Committee 9

Diagnosis and Management of Urinary Incontinence in Childhood

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A. INTRODUCTION

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

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.

I. NORMAL DEVELOPMENT OF BLADDER AND SPHINCTER CONTROL

Normal bladder storage and voiding involve low-pressure and adequate bladder volume filling followed by a continuous detrusor contraction that results in bladder emptying, associated with adequate relaxation of the sphincter complex. This process requires normal sensation and normal bladder outlet resistance. The neurophysiological mechanisms involved in normal bladder storage and evacuation include a complex integration of sympathetic, parasympathetic and somatic innervations 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 foetuses and newborns, micturition is modulated by higher centres and the previous notion that voiding is spontaneous and mediated by a simple spinal reflex is an oversimplification [3]. Foetal micturition seems to be a behavioural state-dependent event: intrauterine micturition is not randomly distributed between sleep and arousal, but occurs almost exclusively while the foetus is awake [3].

During the last trimester the intra-uterine urine production is much higher than in the postnatal period (30ml/hr) and the voiding frequency is approximately 30 times every 24 hours [4].

Immediately after birth voiding is 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 micturition does not occur during sleep [5].

This inhibition (or lack of facilitation) 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 electro-encephalographic evidence of cortical arousal, facial grimaces or limb movements, or actual awakening. Sleeping infants are always seen to wake up before the bladder contracts 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 and may have an intermittent pattern although bladder emptying efficiency is usually good. In over 80 percent of voids the bladder empties completely [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 H2O, respectively) [7,8].

These higher detrusor pressures decrease progressively with increasing age. In up to 70 percent of infants (up to the age of 3 years) with normal lower urinary tracts, intermittent patterns of voiding 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 and 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 need 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 initiate urination even when the bladder is not completely full, and allows 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 depends 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 underlying pathophysiological basis.

II. NORMAL VALUES

1. 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 (**Figure 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. Cystometric capacity is generally less than 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].

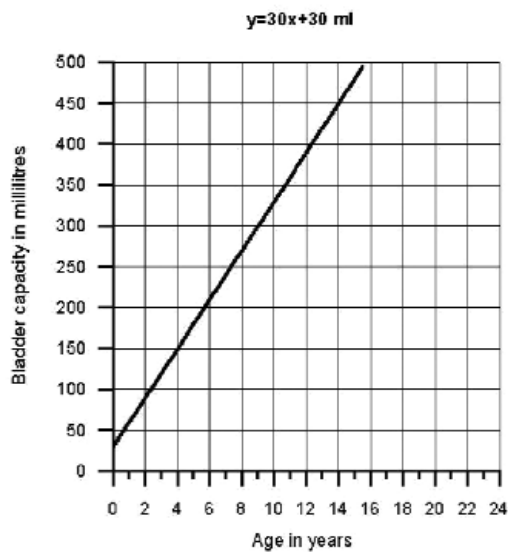Another formula to calculate bladder capacity in infants is: bladder capacity (ml) = 38 + (2.5 x age (mo)) [10].

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

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 (**Figure 2**) [15].
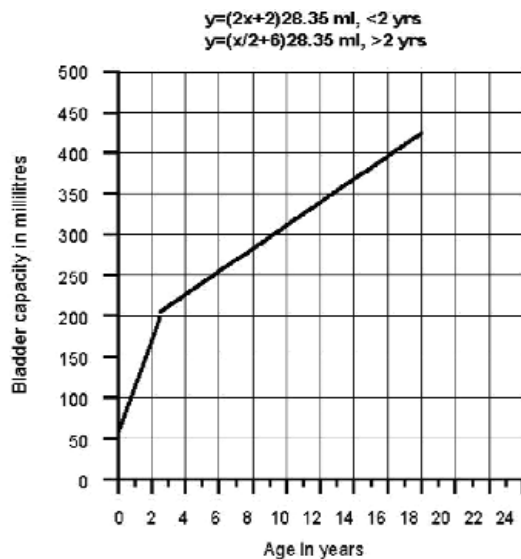

Figure 2. Bladder capacity using the formula
Y = (2 X + 2) x 28.35 ml < 2 years
Y = (X/2+6) x 28.35 ml > 2 years
(Y = capacity in ml, X is age in years)

None of these formulas have been acquired from a population based study and do not reflect normal bladder capacity. Normal bladder capacity should be regarded as the maximum voided volume of urine and shows huge variation.

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.

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 (**Figure 3**) .

2. NORMAL VOIDING

The micturition frequency of the foetus during the last trimester is approximately 30 per 24 hours. It decreases to 12 during the first year of life, and after that it is gradually reduced to an average of 5 ± 1 voidings per day [10, 15].

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: also in individual children, the weight-corrected diuresis could vary up to 10-fold [18].
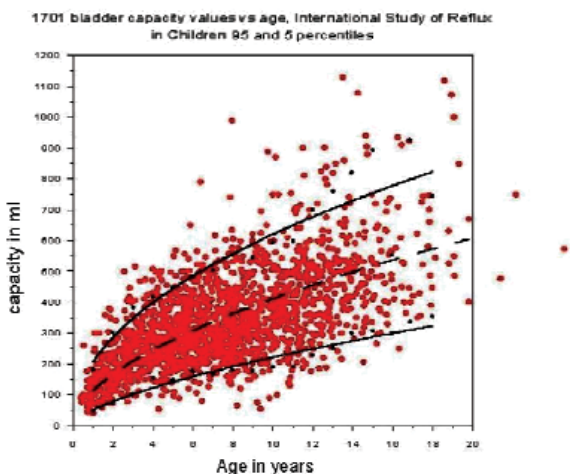

Figure 3. Bladder capacities determined by VCUG in the International Reflux Study

3. NORMAL VOIDING PRESSURES

Bladder dynamics in children have demonstrated developmental changes with age. Detrusor 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 and girls 75 cm H_2O [5].

4. 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].

B. 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 [1].

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 and pelvic floor 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 pelvic floor 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 equivocal results, or results suggesting gross deviations from normal function. Only in these situations is there an indication for invasive investigations, such as:

- Voiding cystourethrography.

- Invasive urodynamics (cystometry, pressure/flow/EMG studies, videocystometry).

- Renal scans or intravenous urography.

- Cystourethroscopy.

I. HISTORY TAKING

For the paediatric age group, where the history is jointly obtained from parents and child, and where the failure to develop bladder control generates specific problems, a structured approach is recommended, with a questionnaire [1,2].

Level of evidence: 3. Grade of recommendation: B

Many signs and symptoms related to voiding and wetting are new to the parents, and they should be specifically asked for, using the questionnaire as checklist. If possible the child should be addressed as the patient and questioned directly, as the symptoms prompting the parents to seek consultation may be different from those are problematic for the child.

A voiding diary is mandatory to determine the child's voiding frequency and voided volumes. Checklists and frequency volume chart can be filled out at home, and checked at the first visit to the clinics. History-taking should also include assessment of bowel function; a similar pro-active process using a questionnaire should be followed for defecation and faecal soiling [3].

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 (in pubertal and older children). 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 [4,5].

Child abuse is very often signalled first by symptoms of vesico-urethral dysfunction [6].

At present there are no validated questionnaires to diagnose the cause of incontinence in children.

Level of evidence: 4. Grade of recommendation: C

II. PHYSICAL EXAMINATION

Apart from a general paediatric 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 [7].

In examining the abdomen for the presence of a full bladder, full sigmoid or descending colon which 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 preventing the pelvic floor relaxation and obstructing the free flow of urine [8] (**Figure 4**).

Level of evidence: 4. Grade of recommendation: D

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 allow the pelvic floor muscles to relax properly.

III. URINALYSIS

In order to be comprehensive, physical examination should include urinalysis to identify patients with urinary tract infection, diabetes mellitus, diabetes insipidus and hypercalciuria if indicated [9].

IV. NON-INVASIVE DIAGNOSTIC TECHNIQUES

1. FREQUENCY / VOLUME CHARTS: BLADDER DIARY

The frequency/volume chart is a detailed diary recording each void by time 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 also recorded: Then, this becomes termed as bladder-bowel diary due to its complexity.

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 [10].

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 [10].

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, even in incontinent children, increase incrementally with age. The frequency volume chart is useful when comparing the mean voided volume and standard deviation 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. Data in normal children and in children with different categories of incontinence are available for comparison [10-12].

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.

Level of evidence: 3. Grade of recommendation: B

2. 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 [12-14].

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.

3. SCORING SYSTEMS

At present two scoring systems, based on validated questionnaires have been described. Specific scores correlated with lower urinary tract dysfunction with a specificity and sensitivity of about 90% [15,16].

The value of these scoring systems to determine the cause of incontinence seems to be of limited value to the individual patient, but can be very useful in studies to determine and compare treatment outcome.

Level of evidence: 3. Grade of recommendation: C

4. QUANTIFICATION OF CONSTIPATION

Scoring a plain X-ray of the abdomen (Barr score) yields inconsistent results in grading constipation. [17-19] Reproducibility seems to be best using the method described by Leech [20-22].

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 and pelvic floor dysfunction habitually use their pelvic floor as an "emergency brake", anomalous defecation frequency and constipation have a high prevalence in this group.

A non-invasive way to determine fecal retention is the estimation of rectal diameter on ultrasound. In children without constipation the mean diameter was 2,4 and 2,1 cm in two different studies respectively [23-24]. In children with constipation the rectal diameter was on average 3,4 cm in one and 4,9 in the second study. Both studies do not mention specificity nor sensitivity. Finding a dilated and filled rectum on ultrasound while the child feels no need to defecate probably can replace a digital rectal examination.

Overt constipation should be dealt with before embarking on treatment of incontinence or detrusor and pelvic floor dysfunction [25,26].

Level of evidence 3. Grade of recommendation: B

5. 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 a standard office procedure. Flow patterns and rates should be repeated 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 [27]. It should be noted that a normal flow does not exclude a voiding disturbance, nor does an abnormal flow pattern automatically means a bladder or voiding dysfunction, as in asymptomatic normal schoolchildren abnormal patterns were also found [28,29].

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 [30,31]. 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 fluctuating. An intermittent flow pattern shows a interrupted flow, whereas in fluctuating voiding the flow does not stop completely, but fluctuates due to incomplete relaxation of the sphincter.

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 [32].

The same parameters used to characterise continuous flow may be applicable, if care is exercised, in children with intermittent, or fluctuating flow patterns (**Figures 5 -7**). In measuring flow time, the time intervals between flow episodes are disregarded. Voiding time is total duration of micturition, including interruptions.

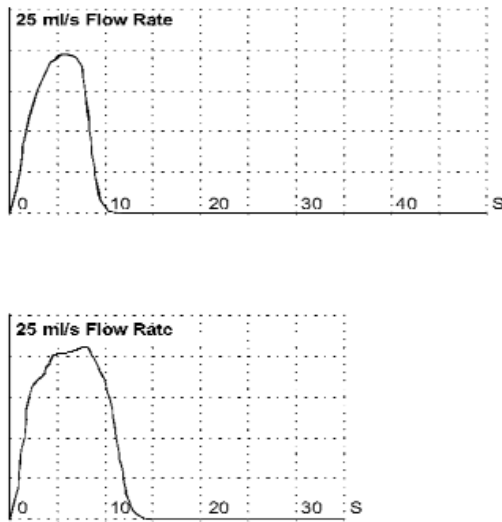Level of evidence: 3. Grade of recommendation: B

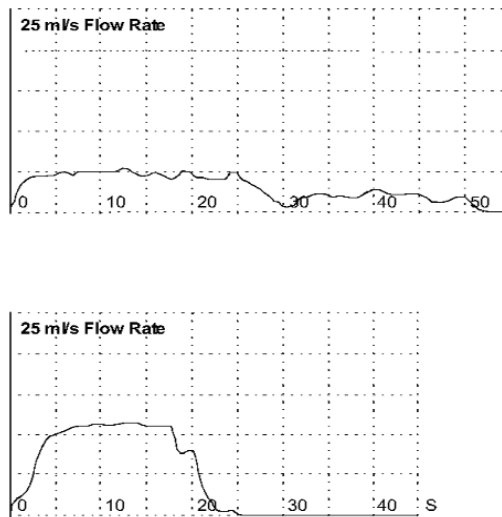*Figure 5: normal urinary flow curves of 2 children.*

Figure 6: flow curve of 2 children with a static, anatomic obstruction; the curve is continuous but the flow is lower than normal and extended in time.

6. 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 [33].

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 millimetres, measured at 50% of expected bladder capacity, is suspicious of detrusor overactivity [34,35]. Because only a few studies have been conducted to compare bladder wall thickness in normal children without complaints and in children with lower urinary tract dysfunction, more studies need to be performed to validate these non-invasive techniques [36, 37].

Another possibility is to assess bladder volume and bladder wall thickness to calculate the Bladder Volume / Bladder Wall Thickness index. In children with nocturnal enuresis this index correlated well with response to treatment [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
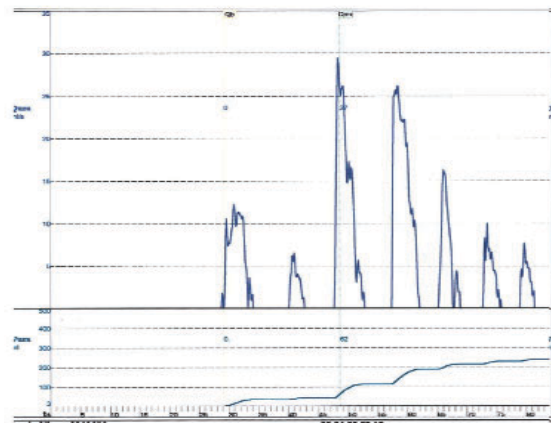

Figure 7: intermittent flow curve in a child with disco-ordination between detrusor contraction and pelvic floor relaxation.

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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 bladder outlet obstruction or detrusor pelvic floor 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 used to obtain representative data on flow rate and flow pattern, as well as post-void residual volumes. With ultrasound, bladder filling is assessed and when the bladder capacity is equal to the functional or expected bladder capacity for age, the child is asked to void into the flowmeter. After recording the flow, post-void residual is assessed again.

This procedure avoids the registration of flow rates at unrealistic bladder volumes.

Alternatively children can be asked to use a flowmeter at home: a special flowmeter has been designed to use at home [40]. Because some children have difficulty voiding in a strange environment, this option can overcome this.

7. 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.

At present there are no studies indicating that a VCUG is useful in children with incontinence, but without urinary tract infections.

In general urodynamic studies will only be done if the outcome will alter the management, and this will also depend on whether the possible treatments being considered are invasive. The diagnostic information needed is that which is necessary to find the correct treatment. Indicators include, 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 bladder outlet obstruction, and an intermittent flow suggesting detrusor –sphincter- pelvic floor dys-coordination [32].

A clinically significant post-void residual on repeated occasions clearly points to incomplete bladder emptying. The pad test will detect the cases with obvious stress and urgency incontinence, or continuous dribbling. Ultrasound imaging will raise suspicion of an ectopic ureter.

In short, invasive diagnostics are indicated when the non-invasive testing raises suspicion of neurogenic detrusor-sphincter dysfunction (occult spinal dysraphism), obstruction (especially posterior urethral valves), genitourinary abnormalities (e.g. epispadias), advanced non-neurogenic detrusor-sphincter- pelvic floor dysfunction (as in children with vesicoureteral reflux and upper tract dilatation 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.

a) Voiding cystourethrogram (VCUG)

1. TECHNIQUE OF VCUG IN CHILDREN

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) with the child in supine position, 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 can be taken during voiding. Also take a spot film of the upper urinary tract during voiding, as the degree of vesicoureteral reflux (VUR) may change with the pressure generated by the detrusor muscle during voiding. Post-void residual volumes vary very considerably 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 in all children, to minimise the risk for post-VCUG urinary tract infection especially in children with an anatomic abnormality.

2. 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 in order to detect reflux and in children with an abnormal flow pattern to detect bladder outlet abnormalities (like valves, strictures or a syringocele). Presence of hydrone-phrosis on ultrasound investigation will certainly obviate the need for this investigation.

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 neurogenic bladder the position and configuration of the bladder neck during filling and voiding should be noted.

In children with non-neurogenic detrusor-sphincter-pelvic floor 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 [41,42].

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

c) (Video)-Urodynamics

In children urodynamic investigations should only be performed if the outcome will have consequences for treatment [43,44]. Furthermore like VCUG it may be considered when invasive or surgical interventions are planned. The main question is whether the urodynamic study will provide new information that cannot be obtained otherwise and will influence the further management. From the few studies that have addressed this issue it can be concluded that urodynamic studies in the majority of cases do not provide significant additional information to justify this type of investigation as a routine procedure in children [45-47].

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 be reflected in the outcome of the study. Especially during the first filling cycle, when the child does not know what to expect, detrusor overactivity may be seen and the voiding phase can be incomplete due to contraction or incomplete relaxation 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. Only if during the first filling cycle, no detrusor contractions are seen and also the voiding phase is in accordance with history and uroflow, it is probably sufficient to do only one complete filling and voiding cycle [48].

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 the pelvic floor muscles is assumed to evaluate 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. Especially in young children some urodynamic parameters, such as capacity and detrusor activity are influenced by the temperature of the filling fluid. Although the clinical relevance is as yet unknown, it is recommended to fill the bladder with fluid of body temperature [49].

When filling by catheter, slow fill cystometry (5 – 10 percent of expected bladder capacity per minute, or < 10ml/min) 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. *Normal 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 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. Also involuntary detrusor contractions occur more often during the first filling cycle (49). This is the reason that in paediatric urodynamics at least two cycles of filling are recommended

Maximum cystometric capacity (MCC) 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 MCC should be interpreted in relation to normal values for age.

Compliance indicates the change in volume for a change in pressure. For children with neurogenic detrusor-sphincter dysfunction, data are available relating poor compliance to the risk of upper urinary tract damage [51].

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) [50].

Immediately prior to micturition the normal closure pressure decreases to allow flow.

Bladder outlet obstruction, recorded with a pressure / flow study, may be anatomical or functional in nature. An *anatomical obstruction* may be present at the bladder neck or in the urethra as a stenosis or a stricture and there is a small and fixed urethral diameter that does not dilate during voiding. As a result, the flow pattern is plateau shaped, 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 or pelvic floor during passage of urine, that creates the narrow urethral segment as a constant or intermittent obstruction. 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 pelvic floor as in clinical practice the urethral sphincter is not readily accessible and 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. Also the use of video urodynamics can be very helpful in this respect, as contractions of the pelvic floor muscles can actually be seen during the voiding phase (**Figure 8 and 9**).

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 [52,53].

c) Cystoscopy

In by far the majority of children cystoscopy is not indicated. In boys with therapy resistant incontinence, an abnormal flow pattern, especially in combination with a history of (recurrent) urinary tract infection is suspicious of infra-vesical obstruction such as bladder neck obstruction, urethral valves, syringocele etc. A VCUG may not always show these abnormalities and pressure flow curves may be equivocal [55].

