Committee 10 A

Conservative Management of Urinary Incontinence in Childhood

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I. INTRODUCTION

In this chapter the different conservative treatment modalities of urinary incontinence in childhood will be discussed. In order to understand the pathophysiology of the most frequent encountered problems in children the normal development of bladder and sphincter control will be discussed briefly.

Most children present with either nocturnal enuresis or day and nighttime incontinence: the underlying pathophysiology will be outlined and the specific investigations for children will be discussed. For general information on epidemiology and urodynamic investigations the respective chapters are to be consulted. Specific information on those conditions that require surgical treatment such as epispadias and ectopic ureter is provided in the chapter on surgical management.

1. NORMAL DEVELOPMENT OF BLADDER AND SPHINCTER CONTROL

Normal bladder storage and voiding involve low-pressure and adequate bladder volume filling followed by a complete and succinct detrusor contraction associated with adequate relaxation of the sphincter complex. This process requires normal sensation and adequate bladder outlet resistance. The neurophysiological mechanisms involved in normal bladder storage and evacuation include a complex integration of sympathetic, parasympathetic and somatic innervation which is ultimately controlled by a complex interaction between spinal cord, brain stem, midbrain and higher cortical structures [1].

Achievement of urinary control is equally complex and as yet not fully understood; various developmental stages have been observed [2].

In newborns the bladder has been traditionally described as uninhibited, and it has been assumed that micturition occurs automatically by a simple spinal cord reflex, with little or no mediation by the higher neural centres. However studies have indicated that even in full-term fetuses and newborns, micturition is modulated by higher centres and the previous notion that voiding is spontaneous and mediated by a simple spinal reflex is probably an oversimplification. Fetal micturition seems to be a behavioural state-dependent event: intrauterine micturition is not randomly distributed over various behavioural (sleep and arousal) states, but occurs almost exclusively while the fetus is awake [3].

During the last trimester the intra-uterine voiding frequency is approximately 30 times every 24 hours [4]. Immediately after birth voiding is usually very infrequent during the first few days of life. The first void may only take place after 12 to 24 hours. After the first week frequency increases rapidly and peaks at the age of 2 to 4 weeks to an average of once per hour. It then decreases and remains stable after 6 months to about 10 to 15 times per day. After the first year it decreases to 8 to 10 times per day, while voided volumes increase by three- to fourfold.

During the postnatal period micturition control mechanisms undergo further changes and extensive modulation. Using ambulatory bladder monitoring techniques in conjunction with polysomnographic recordings it has been shown that even in newborns the bladder is normally quiescent and stable and micturition does not occur during sleep [5]. This inhibition (or lack of fascilitation) of detrusor contractions during sleep is also observed in infants with neurogenic bladder dysfunction who have marked detrusor overactivity while they are awake. In response to bladder distension during sleep, an infant nearly always exhibits clear electroencephalograhic evidence of cortical arousal, facial grimaces or limb movements, or actual awakening. Sleeping infants are always seen to wake up before bladder activity returns and voiding occurs. This arousal period may be transient and the infant may cry and move for a brief period before micturition and then shortly afterward go back to sleep. Because this wakening response is already well established in newborns, it follows that the control of micturition probably involves more complicated neural pathways and higher centres than has been appreciated. There is also strong evidence that a pronounced reorganisation of pre-existing synaptic connections and neural pathways involved in bladder control occurs during the early postnatal period.

In newborns micturition occurs at frequent intervals, may be *intermittent,* but bladder emptying efficiency is usually good. In over 80 percent of voids it is complete after voiding or quick succession of small voidings [6]. During infancy voiding pressures are much higher than in adults. It has also been noted that these pressures are higher in boys than in girls (mean Pdet max of 118 vs. 75 cm H_2O, respectively, P<.03) [7,8]. These higher detrusor pressures decrease progressively with increasing age. Besides in 20-70 percent of infants with normal lower urinary tracts, intermittent voidings were observed. They tend to disappear with increasing age, and are thought to represent variations between individual infants in the maturation of detrusor and sphincteric co-ordination during the first 1 to 2 years of life. Videourodynamic studies have confirmed these findings [5,7,8,9,10].

Between the age of 1 and 2, conscious sensation of bladder filling develops. The ability to void or inhibit voiding voluntarily at any degree of bladder filling commonly develops in the second and third years of life. Central inhibition is crucial to obtain continence.

During the second or third year of life, there is progressive development towards a socially conscious continence and a more voluntary type of micturition control develops. The child becomes more aware of the sensation of bladder distension and the urge to urinate, as well as social norms and embarrassment associated with urinary incontinence. Through an active learning process, the child acquires the ability to voluntarily inhibit and delay voiding until a socially convenient time, then actively initiates urination even when the bladder is not completely full and allow urination to proceed to completion. During the first years of life, gradual development to an adult type of voluntary micturition control that conforms to the social norms depend on an intact nervous system in addition to at least three other events occurring concomitantly: a progressive increase in functional storage capacity, maturation of function and control over the external urinary sphincter and most importantly achievement of volitional control over the bladder-sphincteric unit so that the child can voluntarily initiate or inhibit a micturition reflex [11].

The final steps are usually achieved at the age of 3 to 4 years when most children have developed the adult pattern of urinary control and are dry both day and night. The child has learned to inhibit a micturition reflex and postpone voiding and voluntarily initiate micturition at socially acceptable and convenient times and places. This development is also dependent on behavioural learning and can be influenced by toilet training which in turn depends on cognitive perception of the maturing urinary tract.

It is understandable that this series of complex events is highly susceptible to the development of various types of dysfunction. Various functional derangements of the bladder-sphincter-perineal complex may occur during this sophisticated course of early development of normal micturition control mechanisms. These acquired functional disorders overlap with other types of bladder functional disturbances that may have a more organic but congenital underlying pathophysiological basis.

2. Normal values

a) Normal bladder capacity

The bladder capacity increases during the first 8 years of life roughly with 30 ml per year, so with an average capacity of 30 ml in the neonatal period, a child's bladder volume can be calculated as Y = 30 + 30 X, where Y = capacity in ml and X = age in years (Fig 1) [12].

Hjälmås described a linear correlation that could be used up to 12 years of age: in boys, Y = 24.8 X + 31.6, in girls Y = 22.6 X + 37.4, where Y is capacity in ml, and X is age in years (13). It should be noted that these data were obtained during cystometric investigations and not necessarily reflect normal bladder volumes. Obviously, the relation between age and bladder capacity is not linear for all ages, nor is the relation between body weight and bladder capacity [14].

Another formula to calculate functional bladder capacity in infants is: bladder capacity (ml) = 38 + (2.5 x age (mo)) [10].

Kaefer and co-workers demonstrated that a non-linear model was the most accurate for the relation between age and bladder capacity, and they determined two practical linear equations:

Y = 2 X + 2 for children less than 2 years old, and Y = X/2+6 for those 2 years old or older; Y = capacity in ounces, X = age in years (Fig. 2) [15].

Girls were found to have a larger capacity than boys, but the rate of increase with age was not significantly different between them. Data on 'normal' bladder capacity have been obtained in continent children undergoing cystography, with retrograde filling of the bladder.

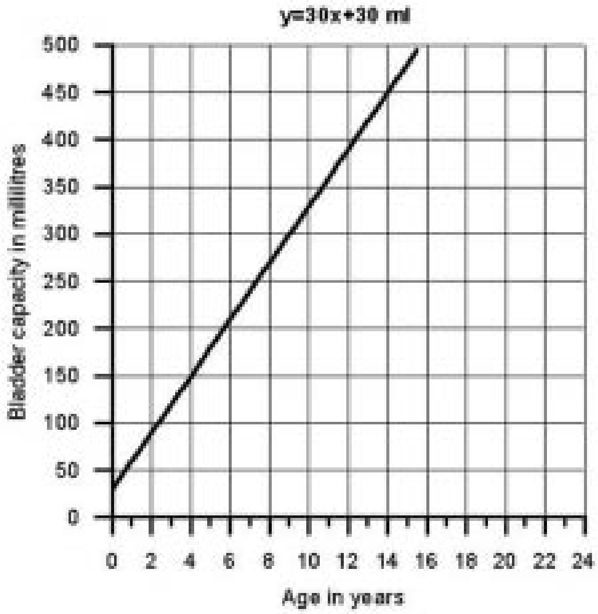

Figure 1 : Bladder capacity using the formula Y = 30 + 30 X (Y= capacity in ml, X = age in years)

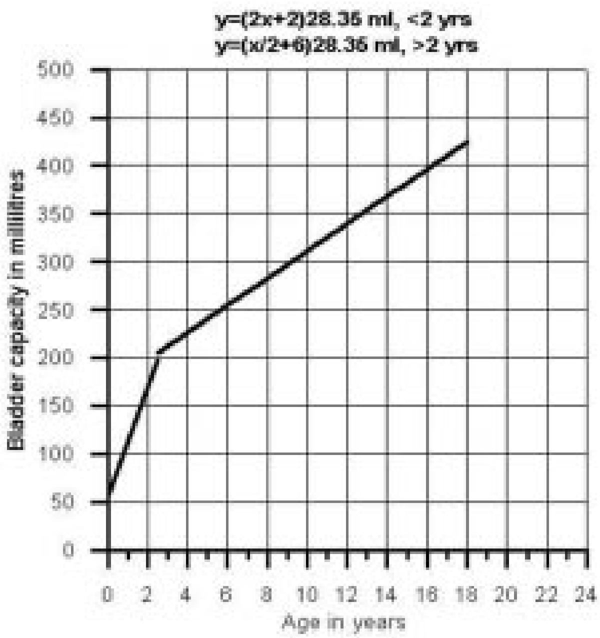

Figure 2 : Bladder capacity using the formula described by Kaefer et al. Y = (2 X + 2) x 28.35 ml < 2 years Y = (X/2+6) x 28.35 ml > 2 years (Y = capacity in ml, X is age in years)

Data obtained from the International Reflux Study indicate that there is not a linear relation between age and capacity and that there is a huge variability. (Fig 3).

b) Normal voiding pattern

The micturition frequency of the fetus during the last trimester is approximately 30 per 24 hours. It decreases

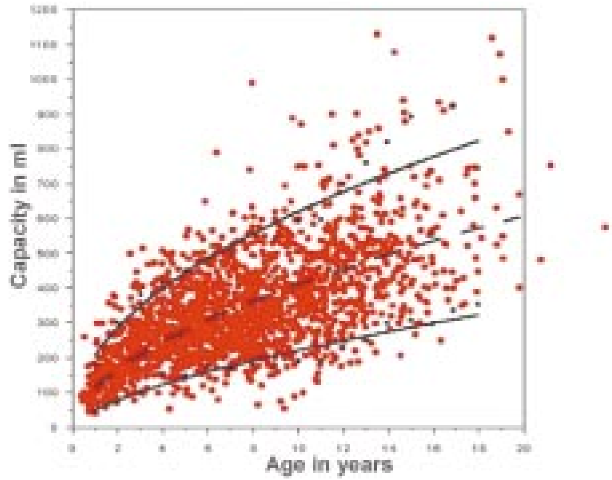

Figure 3 : Bladder capacities determined by VCUG in the International Reflux Study

to 12 during the first year of life, and after that it is reduced to an average of 5±1 voidings per day [10,15].

Thus, the normal range for the micturition frequency at age seven is 3 to 7 [16].

By age 12, the daily pattern of voiding includes 4-6 voids per day [17].

Mattson and Lindström emphasize the enormous variability of voiding frequencies in children: in individual children, the weight-corrected diuresis could vary up to 10-fold [18].

c) Normal pressures at voiding

Bladder dynamics in children have demonstrated developmental changes with age. Bladder pressures at voiding in children are similar to adults, with a mean maximum pressure of 66 cm H_2O in boys, and 57 cm H_2O in girls [19].

These pressures are lower than those reported in infancy by Yeung et al, who found boys having pressures of 118 cm H_2O, girls 75 cm H_2O [5]

d) Normal urinary flow rates

Urinary flow rates in normal children have been only minimally described. Szabo et al Published nomograms for flow rates vs age in normal children [20].

As in adults, flow rates are clearly dependent upon voided volume, and normal values can only be applied to flow rates that have been registered when voiding at a bladder volume approximating the normal capacity for age [18],[21].

The definitions in this chapter comply with "Standardisation and definitions in lower urinary tract dysfunction in children", published in the British Journal of Urology in 1998 on behalf of the International Children's Continence Society (ICCS) [22].

II. EVALUATION IN CHILDREN WHO WET

Even with clear definitions, the approach to history-taking and physical examination has to be structured. The child's complaints at presentation are not synonymous with the signs and symptoms that have to be checked to arrive at a diagnosis. Also, sociocultural aspects and psychomotor development will distort the presentation. Validated questionnaires are very helpful in structuring the history-taking; they at least provide checklists [23].

With a structured approach the diagnosis of monosymptomatic nocturnal enuresis can be made with confidence.

When ultrasound imaging of kidneys and bladder, recording of urinary flow, and measurement of post-void residual are added to history and physical examination, the clinical entities caused by non-neurogenic detrusor-sphincter dysfunction can be diagnosed accurately in the majority of cases, and a high level of suspicion can be maintained towards incomplete bladder emptying in both neurogenic detrusor-sphincter dysfunction and structurally caused incontinence. This is important in view of the potential these conditions have to cause irreversible loss of kidney function.

In a minority of incontinent children the non-invasive assessment yields dubious results, or results suggesting gross deviations from normal function. Only in these situations there is an indication for invasive investigations, such as:

- Voiding cystourethrography.
- Invasive urodynamics (cystometry, pressure-flow, EMG studies, videocystometry).
- Renal scans or intravenous urography.
- Cystourethroscopy.

1. History taking

For the pediatric age group, where the history is jointly obtained from parents and child, and where the development of bladder control generates specific problems, a structured approach is recommended, with a questionnaire [23].

Many signs and symptoms pertaining to voiding and wetting are new to the parents, and they should be specifically asked for, with the questionnaire as checklist. If possible the child should be addressed as a collaborator and questioned directly, as the symptoms prompting the parents to seek consultation may be different from that which is problematic for the child.

A voiding diary is mandatory to determine a child's voiding frequency and voided volumes. Checklists and voiding dairy can be filled out at home, and checked at he first visit to the clinics. History-taking should also include assessment of bowel function; a similar pro-active procedure with a questionnaire should be followed for defecation and fecal soiling [24].

The general history-taking should include questions relevant to familial disorders, neurological and congenital abnormalities, as well as information on previous urinary infections, relevant surgery and menstrual and sexual functions. Information should be obtained on medication with known or possible effects on the lower urinary tract.

At times it is helpful to more formally evaluate the child's psychosocial status and the family situation e.g. using validated question forms such as CBCL (Achenbach) or the Butler forms [25,26].

Child abuse is very often signalled first by symptoms of bladder-sphincter dysfunction [27].

2. Physical examination

Apart from a general pediatric examination, the physical examination should include the assessment of perineal sensation, the perineal reflexes supplied by the sacral segments S1-S4 (standing on toes, bulbocavernosus) and anal sphincter tone and control. Special attention should be paid to inspection of the male or female genital region, and of the urethral meatus. Asymmetry of buttocks, legs or feet, as well as other signs of *occult neurospinal dysraphism* in the lumbosacral area (subcutaneous lipoma, skin discoloration, hair growth and abnormal gait) should be looked for specifically.

In examining the abdomen, the presence of a full sigmoid colon or descending colon is a significant finding with a history of constipation.

