Dysfunctional elimination syndrome: a short review of the literature

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Abstract: The combination of the functional disorders of urination and defecation constitutes the Dysfunctional Elimination Syndrome (DES). DES refers to an abnormal pattern of elimination of unknown etiology characterized by bowel and bladder incontinence and withholding, with no underlying anatomic or neurologic abnormalities. Essential precondition for a child to be subsumed under this entity is the exclusion of either anatomical or neurological causative factors. In the present review study the individual entities of dysfunctional filling, such as the unstable or lazy bladder, or dysfunctional urination, such as the detrusor sphincter dyssynergia and the functional constipation are being described comprehensively. Subsequently, the analysis of the pathophysiological effects of the dysfunctional elimination syndrome such as incontinence, urinary tract infections and the conservation or the deterioration of vesicoureteric reflux, is being accentuated. With the documentation of DES, the therapeutic strategy should aim at treating both the functional disorder of the vesicourethral unit and the functional constipation. The first part does not specify depending on the type of this disorder. Rarely, surgical treatment of functional urinary disorders may be required.

Keywords: dysfunctional elimination syndrome, functional voiding disturbances, functional constipation, urinary tract infection, vesicoureteric reflux.

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Introduction

Dysfunctional elimination syndrome (DES) refers to an abnormal pattern of elimination of unknown etiology characterized by bowel and bladder incontinence and withholding, with no underlying anatomic or neurologic abnormalities [1]. The etiology of the syndrome is unknown and the symptoms begin 3–6 months after the child achieves
control of urination. It affects mostly children under the age of 10 [2]. This is a transitional period in terms of achieving continence, as children are not yet able to inhibit the voiding reflex and stay dry by voluntarily contracting their external sphincter during bladder contractions [3]. The disease most often affects girls (boys / girls = 0.2–0.6) [4, 5]. The main manifestations of dysfunctional elimination syndrome are summarized in Table 1 [2].

**Table 1. Main symptoms of DES.**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Incidence (percent %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Urgency</td>
<td>42</td>
</tr>
<tr>
<td>2. Incontinence</td>
<td>40</td>
</tr>
<tr>
<td>3. High urinary frequency</td>
<td>36</td>
</tr>
<tr>
<td>4. Nocturia</td>
<td>15</td>
</tr>
<tr>
<td>5. Weak urine streak</td>
<td>10</td>
</tr>
<tr>
<td>6. Constipation</td>
<td>66</td>
</tr>
<tr>
<td>7. Urinary tract infections</td>
<td>43</td>
</tr>
</tbody>
</table>

**Functional constipation**

Constipation is the condition that lasts at least 2–3 weeks and is characterized by hard stools, painful and laborious bowel movements, with a frequency of 2 or less per week [2, 6]. This is a common condition as it affects 34–37% of children [6]. The painful evacuation causes, in turn, a negative association subconsciously, which results to the voluntary postponement of the next evacuation, fearing of repeating the (painful) experience. Other causes are a poor digestive fibre diet and delayed defecation either because the child is busy or because he does not want to use shared toilets. Gradually, the stimulation of the receptors in the cerebral cortex decreases, in order to develop the feeling of the full rectal ampulla. The ampulla is gradually congested with a larger volume of stool, which dehydrates so that the next bowel movement is more laborious and painful, developing a catch-22 situation. When the condition gets worse and the ampulla is congested with feces, fecal impaction is palpated, the child complains of abdominal pain, while other symptoms include paradoxical overflow diarrhea as liquid stool passes around the obstruction (fecal soiling).