In girls the flow may be directed upward, indicating an abnormal meatal position or stenosis. A dorsal meatotomy generally solves this problem. It has been postulated that in girls the abnormal direction of the stream triggers the bulbocavernosus reflex resulting in dysfunctional voiding [56].
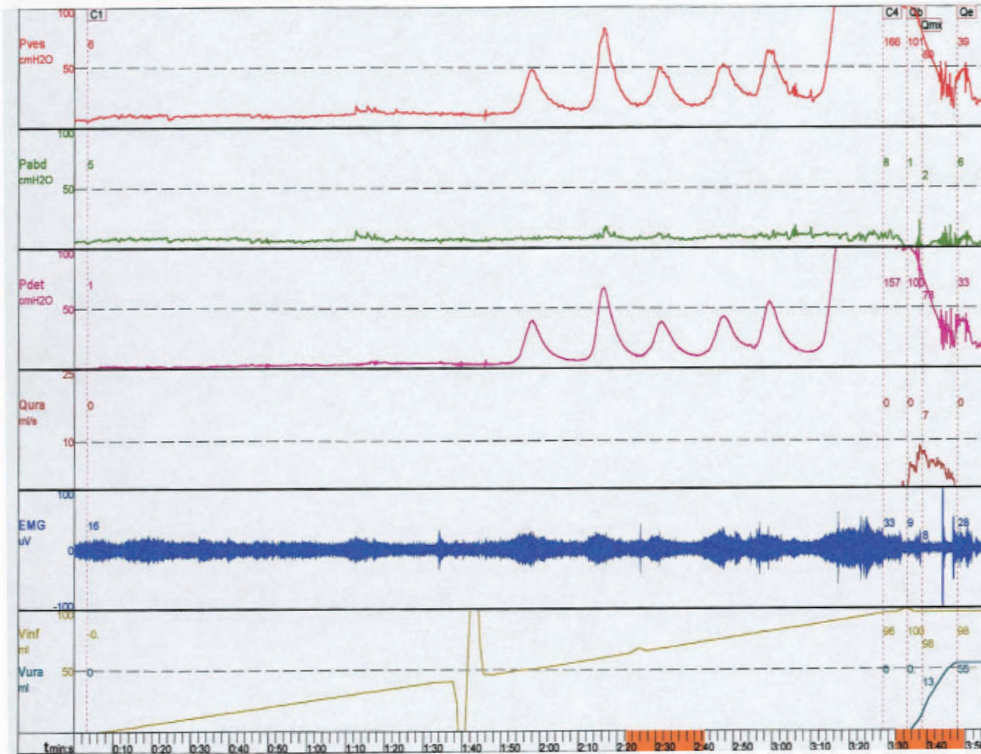
Figure 8 : Urodynamic study illustrating involuntary detrusor contractions, counter action of pelvic floor muscles (guarding reflex) and incomplete pelvic floor relaxation during voiding resulting in post void residual urine (detrusor overactivity + dysfunctional voiding) [50].
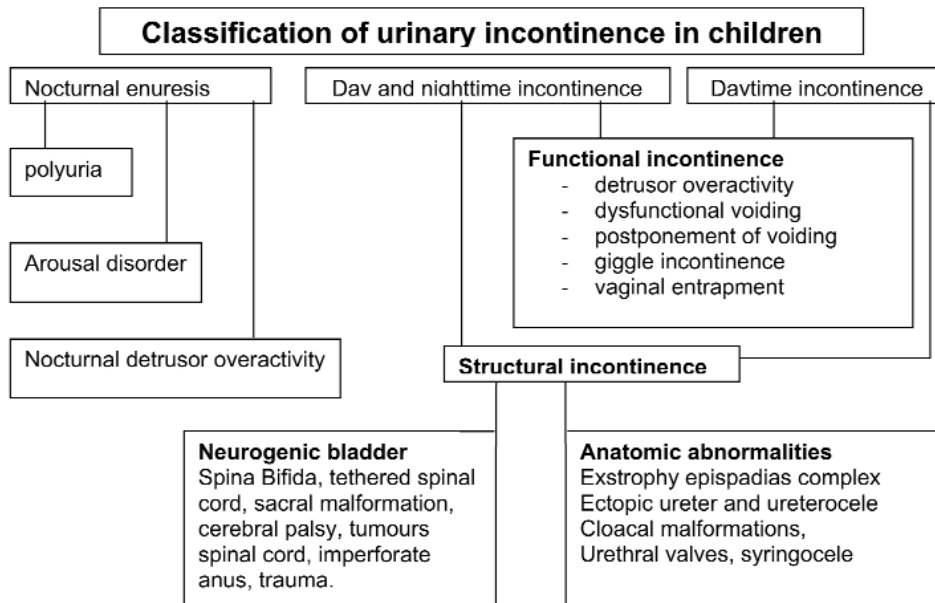
Figure 9 : Classification of urinary incontinence in children.

(Over)activity of the urethral sphincter- pelvic floor 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 B

13

C. NOCTURNAL ENURESIS

I. DEFINITION

Nocturnal enuresis (NE) is involuntary voiding of urine during sleep, 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 [1].

Parental concern and child distress affect the clinical significance of the problem [2].

While most children who wet at night after age five are considered nocturnal enuretics, the child's development level is also important. The age criterion of five is arbitrary but reflects the natural course of achieving bladder control [4]. Verhulst et al argue for flexibility due to different age at which boys develop nighttime continence compared with girls [4]. Extrapolation from Verhulst's figures suggests that the prevalence of nighttime wetting for 8-year-old boys equals that for girls at 5 years [4].

Monosymptomatic NE is bedwetting without daytime symptoms. **Non-monosymptomatic** or polysymptomatic NE describes children with both day and nighttime wetting [5].

II. SEVERITY

Nocturnal enuretics vary in wetting frequency. Although fifteen percent wet each night, most children wet less frequently [4,6]. In a population survey of nearly 1,800 Irish children aged 4 –14 years, 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 month in 25 percent [7]. Some children and parents are concerned about an occasional wet bed, while others 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) [7].

III. PREVALENCE

Bedwetting is common. In the United Kingdom, estimates approximately 750,000 children and young people over 7 years regularly wet the bed. In the United States 5 to 7 million children regularly experience primary NE [8,9,10].

The prevalence of bedwetting varies regionally. In China, where parents take children out of diapers earlier, bedwetting seems to resolve more quickly.

For example, in a large survey from Shandon, the proportion of children attaining nocturnal urinary control before age 2 was 7.7%; by age 3, this had increased to 53.1%, and by age 5 to 93%. The overall prevalence of NE was 4.3%, with a significantly higher prevalence in boys than girls. There was no additional decrease in the prevalence of enuresis between 6 and 16 years [11]. This suggests that structured awakening and toileting is effective treatment for monosymptomatic NE, even in small children.

Bedwetting becomes less common with advancing age. In the West, 15 per cent of children each year develop nocturnal bladder control (12). By adulthood, bedwetting is rare. Hirasing et al sampled over 13,000 adults [18-64 years] and found an overall prevalence rate of NE at 0.5% (13). Of these, 12 percent of men and 29 percent of women had daytime incontinence. Despite persistence of wetting into adulthood, 50 percent of men and 35 percent of the women never seek help for their problem. The enuresis prevalence of 0.5% in otherwise healthy adults in Hirasing's study refers to a largely untreated population. Fifty percent of the men had primary enuresis and had never been consistently dry at night. Assuming a prevalence of enuresis of 8 percent in 7-year-old boys, the risk for an enuretic boy to remain so for the rest of his life is 3 percent [12,14].

Many believe adult enuretics represent a "hard core" group with worse symptoms. These individuals are likely to have associated diurnal enuresis or voiding symptoms. One study included 18 males and 29 females with a mean age of 20 years with persistent NE. Of these patients 37 (79%) had moderate or severe symptoms and 17 (38%) also had daytime urinary symptoms. Thirty patients had urodynamics including 12 males and 16 females (93%) with detrusor overactivity. In addition, 73% of patients had urodynamic evidence of functional bladder outflow obstruction, including dysfunctional voiding and detrusor sphincter or detrusor pelvic floor discoordination. Two male patients (6.7%) had an obstructive pattern on urodynamics and subsequent cystoscopic examination confirmed the presence of congenital urethral stricture/valves. Sixteen patients (53%) had significantly reduced bladder capacity of less than 300 ml [15-18]. These and other studies suggest that persistent NE after childhood is a serious adult problem requiring some investigation and considerable effort to treat.

IV. INHERITANCE

Bedwetting runs in the family of many children who suffer from bedwetting. In one study, A positive family history was found in 94 families (23%) of 411 probands with PNE, including 49% of fathers, 9% of mothers, 6% of both parents, 6% of the siblings and 30% of

grandfathers or (and) mothers. Among the probands the ratio of male to female was 1.3:1 excluding sex-linked inheritance. Autosomal dominant inheritance was in 15%, and autosomal recessive inheritance was consistent in 1.46% of families [19]. Thus, the mode of inheritance is usually autosomal dominant; if both parents were nocturnal enuretics as children, the risk for their children is from 65 to 85 % [20] If only one parent has NE the risk is about 45 percent [21].

Molecular studies have clearly shown that NE is a complex disease with locus heterogeneity and no clear genotype-phenotype association.

Linkage studies to determine the location of the genetic changes have suggested foci on several genes. Linkage studies to markers on chromosomes 8, 12 and 13 demonstrate both clinical, as well as genetic heterogeneity in nocturnal enuresis [22]. But these have not been consistently reported in other studies [23]. So far, there has been no reported association of the genotype with a particular phenotype of enuresis [24].

V. GENDER AND MONOSYMPTOMATIC NE

Boys suffer nocturnal enuresis more frequently. 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 [25]. More recent studies are consistent [26]. Surveys of monosymptomatic NE undertaken in Great Britain, Holland, New Zealand and Ireland suggest that the prevalence for boys is 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 about half that rate: 9-16% at 5 years, 7-15% at 7 years, 5-10% at 9 years and 1-2% in the late teenage years [4,7,27,28]. Although monosymptomatic NE is more common in young boys, by adolescence the incidence in males is the same as in females [16,29].

VI. CLASSIFICATION

1. PRIMARY VERSUS SECONDARY NOCTURNAL ENURESIS

Children who have never been free of bedwetting for 6 months have **primary NE**.

Secondary NE is the re-emergence of wetting after a period of being dry for at least six months. A birth cohort of 1265 New Zealand children studied over 10 years by Fergusson et al found an increased risk of secondary nocturnal enuresis with age [30]. The proportion of children who developed secondary

enuresis was 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 NE is 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 [22, 30,31].

Von Gontard and colleagues found children with secondary enuresis had significantly more emotional difficulties compared to those with primary NE. Their evidence also suggests children with secondary enuresis, compared to those with primary enuresis, are more likely to have behavioural problems, a finding which corresponds to that of McGee et al [32].

Both Jarvelin and Fergusson et al argue that primary and secondary enuretics are similar [30,31]. They believe the two share a common etiological basis. The rate the child acquires primary control influences his or her risk of secondary enuresis. The primary form is 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 he or she acquires control. On the other hand, this capacity determines the child's susceptibility to lapsing back to night wetting when exposed to stress.

Other sources of secondary enuresis must be excluded prior to proceeding with treatment for enuresis. These include sleep apnea from obstructive airway disease, obesity, constipation and infrequent or dysfunctional voiding. Treatment of sleep apnea from obstructive airway has been shown to improve or eliminate NE in some children following surgery or medical management [34,35]. Obesity has been associated with nocturnal enuresis both independently [36] and in the context of sleep apnea [37]

• *Mono-symptomatic versus non-mono-symptomatic NE*

Mono-symptomatic NE refers to those children who report no bladder or voiding problems associated with wetting. **Non-mono-symptomatic NE** refers to bedwetting, that is associated with detrusor overactivity or voiding problems such as urgency and bladder holding during the day [5].

This classification becomes important when 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 NE. Between 10-28% of children with NE have associated daytime wetting. If so, these children should be considered day and night incontinent. In these cases , night time incontinence is not any longer an

isolated phenomenon but part of the symptomatology of day and night time incontinence. These children are more resilient to treatment and more vulnerable to relapse [38]. These boys and girls are more appropriately managed in the context of the primary bladder problem

VII. PATHOPHYSIOLOGY OF MONOSYMPTOMATIC NE

NE stems from a **mismatch of bladder capacity, nocturnal urine output and the ability for the child to arouse during sleep**. Night wetting is normal until age 5. Delayed maturation in one or more of the following systems results in NE: a lack of stability in bladder function, a lack of arginine vasopressin (AVP) release or response, or relative increased solute excretion during the night [39,40], or an inability to wake from sleep to full bladder sensations [41,42]. Combinations of all three problems may be present.

A unifying and simplistic concept with important clinical implications, is that NE is caused by a mismatch between nocturnal bladder capacity and the amount of urine produced during the night, combined with delayed or incomplete arousal response to the afferent neurological stimulus of the full bladder (**Figure 10**).

1. INCREASED NOCTURNAL URINE OUTPUT

In normal children, the circadian rhythm of urine production results in a nocturnal reduction in diuresis to approximately 50% of daytime levels [43,44]. In children this is the result of nocturnal release of hormones that regulate free water excretion (arginine vasopressin, (AVP) or solute excretion (angiotensin II and aldosterone) and may result from circadian changes in glomerular filtration [45]. In the normal child, this results in increased urine concentration and reduced urine volume during sleep. This is why children who are not enuretic sleep through the night without being wet and do not need to rise to void.

Two thirds of patients with mono-symptomatic NE have been found to have a lack of circadian rhythm of vasopressin, resulting in high nocturnal urine production, which exceeds bladder capacity [46,47,48]. Rittig et al and Norgaard et al demonstrated abnormalities in the circadian rhythm of AVP secretion resulting in increased nocturnal urine output that exceeded bladder capacity in children with nocturnal enuresis [46,47]. These children make more urine at night, and often overcome their bladder capacity and wet early in the night. Abnormalities can also be intrinsic, related to reduced nocturnal circadian changes in glomerular filtration rate (GFR) [45] or in sodium and calcium excretion [49].

Detection of low plasma vasopressin levels, GFR assessments or specific sodium and calcium excretion are difficult to measure. Instead, we 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 this may indicate nocturnal polyuria. Nocturnal urine output varies appreciably from night to night [50], but seems larger in children with NE who respond best to desmopressin (dDAVP).
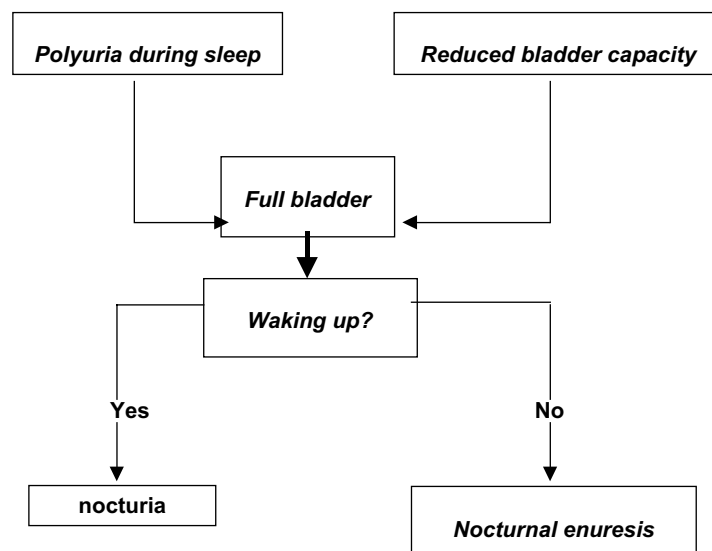

Figure 10 : Basic pathophysiology of NE or nocturia. When the bladder is full because of (relative) polyuria and/or a reduced bladder capacity, the child either wakes up to void (nocturia) or voids while sleeping (NE).

By the time the child becomes an adolescent, the circadian rhythm is less prominent. In adolescents and adults with nocturnal enuresis, there is no diurnal rhythm of plasma vasopressin concentration. The changes in urine production at night occur from a decrease in the urinary sodium excretion that is not due to differences in concentration of AVP but due to a lack of sensitivity to AVP [51] with resultant increased urine output [39]. There may be a small sub-group of children with impaired renal sensitivity to vasopressin or desmopressin [40,52]. Recent work by Devitt et al suggests that 18 percent of children have 'normal' levels of plasma vasopressin release but remain enuretic [48].

These children all failed to respond to a therapeutic dosage of desmopressin. This finding could indicate renal insensitivity to vasopressin but could also be indicative of detrusor overactivity or a small functional bladder capacity.

Total urine output during the night could be helpful in differentiating between the two conditions. The subgroup of patients with NE and increased nocturnal urine output generally has a normal functional bladder capacity and a favourable response to dDAVP [53].

2. DETRUSOR OVERACTIVITY DURING THE NIGHT

The detrusor, in order to function appropriately, needs to be relaxed during filling and allow an appropriate functional capacity. Detrusor overactivity usually causes small voided volumes resulting in a decreased functional bladder capacity [54].

Watanabe and his colleagues, employing EEG and cystometry recording during sleep, discovered that 32 percent of children with NE had involuntary detrusor contractions that resulted in enuresis [60-62]. These children had smaller functional bladder capacities at the point of wetting, than children with enuresis who did not have detrusor overactivity. Functional bladder capacity – defined as the largest daytime void on a frequency- volume (F/V) chart, after excluding the first morning void, may give a reasonably accurate assessment of daytime functional bladder capacity (FBC). Reduced functional bladder capacity, when below 70% of predicted FBC for age, is likely to result in poor response to dDAVP treatment [55]. Daytime bladder capacity is smaller than night time capacity in children without NE [56].

The pattern may be different at night. Yeung et al reported that 44 percent of treatment failures [with desmopressin or the enuresis alarm] have normal daytime bladder function but marked detrusor overactivity during sleep resulting in enuresis [63,64]. Almost none of these children had nocturnal polyuria. Ultrasound studies of the bladder furthermore revealed an increased bladder wall thickness in these children [57].

When further segregated prior to treatment, increased bladder wall thickness and bladder volume predicted the response to therapy in children with their primary nocturnal enuresis (more than three nights weekly). In one study, Yeung, et al [58] correlated ultrasound measured parameters and urodynamic findings. Of 35 children with frequent NE, bladder wall index was normal in only eight patients. It was less than 70% of predicted in 24, and more than 130% in three. When bladder volume and wall thickness index was correlated with ultrasound, 87% of the patients with a normal index exhibited a normal bladder pattern on imaging and 96% of patients with an index less than 70 exhibited detrusor over activity on ultrasound. All the children with a normal index either had a complete or good response to conventional treatment for nocturnal enuresis, whereas only 62% of those with an index less than 70 did not respond to treatment. With longer follow-up, bladder dysfunction had resolved in 38% of the children with an initial index of less than 30, all of whom had a good response to treatment. The bladder dysfunction persisted in the 63% of children who had partial or no response to treatment. What this means is that ultrasound measured bladder parameters may segregate children prior to management of primary nocturnal enuresis into groups that have a favorable outcome and those that do not, following conventional treatment. These studies will become more and more important in helping to predict response of various treatment regiments in the future.

This approach may be even more important in adults with refractory monosymptomatic nocturnal enuresis. Bower, et al. [15] found that in 56 consecutive adolescents and adults compared with 293 normal adults, there were significantly higher childhood scores of urgency, frequency, urge incontinence, infrequent voiding and small volume voids than their normal non-enuretic counterparts. This suggests that adolescents and adults with persistent nocturnal enuresis may have a more significant bladder component particularly since the majority of patients with adult type nocturnal enuresis do not seem to exhibit the nocturnal polyuria problem seen more commonly in the smaller children.

3. LACK OF AROUSAL FROM SLEEP/CNS FUNCTION

The fundamental mechanism resulting in nocturia or NE is that the bladder fills to its capacity during sleep and needs to empty (figure 10). Bladder fullness is due to nocturnal polyuria and/or a reduction of the bladder capacity due to detrusor over activity during sleep. These factors do not fully explain why the enuretic child does not wake up during the night to the sensation of a full or contracting bladder. Regardless of whether the child has detrusor overactivity or nocturnal polyuria, the enuresis event results from the child's inability to awaken from sleep to empty prior to the wetting episode.

There is a widely held belief amongst parents and some clinicians that enuretics are deep sleepers. This is logical, since many of the children exposed to alarm therapy sleep through the alarm while family members awaken. Nevéus reviewed by questionnaire 1413 schoolchildren between the ages of six and ten and noted that enuresis was associated with subjectively high threshold arousal and significant confusion upon awakening from sleep [42]. Wolfish in a study of 15 enuretic and 18 control boys and girls found that enuretics wet most frequently during the first two-thirds of the night and that arousal attempts were less successful in enuretics than in normals [59]. This might explain why the most heavily endorsed view of both children and parents, regarding the aetiology of NE is a belief in deep sleep [60].

More recently Frietag, et al studied brainstem evoked potentials in 37 children with nocturnal enuresis and compared these aged 8 to 14 years, with 40 controls, mean age 10 years, and found that interpeak latencies of the brainstem evoked potentials were increased in children with nocturnal enuresis, suggesting that a maturational deficit of the brainstem was present in children with nocturnal enuresis. Differences in visually evoked potential latencies might point to a reason behind functional cortical differences in children with family history of nocturnal enuresis [61].

Feittag's study would suggest that a maturational effect is present; however, overnight studies in enuretic children with simultaneous sleep electroence-phalographic and cystometry have revealed marked detrusor overactivity, only after sleep at night and not during wakeful periods during the day [62] . Because this pattern has not been observed in normal non-enuretic subjects even during the newborn period, one may hypothesize that this could be due to a small neurologic lesion affecting a tiny area in the vicinity of the Pontine micturition center, the posterior hypothalamus (responsible for secretion of antidiuretic hormone) or the locus coeruleus which may be the cortical arousal center [63].

Another interesting study by Baeyens et al. [64] showed a convincingly significant difference between children with enuresis and control groups, and the startled eye blink reflex which improved with maturation but did not seem to correlate with resolution of enuresis. Clearly there is considerable work that is required to further unravel the mechanisms behind perceived differences in arousal between enuretic and non-enuretic children.

However a raft of evidence counters such a belief. Sleep patterns of children with NE are no different from children who do not have NE [65].

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 occur when the bladder is at a volume equivalent to the maximal daytime functional capacity [66-69].

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

Waking becomes easier as the night progresses. However, several authors have found that children with NE are also more likely to wet in the first third of the night, often in the first two hours following sleep [59,66,67,70,71]. 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.

VIII. TREATMENT OF NOCTURNAL ENURESIS

The age at which the child and his or her parent begins to be concerned about bedwetting varies. In an important review article, Hjalmas, et al. noted that, "for successful treatment of nocturnal enuresis, the child must be brought to the physician by the parents who are concerned and the physician must have the necessary knowledge about the condition and be motivated to start treatment" [43]. In order to fulfill the requirements, parents, teachers, and nurses in primary care need to understand nocturnal enuresis and be ready to treat the child, regardless of age.

Nocturnal enuresis is thought of as a social problem and less of a medical problem; therefore, since the majority of children stop wetting as they mature and since no ill health follows bedwetting in most cases, there is a tendency for many practitioners to take a "wait and see" approach despite the fact that the family and the child in many cases are quite disturbed. In one study, 3803 French school children age five to ten years noted the prevalence of primary nocturnal enuresis to be 9.2%. The majority of the children noted that bedwetting bothered them and hoped that a doctor could help them. In this survey, a question-naire was addressed to mothers of enuretic children, 100 school teachers and 100 school doctors. The mothers had a relatively tolerant attitude but two-thirds had consulted a doctor. Most of the doctors had proposed no solution or a "wait and see" attitude or treatment with a drug rather than an alarm. From this study, we may conclude that considerable work needs to be done to help educate not only parents but teachers and even physicians about the importance of treatment of nocturnal enuresis as well as supportive care [72].

