Dear Colleagues,

I offer an analysis of published work on the diagnosis and treatment of "cloacal" malformation. 30 years ago, there was a change of ideas about the pathological physiology of cloacal malformation. Most of the cases that came to be called cloaca 30 years ago, before that were considered as ARM with fistulas in the vestibule or in the vagina. These changes occurred without prior scientific studies that would justify these changes. Since then, all articles on the cloaca are statistical reports on the application of the proposed, but not reasonable methods of treatment. I did not find any evidence that changing the concept improved the results of treatment. On the contrary, the results of treatment of cloaca are worse than the results of treatment of vestibular and vaginal fistulas.

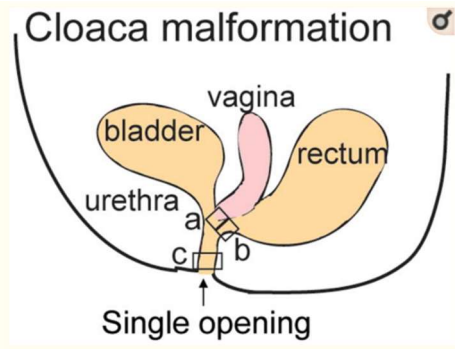
In order not to make mistakes, it is necessary to rely only on scientific facts. You cannot trust the assumptions or unfounded statements. I added a few researchers to the list of the Forum who published articles on the cloaca. I hope that their experience will help get rid of the misconceptions for the benefit of science and for the sake of a better future for our patients.

Respectfully

Michael Levin

P.S. Details on the pathological physiology of ARM can be found on my website: http://www.anorectalmalformations.com/

Recently, in the journal "Frontiers in Pediatrics" was published an article by Wood et al "Cloacal malformations: technical aspects of the reconstruction and factors which predict surgical complexity" [1]. This article provides erroneous data on the pathological anatomy and physiology of the anorectal malformations and on the cloaca. Therefore, the diagnostic and treatment methods described therein are not adequate. Cloaca result from the total failure of the urogenital septum to descend. In this most severe form of congenital anomalies in females, the rectum, vagina, and urethra fail to develop separately and drain via a single common channel known as a cloaca into the perineum (**Figure 1**)



[2]. Fig. 2
Analysis of different regions of the common channel found in cloaca malformation

Figure 1. In cloaca malformation, the urethra, vagina and rectum fail to separate, and drain via a single common channel. From article Gupta et al. [2]

However, the article deals with pathology, where the division into urogenital and rectal parts has already occurred, which means that the embryo has successfully passed the cloacal stage.

Until the early 80s of the 20th century, the authors described isolated cases of cloaca. Probably, Hendren was the first to expand the concept of "cloaca" when «... described 13 more cases of urogenital sinus malformation with an anorectal anomaly, usually rectal atresia with rectovaginal fistula" [3]. Since then, under the name of the "cloaca" began to operate females with vaginal fistula, and the vestibular fistula (**Figure 2**).

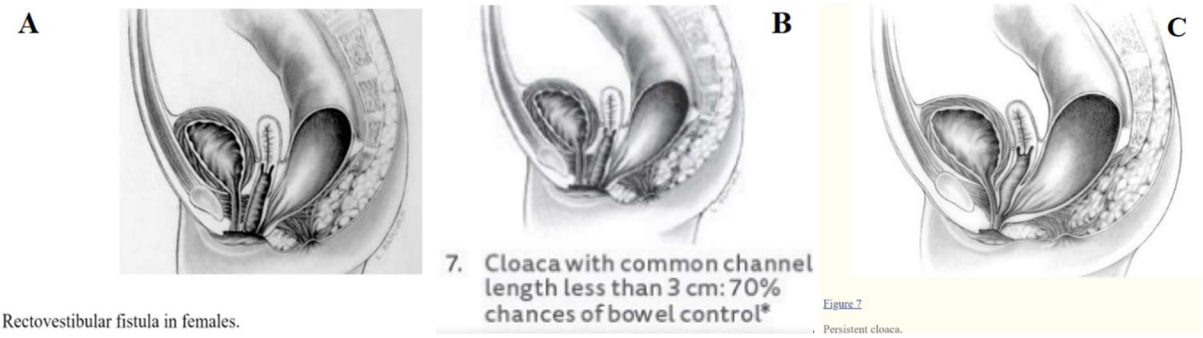


Figure 2. (**A)** The scheme of ARM with vestibular fistula from the article Levitt and Peña [4]. **(B)** It can be verified that the same scheme is currently presented as one form of cloaca. **(C)** Scheme of the defect, described as a cloaca, is an ectopy of the anal canal in the lower part of the vagina with a high location of the urethral orifice (outlet).