Von Gontard and Hollmann [4], while studying 53 children with functional constipation, found that 63.5% had symptoms of urinary dysfunction. Compared to the controlled group, they concluded that the child suffering functional constipation was
15 times more likely to suffer from urinary dysfunction. Due to the fecal congestion in the rectal ampulla, the diameter of the rectum increases (from 2.1 cm to 4.9 cm) causing pressure on the bladder and thus reducing its functional capacity [7]. That results in the early urge to urinate, with a smaller volume of urine. Constipation is responsible for the development of inhibited detrusor contractions, resulting in increased intravesical pressure and the early onset of urinary urgency [8–10]. The child is “forced” to voluntarily stop urination by contracting the external urethral sphincter muscle, resulting in the gradual development of involuntary spasm of the pelvic muscles. The latter is responsible for the failure of complete relaxation of the sphincter during the urination, and progressively leads to dyssynergic urination with increasing post-void residual volume. Chronic contraction of the pelvic floor muscles worsens the functional constipation, thus maintaining a catch-22 situation [11]. Chronic constipation may lead to paradoxical overflow diarrhea, as liquid stool passes due to the overfilling, resulting in contamination of the perineum by germs such as *Escherichia coli*, which are responsible for the development of ascending urinary tract infections. 57% of the children aged 3 to 12 years old suffer from dysfunction during the filling phase of the bladder as a result of delayed maturation of the cortical control in the inhibition of urination. Due to the contraction of the internal urethral sphincter, urine is extruded in the urethra. The child, however, tries to maintain continence by increasing the urinary resistance at the level of the external urethral sphincter. This results to the reflux of urine to the bladder (milk buck phenomenon). Therefore, the refluxed urine is contaminated by germs that have colonized the perineum [12].

Loening and Baucke studied 234 children with constipation and encopresis in relation to the comorbidity of urinary tract infection and urinary incontinence. 12 months after the initiation of the constipation treatment, they found that the colon function had been restored in 52% of the patients. The regression of the constipation contributed positively to the remission of the urinary incontinence in 89% of the patients and the non-development of urinary tract infections in 63% of the patients [13].

**Types of voiding dysfunction**

The term Voiding dysfunction is characterized by the development of functional incontinence due to dysfunction of the urinary phase. The main pathophysiological background of this disorder is the inconsistent coordination within the urinary tract between the detrusor muscle and the urethral sphincter, during the urination. Primary bladder neck dysfunction also falls into this entity.

On the contrary, when urinary incontinence is the result of dysfunctional filling / storage, i.e. dysfunction during the filling / storage phase of the bladder function, it is
attributed to two pathophysiological entities, the overactive bladder (detrusor over activity) and the underactive bladder (lazy bladder). Incontinence of this etiology is attributed as urge incontinence.

The incidence of bladder filling and urination disorders is not well known. However, children who suffer from daytime wetting account for 4.2%–32% of the total [14].

The voiding dysfunction is typically caused by overactive pelvic muscles, which leads to infravesical obstruction. The main clinical manifestations include staccato voiding, fractionated voiding, poor bladder emptying, voiding postponement and finally non neurogenic — neurogenic bladder dysfunction [15]. The main symptoms of a child with dysfunction voiding are incontinence, dysuria, frequent urination, intermittent urination, recurrent urinary tract infections, urgent urination, staccato or fractionated voiding, abdominal straining during urination and constipation.

Staccato voiding is due to intermittent contraction of the pelvic floor muscles that cause intermittent urine flow. The urine flow increase triggers the contraction of the striated sphincter, the urine flow decreases, followed by the relaxation of the striated sphincter, increase of the urine flow and re-triggering of the contraction of the striated sphincter. Eventually, the total urination time is prolonged while the residual volume is gradually increased [15, 16].

Fractionated voiding is characterized by infrequent and incomplete emptying secondary to detrusor inactivity. Micturition occurs in several small and discontinued fractions because of poor and unsustained detrusor contractions, leaving significant postvoid residuals. Abdominal straining is usually evident as an effort to improve the bladder emptying. This straining is often paradoxically counteracted, however, by a reflex increase in activities of the pelvic floor muscles that is triggered by an increase in intravesical pressure, preventing the continuous flow of urine. Eventually, urination is irregular, the bladder volume is usually large for age and may gradually increase as the condition progresses further, and overflow incontinence may ultimately develop [16, 17].

