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# Urinary Tract Infections and Dysfunctional Voiding

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## 1. Introduction

Urinary tract infections are a common disease in the population. It has been estimated that half of all women are likely to suffer from at least one episode of UTIs in their life and one third will require an antibiotic treatment (Foxman, 2003).

Pathogen-related conditions (such as the presence of invasion or virulence factors) affect the severity of the infection and its resistance to antibiotic therapy, but also different host-related characteristics have been individuated, that play a role, in particular in the possibility of infection recurrence.

There are defence mechanisms that allow to counteract every attempt of the microorganisms to ascend the urinary tract. The basis of this defence is represented mainly by the semi-continuous stream of new (sterile) urine, coming from the upper urinary tract, that is stored only for a limited period of time in the bladder and afterwards completely eliminated. In this way the possibility of the microorganisms to proliferate is limited to a very narrow period of time and the immune system becomes able to eliminate efficiently the residual limited amount of colonies. Obstructing conditions causing incomplete bladder emptying after micturition set the patients at risk of infection development through overgrowth of ascending bacterial colonies.

The main causes of retention in women are listed in Table 1. Some of them are secondary to anatomic factors, while others depend on neurologic alterations affecting, in last consequence, the mechanisms of pelvic floor relaxation and detrusor contraction and their coordination. A particular category of voiding disturbances is represented by patients with alterations of detrusor-sphincter coordination in the absence of uropathy or neuropathic disorders. The individuals affected, mainly women, present frequently recurrent UTIs associated to a tendency to urinary retention.

In this chapter this disorder and its relation with infection recurrence are presented; the most common diagnostic procedures and their findings in the dysfunctional voiding and the possible treatment options are considered.

## 2. Pathophysiology of dysfunctional voiding

The normal micturition cycle can be divided in two phases: a storage phase, with passive filling by bladder relaxation and sphincter muscle contraction, and a voiding phase, with

pelvic floor muscle relaxation and bladder contraction allowing micturition. In physiological conditions the two phases are well distinguished, and muscular groups aimed at filling and emptying switch alternatively from a relaxed to a contracted condition. This system is guaranteed by a correct voluntary and involuntary coordination of the nervous circuits and allows the individual to conduct a regular everyday life, without involuntary wetting or urine accumulation.

There are conditions in which, although the circuit is correctly functional and no anatomical obstructions are present, there is an impaired capacity of emptying the bladder. This situation, called dysfunctional voiding (DV), is often shown in particular in young healthy women, who go to the physician because of frequent episodes of recurrent UTIs.

DV is defined as an abnormality of bladder emptying in neurologically normal individuals in whom there is increased external sphincter activity during voluntary voiding (Carlson et al., 2001; Messelink et al., 2005).

It has been referred to by various terms, including pseudodyssynergia, external sphincter spasticity and non relaxing external urethral sphincter (Carlson et al., 2001). Its etiology is to date controversial, the clinical presentation varies and the precipitating event in autonomic somatic dyssynergia usually remains obscure (Yagci et al., 2005).

The prevalence of learned voiding dysfunction among adults is unknown, but it has been suggested that this disorder is more frequent than commonly recognized (Groutz et al., 2001): Jorgensen reported 0.5% prevalence rate among patients referred for urodynamic evaluation.

As far as it is known, DV seems to be the result of the combination of both inherited factors and behavioural conditions (Everaert et al., 2000). It is thought to be often acquired in the childhood, during toilet training when the children learn to control sphincteric activity, but can also appear in older ages, with higher frequency in the female sex. An inappropriate contraction of pelvic floor muscles, thereby tightening the urinary sphincter complex represents the key point of this mechanism. Activation of the pelvic floor muscles seems to start in consequence of the flow-rate exceeding a certain threshold and to cease spontaneously after it has fallen again below it.

