Dear colleagues,

Recently, a huge number of articles have appeared on manometry of the colon and anorectum in functional constipation (FC). Unfortunately, this coincided with a historical decline in morals called political correctness. In practice, this means a lack of discussion and critical analysis of published works. Through this mental breach, huge amounts of money from medical equipment manufacturers are poured in, and in their own interests, they direct the solution of medical problems. I decided to analyze the impact of colonic manometry on the diagnosis and treatment of FC. I will start with the recently published article by Gupta et al "Surgically treated intractable constipation in children evaluated with colonic manometry." [1].

1. Scientific criteria in this area of knowledge are not presented.

A) "Intractable constipation (IC) was defined as unresponsive to optimal conventional treatment for at least 3 months" [2]. This definition does not make sense, since multiple methods of treatment of FC are described [3,4,5] and there is no article that would compare them and determine the most optimal one. Such work is not justified in terms of political correctness, because it can offend many researchers and embarrass the author of the article. Can, for example, be considered the optimal tactics of conservative treatment of FC in the Peña and Levitt colorectal centers? "The initial dosage Senna is empirically determined and adjusted daily, during a one-week period, until the amount of Senna that empties the colon is reached (range: 5–175 mg). If the dose of the laxative provokes abdominal cramping, distension, and vomiting, without producing bowel movements, patients are considered non manageable" [3]. Such large doses of Senna are not recommended for children, especially since in such cases not only the tone of the colon and rectum increases but also the tone of the anal canal, which prevents the emptying of the rectum. «It is important to stress that the untoward effects which may result from laxative abuse could be greater than

those of constipation" [6]. Thus, the authors of the peer-reviewed article hospitalized patients diagnosed with 'Intractable constipation' who did not receive optimal treatment.

B) Knowledge of the etiology and pathogenesis of FC is the key to effective diagnosis and treatment of the disease. On this issue, the article cites conflicting assumptions and not a single scientific study. For example, a reference to an article by Levitt et al [7] states: "Different etiological explanations exist, which can be broadly categorized as normal transit, panintestinal dysmotility, isolated colonic dysmotility or evacuation disorders." First, there is no evidence in the paper by Levitt et al. Secondly, the same group of authors published an article in which, because of methodological errors, they came to the paradoxical conclusion that the upper limit of the normal width of the rectum in children under 5 years of age is the same (6.5 cm) as in adults [8,9]. Thus, the authors believe that in all children with FC, the rectal width is within the normal range (i.e., less than 6.5 cm). From which they make a false conclusion that the cause (etiology) of FC is in the primary dysfunction of the clearly dilated colon. Thirdly, since 2017, the criterion for selecting patients for surgery in the Peña and Levitt colorectal centers is the response to high doses of Senna and not the results of manometry [3]. В 2010 году Dinning and Di Lorenzo believed that "Colonic motor dysfunction remains the leading hypothesis to explain symptom generation in the most severe cases of chronic constipation" [10]. Since then, no studies have been published to prove that chronic constipation is due to primary damage to the colon. Therefore, the reference to this article that allegedly "'colonic dysmotility' as a distinct entity in children with slow transit constipation (STC)" is not correct.

The authors further write: "It has been suggested that apart from colonic dilatation, fecal stasis and immaturity of the enteric nervous system may contribute to dysmotility". "Whether this is a cause or an effect, or whether the two conditions should be regarded as synonymous, is debatable" [1]. Usually, a

hypothesis is based on known scientific facts and one assumption, which together create a new understanding of the phenomenon. But if a hypothesis is based on assumptions alone, it leads to absurdity. (cause and effect cannot be synonymous).

C) An alternative hypothesis of the etiology and pathogenesis of FC is not mentioned at all, although it is recognized by most researchers and explains all the clinical, manometric, and radiological features of FC.