A special condition is the wetting that occurs during laughing, usually in females, this entity is called giggle incontinence or enuresis risoria. It is a benign and self-limiting disorder, but it can also occur in older people. The pathogenesis is postulated to be centrally mediated and related to a receptor imbalance of cholinergic and monoaminergic systems. This results in loss of the muscle tone (hypotension). Medication is rarely required with anticholinergic or sympathomimetic or methylphenidate (dosage 0.3–0.5 mg/kg/4–6 hours) [12].

Post void dribbling ή vagina voiding refers to obese girls who urinate while sitting more supine and have their legs closed. When urinating, a small amount of urine regress to the vulva vestibule and as the little girl rises from the toilet at the end of urination, urine comes out of the vestibule to the underwear [12].
Pathophysiology of voiding dysfunction

The main types of voiding dysfunction are the unstable bladder, the lazy bladder and the detrusor sphincter dyssynergia [1, 2, 8].

The unstable or overactive bladder is responsible for a) the reduced bladder compliance (increased intravesical pressure during the filling of the bladder. Despite the increased intravesical pressure, the bladder does not void completely (increased post-void residual volume). And b) at the beginning of urination the external urethral sphincter normally relaxes, but due to discomfort of the child it contracts, blocking the complete emptying of the bladder. The discomfort is attributed to the development of inflammation at the level of the bladder trigone and is an endoscopic finding. In the attempt to inhibit the urination, the striated urethral sphincter contracts voluntary and intermittently causing a) worsening of the infravesical resistance of urine output and b) urine regression from the urethra to the bladder (milk buck phenomenon) which leads to recurrent urinary tract infections.

A child with a lazy or underactive bladder urinates 1–2 times per day, while usually the bladder does not empty completely, but as long as it takes for the feeling of the bladder pressure to disappear. The intensity of the message of the full bladder to the cerebral cortex reduces gradually, resulting in overstretching if the bladder, urinary retention and finally development of increased residual volume. These changes are responsible for recurrent urinary tract infections as a result of urinary retention and overflow incontinence. The bladder is characterized by thinning of the wall, large functional capacity and low intravesical pressure (increase if the bladder compliance). Abdominal straining is necessary in order to achieve urinary voiding. Eventually, however, there remains an increased residual volume, while in the most severe version of this condition there is complete detrusor myogenic failure.

Dyssynergia of the detrusor muscle and the striated urethral sphincter is characterized by contraction of the striated sphincter during urination, which results to development of infravesical obstruction. Normally, as it is known, the sphincter relaxes during the contraction of the detrusor muscle, in order to achieve bladder voiding. This dyssynergia strains the upper urinary system, as it leads to development of hydronephrosis (2/3 of these children, scarring of the renal cortex due to pyelonephritis, while at the same time, the co-existing veicoureteral reflux (in 50% of the cases) worsens. Progressive lesions develop both in the low urinary tract and in the function of the large intestine, such as a) large dilation of the bladder with multiple diverticula and b) stenosis (fixed or intermittent) in the striated sphincter, in 50% of these children, while eventually functional constipation is established. The possible mechanisms responsible for the development of this disorder are a) a “training mistake” during the development of urinary control, as the child voluntarily contracts the pelvic floor muscles, in order to prevent the impending unwanted urination and b) pre-existing inhibited detrusor contractions, which result to
gradually development of abnormal activity of the detrusor muscle, in the child’s attempt to prevent unwanted urination. Trying to prevent unwanted urination or defecation, the child voluntarily contracts the pelvic floor muscles, worsening the situation. This increases the chance of chronic functional constipation and the happenings of wetting. The main symptoms that might be observed in these children are urgency, incontinence, especially during the filling phase, infrequent voluntary urination, weak urine stream and fractionated voiding. The child at the beginning of urination, spontaneously increases the intra-abdominal pressure, in order to overcome the contracted striated urethral sphincter.