This incoordination of bladder-sphincter function in children may represent a developmental abnormality (Allen & Bright, 1978), that can lead not only to lower urinary tract symptoms, but may cause structural and functional changes, including obstruction and consequent bladder trabeculations, residual urine and bacteriuria; detrusor hypertrophy and consequent vesico-ureteral reflux (VUR) or hydroureter/hydronephrosis may develop (Hinman, 1986; Groutz et al., 2001).

DV could represent the result of a learned behavior, evolving from attempt to suppress impending or active bladder contractions by inappropriately contracting the pelvic floor muscles, thereby tightening the urinary sphincter complex. The first step in the development of dysfunctional voiding could then reside in an underlying form of bladder overactivity, which the patient learns to control from the childhood through volitional contractions of the muscles of the pelvic floor. This leads to a condition of insufficient pelvic floor relaxation (or contractions) also in response to the physiological contractions during micturition. As the time goes by, this condition can evolve to a situation of high-pressure voiding, as in all obstruction sets. VUR, if not already present, can develop and, combined with the increased tendency to the development of recurrent UTIs, can further facilitate the occurrence of pyelonephritis and subsequent renal scarring (Chandra, 1995; Acar et al., 2009).

As a result, people affected from DV tend to develop chronic urinary retention, since high urethral pressures during micturition, due to incomplete sphincter relaxation, do not allow complete bladder emptying, and to develop, in the mid-long term, recurrent UTIs from an ascending way.

Also incontinence can develop during this process. This can be due to the accentuation of the primitive condition of detrusor overactivity, or, later, to the development of bladder underactivity, resulting in inability to empty and overflow incontinence (lazy bladder syndrome) (Norgaard et al., 1998).

An additional role for urethral instability in the pathogenesis of DV has been claimed, to explain the symptoms of urgency in DV. Sudden variations in the urethral pressure during bladder filling in people affected by DV were demonstrated, represented by pressure decreases with short periods of electromyography silence, intermittent urethral pressure increases with short perineal spasms, or urethral pressure decreases with silent electromyography, combined with different degrees of bladder instability (Vereecken & Proesmans, 2000).

Furthermore, some degree of external sphincter hypertrophy was noted in some studies conducted on females affected from dysfunctional voiding and a positive correlation between dysfunctional behaviors and sphincter volume postulated (Minardi et al., 2008). Its role in the pathogenesis is, anyway, still to be determined.

Behavioral or functional abnormalities which predispose to UTIs in women with normal urinary tract or only minor abnormalities are neglected in most recommended protocols for evaluation of urinary tract infections (McKenna & Herndon, 2000).

The commonest cause of urinary retention in young women in dysfunctional voiding is a primary disorder of sphincter relaxation (Fowler's syndrome). It is defined as the combination of urinary retention, abnormal electromyographic activity of the urethral rhabdosphincter and polycystic ovaries (Fowler et al., 1988); it was further observed that this overactivity can lead to hypertrophic changes of the urethral rhabdosphincter (Wiseman et al., 2002). The full etiology of this condition remain to be elucidated but it has been hypothesized that the disorder is due to a hormonally sensitive channel alteration, which results in a sustained involuntary contraction of the striated urethral sphincter (Kavia et al., 2006). This in turn has an inhibitory effect on detrusor contractions as well as inhibiting sensations of the desire to void.

On light microscopy the urethral rhabdosphincter fiber diameter did not differ among patients with disorder of sphincter relaxation compared to normal patients, but electron microscopy showed excessive peripheral sarcoplasm with lipid and glycogen deposition, and sarcoplasmic accumulation of normal mitochondria, reflecting the increased energy requirement of an overactive urethral rhabdosphincter (Andrich et al., 2005).

EMG of the pubo-coccygeal muscles (together with recordings of other urodynamic variables) is helpful in revealing inappropriate EMG activity during micturition (Deindl et al., 1998).