Detailed questioning of the parents' observation of the child's voiding habits is essential as is direct observation of the voiding, if possible. Children may have their voiding dysfunction ameliorated or even eliminated by correcting anomalies of body position detected when observing the child's micturition. Children may void in awkward positions, e.g. with their legs crossed or balancing on the toilet without proper support of the legs, thereby activating the pelvic floor and obstructing the free flow of urine (Fig. 4) [28].

3. Urinalysis

In order to be comprehensive, physical examination should include urinalysis to identify any infection and glucosuria.

Figure 4 : Improper position for voiding: the feet are not supported (unbalanced position) and the boy is bent forward. Support of the feet will correct this and will the pelvic floor muscles allow to relax properly.

4. Non-invasive diagnostic techniques

a) Frequency/volume charts: bladder diary

The frequency/volume chart is a detailed diary recording fluid intake and urine output over 24-hour periods. The chart gives objective information on the number of voidings, the distribution of day and night voids, along with the voided volumes and episodes of urgency and leakage, or dribbling. In order to obtain a complete picture defecation frequency and/or soiling are often recorded.

From the frequency/volume chart the child's "functional" bladder capacity may be assessed as the largest voided volume, with the exception of the morning micturition which actually represents nighttime bladder capacity. Whenever possible, filling out the chart is the responsibility of the child: the parents provide assistance and support. Ideally the chart should cover 3 complete days, but in reality completion over a weekend restricts the record to 2 days.

The frequency volume chart is a reliable non-invasive measure of maximum bladder storage capacity and can be used as an outcome measure in children with bladder dysfunction if care is taken to minimise confounding factors and sources of error during chart completion [29].

The amount of urine voided by a non-supervised child during the day varies considerably since the child's voidings are dictated more by social circumstances and /or bladder activity rather than by bladder capacity. Children with bladder symptoms void smaller volumes of urine than may be expected from traditional estimates [29]. This is unrelated to either gender, type of presenting incontinence or a positive family history of bladder dysfunction. The only significant influence upon voided volumes recorded on a frequency volume chart is the age effect, and voided volumes in incontinent children increase incrementally with age. The frequency volume chart is useful when comparing the mean voided volume and SD by a child's age.

Validation and test/retest data on frequency/volume charts whilst scarce indicate that voiding interval is the most variable parameter [29]. Data in normal children and in children with different categories of incontinence are available for comparison [29,30,31].

In order to obtain a complete picture it is better to ask for a bladder diary: fluid intake as well as voiding frequency, voided volumes, incontinence episodes and defecation frequency and/or soiling are recorded.

Test/retest evaluation is not available; trend analyses of frequency/volume charts can be extracted from currently available data.

b) Quantification of urine loss

Subjective grading of incontinence may not indicate reliably the degree of dysfunction. For objective grading, 12-hour pad test and frequency/volume charts are validated instruments [30, 31].

In children, the 12-hour pad test should also give information about fluid intake. The pad test is complementary to the bladder diary, which denotes more the frequency of incontinence and the distribution of wetting episodes than the quantities of urine lost.

The amount of urine lost during sleep can be determined by weighing diapers or absorbent pads, before and after sleep. To obtain a measure of the total nocturnal urine output, the volume of the early-morning voiding should be added to the amount lost during sleep.

c) Quantification of constipation

In grading constipation, scoring a plain X-ray of the abdomen (Barr score) yields inconsistent results [33,34,35].

A better way to match clues from the medical history with signs and symptoms is the measurement of colonic transit time. As many children with non-neurogenic detrusor-sphincter dysfunction habitually use their pelvic floor as emergency brake, anomalous defecation frequency and constipation have a high prevalence in this group. Overt constipation should be dealt with before embarking on treatment of incontinence or detrusor-sphincter dysfunction [36].

d) Urinary flow

Voiding should be analysed in detail in all incontinent children with the exception of monosymptomatic bedwetting where voiding, as far as we know, is normal.

Graphic registration of the urinary flow rate during voiding is becoming a standard office procedure. Flow patterns and rates should be consistent to allow for evaluation, and several recordings are needed to obtain consistency.

Approximately 1% of school children have a voiding that can be labelled abnormal with flattened or intermittent flow curves. The remaining 99% have a bell-shaped flow curve [21].

Flow recordings with a voided volume of less than 50% of the functional capacity are not consistent: they represent voiding on command, and many children will try to comply by using abdominal pressure. A helpful tool in this respect is the bladder scan: before micturition the bladder volume can be assessed. If the bladder is still nearly empty the child should be asked to drink some water until the bladder is full enough for a reliable flow.

Urinary flow may be described in terms of rate and pattern and may be continuous, intermittent (in fractions), or staccato.

Measurement of urinary flow is performed as a solitary procedure, with bladder filling by diuresis (spontaneous or forced), or as part of a pressure/flow study, with bladder filling by catheter. Patterns and rates should be consistent to allow for evaluation, and several recordings are needed to obtain consistency [37].

The same parameters used to characterise continuous flow may be applicable, if care is exercised, in children with intermittent, or staccato flow patterns. In measuring flow time, the time intervals between flow episodes are disregarded. Voiding time is total duration of micturition, including interruptions.

5. Ultrasound imaging of upper and lower urinary tract

In most clinical settings, ultrasound imaging techniques are routinely used in children with incontinence. Upper tract abnormalities such as duplex kidney, dilatation of the collecting system, and gross reflux nephropathy can be readily detected, but detection of the more subtle expressions of these abnormalities require urological expertise on the part of the ultrasound operator.

Lower urinary tract abnormalities are even more difficult to assess for the inexperienced, aside from bladder wall thickness: a bladder wall cross-section of more than 3-4 milimeters, measured at 50% of expected bladder capacity, is clinically suspect for long-standing detrusor overactivity [38].

a) Post-void residual volume

Except in small infants, the normal bladder will empty completely at every micturition [39].

The identification or exclusion of post-void residual is therefore an integral part of the study of micturition. However, an uneasy child voiding in unfamiliar surroundings may yield unrepresentative results, as may voiding on command with a partially filled or overfilled bladder. When estimating residual urine, voided volume and the time interval between voiding and estimation of post-void residual should be recorded. This is of particular importance if the patient is in a diuretic phase. In patients with gross vesicoureteral reflux urine from the ureters may enter the bladder immediately after micturition and may falsely be interpreted as residual urine. The absence of residual urine is an observation of clinical value, but does not exclude infravesical obstruction or bladder-sphincter dysfunction with absolute certainty. An isolated finding of residual urine requires confirmation before being considered significant, especially in infants and young children.

b) Ultrasound-flow-ultrasound

This combination of imaging and non-invasive urodynamics is a standardised procedure to obtain representative data on both flow rate and flow pattern, as well as on post-void residual volumes. With ultrasound, bladder filling is assessed and compared with the functional or expected bladder capacity for age—when these values correspond, the child is asked to void in the flowmeter. After recording the flow, post-void residual is assessed again. This procedure avoids the registration of flow rates at unrealistic bladder volumes.

6. Invasive diagnostic techniques

The important question (for the incontinent child) whether invasive diagnostic procedures are necessary is decided by the results of the non-invasive procedures. The diagnostic information needed is that which is necessary to find the correct treatment. Indicators include voiding frequency of 3 or less per day, straining or manual expression during voiding, a weak urinary stream, previous febrile urinary tract infection, continuous dribbling incontinence or pronounced apparent stress incontinence, or previously identified dilating vesicoureteral reflux.

The finding of genitourinary abnormalities or signs of occult spinal dysraphism at physical examination also indicate the need for further diagnostics. Urinary flow registration will detect the plateau-shaped flow curve typical for structural infravesical obstruction, and the intermittent flow suggesting detrusor-sphincter dyscoordination [37].

A clinically significant post-void residual at repeated occasions clearly points to incomplete bladder emptying. The pad test will detect the cases with obvious stress incontinence, or continuous dribbling. Ultrasound imaging will raise suspicion for extravesical ectopic ureters, even when history and pad test do not point to dribbling incontinence.

In short, invasive diagnostics are indicated when the non-invasive program raises suspicion on neurogenic detrusor-sphincter dysfunction (occult spinal dysraphism), infravesical anatomical obstruction (especially posterior urethral valves), genitourinary abnormalities (e.g. epispadias), advanced non-neurogenic bladderdetrusor-sphincter dysfunction (as in children with dilating vesicoureteral reflux and/or febrile urinary tract infections), or significant post void residuals.

To diagnose the complex of non-neurogenic detrusor-sphincter dysfunction, recurrent urinary tract infections and vesicoureteral reflux, urodynamic studies are needed in only a minority of all incontinent children.

• TECHNIQUE

Cleanse and rinse the external genitalia with lukewarm water: do not use detergents. Use a feeding tube with side holes and a rounded tip (Ch 06-08) or balloon catheter to catheterise the bladder; check the urine for infection. Empty the bladder completely before filling. Use a radio-opaque dye of maximum 30% concentration, at body temperature, and fill the bladder by slow-drip infusion, with a hydrostatic pressure of not more than 40 cm H_2O. Note the volume of the contrast medium instilled. Use fluoroscopy during filling at regular intervals.

Take spot-films (70mm or 90mm camera) supine, with partial filling and at the end of filling, in AP projection, of the complete urinary tract. Upper tracts and lower tract should be visible.

When voiding is imminent, change the position of the child so that spot films of bladder and urethra in 3/4 projection during actual voiding can be taken. Also take a spot film during voiding of the upper urinary tract: the degree of vesicoureteral reflux (VUR) may change with the pressure generated by the detrusor muscle during voiding. Post-void residual volumes are a very inconsistent finding with VCUG. The voiding phase is critically important to VCUG, both for reflux detection and for assessment of voiding dynamics. Without a voiding phase, the VCUG is incomplete.

Prophylactic antibiotics are indicated, to minimise the risk for post-VCUG urinary tract infection especially in children with an anatomic abnormality.

• INDICATIONS FOR VCUG

A VCUG is an invasive procedure and should only be done if the outcome will influence the management. It is indicated in children with recurrent urinary tract infections to detect reflux and in children with an abnormal flow pattern to detect infravesical abnormalities (like valves, strictures or a syringocele).

In children with incontinence the lateral projection during voiding is the most important part of the study. Especially in children with stress incontinence or a neuropathic bladder the position and configuration of the bladder neck during filling and voiding should be noted.

In children with non-neurogenic detrusor-sphincter dysfunction as well as in children with neurogenic detrusor-sphincter dyssynergia, the proximal urethra may show the so-called ‘spinning top’ configuration, during filling and during voiding. With detrusor and pelvic floor muscles contracting at the same time, the force of the detrusor contraction will dilate the proximal urethra down to the level of the forcefully closed striated external sphincter. The resulting ‘spinning top’ configuration used to be seen as a sure sign of distal urethral stenosis, a concept held responsible for recurrent urinary tract infections in girls, with urethral dilatation or blind urethrotomy as the obvious therapy. However, urodynamics made it clear that the ‘spinning top’ will only appear when detrusor and pelvic floor contract synchronously, which makes it a functional anomaly, not an anatomical one [40, 41]

Women often recall their experience with VCUG as young girls in terms bordering to abuse. The use of VCUG in children should be limited to the absolutely necessary.

a) Urodynamics

Especially in children urodynamic investigations should only be performed if the outcome will have consequences for treatment. Both children and parents need careful preparation and adequate information before the study is done. It is an invasive procedure and artefacts may occur. Because of the invasiveness of the investigations all children are anxious and this may reflect in the outcome of the study. Especially during the first filling cycle, when the child does not know what to expect, instability may be seen and the voiding phase can be incomplete due to contraction of the pelvic floor muscles during voiding. Once the child knows that filling and voiding are not painful a subsequent filling and voiding cycle may show a completely different pattern. The study should be repeated at least 2 or 3 times. Still the results may not always be reproducible and it should be stressed that the primary objective is to treat the child and not a "urodynamic abnormality" per se.

Special attention should be given to a pleasant surrounding for the child: one or both parents should be present and young children may be given a bottle. Older children may be distracted by watching a video movie. The child should be awake, unanaesthetised and neither sedated nor taking any drugs that affect bladder function

During the study the investigator has the opportunity to observe the child and discuss various findings and correlate them to what the child feels and/or normally would do in such circumstances.

In children, the transition from filling phase to voiding phase is not as marked as in adults. To avoid missing this important transition, cystometry and pressure-flow/EMG measurements are performed as one continuous study in paediatric urodynamics.

Electromyography of pelvic floor muscles evaluates the activity of the striated urethral sphincter, in the filling phase and in the voiding phase. Surface skin electrodes are usually used to record the EMG. In children the pelvic floor EMG is probably of much more importance than in adults as it helps to differentiate the different voiding disorders.

Filling the bladder can be achieved by diuresis (natural fill cystometry) or retrograde by catheter. For retrograde filling by catheter, saline 0.9% or contrast medium at body temperature is recommended in children, without additives; CO_2 is not recommended.

When filling by catheter, slow fill cystometry (5 – 10 percent of expected bladder capacity per minute) is recommended in children, as certain cystometric parameters, notably compliance, may be significantly altered by the speed of bladder filling.

Involuntary detrusor contractions may be provoked by rapid filling, alterations of posture, coughing, walking, jumping, and other triggering procedures.

The presence of these contractions does not necessarily imply a neurologic disorder. In infants, detrusor contractions often occur throughout the filling phase.

Bladder sensation is difficult to evaluate in children. Only in toilet-trained cooperative children is it a relevant parameter. *First desire to void* is not relevant in the infant, but can be used as a guideline in children of 4 years and older. *Normal desire to void* should be considered the volume at which some unrest is noted, e.g. wriggling with the toes; this usually indicates voiding is imminent. In the older child, the volume may be small with the first cystometry, for fear of discomfort. This is the reason that in pediatric urodynamics several cycles of filling are recommended. The difference between strong desire to void and urgency may be too subtle for children to perceive.

Maximum cystometric capacity (CBC) is the volume in the bladder at which the infant or child starts voiding. The value for maximum cystometric capacity is derived from volume voided plus residual volume. Values for CBC should be interpreted in relation to normal values for age.

Compliance indicates the change in volume for a change in pressure. For children with neuropathic bladder-sphincter dysfunction, data are available relating poor compliance to the risk of upper urinary tract damage [41].

The urethral closure mechanism during storage may be normal or incompetent. The normal urethral closure mechanism maintains a positive urethral closure pressure during filling, even in the presence of increased abdominal pressure or during detrusor overactivity (guarding reflex) [42]. Immediately prior to micturition the normal closure pressure decreases to allow flow.