The etiology of FC flawlessly reflected in the Nurko and Zimmerman article: «Outside of the neonatal period, childhood constipation is usually functional (i.e., there is no evidence of an organic condition). Functional constipation is most commonly caused by painful bowel movements that prompt the child to voluntarily withhold stool. To avoid the passage of another painful bowel movement, the child will contract the anal sphincter or gluteal muscles by stiffening his or her body, hiding in a corner, rocking back and forth, or fidgeting with each urge to defecate. Withholding of stool can lead to prolonged fecal stasis in the colon with reabsorption of fluid, causing the stool to become harder, larger, and more painful to pass. Over time, as the rectum stretches to accommodate the retained fecal mass, rectal sensation decreases, and fecal incontinence may develop. This cycle commonly coincides with toilet training, changes in routine or diet, stressful events, illness, or lack of accessible toilets, or occurs in a busy child who defers defecation» [11].

Pathogenesis of FC. The reason for the violation of the evacuation of feces from the rectum is the discrepancy between the large width of the feces with the maximal width of the open anal canal. Those volumes of feces that normally cause a defecation reflex, in FC (megarectum) cause a retention reaction, i.e., a contraction in PRM and EAS. When the stool volume reaches the width that causes the defecation reflex, the stool is too wide. The passage of wide stool through the anal canal causes pain and resistance of the child, who by voluntary

contraction of the EAS stops defecation. This creates a vicious circle that leads to the megarectum and megacolon **(Figure 1).**

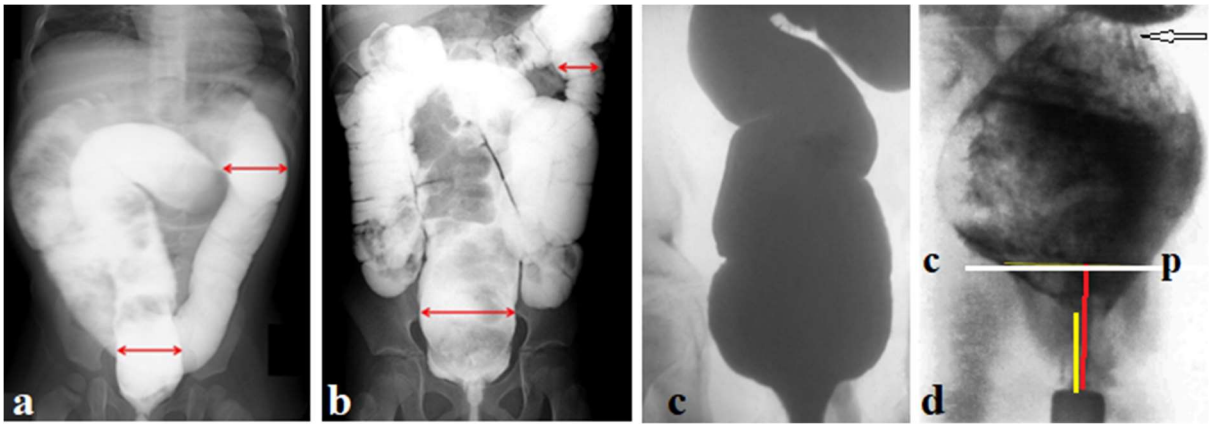

Figure 1. Radiographs **(a, b)** with contrast enema in patients with FD from the article by Bischoff et al [3]. In both cases, there is an expansion of the rectum and megacolon. **(c, d)** Radiographs with barium enema in frontal and lateral position of patient 11 years old with FC and descending perineum syndrome. (d) The red line shows how long the anal canal should be at this age. The yellow line is a functioning anal canal. The black arrow shows the contraction of the rectosigmoid sphincter (RSS). White line - pubococcygeal line. The true diameter of the marker located near the anus is 1.6 cm.

The key to understanding the pathogenesis of FC and diagnosing the disease is the triad of symptoms: the width of the rectum, the length of the functioning anal canal, and the general characteristic of the size of the colon (megacolon) [12].