Women perceive voiding dysfunction less commonly as an important urinary symptom. The most reported voiding symptom was poor urinary stream. Its prevalence with or without hesitancy ranged from 15% to 45%, intermittency (20% to 35%), incomplete emptying (30% to 50%), and abdominal straining (10%). These seem more severe in younger women than older women, except for poor stream which is common in older women (10% of women aged 19 to 29 years and 40% of women aged  $\geq 80$  years) (Al-Hayek & Abrams, 2004).

The association of dysfunctional voiding with recurrent UTIs is documented; dysfunctional voiding can disrupt the laminar urinary flow through the urethra, causing UTIs as bacteria are transferred back from the meatus to the bladder as a result of the “milk-back” phenomenon (Carlson et al., 2001; Yagci et al., 2005). It has been estimated that up to 42% with dysfunctional voiding suffer from recurrent UTIs episodes.

An extreme form of dysfunctional voiding is represented by Hinman-Allen syndrome, also called non-neurogenic neurogenic bladder syndrome (NNNBS). Hinman and Baumann and Allen described, independently, in the 70s, this condition in two series of children with severe functional dysfunction producing changes indistinguishable from an obstructive factor (Hinman & Baumann, 1973). Objective findings of NNNB syndrome are represented by severe obstructive uropathy, with elevated postvoid residual (PVR) urine volume, thickened, trabeculated bladder wall, recurrent UTIs, and acquired VUR and hydronephrosis. It often presents in the more complex form of dysfunctional elimination syndrome, including also the development of fecal disturbances and usually leads to very serious consequences including renal failure (Claudon et al., 2010).

Clinical criteria have been developed to help in distinguishing between NNNB syndrome and neurogenic bladder: in Hinman-Allen syndrome there is intact perineal sensation and anal tone, normal anatomy and function of the lower extremities are found, there is no evidence of skin lesions overlying the sacrum, normal lumbosacral spine at plain radiography, and normal spinal cord at MR imaging (Johnson et al., 1992). A relation between this abnormal bladder behavior in children, developed during their period of toilet training and a difficult familial-social condition (in particular the presence of a history of sexual harassment) has been reported in over 50% of the subjects affected (Ellsworth et al., 1995; Davila et al., 2003).

### 3. Diagnostic procedures

Some parameters have been developed, in order to classify a voiding disturbance as true Dysfunctional Voiding. There are clinical and laboratory requirements. Furthermore, a deep evaluation of all possible complicating factors need to be performed and the results must also be monitored after a treatment.

#### 3.1 History taking, examination and questionnaires

A correct case history collection represents the first and most important step in the diagnosis of DV.

Voiding habits of patients presenting with symptoms of recurrent cystitis (pelvic pain or burning, frequent voiding, nocturia, blood in urine) must be carefully collected. A voiding diary can also be useful. In older patients also a pediatric history should be deeply collected, as far as possible.

Examination of the external genitalia, with particular care for eventual secretions can allow to exclude different etiologies, or address to particular infectious agents. Furthermore, in the female, a thorough inspection for vaginal wall prolapse should be always made, since they could account for obstructive symptoms, even in initial cases (Dancz & Ozel, 2011).

For pediatric patients also several questionnaires have been developed to assess voiding dysfunction (Tuygun et al., 2007). The most accepted is represented by the standardized dysfunctional voiding symptom score (DVSS) (Farhat et al., 2000). It consists of questions, the pediatric patient can easily understand and answer, while the parents are asked to



evaluate whether possible traumatic events have recently occurred that could justify the raise of the symptoms. The reliability of the test in predicting voiding dysfunction in the subsequent strumental iter was proven through different studies and could be successfully adapted to settings presenting cultural differences from western countries (Bartkowski & Doubrava, 2004; Calado et al., 2010).

A similar but more complex test, that can better fit to an adult population is represented by the Pelvic Floor Inventories Leiden (PelFIs), developed at the University of Leuven, aimed at the evaluation of a broader spectrum of different pelvic floor disorders. It consists of 83 items related to micturition, defecation and sexual dysfunction symptoms (Voorham-van der Zalm et al., 2008). It offers very good results in terms of validity and reliability. (Voorham-van der Zalm et al., 2011).