The actual timing of treatment for nocturnal enuresis may vary depending on the needs of the child and the parent. Toilet training age may be different in different societies. For example, toileting in Asia may begin earlier than in North America or other parts of the

world [72,73,74]. Toilet training should be started when both the child and parents are ready. Most studies appear to show that children start training between 24 and 36 months of age with a current train toward later completion than in previous generations. This is markedly different than noted in some Asian cultures where training appears to begin much earlier. Toilet training should occur in an environment that is comfortable for the child. Unfortunately, toilets in most household bathrooms are adult sized, making it difficult for the child who needs to climb to the top of the toilet to relax. In these cases, a potty chair to toilet train the child, and once the child is old enough, he or she should be transitioned to an over-the-toilet seat with a footstool to allow optimal posture for voiding. Parents should encourage children to relax and take time to completely empty the bladder [43].

It is essential that both the child and his or her parents understand bedwetting pathophysiology and treatment philosophy. The clinician should give the child general advice such as what to eat and drink and to void regularly during the day, abstain from drinking too much during the late afternoon and evening and have relaxed routines at bedtime. The clinician should stress that NE is common and usually represents a delay in maturation without any psychopathological undertone. Up to 19 percent of children will become dry within the next 8 weeks without any further treatment besides good counselling [43,73,74].

1. EVALUATION

Hjalmas, et al. have recommended a careful history which we will summarize in these next few paragraphs. This approach, which has been recommended by the International Children's Continence Society, provides an excellent guide toward the taking of a history for a child with nocturnal enuresis [43] (**Figure 11**).

a) The frequency volume chart (FVC)

Parents are asked to record a two-day three-night record. This includes recording the child's fluid intake and urine output, frequency of micturition and the frequency and pattern of voiding. The largest single micturition is considered the functional bladder capacity. This chart can be performed beginning on a Friday evening and concluding on Sunday on any weekend.

b) Symptoms of nocturnal enuresis

A careful history should include questions about the age of onset of nocturnal enuresis, length and circumstances of dry spells, number and time of episodes of nocturnal enuresis or nocturia, presence of daytime voiding symptoms or urinary tract infection, posture while voiding, daytime and evening fluid intake, sleep habits, frequency and consistency of bowel movements and psychosocial situation. One must establish whether or not symptoms represent primary
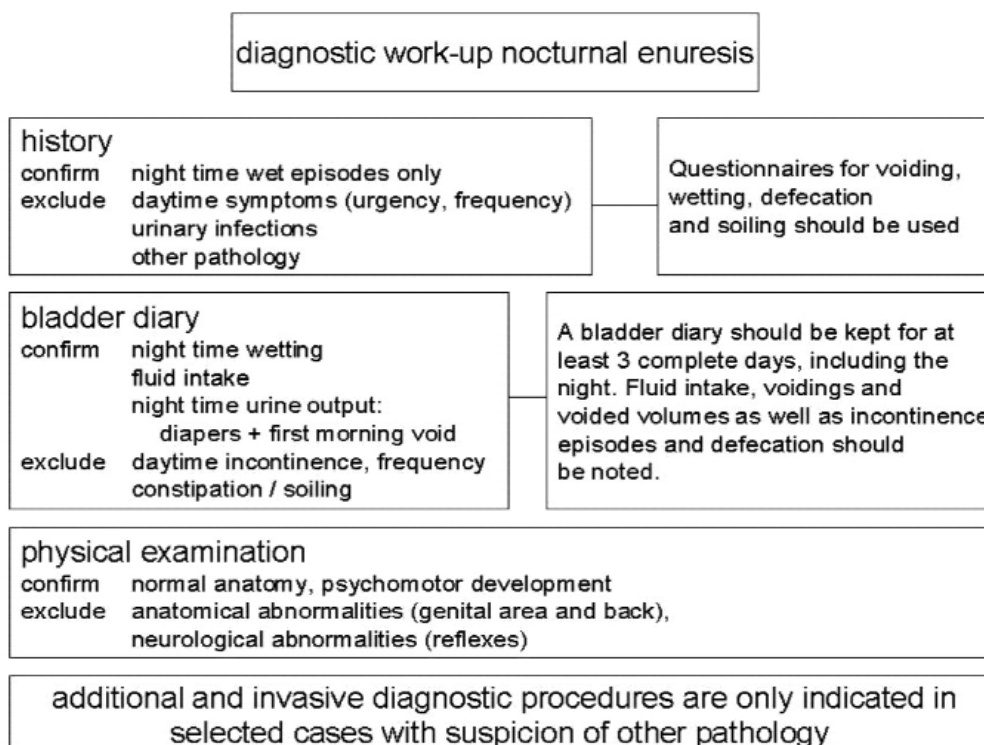

Figure 11 : Schematic work-up in patients presenting with night-time wetting only.

or secondary nocturnal enuresis. It is critical to search for new psychological problems results in secondary nocturnal enuresis, particularly when the child presents with nocturnal enuresis after a prolonged period of dryness. The personality of the child, family situation, school environment, and presence of alternate care givers might have an appreciable impact on voiding habits and will influence management options [43]. Children may drink large volumes of fluid in the hours before sleep and this may result in nocturnal enuresis or nocturia.

It is helpful to determine the number of hours of sleep and to compare this to standard charts of average duration of sleep by age. Morning fatigue may be the result of obstructive sleep apnea. Other symptoms of sleep apnea include mouth breathing, snoring, and restless sleep [43].

It is important to rule out symptoms of anatomical or physiologic urologic conditions that may lead to nocturnal enuresis. Many of these conditions are covered in other parts of this section, and include a failure to store urine or failure to empty urine. Storage symptoms include increased frequency, urgency, and urgency incontinence including squatting behavior, daytime incontinence and the sensation to need to void again. The clinician must carefully assess daytime wetting, particularly in older children. In many cases, the child may hide these symptoms from the clinician and the family.

Children void four to seven times a day or about every two to three hours [75]. If the child is voiding significantly more frequently than eight or more times a day, this may suggest incomplete emptying or overactive bladder symptoms. Urgency is present in many children and posturing, including squeezing or crossing the legs, squirming while standing or sitting, or physically compressing the genital area with a hand is all suggestive of overactive bladder due to detrusor overactivitiy which may or may not bw associated with dysfunctional voiding. Other causes include urinary tract infection, polyuria from diabetes mellitus or diabetes insipidus which can also cause more frequent voiding [43]. Treatment for these symptoms is covered in other sections within this chapter.

Additional symptoms during the daytime include continuous dribbling between voids that can come from an ectopic ureter bypassing sphincter mechanisms or from failing to empty the bladder or sphincter incompetence. Also continous leakage can result can result from neurologic causes or anatomical causes such as epispadias, or a closed bladder exstrophy or urogenital sinus.

Lastly, children may have incomplete emptying from true dysfunctional voiding which results from the detrusor contraction at the same time that the sphincter or pelvisc floor is contracting. In addition, a detrusor underactivity may result from neuropathy from diabetes mellitus and in some cases conditions such as the prune belly syndrome will result in detrusor underactivity. Lastly, urethral strictures may result in incontinence due to detrusor overactivity with poor bladder emptying. Boys with posterior urethral valves or Cobb's collar may also have incomplete emptying. Lastly, the clinician should be alert for symptoms of constipation and faecal incontinence. It is a common misconception that if a child is stooling once per day then he or she is not constipated. In fact, the best symptom of constipation includes infrequent or painful passage of hard small pellet-like stools. Faecal incontinence may also be present, the principal sign of this being faecal material in the underwear. Excessive stool retention may result in bladder dysfunction. In these cases [76] this may result in increased urethral sphincter and pelvic floor activity and explain the association of voiding dysfunction with incomplete voiding. Treatment of constipation may result in improvement in enuresis.

c) Physical examination

Anatomic and behavioral causes for enuresis may be identified through a careful physical examination. Evidence of improper gait, spinal deformities, and foot abnormalities including asymmetry, high-arched feet, or hammer toes are signs of sacral neuropathy. Physical signs of occult spinal abnormalities such as dimples, tufts of hair, skin discoloration, lipoma, asymmetrical buttocks and gluteal clefts are also important. A careful abdominal examination with particular emphasis on the left lower quadrant may identify the colon full of firm stool. In most cases, a rectal examination is not performed but in some cases this may also be indicated. Occult feacal impaction, poor perineal sensation and reduced anal sphincter tone can be indicative of neuropathy.

In boys, marked narrowing of the urethral meatus (when the meatal lips are separated and no mucosa is seen), must be identified and carefully noted. If these signs are present, the boy should be asked to void so the clinician can witness and record the flow rate and residual urine. Narrowed or displaced urinary stream is suggestive of meatal stenosis.

In girls, the introitus should be identified for the position of the urethra. Evidence of wetting or irritation of the labia or vagina should be identified as this could be suggestive of post-void dribbling or incomplete emptying with and incontinence due to either detrusor overactivity or sphincter weakness [77].

d) Laboratory examination

There is very little laboratory examination that is required in patients with nocturnal enuresis other than a urinalysis to rule out UTI and evidence of glycosuria and a urine culture if the urinalysis is suggestive of infection.

Urodynamics and imaging are rarely important in the child with monosymptomatic nocturnal enuresis. If there is any suggestion, however, that daytime wetting is occurring, and then a full evaluation of the daytime problem should precede the evaluation for nocturnal enuresis.

The management of NE 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, regular voidings, and relaxed routines at bedtime
- regular review of the new intervention

The therapist should convey a sense of understanding and compassion to both the child and the family. Education about the problem and a realistic discussion about the prognosis will help instil competence in the treatment offered which may improve both compliance and outcome [78]. What follows is taken in part from the excellent review article by Hjalmas, et al [43].

EVIDENCE BASED RECOMMENDATIONS FOR TREATMENT OF NE

First line treatment and preliminary steps: Primary and secondary forms of nocturnal enuresis are treated the same if faecal incontinence, constipation or daytime wetting is present, these should be treated first [76].

Initial management: 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 strongly recommend any of these [93-100]. However, non invasive behavioural modifications such as resisting over hydration in the evening are appropriate recommendations at the initiation of therapy. The child must void before bed. Excessive calcium or sodium intake should be avoided as well [79].

During the day the child should be instructed to void regularly, not to hold urine until the last minute, and to relax and take time to completely empty. If deemed important by the parents, a letter should be sent to the school to explain this.

Timing of treatment for the child who wets is dependent on the family's desire and the child's desire. As a good rule of thumb, children should be six to eight years of age. Some children, however, may want to wait until later. Others may be ready closer to age six. We try very hard not to treat children that are much younger than six, however. It is important for the parents to know that relapses can occur and that the older the child is, the better chance they have the enuresis resolving. The successful treatment of

children with nocturnal enuresis has a foundation of realistic expectations and a motivated family [43].

Before starting treatment, a "baseline" meeting with counselling, provision of information, positive reinforcement, reassurance that 15% of children resolve each year, and increasing motivation should occur first. Children are asked to fill out a calendar or chart depicting the wet and dry nights. Children became significantly drier in two non-randomized trials associated with fewer wet nights simply by focusing them more on record keeping and true reward charts [80].

1. PHARMACOLOGICAL TREATMENT

We have noted three main causes of enuresis. (1) Nocturnal polyuria, (2) detrusor overactivity, and (3) Disorder of arousal. Pharmacological treatment is designed to address these three areas.

a) Desmopressin

Arginine vasopressin (AVP) or antidiuretic hormone (ADH) is normally produced in the hypothalamus and released in the pituitary in response to hyperosmolality or hypovolemic conditions. Vasopressin acts on the collecting ducts and distal tubules to enhance water absorption. AVP by virtue of an independent vaso-constrictor effect is also a potent vasopressor. Desmopressin (or dDAVP) is an analog of vasopressin created by deaminating the cystine residue at position 1 and substituted D-argenine for L -argenine at position 8. These changes result in significantly increased antidiuretic activity but loss of vasopressor activity. The half-life of Desmopressin is 1.5 to 3.5 hours. In a larger portion of children with monosymptomatic nocturnal enuresis, the normal circadian variation in urine production with nocturnal rise of vasopressin is absent. In these cases, dDAVP would seem to be particularly appropriate. Desmopressin is easy to administer and the clinical effects appear immediately. The usual dose is 0.2 to 0.4 mg orally, or 20-40 micrograms intranasally at bedtime. The intranasal form is no longer recommended for nocturnal enuresis in many places around the world. Some patients have a delayed response and a small group of children who do not respond to desmopressin in ordinary dosage will become dry when the dose is increased [81].

Desmopressin may be particularly beneficial in the child with limited numbers of wet episodes per month who wants added security on special nights such a sleepovers, etc.

Nocturnal polyuria is a characteristic of children that respond the best to desmopressin [82].

But detrusor dependent enuresis does not easily respond as well to desmopressin treatment. The presence of daytime urgency of daytime incontinence is common in this group and constipation or faecal

incontinence is a regular finding and these must be treated before offering dDAVP. In the short term, desmopressin is reported to produce more rapid improvement than alarm therapy. The results of various long-term studies which have followed children for six to 24 months after treatment cessation indicate an annual cure rate in children on long-term treatment of approximately 30% [83,84].

1. TOLERABILITY AND SAFETY

Large amounts of liquid should not be consumed the nights when the drug is taken. There have been several reports that note Desmopressin toxicity [85,86,87].

This data would suggest that a fairly rigid regimen of water restriction must be enforced for two hours prior to bedtime and to allow one eight-ounce glass of water at dinner and nothing for the two hours prior to bedtime.

The results of numerous clinical trials have shown that desmopressin is well tolerated even during long-term treatment and associated with a low risk of adverse events. In the SWEET study, only six of 242 children (2.5%) withdrew during the long-term treatment because of very mild adverse events following the administration of intranasal desmopressin. With the exception of water intoxication, which can be serious, this drug seems to be tolerated quite well.

In a survey on hyponatremia in patients with nocturnal enuresis by Robson and Norgard in 1996 was found in the majority of children water intoxication was due to considerable intake of water during the time the child was actually taking the desmopressin.

2. PREDICTORS OF RESPONSE

The SWEET study found that those who improved or became dry during desmopressin were older (greater than 8 years), had fewer wet nights during baseline, and had only one wet episode during the week and responded initially to the smallest dose of desmopressin used in the study [88,89].

The practical approach, however, is to offer the treatment to enuretic children since it is difficult to absolutely predict those that will respond.

There is considerable evidence that desmopressin works better than placebo. In one study, patients on desmopressin were 4.6 times more likely to achieve 14 consecutive dry nights compared with placebo [90].

However, relapse after short-term treatment is common. Sixty-one percent of 399 patients six to 12 years of age recruited from a primary care in one study responded to desmopressin initially [83]. Using intention to treat analysis 19% (77 of the 399) remained dry off medication and 18% were dry while still on desmopressin, thus not significantly better than the spontaneous cure rate. This suggests that desmopressin, by reducing the urine output over night, reduces nocturnal enuresis but does not significantly affect the resolution rate over time above the spontaneous rate.

Although several studies have shown that dDAVP is a well tolerated and safe drug, even during long-term usage, one has to be aware that dDAVP is a potent antidiuretic drug and that there have been reports on severe water retention with hyponatremia and convulsions, but these are infrequent [91-97].

Level of evidence: 1. Grade of recommendation: A

b) Antimuscarinic drugs

1. OXYBUTYNIN

Oxybutynin should not theoretically be efficacious in children with monosymptomatic nocturnal enuresis. However, because there is considerable overlap in the diagnosis of monosymptomatic nocturnal enuresis, a number of children with few daytime symptoms of overactive bladder may have symptoms of overactive bladder at night. Moreover, it has been shown that on urodynamics 73% of adults with primary nocturnal enuresis have some form of functional bladder outlet outflow obstruction classified as (1) "primary bladder neck dysfunction" or "detrusor sphincter dyssynergia". [18]. That would suggest then that Oxybutynin might be a useful alternative in some children who are unresponsive to DDAVP. The drug is also indicated in combined day and nighttime incontinence [52, 98,99].

In general, oxybutynin is well tolerated but there are some side effects, namely dryness of the mouth, constipation and vertigo (rare). Constipation can also pose a problem since detrusor overactivity have a predilection for constipation and the development of constipation may aggravate detrusor overactivity and thus counteract the beneficial effects of the drug. It may also result in increased residual volumes which may make it difficult for the child to empty prior to bedtime. Oxybutynin treatment in conjunction with desmopressin may have a role in cases with suspected day and night time detrusor overactivity.

Level of evidence : 2 . Grade of recommendation: B.

In those children who have NE due to detrusor overactivity during the night, treatment with an antimuscarinic drug should be considered [100]. Because it is difficult to perform a night time cystometry in these children it may be tried in children who have more than 2 wetting episodes per night and who do not respond to dDAVP or be given in combination with alarm or dDAVP [101,99]. At present no studies have been performed to demonstrate its efficacy.

Level of evidence: 3. Grade of recommendation: C

c) Tricyclic antidepressants

Although tricyclic antidepressant drugs, imipramine in particular, have worked in a number of children, most of the studies that recommend this drug are relatively old. The major drawbacks to imipramine therapy are cardiotoxic side effects, in some cases even with therapeutic doses, and the possibility of death with overdose.

Because imipramine and other drugs of the same family have potential cardiotoxic side effects they cannot be generally recommended for treatment of this non-lethal disorder [102].

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 [103].

Only in selected cases (like adolescent boys with Attention Deficit Hyperactivity Disorder and persistent NE) it should be considered [104].

Level of evidence: 1. Grade of recommendation: C (due to potential cardiotoxicity).

In addition to dDAVP and imipramine, other drugs, such as carbamazine and indomethacin have been investigated as well: based on study design as well as study outcomes, these drugs are not recommended at this stage [105-107].

d) Inhibitors of prostaglandin synthesis

Because nocturnal polyuria in children with NE may not be entirely attributed to a defect in free water excretion, but rather to an increase in nocturnal excretion of sodium, cyclo-oxygenase inhibitors (like diclofenac), which reduce urinary sodium excretion, have been tried and in a randomised double blind placebo controlled study proved to be effective [128]. Further studies need to be done to elucidate the role of these drugs.

2. ENURESIS ALARM

The enuresis alarm is the most effective means of facilitating arousal from sleep and remains the most effective way to treat mono-symptomatic NE(107,108). Intervention with an alarm is associated with nine times less likelihood of relapse than antidiuretic therapy. Relapse rates in the 6 months following treatment are in the order of 15 - 30 %. Alarm therapy has been shown in a meta-analysis to have a 43 percent lasting cure rate [109,110]. Alarm therapy should be considered in every patient. There is an average success rate of nearly 68% with efficacy increasing with the duration of therapy.

Better results occur with optimal motivation of the child and family and higher frequency of wet nights. Reduced efficacy associated with the lack of concern shown by the child, lack of supervision, inconsistent use, family stress, abnormal scores on behaviour system checklists, psychiatric disorder of the child, failure to awaken in response to the alarm, unsatisfactory housing conditions and more than one wetting episode per night. Enuresis alarms require several months of continuous use and are, therefore, unsuitable for some families [111-112].

For optimal results, alarm therapy requires a motivated family and child with significant commitment to time and effort. We sometimes recommend that this be done during the summer holiday if possible. The impact on other family members should be considered. In some families alarm therapy may wake other members of the family and may increase parental annoyance and place a child at increased risk for physical or emotional abuse. Close follow-up is important to sustain motivation, troubleshoot technical problems and otherwise monitor the therapy [43].

The exact mechanisms for alarm treatment are not known. The effects are not due to classical conditioning as stimulus awakening occurs after and not before wetting. Instead it is clearly an operant type of behavioural approach, i.e. a learning program with positive reinforcement that includes aversive elements. Dryness is reached either by waking up leading to "nocturia" in 35% of children or by sleeping through the night with a full bladder in 65%. Body worn alarms are as effective as bedside alarms (general assessment for alarm treatment [113].

The family should continue alarm therapy for at least 6 to 8 weeks before discarding it as ineffective. Compliance remains a problem: dropout rates are rarely disclosed in reported studies. Proper guidance and instructions are mandatory.

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

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 [114, 115].

Level of evidence 1. Grade of recommendation A

In some cases, alarm therapy can be enhanced using the alarm in addition to other behavioral components. Overlearning (giving extra fluids at bedtime after successfully becoming dry using an alarm) and avoiding penalties may further reduce the relapse rate (108).

3. DRY BED TRAINING

This is a package of behavioural procedures used in conjunction with the enuresis alarm first described by Azrin et al [116]. It incorporates:

- the enuresis alarm
- 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 needs to void, and on returning to bed the child is encouraged to have a further drink

2. On the second night the child is awakened and taken to the toilet 3 hours after going to sleep. For each dry night, the clinician moves the waking time later by 30 minutes. If the child is wet on any night, the waking time stays at the time of the previous evening. The clinician discontinues the sense when the waking time reaches 30 minutes following sleep. The clinician restarts the waking schedule if the child begins wetting twice or more in any week, stating again 3 hours after sleep.