1**) The rectal width.** The rectal width is measured on a lateral radiograph. In Figure 1a, the width of the rectum is significantly smaller than in Figure 1b. However, these patients are of different ages. The width, which is normal for a 14-year-old patient, is a sign of a megacolon for a 4-year-old patient. To accurately evaluate the rectal width, it must be compared with the age norm **(Table 1).**

Table 1. The normal size of the rectum and anal canal in different ages.

Ages	The width of the rectum (cm)	The length of the anal canal (cm)
5 days – 11 months	1.3 – 3.0 (2.24±0.09)	1.7 – 2.5 (2.21±0.15)
1 – 3 years	3.0 – 3.7 (3.21±0.11)	2.3 – 2.8 (2.55±0.10)
4 – 7 years	3.0 – 3.9 (3.43±0.14)	2.5– 3.6 (3.17±0.14)
8 – 10 years	3.2 – 4.1 (3.72±0.05)	2.6 – 3.7 (3.11±0.10)
11 – 15 years	3.6 – 4.6 (3.95±0.07)	3.1 – 3.9 (3.43±0.10)
23 – 64 years	3.5 – 4.8 (3.95±0.21)	3.4 – 4.2 (4.08±0.07)

2) The anal canal length. A strong peristaltic wave of the rectum, which starts from the rectosigmoid sphincter (RSS), tries to push the stool through the anal canal. However, the anal canal cannot pass feces of this diameter. Repeated bougienage of feces results in stretching and weakening of the pelvic floor muscles (levator plates and puborectalis muscles). Radiographically, this is manifested by shortening of the functioning anal canal (**see Figure 1d**). This picture is called descending perineum syndrome [13] and often combined with encopresis.

3) The value of megacolon (constant- C) is determined by the formula:

$$C = \frac{R \times V \times K}{h};$$

Where: C-constant, V-colon volume (ml) after filling the empty colon with barium to the cecum, R- rectal width (cm); K -projection distortion factor, which is the ratio of the true width of the marker, which is located near the anus, to its image on the radiograph; h – the patient's height. In healthy children, "C" is "31", regardless of age. In patients with FC, it is always more than 31. We subdivide megacolon into 3 degrees: 1st degree (C=32-45), 2nd degree (C=46-60), 3rd degree (C > 60). Comparison of "C" before and after treatment allows you to accurately determine the dynamics of the process.

X-ray analysis showed that all children with FC have an expansion of the rectum and a varying degree of megacolon, which indicates the obstructive nature of the pathological process. Anorectal reflexes are stimulated by rectal pressure. Those volumes of rectal balloons, which normally cause rectal defecation pressure, in patients with megarectum cannot cause a threshold defecation pressure. On the contrary, it stimulates a rectoanal inhibitory reflex and the associated retention reaction, i.e., a contraction of PRM and EAS. This is not a paradoxical [14], but a normal reaction of anal sphincters in megarectum. Failure to respond to conventional rectal balloon volumes [15] is not evidence of rectal hyposensitivity. It is described that stagnation of wide feces in the rectum causes a deficiency of mucosal nerves [16]. Obviously, with megarectum and megacolon, the area of the mucous membrane is sharply increased. Naturally, a unit of the area contains fewer nerve elements than normal. Shafik and El-Sibai found that the pressure of the lower esophageal sphincter and pyloric sphincter significant rise ($p < 0.05$) with rectal distension up to 70 ml [16]. This is a reflex slowing down of the peristalsis of the digestive tract to prevent overfilling of the rectum. Obviously, the slow transit constipation in megacolon serves the same function. An extended colon with a hypertrophic wall can not create the same peristaltic waves as a healthy gut. From this, it follows that the expansion of the colon with lengthening of the sigma, as well as changes in its wall, delayed transit through the colon, and disturbance of peristalsis is the result (complication) of a violation of the evacuation of the rectum.

2. Diagnostic capabilities of the colonic manometry

A) Indiscriminate quotation. Referring to the article by Koppen et al, the authors write: Colonic manometry has been recommended as a diagnostic modality in children with IC to evaluate pathophysiology and underlying neuromuscular abnormality [17]. However, there are no such recommendations in this article.