Although self assessment questionnaires represent a valid item in the evaluation of pelvic disorders, as reported in the literature, it is authors' belief that they cannot be considered as a substitute of the general clinical assessment on the basis of the personal judgement and experience of the physician, and a complete evaluation must be always be made after a (video)urodynamic , that is able not only to give a more correct and quantitative assessment of the disturbances felt by the patient, but also to discover mechanisms that could not be directly correlated with the symptoms and would therefore remain undiscovered, only based on patient's perceptions.

### 3.2 Urinalysis

In women presenting to their physician compelling of recurrent pelvic pain symptoms, chemical and cultural urine analysis represent the first line examination. The finding of high levels of nitrate in the urine, or the presence of leucocytes, is highly suggestive for the presence of urease producing bacteria. The importance of urinalysis in dysfunctional voiding relies on the need of stating the actual presence of recurrent UTIs; at the same time, it is necessary to prove the efficacy of an antibiotic therapy and to exclude the onset of an asymptomatic bacteruria.

### 3.3 Urodynamics

Functional assessment through urodynamics (UD) or with video-urodynamics (VUD) represents a second-level examination for UTIs assessment, but become mandatory in cases of treatment refractory recurrent UTIs. Some findings are typical of DV at the urodynamic evaluation. In these cases the contextual registration of needle EMG is very helpful (Minardi et al., 2008).

### 3.4 Ultrasound

Genito-urinary ultrasound (US) - in experts hands - represents an important tool in the evaluation of all cases of urinary tract dysfunctions, allowing a first examination of morphological changes, that are present in case of obstructed voiding, and a first assessment of the integrity of the urinary system. Advances in ultrasound equipment such as the development of vaginal probes allowing the use of higher frequency ultrasound have led to a dramatic increase in the resolution of images obtained and to date perineal US is held as an effective, well-tolerated and affordable diagnostic procedure (Sendag et al., 2003).

In the evaluation of the characteristics of the lower urinary tract US can also be used to evaluate the anatomy of the urethro-vesical junction and the mobility of the bladder neck

for the study of stress urinary incontinence (Kolbl et al., 1988; Quinn et al., 1988; Khullar et al., 1996; Sarnelli et al., 2003).

Bladder neck mobility can be demonstrated by perineal or vaginal ultrasound and measured using the symphysis pubis as the immobile reference point; perineal ultrasonography allows visualization and measurement of the angle between the proximal mobile part and the distal fixed part of the urethra.

Under these aspects US offers several advantages over other imaging modalities: using US urethral sphincter volume and detrusor wall thickness could be investigated in women with urinary incontinence, urinary retention and detrusor instability (Kondo et al., 2001; Schafer et al., 2002; Oliveira et al., 2006); in patients with detrusor overactivity a positive correlation was observed between rhabdosphincter thickness and detrusor contraction pressure, and between rhabdosphincter thickness and urethral resistance, and mean maximum urethral closure pressure and sphincter volume (Major et al., 2002; Wiseman et al., 2002).

Sendag et al., applying perineal ultrasound, found that posterior urethro-vesical angle was significantly different both at rest and on straining in patients with stress incontinence, as well as the angle between the vertical axis and urethral axis and the descensus diameter (Sendag et al., 2003).

Perineal ultrasonography provides also serial non-invasive examinations for assessing the condition of the bladder wall; the normal bladder wall is 3 to 6 mm thick although it varies with intravesical volume; it may be thickened secondary to chronic infection, inflammation after surgery, or radiation; a decrease in bladder wall thickness may suggest clearing of an infection or inflammation; measurement of bladder wall thickness may be helpful for detecting detrusor overactivity (Schaer et al., 1995; Khullar et al., 1996; Yang & Huang, 2003; Minardi et al., 2007).