High success rates and low drop out have been reported although relapse rates are no different than enuresis alarm treatment alone. Modifications are advocated to remove some of the more punitive elements of the programme but at best, it is a complex, time consuming and demanding technique [113,117,118].

Hirasing et al found 80 percent success with group administered dry bed training. Girls responded better than boys [119]. 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.

In another study they found a positive effect on behavioural problems [120].

An important component analysis by Bollard & Nettelbeck found that the enuresis alarm accounted for most of the success achieved through dry bed training. They believe that a large proportion of the components of the procedure can be eliminated without sacrificing much of its overall effectiveness and that the waking schedule coupled with the enuresis alarm is as effective as the complete dry bed-training programme [121].

Level of evidence: 2. Grade of recommendation D (no more effective than alarm treatment alone)

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 [122].

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 ? 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 enuretic children between 6 and 12 years'. Compared with other studies and considering experience of daily practice one may question the very high success rate in this particular group of patients.

Level of evidence: 3. Recommendation: grade C

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.

5. ACUPUNCTURE

In one randomised controlled trial that examined acupuncture, 40 children were allocated either to dDAVP or acupuncture, 75% of children were dry after 6 month of therapy (while still on medication), while 65% of patients were completely dry after a mean of 12 sessions.

From this study it is concluded that as an alternative, cost-effective and short-term therapy acupuncture should probably be counted among available treatment options. Another meta analysis provides some evidence for the efficacy of acupuncture for the treatment of childhood nocturnal enuresis [123].

Comparison of treatment outcome and cure rates is difficult because of the inconsistent use of definitions, the inclusion of children with daytime symptoms, and the variable follow-up periods in most studies. For a pragmatic approach, see Figure 11.

Level of evidence: 4. Recommendation: grade D

6. COMBINED TREATMENT WITH ALARM AND DESMOPRESSIN

Combined treatment may be superior to alarm alone especially for non-responders of each individual treatment. In this approach, treatments are started at the same time: the rapid action of dDAVP is believed to facilitate the child's adaptation to the alarm [124, 125]. 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 is particularly effective in children with high wetting frequencies and behavioural problems.

Combination with full-spectrum therapy may even yield higher success rates [126-127].

Van Kampen et al reported their results of 'full-spectrum' therapy in 60 patients: they were treated for 6 months with a combination of alarm, bladder training, motivational therapy and pelvic floor muscle training: 52 patients became dry [126].

Hjälmås et al have proposed the following (not validated) protocol [43].

1. careful screening to identify any functional or mechanical outlet obstruction and appropriate management,

2. monotherapy with either alarm or desmopressin for a minimum of 12 weeks,

3. combination of alarm and half-therapeutic or titrated dose of desmopressin that allows wetting up to 4 nights per week,

4. maintain both interventions for 8-10 weeks,

5. increase desmopressin to dose that allows only one wet episode per week,

6. withdraw alarm when dry for one month,

7. reduce desmopressin to half dose after a further 8 weeks,

8. withdraw desmopressin after a further 8 weeks.

7. NON RESPONDERS

About one third of children do not respond to treatment with alarm and/or dDAVP. The majority of these children are likely to have a small nocturnal bladder capacity and suffer from "detrusor dependent NE". These children may void more frequently than their peers or have urgency and day-time incontinence. They are also often constipated. Prescription of dDAVP plus antimuscarinics should be considered, although evidence from the literature is lacking. Most likely the reduced urinary output during the night leads to a lower filling rate which may reduce the nocturnal involuntary detrusor contractions and enhance the action of antimuscarinic drugs. Treatment success is usually noted between 1-2 months. Treatment should be continued for 6 -12 months, but clinical evidence is lacking.

On the other hand some of these children may have day time incontinence, which was not discovered during the initial workup. They should be given a strict voiding regimen and a combination of dDAVP with the alarm [54].

Some children who remain non-responders to desmopressin in combination with alarm and / or anticholinergic drugs may have absorptive nocturnal hypercalciuria which may be responsible for the NE in some of these patients. With an appropriate (low calcium) diet these patients can became desmopressin responders [129].

NE is a symptom, not a homogeneous disorder. A really efficient treatment will never become possible until we have clarified all the different pathophysiological subgroups that go under the heading of NE.

8. SUMMARY (Figure 12)

Table 1. Response and cure rates of different treatment modalities

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 %

- Gaining the confidence of the child and the family is paramount. The development of structure in the child's life, early bedtime, careful calendaring, avoidance of fluids late in the day, are critical.

- Secondly, identifying compounding psychological or physiologic factors of the child such as constipation and diurnal enuresis are critical.

- Third, alarm treatment should probably be recommended as the first choice of treatment with the modifications listed above. Single parents have a difficult time with the effort that is required to awaken with the child for the alarm management and, in some cases when children are not frequently wet, dDAVP may provide effective therapy for the last few years that they are at risk. In general, those that do the best with the alarm therapy are those with frequent bedwetting, normal estimated bladder volume, parents who are willing to participate, and true monosymptomatic nocturnal enuresis.

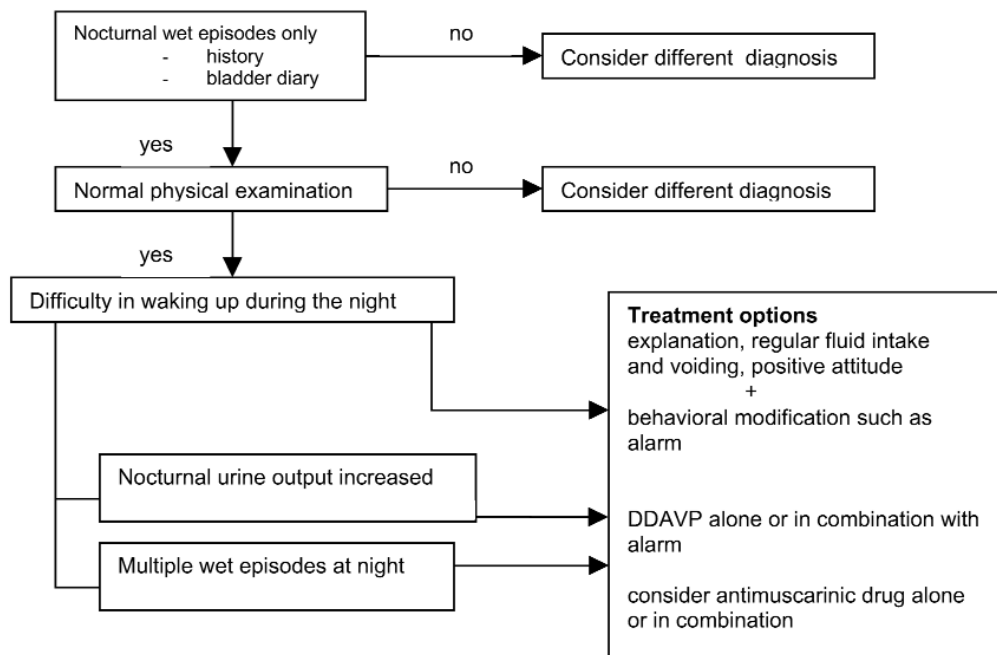- Desmopressin seems to work best in children

Figure 12 : Pragmatic approach to the diagnosis and treatment of nocturnal enuresis

who are unable to participate in alarm therapy who have truly monosymptomatic nocturnal enuresis, who are wetting only once on a wet night and are relatively devoid of bladder dyssynergia.

- If the initial treatment does not provide satisfactory results in two months, the child can switch to another. In some cases, using both the alarm and Desmopressin can be effective [124,130].

- Lastly, combinations of therapy including Desmopressin plus an antimuscarinic can be used in some cases as well if detrusor overactivity at night is suspected.

D. CHILDREN WITH BOTH DAY AND NIGHT TIME INCONTINENCE

Urinary incontinence in children may be caused by a congenital anatomical or neurologic abnormality, such as ectopic ureter, bladder exstrophy or myelome-ningocele (MMC). In many children, however, there is no such obvious cause for the incontinence and they are referred to as having "functional incontinence."

Previously the bladder in infancy was considered overactive during filling with emptying being initiated by an detrusor overactivity contraction, however natural fill studies in infants demonstrated a stable detrusor during filling and dyscoordinated emptying[1,2,3].

Male infants void with significantly higher pressure than female infants and demonstrate a smaller bladder capacity than girls. However these dysfunctions are transitory as on follow-up detrusor overactivity has resolved, post void residual volumes have improved and voiding detrusor pressures are normalized. A continuous voiding pattern was seen consistently after 2 years of age.

Bladder control is believed to be under influence of the central nervous system. The pontine region is considered to be responsible for detrusor sphincter coordination while the cortical area is responsible for detrusor overactivity control. Formerly it was believed that bladder maturation followed maturation of cortical inhibition processes, However, recent work of CK Yeung suggests bi-directional maturation of both the coordinating influence on the bladder and the pons may be implicated. This implies that a condition such as detrusor overactivity would be the result of loss of cortical control or of deficiency in cortical control, while dysfunctional voiding would be the result of non maturation of the coordination.

With the emergence of functional MRI future studies will be able to illuminate this enigma.[4] This opens an era of corticocentric thinking on lower urinary tract dysfunction away from the current trend of vesicocentric thinking. Detrusor overactivity may be a symptom of a centrally located dysfunction affecting bladder, bowel, sexual function and even mood and behaviour.[2] Indeed many studies indicate that there exists a link between lower urinary tract dysfunction and ADHD (attention deficit and hyperkinesia) [5, 6].

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 [7]. Voiding in these circumstances can only be achieved by abdominal straining. The positive reinforcement that the child receives by voiding even a small amount may lead to the development of an abnormal voiding pattern.

The same is true when children receive negative feedback related to voiding [8]. Urinary incontinence in children may be due to disturbances of the filling phase, the voiding phase or a combination of both. . In the new ICCS terminology document these conditions are termed functional bladder disorders or Lower Urinary tract (LUT) conditions. They are divided into either detrusor overactivity (DO) or dysfunctional voiding.[9] While the former condition is a filling disorder the latter is considered an emptying disorder. They can of course coincide and one may be causative of the other.

Detrusor overactivity may lead to disturbances in the filling phase characterized by urgency, frequency and at times urge incontinence. Girls present with DO symptoms more often than boys. In addition to the urinary symptoms, children with functional urinary incontinence may also have recurrent urinary tract infections and constipation.

Incomplete relaxation or tightening of the sphincteric mechanism and pelvic floor muscles during voiding results in an intermittent voiding pattern, that may be associated with elevated bladder pressures and post-void residuals. Such individuals with dysfunctional voiding are also prone to constipation and recurrent urinary tract infections[10]. Bladder function during the filling phase in these children may be essentially normal, alternatively DO may be present. In children with a underactive detrusor, voiding occurs with reduced or minimal detrusor contractions, and post-void residuals and incontinence are characteristic symptoms.

I. PREVELANCE

For more 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. Furthermore, it is virtually impossible to identify the prevalence of detrusor overactivity or dysfunctional

voiding as the studies tended to look primarily at daytime versus nighttime incontinence and made no effort to evaluate the type of daytime incontinence.

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 [11]. 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 [12-17]. Sureshkumar et al in a population based survey of over 2000 new entrant primary school children [age 4-6 years] in Sydney Australia noted an overall prevalence of daytime wetting of 19.2% defined as at least one daytime wetting episode in the prior 6 months with 16.5% having experiencing more than one wetting episode and only 0.7% experienced wetting on a daily basis [18]. Multivariate analysis showed that recent stress, a history of daytime wetting along the paternal line, and a history of wetting among male sibs were independent risk factors for moderate to severe daytime wetting. Because this was a cross sectional study recall bias may have resulted in an overestimate of risk of daytime wetting being caused by such factors as emotional stress and family history. In addition, urine cultures were not obtained so occult UTIs could not be identified.

In a questionnaire based study supplemented by telephone calls Hellstrom assessed the prevalence of urinary incontinence in 7 year old Swedish school entrants [19]. Diurnal incontinence was more frequent in girls than boys, 6.7% vs 3.8%, respectively. Wetting every week was reported in 3.1% girls and 2.1% of boys. The majority of children with diurnal incontinence had concomitant symptoms: urgency was reported in 4.7% girls and 1.3% boys. Nocturnal incontinence combined with daytime wetting was equally common in males versus females, 2.2% versus 2%, respectively. At the age of 17 years daytime wetting, at least once a week, was found in 0.2 % of boys and 0.7% of girls. A limitation of this study is its dependency on recall. 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 [20]. Urgency 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 [20, 21].

Most children are toilet-trained by the age of 3 years, although the mean age may range from 0.75 to 5.25 years, with girls being trained earlier [2.25 years] than boys (2.56 years) [22]. Although a recent study reported day dryness at a mean age of 17.4 months in the majority of countries the age of commencing toilet training has increased [23]. This is thought to be associated with higher education levels in parents and the popularity of the child-oriented approach

rather than parent-initiated methods [24]. Children who exhibited elimination signals for voiding became dry sooner than those who did not show such signs. There is huge social and cultural variation in toilet training practices with some of the implicated issues being availability of inside toilet, washable versus disposable diapers, working or home-based mothers, rural or urban location and use or not of punishment methods [24].

Swithinbank et al have found a prevalence of day wetting [including also "occasional" wetting] in 12.5% in children age 10-11 years which decreases to 3.0% at age 15-16 years [25]. Based on these findings, it seems that the prevalence of all kinds of daytime incontinence diminishes by 1-2% per year from age 10-11 to age 15-16 years, while daytime incontinence, at least once a week, seems to diminish by 0.2% per year from age 7 to age 17 years. Because of treatment interventions the studies may not recount the true natural history.

A more recent cohort study of all school children in the first and fourth grades in the city of Eskilstuna (Sweden), daytime urinary incontinence (at least once a month) was reported in 6.3% of the first graders and 4.3% of the fourth graders, while bedwetting (at least once a month) was reported in 7.1% and 2.7% and faecal incontinence in 9.8% and 5.6%, respectively. This study demonstrates that soiling and daytime urinary incontinence often coexist.[26]

The natural history of detrusor overactivity in children is not well understood. It is no longer held that an detrusor overactivity in children is idiopathic or due to a maturational delay but more likely to be associated with feed forward loops from the generation of a high pressure system during voiding or filling. Both the interplay of neural drive with motor control and the dynamic nature of the growing bladder could be causative. This is in contrast to the adult population where detrusor overactivity is considered a chronic condition whose origin is unrelated to functional use. There is no long-term data to determine if childhood detrusor overactivity predicts detrusor overactivity as an adult.

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. In children who present with a change in voiding habits, such as a new onset of voiding dysfunction, one should consider the possibility of child sexual abuse [27].

This is difficult to prove but should be kept in mind, especially when invasive diagnostic and therapeutic procedures are contemplated. One may want to simply ask the parent or caregiver if there were any precipitating events or concerns that they feel may have led to the changes in the child's voiding habits. The appropriate individuals should be contacted if there is a high index of suspicion. Of adult women with complex urinary symptoms, a significant proportion report sexual abuse as a child.

II. INTRODUCTION TO CLINICAL ASSESSMENT

The evaluation of daytime wetting is based on the medical and voiding history, a physical examination, a urinalysis, bladder diaries and uroflowmetry with postvoid residual. The upper urinary tract should be evaluated in children with recurrent infections and dysfunctional voiding. Uroflowmetry can be combined with pelvic floor electromyography to demonstrate overactivity of the pelvic floor muscles. Urodynamic studies are usually reserved for patients with therapy resistant dysfunctional voiding and those not responding to treatment who are being considered for invasive treatment [28-31].

Treatment is usually a combination of 'standard therapy' (see below), behaviour therapy, bladder training, physiotherapy and medical treatment. Surgery is rarely needed for the management of daytime wetting in the absence of a structural abnormality. The roles of neuromodulation, botulinum toxin and intravesical therapies in the management of pediatric urinary incontinence are less well-defined. Clean intermittent self-catheterization is sometimes necessary in children with poor bladder emptying, due to underactivity of the detrusor and subsequent large residuals, who do not respond to a more conservative approach.

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 urgency incontinence. Eight percent noted severe symptoms. Women who at age six years had wet episodes during the day or were wet several nights per week, were more likely to suffer from severe incontinence and report urgency symptoms: occasional bedwetting was not associated with an increased risk in adult life [31].

III. CONFOUNDING FACTORS: LOWER URINARY TRACT DYSFUNCTION, RECURRENT URINARY TRACT INFECTION AND VESICOURETERIC REFLUX (VUR)

The relationship between detrusor dysfunction and VUR associated with a urodynamic anomaly was first described by Allen and Koff and has been confirmed by several authors [32-35]. Koff demonstrated that

treatment of detrusor overactivity reduced the incidence of infection and resulted in a 3 fold increase in the rate of reflux resolution. In a study by Sillen of children with gross bilateral reflux, extreme detrusor overactivity without signs of bladder outlet obstruction was found in boys. Infant girls with gross bilateral reflux did not show the same degree of detrusor overactivity [36]. Other investigators assessing high grade VUR in newborns noted similar findings. Van Gool et al noted that 40% of 93 girls and boys evaluated for urgency incontinence and recurrent UTIs had reflux [37].

These studies in infants and the association of 'dysfunctional elimination syndromes' with reflux and infection in older children support the controversial suggestion that in some individuals vesicoureteral reflux is a secondary disorder related more to abnormal detrusor function than to a primary anatomic defect at the ureterovesical junction. 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 [38].

In support of this concept is the common finding of vesicoureteral reflux in children with neuropathic bladders and detrusor-sphincter dyssynergia. In such children, the institution of clean intermittent catheterization and anticholinergic therapy leads to the resolution of VUR in a large number 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 [39]

Koff et al evaluated the effects of antimuscarinic therapy in 62 children with a history of recurrent UTIs, VUR and detrusor overactivity, and compared these children with an age-matched control group with a normal urodynamic study [40]. The overall small sample size and the small number of compliant patients limit the study, however, it did demonstrate a statistically significant difference in the resolution rate of VUR between the treated group and the control group. The overall infection rate was lower in the treated group [16%] compared to the non-medically treated group [63%] and the age-matched control group [71%]. Several authors have documented the relationship between detrusor overactivity and dysfunctional voiding with recurrent UTIs.

Proposed etiologies for the increased incidence of UTIs in these patient populations include a milk back phenomenon whereby bacteria in the proximal urethra are "milked back" into the bladder during contraction of the pelvic floor muscles. Alternatively, decreased blood flow and relative hypoxia during periods of increased detrusor pressure such as during involuntary detrusor contractions and voiding against functional obstruction, may induce transient bladder mucosal injury.

Constipation is prevalent among children with bladder symptoms, but often poorly identified by parents [41]. It is a risk factor for recurrent UTIs. Contrary to expectations, findings from the European Bladder Dysfunction Study suggested that symptoms of disordered defecation did not influence the cure rate of treatment for bladder symptoms [42]. In a prospective non-randomized clinical series of day wetting children a strong correlation was found between recurrent urinary tract infections, detrusor overactivity and detrusor-sphincter dysfunction [43, 44]. In a study by Hansson et al, symptoms of an detrusor overactivity, such as urgency and daytime incontinence were found in a high percentage of girls with asymptomatic bacteriuria [45].

In the majority of children with detrusor-sphincter-pelvic floor dysfunction the recurrent infections disappeared following successful treatment of the detrusor dysfunction. This finding confirms the hypothesis that detrusor- sphincter-pelvic floor dysfunction is the main factor responsible for the infections (and to a lesser extent vice versa) [46, 47]. Additionally, since such children typically have coexistent constipation, attempts at restoring normal bowel habits will also contribute to decreasing the risk of UTIs. 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 [48]. Those children with VUR in association with detrusor overactivity and/or voiding dysfunction may be at increased risk for upper tract damage given their increased risk of developing UTIs. With this in mind, aggressive treatment of the underlying filling/voiding disorder, the addition of prophylactic antibiotics, and attention to their bowel habits should be given in an effort to decrease the risk of UTIs in this higher risk group [49-52].

In a recent study evaluating retrospectively a large group of children with LUT conditions it was shown that in patients who had urinary tract infection the presence of reflux increased the rate of renal cortical abnormalities. [53]

IV. CLASSIFICATION

Numerous classifications have been used for children who present with varying degrees of 'functional' urinary symptoms, unrelated to apparent disease, injury or congenital malformation. In 2006 the International Children's Continence Society (ICCS) released a standardized terminology to provide guidelines for the classification and communication about LUTS in

children [9]. Symptoms are classified according to their relation to the voiding and or storage phase of bladder function.

In addition to gaining a comprehensive history, observing micturition and examining a child form the basis of assessment, the information derived from a 48-72 hour bladder diary, stool record, voiding uroflowmetery and lower urinary tract ultrasonography is essential in making the initial diagnostic classification. Urodynamic investigations elucidate the basis of clinical findings but are first line evaluation techniques only in tertiary referral centers where children have not responded to previous treatment or have symptoms suggestive of neural involvement or anatomical anomalies.

The ICCS has classified daytime LUT conditions into groups that currently align with understanding of underlying pathophysiology. The groups commonly overlap and allocation is based on the 4 symptoms of urinary incontinence, frequency of volitional voiding, micturition volumes and fluid intake.