The concept change occurred without scientific justification, without any research. The number of females with "cloaca" has increased dramatically. For example, Dr. Alberto Peña operated 570 patients with cloaca for 8 years (71 cases per year) [5]. An analysis of the literature shows that many pediatric surgeons do not support the expansion of the concept of "cloaca". For example, in 2010, the European consortium of anorectal malformations registered 8 cases of cloaca, which were born between 2007 and 2012 in 15 surgical centers (0.5 case per center) [6], i.e. 140 times less than Dr. Peña operated on. The purpose operation in ARM with a vestibular and vaginal fistula is to create the anus in a normal place, i.e. in the center of the subcutaneous portion of the external anal sphincter. In patients with cloaca with three divided anatomical channels (urethra, vagina and anal canal), the authors of the article, in addition to creating a new anus, describe two types of operations: a total urogenital mobilization (TUM) and a urogenital separation [1]. In each of these stages, the authors ignore the pathophysiology of malformations. Therefore, we must stop at each stage separately.

1. **Anorectal correction.** First, the authors of the article draw attention to the importance of the location of the rectal fistula and the true rectum and its position in the pelvis, notably the pubococcygeus (PC) line. “The P-C line is a good guide as to whether the true rectum can be mobilized from a posterior sagittal approach or will require a trans-abdominal approach. If the normal lumen of the rectum lies below the P-C line it can reliably be mobilized through a posterior sagittal incision” [1]. However, in 1953, Stephens proposed the concept of a pubococcygeal (P-C) line. He showed that this line corresponds to the location of the PRM, which is located between the rectum and the anal canal [7]. This means that the intestine located caudal to the P-C line is the anal canal. Since then, there has not been a single study that would reject this scientific fact. The anal canal is in constant contraction. Therefore, some surgeons, by mistake, call it a fistula or

rectal pouch. It can be seen only during its opening, when a contrast agent or gas penetrates the anal canal from the rectum. For this, it is necessary to create high pressure in the rectum, like in boys with urethral fistula [8]. The authors of the article do not produce the study with high rectal pressure. In this case, there is no way to correctly judge the level of ARM. Secondly, it was shown that females with vestibular fistula have normal basal pressure for the anal canal and a normal anorectal inhibitory reflex [9]. Thirdly, in patients with a vaginal fistula, where the opening was wide enough, the function of fecal retention and defecation did not differ from the norm [10].

Analysis of the literature suggests that all patients with vestibular fistula and a significant number with vaginal fistula have a functioning anal canal. Instead of preserving all the elements of the anal canal, the authors recommend the PSARP, in which the resection of the internal anal sphincter (IAS) is performed, the PRM is crossed, the levator plates are cut off from the rectum, and the rectum moves to place of IAS. During a wide dissection of the perineum, the nerve pathways of the anorectal and vesicourethral reflexes intersect. In a systematic review including 455 patients with a history of anorectal malformation repair (except for cloaca), the range of reported prevalence of long-term active problems was as follows: fecal incontinence, 16.7% to 76.7%; chronic constipation, 22.2% to 86.7%; urinary incontinence, 1.7% to 30.5%; ejaculatory dysfunction, 15.6% to 41.2%; and erectile dysfunction, 5.6% to 11.8%. The wider the dissection of tissue (high type) the worse long-term functional results [11]. In the scientific community, despite scientific evidence and common sense, cultivated opinion that PSARP is the ideal method of treatment of ARM, and poor results are due to congenital absence of the anal canal and violation of the nervous regulation.

2. **Urinary reconstruction.** In the article under discussion, it is stated that “The goals of urinary reconstruction in urogenital sinus and cloacal repair include: (1) positioning of the bladder neck above the urogenital diaphragm to maximize

future urinary continence, and (2) creating a visible urethra that can be catheterized if needed" [12]. In addition, the authors declare that "…the minimum length for the urethra after reconstruction of a cloacal malformation should be 1.5 cm" [1].

First, in the literature there is no evidence that in the ARM with a single perineal orifice, which the authors call the cloaca, the bladder neck is offset from the pelvic diaphragm and this somehow affects urine retention.

Secondly, on all radiographs of this group of authors, the neck of the diaphragm is located normally at the P–C line level, i.e. at the PRM level (**see Figure 2, C**).