Infravesical obstruction, recorded with a pressure/flow study, may be anatomical or functional in nature. An *anatomical obstruction* creates a urethral segment with a small and fixed diameter, that does not dilate during voiding. As a result, the flow pattern will be plateauing, with a low and constant maximum flow rate, despite high detrusor pressure and complete relaxation of the urethral sphincter. In a *functional obstruction*, it is the active contraction of the urethral sphincter during passage of urine that creates the narrow urethral segment, constantly or intermittently. To differentiate anatomical from functional obstruction, information is needed about the activity of the urethral sphincter during voiding. This information can be obtained, and recorded together with pressure and flow, by monitoring the urethral pressure at the level of the urethral sphincter, or by recording a continuous electromyogram of the striated urethral sphincter sensu stricto. For clinical purposes, in patients where the urethral sphincter is not readily accessible, the electromyogram of the external anal sphincter is often used to monitor activity of the striated urethral sphincter. This corresponds to activity of the pelvic floor muscles (Fig. 5). Also the use of video

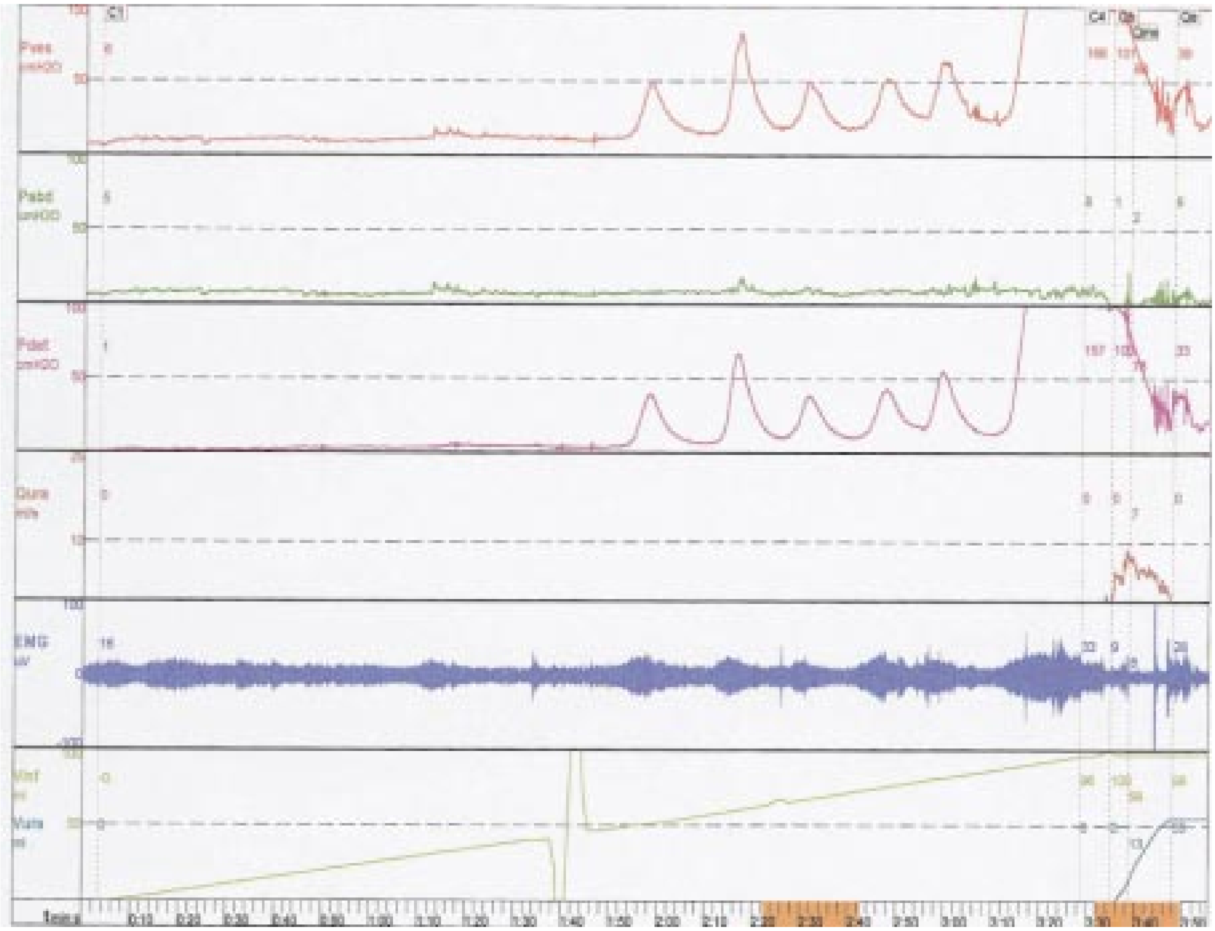

Figure 5 : Urodynamic study illustrating bladder overactivity, counter action of pelvic floor muscles (guarding reflex) and incomplete relaxation during voiding resulting in post void residual urine (bladder instability + dysfunctional voiding).

urodynamics can be very helpful in this respect, as contractions of the pelvic floor muscles can actually be seen during the voiding phase.

In infants and small children, pelvic floor muscle overactivity during voiding (with post-void residuals) is not uncommon: in all probability it is a normal developmental feature [5, 7]

(Over) activity of the urethral sphincter may occur during the voiding contraction of the detrusor in neurologically normal children; this set of events is termed dysfunctional voiding.

Grade of recommendation: for all diagnostic procedures level 2

III. NOCTURNAL ENURESIS

1. Definition

Nocturnal enuresis can be defined as an involuntary voiding of urine during sleep, with a severity of at least three times a week, in children over 5 years of age in the absence of congenital or acquired defects of the central nervous system [44].

It has been argued that parental concern and child distress should also play a part in determining the clinical significance of the problem [45].

Although there is general consensus about the core descriptors of nocturnal enuresis, divergent opinions flourish over many specific aspects of the definition [46].

Age is one such issue. Most definitions refer to 5 years as the watershed although occasionally the child's 'mental age' is taken into account. The age criteria is somewhat arbitrary but reflects the natural course of bladder acquisition. It has been contested that 5 years is appropriate as it is around this time that a child normally is able to start micturition at will and has thus developed cognitive control over voiding [47].

Verhulst et al argue for flexibility in age criteria due to different rates of acquisition for boys and girls. Extrapolation from Verhulst's figures suggests that the prevalence rate for 8 year old boys is equivalent to that for girls at 5 years [48].

2. Severity

Children manifestly vary in wetting frequency. Only some 15 percent of children wet every night although most children wet more than once a week [49, 48].

In a population survey of nearly 1,800 Irish children aged 4 –14 year olds, Devlin found the frequency of wetting as follows: less than once per week in 33 percent, once per week in 11 percent and 2 to 4 times per week in 25 percent [50].

Epidemiological surveys may seek to define the problem if bedwetting occurs more than once a month whereas, in contrast, most trials of treatment effectiveness work to a more severe criteria of perhaps at least 4 wet beds per week. In clinical practice, parental and child concern over the bedwetting, rather than severity itself, seems the relevant issue. Some children and parents are concerned over an occasional wet bed, while others will accept regular wetting. Clinically severity can be defined as: infrequent (1-2 wetting episodes per week), moderately severe (3 – 5 wetting episodes per week) or severe (6 – 7 wetting episodes per week).

3. Prevalence

The extent of bedwetting is widespread. It has been argued that nocturnal enuresis is the most prevalent of all childhood problems [51].

In the United Kingdom estimates suggest around 750,000 children and young people over 7 years will regularly wet the bed. In the USA recent evaluations of prevalence suggest some 5 to 7 million children regularly experience primary nocturnal enuresis [52, 53, 54].

Epidemiological surveys tend to adopt 'lenient' criteria in defining nocturnal enuresis. They survey a sample or the whole community asking parents to check against a list should their child wet the bed. Such surveys (including any episodes of nocturnal enuresis) undertaken in Great Britain, Holland, New Zealand and Ireland suggest that the prevalence for boys is around: 13-19% at 5 years, 15-22% at 7 years, 9-13% at 9 years and 1-2% at 16 years. For girls the prevalence rates are reported to be:

• 9-16% at 5 years, 7-15% at 7 years, 5-10% at 9 years and 1-2% in the late teenage years [48, 50, 55, 56].

All surveys suggest the rate of bedwetting reduces with advancing age. The rate of decline in incidence with the child's age has been assessed as around 14% for 5-9 year olds and 16% for those 10-18 years old. A small percentage of individuals each year do therefore establish nocturnal bladder control. It might be construed that rather than 'growing out of the problem', they are able to develop improved nocturnal bladder control through maturational processes (Fig. 6).

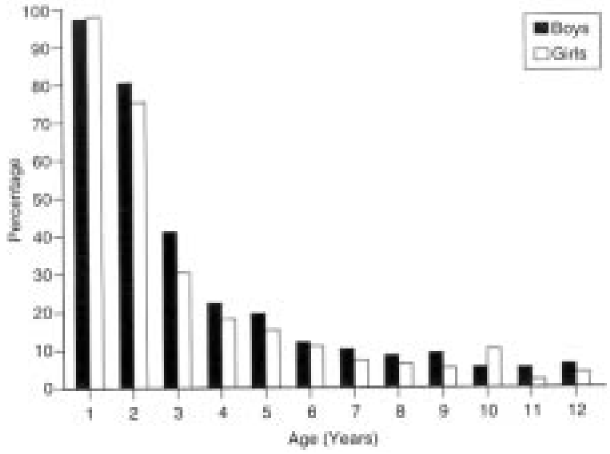

Figure 6 : Prevalence of nocturnal enuresis by age, redrawn from Verhulst et al.

Many adults will be reluctant to come forward or admit to currently having a problem of bedwetting. Hirasing et al sampled over 13,000 adults [18-64 years] and found an overall prevalence rate of nocturnal enuresis at 0.5% [57]. Of these, 12 percent of men and 29 percent of women had daytime incontinence. Fifty percent of men and 35 percent of the women had never consulted a health professional about their bedwetting. Thirty eight percent of the men and 26 percent of the women had never done anything to try and become dry.

The enuresis prevalence of 0.5% in otherwise healthy adults in this study refers to a largely untreated population. Fifty percent of the men had primary enuresis so they had never been consistently dry at night. Assuming a prevalence of enuresis of 8 percent in 7-year-old boys, this could be translated to mean that the risk for an enuretic boy to remain enuretic for the rest of his life is 3 percent if he does not receive active treatment during childhood. Three per cent equals the prevalence found in patients after the age of 20 years in the study by Forsythe and Redmond and in the Finnish 14-year-olds as described by Moilanen [58, 59]. It is still not clear whether active treatment of nocturnal enuresis in childhood is able to reduce the number of adult enuretics.

4. Inheritance

In most children bedwetting is a familial problem. Sporadic bedwetting with no affected relatives is found in 30 percent of children.

The mode of inheritance is autosomal dominant, so if both parents were nocturnal enuretics as children, the risk for their offspring is 77 percent. If only one parent had nocturnal enuresis the risk is about 45 percent. As a genetically determined disorder, nocturnal is unusual as the great majority of patients show a spontaneous resolution of their enuresis with time. Thus the hereditary trait leads to a delay of maturation of the mechanisms responsible for sleeping without wetting the bed, not to a permanent disorder in most cases.

With linking analysis, foci have been found on chromosomes 8, 12, 13 and 22 [60,61,62].

It is conceivable that more than 10 chromosomes are involved. With increasing knowledge a picture of pronounced heterogeneity of both genotype and phenotype is emanating. The etiology of nocturnal enuresis is characterised by a complex interaction of genetic and environmental factors.

5. The gender difference

In a population survey of 706 families in London ,Weir found a higher prevalence for boys than girls at age 3 years with 56 percent of boys and 40 percent of girls being wet at night more than once a week [63].

A recent survey of over 2900 three year old twin pairs born in England and Wales in 1994 found a significant difference between boys and girls in development of nocturnal bladder control with 54.5 percent of girls and 44.2 percent of boys being dry at night [64].

Historically girls have been reported as more likely to experience secondary enuresis and associated daytime incontinence, urinary frequency, emotional and behavioural problems, urinary tract infections, along with tolerant mothers, and a high level of concern about their enuresis [50,55,65,66,67].

Girls have also been reported to be less likely to have a family history or genetic pre-disposition to bedwetting [64,68].

6. Classification

The traditional classification is based on the child's history of enuresis. Children who have never achieved a period of up to 6 months free of bedwetting are considered to have primary nocturnal enuresis. There may be indications of slight maturational delay in primary nocturnal enuresis with low birth weight, soft signs of neurological delay, delayed motor development and shorter height [65,69,70,71,72].

However children with primary nocturnal enuresis do not have an increased likelihood of behavioural problems compared with children who are not bedwetters or former bedwetters [57,73,74,75].

Secondary or onset nocturnal enuresis is the re-emergence of wetting after a period of being dry. The time period is usually considered to be a minimum of 6 months, although some take 1 year to be the specified enuresis-free period. A birth cohort of 1265 New Zealand children studied over 10 years by Fergusson et al found an increased risk of secondary enuresis with age [76]. They found the proportion of children who developed secondary enuresis were: 3.3 percent at 5 years, 4.7 percent at 6 years, 6.2 percent at 7 years, 7.0 percent at 8 years, 7.5 percent at 9 years and 7.9 percent at 10 years.

Secondary nocturnal enuresis appears to be associated with a higher incidence of stressful events particularly parental separation, disharmony between parents, birth of a sibling, early separation of the child from parents and psychiatric disturbance in a parent [76,77,78].

Von Gontard and colleagues found children with secondary enuresis had significantly more emotional difficulties compared to those with primary nocturnal enuresis [78]. Their evidence also suggests children with secondary enuresis, compared to those with primary enuresis, are significantly more likely to have behavioural problems, a finding which corresponds to that of McGee et al [73].

Both Jarvelin and Fergusson et al compellingly argue that primary and secondary enuresis are aspects of the same problem [69,76]. They claim the two classifications share a common etiological basis. The rate at which a child acquires primary control influences his or her susceptibility to secondary enuresis. The primary form is regarded as being the consequence of a delay in maturation of the physiological mechanisms. The child's capacity to sustain and maintain nocturnal bladder control is manifest in the rate at which control is acquired. On the other hand this capacity determines the child's susceptibility to lapsing when exposed to stress.

a) Mono-symptomatic versus non-mono-symptomatic

Mono-symptomatic nocturnal enuresis refers to those children who report no bladder or voiding problems associated with their wetting. Non-mono-symptomatic nocturnal enuresis refers to bedwetting which is associated with bladder instability and voiding problems such as urgency and postponement during the day, but no daytime wetting [79].

This classification becomes extremely important in considering the most appropriate treatment intervention.

Many parents are unaware of daytime symptoms when seeking help for bedwetting and when identified these symptoms should be treated prior to intervention for the nocturnal enuresis.

Between 10-28% of children with nocturnal enuresis have associated daytime problems and if they have urinary incontinence during the day these children should not be regarded as having nocturnal enuresis: they should be considered to be incontinent. The night time incontinence is not any longer an isolated phenomenon but part of the symptomatology of functional incontinence. They are more resilient to treatment and more vulnerable to relapse 58, 80.

7. Understanding nocturnal enuresis

The pathophysiology of nocturnal enuresis has been studied extensively and is still not fully understood. A conceptual model has been proposed for understanding nocturnal enuresis, envisaging it as a problem or delayed maturation in one or more of the following systems: a lack of stability in bladder functioning, a lack of arginine vasopressin release and an inability to wake from sleep to full bladder sensations (Fig. 7) 81.

The clinical benefits of employing this model are extensive:

1. It provides an explanation, for both child and parents, as to the reasons for the ongoing problem
2. It assists the assessment process in that the focus is on which aspect[s] of the system is letting the child down
3. Following from the assessment, the model enables the appropriate treatment interventions to be selected
4. Having an understanding as to why a particular treatment might be advocated, improves compliance with treatment
5. Because the model emphasises the child's difficulty in acquiring processes that are outside of his or her control, it removes the child from blame

This is supported by the work of Neveus et al, who sought to evaluate differences in sleep factors between children with wetting problems and dry children 82.