Over active bladder (OAB) including urgency

• incontinence

• Dysfunctional voiding

• Underactive bladder

The symptom-specific conditions of

• Voiding postponement

• Vaginal reflux

• Giggle incontinence

• Extraordinary daytime urinary frequency

• Elimination syndrome

The term 'non-neurogenic dysfunction' is commonly encountered in the literature and describes the whole spectrum, from simple detrusor overactivity to severe cases with deterioration of the upper tracts. The fact that a neurologic deficit is not demonstrated at the time of evaluation, does not, however exclude the possibility that a neurologic abnormality was present at the onset of the problem.

It has been postulated that detrusor overactivity may eventually lead to poor bladder emptying due to underactivity of the detrusor or severe dys-coordination between detrusor, sphincter and pelvic floor. 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, VUR [15%] and constipation [17%] [54].

1. OVER ACTIVE BLADDER IN CHILDREN

The term detrusor overactivity is used to describe the symptom complex of urgency, which may or may not be associated with urgency incontinence and is not a direct result of known neurological damage. Recent suggestions describe DO as a symptom of cortico-central dysfunction that affects multiple systems rather than a dysfunction isolated to the urinary bladder [55],.Urge syndrome is characterized clinically by frequent episodes of an urgent need to void, countered by contraction of the pelvic floor muscles (guarding reflex) and holding manoeuvres, such as squatting and the Vincent curtsey sign. The term urgency refers to a sudden compelling desire to void that is often difficult to defer, unlike the need to void which is experienced by all individuals and may be intense if one holds one's urine for a prolonged period of time. The symptoms arise from detrusor overactivity during the filling phase, causing urgency. These detrusor contractions are countered by voluntary contraction of the pelvic floor muscles to postpone voiding and minimize 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'). Such strong bladder and pelvic floor muscle contractions have been postulated to result in damage to the bladder mucosa increasing the risk of UTIs. In addition these children may note suprapubic or perineal pain. A cohort of patients presenting with nighttime pain syndromes based on pelvic floor spasms was described by Hoebeke et al. Good response to pelvic floor relaxation biofeedback is described in this study [56]

Over active bladder (OAB) should also be considered in "continent" children with recurrent UTI and vesicoureteral reflux. Depending on fluid intake and urine production, the complaints of incontinence become worse towards the 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 minimize wetting, and therefore incontinence may not be the main complaint or symptom.

Frequent voluntary contractions of the pelvic floor muscles may also lead to postponement of defecation. Constipation and fecal soiling are often found in children with detrusor overactivity [57]. The constipation is aggravated by the decreased fluid intake. Constipation contributes to an increased risk of UTIs and may exacerbate the detrusor overactivity. An investigation of the natural history of combined emptying dysfunction of bladder and bowel using an elimination score in women and without urogy-

naecological problems demonstrated that childhood lower urinary tract dysfunction may have a negative impact on bladder and bowel function in later life. [58]

A careful history, physical examination and scrutiny of the child's bladder diary will identify symptoms of detrusor overactivity. Urine flow rate registration and post-void residual urine measurement help to identify c0-exsisting dysfunctional voiding. Thus in the majority of children, invasive studies such as urodynamic studies are not indicated as part of the initial evaluation. Such studies are reserved for those children with a question of an underlying neurologic defect and those who fail to improve with medical and behavioral therapy, if invasive therapiesa are being considered.Those children with a history of recurrent UTIs should undergo assessment with a renal/bladder ultrasound and depending on the age of the child and the severity of the UTI(s) a voiding cystourethrogram (VCUG) to assess reflux is occasionally performed [59, 60]. By adopting a structured approach to history and physical examination, the diagnosis of urge syndrome can be made in the majority of children without the need for invasive diagnostic procedures.

Treatment

The treatment of urge syndrome involves a multimodal approach. involving strategies such as behavioral modification, antimuscarinic medication, adjunctive biofeedback and neuromodulation. Underlying and potentially complicating conditions such as constipation and UTIs are managed prior to intervention.

Level of evidence: 3 . Grade of recommendation: C

2. DYSFUNCTIONAL VOIDING

Dysfunctional voiding refers to an inability to fully relax the urinary sphincter or pelvic floor muscles during voiding. There is no identified underlying neurologic abnormality. Children with dysfunctional voiding usually present with incontinence, urinary tract infections and constipation and demonstrate fluctuating or intermittent patterns during repeated uroflowmetry. A recent study report mild and severe obesity occurring in 51% and 31% respectively of children with daytime incontinence. These figures compare to population prevalence rates of 30% and 15% respectively and highlight a potential association between lower urinary tract dysfunction and obesity.

No clear data are available on the possible causes of dysfunctional voiding. It may be that an detrusor overactivity eventually leads to overactivity of the pelvic floor muscles, with subsequent insufficient relaxation during voiding [61]. Alternatively, poor relaxation of the pelvic floor muscles during voiding may be a learned condition during the toilet training years, adopted following episodes of dysuria or constipation or occur secondary to sexual abuse [62]. The child's environment, in particular toilet conditions

and privacy issues, can trigger or exacerbate voiding anomalies [63]. In some girls, anatomical anomalies of the external urethral meatus seem to be associated with a higher incidence of dysfunctional voiding. The urine stream may be deflected anteriorly and cause stimulation of the clitoris with subsequent reflex activity of the bulbocavernosus muscle causing intermittent voiding [64]. Since no true structural obstruction can be identified the intermittent incomplete pelvic floor relaxation that occurs during abnormal voiding is termed a functional disorder.

Abnormal flow patterns seen in children with dysfunctional voiding:

- Fluctuating (Staccato) voiding: continuous urine flow with periodic reductions in flow rate precipitated by bursts of pelvic floor activity. Voids are commonly prolonged and incomplete.

- Interrupted voiding: characterized by unsustained detrusor contractions resulting in infrequent and incomplete voiding, with micturition in separate fractions. Bladder volume is usually larger than age-expected capacity. Residual urine is often present. Detrusor overactivity may be seen but it may also be absent [43, 47, 59, 65]

Sustained alteration of voiding is associated with subsequent filling phase anomalies such as phasic detrusor overactivity and inappropriate urethral relaxation [66]. Urinary tract infections and kidney damage are common sequelae[67]. Over time, routine incomplete bladder emptying can progress to detrusor over-distension associated with chronic urinary retention. The child with this presentation is often classified as having poor bladder emptying due to detrusor underactivity.

Urinary symptoms associated with dysfunctional voiding range from urgency to complex incontinence patterns during the day and night [68]. Children with dysfunctional voiding have a higher rate of recurrent urinary tract infections than children with no voiding abnormality and also demonstrate increased incidence of higher grades of VUR [54, 69]. Symptoms are significantly more common in children with Attention Deficit Disorder than in 'normal' children [70].

Signs of dysfunctional voiding reflect initial "compensatory" overactivity of the detrusor along with poor emptying ability. They may include small bladder capacity, increased detrusor thickness, decreased detrusor contractility, impaired relaxation of the external urinary sphincter/ pelvic floor during voiding, weak or interrupted urinary stream and large post-void residual volumes of urine. There may also be ultrasound abnormalities, secondary vesicoureteric reflux, fecal soiling or constipation [54, 71, 72],.

Treatment

Symptoms are often refractory to standard therapy of

hydration, bowel management, timed voiding and basic relaxed voiding education. Effective intervention requires combination therapy, generally with a sizeable investment of time over a long period. Treatment is aimed at optimizing bladder emptying and inducing full relaxation of the urinary sphincter or pelvic floor prior to and during voiding.

Specific goals are:

- consistent relaxation of the pelvic floor throughout voiding,
- normal flow pattern,
- no residual urine and
- resolution of both storage and voiding symptoms.

Strategies to achieve these goals include pelvic floor muscle awareness and timing training, repeated sessions of biofeedback visualization of pelvic floor activity and relaxation, clean intermittent self-catheterization for large post-void residual volumes of urine, and antimuscarinic drug therapy if detrusor overactivity is present. If the bladder neck is implicated in increased resistance to voiding, alpha-blocker drugs may be introduced. Recurrent urinary infections and constipation should be treated and prevented during the treatment period.

Treatment efficacy can be evaluated by improvement in bladder emptying and resolution of associated symptoms [73]. Controlled studies of the various interventions are needed. As with detrusor overactivity, the natural history of untreated dysfunctional voiding is not well delineated and optimum duration of therapy is poorly described.

Level of evidence: 4. Grade of recommendation: C

3. UNDERACTIVE DETRUSOR

Children with underactive detrusor function may demonstrate low voiding frequency and an inability to void to completion using detrusor pressure alone. Voiding is of long duration, low pressure, intermittent and often augmented with abdominal straining.

Children with this condition usually present with urinary tract infections and incontinence. Urodynamically, the bladder has a larger than normal capacity, a normal compliance and reduced or no detrusor contraction during voiding. Abdominal pressure is the driving force for voiding. The previously used term 'lazy bladder' is incorrect and should no longer be used.

A correct diagnosis can only be made by urodynamic evaluation. 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

Treatment is aimed at optimizing bladder emptying after each void. Clean intermittent (self) catheterization is the procedure of choice to promote complete bladder emptying, in combination with treatment of infections and constipation [which may be extreme in these patients]. Intravesical electrostimulation has been described, but at this time it is still not recommended as a routine procedure for children.

Level of evidence 4. Grade of recommendation C

4. VOIDING POSTPONEMENT

A new classification of voiding dysfunction in which children postpone imminent micturition until overwhelmed by urgency, resulting in urgency incontinence [74] . A recent study comparing children with typical OAB to those with voiding postponement revealed a significantly higher frequency of clinically relevant behavioral symptoms in postponers than in children with OAB, suggesting that voiding postponement is an acquired or behavioral disorder [74]. In the children with voiding postponement only 20% exhibiting a fluctuating voiding pattern. It remains to be determined whether or not voiding postponement can develop in the setting of a perfectly normal urinary tract or whether OAB is a necessary precursor.

Level of evidence 4. Grade of recommendation C

5. GIGGLE INCONTINENCE

In some children giggling can trigger partial to complete bladder emptying well into their teenage years, and intermittently into adulthood [75]. The condition occurs in girls and occasionally in boys and is generally self-limiting. The etiology of giggle incontinence is not defined. Urodynamic studies fail to demonstrate any abnormalities, there is no anatomic dysfunction, the upper tracts appear normal on ultrasound, the urinalysis is normal and there are no neurologic abnormalities [76, 77].

It is postulated that laughter induces a generalized hypotonic state with urethral relaxation, thus predisposing an individual to incontinence, however the effect has not been demonstrated on either smooth or skeletal muscle. It has also been suggested that giggle incontinence is due to laughter triggering the micturition reflex and overriding central inhibitory mechanisms. One small study hinted at an association with cataplexy (a state of excessive daytime sleepiness), suggesting involvement of central nervous structures, however with only 7 subjects further evidence is needed [78].

Since the etiology of giggle incontinence is not known it is difficult to determine the appropriate form of treatment. Positive results have been reported with conditioning training, methylphenidate and imipramine [76, 78-80]. Others have tried antimuscarinic agents and alpha-sympathomimetics. There is no acceptable

evidence that any form of treatment is superior to no intervention.

Level of evidence 3. Grade of recommendation D

6. VESICOVAGINAL ENTRAPMENT

Urinary leakage that occurs in girls a short time after voiding to completion, that is not associated with any strong desire to void, may be the result of vesicovaginal reflux

[81]. Urine may become entrapped in the vagina during voiding due to labial adhesions, a funnel shaped hymen, or an inappropriate position on the toilet. The classic presentation is that of a girl who does not spread her legs apart during voiding and who is not sitting all the way back on the toilet seat, but who is rather sitting near the end of the toilet seat tilting forward. Obesity may be an associated risk factor. Changes in voiding position and treatment of labial adhesions will lead usually to resolution of the urine leakage.

Level of evidence 4. Grade of recommendation C

7. ELIMINATION SYNDROME

This is a term used to describe dysfunctional emptying of bowel and/or bladder presenting with symptoms of detrusor over activity, constipation and infrequent voiding.

The genitourinary tract and the gastrointestinal system are interdependent, sharing the same embryologic origin, pelvic region and sacral innervation. Although children with voiding disturbances often present with bowel dysfunction, until recently this co-existence was considered coincidental. However, it is now accepted that dysfunction of emptying of both systems, in the absence of anatomical abnormality or neurological disease, is inter-related. The common neural pathways, or the mutual passage through the pelvic floor musculature, may provide a theoretical basis for this relationship, as may the acquisition of environmental and developmental learning. The latter can be influenced by episodes of urinary tract infection, constipation, anal pain or trauma, childhood stressors, reluctance to toilet and poor toilet facilities [57, 63, 82].

There is also evidence to suggest that in severe cases symptoms may have a neurological basis.

The Elimination Syndrome [ES] is seen more frequently in girls than boys and is significantly associated with the presence of both VUR and UTI [83]. VUR is slower to resolve and breakthrough urinary tract infections are significantly more common in children with ES when compared to those without the diagnosis. Infections do not ameliorate with antibacterial prophylaxis. Age of first febrile UTI does not appear to be an etiological factor [84], however, recurrence of UTI in children older than 5 years is associated with the presence of ES [84, 85].

Abnormal recruitment of the external anal sphincter during defecation or at call to stool is considered causative, in that it elicits concomitant urethral sphincter and pelvic floor co-contractions. Thus in both systems a functional obstruction to emptying is generated. In the case of the urinary system, high pressures generated by the detrusor muscle to overcome a decrease in urethral diameter can stimulate detrusor hypertrophy, detrusor overactivity, and lead to incompetence of the vesicoureteric junctions. In the early stages of defecation disorders, bowel emptying is incomplete, infrequent and poorly executed. As the dysfunction progresses stool quality becomes abnormal, the child develops distension of the rectum and descending colon, seems to lose normal sensation and develops fecal retentive soiling. If constipation was not present as a predisposing factor, it rapidly develops [82].

Children with elimination syndrome commonly complain of urinary incontinence, non-monosymptomatic nocturnal enuresis, recurrent urinary tract infections, imperative urgency to void (OAB) exceptional urinary frequency and on investigation are often noted to have poor voiding efficiency, vesicoureteric reflux, constipation, soiling, no regular bowel routine and infrequent toileting. The incidence of children with elimination syndrome and sub-clinical signs and symptoms is unknown.

Assessment follows the same process as for other aspects of pediatric bladder dysfunction, with the addition of a 2 week bowel diary and relevant symptom score. The inclusion of an ultrasound rectal diameter measure, either via the perineum or when assessing the bladder, has been shown to be discriminative for children with elimination syndrome. Urinary flow curve, perineal EMG and post void residual urine estimate, when considered in isolation, are not conclusive for the diagnosis of elimination syndrome. There is no evidence to suggest that anorectal manometry is warranted as a first line investigation in these children. Recently a symptom scale for DES has been developed providing objective assessment for diagnosis and quantification of severity [86].

Treatment

Treatment aims at assisting a child to become clean and dry in the short term, by retraining appropriate bladder and bowel awareness and teaching dynamic elimination skills. As bowel dysfunction is more socially isolating than urinary incontinence, and in the light of evidence that amelioration of underlying constipation can relieve bladder symptoms, most clinicians begin with treatment of the bowel. Strategies include disimpaction [if needed], prevention of stool reaccumulation, and post-prandial efforts to empty the bowel while maintaining optimal defecation dynamics. Once stools are being passed regularly, treatment focuses on teaching awareness of age

appropriate fullness in the bladder and training unopposed emptying (without straining or pelvic floor muscle recruitment), at pre-scheduled times. Pelvic floor awareness training and biofeedback therapy are integral.

There are currently no known studies of the efficacy of treatment in children with elimination syndrome. Several authors have evaluated the outcome of constipation management on bladder symptoms, however until last year the baseline characteristics of subjects were not described adequately enough to allow clear diagnosis of elimination syndromes [57, 87].

Level of evidence 4. Grade of recommendation C

V. PRINCIPLES OF NON PHARMACOLOGICAL TREATMENT FOR ALL DIFFERENT STATES

Treatment of the over active bladder focuses on both the involuntary detrusor contractions and the child's response to these. The initial treatment of daytime urinary incontinence involves a behavioral and cognitive approach. The child and parent[s]/ caregiver(s) are educated about normal bladder function and responses to urgency. Voiding regimens are instituted and UTIs and any constipation are managed. Additional treatment involves pharma- cotherapy, pelvic floor muscle relaxation techniques and biofeedback, either alone or in combination.

Although there are many studies reported in the literature assessing the effects of various forms of therapy on daytime incontinence and urinary symptoms, many of these are case series rather than being randomized or controlled trials. The paucity of studies evaluating basic standard therapy initiatives has precluded double-blinded trials of novel and multimodal interventions. Whilst clinically important benefits are commonly described, patient numbers, objective outcome measures and length of follow-up are sub-optimal.

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. Children learn to recognize the desire to void and to suppress this by normal central inhibition instead of resorting to holding manoeuvers [i.e. immediate voiding without postponement] to generate urethral compression. Children with dysfunctional voiding learn to initiate voiding with a completely relaxed pelvic floor and to pass urine in association with a detrusor contraction rather than via generation of abdominal pressure. Dietary changes and bowel regimens are used to treat the constipation [87]. Antibiotic prophylaxis may

prevent recurrent UTIs, however, data to support this is limited.

"Bladder training" is used widely, but the evidence that it works is variable [50, 88]. 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 [37] . More active conventional management involves a combination of cognitive, behavioral, 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 [25, 89-91]. 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.

1. BLADDER REHABILITATION AND UROTHERAPY

Initial intervention for OAB and dysfunctional voiding uses a non-pharmacologic approach. This is often termed Urotherapy. Despite its use for many years there is no set format to urotherapy and many clinical studies utilize differing combinations of therapies, which makes it difficult to evaluate the results [25, 51, 90]. The aim of urotherapy is to normalize the micturition pattern and to prevent further functional disturbances. This is achieved through a combination of patient education, cognitive, behavioral and physical therapy methods.

A Danish report of the outcome of standard urotherapy in 240 children with daytime incontinence noted achievement of dryness in 126 children (55%). Alarm therapy has traditionally been used for the treatment of nocturnal enuresis and but was recently used in management of daytime wetting. When a time watch was utilized as a reminder to void at regular intervals 70% of children became dry. An earlier study of a contingent alarm [which sounded when the child wets] versus a noncontingent alarm system (which sounded at intermittent intervals to remind the child to void) over 3 months in 45 children [92] was equally successful for the achievement of continence. Predictors for dryness included a low voiding frequency, larger volumes voided in relation to age- expected storage and fewer incontinent episodes per week [93].

Following a 3 month training programme, 42.8% of daywetting children were cured at 1 month, 61.9% by 6 months, and 71.4% by 1 year [94]. Allen et al [95] reported that urotherapy patients with good compliance with timed voiding were significantly more likely to improve their continence than those with poor

compliance. It has recently been highlighted however, that there is frequently conflict between school rules, routines and toilet facilities and the urotherapy programme components. Adaptive coping techniques added to urotherapy training may enhanced gains in dryness.

In children with OAB and dysfunctional voiding the pelvic floor muscles relaxation is impaired during voiding. Physiotherapy is concerned with re-training of specific muscle groups. Adjunctive physiotherapeutic input offers children different strategies to achieve pelvic floor relaxation during micturition.

Level of evidence 3. Grade of recommendation C

2. ADJUNCTIVE BIOFEEDBACK

Biofeedback is a technique in which physiological activity is monitored, amplified and conveyed to the patient as visual or acoustic signals, thereby providing the patient with information about unconscious physiological processes. Biofeedback may be utilized for the management of both filling phase (detrusor overactivity) and voiding phase (dysfunctional voiding due to pelvic floor muscle overactivity) abnormalities.

Biofeedback can help children to identify how to relax their pelvic floor muscles or recognize involuntary detrusor contractions.

Training with biofeedback can be used as a single treatment [96, 97], or in conjunction with a compre-hensive rehabilitation program [98, 99]. It may be performed by a cystometrogram during which the child is taught to recognize and inhibit involuntary detrusor contractions by watching the pressure curve during cystometry. This is invasive and a time consuming process with limited use as a routine treatment.

More commonly pelvic floor muscle relaxation is taught through the use of EMG biofeedback and real-time uroflow. The child sits on a toilet with a flow transducer, watching both the flow curve and EMG on a computer display, and attempts to empty completely in one relaxed void. Ultrasound may be used to determine the post void residual and demonstrate complete emptying. Interactive computer games are commonly used to make biofeedback training more attractive to children [100, 101], however care should be taken that posture and muscle recruitment approximates that of the voiding position.

The results of biofeedback are commonly reported as case series rather than RCTs. Results are generally positive but overall may not be superior to high quality standard urotherapy. The group receiving adjunctive biofeedback in the Vasconcelos study [94] did not achieve greater continence rates at the study end point, although a greater proportion of subjects achieved earlier dryness. Furthermore, the post void residual volumes were significantly reduced in the biofeedback group compared to the standard therapy only group.

Long duration follow-up, whilst desirable, confounds results of intervention in children who are continually growing and maturing. Hellstrom et al report results of a 6 week bladder rehabilitation program inclusive of biofeedback and [90] and note that at 3 years 71% of the children with detrusor overactivity, 70% of those with dysfunctional voiding and 73% of those with a combined disturbance had a normal micturition pattern. The potential for bias from intercurrent events and interventions precludes statements about the efficacy of biofeedback alone.