Third, during PSARP, surgeons cross the PRM, which constitute the basic structure of the pelvic floor and play a large role in the retention of feces and urine. Therefore, this goal cannot serve as an excuse for additional dissection of the urogenital structures.

Fourthly, urinary incontinence is observed in 30% of patients with ARM without a "cloaca" [11]. It is time to decide whether the deterioration of the results in patients with "cloaca" congenital underdevelopment of the low urinary system, or is it the result of additional dissection of the urinary tract.

The authors of the article under review describe operations to isolate the urethra, while there is no research on the tone and effective length of the urethra, which is the internal urethral sphincter. There is no information about the function of the external urethral sphincter, as well as the vesico-urethral reflex. The urethra is considered as a tube, the effect of which for urinal retention is estimated by its length. They describe «... urogenital separation with common channel kept as urethra...» [1]. They believe "...that a minimum urethral length for a normal female between age 6 and 36 months is 1.5 cm and the mean length is 2.5 cm ...". And the goal of the operation is "... that the minimum length for the urethra after reconstruction of a cloacal malformation should be 1.5 cm". The link to1.5 cm is

not accurate. For example, in twenty-seven consecutive adult females urethral length varied from 19 to 45 mm [13]; 2-4 cm [14]. If we consider that the length of the internal urethral sphincter is proportional to the height and weight of the woman, then its length in infants of 1.5 cm not possible to be the minimum limit of the norm. Secondly, as seen in these figures, the sphincter function is not directly dependent on its length. As the internal anal sphincter is not a fistula, so the internal urethral sphincter (urethra) is not a water pipe.

It is known that voluntary voiding (micturition) involves the parasympathetic nervous system and the voluntary somatic nervous system. Influences from these systems cause contractions of the detrusor muscle and corresponding somatic nervous activity, leading to the internal and external urethral sphincters relaxation (**Figure 3**) [15].

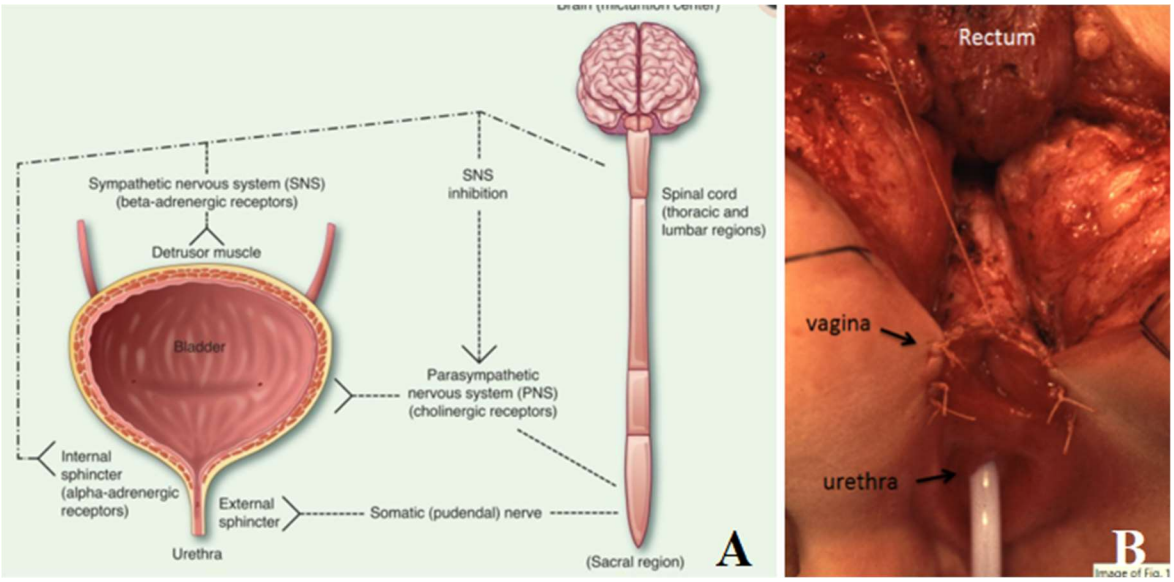


Figure 3. (A) Scheme of neural regulation of lower urinary system [15]. (B) The surgical repair in a cloaca with a 1 cm common channel length. From the Bischoff article [16]. It is hard to imagine that any nervous routines remained uncrossed.