Children with nocturnal enuresis aged between 6 and 10 years were found to have both impaired arousal and bladder instability.

a) Lack of nocturnal vasopressin release

Normal subjects have a marked circadian variation in urine output, leading to a significant reduction of urine excretion and a corresponding increase of urine osmo-

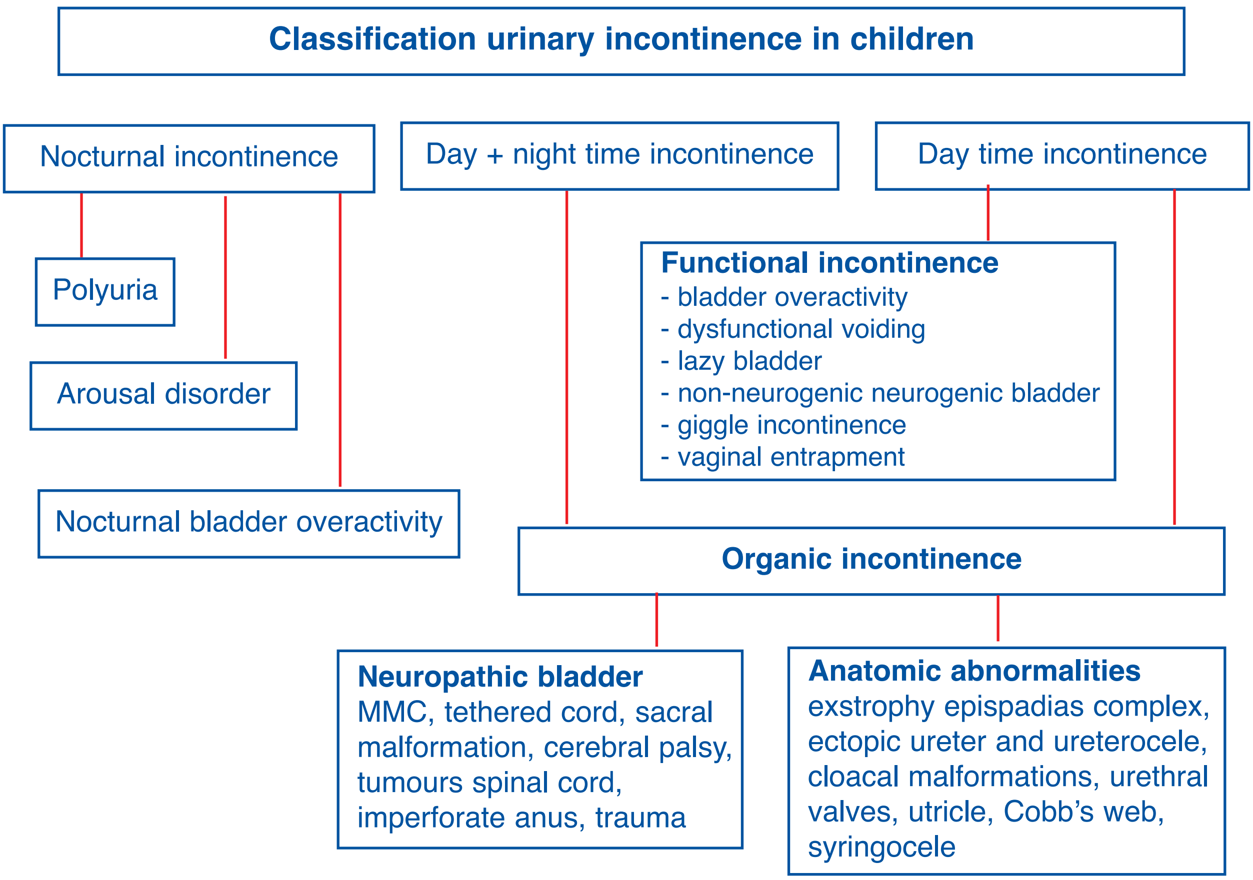

Figure 7 : Classification of urinary incontinence in children. Most causes of anatomic abnormalities need surgical treatment and are not discussed in this chapter.

lality during sleep [83]. Decrease of renal urine production during the night allows for sleep not disturbed by a full bladder. In children this is the result of nocturnal increase of plasma vasopressin (a polypeptide containing nine amino acids, produced in the hypothalamus and stored in the posterior pituitary gland), which results in increased urine concentration and reduced urine volume during sleep. This could explain why most children who are not enuretic tend to sleep through the night without being wet [30].

In adolescence and adult age there is no diurnal rhythm of plasma vasopressin concentration, and the changes in urine production occur entirely owing to a decrease in the urinary sodium excretion [84].

Two thirds of patients with mono-symptomatic nocturnal enuresis have been found to have a lack of circadian rhythm of vasopressin, resulting in high nocturnal urine production which exceeds bladder capacity [85, 86, 87].

Detection of low plasma vasopressin levels cannot realistically be considered as part of a routine clinical assessment. Alternatively we can look for clinical signs of low vasopressin during the assessment interview. Weighing the diapers and adding the first morning void provides the total nocturnal urine output: if this total exceeds the child's functional bladder capacity it could be an indication for nocturnal polyuria.

Wolfish et al interestingly found that most nocturnal enuretic episodes occur in the first third of the night and many studies report that the enuretic episode is most likely to occur in the first 2 hours of sleep [88, 89].

There may be a small sub-group of children with impaired renal sensitivity to vasopressin or desmopressin [90, 91] Recent work by Devitt et al suggests that 18 percent of children have 'normal' levels of plasma vasopressin release but remain enuretic [87]. These children all failed to respond to therapeutic dosage of desmopressin. This finding could indicate renal insensitivity to vasopressin but could also be indicative for bladder overactivity or a small functional bladder capacity. Total urine output during the night could be helpful in differentiating between the two conditions (is there really nocturnal polyuria?).

b) Bladder overactivity during the night

The bladder, in order to function appropriately, needs to be stable during filling and have an appropriate functional capacity. Bladder instability usually causes functional bladder capacity to be decreased [92].

Watanabe and his colleagues, employing EEG and cystometry recording during sleep, discovered that in 32 percent of children with nocturnal enuresis uninhibited bladder contractions occurred resulting in enuresis [93, 94, 95]. These children had smaller functional bladder capacities at the point of wetting, than children with enuresis who did not have bladder instability.

Yeung et al have recently reported that 44 percent of treatment failures [with desmopressin or the enuresis alarm] have normal daytime bladder functioning but marked unstable bladder contractions during sleep resulting in enuresis [96]. Almost none of these children had nocturnal polyuria.

It is important clinically to be aware of the possibility of bladder instability as a cause of the child's nocturnal enuresis. Under the new classification system, such children might be described as having non-monosymptomatic nocturnal enuresis.

The following signs are indicative of bladder instability [85, 96, 97]:

In the daytime: frequency (more than 7 times per day), urgency, (unsuccessful) holding manoeuvres such as squatting and low or variable functional bladder capacity (small voided volumes)

At night: multiple wetting episodes, variability in the amount of urine in the diaper and waking during or immediately after wetting

c) Lack of arousal from sleep

The fundamental mechanism resulting in nocturia or nocturnal enuresis is that the bladder fills to its capacity during sleep and needs to be emptied. Bladder fullness is due to nocturnal polyuria and/or a reduction of the bladder capacity due to improper relaxation of the detrusor during sleep. These factors can not by themselves explain why the enuretic child does not wake up during the night to the sensation of a full or contracting bladder.

Whether the child has bladder instability or lack of vasopressin release resulting in over production of urine, the enuresis event results from the child's inability to awaken from sleep (Fig. 8).

Non-enuretic children are more likely to wake to void than enuretic children [98].

This might explain why the most heavily endorsed view of both children and parents, regarding the aetiology of nocturnal enuresis is a belief in deep sleep [99].

However a raft of evidence counters such a belief. Sleep patterns of children with nocturnal enuresis are no different from children who do not have nocturnal enuresis [85].

Enuretic episodes occur during all stages of sleep in proportion to the amount of time spent in that stage and appear to occur independent of sleep stage but when the

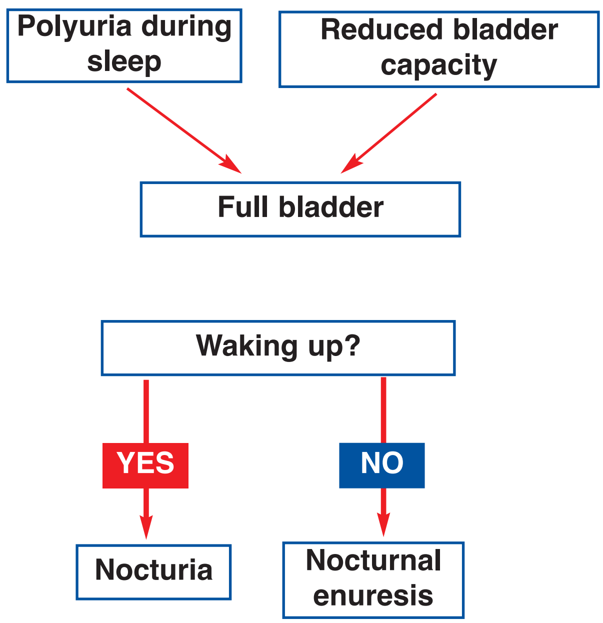

Figure 8 : Basic pathophysiology of nocturnal enuresis or nocturia. When the bladder is full because of (relative) polyuria and/or a reduced bladder capacity, the child either wakes up to void (nocturia) or voids while sleeping (nocturnal enuresis).

bladder is filled to the equivalent of maximal daytime functional capacity [88,100,101,102].

Bedwetting children sleep normally but are unable to suppress nocturnal bladder contractions or awaken in response to them or to bladder fullness.

The issue is one of the child's inability to arouse from sleep when the bladder reaches its maximum capacity, which Watanabe and colleagues have demonstrated in a series of EEG studies. Watanabe et al make the distinction between two forms of arousal difficulty based on EEG recordings. They suggest 'Type I' is a mild disturbance of arousal where the full bladder creates changes in arousal so the child moves to a lighter stage (1 or 2) of sleep, but the child does not waken. This accounts for 57 % of the enuretic population. 'Type IIa' is much less common (9 percent of the enuretic population) and caused by a more severe 'disturbance in arousal'. They found no EEG changes in response to the full bladder and no arousal from sleep in 'Type IIa' enuresis, whereas in 'Type IIb' (34 percent) in addition continuous detrusor overactivity is found during sleep.

Wolfish et al suggest the most difficult part of the night for all children to arouse from sleep, is the first third [88].

Waking becomes easier as the night progresses. However, Norgaard, Mikkelsen et al and Wolfish et al have all found that children with nocturnal enuresis are also more likely to wet in the first third of the night, often in the first two hours following sleep [88,100,101]. Thus the point of bladder fullness for most enuretic children coincides with a time of night where they find it most difficult to wake from sleep.

It is possible to gauge a child's level of arousability by asking about their ability to arouse to the external signals such as bad weather, noise or unusual sounds, internal signals such as illness worry or self instructions, full bladder signals.

Some children demonstrate an ability to wake but fail to complete voiding in the toilet. They may find leaving bed difficult because of the cold, a fear of the dark, or practical reasons such as the toilet being not readily accessible. Such children benefit from practical ways of help, such as warmth in the room, a torch or a receptacle for urination in the bedroom.

8. Treatment of nocturnal enuresis

The normal annual resolution rate of monosymptomatic nocturnal enuresis is not always accounted for in cure rates reported. When reporting is done with survival analysis, the resolution rate remains visible throughout follow-up [58,79,103].

The outcome of pharmacological treatment for nocturnal enuresis is expressed as either full response or partial response, while on the prescribed medication. A ***full response*** is defined as a reduction in wet nights of at least 90%, ***partial response*** is defined as a reduction in wet nights of 50%-90%; less than 50% reduction in wet nights is considered to be non-response [45,104,105].

A ***lasting cure*** is defined as a full response, still present 6 months or longer after discontinuation of pharmacotherapy. With other forms of therapy (alarm treatment, dry-bed training), full response or partial response are noted immediately after the actual intervention.

With a follow up of at least 6 months, response can become a *lasting cure* (>90% reduction) or a *lasting improvement* (50%-90% reduction). In reports on the outcome of nocturnal enuresis, it should be ascertained if nocturia did replace the nighttime wetting [106].

Nocturia occurs when a child wakes up at night to void.

The older definition of full response, 1 wet night or less per month, correlates closely with a reduction of 90% or more in the number of wet nights.

The 90 percent cut-off point has been chosen in order to allow for the occasional wetting that can occur up to 2 years after otherwise successful treatment during a night when the child sleeps very deeply after a tiring day or runs a fever.

For the individual patient who has achieved a significant reduction in wet nights, the occasional wet episodes (eg once or twice a month) still remain a problem not to be underestimated, especially in the adolescent and adult patient population. Therefore the 90 percent cut-off point should really only apply to the pre-pubertal child.

It is essential to explain the problem to children with mono-symptomatic nocturnal enuresis and their parents and give general advice such as to eat, drink and void regularly during the day, abstain from drinking too much during the late afternoon and evening and have relaxed routines at bedtime. It should be stressed that the condition is common and usually a benign delay in maturation without any psychopathological undertone. A positive attitude towards the child should be utilised and explained that the bed-wetting eventually will cease "but nobody knows exactly when that will happen". Up to 19 percent of children will become dry within the next 8 weeks without any further treatment [107].

The management of Nocturnal enuresis (Figs. 9 and 10) depends on:

- the child's motivation to participate in treatment
- exclusion of confounding psychosocial factors
- providing information and instruction about daily habits underlining the importance of having regular fluid intake and voidings and relaxed routines at bedtime
- regular review of intervention

Although treatment modalities like lifting, fluid restriction, dry-bed training, retention control training, psychotherapy, acupuncture, hypnosis all have been used, there is not sufficient data in the literature to recommend any of these.

Comparison of treatment outcome and cure rates is difficult because of the inconsistent use of definitions and the inclusion of children with daytime symptoms and variable follow-up periods in most studies.

a) Enuresis alarm

The enuresis alarm is the most effective way to treat mono-symptomatic nocturnal enuresis [103] Intervention with an alarm is associated with nine times less likelihood of relapse than antidiuretic therapy [108].

Alarm therapy has been shown in a meta-analysis to have a 43 percent lasting cure rate [109,110].

Alarm treatment is slow in the beginning so it should be continued at least 6 to 8 weeks before it is considered

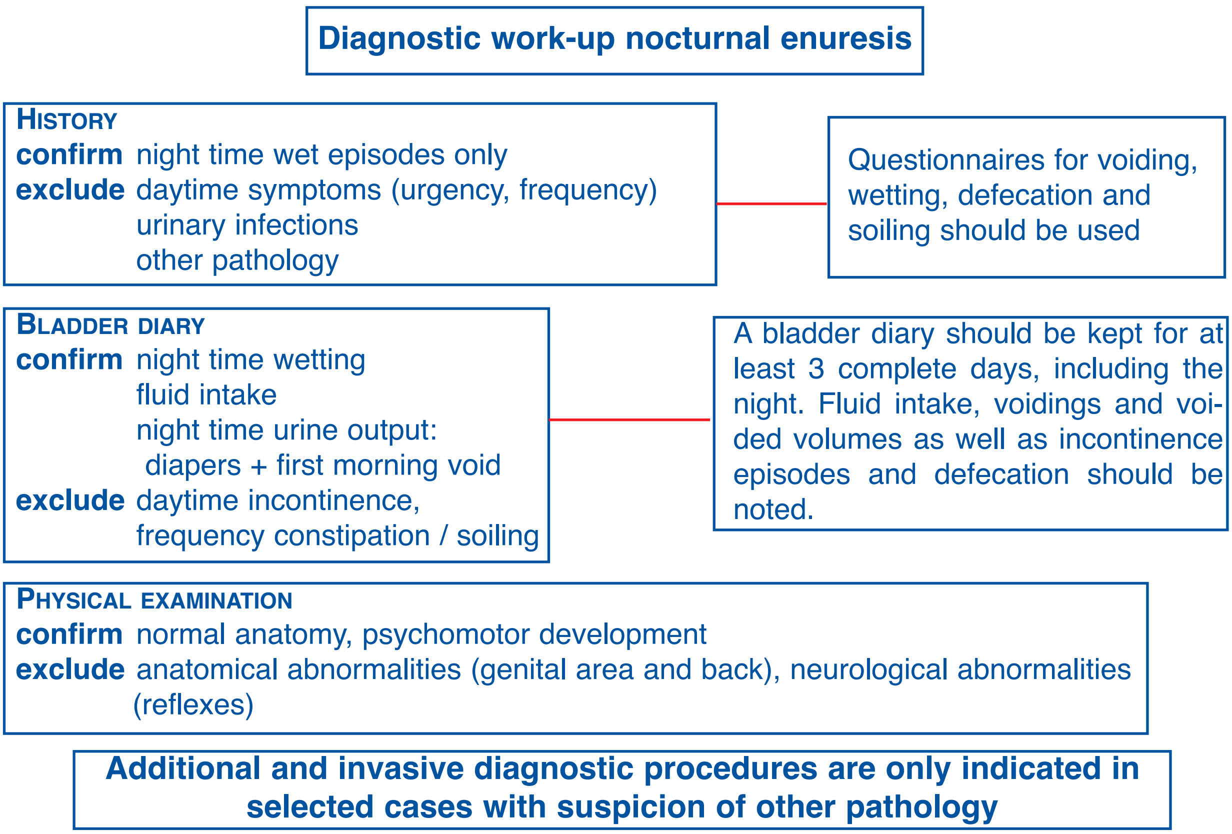

Figure 9 : Schematic work-up in patients presenting with nighttime wetting only.