**DES and Urinary Tract Infections**

The pathogenetic mechanism of the development of urinary tract infections in a child with DES is quite complex and the impact of colon dysfunction is catalytic.

The natural immunity of the urinary tract is characterized by its organisation in 4 levels: the periurethral area, the bladder, the vesicoureteric junction and finally the renal papilla. The main parameters that prevent urinary tract infection are the complete emptying of the bladder frequently, the acidic pH and the normal osmolality of the urine, the urothelial cells that help to prevent germs growing, and also to kill them. In addition, they produce a mucopolysaccharide that prevents pathogenic germs from attaching to the urothelium, and immunoglobin A (IgA). Finally, the conical shape of the renal papilla prevents the development of intrarenal reflux.

Pathophysiologically, it is worth mentioning the parameters that are responsible for the growth of pathogenic microorganisms, such as the speed that they multiply, the dilution of urine, the hourly urine output, and finally conditions that favour urinary retention.

Regarding the association of urinary tract infections developed prior to the second age of life with the impending development of DES, there are conflicting views in the international literature. Hansen et al. consider that there is a positive correlation between urinary tract infections prior to the second year of life and the development of DES later [18]. On the contrary, in a Shaikh et al. study it was concluded that this correlation is not valid [6].

**DES and Vesicoureteral Reflux**

Halachmi et al. in a recent study estimated the association between the dysfunctional elimination syndrome, the vesicoureteral reflux (VUR) and urinary tract infections. The coexistence of these conditions is found in 36% of boys and 21% of girls [2]. O’Regan et al. in a study of 17 children recorded the development of a catch-22 situation in the context of the interaction of vesicoureteral reflux, constipation, and overactive bladder [19].
The development of urinary tract infections in patients with VUR, despite the chemoprevention, is observed in 77% of the children with DES, while this percentage is decreased to 23% in children without DES [2, 7]. In young patients who suffer both VUR and DES, the spontaneous remission of VUR is delayed by 1–2 years (Avg: 1.6 years). Children with DES and surgically treated VUR are more likely to develop complications, such as recurrence of VUR, bilateral VUR and recurrent urinary tract infections, in relation to children with non-surgically treated VUR and no background of DES [20].

Naseer et al. in a 538 cases study associated the presence of DES with renal scarring development in children with VUR: 13.5% had renal scarring during the first evaluation, while 2.1% developed new scars, despite the standard treatment that underwent. Finally, 6/11 patients that underwent a successful surgery developed new scars [21].

Silva et al. analysed the prognostic factors for the remission of VUR, concluding that in any child with VUR, the possible presence of DES should be considered, prior to the decision of surgical treatment. In that case, the dysfunctional elimination syndrome should be treated first [22].

**Diagnostic approach**

It derives from the utilization of the data obtained from the history, the clinical examination and the lab and imaging tests.

**History**

The main issue in the diagnostic approach of the DES is the detailed history, as taken by the parents and the child and the collection of information about the frequency and severity of wetting episodes, the coexistence of symptoms from the low urinary tract, the reporting of urinary tract infections, the urination and defecation habits, the eating habits and the amount of fluid intake in a daily basis. All this information is included in the bladder diary, as suggested by International Children’s Continence Society (Table 2) [23].