B) The authors unreasonably excluded children with "foregut bowel motility disturbances or anorectal retention (as defined by high internal anal sphincter pressure or dyssynergia on anorectal manometry".

1). As shown above [16], FC may be accompanied by foregut bowel motility disturbances.

2). Anorectal manometry cannot differentiate the pressures of different sphincters. Hou et al found no significant differences between FC and control in median resting anal sphincters pressure [18]. Anal pressure can be relatively high, for example at the onset of the disease, because of a spasm of the PRM. It can be low, especially in descending perineum syndrome. The authors unreasonably assumed that they excluded patients with obstructive constipation and examined patients in whom the root cause of FD is dysfunction of the colon. This hypothesis has no scientific basis.

3). "Colonic manometry findings were classified as normal, left-sided colonic dysfunction (abnormal findings proximal to descending colon) and total colonic dysfunction (when abnormalities were noted in the entire colon)" [1]. Neither digital nor descriptive characteristics are presented in the article. These results are difficult to trust since they cannot be verified. They cannot be compared with other studies and cannot be used. The results of the manometric study contradict the conclusions of the authors, which state that colonic manometry should be seen as a useful diagnostic test. There is no information in the article that colonic manometry in any way influenced the tactics of treatment. For example, 8 (14%) patients were operated on despite normal manometry findings.

3. Surgical treatment

This paragraph contains only excerpts from the analyzed article. "Overall, 39 children underwent an ACE, 21 a colostomy and 21 an ileostomy with a high risk of complications. The complications of an ACE stoma are potentially avoidable

with the use of transanal irrigation. At 3.2 years (4 months–9.9 years) follow-up, 18 remain on ACE washout, 9 on colostomy, 19 on ileostomy, and 10 are off all treatment and doing well. A successful outcome was defined as adequate decompression (no longer fulfilling the Rome IV criteria for functional constipation in those without a stoma, or having a functional stoma) without need for further unplanned surgical intervention" [1].

Thus, by the time of this writing, 10 (22%) of 46 patients have recovered. The remaining 36 (78%) patients remain with different intestinal stomas. Since the authors do not compare these results with another group of patients, it is not possible to evaluate their results. Are they better or worse than other treatments? The authors' remark that ACE stoma is potentially avoidable with the use of transanal irrigation seems rational. From a physiological point of view, antegrade and retrograde enemas do not differ from each other. Antegrade enema was proposed for adult patients after oncological operations, with damage to the spine, etc., so that it was convenient for them to take care of themselves. Children who are cared for by parents do not have this goal. However, this idea is not supported by scientific facts. Why 18 remain on ACE washout despite the possibility of multiple complications? Twenty children (18 with stoma and 2 with ACE) underwent repeat manometry 2.2 years (10 months–7.6 years) after surgery, but the results of manometry did not affect treatment tactics.

Conclusion.

Gupta et al reported on the surgical treatment of some patients with FC. There is not a single proven scientific fact in this article. From the point of view of etiology and pathogenesis, it is a one-sided compilation of assumptions. A manometric study confirmed the already known fact that in some patients with FC, the motility of the large intestine differs from the norm. This study showed low sensitivity of the described method since theoretically all patients with FC should have impaired motor function of the colon. As can be seen from the study, colonic

manometry did not affect treatment tactics and did not evaluate the results of the operation with its help. Therefore, the authors' assertion that colonic manometry should be seen as a useful diagnostic test is unfounded.

Two especially important questions remain: (1) Who and why gave a positive review of this article? (2) Why GEORGE W. HOLCOMB, III, M.D., MBA; the Editor-in-Chief of the Journal of Pediatric Surgery published this article?