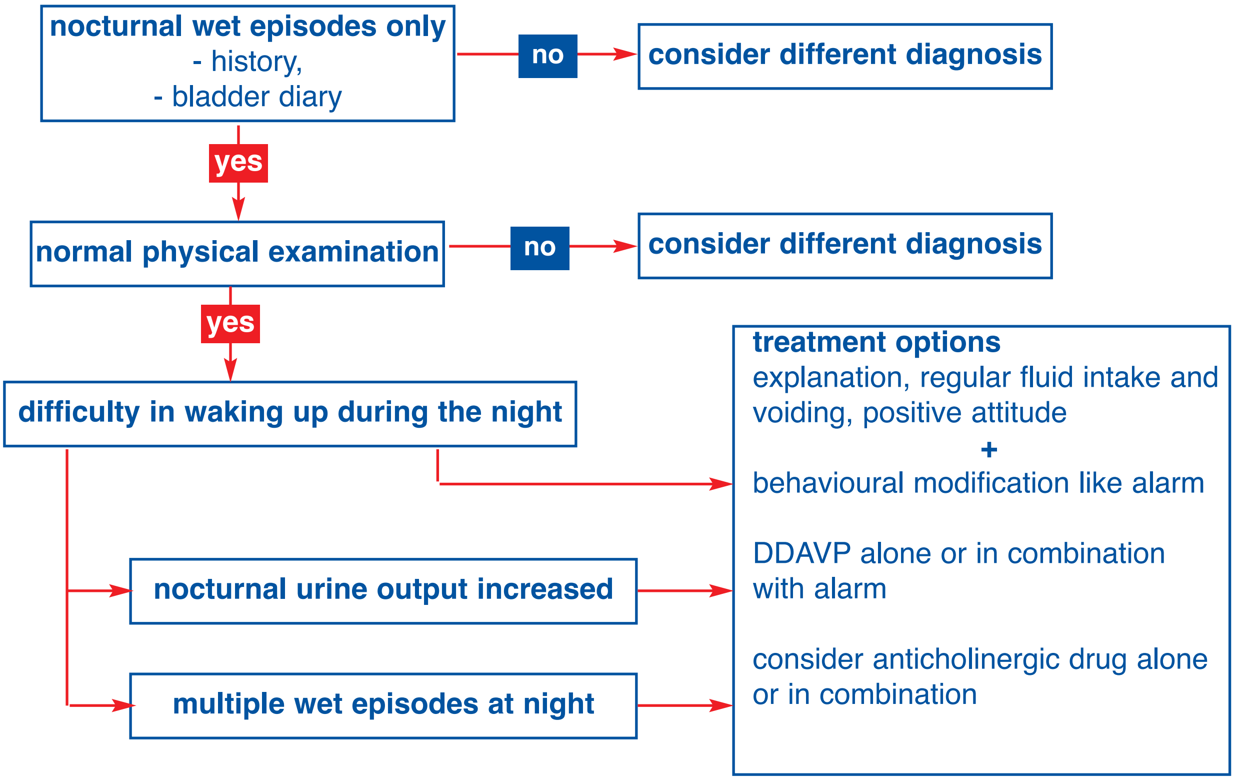

Figure 10 : Pragmatic approach to diagnosing and treatment of nocturnal enuresis.

effective or not. Compliance remains a problem: dropout rates are rarely disclosed in reported studies. Proper guidance and instructions are mandatory.

The mode of action of the alarm has been believed to be an amelioration of arousal to a full bladder, which may be true but lacks scientific validation (see also section IV.3). An interesting finding is that alarm increases nocturnal bladder capacity, which may explain why children after successful treatment are often able to sleep dry without nocturia [111].

Possible future alarm design could include a small ultrasound transducer to monitor bladder volume during the night, so that at a predetermined volume a sound signal is emitted, thus waking the child before the enuresis occurs. ***Level of evidence: 1***

b) Desmopressin

Placebo controlled studies have shown that the antidiuretic drug DDAVP is significantly more effective than placebo [112], [113]. Patients on desmopressin were 4.6 times more likely to achieve 14 consecutive dry nights compared with placebo [114]. However, there was no difference after treatment was finished.

In most trials a response rate (more than 50 percent reduction of wet nights) of 60 to 70 percent is found. This corresponds with the number of patients who have nocturnal polyuria as main factor responsible for their nocturnal enuresis.

It has also been established that responders have in fact nocturnal polyuria

Relapse after short-term treatment is rather the rule, whereas long-term treatment may yield better cure rates [115].

Long-term results have been found to be 23 percent of children treated and 31 percent of those who responded to treatment. The 23 percent is not significantly better than spontaneous resolution [116].

Because DDAVP is a potent antidiuretic drug, there have been reports on severe water retention with hyponatremia and convulsions, but these are sporadic [117], [118]. ***Level of evidence: 1***

c) Combined treatment with alarm and Desmopressin

Combined treatmen is superior to alarm alone especially for nonresponders of each individual treatment. Both treatments are started at the same time : the vast action of DDAVP is believed to fascilitate the child's adaptation to the alarm [119]. After 6 weeks the DDAVP is discontinued while the alarm treatment is continued until the child becomes completely dry. Compared with either therapy alone, the combination has been found to be particularly effective in children with psychosocial problems. ***Level of evidence: 1***

d) Anticholinergic drugs

In those children who have bladder overactivity during the night, treatment with anticholinergic drugs should be considered [120]. Because it is difficult to perform a nighttime cystometry in these children it may be tried in children who not respond to DDAVP or given in combination with alarm. At present no studies have been performed to demonstrate its efficacy.

e) Tricyclic antidepressants

Because Imipramine and other drugs of the same family have potential lethal side effects they can not be generally recommended for treatment of this non-lethal disorder [121].

Although treatment with tricyclic drugs is associated with a decrease of one wet night per week, the lasting cure rate of only 17 percent restricts the use of these drugs.

Only in selected cases (like adolescent boys with Attention Deficit Hyperactivity Disorder and persistent nocturnal enuresis) it could be considered. ***Level of evidence: 2***

f) Inhibitors of prostaglandin synthesis

Because nocturnal polyuria in children with Nocturnal enuresis may not be entirely attributed to a defect in free water excretion, but rather to an increase in nocturnal excretion of sodium, cyclooxygenase inhibitors (like diclofenac) which reduce urinary sodium excretion, have been tried and in a randomised double blind placebo controlled study proved to be effective [122]. Further studies need to be done to elucidate the role of these drugs.

Full response (while on medication) and cure rates (6 months after cessation of treatment) of Nocturnal Enuresis are summarisez in table 1.

Table 1 : Full response (while on medication) and cure rates (6 months after cessation of treatment) of Nocturnal Enuresis.

	Full response	**Cure**
Alarm treatment	65 %	43 %
Desmopressin	31 %	22 %
Dry-bed training	40%	18 %
Imipramine		17 %

g) Non responders

About one third of children do not respond to treatment with alarm and/or DDAVP. This should arouse suspicion on nocturnal detrusor overactivity. Prescription of anticholinergics should be considered although evidence from the literature is lacking.

On the other hand some of these children may have functional incontinence (lazy bladders , children with overdistended bladders and infrequent voiding), which was not discovered during the initial workup. They should be given a strict voiding regimen and a combination of DDAVP with the alarm [92].

IV. BEHAVIOUR THERAPY

Behaviour therapy can be considered to be an approach that seeks to change behaviour patterns through altering the individual's environmental contingencies. Its theoretical roots lie in behaviourism which suggests that behaviour derives from contingencies of reinforcement and particular responses made in the presence of stimulus situations.

The focus is on the behaviour itself, rather than any underlying dynamics possibly causing the behaviour. Behaviour is now considered to include an individual's thinking processes and thus the emergence of cognitive behaviour therapy.

Effective treatment within a behaviour therapy tradition aims to modify behaviour which the individual finds distressing or inappropriate. Behaviour therapy is technique driven and includes a range of procedures which can assist the individual in altering their behaviour patterns.

Techniques that have been advocated in treating nocturnal enuresis include:

- positive reinforcement
- cognitive re-structuring
- arousal training
- normalised voiding
- positive practice
- retention control training
- dry bed training
- full spectrum home training

1. POSITIVE REINFORCEMENT

Positive reinforcement of a behaviour increases the frequency or strength of that behaviour. Rewards and star charts for 'dry beds' has been traditionally adopted by many parents and health professionals yet they tend to be largely unsuccessful. Children quickly loose faith in them. Generally this is because such reward schedules focus on the outcome (dry night), which the child has little, if any, control over. For most children the dry night is a reward in itself.

There are no reported studies on the effectiveness of such contingent positive reinforcement with nocturnal enuresis. However, there is one study where the alarm has been coupled with 'tangible rewards' contingent on outcome. Kaplan et al described a study of 70 children aged over 6 years with severe nocturnal enuresis (75 percent had tried other methods unsuccessfully) [123]. They allocated 38 children to the alarm plus rewards and 32 were treated with alarm monotherapy in a non-randomised process. Success rates (14 consecutive dry nights) were 87 percent with alarm + rewards compared to 65 percent for alarm monotherapy. The combination of alarm + rewards tended to produce higher success rates but there were no significant differences across the treatment methods on any of the outcome measures.

Rewarding dry nights raises theoretical and ethical concern over the issue of control. A child experiences little control over whether they are wet or dry during sleep and the three main causes (bladder overactivity, lack of vasopressin release and failure to arouse) responsible for nocturnal enuresis are not conceptualised as within the child's control or will [81].

However rewarding a dry night implies that the mechanisms responsible for being dry (bladder stability, release of vasopressin and waking to a full bladder during sleep) are within their control. It might be argued that being dry itself is the intrinsic reward and Harter has argued that tangible rewards for actions the child wishes to engage in will decrease or undermine intrinsic motivation by decreasing the child's sense of self-determination and competence [124].

Current thinking suggests the process, not the outcome, should be rewarded. This means rewarding what is controllable. Rewarding the behaviour or efforts the child makes towards improving the chances of being dry. Thus stars or small rewards might be made contingent on:

- increased daytime drinking
- regular daytime voiding
- waking up to go to the toilet
- voiding before sleep
- waking quickly to an alarm triggering

2. Cognitive re-structuring

There are anecdotal reports concerning the promotion of 'appropriate' thought processes to facilitate improved bladder control. Butler suggested three cognitive processes – auto-suggestion, restructuring beliefs and visualisation. Few studies have however, investigated cognitive change directly [45].

With auto-suggestion the individual is encouraged to cue self statements to a particular event. Thus when passing a toilet door, a child may be taught to think to him or herself 'I can only wee in the toilet'. An investigation by Edwards and van der Spuy found that self instructions were more important than the trance state during hypnotherapy but with a success rate of only 19 percent, autosuggestion cannot be considered a primary form of treatment for nocturnal enuresis [125].

Re-structuring beliefs focuses on enhancing the child's belief that they are active and responsible for behaviour change. Thus an internal attribution for success, it is argued, fosters the child's belief that 'dryness' is due to a change in their functioning, not due to the treatment intervention. Butler et al found that with a structured withdrawal programme over 70 percent of children remained dry when medication was withdrawn [126, 127].

They argue that the effective element was that children were encouraged to internalise the success rather than consider the medication as the reason for success.

Visualisation is the employment of imagery as a vehicle for establishing improved bladder control. Only one case study can be found in the literature [128].

An immediate response was noted in this case with a child who had become dependent on the enuresis alarm to wake him.

3. Enuresis alarm

The enuresis alarm remains the most effective means of facilitating arousal form sleep. The essential principle is to alert and sensitise the child to respond quickly and appropriately to a full bladder during sleep, converting the signal from one of urination to that of inhibition of urination and waking. The child usually reacts to the alarm triggering by contracting the muscles of the pelvic floor (and thus stopping urination) and waking. The key to success is not the stimulus intensity of the alarm triggering, but the child's preparedness to awake and respond to the signal [88].

There are variables that coincide with the use of the alarm that may enhance its effectiveness:

- an expectation of success [99],
- avoidance conditioning, whereby the child seeks to avoid the unpleasantness of the noise by spontaneous waking or contraction of the pelvic floor muscles [129],
- increased functional bladder capacity [130],
- increased production of vasopressin in response to the stress of waking to the alarm, which might explain why some 80% of children who become dry with the enuresis alarm are able to sleep through the night and [52],
- a conditioned response whereby waking after urina-

tion serves as an unconditioned stimulus while the startle response of pelvic floor contractions which stops urination is the unconditioned response [131]. With repeated triggerings the alarm produces a conditioned response of inhibition of urination in the presence of detrusor contractions during sleep. Learning to control the pelvic floor muscles during the night, it is argued enables the child to sleep through the night.

Given such possible mechanisms of action it may be postulated that enhanced effectiveness might be facilitated by a positive expectation of success, an emphasis on the importance of waking when the alarm is triggered, reinforcement for waking quickly to the alarm triggering, increasing the child's understanding of the process and keeping detailed records of progress

Reviews of alarm treatment effectiveness suggest a success rate of between 65-75% on undifferentiated samples of children with nocturnal enuresis, where the duration of treatment was between 5 and 12 weeks [103, 132, 133].

Relapse rates in the 6 months following treatment are in the order of 15 - 30 % [103].

Children successfully treated with an enuresis alarm are less likely to relapse compared with pharmacological interventions [134].

Comparison of the different types of alarm did not show significant outcomes [103].

In general it can be stated that alarm treatment is more effective than other forms of treatment and the lasting cure rate about twice as high [135].

Alarm treatment appears to result in the child learning to sleep through not wake to a full bladder as expected. Monda and Husmann found that during treatment children did wake up to void but following treatment, 70 percent of those who became dry, successfully slept through the night [136]. ***Level of evidence: 1***

4. AROUSAL TRAINING

Arousal training entails reinforcing appropriate behaviour [waking and toileting] in response to alarm triggering. The aim is to reinforce the child's rapid response to the alarm triggering, not on 'learning to keep the bed dry'.