In their study, Khullar et al averaged the bladder wall thickness at the trigone, dome, and anterior bladder wall to develop criteria for detection of detrusor overactivity, others assumed that measurement of the bladder dome is sufficient to define bladder wall thickness, even if they did not find that women with detrusor overactivity had an appreciably thicker bladder wall than other study groups (Khullar et al., 1996; Yang & Huang, 2003).

US has also been shown to be a reproducible method of assessing urethral sphincter volume (Digesu et al., 2009).

Using 2D ultrasound, on axial US images the normal urethra has a characteristic target-like appearance and is seen as composed by four concentric rings of different echogenicity (Minardi et al., 2007).

In patients with detrusor overactivity a positive correlation was observed between rhabdosphincter thickness and detrusor contraction pressure, and between rhabdosphincter thickness and urethral resistance, as measured by maximal urethral closure pressure (Major et al., 2002).

Morphologic changes in the sphincter echo-texture can occur as result of a variety of factors; but while an intrinsic sphincter deficiency can easily be suggested on axial US images by loss of its normal characteristic target-like appearance, the coexistence of abnormal urethral rings and increased detrusor wall thickness might be due to functional compressive urethral obstruction from sphincter overactivity, both of idiopathic or neurological origin (Minardi et al., 2007).

Under this aspect the introduction of three-dimensional (3D) ultrasound has proven very useful to the morphologic assessment of the pelvic floor.

The advent of 3D images has improved the potential of US technique to measure volumes of structures. The advantages of 3D technology over two dimensions specifically include an ability to cross reference measurements so that the image measured is the best possible one obtainable and therefore in theory reduce the error of these measurements (Tooze-Hobson et al., 2001).

In fact, 3D measurements are produced from assessment of all three planes, each of which will have a biological variation. 3D ultrasound offers a potential advantage over 2D scanning of increased sensitivity, with a reduction in the error from conventional 2D imaging as the operator can constantly cross reference in all three major planes simultaneously and therefore ensure that any surface area being measured is the best possible reproduction. Since the scan may be manipulated in any plane, the image may be viewed from several perspective prior to the actual measurement (Tooze-Hobson et al., 2001). Technical developments enable rapid automated volume acquisition in real time, and currently available transducers designed for abdominal use are well suited for translabial/transperineal imaging (Dietz, 2004). Useful applications are represented by imaging of the urethra, the levator ani and paravaginal supports, prolapse and implants used in pelvic floor reconstruction and anti-incontinence surgery (Dietz, 2004).

Three-dimensional reconstruction of the female human urethral sphincter have shown the precise structure of the muscle layers (smooth and striated muscle fibers) and nerve fibers (myelinated and unmyelinated) and their relations with the urethra and vaginal wall. The proximal third consisted of a circular smooth muscle sphincter, the middle third consisted of two circular layers of smooth and striated muscle fibers and the distal third consisted of a circular layer of smooth muscle fibers surrounded by omega-shaped layer of striated muscle fibers (Karam et al., 2005).

In studies conducted on women with stress-urinary incontinence three-dimensional ultrasound has been shown to be a reproducible method of assessing urethral sphincter volume, where it has been shown to correlate with the area under the urethral pressure profile curve, suggesting a relationship between structural and functional anatomy (Tooze-Hobson et al., 2001; Athanasiou et al., 1999; Robinson et al., 2004).

Perineal ultrasound was used by our group to assess function and morphology of the urethral sphincter and of the detrusor muscle in the evaluation of dysfunctional voiding in female patients with recurrent urinary tract infections (UTIs) (Minardi et al., 2008).

The study population comprised women referred to our Department with more than a 3-year period of recurrent UTIs, and dysfunctional voiding. The diagnosis of dysfunctional voiding was made according to Carlson et al., where an increased external sphincter activity during voiding was recorded on multichannel video urodynamics (Carlson et al., 2001).