References

1. Gupta A, Basson S, Borrelli O, et al. Surgically treated intractable constipation in children evaluated with colonic manometry. J Pediatr Surg. 2020 Feb;55(2):265-268. doi: 10.1016/j.jpedsurg.2019.10.046.
2. Tabbers MM, DiLorenzo C, Berger MY, et al. Evaluation and treatment of functional constipation in infants and children: evidence-based recommendations from ESPGHAN and NASPGHAN. J Pediatr Gastroenterol Nutr. 2014 Feb;58(2):258-74. doi: 10.1097/MPG.0000000000000266.
3. Bischoff A, Brisighelli G, Dickie B, et al. Idiopathic constipation: A challenging but manageable problem. J Pediatr Surg. 2018 Sep;53(9):1742-1747. doi: 10.1016/j.jpedsurg.2017.09.022.
4. Zar-Kessler C, Kuo B, Belkind-Gerson J. Botulinum toxin injection for childhood constipation is safe and can be effective regardless of anal sphincter dynamics. J Pediatr Surg. 2018 Apr;53(4):693-697. doi: 10.1016/j.jpedsurg.2017.12.007.
5. Bharucha AE, Wald A. Chronic Constipation. Mayo Clin Proc. 2019 Nov;94(11):2340-2357. doi: 10.1016/j.mayocp.2019.01.031.
6. Shafik A. Constipation. Pathogenesis and management. Drugs. 1993 Apr;45(4):528-40. doi: 10.2165/00003495-199345040-00005.
7. Levitt MA, Mathis KL, Pemberton JH. Surgical treatment for constipation in children and adults. Best Pract Res Clin Gastroenterol. 2011 Feb;25(1):167-79. doi: 10.1016/j.bpg.2010.12.007.
8. Koppen IJN, Yacob D, Di Lorenzo C, et al. Assessing colonic anatomy normal values based on air contrast enemas in children younger than 6 years. Pediatr Radiol. 2017 Mar;47(3):306-312. doi: 10.1007/s00247-016-3746-0.
9. Levin MD. Reaction to Koppen et al., 'Assessing colonic anatomy normal values based on air contrast enemas in children younger than 6 years'.

Pediatr Radiol. 2018 Oct;48(11):1674-1677. doi: 10.1007/s00247-018-4181-1.
10. Dinning PG, Di Lorenzo C. Colonic dysmotility in constipation. Best Pract Res Clin Gastroenterol. 2011 Feb;25(1):89-101. doi: 10.1016/j.bpg.2010.12.006.
11. Nurko S, Zimmerman LA. Evaluation and treatment of constipation in children and adolescents. Am Fam Physician. 2014 Jul 15;90(2):82-90.
12. Levin MD. Radiological anatomy of the colon and rectum in children. Gastroenterology & Hepatology. 2019; 10 (2):82-6. (Open access).
13. Levin MD. Pathophysiology and diagnosis of descending perineum syndrome in children. (2018) Pelviperineology. 37(2):52-56. (Open access).
14. Rao SS, Welcher KD, Leistikow JS. Obstructive defecation: a failure of rectoanal coordination. Am J Gastroenterol. 1998 Jul;93(7):1042-50. doi: 10.1111/j.1572-0241.1998.00326.x.
15. Gladman MA, Aziz Q, Scott SM, et al. Rectal hyposensitivity: pathophysiological mechanisms. Neurogastroenterol Motil. 2009 May;21(5):508-16, e4-5. doi: 10.1111/j.1365-2982.2008.01216.x.
16. Shafik A, El-Sibai O. Esophageal and gastric motile response to rectal distension with identification of a recto-esophagogastric reflex. Int J Surg Investig. 2000;1(5):373-9.
17. Koppen IJN, Kuizenga-Wessel S, Lu PL, et al. Surgical decision-making in the management of children with intractable functional constipation: What are we doing and are we doing it right? J Pediatr Surg. 2016 Oct;51(10):1607-12. doi: 10.1016/j.jpedsurg.2016.05.023.
18. Hou XY, Wang LY, Wang WL, Li Y, Bai YZ. [Clinical significance of detection of internal anal sphincter in children with functional constipation]. Zhonghua Wei Chang Wai Ke Za Zhi. 2011 Oct;14(10):753-5.