The instructions involve:

- setting up the alarm before sleep
- when the alarm is triggered the child must respond by turning it off within 3 minutes
- the child completes voiding in the toilet, returns to bed and re-sets the alarm
- when the child reacts in this fashion he is rewarded with 2 stickers
- when the child fails to respond in this way the child pays back one sticker

Van Londen et al first described this procedure with a group of 41 children, aged 6-12 years, with predominantly primary enuresis [137]. They reported 98 percent success (14 consecutive dry nights) compared to 73 percent success with alarm monotherapy.

The difference was significant ($p<0.001$). Ninety two per cent remained dry after $2^{1/2}$ years suggesting very low relapse rate. An extraordinary aspect of this study was the lack of contact between therapist and parents. All those included were parents who had ordered an alarm from a rental agency and were given the instructions with the alarm. The authors conclude that arousal training is 'definitely the treatment of choice for non-clinical enuretic children between 6 and 12 years'. Compared with other studies and considering experience of daily practise one may question the very high success rate in this particular group of patients.

5. NORMALISED VOIDING

Normalised voiding involves:

- increasing daytime fluid intake
- increasing the frequency of micturitions during the day by voiding regularly at pre-determined times [every 2-3 hours] and
- avoidance of postponing urination.

This is usually used in combination with other treatment modalities. It is an attempt to normalise voiding, whereas many of the children postpone voiding. Although this form of treatment in itself may be the cornerstone of success, it has never been tested as a stand-alone treatment. In a study by Kruse et al, a small group of patients (n=5) was described, aged 10 years and older, all of whom had a history of several treatment failures and who tended to hold in the daytime [92].

Most children also had a small functional bladder capacity and day-time urgency: most likely due to detrusor overactivity. They found using an alarm with normalised voiding was successful (<1 wet per fortnight) with two individuals at 1 month; successful with another child at 5 month and a further success at 9-12m. The 1 'failure' reduced wetting frequency to twice a fortnight, from 50 percent wet at baseline after 1 month of treatment.

6. POSITIVE PRACTICE

The aim of positive practice is to develop an alternative response to bedwetting. Following a wet bed, the child is encouraged to practice the following, both immediately and prior to bed-time the next night:

- the child is encouraged to lie in bed with the lights off,
- count to 50,
- go to the toilet and attempt to urinate,
- repeat this 20 times.

For younger children the procedure is reduced to 10 repetitions counting to 20. Bollard and Nettelbeck in their component analysis of dry bed training employed this strategy with 12 individuals with a success rate of 83 percent [138].

It may be clear that this can only be attempted in motivated children and good parental support.

7. Retention control training

The aim is to assist the detrusor muscles in adapting to increased bladder pressure and volumes and make the child aware of to full bladder sensations [139].

Once a day the child is asked to drink 3 glasses of water. When the child indicates a need to void, he/she is asked to hold (postpone micturition) for increasing amounts of time (in 3 minute increments). Rewards are given for each increase and the process discontinued when the child is able to postpones for 45 minutes. When used with children with nocturnal enuresis it has been combined with the enuresis alarm. Houts et al found a success rate of 87 percent with 15 children when combined with an enuresis alarm [131].

There has been an attempt to use night time retention control training in combination with an alarm. The aim is to increase functional bladder capacity and practice inhibiting urination. Before bedtime the child is given a large drink (at least 2 glasses). Every hour during sleep, the child is woken and directed to the toilet (see next section *scheduled waking*) At the toilet door the child is then asked if he/she can hold for another hour. If the child elects to hold, he or she is praised, but if the child elects to void, he or she is encouraged to hold for a few minutes before voiding. At the bedside the child is given another large drink. This procedure was discontinued after one night with Bollard & Nettelbeck finding a success rate of 92 percent in 12 children [138]. Motivation and parental support are essential in this type of training.

8. Scheduled waking

The aim is to encourage arousability from sleep. As originally described, there are two aspects: hourly waking on the first night and scheduled waking thereafter [129].

With the hourly waking on one night only, the child is:

- woken each hour with a minimal prompt,
- asked to void in the toilet and
- praised for having kept the sheets dry.

On subsequent nights, scheduled waking involved waking the child three hours after sleep and encouraging him or her to void. For every dry night the waking time is brought forward by a 1/2 hour until it is timed to occur one hour after going to sleep.

Bollard & Nettelbeck found this procedure was 100% effective when combined with the alarm in 12 children [138].

9. Dry bed training

This is a package of behavioural procedures used in conjunction with the enuresis alarm first described by Azrin et al [129]. It incorporates**:**

- the enuresis alarm,
- positive practice (practice of waking),
- cleanliness training (encouraging the child to take responsibility for removing of wet night clothes and sheets, re-making the bed and resetting the alarm),
- waking schedules – to ease arousability from sleep as described above and involving:

1. for the first night, waking the child each hour, praising a dry bed, encouraging the child to decide at the toilet door whether he or she needed to void, and on returning to bed the child is encouraged to have a further drink and
2. on the second night the child is woken and taken to the toilet 3 hours after going to sleep. For each dry night the waking time is brought forward by 30 minutes. If wet on any night the waking time stays at the time of the previous evening. The waking schedule was discontinued when the waking time reached 30 minutes following sleep. The waking schedule is resumed if the child begins wetting twice or more in any week, starting again 3hours after sleep.

- social reinforcement and
- increased fluid intake.

High success rates and low drop out have been reported although relapse rates are no different to enuresis alarm treatment. Modifications have been advocated to remove some of the more punitive elements of the programme but it remains a complex, time consuming and demanding procedure.

Hirasing et al found 80 percent success with group administered dry bed training. Girls responded better than boys [140]. The majority of parents were satisfied with the programme but opinions of the children were divided. Factors not related to success were the child's age, bedwetting frequency, secondary enuresis or family history.

An important component analysis by Bollard & Nettelbeck found that the enuresis alarm accounted for most of the success achieved through dry bed training, that a large proportion of the components of the procedure could be eliminated without sacrificing much of its overall effectiveness and that the waking schedule coupled with the enuresis alarm was as effective as the complete dry bed training programme [138]. ***Level of evidence: 3***

10. Full spectrum home training.

This programme incorporates:

- the enuresis alarm,
- retention control training,
- cleanliness training and
- overlearning,

Whelan and Houts claim a 75 percent success rate after an average of 12 weeks. This is not dissimilar to success rated with the alarm on its own. As with dry bed training, the enuresis alarm has proved to be by far the most effective component of the programme leading some clinicians to consider all the other procedures to be adjuncts to the alarm and employed for specific situations [140].

The enuresis alarm remains the most effective means of facilitating arousal from sleep. The key to success is not the stimulus intensity of the alarm triggering, but the child's preparedness to awake and respond to the signal.

V. DAY AND NIGHT TIME INCONTINENCE

1. Introduction

Urinary incontinence in children may be caused by a congenital anatomical or neurologic abnormality, such as ectopic ureter, bladder extrophy or myelomeningocele (MMC). Many children, however, do not have such an obvious cause for their incontinence and they are referred to as having 'functional incontinence'.

The process of gaining control over bladder and sphincter function is complex and it is understandable that this series of complex events is highly susceptible to the development of various types of dysfunction. These acquired functional disorders overlap with other types of bladder functional disturbances that may have a more organic but congenital underlying pathophysiological basis.

The desire to void is a sensation which, in the developing child, is incorporated into daily life so that voiding takes place at an appropriate time and place. Problems with training or psychological difficulties can have a great impact on the results of training: some parents send their child to the toilet many times, though his/her bladder may be empty [142].

Voiding in these circumstances can only be achieved by abdominal straining. As the child will be rewarded when he or she produces even the smallest amount of urine, the result may be an abnormal voiding pattern. The same is true when children receive negative feedback related to voiding [143].

Functional urinary incontinence in children may be due to disturbances of the filling phase, the voiding phase or a combination of both. Detrusor overactivity may cause frequency and urgency, with or without urge incontinence. Girls present with symptoms of detrusor overactivity more often than boys, but sometimes other symptoms, such as urinary tract infections or constipation, prevail. Incomplete or no relaxation of the sphincteric mechanism during voiding results in intermittent voiding. When incontinence is the result of urethral overactivity during voiding the term 'dysfunctional voiding' is used [144].

Bladder function during the filling phase in these children may be essentially normal, but instability may be present. In children with a lazy bladder, voiding occurs without detrusor contractions, and post-void residuals and incontinence are the main characteristics.

Diagnosis is based on the medical and voiding history, a physical examination, bladder diaries and uroflowmetry. The upper urinary tract should be evaluated in children with recurrent infections and dysfunctional voiding (reflux). Uroflowmetry can be combined with pelvic floor electromyography to demonstrate overactivity of the pelvic floor muscles. Urodynamic studies are usually reserved for patients with dysfunctional voiding and those not responding to treatment [145].

Treatment is usually a combination of 'standard therapy' (see below), behaviour therapy, bladder training, physiotherapy and medical treatment. The importance of treatment during childhood was pointed out in a general population study of 1333 adult women. Fifty percent reported symptoms of stress incontinence and 22 percent reported symptoms of urge incontinence. Eight percentage had severe symptoms. Women who at age six years had wet episodes during the day or several nights a week were more likely to suffer severe incontinence and report urge symptoms: occasional bedwetting was not associated with an increased risk in adult life [146].

The role of α-blockers needs to be evaluated further. Also, neuromodulation may have a place in treatment but the exact indications need to be defined. Clean intermittent self-catheterization is sometimes necessary in children with a lazy bladder and large residuals who do not respond to a more conservative approach.

2. Prevalence

For detailed information on the prevalence of daytime incontinence the Chapter on Epidemiology should be consulted, where an overview is presented on the currently available data. The main problem is that it is impossible to draw any conclusions from the presented data as different studies have used definitions and criteria that differ from others. Daytime or combined daytime and nighttime incontinence at least once a week seems to occur in about 2-4 percent of 7-year old children and is more common in girls than in boys 17].

Overall the rates of prevalence vary from 1 to 10 percent, but in general for 6 to 7 year old children the prevalence is somewhere between 2 and 4 percent, and rapidly decreases during the following years [65,66,98, 147,148,149,150,151.

Children with daytime or mixed wetting were found to suffer from urgency in 50.7 percent of the cases, with 79.1 percent wetting themselves at least once in 10 days 65.

Urge symptoms seem to peak at age 6–9 years and diminish towards puberty, with an assumed spontaneous cure rate for daytime wetting of about 14% per year 58,193.

Most children are toilet-trained by the age of 3 years, though there is a huge social and cultural variation. In a recent study by Bloom et al, the mean age ranged from 0.75 to 5.25 years, with girls being trained earlier (2.25 years) than boys (2.56 years) 147].

Hellström et al found day wetting at least once a week at age 17 in 0.2% of boys and 0.7% of girls and as compared to 2.1% and 3.1%, respectively, at age 7 years 152.

Swithinbank et al had found a prevalence of day wetting (including also “occasional” wetting) in 12.5% in children at age 10-11 years declining to 3.0% at age 15-16 years 153.

Based on these, it seems that the prevalence of all kinds of daytime incontinence diminishes with 1-2% per year of life from age 10-11 to age 15-16 years, while daytime incontinence at least once a week seems to diminish with 0.2% per year of life from age 7 to age 17 years. Because of treatment the studies may not recount the true natural history.

By the age of 5 years, unless organic causes are present, the child is normally able to void at will and to postpone voiding in a socially acceptable manner. By this age, night-time and daytime involuntary wetting become a social problem and a cause for therapeutic intervention.

Some children are diagnosed with an urge syndrome or dysfunctional voiding, but are actually victims of child abuse. This is difficult to prove but should be kept in mind, especially when invasive diagnostic and therapeutic procedures are contemplated. Of adult women with complex urinary symptoms, a significant proportion report sexual abuse as a child 154.

3. Bladder-sphincter dysfunction, recurrent urinary tract infection and vesicoureteric reflux

The relationship between bladder dysfunction and VUR was first described by Allen and Koff and since confirmed by several authors 155,156,157,158 (Fig. 11).

In a study by Sillen of children with gross bilateral reflux, extreme detrusor overactivity without signs of infravesical obstruction was found in boys. Infant girls with gross bilateral reflux did not show the same degree of detrusor overactivity 159.

Similar findings were noted by other investigators assessing newborns with severe reflux. These studies in infants and the association of dysfunctional elimination syndromes with reflux and infection in older children strongly suggest that vesicoureteral reflux is a secondary disorder related more to abnormal bladder function than to a primary anatomic defect at the ureterovesical junction.

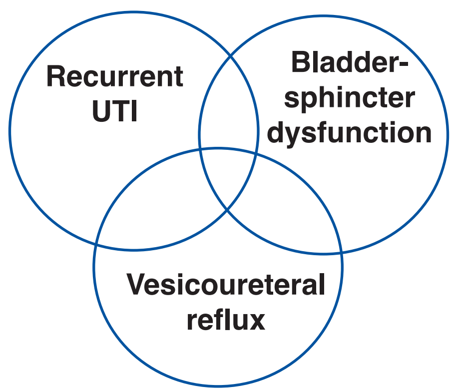

Figure 11 : Association of recurrent UTI, bladder-sphincter dysfunction and vesicoureteral reflux: each occurs separately, but the combination increases the risk of renal damage.

It has recently been shown that increased intravesical pressure, without reflux may be detrimental for the upper tracts: renal scarring without reflux was described by Vega at al recently [160].

Vesicoureteric reflux is a common finding in children with a neuropathic bladder and detrusor-sphincter dyssynergia: with the institution of clean intermittent catheterisation combined with anticholinergic drugs, reflux disappears in a high percentage of cases. It is believed that the decrease of detrusor overactivity and restoration of functional capacity in combination with regular and complete emptying of the bladder are the responsible co-factors [161].

In a prospective non-randomised clinical series of daywetting children a strong correlation was found between recurrent urinary tract infections and bladder-sphincter dysfunction [162,163]. Girls with asymptomatic bacteriuria were found to have symptoms of an overactive bladder, such as urgency and daytime incontinence in a high percentage [164].

In the majority of children with detrusor-sphincter dysfunction the recurrent infections disappeared following successful treatment of the bladder dysfunction. This finding confirms the hypothesis that detrusor-sphincter dysfunction is the main factor responsible for the infections (and to a lesser extend vice versa) [165 166].

At present, current opinion is that vesicoureteral reflux as such does not predispose to UTI: however it may facilitate renal involvement (causing pyelonephritis) once bacteriuria has been established in the bladder. This concept has not been scientifically validated and the incidence of renal scars as a consequence of pyelonephritis is reportedly the same, regardless of whether reflux has been documented or not [167].

In clinical studies there is a strong association between bladder-sphincter dysfunction, recurrent UTI and reflux, but the causal relationships still need to be scientifically investigated. Because of this association, bladder-sphincter dysfunction in combination with vesicoureteral reflux and infection is a potentially hazardous situation for the upper urinary tract and should be treated with appropriate care and sometimes even aggressively [23,168,169,170].

4. Classification

Several classifications have been used for children who present with varying degrees of 'functional' urinary symptoms unrelated to apparent disease, injury or congenital malformation. Some are based on urodynamic patterns, others on clinical presentation. The majority of children present with frequency, urgency and infections, with or without incontinence. Although the correlation between urodynamic findings and presenting symptoms does not seem to be very high, urodynamic investigations have given us more insight into the pathophysiology behind the symptoms and signs, and made the clinical expression of non-neurogenic bladder–sphincter dysfunction more specific [171,172].