The sonographic examination (ESAOTE, model. Technos MP, Genova, Italy) was performed with the patients supine, using both the translabial approach (3.5 MHz sector probe) and the introital approach (6.5 MHz end fire endovaginal probe); the latter was used to allow proper location of the end extremity of the probe close to mid urethra and, due to its superior spatial resolution, to provide a more detailed depiction of minute structure when examining the echogenic texture of the urethra. Image orientation and display on the screen were standardized so that the transducer appears at the bottom, the left side is the ventral aspect of the patient and the upper is the cranial aspect, as described (Schaer et al., 1995; Minardi et al., 2007). The posterior urethro-vesical angle, the proximal pubo-urethral distance and the angle of urethral inclination were calculated, as described (Minardi et al., 2007). The thickness of the bladder detrusor wall was measured at the dome of the bladder.



Visualization of the four-rings different echo texture of the urethra was performed in the same scan plane. Urethral sphincter volume was assessed by measurements of 3 dimensions; they were first determined in the axial plane by measuring the transverse and anteroposterior dimension at the estimated point of widest transverse dimension; the longitudinal dimension was measured in the sagittal plane just off the midline; the ellipsoid volume formula was then applied as follows:  $\text{volume} = \text{height} \times \text{width} \times \text{length} \times 0.52$ .

Urethral sphincter volume was measured using a 7.5 MHz transvaginal ultrasound probe, where volume was calculated using formula for the volume of a cylinder, as described (Kondo et al., 2001; Wiseman et al., 2002).

We observed that maximum urethral sphincter volume was significantly increased in patients with recurrent UTIs and dysfunctional voiding ( $2.87 \pm 0.41 \text{ cm}^3$ ) compared to patients with recurrent UTIs and normal perineal activity during voiding and to control patients ( $1.77 \pm 0.62 \text{ cm}^3$  and  $1.61 \pm 0.32 \text{ cm}^3$  respectively); abnormal findings at ultrasound included thickening of individual rings, haziness of contours and change in echogenic texture with loss of the characteristic four-rings appearance; these findings were observed only in patients with dysfunctional voiding (Minardi et al., 2008).

Detrusor wall thickness as assessed by suprapubic ultrasound ranged from 2.2 to 9.3 mm.; it was significantly thicker in patients with dysfunctional voiding ( $7.83 \pm 0.8 \text{ mm}$ ) compared to patients with recurrent UTIs and normal perineal activity during voiding and to control patients ( $3.81 \pm 1.1 \text{ mm}$ . and  $3.92 \pm 1.8 \text{ mm}$ . respectively).

The ROC analysis showed that, to identify a patient with dysfunctional voiding, a sphincter volume threshold of  $1.94 \text{ mm}^3$  has 100% sensitivity and 63.2% specificity; a detrusor thickness threshold of 4.95 mm has 100% sensitivity and 85.4% specificity; at these cut-off values, 56.9% of patients with dysfunctional voiding had both the two ultrasound parameters above the threshold level (Minardi et al., 2008).

In our study by the analysis of opening/maximum flow detrusor pressure and mean/maximum urethral closure pressure, patients with recurrent UTIs associated with dysfunctional voiding are obstructed; similarly, by the analysis of detrusor thickness and striated sphincter volume at ultrasound, we can diagnose obstruction. We have found positive correlations between opening/maximum flow detrusor pressure and urethral sphincter volume, between mean/maximum urethral closure pressure and urethral sphincter volume, and between detrusor thickness and urethral sphincter volume in patients with recurrent UTIs associated with dysfunctional voiding; the increased urethral sphincter volume, as a consequence of a dysfunctional voiding, can be the cause of a functional obstruction (Minardi et al., 2008). An increased urethral sphincter volume, as a consequence of a dysfunctional voiding, can be the cause of functional obstruction.

Based on our experience, dysfunctional voiding can be suspected by ultrasound in women with recurrent UTIs, when an increase of detrusor thickness and of striated sphincter volume is observed. Data derived from the ROC curves about cut-off values of urethral sphincter volume and detrusor thickness allow us to propose perineal ultrasound as a first line diagnostic approach in the evaluation of dysfunctional voiding in women with recurrent UTIs.