From this scheme it can be seen that denervation with the intersection of reflex arcs during mobilized of the urethra inevitably causes disintegration of the nervous system: filling the bladder to a certain level causes its contraction [17],

but this is not accompanied by the relaxation of the sphincters. Here in such cases, periodic bladder catheterization is necessary.

Results. In the systematic review of Versteegh et al eight records were analyzed according to the Rangel score. After meta-analysis of data, postoperative complications were seen in 99 of 327 patients (30 %). The most common reported complications were recurrent or persistent fistula (n = 29, 10 %) and rectal prolapse (n = 27, 10 %) [18]. Versteegh et al studied of urogenital function after cloacal reconstruction. "Median follow-up was 142 months (range 15-289). At follow-up spontaneous voiding was seen in 29 patients (69%). Clean intermittent catheterization (CIC) was needed in 14 patients (33%); a urinary diversion was created in 10 patients (24%). In total 32 patients (76%) were dry with no involuntary loss of urine per urethra. Recurrent urinary tract infections were seen in 23 patients (55%)" [19]. These results concerned only the urinary system, and surprisingly, were not considered as a complication of the operation. The surprise is that, on the one hand, operations on the urinary system are not justified, on the other hand, there is no scientific analysis of the results. In the systematic review of Versteegh et al the long-term of functional outcome in patients with a cloacal malformation was evaluated. Twelve publications were eligible for inclusion. Voluntary bowel movements were reported in 108 of 188 (57%), soiling in 146 of 205 (71%), and constipation in 31 of 61 patients (51%). Spontaneous voiding was reported for 138 of 299 patients (46%). 141 of 332 patients (42%) used intermittent catheterization, and 53 of 237 patients (22%) had a urinary diversion [20].

Conclusion: The cloaca is a very rare and severe form of congenital anomalies in females, when the rectum, vagina, and urethra fail to develop separately and drain via a single common channel. The ARM with a single perineal orifice, where the urethra, vagina and intestine are separated, is an ectopy of the anal canal into the vestibule or into the vagina. The deep location of the external

urethral opening and the short urethra are the result of delayed development. Their maturation does not end at the point of birth. There is no evidence that the function of the internal and external urethral sphincters, as well as the ectopic anal canal, is seriously damaged due to congenital malformation. There is no doubt that the PSARP destroys the anal canal and the function of the lower urinary tract.

I am sure, that a broad scientific discussion involving independent scientific urologists and physiologists will expand scientific research, that, ultimately, allow to choose rational treatment methods.

As one of the panelists, I offer the following diagnostic and therapeutic methods.

First, it is important to determine the level of ARM. If there is an anal canal (low type), it is necessary to preserve all its elements so that the anorectum function was normal. If the distal intestine ends above the P-C line, there is a need for a pull-through procedure with the obligatory preservation of puborectalis muscle.

Diagnostic method in ARM with visible fistula. The purpose of diagnosis, first, to estimate the width of the rectum. Secondly, to determine the condition of the pelvic floor muscles. Third, to determine the distance between the wall of the anal canal and the anal dimple. Hydrostatic barium enema [21] and comparison of the obtained data with the standards **(see Table in article 21)** allow us to answer the first two questions **(Figure** 4, A-B).