On the basis of urodynamic studies, the functional dysfunctions can be termed unstable bladder, bladder-sphincter dyscoordination, lazy bladder and occult neurogenic bladder. According to the definition of the International Children's Continence Society, incontinence as a result of a filling phase dysfunction (mainly bladder instability) is called urge syndrome and urge incontinence [22]. When incontinence is the result of a voiding phase dysfunction it is called dysfunctional voiding, being subdivided into staccato voiding, interrupted voiding and lazy bladder syndrome.

The term 'non-neurogenic detrusor–sphincter dysfunction' is used to describe the whole spectrum, from simple detrusor instability to severe cases with deterioration of the upper tracts. The fact that we cannot demonstrate a neurologic deficit, however, does not exclude the possibility that a neurologic abnormality was present at the onset of the problem. It has been postulated that detrusor instability may eventually lead to lazy bladder syndrome or severe dys-coordination between detrusor and sphincter. However, the natural history of many of these children does not confirm this hypothesis, nor the early onset of severe pathology in some of them.

Hoebeke et al found no evidence for this dysfunctional voiding sequence: children with functional incontinence have different primary diseases, but all have a common risk of incontinence, UTI (especially in girls with a lazy bladder), reflux (15%) and constipation (17%) [173] (Fig. 12).

a) Urge syndrome and urge incontinence

Clinically, this condition is best characterised by frequent episodes of an urgent need to void, countered by contraction of the pelvic floor muscles (guarding reflex) and hold manoeuvres, like squatting. The symptoms are caused by detrusor overactivity during the filling phase, causing the imperative urge to void. These detrusor contractions are countered by voluntary contraction of the pelvic floor muscles to postpone voiding and minimise wetting. The detrusor contractions can be demonstrated urodynamically, as can the increased activity of the pelvic floor muscles during each contraction. The voiding phase is essentially normal, but detrusor contraction during voiding may be extremely powerful. The flow rate reaches its maximum quickly and may level off ('tower shape').

Depending on fluid intake and urine production, the complaints of incontinence become worse towards the

Diagnostic work-up functional incontinence

HISTORY
confirm daytime (and night time) symptoms (urgency, frequency, with or without incontinence), infections, soiling
exclude other pathology, previous surgery

Questionnaires for voiding, wetting, defecation and soiling should be used

BLADDER DIARY
confirm daytime frequency and wetting fluid intake, voided volumes soiling, defecation

A bladder diary should be kept for at least 3 complete days, including the night.

PHYSICAL EXAMINATION
confirm normal anatomy, psychomotor development
exclude anatomical abnormalities neurological abnormalities

ADDITIONAL STUDIES
urinalysis
uroflowmetry + residual urine
Xray Lumbar + Sacral vertebrae
Ultrasound of kidneys + bladder
VCUG (if UTI positive)

Urodynamic studies only with abnormal flow, residual urine, initial treatment failures and suspicion of other pathology. Cystoscopy is rarely indicated

Figure 12 : Schematic work-up of children presenting with daytime (and night time incontinence)

end of the day, due to loss of concentration and fatigue and may also occur during the night. Children usually diminish their fluid intake to minimise wetting, and therefore incontinence may not be the main complaint or symptom. Urge syndrome should also be considered in "continent" children with recurrent UTI and vesicoureteral reflux: the bladder diary will usually demonstrate that fluid intake is minimal and voided volumes are smaller than expected.

Some children with bladder overactivity are not incontinent during the day but only at night: during the day they usually also demonstrate the symptoms of bladder overactivity and should be treated accordingly. They do not have monosymptomatic nocturnal enuresis but "incontinence".

The powerful flow resulting from urge syndrome can cause further problems, particularly when the pelvic floor muscles have become overactively trained and act as a bladder outlet funnel. It has been postulated that in children with recurrent urinary tract infections this may damage the mucosa and be the cause of pain and more infections.

Frequent voluntary contractions of the pelvic floor muscles inevitably lead to postponement of defecation, and constipation and faecal soiling are common signs in children with overactive bladder [174]. The constipation is worsened by diminished fluid intake. Constipation may be the leading symptom.

By adopting a structured approach to history and physical examination, the diagnosis of urge syndrome can be made in the majority of patients with confidence, without the need for invasive diagnostic procedures. Urine flow rate registration and post-void residual urine measurement can be helpful. Children with recurrent urinary tract infections require an ultrasound evaluation of the upper tracts as well as a voidingcystourethrograph (VCUG) to assess reflux [23,175].

The primary mode of therapy in urge syndrome is antimuscarinic medication. Attention should however also be given to explanation and demystification of the problem, together with voiding instructions, treatment of concomitant constipation and urinary infections.

By adopting a structured approach to history and physical examination, the diagnosis of urge syndrome can be made in the majority with confidence, without the need for invasive diagnostic procedures.

There is no evidence that medical treatment is better than standard therapy.

b) Dysfunctional voiding

Children with dysfunctional voiding usually present with incontinence, urinary tract infections and constipation. It is primarily believed to be a voiding disorder, but detrusor dysfunction is common.

No clear data are available on the possible causes of dysfunctional voiding. It may be that overactive bladder eventually leads to overactivity of the pelvic floor muscles, with subsequent insufficient relaxation during voiding. Alternatively, poor relaxation of the pelvic floor muscles during voiding may be a learned condition.

In some girls anatomical anomalies of the external urethral meatus seem to be associated with a higher incidence of dysfunctional voiding. The stream may be deflected anteriorly and cause stimulation of the clitoris with subsequent reflex activity of the bulbocavernosus muscle causing intermittent voiding [176].

In those children with poor or no coordination between detrusor contraction and sphincter relaxation, there may be many similarities with true detrusor–sphincter dyssynergia, which by definition is a neurologic problem.

Several forms of abnormal flow patterns in children with dysfunctional voiding have been described, including the following:

- Staccato voiding: characterised by periodic bursts of pelvic floor activity during voiding, with prolonged voiding time and sometimes residual urine. The flow is still continuous.
- Interrupted voiding: characterised by incomplete and infrequent voiding, with micturition in several separate fractions. Bladder volume is usually enlarged and unsustained contractions can be seen during voiding. Residual urine is usually present.

Detrusor instability may be seen in both forms of dysfunctional voiding during urodynamic studies, but it may be absent [23,162,166,172,177].

Diagnosis should be based on a careful history and physical examination, complemented by bladder diaries, renal ultrasound studies, and urinary flow and residual urine measurements. The pattern of the flow curve is usually indicative. The combination of uroflowmetry with pelvic floor electromyography (EMG) registration and post-void measurement of residual urine may obviate the need for an invasive urodynamic study.

Primary aim in the treatment of dysfunctional voiding is relaxation of the pelvic floor muscles: if bladder overactivity is present as well, anticholinergic drugs can be added to relax the detrusor muscle and increase functional capacity. Recurrent urinary infections and constipation should be treated and prevented during the treatment period. Rehabilitation of the pelvic floor aims at complete relaxation of the pelvic floor muscles and complete emptying of the bladder.

c) Lazy Bladder syndrome

Children with a lazy bladder void infrequently, and usually present with urinary tract infections and overflow incontinence. Urodynamically, the bladder has a greater than normal capacity, a normal compliance and there is no detrusor contraction during voiding. Abdominal pressure is the driving force for voiding.

A correct diagnosis can only be made through urodynamic investigation. Renal function studies, renal ultrasound and VCUG should be performed to assess the extent of renal damage and reflux. Long-standing overactivity of the pelvic floor may in some children be responsible for decompensation of the detrusor, leading to a non-contractile detrusor. However, no data are available to support this theory.

Treatment is aimed at optimising bladder emptying after each void. Clean intermittent (self) catheterisation is the method of choice in combination with treatment of infections and constipation (which may be extreme in these patients). Intravesical elctrostimulation has been described, but is as yet not recommended as a routine procedure in these children.

d) Non-neurogenic neurogenic bladder

This condition has been described by Hinman and Bauman, and was looked upon as an acquired personality disorder [178,179,180].

It is also referred to as 'occult neuropathic bladder' [181].

The psychogenic model has since been abandoned and the condition is now considered to be the extreme endstage of dysfunctional voiding, though no studies confirm this pathophysiological chain of events.

Urodynamically, non-neurogenic neurogenic bladder is characterised by diminished bladder volume and compliance. Bladder instability is usually present (resembling hyperreflexia in the neuropathic bladder) and overactivity of the pelvic floor muscles occurs during voiding. Videourodynamics or a VCUG usually shows all the features of a true neuropathic bladder. It is believed that long-standing detrusor overactivity in combination with pelvic floor overactivity may lead to this condition.

Although physical and neurologic examination, as well as an MRI of the spinal cord, may be completely normal, a hidden neurologic disorder must be considered. This is because, in many patients, the early onset of the problems and severe renal impairment make the 'end-stage theory' less likely.

Treatment is complex in these patients. Sometimes anticholinergic drugs in combination with clean intermittent (self) catheterisation is sufficient, but occasionally surgical bladder augmentation to safeguard the upper urinary tract and promote continence is necessary.

e) Giggle incontinence

Laughter can trigger partial to complete bladder emptying in some children well into their teenage years, and intermittently into adulthood [182].

The condition occurs in both boys and girls and is generally self-limiting. The exact mechanism of leakage is poorly understood as demonstrable urodynamic studies do not reveal abnormality, there is no anatomical dysfunction and both urinalysis and upper tract visualisation are normal.

It has been postulated that laughter induces a general hypotonic state with urethral relaxation, thus predisposing an individual to incontinence, however the effect has not been demonstrated on either smooth or skeletal muscle [183]. It has also been suggested that giggle incontinence is due to laughter triggering the micturition reflex and overriding central inhibitory mechanisms.

Suffererers are neurologically normal but display physiological variations in response or control [184,185].

Treatment is notoriously difficult and often long term, such that positive results may simply reflect a natural history of the disorder. There are reports of positive results with conditioning training, methylphenidate, and Imipramine [183,184,186].

There is no acceptable evidence that any of these treatments are better than no intervention.

f) Vesicovaginal entrapment

Urinary leakage that occurs in girls within a short time following micturition to complete bladder emptying and is not associated with any urge to void may be associated with entrapment of urine in the vagina. The hymen can be funnel shaped or the labia partially fused or functionally unable to be spread during voiding. The classic presentation is of a girl who does not spread her legs during voiding or who on questioning has a posterior pelvic tilted position on the toilet. Alteration of voiding mechanics results in an immediate improvement in post-void continence.

5. NON-PHARMACOLOGICAL TREATMENT

The main objectives of treatment are to normalise the micturition pattern, normalise bladder and pelvic floor overactivity and cure the incontinence, infections and constipation.

Traditional therapy for day-wetting children is cognitive and behavioural, using explanation of bladder function, learning to recognise the sensation of urge, and eradication of holding manoeuvres (i.e. immediate micturition without postponement). Micturition charts and diaries are established aids for bladder retraining, sometimes in combination with alarm clocks, reminding the child to urinate every 3–4 hours. Ultrasound can be used as a biofeedback mechanism to aid reduction of residual volume.

"Bladder training" is used widely, but the evidence that it works is variable [168,187,188]. Some authors contend that in less severely affected children a thorough explanation of the underlying causes and the expected progress of resolution is sufficient treatment in itself [149]. More active conventional management involves a combination of cognitive, behavioural, physical and pharmacological therapy methods. Common modes of treatment include parent and child reassurance, bladder retraining (including timed toileting), pharmacotherapy, pelvic floor muscle relaxation and the use of biofeedback to inhibit rises in detrusor pressure associated with urinary incontinence [189,190,191,192,193] Further treatment options include suggestive or hypnotic therapy and acupuncture.

A combination of bladder training programs and pharmacological treatment, aimed specifically at reducing detrusor contractions, is often useful and sometimes necessary.

Curran et al described the long term results of conservative treatment of children with idiopathic bladder overactivity [194]. Of 30 patients follow-up was long enough to draw conclusions; it showed complete resolution in 21 and markedly improvement in five patients. The average time to resolution of symptoms was 2.7 years. Children with very small or large bladders were less likely to benefit from this treatment. Age and gender were not significant predictors of resolution although girls were more likely to have resolution than boys.

a) Bladder rehabilitation

Urotherapy is used in the rehabilitation of the dysfunctional bladder and is a combination of cognitive, behavioral and physical therapy methods. The program is based on careful evaluation of bladder function and knowledge about normal development of bladder control. The evaluation also includes how the child itself handles the situation.

The aim of urotherapy is to normalise the micturition pattern and prevent further functional disturbances: it is an integrated concept, from filing to the emptying phase.

Although the concept of urotherapy dates back to the late 1970's, clinical studies are still scarce and describe compound therapies rather than single interventions, which makes it difficult to evaluate the results 169,190, 191.

Rehabilitation of bladder and pelvic floor muscles using different modalities, such as explanation and instructions, in combination with medical treatment of constipation and infections, physiotherapy and biofeedback play a major role in the treatment of children with bladder and sphincter dysfunctions.

1. STANDARD THERAPY

Once the child is interested in its own bladder and voiding problem, careful instructions can be given to the child. The function of the bladder and sphincteric mechanism is explained and the child has to learn how to void again. This can obviously be done in several ways and much depends on the child's abilities and parental support.

The main points are:

- explanation and demystification
- instructions on how and when to void (at regular intervals and in a good position)
- bladder diaries
- treatment of concomitant constipation
- treatment of concomitant infections and antibiotic prophylaxis

Regular voidings, sufficient fluid intake and dietary measures to promote easy defecation are of utmost importance. Also voiding in such a way that the pelvic floor muscles can relax completely during voiding is important. Bladder diaries are filled in by the child to follow the daily life of the child. Children with urge syndrome start with shorter intervals, gradually increasing them as soon as urgency attacks disappear. Children with dysfunctional voiding have to learn how to decrease the intervals.

During the treatment period it is important to have the child frequently visit the clinic in order to offer sufficient support to the child and parents and to discuss the diaries and check for residual urine. Home training programs, including reminders, are designed for use between the visits to the clinic.

This standard approach is always used as a first step. Although this method has been described by several authors, there are no prospective randomised studies available to evaluate the success rate. ***Level of evidence: 2***

2. PHYSIOTHERAPY

In children with urge syndrome and dysfunctional voiding the pelvic floor muscles are almost always overactive: the primary objective of physical therapy therefore should be to teach the children to relax the pelvic floor muscles during voiding.

Success rates vary between 50 and 80 percent: all studies describe a heterogenous group of children, use more than one treatment modality (like standard therapy in combination with physical therapy and biofeedback) and outcome is defined inconsistently 196 197

The cited studies describe physiotherapy exercises in an excellent way and show definite improvement of signs and symptoms. Controlled studies about pelvic floor exercises are still missing. The finding of these studies that children who previously had been treated unsuccessfully with biofeedback or standard therapy alone responded to the comprehensive package suggests that the comprehensive program is more effective. ***Level of evidence: 3***

b) Biofeedback

Biofeedback implies perception to some degree of detrusor contraction (filling phase) or pelvic floor relaxation (emptying phase). This achieved by monitoring continuously a signal that carries information about detrusor or pelvic floor muscles. The feedback loop enables the child to influence the process provided cognitive capabilities are developed normal. The feedback loop also graphically demonstrates the habitual non-physiological response of children with urge syndrome or dysfunctional voiding. Training with biofeedback can be used as a single treatment 198, 199, or in conjunction with a comprehensive rehabilitation program 195,196 200.

An overactive detrusor contraction with imperative urge should be inhibited before it escalates. With central inhibition, the emergency brake of forceful pelvic floor muscle contraction need not be applied.