Therefore, we have suggested that a first line approach in female patients with recurrent UTIs can be done by flow electromyography, with recording of urine flow and perineal activity during voiding, and by perineal ultrasound, with the evaluation of detrusor wall thickness and of sphincter volume; these investigation in our experience are able to select

patients with dysfunctional voiding. According to results of our study, multichannel video urodynamics can therefore represent a second line diagnostic approach in selected patients.

#### 4. Treatment options

DV treatment is particularly problematic: the aim is to restore a normal voiding pattern, to reduce excessive detrusor and pelvic floor activity, to improve voiding and storage symptoms and especially to reduce UTIs incidence. DV therapy combines pharmacological treatment, physical therapy and behavioral therapy.

DV treatment, with particular reference to UTIs, benefits, from a long time, of biofeedback, which has been employed for the first time in the 80's, on babies followed up for 3 years, with complete voiding pattern normalization (Hellstrom et al., 1987). Afterwards, many studies were focused on the linkage between DV and UTIs, trying to find therapeutic protocols which would be able to normalize voiding pattern and reduce UTIs recurrence and, from the other side, be simple to manage for the patient and, when in the pediatric age, for his family.

De Paepe et al. published in 1998 the first prospective clinical trial aimed to investigate the role of biofeedback modulation (BFM) in UTIs prevention in young girls (De Paepe et al., 1998). Girls of age under 14 were enrolled, with urodynamic-confirmed DV diagnosis. In the first phase of the treatment, patients were taught to take self-consciousness of perineal musculature and afterwards they started BFM. During this period, trimethoprim and anticholinergic drugs, in case of overactivity, were prescribed. The antibiotic treatment was stopped at the end of the BFM protocol and the patients were followed-up for 6 months. Considering an UTIs-free period of 6 months, at least the 83% of patients of age over 6 years were free from infections. Moreover, the Authors reported also a complete resolution of vesico-ureteral reflux in 5 of 6 cases. This study, which was of great importance because it shed light on the ability of BFM in reducing urinary infections, had several limitations, especially the absence of a control group (very important in this setting, because of the frequent spontaneous resolution of predisposing factors at this age, e.g reflux), and relatively short follow-up.

VUR is a determinant factor which is able to predispose DV patient to recurrent UTIs. In this regard, Kibar et al studied in deep the linkage between BFM treatment and frequency of VUR in children with DV (Kibar et al., 2007). Eighty-six patients of age over 5 years were enrolled in a BFM program; of these, 78 completed the protocol. At the end of 6 months follow-up, the Authors reported a significant improvement in all the considered parameters, both in symptoms (enuresis, incontinence, frequency, urgency) and urodynamics parameters. Moreover, the 29% of VUR improved, with a complete resolution in 63% of cases. Considering the frequency of spontaneous resolution of VUR in this age group, Authors concluded that BFM treatment could be considered as a good option alternative to watchful-waiting.

In the pathophysiology of recurrent UTIs in DV patient, post-void residual is of crucial importance. Kibar and coll focused their attention in a prospective randomized trial in which 94 kids with flowmetric and electromiographic profile compatible with DV, and a PVR higher than 20 ml were enrolled (Kibar et al., 2010). Patients were randomized in two groups, in the first one kids were informed with behavioral rules, in the other patients received also BFM. At the end of the treatment, there was a complete resolution of PVR in 64,5% in the group which received both treatments vs. th 34,4% in the first group. Moreover, Authors reported a reduction of UTIs in both groups.