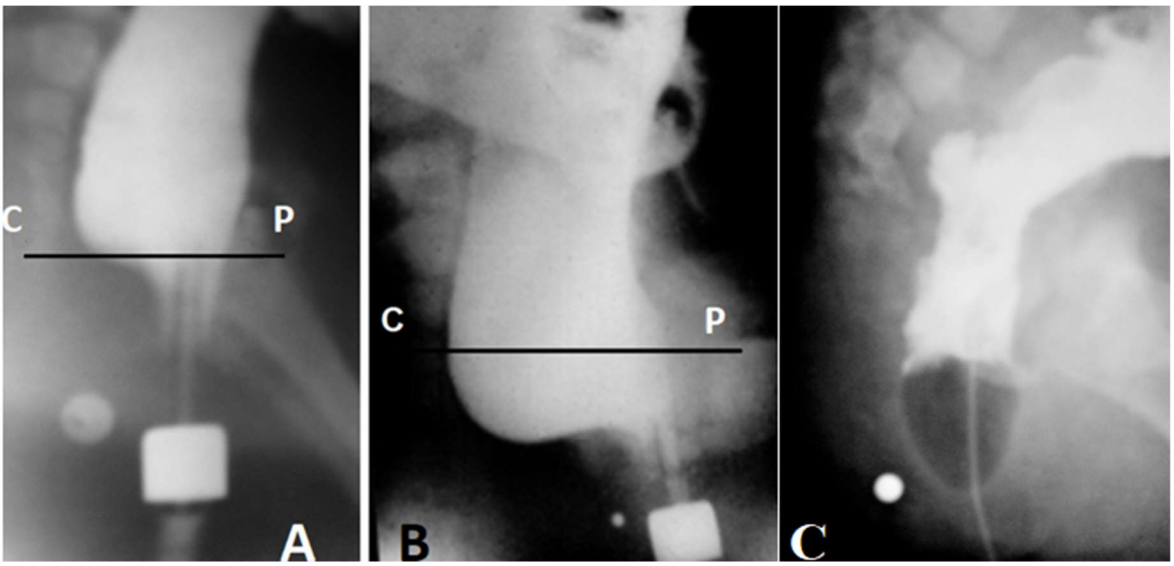


Figure 4. Lateral radiographs of the anorectum made in the same girl with vestibular fistula at a different age. P-C is the pubococcygeal line. The true diameter of the contrast marker, strung on the tip of the enema is 1.6 cm. It is located near the fistula orifice. **(A).** At the age of 8 months. Permanent contraction of the ectopic anal canal was observed during the barium enema. Its length is 2.5 cm, which corresponds to the anal canal age norm. The width of the rectum is 3.4 cm, which is greater than the maximum normal limit (3 cm) (megarectum). Barium penetrates the anal canal behind the tip of the enema. This shows the weakness of the PRM, which is not pulls of the posterior wall forward. **(B).** At the age of 1.5 years she had a severe constipation and soiling. The width of the rectum is 5.5 cm, which significantly exceeds the maximum limit of the norm for this age (3.7 cm). A megarectum is combined with significant shortening of the anal canal. Its length is 1.9 cm (minimal limit is 2.3 cm). Conclusion. ARM with vestibular ectopy, megarectum and descending perineum syndrome. **(C).** After emptying the gut, the Foley catheter was inserted into the rectum. After inflating the balloon, the catheter is retracted down 19 until it stops. It lingered over the narrow and rigid ring of the ectopic anus. The distance from the wall of the anal canal to the marker near the anal dimple is 2 mm.

In newborns with ARM, the rectum is of normal size. It expands as a result of chronic constipation caused by a stool retention due to stenosis of an ectopic anus (secondary megacolon or organic chronic constipation). In severe cases, wide fecal masses that cannot pass through the anal canal, under the influence of a strong peristaltic wave of the rectum, stretch the muscles of the pelvic floor. As a result of the weakness of the PRM and the levator plates, the upper part of the anal canal does not function to hold the feces, and becomes, as it were, a part of

the rectum (descending perineum syndrome). In such cases, even an ideal operation cannot bring success, since chronic constipation and fecal incontinence or encopresis will result from weakness of the pelvic floor muscles and megarectum. Therefore, correction of the ARM with visible fistulas, should be performed before the appearance of the hard feces.

Diagnostic method in ARM with vaginal fistula in patients with colostomy. Balloon-tipped catheter is inserted into the stoma far enough so that the balloon is into the proximal lumen of the ostomy of the mucous fistula. The balloon is then carefully inflated with 1–2 mL of air, just enough to occlude the stoma but not over-distend the bowel lumen. A 60-mL catheter-tipped syringe, without a piston, is filled with 50 ml isosmotic watersoluble contrast agent. It is connected to the catheter and rises above the baby so that the tip of the syringe was 40 cm from the anus. Then need to open the faucet and wait until the level of the contrast agent in the syringe stops falling. This means that the rectum is filled with a contrast agent under low hydrostatic pressure, at which bowel perforation is impossible. Then under the control of fluoroscopy the abdominal compression is produced. In the presence of a low type of ARM, the contrast agent will approach the marker in the anal dimple.

The treatment strategy I proposed consists of 4 stages: (1) creating a colostomy, (2) forming a new anus, (3) closing an ectopic anus (4) closing a colostomy. Below I describe in detail the second stage. The first and fourth stages are extensively covered in the literature. The closure of the ectopic anus can be done in different ways (closure through the anus, using a fibroscope, etc.). The treatment process can last for many months, but the result is worth it.

Perineal perforation procedure (PPP) in ARM with vaginal fistula in patients with colostomy.