Cystometric biofeedback is used to teach the child how to recognise and inhibit overactive detrusor contractions by watching the pressure curve during cystometry: this is invasive and time consuming and therefore has limited use and is not used as a routine treatment.

Using the flowpattern as biofeedback, with or without EMG of pelvic floor muscles, will teach the child how to relax the pelvic floor during micturition: the child sits on a toilet with a flow transducer, watching the flow curve and EMG on line on a computer display, trying to empty completely in one relaxed voiding. Ultrasound can be used to determine residual urine. Sometimes interactive computer games are used to make it more attractive to children [201].

The results of biofeedback are reported only in a few studies. In one study the results were classified as good in 68%, improved in 13 % and not improved in 29%: the positive effect of biofeedback is confirmed by others. In most studies no information is provided on residual urine. Also inclusion criteria and outcome measures vary considerably between the various studies [202,203,204,205]. ***Level of evidence: 2-3***

In its most simple form it can be regarded as a self-disciplinary measure to correct a long-standing bladder habit. The principle of "re-education" using biofeedback has also been used to train individual children to inhibit inappropriate rises in detrusor pressure during bladder filling. The practice of biofeedback can help children learn both inhibition of vesical pressure increase and improved recruitment of skeletal muscle urethral closure mechanisms [206].

c) Clean intermittent (self) catheterisation

In children with a lazy bladder, when the detrusor contractions are minimal or absent, bladder emptying can be achieved with timed and double voiding. If this does not provide adequate results, clean intermittent self-catheterization (CISC) may be tried. This requires careful guidance for both the child and the parents. Sometimes it is necessary to give the child a suprapubic catheter for a while and gradually prepare him/her to accept CISC. Once the infections have cleared and the child is continent it will become easier for both the parents and the child to accept. The frequency of CISC depends on the severity of the problem and may vary between four times a day and once a day before going to bed.

d) Electrostimulation

Neuromuscular electrical stimulation may be directed at the pelvic floor or the detrusor. However, the invasive nature of the procedure makes it less attractive, particularly for children. A recently described technique using transcutaneous stimulation with surface electrodes stimulating the sacral root (S3) provided promising results but needs further validation [207]. Stimulation of 2 Hz was applied for 2 hours daily over 6 weeks in 16 children with proven detrusor instability. Two did not respond at all, but bladder capacity increased in nine patients and incontinence decreased in six.

At present there is insufficient data available to justify intravesical electrostimulation or transcutaneous neuromodulation routinely in children. Some centres are using different modalities to test their efficacy in children [208,209,210,211].

e) Alarm treatment

This modality is not frequently used for daytime wetting, but occasionally individual patients may benefit. Only one randomised clinical trial has been published to establish the efficacy of this form of treatment. Halliday et al compared a contingent alarm (which sounded when the child wet) with a non-contingent alarm system (which sounded at intermittent intervals) [212]. The trial included 44 participants half of whom were assigned to each of the two types of alarm by a quota allocation system that considered age, sex, type and frequency of daytime wetting. After 3 months of treatment success was measured as 6 consecutive weeks without daytime wetting. All children who failed to achieve this dryness were said to be persistently wetting during the day. By this definition 9 children in the non-contingent group and 6 children in the contingent group had persistent wetting. Although the risk of persistent wetting with the contingent alarm was 67 percent of the risk of persistent wetting with the non-contingent alarm, the difference in reduction in wetting between the two groups was not significant (RR 0.67, 95% CI 0.29 to 1.56).

f) Conclusion

Most clinical studies describe compound therapies rather than single interventions, which makes it difficult to evaluate the results. Physiotherapy and biofeedback both focus on the pelvic floor. Relaxation of the pelvic floor during voiding is essential for normal voiding and most of these patients are unable to relax their pelvic floor muscles. Biofeedback is important for showing the children the effect of their efforts.

Most studies only state the clinical responses, and do not provide information on urodynamic parameters before and after treatment. A 'normal' flow curve does not mean normal voiding if no information is provided on post-void residual urine. In most papers the inclusion and exclusion criteria are not clearly documented, and it may very well be that the more difficult patients with both storage and voiding dysfunction were included in the study population. Furthermore, different series may describe different groups of patients due to poor definitions and an inadequate classification system.

In children with a suspected infravesical anatomic obstruction or abnormality, endoscopic investigations should be performed. Most often the abnormality can be treated at the same time. In girls, a meatal web may cause a deflection of the stream upwards (causing stimulation of the clitoris and bulbocavernosus reflex). A meatotomy may cure this problem, though no information on the long-term effects is available [176].

6. PHARMACOLOGICAL THERAPY

Many clinicians use adjunctive anticholinergic drug therapy to decrease detrusor contractility and facilitate greater functional bladder storage. Detrusor overactivity is believed to play an important role in many children with functional incontinence, vesicoureteral reflux and urinary infections [213].

In the presence of moderate to severe daytime incontinence some clinicians bypass bladder training and institute pharmacotherapy alone [169].

The outcome of pharmacological treatment for incontinence during the day is "unpredictable and inconsistent" and few randomised studies have been performed to evaluate safety and efficacy.

Currently, the drug most widely used to relax the overactive detrusor is oxybutynin-HCl. It has antimuscarinic, local anaesthetic and muscle relaxant properties [214].

If oral medication is poorly tolerated, it may be administered intravesically, but in these children this is rarely an option, whereas in children with neuropathic bladder dysfunction who are catheterised at regular intervals it may be a good alternative [215].

Side-effects are common – up to 10 percent of children have to discontinue the drug because of intolerable side-effects, such as headache, blurred vision, constipation, altered behaviour, dry mouth and flushed cheeks. Reduced saliva production may induce tooth decay, and constipation may worsen [170, 182]. The incidence of side effects seems to be a dose related, both for oral and intravesical administration [216].

Oxybutynin crosses the blood–brain barrier and psychological and personality changes may be seen. Anecdotal documentation of dramatic improvement in school achievements following withdrawal of the drug in MMC patients further supports the need for more sophisticated drugs with fewer side-effects.

A novel drug, tolterodine, with a more pronounced and specific antimuscarinic effects on the detrusor has become available and is currently being evaluated in children. Preliminary results from a dose finding/pharmacokinetics study show that the optimal dosage in children aged 5–10 years is 1 mg b.d. No safety concerns have been noted [217, 218, 219].

The only drug which has been investigated in a randomised placebo controlled way is terodiline [220, 221].

Because of serious cardiac side effects terodiline has been withdrawn from the market.

Other drugs like trospium and propiverine have been used in children, but results are variable and inclusion and outcome criteria were not in accordance with ICCS definitions which make comparison with other studies difficult [222, 223, 224].

Treatment of the overactive pelvic floor and sphincter is much more difficult. Recently the results of α-adrenergic blockade were presented [224]. The initial results are promising but further studies are needed to define the place of alpha-blockers.

To evaluate the efficacy of different treatment modalities a prospective multi-centre trial (European Bladder Dysfunction Study (EBDS, EEC Biomed I, CT 94-1006) has been designed, in which pharmacotherapy (oxybutynin vs placebo) is compared with biofeedback and standard therapy. Although preliminary results are available, final outcome results will become available in 2002.

In preparation of this chapter an extensive review of the literature has been performed: only 6 studies (out of 1013) qualified for analysis. But the limited number of identified randomised controlled trials does not allow a reliable assessment of the benefits and harms of different methods of management in children. Further studies on the different behavioural (bladder training, psychotherapy), physical (pelvic floor muscle relaxation), electrical stimulation and drug therapies that are currently being used in children as standard treatment are required.

7. CONCLUSION

Although the condition of urinary incontinence in children is distressing, significantly effective treatment has not been identified. Of the studies reviewed the only treatment found to be beneficial was the drug terodiline, an anticholinergic with calcium agonist properties. Although the particular study did not demonstrate adverse effects on blood pressure, subsequent work established an association with ventricular arrhythmia and terodiline was ultimately withdrawn.

Three specific problems were identified concerning the evaluation of interventions for children with daytime urinary incontinence.

Firstly, few trials exist and of those identified three were of historical interest only. The most recent trial (EBDS) concerns current clinical intervention, namely the use of biofeedback and oxybutynin, and is therefore clinically relevant, but the final results are not yet available. Other interventions in routine clinical use, such as the combination of education, bladder training, physical therapies, bowel management and antibiotic prophylaxis have never been evaluated with respect to no intervention or placebo. New trials are warranted to evaluate these and other interventions which are commonly used by clinicians to treat childhood incontinence. It would be ideal if randomised and controlled trials were conducted when an intervention is first identified rather than after the unproven treatment has become routine practice. It is acknowledged that many clinicians feel an ethical dilemma about randomising children to a study arm that offers no genuine assistance. However, if routine conservative treatment has a proven benefit, randomised controlled trials can use this therapy as the control arm.

The second problem involves the size and design of existing trials being inappropriate to allow identification of the true effects of interventions studied. As is well known the power of the trial to detect effects of interventions is proportional to the event rates in the groups and the number of patients in the trial. Small trials may miss modest but clinically important effects. In our systematic review four of the five trials enrolled 61 patients or fewer. Other design parameters that warrant particular attention include randomisation of participants, control for intervention, and blinding for each of the subjects, assessors and data analysts. Since problems in trial design and reporting may bias the observed intervention effects, editors of the major biomedical journals have published guidelines for the reporting of trials in the form of CONSORT statement (Consolidated Standards for Reporting of Trials).

Finally, standardised outcome measures would be beneficial and allow synthesis of data from different studies. Four areas of quantification can be identified: severity of incontinence, bladder storage, features of bladder emptying, and quality of life. In measuring incontinence a clinician may be interested in either the severity or the frequency of episodes. Bladder storage has routinely been evaluated by both cystometry and the bladder diary, while bladder emptying requires data from uroflowmetry in addition to estimates of pre and post void urine volumes. Measures of quality of life in children with childhood incontinence are also rare. In summary, studies to establish reliable valid outcome measures would inform higher quality clinical trials.

In conclusion, further work is required in this difficult clinical area. Firstly, the establishment of outcome measures is warranted, thence randomised controlled trials of routine therapy to allow the use of such management in a control capacity for other studies. Such interventions that would reward further investigation include: bladder and voiding education, bladder drill, retention training, bowel management, hypnotherapy and alternative therapies, psychology, prophylactic antibiotic medication, neuromodulation, biofeedback therapy and pelvic floor muscle awareness and specific relaxation. Only then can the efficacy of new interventions be measured in children with voiding dysfunction or the urge syndrome.

In summary, while there is a wide therapeutic choice available to clinicians, many of the commonly used treatments are of dubious value and have not been rigorously evaluated in careful clinical trials with an appropriate study design.

Children who suffer this distressing condition, and their families, and those who care for them clinically, need clear guidance as to which treatments are of proven value. They need access to treatments which work, and they need protection from treatments which do not work.

VI. NEUROGENIC DETRUSOR-SPHINCTER DYSFUNCTION

1. INTRODUCTION

Although significant advances have been made in the diagnosis and management of children with incontinence secondary to neurogenic detrusor-sphincter dysfunction, the primary objective of treatment has remained the same i.e. preservation of the upper urinary tract and renal function.

Most neuropathic bladders are encountered in children with Myelomeningocele (MMC), tethering of the cord or sacral anomalies. Traumatic spinal lesions in children are less frequent.

In most cases the defect will be apparent at birth: only occasionally children with tethering of the cord will come to the attention of the physician with minor defects, such as Spina bifida occulta with slight discoloration of the skin, abnormal hair growth or a sacral dimple.

At birth the majority of these patients have normal upper tracts: without proper management urinary tract infections and secondary changes of the bladder may cause upper tract deterioration in up to 60 percent within 5 years [226, 227].

Treatment of the bladder dysfunction is therefore primarily aimed at preservation of the upper urinary tract and secondarily at gaining continence and improvement of quality of life.

Management goals are directed at promoting a low pressure reservoir and regular emptying (in the first years of life), while later in life, as the child grows up, promoting continence is added.

2. Pattern recognition

In children with neuropathic bladder dysfunction the detrusor may be normal, overactive or inactive. The urethral sphincter may be normal, overactive or paralysed. These conditions may exist in any combination [228,229,230].

Urodynamic evaluation (preferably in combination with fluoroscopy) makes pattern recognition possible. Four major types are usually used to describe the detrusor-sphincter dysfunction:

1. Detrusor overactivity (hyperreflexia) with overactivity of the sphincter,
2. Detrusor hyperreflexia with underactivity of the sphincter,
3. Detrusor underactivity with sphincter overactivity and
4. Detrusor underactivity with sphincter underactivity.

Urodynamic investigations make it possible to establish a management plan for each individual patient. For the very young child the combination of an overactive detrusor and sphincter is potentially dangerous because of the high intravesical pressures, which will put the upper tract at risk (vesicoureteral reflux and hydronephrosis), whereas an inactive detrusor and paralysed sphincter is relatively safe, providing low pressure reservoir [231]. ***Level of evidence: 2***

3. Management

The urological problems in children with a neuropathic bladder are either associated with high intravesical pressures or insufficiency of the sphincteric mechanism.

In the first years of life the kidneys are highly susceptible to back-pressure and infection. In this period emphasis will be on documenting the pattern of neurogenic detrusor- sphincter dysfunction and assessing the potential for functional obstruction, vesicoureteral reflux. Ultrasound studies and a VCUG to exclude reflux have to be performed soon after birth. A urodynamic evaluation can be done after some weeks and needs to be repeated at regular intervals, in combination with evaluation of the upper tracts [232]. ***Grade of recommendation: 2***

Initial treatment consists of oral or intravesical anticholinergic treatment in combination with clean intermittent catheterisation, to start soon after birth.

At present Oxybutynin, Tolterodine, Trospium and Propiverine are the most frequently used drugs: some clinical studies are available, but no randomised placebo controlled studies have been performed [218,233,234,235,236,237,238,239]. ***Level of evidence: 2***

As fecal evacuation is also impaired in most patients, colonic lavage may have to be started even at this very young age.

In children the early institution of intermittent catheterisation has the advantage that it becomes an integral part of daily routines and is well accepted by the parents.

Children with a good response to anticholinergic treatment and an overactive sphincter may be continent in between catheterisations. Bladder pressure and development of the upper tracts will determine whether additional treatment is necessary.

Therapy resistant overactivity of the detrusor, or small capacity and poor compliance will usually need to be treated by bladder augmentation.

It has been postulated that overactivity of the sphincter in combination with an overactive detrusor (classical detrusor sphincter dyssynergia) causes secondary changes of the bladder wall, due to the frequent increased intravesical pressures. These bladder wall changes (collagen deposition in the muscular layer) may cause further loss of elasticity and compliance: resulting in a small non-compliant bladder with continuously elevated pressures. It is believed that early institution of intermittent catheterisation and anticholinergic drugs may prevent this in some patients [233].

At present there is not enough evidence that this management protocol indeed decreases the need for later augmentation. No prospective trials have been described.

Children with detrusor overactivity (hyperreflexia) but without sphincter activity will fare better in terms of their upper tracts, but they will be severely incontinent. Initial treatment will be intermittent catheterisation (as it may reduce the degree of incontinence and offers a much better control over urinary infections) with anticholinergic drugs: at a later age the outlet resistance has to be increased in order to render them continent [240].

No validated medical treatment is available to enhance the bladder outlet, although some authors have advocated alpha-receptor stimulation of the bladderneck. For permanent continence surgical procedures need to be considered [241,242,243,244,245,246].

It is important to establish adequate bowel emptying before attempting to correct bladder dysfunction surgically or medically.

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