**Table 2.** Bladder diary data.

<table>
<thead>
<tr>
<th>Data</th>
<th>Evaluation period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. volume and frequency of urination</td>
<td>For 48 hours</td>
</tr>
<tr>
<td>2. nocturia episodes</td>
<td>For 14 days</td>
</tr>
<tr>
<td>3. nocturia episodes — urine volume in each of the episodes</td>
<td>For 14 days</td>
</tr>
<tr>
<td>4. daytime wetting episodes — other urinary tract symptoms</td>
<td>For 14 days</td>
</tr>
<tr>
<td>5. liquid intake</td>
<td>For 48 hours</td>
</tr>
<tr>
<td>6. sleep and awakening time</td>
<td>For 14 days</td>
</tr>
<tr>
<td>7. defecation frequency — encopresis episodes</td>
<td>For 14 days</td>
</tr>
</tbody>
</table>
Utilization of the history of urination and defecation of the child and the conversion to a score (dysfunctional elimination scoring system) contributes to the diagnostic documentation of the syndrome [6, 24]. In particular, the answers to targeted questions are evaluated, in order to explore possible urine incontinence, nocturia, dysuria and constipation. The questions are also addressed to a control group for benchmarking. Each answer is scored with 0 (no symptom), 1 (presence of the symptom sometimes) and 2 (continuous presence of the symptom). If the score is >9 in the examined boy, the diagnosis of DES is established, with a sensitivity of 81% [6]. Respectively, in the examined girl the diagnosis is established with a score >6, with a sensitivity of 93%. The specificity of the method accounts for 87% in girls and 87% in boys [25].

Physical Examination

A thorough examination of all systems should not be neglected. Next the clinician needs to focus on:
— examination of the external genitalia (indication of urethritis, vulvitis, labial adhesions, indication of sexual abuse)
— lower abdomen examination (indication of dilated bladder, fecal impaction)
— examination of the lumbar region for the existence of findings indicative of occult myelodysplasia such as lipoma, sinus, fistula, tufts of hair
— neurological examination focusing on posture, gait, control of muscle tone, sensory functions. Also, in the evaluation of the recto-anal inhibitory reflex and the bulbocavernosus reflex. And finally,
— examination of the upper respiratory system for the presence of hypertrophic parietal tonsils or adenoids hypertrophy.

Laboratory Examinations

Initially, a general urine test and urine culture are performed. From the data of the general urine test, the specific gravity, glucosuria, hypercalciuria, the presence of leukocytes, pyospheres, red blood cells and nitrates are evaluated. If the urine culture is negative, then urinary tract infection or bacteriuria is ruled out.

If reservations remain regarding the existence or not of an anatomical or neurological background, a thorough diagnostic approach should be followed by:
— abdominal ultrasound. It evaluates particularly a) the bladder during the filling phase (urine volume, presence of irregular contractions of the detrusor muscle, wall thickness, presence of a diverticulum) and during urination (mobility of the cystic neck, residue volume). The anatomy of the vesicoureteric junction should be evaluated in both phases. And b) the rectosigmoid ration (sigmoid diameter / rectal diameter).
— X-rays of the lumbar region to highlight findings of masked myelodysplasia e.g., spina bifida.
— voiding cystourethrography in indication of infravesical obstruction or neurogenic bladder and finally if necessary.
— urodynamic assessment or bladder-pressure study (cystomanometry, urometry and electromyogram of the pelvic floor muscles) [14, 26]. For the reliability of the urometry the child should be calm and hydrated. If the urine flow curve is normal and the volume of urine excreted is at least 100 ml with no residual volume at the end of urination, then dysfunctional urination can be ruled out.

Management

With the documentation of DES, the therapeutic strategy should aim at treating both the functional disorder of the vesicourethral unit and the functional constipation. The first part does not specify depending on the type of this disorder. Rarely, surgical treatment of functional urinary disorders may be required. A — rare — indication is the resistant to dysfunction of the detrusor muscle and the striated urethral sphincter in order to remove the effects on the upper urinary tract of increased intravesical pressure and decreased compliance.

Firstly, certain non-pharmaceutical principles, which we include in the term urotherapy [14], should be applied. The general principles of this approach include organizing a regular urination and defecation program at regular intervals. The child should sit properly so that the pelvis forms a right angle with the torso while the legs are in abduction. In this position there is the possibility of both contraction of the abdominal wall muscles and relaxation of the pelvic floor muscles. Biofeedback is defined as the set of actions aimed at the coordinated relaxation of the pelvic floor muscles during the contraction of the detrusor muscle [27, 28]. Additional measures are the treatment of constipation, hygiene, increased liquid intake, encouraging the child to empty the bladder completely, even with double urination, and the application of positive feedback methods. Behavioral therapy might help and the treatment of urinary tract infections, if present, can be treated with the administration of appropriate antibiotics and then chemoprophylaxis.