Level of evidence: 3. Grade of recommendation C

3. CLEAN INTERMITTENT (SELF) CATHETERISATION

In children with an underactive detrusor, bladder emptying can be achieved with timed and double voiding. If this does not adequately empty the bladder clean intermittent self-catheterization (CISC) may be tried [102-104]. 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.

Level of evidence 4 Grade of recommendation C

4. NEUROMODULATION

Neuromodulation has been used in adults for a variety of lower urinary tract symptoms and has recently been applied in children. The use of transcutaneous stimulation with surface electrodes stimulating the sacral root (S3) has shown promising results, especially when tested as part of a randomized controlled trial [105]. Transcutaneous and percu-taneous neuromodulation delivered over either the sacral outflow or peroneal region of the ankle at a frequency between 10-25 Hz, has proven a useful adjunctive treatment in children with an detrusor overactivity [22, 24, 25]. Intravesically stimulation can impact function of an underactive detrusor and potentially improve detrusor contractility and enhance bladder emptying [106, 107]).

Electrical current directly affects the central nervous system by artificially activating neural structures; facilitating both neural plasticity and normative afferent and efferent activity of the lower urinary tract. For children with structural abnormalities, for example imperforate anus, electrostimulation is one method of facilitating strength gains in the skeletal muscle and its fascial attachments. Treatment is particularly useful in patients with very little pelvic floor awareness

to stimulate muscle recruitment. Once neural efficiency has improved, training is augmented by active pelvic floor contractions.

A literature search revealed 10 reports of the use of neuromodulation in children with non-neurogenic bladder dysfunction. Only one of these studies was randomized and controlled, whilst the rest were case series. Use of neuromodulation in children with neurogenic LUT dysfunction has been reported in 6 studies, 2 of which were randomized controlled trials. From **Table 2** it is clear that different modes of application have been trialed in mostly small series of children. There is minimal standardization of populations, application parameters or outcome measures. Thus evidence is largely drawn from low quality studies. Clearly neuromodulation in children warrants larger, controlled and randomized studies.

Reported changes with neuromodulation include: significantly increased bladder capacity, decreased severity of urgency, improved continence, and decreased frequency of urinary tract infection. Significant improvement in urodynamic parameters of bladder compliance, number of involuntary contractions, and bladder volume at first detrusor contraction have also been noted.

More recently the first reports on sacral nerve stimulation with implantable electrodes have been published. In a group of 20 patients between 8 and 17 years old followed prospectively, urinary incontinence, urgency and frequency, nocturnal enuresis and constipation were improved or resolved in 88% (14 of 16), 69% (9 of 13), 89% (8 of 9), 69% (11 of 16) and 71% (12 of 17) of subjects, respectively. Complications were seen in 20% of patients. [108] Due to the uncontrolled design the level of evidence is low. Experience from adults offered this treatment modality suggests future positive development in children to be likely.

Level of evidence: 4. Grade of recommendation D

5. ALARM TREATMENT

Alarm therapy has traditionally been used for the treatment of nocturnal enuresis and has rarely been used for daytime wetting. 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 wets] with a noncontingent alarm system (which sounded at intermittent intervals to remind the child to void) [92]. Forty-four children participated in the study, 50% were assigned to each form of therapy for a 3 month period. Success was measured as 6 consecutive

weeks without daytime wetting. Nine 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%

of the risk of persistent wetting with the noncontingent alarm, the difference in the reduction in wetting between the groups was not significant (RR 0.67, 95% CI 0.29 to 1.56). In a more recent retrospective review by Van Laecke et al, a cure rate of 35% after the use of a daytime alarm was described[109]. Due to the retrospective design of the study the level of evidence is low.

Level of evidence: 3. Grade of recommendation C

6. CONCLUSION

Most clinical studies describe combinations of therapies rather than single interventions, which makes it difficult to evaluate the results. Physio-therapy and biofeedback both focus on the pelvic floor. Relaxation of the pelvic floor during voiding is essential for normal voiding and most of which 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 may 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 bladder outlet obstruction, endos-copic investigations should be performed. Most often the anatomic abnormality causing abstruction 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 [64].

VI. PHARMACOLOGICAL TREATMENT

Antimuscarinic therapy remains one of the common forms of therapy for the detrusor overactivity. Its use is predicated on the concept that parasympathetic mediated stimulation of muscarinic receptors in the bladder causes detrusor overactivity, which is responsible for the symptoms of detrusor overactivity. Antimuscarinic agents have been demonstrated to increase bladder capacity, increase bladder compliance and decrease detrusor contractions in neurogenic detrusor overactivity. Detrusor overactivity is believed to play a role in many children with functional incontinence, vesicoureteral reflux and

Table 2. Study parameters in paediatric neuromodulation trials

Author and year of publication	Population	Design	N	Mode of application	Outcome measure
Gus 2004	Neurogenic (Spina bifida)	RCT	42	Sacral implant	n/s difference from controls for continence
Marshall 1997	Neurogenic (MMC)	RCT	50	Transcutaneous	n/s difference from controls for continence
Johnston 2005	Neurogenic (spinal cord injury)	Series	2	FES implant	Suppression of detrusor overactivity in 1 pt
Han 2004	Neurogenic (MMC)	Series	24	Intravesical	Significant ↓ in faecal incontinence
De Gennaro 2004	Neurogenic and Non neurogenic	Series	6 17	Percutaneous tibial nerve	n/s difference in neuropathic pts 5/9 with incontinence cured
Gladh 2003	Neurogenic and Non neurogenic	Series	20 24	Intravesical	40% cure neurogenic 83% cure non neurogenic
Hagstrom 2008	Non neurogenic	RCT	25	Transcutaneous sacral	8/13 partial response
Humphreys 2006	Non neurogenic (severe DES)	Series	23	Sacral implant	3/19 cured of incontinence 2/16 able to stop CIC
Barroso 2006	Non neurogenic (urge syndrome)	Series	36	Transcutaneous sacral	12/19 "complete" improvement
Lee 2005	Non neurogenic (infrequent voiding)	Series	12	Intravesical	Signif ↑ max flow rate, signif ↓ PVR
Bower 2001	Non neurogenic	Series		Transcutaneous sacral	73% improved continence
Gladh 2001	Non neurogenic (DI diagnosis)	Series	48	Anal plug	18/48 cured
Hoebeke 2001	Non neurogenic	Series	41	Transcutaneous sacral	56% cured after 1 year
Trsinar 1996	Non neurogenic	Controlled trial	73	Anal plug	+ve gains in active group

urinary tract infections [110]. More commonly, pharmacotherapy is instituted when behavioral therapy has failed to achieve a satisfactory outcome. Some clinicians use pharmacologic therapy as a first line therapy in children with moderate to severe daytime incontinence [51].

Despite the frequent use of anticholinergic therapy, often in conjunction with a behavioral therapy regimen, the outcome of pharmacologic therapy for daytime urinary incontinence is "unpredictable and inconsistent" and there are few randomized studies available to assess drug safety and efficacy. Currently the pharmacologic therapy most widely used in children with detrusor overactivity is oxybutynin [111]. More recently, a long-acting formulation, Oxbutynin- XL, has been approved by the FDA for use in children [112]. Historically, oxybutynin use has been limited by its adverse effect profile with such side effects as dry mouth, constipation, facial flushing and CNS effects. The incidence of side effects seems to be dose-related, both for oral and intravesical administration [113].

The CNS effects are related to the ability for oxybutynin to cross the blood brain barrier. Oxybutynin- XL utilizes a novel delivery system, which results in absorption in the large intestine, thereby bypassing the first pass metabolism in the liver. This leads to a decrease in the amount of active metabolite [produced in the liver]: resulting in a more favorable tolerability profile. The delivery system requires an intact tablet and thus it cannot be cut or crushed to facilitate swallowing. Another method of delivery of oxybutynin is intravesical therapy. This method of delivery also avoids the first pass effect and leads to increased amounts of oxybutynin available compared to immediate release oxybutynin. Its use in the neurologically intact patient is limited by the need for catheterization [114].

There are only a few studies, none randomized and double blinded, assessing the efficacy of oxybutynin in detrusor overactivity in children. Curran et al, in a retrospective review assessed the efficacy of several agents, primarily oxybutynin in children with non-neurogenic detrusor overactivity, confirmed by urodynamics who were refractory to behavioral therapy. Some children were treated with combination therapy. Eighty percent had complete resolution or a significant improvement in their urinary symptoms. The authors noted an average time to resolution of symptoms of 2.7 years [range 0.2 to 6.6], however patients were not followed frequently

[115]. In a recent study by Van Hoeck et al, holding exercises with and without oxybutinin showed no beneficial effect of adding oxybutinin.[116].

Level of evidence: 3. Grade of recommendation C

Tolterodine, a nonselective antimuscarinic is currently being used for the treatment of detrusor overactivity

in adults. It is the first antimuscarinic agent designed specifically for use in detrusor overactivity and is felt to be "bladder selective". It's affinity for the bladder compared to other organ systems leads to an improved tolerability profile. The chemical nature of tolterodine makes it less likely to penetrate the blood brain barrier, which is supported by EEG studies [117]. The delivery system of the long acting preparation is such that the capsule may be cracked and "sprinkled" on food. Tolterodine has not been approved for use in children but there are several studies, which evaluate its safety and efficacy in children with detrusor overactivity. Hjålmas reported the results of an open label, dose escalation study using immediate release tolterodine in 33 children [118]. Doses ranged from 0.5 mg po BID to 2 mg po BID for 14 days. The results demonstrated a 21% (23% with 2 mg po BID) mean decrease from baseline in micturition frequency and a 44% mean decrease from baseline for the number of incontinence episodes in children treated with 1 mg and 2 mg po BID. Bolduc et al reported on a prospective crossover study of 34 children followed for > 1 year who were crossed over from oxybutynin to tolterodine because of adverse effects with oxybutynin [119]. Detrusor overactivity was confirmed in 19/20 who had urodynamic studies performed prior to therapy. Children received either 1 mg or 2 mg po BID and the median treatment period was 11.5 months. Efficacy was assessed by a questionnaire and was comparable for oxybutynin and tolterodine. Sixty-eight percent noted a > 90% reduction in wetting episodes at 1 year and an additional 15% noted a > 50% reduction in wetting episodes. Fifty nine percent reported no side effects with tolterodine and 18% reported the same side effect as with oxybutynin, but felt it was less severe. Eight patients [24%] discontinued tolterodine.

Munding et al reported on the use of tolderodine in children with "dysfunctional voiding" manifested as daytime wetting, frequency or urgency [120]. There was no documentation of uroflow studies to make the diagnosis of "dysfunctional voiding" and from the symptoms these children appeared to have detrusor overactivitys. Children were started on behavioral modification for 4-6 weeks and pharmacologic therapy was instituted if they failed or had only slight improvement with behavioral therapy. A minimum of 1 month's follow-up was needed for inclusion, but the mean follow-up was only 5.2 months. Doses ranged from 1 mg po BID to 4 mg po BID. Assessment of results was made by telephone survey. Thirty three percent had > 90% reduction in daytime and nighttime wetting episodes and 60% had > 50% reduction. Four patients [13.3%] had side effects, constipation in 2, dry mouth in 1 and diarrhea in 1.

Reinberg et al performed an open label parallel group retrospective study of the efficacy and safety of immediate release and long acting tolterodine and extended release oxybutynin [121]. Children started

out with the lowest possible dose, 2 mg tolterodine and 5 mg oxybutynin and titrated up according to response and side effects. Children were arbitrarily assigned to therapy based on the formulary restrictions of the health plan and there was an uneven distribution of patients in the treatment groups. Final dose and duration of treatment were not noted. Study nurses asked about side effects and a voiding diary was used to assess efficacy. The authors concluded that extended release tolterodine [p<0.05] and oxybutynin [p<0.01] were more effective than immediate release tolterodine in improving urinary incontinence symptoms and that extended release oxybutynin was more effective than extended release tolterodine in resolving diurnal incontinence (p<0.05) Long term tolerability of tolterodine extended release in a large pediatric population has been shown. [122]

Level of evidence: 3. Grade of recommendation C

One of the drugs which has been investigated in a randomized placebo controlled trial was terodiline [123, 124]. Because of serious cardiac side effects terodiline has been withdrawn from the market. Trospium chloride is another agent, which has been used in small series in children. It is currently available in a twice a day dosing formulation. In the adult population, there is a 16% intra-individual variability in bioavailability and 36% inter-individual variability. Absorption is affected by food intake. Trospium's chemical structure make it unlikely to penetrate the blood brain barrier as supported by EEG studies [117]. Lopez Periera et al evaluated the use of trospium in 62 children with documented detrusor overactivity and absence of 'detrusor sphincter dyssynergia' [125]. Children were randomly assigned to 10, 15, 20 or 25 mg of trospium administered in 2 divided doses or placebo. Fifty-eight children were evaluated. Response rates were assessed by incontinence episodes and urodynamic parameters. Overall, 32% had an excellent response, 42% a good response and 8% a fair response. Detrusor overactivity completely resolved in 35%. Four children had medication related adverse effects including headache, dizziness, abdominal cramps and dry mouth.

Level of evidence: 3. Grade of recommendation C

Like trospium, propiverine has been used in children, but results are variable and inclusion and outcome criteria were not in accordance with ICCS definitions making comparison with other studies difficult [19]. Recently a randomized, double-blind, placebo-controlled phase 3 trial with propiverine in children aged 5-10 yr was performed. Of 171 randomized children, 87 were treated with propiverine and 84 with placebo. The primary efficacy parameter showed a decrease in voiding frequency (-2.0 episodes for propiverine versus -1.2 for placebo; p=0.0007). Superiority could also be demonstrated for voided volume (31.4 vs. 5.1ml; p<0.0001) and reduction in incontinence episodes (-0.5 vs. -0.2 episodes per d; p=0.0005. This clinical trial showed superior efficacy of propiverine over placebo and good tolerability for the treatment of children suffering from DO and urinary incontinence.[126] This is the first study with level of evidence 1 that shows beneficial effect of anti-cholinergic therapy.

Level of evidence: 1. Grade of recommendation B/C (only single study)

Botulinum toxin is currently being used in children, mainly with neurogenic detrusor overactivity. Initial results seem promising, but more studies need to be done. In children. 300 Units on average, are injected in 30-40 spots [127]. The trigone should not be injected, as there is an increased risk of reflux developing. The results last about 6-9 months. Botulinum toxin is not registered for injection in the detrusor or the sphincter in children. It is off label used and further prospective studies are needed before general recommendation.

One prospective uncontrolled study by Hoebeke et all shows beneficial effects of botulinum toxin in 70% of children with therapy resistant detrusor overactivity. [128]. Injection of botulinum toxin is also possible into the external sphincter, but the results are more variable and last only 3-4 months [129]. Radojici et al describe excellent results in the treatment of dysfunctional voiding. In 20 children good results are described for 17 patients. [130] In a retrospective study by Franco et al, similar results are described in 16 children, however using a higher dosage. [130, 131]

Level of evidence: 3. Grade of recommendation C

Treatment of the overactive pelvic floor and sphincter is much more difficult. Treatment with **alpha-adrenergic blockade** seems promising, but from the presented studies it is difficult to draw firm conclusions: as most series are small, not randomized and describe a mixed patient population [132-134].

In a more recent uncontrolled study by Donohoe et al a total of 26 patients with Primary Bladder Neck Dysfunction (20 males, 6 females, mean age 12.8 years) were treated with alpha-blockers. Mean average and maximum uroflow rates improved from 5.5 to 12.6 cc per second and from 10.3 to 19.7 cc per second, respectively, while mean EMG lag time decreased from 24.4 to 5.7 seconds and post-void residual urine volume from 98.9 to 8.9 cc (all p <0.001). Mean follow-up was 31 months and no major adverse side effects were observed.[135] Further randomized controlled studies are needed to define the place of alpha-blockers.

Level of evidence: 3. Grade of recommendation C

Because there is much variability in presenting symptoms as well as the underlying pathology an individual approach is advisable: a step by step algorithm has been developed by Marschall-Kehrel,

which seems to deal with many of these variables [136].

Level of evidence 3. Grade of recommendation B/C

The limited number of identified randomized controlled trials does not allow a reliable assessment of the benefits and harms of different methods of management in children. Further work is required in this difficult clinical area. The establishment of outcome measures is needed, to facilitate randomized controlled trials of routine therapy. Interventions that would benefit from further investigations include: bladder and voiding education, bladder 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 detrusor overactivity or dysfunctional voiding.

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.

Children who present with urinary symptoms may have been victims of sexual abuse. In these cases, the use of invasive diagnostic procedures (VCUG and urodynamic studies) must be regarded as contraindicated, as must the use of invasive intra-anal treatment devices. Development of less invasive methods of diagnosis and treatment should therefore be encouraged.

E. NEUROGENIC DETRUSOR-SPHINCTER DYSFUNCTION

I. INTRODUCTION

Neurogenic detrusor-sphincter dysfunction (NDSD) can develop as a result of a lesion at any level in the nervous system. This condition contributes to various forms of lower urinary tract dysfunction which may lead to incontinence, urinary tract infections (UTIs), vesicoureteral reflux (VUR), and renal scarring. Surgery may be required to establish adequate bladder drainage, and potentially, if not managed properly, NDSD can cause renal failure, requiring dialysis or transplantation.

Management of neurogenic detrusor sphincter dysfunction in children has undergone major changes over the years. While the use of diapers, permanent catheters, external appliances and various forms of urinary diversion were acceptable treatment modalities; these are now reserved for only a small number of resistant patients [1]. Initially long term renal preservation was the only aim of therapy and early diversion had the best long term results for preserving renal function. Despite some of the complications of ileal conduits and cutaneous urostomies requiring secondary surgery, this form of treatment offered the best outcome for renal preservation with socially acceptable continence [2].

Introduction of clean (self) intermittent catheterization revolutionized the management of children with NDSD. It, not only made conservative management a very successful treatment option, but also made surgical creation of continent reservoirs a very effective alternative with a good quality of life [3].

The most common cause of NDSD in children is neurospinal dysraphism and this condition presents with various patterns of detrusor-sphincter dysfunction within a wide range of severity. About 15 % of neonates with myelodysplasia have no signs of lower urinary tract dysfunction (LUTD) when initially studied [4]. However there is a high chance of progressive changes in the dynamics of the neurological lesion in time and even babies with normal LUT function at birth have a 1 in 3 risk of developing either detrusor sphincter dyssynergia or areflexia by the time they reach puberty [5]. Nearly 60 % of the neonates with neurospinal dysraphism may develop upper tract deterioration due to increased detrusor filling pressures and infections, with or without reflux [6,7].

As our understanding of urodynamic studies has evolved it allowed us to understand the nature and severity of the problems and administer management in a more rational manner differing according to the functional characteristics of each detrusor sphincter unit. Although the last quarter century has witnessed a remarkable progress in understanding pathophysiology, pathogenesis and the management of these children, the main goals of treatment remained the same i.e. the prevention of urinary tract deterioration and the achievement of continence at an appropriate age.

II. PRESENTATION OF NEUROGENIC DETRUSOR SPHINCTER DYSFUNCTION IN CHILDREN

Neurogenic detrusor sphincter dysfunction can develop as a result of a lesion at any level in the nervous system, including the cerebral cortex, spinal cord or the peripheral nervous system. The type and degree of detrusor sphincter dysfunction is poorly correlated with the type and spinal level of the neurologic lesion.

The closure of spinal canal in utero takes place in caudad direction from cephalic end and is completed at around 35 days of gestation. The failure of mesodermal in-growth over the developing spinal canal results in an open lesion most commonly seen in the lumbosacral area. The degree of this closure deficiency contributes to a variable presentation of neural injury with varying degrees of LUTD and lower extremity problems. Developmental anomalies that result from defects in neural tube closure are termed as **myelodysplasia.** This term includes a group of lesions like spina bifida occulta, meningocele, lipomyelomeningocele, or myelomeningocele.

Myelomeningocele is by far the most common defect seen and the most detrimental. Traumatic and neoplastic spinal lesions of the cord are less frequent in children [8].

The neurologic lesions produced by myelodysplasia are variable contingent on the neural elements that protrude within the meningocele sac. The bony vertebral level correlates poorly with the neurologic lesions produced. Additionally, different growth rates between the vertebral bodies and the elongating spinal cord can introduce a dynamic factor to the lesion and scar tissue surrounding the cord at the site of meningocele closure can tether the cord during growth [9-10].

In occult myelodysplasia the lesions are not overt and often with no obvious signs of neurologic lesion. The diagnosis of this condition has increased since the advent of spinal ultrasonography and magnetic resonance imaging. Yet, in nearly 90% of patients, a cutaneous abnormality overlies the lower spine and this condition can easily be suspected by simple inspection of the lower back .These cutaneous lesions can vary from a dimple or a skin tag to a tuft of hair, a dermal vascular malformation, or an obvious subdermal lipoma [8]. Alterations may be found in the arrangement or configuration of the toes, along with discrepancies in lower extremity muscle size and strength with weakness or abnormal gait. Back pain and an absence of perineal sensation are common symptoms in older children.

Incidence of abnormal lower urinary tract function in patients with spina bifida occulta is as high as 40%. Occult lesions may also become manifest with tethering of the cord later in life. This can lead to changes in bowel, bladder, sexual and lower extremity function.

