Epub 2018 Mar 20.
- 11. Posadzki P, Watson LK, Ernst E. Adverse effects of herbal medicines: an overview of systematic reviews. Clin Med (Lond). 2013 Feb;13(1):7-12. doi: 10.7861/clinmedicine.13-1-7.