The treatment of the unstable cyst is established with the administration of muscarinic (cholinergic) antagonists and especially of the M_2 and M_3 receptors. Drugs of this group are oxybutynin, tolterodine, propiverine, etc. The main contraindications for their administration are angle-closure glaucoma, gastrointestinal obstruction, infravesical obstruction and myasthenia Gravis. In persistent cases of an unstable cyst, intravesical instillation of botulinum-A toxin may be performed endoscopically. It should be noted that its injection near the ureters should be avoided. The dose is 10 unit/kg with a maximum dose of 100–300 units for Botox and 500–1500 units for
Dyspot. The main side effect of its administration to the detrusor muscle is urinary retention. Muscular weakness of the lower extremities has been reported in cases of neurogenic cyst. The treatment must be repeated, as new neuromuscular synapses and antibodies against the toxin develop over time [29–32].

Neurostimulation is a promising alternative and can be applied transdermal at the height of the I-3 vertebra (sacral transcutaneous ENS-STENS) [33]. The mechanism of action, although not fully known, results in the modification of bladder function, either due to sympathetic stimulation or due to relaxation of parasympathetic neurons or finally through effect in the cerebral cortex [34].

For the treatment of lazy bladder, bethanechol chloride (cholinergic agonist) can be administered at a dose of 0.7–0.8 mg/kg/day. Its action lies in the stronger sense of urgency to urinate. In rare and persistent cases with muscular insufficiency of the detrusor muscle, a program of sterile intermittent catheterization may be required, temporarily, until the bladder regains the necessary contractility to empty satisfactorily.

To improve the excretion of urine in dyssynergia of detrusor muscle and urethral sphincter, which is characterized by increased urine residue volume, staccato voiding and dysuria, if urotherapy does not work, it can be administered:

1. inhibitor of α-1 receptors of the sympathetic system (terazosin at a dose of 1 mg/20 kg of the child, doxazosin at a dose of 0.5–1 mg/day, tamsulosin at a dose of 0.001–0.004 mg/kg with a maximum daily dose of 0.4 mg). It is a selective inhibitor that does not cause side effects such as hypotension, headache and dizziness. This promising group of drugs has not been widely used in childhood.

2. botulinum-A toxin (Botox). It is injected either transurethrally or transperineally at the level of the urethral sphincter. The therapeutic effect is impermanent and lies in inhibiting the release of acetylcholine from the presynaptic vesicles of neuromuscular synapses, causing muscle relaxation of the urethral sphincter. Disadvantage is the fact that it is not widely applied in childhood.

The general measures for the treatment of functional constipation are:

— daily visit of the child to the toilet on a regular basis, where he stays for 10 minutes trying to defecate. This can be done after a main meal to help activate the gastrocolic reflex.

— increase in the intake of dietary fiber in the child’s diet, increase in liquid (water) intake, physical exercise.

— planning of 4–6 daily meals at regular intervals and finally,

— treatment of painful perianal diseases.

The mentioned strategy should be supplemented with the administration of a laxative. If there is neglected fecal impaction, glycerin suppositories or an enema containing 50% glycerol solution in saline may be given initially. Then an oral laxative such as paraffin oil can be administered (2–4 ml/kg/day), magnesium milk (1–3 ml/kg/day),
sorbitol (1–2 ml/kg/day) or lactulose (1–2 ml/kg/day). The treatment will last 2–3 months with gradual interruption in order to achieve on one hand the return of the colon tone to normal levels, on the other hand the child to defecate daily, with soft stools.

Conflict of interest

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References