Sacral agenesis is a rare congenital anomaly that involves absence of part or all of one or more sacral vertebrae. Perineal sensation is usually intact and lower extremity function is usually normal and the diagnosis is made when a flattened buttock and a short gluteal cleft is seen on physical examination. This lesion may produce variable degrees and patterns of LUTD.

Cerebral palsy patients may also present with varying degrees of LUTD usually in the form of overactive detrusor and wetting.

Imperforate anus is a rare anomaly and presents with a closed rectum that does not open onto anal skin verge. These children may present with accompanying spinal cord pathology. This is more common when the rectum ends above the pelvic floor muscles and they should undergo a MR imaging for detection. Early detection of this problem in imperforate anus patients is important to improve the child's chance of maintaining healthy kidneys and becoming continent.

III. CLASSIFICATION: PATTERN RECOGNITION

The purpose of any classification system is to facilitate the understanding and management of the underlying pathology. There are various systems of classification of the neurogenic bladder.

Most systems of classification were formulated primarily to describe those types of dysfunction secondary to neurologic disease or injury. Such systems are based on the localization of the neurologic lesion and findings of the neuro-urologic examination. These classifications have been of more value in adults as neurogenic lesions are usually due to trauma and more readily identified.

In children the spinal level and extent of congenital lesion is poorly correlated with the clinical outcome. Indeed, severe detrusor sphincter dysfunction has been associated with minimal bony defects. Various possible neuropathologic lesions of the spinal cord including syringomyelia, hydromyelia, tethering of the cord and dysplasia of the spinal cord are the causes of these disparities and they may actually extend several segments above and below the actual site of the myelomeningocele. Therefore urodynamic and functional classifications have been more practical for defining the extent of the pathology and planning treatment in children.

The detrusor and sphincter are two units working in harmony to make a single functional unit. The initial approach should be to evaluate the state of each unit and define the pattern of bladder dysfunction. Determined by the nature of the neurologic deficit, they may be either in an overactive or in an inactive state. The detrusor may be overactive with increased contractions, with a diminished bladder capacity and compliance or be inactive with no effective contractions; the bladder outlet (urethra and sphincter) may be independently overactive causing functional obstruction or paralyzed with no resistance to urinary flow leading stress incontinence.

These conditions may exist in any combination [9-14].

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 with overactivity of the sphincter (mostly dyssynergia),

2. Detrusor overactivity with normal or underactivity of the sphincter,

3. Detrusor underactivity with sphincter overactivity and

4. Detrusor underactivity with sphincter underactivity.

Besides these 4 patterns, one can use the ICS classification: overactive detrusor, underactive detrusor, overactive sphincter and underactive sphincter. Sometimes this is more helpful, as the detrusor may be overactive during filling, but underactive during 'voiding'.

The urodynamic investigation is considered normal when there is suitable age matched capacity, good compliant bladder with no overactivity and normal innervation of the sphincter with normal sacral reflexes and an increase in pelvic floor activity during filling and no activity during voiding. Presence of overactivity during filling with or without decreased capacity and compliance is usually seen when there is upper motor neuron lesion and this is usually accompanied by overactivity of the sphincter and failure to relax during voiding. A lower motor neuron lesion is considered when the detrusor contractions are weak or lost and the sphincter is underactive. Urodynamic investigations make it possible to establish a management plan for each individual patient.

Evidence level 3. Grade of recommendation B

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 underactive detrusor and paralysed sphincter is relatively safe, providing a low-pressure reservoir [15-17].

Level of evidence: 2

IV. MANAGEMENT

The main aim in management of NDSD in children is to ensure and maintain a reservoir with normal age-matched capacity and good compliance that can be emptied completely at low pressures and at regular intervals.

In the first years of life the kidneys are highly susceptible to backpressure and infection. In this period emphasis will be on documenting the pattern of neurogenic detrusor- sphincter dysfunction and assessing the potential for functional obstruction and whether or not there is vesicoureteral reflux [17,18]. Ultrasound studies and a VCUG or video-urodynamics to exclude reflux have to be performed soon after birth. Measurement of residual urine during both ultrasound and cystography should also be done. These studies provide a baseline for the appearance of the upper and lower urinary tracts, can facilitate the diagnosis of hydronephrosis or vesicoureteral reflux, and can help identify children at risk for upper urinary tract deterioration and impairment of renal function.

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 [19].

Level of evidence 3. Grade of recommendation: B

Overwhelming experience gained over the years with early management of neurogenic bladder in infants has lead to a consensus that children do not develop upper tract deterioration when managed early with **CIC and antimuscarinic medication** [19-22]. Therefore initial treatment should consist of oral or intravesical antimuscarinic drugs in combination with clean intermittent catheterisation, to start soon after birth in all babies and especially in those with signs of possible outlet obstruction [23-27].

Level of evidence 2. Grade of recommendation: B

The early initiation of **intermittent catheterization** in the newborn period, makes it easier for parents to master it and for children to accept it as they grow older [28,29].

With early management not only are upper tract changes less, but also bladders are better protected and incontinence rates are much lower.

It has been suggested that increased bladder pressures due to **detrusor sphincter dyssynergia** cause secondary changes of the bladder wall. These fibroproliferative changes in the bladder wall may cause further loss of elasticity and compliance: resulting in a small non-compliant bladder with progressively elevated pressures. It is believed that early institution of intermittent catheterization and anticholinergic drugs may prevent this in some patients [30-32].

Level of evidence 3

Retrospective evaluation of patients has also shown that significantly fewer augmentations were required in patients with early start of CIC [23,24].

Level of evidence 4

The main disadvantage of CIC is bacteriuria which is found in 60% of the patients, but symptomatic UTIs are less common (20%) with CIC when compared to the group without CIC (40%). Since the risk of reflux is similarly lower with CIC the renal scar rates are

lower. CIC alone when begun in infancy can achieve continence at a rate of 60 %. When combined with newer and more potent antimuscarinic drugs continence rates approach 75-80% [33-36].

At present oxybutynin, tolterodine, trospium and propiverine are the most frequently used **anti-cholinergic drugs** to treat detrusor over activity in children. Some clinical studies are available, but no randomised placebo controlled studies have been performed [31,37-41].

A prospective controlled trial evaluating trospium in children reports that trospium is effective and safe in correcting detrusor overactvity in children but this study does not include patients with a neurogenic bladder [42].

Two different forms of tolterodine have been investigated in children with neurogenic bladder and extended release formulation of tolterodine is found to be as efficient as the instant release form with the advantages of being single dosage and less expensive [43].

Level of evidence 3. Grade of recommendation: B

Use of medication in children with neurogenic bladder to facilitate emptying has not been studied well in the literature. Few studies investigating the use of **alpha-adrenergic blockade** in children with neurogenic bladder report good response rates but they are non-controlled studies and long-term follow-up is lacking [44-46].

Level of evidence 4

Use of **intravesical oxybutynin** in children with poorly compliant neurogenic bladder has been investigated in some studies and incontinence has been shown to be improved significantly in most studies, with "dry and improved" rates ranging from 61% to 83% [47]. Use of lidocain intravesically also has been shown to be effective to improve bladder capacity and compliance and decrease overactivity in children with neurogenic bladder [48]. None of these studies are randomized controlled trials and evidence available is insufficient to strongly recommend this therapy. There are no data available on long term use.

Level of evidence 3. Grade of recommendation: C

In neurogenic bladders that are refractory to antimuscarinics and still remain to be in a small capacity and high-pressure state, injection of **botulinum toxin** into the detrusor has been introduced to be a new treatment alternative [49-50]. Initial promising results in adults have also initiated its use in children. So far pediatric studies have been open-label studies and prospective controlled trials are lacking [51-53]. Injection of botulinum toxin in therapy resistant bladders seems to be an effective and safe treatment alternative. This treatment seems to be more effective in bladders with evidence of detrusor

overactivity, while non-compliant bladders without obvious detrusor contractions are unlikely to respond to this treatment. Dosage in children should be determined by body weight, with caution regarding total dose if also being used for treatment of spasticity, and minimum age [54-57].

Level of evidence 3. Grade of recommendation C

In a single study urethral sphincter botulinum-A toxin injection has been shown to be effective in decreasing urethral resistance and improve voiding.The evidence is still too low to recommend its routine use in decreasing outlet resistance, but it could be considered as an alternative in refractory cases [58].

Intravesical electrical stimulation of the bladder has been introduced more than four decades ago and it has been tested in some open clinical trials in children since 1984. Its practice is limited to a few centres who have reported varying results. The nature of this type of treatment (time consuming and very dedicated personal) does not make it attractive for the majority of treatment centres [59].

Level of evidence 3. Grade of recommendation C

Children with neurogenic bladder also have disturbances of bowel function. Fecal incontinence in these children is frequently unpredictable; it is related to the loss of lower bowel sensation and function, altered reflex activity of the external sphincter and the consequent failure to fully empty the rectum [60].

The majority of children with a neurogenic bladder also have constipation and this is managed most commonly with **laxatives**, such as mineral oil, combined with enemas to facilitate removal of bowel contents. A regular and efficient bowel emptying regimen is often necessary to maintain fecal continence and this may have to be started even at a very young age. With antegrade or retrograde enemas, the majority of these children's constipation can be managed and they may attain some degree of fecal continence [61-65].

Level of evidence 3. Grade of recommendation C

Biofeedback training programs to strengthen the external anal sphincter have not been shown to be more effective than a conventional bowel management program in achieving fecal continence [66]. Electro-stimulation of the bowel may also offer a variable improvement in some patients [67].

Level of evidence 3. Grade of recommendation D

Urinary tract infections are common in children with neurogenic bladders. In the absence of reflux, patients with urinary tract infections should be treated if symptomatic. There is strong evidence not to prescribe **antibiotics** to patients with bacteriuria without clinical symptoms [68-71]. Bacteriuria is seen in more than

half of the children on clean intermittent catheterization (CIC), but patients who are asymptomatic do not need treatment.

Level of evidence 3. Grade of recommendation B

Patients with vesicoureteral reflux and urinary trac infection often should be placed on **prophylactic antibiotics** to reduce the incidence of pyelonephritis, which can potentially lead to renal damage [72].

Sexuality, while not an issue in childhood, becomes progressively more important as the patient gets older. This issue has historically been overlooked in individuals with myelodysplasia. Patients with myelodysplasia have sexual encounters, and studies indicate that at least 15-20% of males are capable of fathering children and 70% of females can conceive and carry a pregnancy to term. Therefore counseling patients regarding sexual development is important in early adolescence.

Children with a **good response to antimuscarinic treatment** and an overactive sphincter may be continent in between catheterizations. Bladder pressure and (normal) development of the upper tracts will determine whether additional treatment is necessary.

Children with **therapy resistant overactivity** of the detrusor, or small capacity and poor compliance will usually need additional surgical treatment such as bladder augmentation.

Children with **detrusor overactivity but with underactive sphincters** will be in a better shape in terms of protecting their upper tracts, but they may be severely handicapped because of their incontinence. Initial treatment will be intermittent catheterization (as it may reduce the degree of incontinence and offers a much better control over urinary infections) in combination with antimuscarinic drugs. At a later age the outlet resistance has to be increased in order to render them continent [73]. There is no medical treatment of proven efficacy that increases bladder outlet resistance. Alpha-receptor stimulation of the bladder neck has not been very effective. Surgical procedures need to be considered for maintaining continence [75-77].

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

Patients with a neurogenic bladder require **lifelong supervision** and monitoring of **renal function** is extremely important. Periodic investigation for upper tract changes, renal function and bladder status is mandatory. Therefore repeat urodynamic studies are needed more frequently at younger ages and less frequently at later ages. A repeat urodynamic study is warranted when the patient has a change in symptoms or undergoes any neurosurgical procedure.

In case of any apparent changes both in the upper and lower urinary tract or any changes of neurological symptoms, a more detailed examination including urodynamics and MRI of the spine is indicated. Renal failure usually progresses slowly but may occur with startling rapidity in these children.

F. SURGICAL MANAGEMENT OF URINARY INCONTINENCE IN CHILDREN

Intermittent catheterization and drug therapy are usually sufficient in the majority of cases for maintaining continence and preserving upper tracts. Surgical procedures should be considered if conservative measures fail to achieve continence between catheterizations or preserve upper tracts.

Surgical intervention is required for congenital and acquired diseases interfering with the function of the storage function of the bladder, the sphincter mechanisms or which bypass normal sphincter mechanisms. A plethora of different surgical procedures has been proposed to maintain continence by using different mechanisms. Various procedures using different mechanisms for maintaining continence may be used in the same patient.

In many cases measures such as intermittent catheterization and drug therapy are needed in addition to surgery since most of the surgical procedures can achieve 'dry- ness', but rarely restore normal voiding.

Patients with bladder neck incompetence pose a real challenge and require a different approach. All surgical procedures to "reconstruct" the bladder neck have one thing in common; an obstruction is created to enhance bladder outlet resistance. Even if successful, normal spontaneous voiding with low pressures without external help is not possible in most patients. Considering the long-term outcome, it may be better *not* to void spontaneously when bladder outlet resistance is increased because longstanding outlet resistance may cause secondary changes of the bladder wall.

The rarity and complexity of the conditions associated with congenital incontinence in children precludes the establishment of higher levels of evidence because of the rarity and spectrum of the pathology. Results are highly dependent on the skills of the individual surgeon. Therefore graded recommendations for specific procedures cannot be provided. There are no randomized controlled trials (level 1 and 2 evidence). Based on the available literature most studies have a level of evidence 3-4 and grade of recommendation C or D.

I. ABNORMALITIES OF STORAGE

1. BLADDER EXSTROPHY

The incidence of bladder exstrophy is 1 per 30,000 live births. (male to female ratio 2:3.1-6.1). Closure of the bladder is generally performed within the first days of life; pelvic osteotomies facilitate reconstruction of the abdominal wall and may improve ultimate continence [1,2,3]. Some children will develop more or less normal capacities. Even after successful closure there will be some children who end up with a poorly compliant small bladder requiring later bladder enlargement or urinary diversion (ureterosigmoidostomy) [4,5,6,7]. Patients with a good bladder template who develop sufficient bladder capacity after successful primary closure and epispadias repair can achieve acceptable continence without bladder augmentation and intermittent catheterization [8,9,10].

Reconstruction of the bladder neck can either be done at the time of bladder closure or at a later stage. Early reconstruction may facilitate normal bladder function, but should be attempted only at centers experienced with such surgery [11,12]. Continence rates vary from center to center and may range between 43 to 87% [13,14].

2. CLOACAL EXSTROPHY

The incidence of cloacal exstrophy is 1 per 200,000 live births. This is a much more complex deformity that requires an individual approach. Most of these children have anomalies of the nervous system, upper urinary tract and gastrointestinal tract that can adversely affect urinary tract reconstruction. Before reconstructive procedures are considered, an extensive evaluation has to be carried out.

3. AGENESIS AND DUPLICATION OF THE BLADDER are both extremely rare. Agenesis is rarely compatible with life. In bladder duplication other associated congenital anomalies are often observed such as duplication of external genitalia or lower gastrointestinal tract.

4. ABNORMAL STORAGE FUNCTION in combination with other anomalies is usually caused by a neurologic deficit or is secondary to bladder outlet obstruction. Sacral anomalies are frequently seen with cloacal malformations and imperforate anus [15, 16, 17,18].

Posterior urethral valves may cause severe hypertrophy of the detrusor with a small poorly compliant bladder [19,20].

Unfortunately, following valve ablation, these bladders may not return to normal function [21,22].

II. ABNORMALITIES OF SPHINCTERIC FUNCTION

1. EPISPADIAS (without exstrophy): incidence 1 in 60,000 live births, male to female ratio: 3-5:1. All patients with bladder exstrophy also have complete epispadias.

In male patients with complete epispadias and all females the sphincteric mechanism is deficient and the child has complete incontinence. Reconstruction of the bladder neck is either performed at the time of epispadias repair or at a later stage. The bladder function may or may not be normal in these patients [23,24].

2. MALFORMATION OF THE UROGENITAL SINUS occurs exclusively in phenotypic females. The incidence is 1 in 50,000 live births. In patients with classical urogenital sinus or cloaca, the sphincteric mechanism is insufficient and due to associated neurological abnormalities the bladder function may be abnormal.

3. ECTOPIC URETEROCELES protruding into the urethra may be responsible for a partial defect of the bladder neck. In these rare cases, sphincteric incontinence may be the result.

4. SPHINCTER ABNORMALITIES secondary to spina bifida and other neurologic disorders are of particular importance. The sphincter may be *overactive* (like in detrusor sphincter dyssynergia) or *underactive*. *Overactivity* of the sphincter causes secondary changes of the bladder wall (increased collagen type III with decreased elasticity and compliance). Continence is usually achieved with antimuscarinic drug treatment or bladder augmentation (using the overactivity of the sphincter for continence). In cases of incompetence of the sphincter, different types of surgical intervention are possible to enhance the sphincteric mechanism. In general all patients with a neurogenic bladder need Clean Intermittent Catherization (CIC). In patients bound to a wheelchair a suprapubic channel can be created (Mitrofanoff) to facilitate CIC.

5. BYPASS OF SPHINCTERIC MECHANISM

a) Ectopic Ureter is an abnormally located terminal portion of the ureter. Instead of the ureter opening in the bladder, it opens in the urethra, vagina, or uterus. Ectopic ureters occur more frequently in girls and are commonly part of a duplex system: in girls the ectopic orifice of the upper pole moiety drains into the urethra below sphincteric level or vaginal vestibule, thus causing incontinence [25].

When the ectopic ureter represents a single system, the trigone is usually asymmetrical and not well developed. These children may suffer from continuous

incontinence as well as a deficient sphincteric mechanism: this is particularly true in bilateral ectopia of single systems. In these patients the trigone and bladder neck are functionally abnormal and treatment includes surgical reconstruction of the bladder neck. When the upper pole ureter opens in the mid or distal female urethra or outside the urinary tract (i.e. vulva or vagina) incontinence results. Upper pole nephrectomy or ipsilateral uretero-ureterostomy solves the problem.

A rare and a challenging condition is when there are bilateral ectopic ureters. Since bladder is hypoplastic in these children achieving normal bladder capacity and function may require additional procedures to ureteric reimplantation [26,27,28].

b) Urethral duplications

Most patients with urethral duplication will leak urine from the abnormal meatus during voiding. In rare cases, when the urethra bypasses the sphincteric mechanisms, continuous leakage may be present [29].

c) Vesicovaginal fistulas

Acquired fistulas may be traumatic or iatrogenic, following procedures on the bladder neck.

III. EVALUATION AND DIAGNOSIS

A detailed history and physical examination in combination with imaging studies and urodynamic evaluation are the corner stones for successful management. Imaging studies are essential to define the anatomical abnormalities responsible for and associated with incontinence. Ultrasonography of bladder and kidneys as well as a voiding cystourethrogram are the basic studies. In infants and small children sacral ultrasonography can demonstrate normal position and mobility of the spinal cord.The scout film of the contrast voiding cystourethrogram (VCUG) assesses the lower spine and sacrum, intersymphyseal distance, and fecal retention. The contrast films will show bladder configuration, presence of vesicoureteral reflux, incomplete voiding, bladder neck competence, urethral anatomy, and vaginal reflux. Occasionally, an intravenous urogram will provide the clearest assessment of the urinary tract. MRI and CT scanning can be helpful in defining spinal abnormalities as well as congenital abnormalities in the urinary tract.

In addition to imaging studies, urodynamic studies (cystometrography and when needed electromyography of the sphincters and urinary flow studies) are useful for all patients with neurogenic incontinence, and after surgery in some cases of bladder exstrophy and after posterior urethral valves resection to help define the mechanism of any continued incontinence. However in many patients much useful information on the function of the lower urinary tract can be obtained with very basic studies including ultrasound and cystometry.

IV. INDICATIONS FOR SURGICAL PROCEDURES TO CORRECT URINARY INCONTINENCE

1. STORAGE FUNCTION

Reduced bladder capacity is the main indication for simple bladder augmentation. Reduced capacity can be congenital (bilateral single ectopic ureters, bladder exstrophy) or caused by previous surgery e.g. bladder neck reconstruction in exstrophy patients, where a part of the bladder is used to create an outlet resistance. Other indications are low functional bladder capacity as it may be present in neurogenic bladder (meningomyelocele) or bladder scarring from previous surgery or obstruction. Bladder scarring from bilharzia remains common in endemic areas and is increasingly common with immigration to the developed world. In all such cases surgery is indicated when conservative treatment has failed.

Several studies suggest that aggressive early intervention with CIC and anticholinergic therapy improves bladder compliance and may protect children from augmentation surgery [30,31].

Yet in a recent survey has reported that there has been no change in augmentation rates during the last 5 years: they demonstrated significant interinstitutional variability [32].

2. SPHINCTER FUNCTION DURING STORAGE

Most of the diseases in childhood requiring surgical repair for incontinence not only have an influence on bladder capacity but also on sphincter function. Conservative measures to improve sphincter function have limited value and surgery is required in many cases. There are different surgical options; either to increase outlet resistance or to create or implant a new sphincter mechanism. In neurologically normal patients such as classic exstrophy patients, early anatomic reconstruction may allow 'normal' bladder and sphincter function. Sling procedures are indicated when the residual sphincter function is not sufficient to avoid incontinence. This may be the case in patients with neurogenic bladder disturbances and urethral incontinence. If there is no residual sphincter function or outlet resistance, an artificial sphincter may be required. Primary urinary diversion (rectal reservoirs/continent stoma) offers an alternative solution to this problem.