BFM was applied not only in pediatric population, but also recently in adult female patients with recurrent UTIs and DV. In a prospective randomized clinical trial, we examined 142 women assigned to 4 treatment groups (Minardi et al., 2010) The first group underwent only uroflowmetry BFM, the second only BFM, the third both the two treatments and the fourth only antibiotic treatment when needed. During the treatment and at the end of the protocol, patients underwent periodic urine cultures and periodic evaluation of symptom scores and urodynamics parameters, trying to show variation in the subjective and objective domain. Only 86 subjects completed the protocol. Authors observed an improvement not only in the obstructive symptoms but also on irritative domain, as well as on urodynamic parameters, with results that remained stable until the end of follow-up period of 24 months. UTIs incidence was dramatically reduced in all the three group of treatment, but remained unchanged in the group that received only antibiotic therapy. The low compliance that emerged from this protocol, stresses the commitment, sometimes considerable, required to the patient in order to complete the protocol and to keep in touch with the hospital. This is of utmost importance because dropping out the protocol leads to a significant worsening of the results.

<b>Neurologic causes</b>	Neurologic diseases (e.g. Multiple sclerosis, Lateral amyotrophic sclerosis, Parkinson disease)
	Spinal lesions/trauma
	Pharmacological treatments (e.g. TCA, antimuscarinic agents, alpha agonists, ganglion-blockers)
	Endocrine (e.g. Diabetes mellitus, hypotiroidismus)
<b>Non-neurologic causes</b>	Mechanic intrinsic bladder outlet obstruction (e.g. prostatic hyperplasia, bladder neck disease, urethral stenosis, bladder prolapse)
	Extrinsic obstruction (e.g. pelvic masses, pelvic organs prolapse)
	Psychogenic (e.g. anxiety syndrome, hysteria)
	Inflammatory (e.g. urethritis, prostatitis, herpes)
	Myopathy (detrusor myopathy, myasthenia gravis)
	Iatrogenic (e.g. after pelvic surgery)
	Idiopathic causes

Table 1. Most common causes of Urinary retention.

Anyway, some open questions remain, in particular on which parameters should be considered to establish the success of therapy and which prognostic factor the clinician can use in this setting. Nelson and coll evaluated the importance of urodynamic parameters in the evaluation of BFM treatment outcomes in DV patients (Nelson et al., 2004). This study confirmed the beneficial effect of BFM on the resolution of recurrent UTIs, but there was no correlation between the clinical improvement and urodynamic parameters improvement. In this study, which involved 81 pediatric patients followed up for more than 9 months after the end of BFM, there was no statistically significant difference in urodynamic parameters (in particular PVR and maximum flow) between those who had persistence of UTIs and those who benefit from this therapy.

In a retrospective study on 77 boys with DV, Drzewiecki and coll. showed that some parameters are able to predict the success of BFM therapy (Drzewiecki et al., 2009). The Authors noted that compliance and commitment during the treatment are both determinant factors, considering that at least 6 sessions are required for pediatric patients and that the probability of flow normalization after the third session are reduced to 5%.

At present, there is no evidence about this point in the adult population; so future randomized trials should also aim to identify predictive factors in order to tailor the treatment to any specific patient as much as possible.

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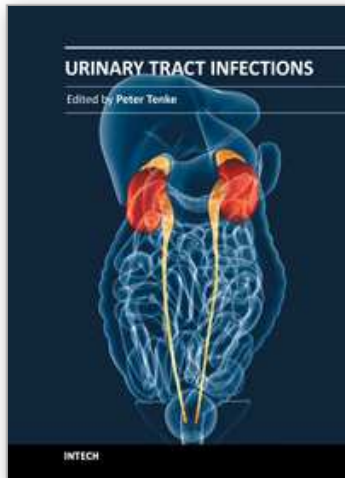
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Urinary tract infections (UTIs) are among the most common bacterial infections worldwide, and they are also the leading cause of hospital-acquired infections. Therefore, the appropriate management of UTIs is a major medical and financial issue. This book covers different clinical manifestations of UTI, with special emphasis on some hard-to-treat diseases, and special conditions in respect of treatment; antibiotic resistance and the available alternative strategies for the prevention and treatment of UTIs and it deals with urinary tract infections in children. The aim of this book is to give a summary about the different aspects of the diagnosis, management and prevention of urinary tract infections for all medical disciplines.

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