On the X-Ray table under general anesthesia the cross-section of skin is done above contraction of the subcutaneous portion of external anal sphincter (EAS). After stretching of its fibers, the child is transferred to a lateral position. During fluoroscopy, when the anal canal is opened during abdominal compression, the needle is inserted from an incision in the skin into the rectum through the open anal canal (**Figure 5, A-B**). Only that step is performed under fluoroscopic control. Before proceeding it is necessary to make sure that the needle is in the rectal lumen. This is evidenced by the sound of the outgoing gas or the appearance of meconium. If there is no certainty that the needle is in the rectum, appropriate to introduce a contrast agent into the intestine through the needle. Then, a conductor with soft floating end is inserted through the needle into the rectum (**Figure 5, C**). The needle is removed and the tight conical bougie with a maximum diameter of 0.8 cm is introduced into the gut along the conductor (**Figure 5, D**). After that, the tracheostomy tube with diameter 0.8 cm introduced into the rectum and the conductor is removed (**Figure 5, E**). Four cm^3 of air is introduced into the balloon of this tube that allows to fix the tube for 7 days. After 7 days, the tube is removed.

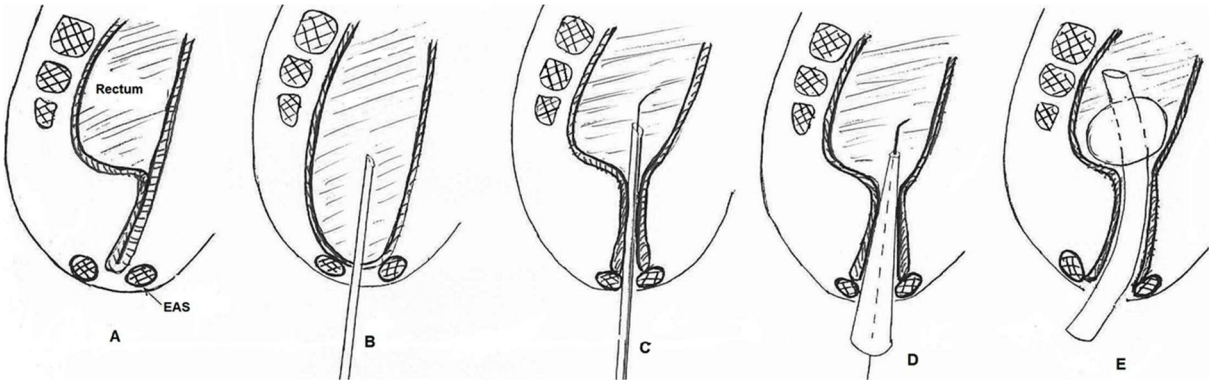


Figure 5. Scheme of the "perforation perineum procedure" (PPP) to treat low imperforate anus without visible fistula. Lateral view. **A**. The anal canal is closed. **B.** Anal canal is opened due to abdominal compression. Under X-ray control a needle is introduced into the anal canal. **C**. Conductor for 27 vascular catheterization is introduced into the rectum through the needle. **D**. The tapered

dilator introduces on a conductor for expansion of the newly created channel. **E.** After removal of the dilator, the tracheostomy tube introduced along the conductor. Its balloon is inflated in the rectum.

The tube is removed through a week after the procedure. During this time, the emptying of the rectum there is through the tracheostomy tube. The internal anal sphincter is not separating and is not sewn to the skin.

I am sure that the preservation of all elements of the anal canal without damaging the nerve pathways will dramatically reduce the complications that are observed after PSARP in patients with ARM excluding cloaca (fecal incontinence, 16.7% to 76.7%; chronic constipation, 22.2% to 86.7%; urinary incontinence, 1.7 % to 30.5%; ejaculatory dysfunction, 15.6% to 41.2%; and erectile dysfunction, 5.6% to 11.8% [11]). I consider it necessary that urological problems be solved by pediatric urologists, who call the bladder to be a detrusor, consider the urethra to be the internal urethral sphincter and cherish function of the external urethral sphincter. I am sure that gynecological problems should be solved by gynecologists - the acute problems at birth, and the chronic one during puberty. It is unacceptable to produce surgery without scientific justification.

M.D. Levin, MD, PhD, DSc. Radiologist,

Department of Pediatric Radiology of the 1-st State Hospital, Minsk, Belarus.

Dorot-Netanya Geriatric Medical Center, Israel.

Amnon VeTamar, 1/2, Netanya, 42202, Israel.

nivel70@hotmail.com; michael.levin@dorot.health.gov.il

https://orcid.org/0000-0001-7830-1944

https://www.anorectalmalformations.com

Scopus Author ID: 7402571390

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