3. PROCEDURES TO BYPASS THE SPHINCTER

If bladder outlet surgery fails or urethral catheterization is not possible, a continent stoma may be constructed.

Some patients prefer catheterizing through a continent stoma rather than through the sensate urethra. The continent stoma (Mitrofanoff principle) may be combined with bladder augmentation and/or bladder neck reconstruction or closure. An alternative to such procedures would be the use of the anal sphincter for urinary continence with the use of colon as the storage reservoir.

V. BLADDER RESERVOIR CONSTRUCTION

1. URETEROSIGMOIDOSTOMY

This type of continent urinary reconstruction may be utilized in reconstruction for bladder exstrophy, an incontinent urogenital sinus or the traumatic loss of the urethral sphincter. As this reconstruction is totally dependent on the normal function of the anal sphincter, contraindications include incompetence of the anal sphincter, anal prolapse, previous anal surgery, and irradiation. Because of the potential for electrolyte resorption, renal insufficiency is also a contraindication.

Low pressure rectal reservoirs are superior to simple ureterosigmoidostomy because the augmented or reconfigured rectal bladder achieves lower pressure storage and accordingly, enhances continence.

There are two techniques which have been utilized:

a) The augmented rectal bladder in which.the rectosigmoid is opened on its antimesenteric border and augmented by an ileal segment. The sigmoid may be invaginated to form a nipple valve to avoid reflux of urine into the descending colon and thus to minimize metabolic complications.

b) The sigma-rectum pouch (Mainz pouch II) in which there is an antimesenteric opening of the recto-sigmoid and a side to side detubularization anastomosis. Ureteral reimplantation of normal sized ureters is by a standard submucosal tunnel (Goodwin, Leadbetter). If the ureter is dilated the technique utilizing a serosa lined extramural tunnel may be more appropriate [33,34] .

As reported by D'elia et al, the results of these low-pressure rectal reservoirs are excellent with day and night continence better than 95% and complications related to the surgical procedure range from 0 -10% with the sigma-rectum pouch to 34% for the augmented rectal bladder [35]. Late complications for the sigma-rectum pouch range from 6-12.5% and the late complications for the augmented rectal bladder are 17%. Early complications include pouch leakage while late complications are mainly related to the ureteral implantation into the bowel and pyelonephritis. Metabolic acidosis also occurs (69% of the patients had a capillary base excess of –2.5 mmol/L and used oral alkalinizing drugs to prevent hyperchloraemic acidosis).

Periodic follow-up studies are important to check the upper urinary tract and prevent metabolic acidosis. Due to the risk of malignancy at the ureterointestinal anastomosis, colonoscopy should be performed annually beginning at postoperative year 10 [30, 36,37,38,39].

Level of evidence : 3. Grade of recommendation: B

2 BLADDER AUGMENTATION, BLADDER REPLACEMENT AND CONTINENT URINARY DIVERSION, USING INTESTINE

The indication for bladder augmentation, replacement of the bladder, or the creation of a continent urinary diversion, is either the morphological or functional loss of normal bladder function. The main goal of this surgery is to relieve high pressure and low capacity of the urinary bladder and create a new reservoir with low storage pressures that can be emptied periodically. It is particularly important that the patients understand that spontaneous voiding will not be possible after such surgery and life long intermittent catheterization will be required.

Before deciding on what type of procedure can be performed some significant factors must be addressed. These are

1. Physical and mental capacity of the patient to do intermittent catheterization.

2. Previous surgery (on urinary tract and bowel)

3. Renal function status (including acid base state)

4. Absence or presence of reflux

5. Outlet resistance

6. The need for a catheterizable channel

The different technical approaches to bladder augmentation or replacement are dependent on the clinical presentation of the patient:

- a simple bladder augmentation using intestine may be carried out if there is any bladder tissue, a competent sphincter and/or bladder neck, and a catheterizable urethra,

- an augmentation with additional bladder outlet procedures such as bladder neck reconstruction or other forms of urethral reconstruction are required when both the bladder and outlet are deficient. This occurs most commonly in spina bifida or bladder exstrophy. It must be appreciated that bladder outlet procedures may complicate transurethral cathe-terization.

- augmentation with surgical closure of the bladder neck may be required primarily, or as a secondary procedure in certain rare clinical situations. In this situation a continent stoma will be required. Most urologists however prefer to leave the bladder neck and urethra patent as a safety precaution:

when the bladder is very full leakage will occur and it allows transurethral manipulations such as catheterization if the continent reservoir cannot be emptied through the suprapubic catheterizable channel.

- an augmentation with additional continent stoma is utilized primarily following failure of previous bladder outlet surgery. It is advisable also when it can be anticipated that there will be an inability to catheterize transurethrally. An abdominal wall continent stoma may be particularly beneficial to the wheelchair bound spina bifida patient who often can have difficulty with urethral catheterization or who is dependent on others to catheterize the bladder. For continence with augmentation and an abdominal wall stoma, it is essential that there be an adequate bladder outlet mechanism to maintain continence.

- total bladder replacement in anticipation of normal voiding in children is very rare, as there are infrequent indications for a total cystectomy, with preservation of the bladder outlet and a competent urethral sphincter. This type of bladder replacement is much more common in adult urologic reconstruction.

The main contraindications are the inability of the patient to be catheterized, or perform CIC him or herself and the anticipation of poor patient compliance. When there is reduced renal function generally with a creatinine above 2 mg/dl or a creatinine clearance below 40 ml./min/1.73 m^2, there is a relative contraindication to the use of ileum or colon because of metabolic acidosis secondary to reabsorption. The stomach with its excretion of acid may be used with a low creatinine clearance possibly in preparation for transplantation. It is, however, not wise to use stomach in any voiding patient or one with any questions of an incompetent bladder outlet because of the severe skin irritation that the acid urine may produce (hematuria-dysuria syndrome).

a) Which intestinal segment should be utilized?

1. STOMACH

Stomach has limited indications primarily because of the complications that have been seen. It is the only intestinal segment suitable in patients with significantly reduced renal function [40,41,42].

Additionally, when no other bowel may be available, as after irradiation or there exists the physiology of a short bowel syndrome, as in cloacal exstrophy, this may be the only alternative remaining.

2. ILEUM / COLON

Clinically these two intestinal segments appear to be equally useful. In children, sigmoid colon is widely used except in those who have been treated for imperforate anus. Use of the ileocecal region can be associated with transient and sometimes prolonged diarrhea. This segment should be avoided in patients with a neurogenic bowel such as in myelomeningocele or who have been subject to previous pelvic irradiation. If the ileocecal valve must be used, it can easily be reconstructed at the time of performing the ileo-colonic anastomosis. The ileum can be satisfactorily used for bladder augmentation: however because of its smaller diameter a longer segment of ileum is required to create a comparable reservoir to that created from colon. Colon has greater flexibility for ureteral implantation and construction of a continent catheterizable channel.

3. GENERAL PRINCIPLES

There are several important principles for bladder augmentation and replacement that should be respected:

- use the minimal amount of bowel and if available use hindgut segments or conduits from previous surgical procedures,

- a low-pressure large capacity reservoir is essential. This requires detubularization of any intestinal segment used.

- for colonic reservoirs a sigmoid segment of 20-30 cm is generally satisfactory. A slightly longer segment of ileum is generally used. The length of the segments can be scaled down in smaller children. Care should be taken not to use more than 50 to 60 cm of ileum in adolescents and comparable lengths in younger children because of reduction of the intestinal resorptive surface.

- the jejunum is contraindicated in intestinal reconstruction of the urinary tract because of its metabolic consequences (hyponatremia, hypercalcemia, and acidosis).

- it is wise to strive to achieve an anti-reflux ureteral anastomosis into the reservoir to avoid the potential for reflux and consequently ascending infection: in high pressure bladders with reflux the reflux usually disappears spontaneously following augmentation [43,44].

- a reliable continence mechanism (continent urinary outlet) must be assured.

- because of the risk of stone formation only resorbable sutures and staples should be used in bladder augmentation and reservoir construction.

4. BLADDER AUGMENTATION TECHNIQUES

i. In *gastric augmentation* a 10-15 cm wedge-shaped segment of stomach is resected. Most commonly this is based on the right gastroepiploic artery but can be based on the left one as an alternative. The segment is brought down to the bladder easily in the retroperitoneal space along the great vessels.

ii. When using large or small bowel the segment to

be utilized is opened on the antimesenteric border and detubularized prior to anastomosis to the bladder remnant. The anastomosis of the intestinal segment to the bladder remnant and to itself is usually carried out in one running layer of inverting absorbable sutures.

iii. The techniques for *urinary diversion with continent stoma* (Mainz pouch, Indiana pouch, Kock pouch) are covered in the chapter on urinary diversion in adults [45,46,47].

Currently, augmentation cystoplasty is the standard treatment for low capacity and/or low compliance bladders secondary to neurogenic, congenital and inflammatory disorders. Due to the relatively high morbidity of conventional augmentation there is renewed interest in alternative methods [48, 49, 50,51,52,53]. These alternative techniques try to avoid the contact between urine and intestinal mucosa and include gastrocystoplasty, bladder auto-augmentation, seromuscular augmentation, alloplastic or biodegradable scaffolds grafted with autologous urothelium developed in cell culture, and ureterocystoplasty.

5. SEROMUSCULAR PATCH

To overcome one of the major disadvantages of a conventional augmentation that is mucus formation several techniques have been developed to use intestinal segments free of mucosa. The first attempts at using intestinal segments free of mucosa to improve bladder capacity resulted in viable seromuscular segments covered with urothelial mucosa [67,68]. The intense inflammatory response and shrinkage observed in the intestinal segment discouraged its use in humans [69]. Further attempts consisted of using the association between demucosalized intestinal segments and auto-augmentation. In the initial model using sheep, the animals tolerated the demusculization procedure poorly, reflected by inflamed, hemorrhagic colonic segments in the animals sacrificed within one month. In addition, colonic mucosa regrowth occurred in one third of the animals [70] . Follow-up studies in a dog model with previously reduced bladder capacity suggested that the contraction of the intestinal patch in seromuscular enterocystoplasty can be avoided by the preservation of both the bladder urothelium and lamina propria, together with the submucosa and muscularis mucosa of the intestinal patch [71,72]. This form of bladder augmentation was shown to prevent absorption of toxic substances like ammonium chloride [73]. Other authors using the same technique to line de-epithelialized gastric patches in the mini-pig model found it useless due to the fibrotic changes and decreased surface of the patch [74].

The initial experience in treating humans with colocystoplasty lined with urothelium were reported by Gonzales and Lima who developed a slightly different technique independently [75,76]. Bladder

capacity increased significantly while bladder pressures decreased. Biopsies demonstrated urothelium covering the augmented portion of the bladder in the majority of cases.

Longer term follow-up is now available and although the results are very encouraging, the results seem to be highly operator dependent and the way the mucosa is removed seems to be a crucial factor. Lima et al do no longer preserve the bladder urothelium and use a silicone balloon to prevent the augmented segment from contracting (they remove the balloon after 2 weeks: urine is diverted using ureteral stents): in 123 patients no ruptures were found and only 10% were regarded as failures [77].

Gonzalez et al found seromuscular colocystoplasty in combination with an artificial urinary sphincter successful in 89% of their patients and that it effectively achieves continence with no upper tract deterioration, and concludes that this is their preferred method of augmentation when adverse bladder changes occur after implanting the AUS [78].

Although more authors have now reported their results it still remains a more complex form of augmenting the bladder. This procedure has not receive a general acceptance among the paediatric urological community but is being done in some designated centres [79, 80, 81,82]. A recent comparison of the long term outcome of this technique with standard intestino-cystoplasty has indicated that most of the risks and benefits of augmentation cystoplasty performed using intestine and seromuscular patch appear similar.

Level of evidence 3. Grade of recommendation C

3. AUTO-AUGMENTATION

The principle of auto-augmentation of the bladder is the excision of a great portion of the detrusor while leaving the urothelium intact, creating a large diverticulum for the storage of urine at lower pressures. This urine stored at a low pressure can be drained by intermittent catheterization. The theoretical advantages of this procedure are the low complication rates of the surgery, reduced operative morbidity with shorter stay in the hospital, absence of urine salt resorption, less mucous production in the urine and possibly absence of carcinogenic potential. Although some series showed good results with this procedure [54,55,56,57], most authors have been unable to achieve previously reported success [58].

Long-term results have been rather disappointing: MacNeily et al concluded that of 17 patients with neurogenic bladder following auto-augmentation, 71% were clinical failures and 14 out of 15 were urodynamic failures (59). Similar findings have been reported by others (60,61). The inability of this procedure to achieve long-term good results may be due to the regeneration of nerve fibers divided during the surgery as well as the ischemic atrophy of the mucosa.

Although there are many potential advantages to this approach to a small poorly compliant bladder the inconsistency of success make it a less favorable option at this time. It is generally felt that pressures can be lowered but that capacity remains unchanged.

More recently, some authors have proposed the laparoscopic auto-augmentation as a minimally invasive procedure for the treatment of low capacity/low compliance bladder [62,63]. Despite the indifferent results some still suggest its consideration before a standard augmentation because of the reasons listed above [64,65,66].

Level of evidence 4. Grade of recommendation C

4. URETERAL BLADDER AUGMENTATION

Another alternative to avoid the morbidity of intestinal bladder augmentation is the use of ureteral segments to improve bladder capacity and/or compliance. Megaureters associated with poorly or nonfunctioning kidneys provide an excellent augmentation material with urothelium and muscular backing, free of potential electrolyte and acid base disturbance, and mucus production [83,84].

Another alternative in patients with ureteral dilation and good ipsilateral renal function, is to combine trans-ureteroureterostomy with ureterocystoplasty [85]. Another alternative in bilateral dilated ureters with preserved renal function is bilateral reimplantation and the use of bilateral distal ends for detubularized bladder augmentation [86,87].

Bladder augmentation with ureter may be effective in a small sub group of patients with ureteral dilatation and poor bladder capacity. Overall long-term results are good and remain so over a longer period of time [88,89,90,91,92,93].

In a recent evaluation of the long term functional outcome of this technique it is reported that ureterocystoplasty provides durable functional urodynamic improvement, yet some patients (4 out of 17 in this series) would eventually need a standard intestinal cystoplasty [94].

Level of evidence 3. Grade of recommendation B

It has been shown that this type of augmentation can also be employed in children who require a kidney transplantation [95,96,97].

5. EXPERIMENTAL METHODS

The artificial bladder has been the topic of speculation and experiment that remains still outside the bounds of clinical application. Somewhat nearer to clinical application may be the concept of tissue engineering using autologous urothelium and bladder muscle cells. These cells may be grown on biodegradable scaffolds—both naturally derived and synthetic—for the temporary support of growing tissues and then can be used for augmenting the bladder. A number of synthetic materials and natural matrices have been used in experimental and clinical settings and major improvement have been gained in techniques of cell harvest, culture, and expansion as well as polymer design.

A range of applications of engineered bladder tissues are at different stages of development. There have been a few in preclinical trials, recent progress suggests that engineered bladder tissues may have an expanded clinical applicability in the future.

Clinical trials with these methods are not far away [98-110].

Although this field of research may represent the future of bladder reconstructive surgery, currently only few experimental studies are available and it may be some time before all this knowledge can be used clinically. We strongly encourage further research in this field.

VI. BLADDER OUTLET SURGERY

1. URETHRAL ENHANCEMENT

In those children where sphincteric incompetence is the only cause of incontinence or plays a mayor role in association with decreased bladder capacity or compliance, surgical procedures to enhance outlet resistance should be considered. In many cases bladder outlet surgery needs to be combined with other procedures aimed at creating a large low pressure storage reservoir.

2. BULKING AGENTS

The injection of bulking substances in the tissues around the urethra and bladder neck to increase outlet resistance in children dates back to at least 1985. However, concern about distant migration of the injected substance and risk of granuloma formation prevented this technique from gaining widespread acceptance [111,112].

The search for safer, biocompatible substances to create periurethral compression has first led to the use of cross-linked bovine collagen, with initially reported success in about 20-50% of children [113,114,115].

Collagen injection appeared to effectively improve urethral resistance, but this did not always translate into satisfactory dryness, besides, the effect of the injection is of short duration and repeated injections were often necessary [116,117]. Because of this collagen is no longer recommended for this indication.

At present the following substances are available and have been tested in children with incontinence: dextranomer / hyaluronic acid copolymer (a nontoxic, nonimmunogenic, non-migrant synthetic substance) and polydimethylsiloxane.

Usually the substance is injected endoscopically in the bladder neck area (finding the best spot is often the most difficult part of the procedure): more than one procedure may be necessary. On average 2.8 – 3.9 ml is injected. More than 50% of patients need more than one injection. Initial results of 75% success have been reported, but after 7 years there is a gradual decrease and only 40% remained dry [118,119,120].

Others have reported success rates of 0 - 70% [121-128].

Despite limited success it remains an option for all patients who are poor surgical candidates and those who want to avoid extensive BN reconstruction.

An alternate route may be the injection around the urethra using laparoscopy [129].

Level of evidence : 3. Grade of recommendation C

3. ARTIFICIAL URINARY SPHINCTER

Since its introduction in 1973 the AUS has undergone major transformations over the years. Different devices are currently in use: one of the most frequently used devices is the AS800-T that has been in use for almost 20 years [130]. It consists of an inflatable cuff, a pressure regulating balloon and a unit containing a pump and control mechanisms. The inflatable cuff can only be implanted around the bladder neck in females and pre-pubertal males. In post-pubertal males the bulbar urethral placement is possible but not recommended for wheelchair patients or those who perform intermittent catheterization [131]. In patients who have had extensive urethral surgery (exstrophy and epispadias) it may also not be technically feasible.

Implantation of an AUS requires special training and difficulties may be encountered in the dissection of the space around the bladder neck in obese, post-pubertal males or in patients with a history of previous bladder neck procedures. A 61-70 cm H_2O pressure balloon is used exclusively when the cuff is around the bladder neck and a lower pressure balloon when it is around the bulbous urethra. Although high in cost, the artificial sphincter remains the most effective means or increasing urethral resistance and preserving the potential for voiding.

The ideal candidate for AUS implantation is a patient with pure sphincteric incompetence who voids spontaneously and has good bladder capacity and compliance. Unfortunately only a small proportion of children with sphincteric incontinence meet the criteria. The AUS may also be used in patients dependent on clean intermittent catheterization. The compatibility of the AUS with intermittent catheterization and enterocystoplasty is well documented [132,133,134].

The ability to empty the bladder spontaneously or by Valsalva maneuver may be preserved after AUS implantation. In series reporting children with AUS, the majority having neurogenic incontinence, 25% void spontaneously [135]. When the AUS is implanted before puberty, the ability to void spontaneously may be lost after puberty.

Overall, 40 to 50% of neurogenic patients require a bladder augmentation concomitantly or subsequently to the AUS implantation [133,136,137,138].

The continence rate ranges from 63 to 97% [139-146].

Herndon et al reported a success rate of 86% (of 134 patients): 22% voided, 11% had to perform CIC after voiding, 48% only performed CIC through the urethra, 16% performed CIC through a continent channel and 3% used diversion [147]. Mechanical problems occurred in 30% of patients who had an 800 model implanted (versus 64% in the old model). Revisions (in 16%) were significantly less in the 800 model. Erosion occurred in both groups (16%). A major complication was perforation of the augmented bladder in this group (it occurred in 10 patients). In 28% a secondary bladder augmentation was necessary.

Another interesting aspect of the AUS is that in some children the device is either deactivated or no longer functions but they remain dry: others have reported that placing a cuff only without activation is all that is required to make them dry [148].

The complications most commonly encountered in patients with AUS are mechanical failures. The longevity of the present devices is expected to exceed 10 years, although Spiess et al reported a mean lifetime of only 4.7 years [149].

The second most common problem is the development of reduced bladder compliance with time. This may result from an error in the preoperative evaluation or the reaction of the detrusor to obstruction (a reaction noted in some patients with spina bifida). These changes can be seen after many years of follow-up. The results of decreased capacity and compliance may be incontinence, upper tract deterioration, or the development of vesicoureteral reflux. Therefore long term follow-up with ultrasound, renal scintigraphy and if indicated urodynamics is mandatory in all patients with an AUS.

Infection of the prosthesis should occur in no more than 15% of all cases. Erosions of the tissues in contact with the prosthesis are rather infrequent. Bladder neck erosions are practically non-existent when the sphincter is implanted around a "virgin" bladder neck. When the AUS is used as a salvage procedure following bladder neck reconstruction, the erosion rate may be as high as 30% [137]. Despite the high complication and revision rate, AUS results show that acceptable continence rates can be achieved in the long-term. For this reason AUS implantation may be better considered as the initial treatment in selected cases [150].

4. FASCIAL SLINGS

Fascial slings constructed with the fascia of the anterior rectus muscle have been used to increase outlet resistance in incontinent children, particularly those with neurogenic dysfunction since 1982 [151]. The sling is used to elevate and compress the bladder neck and proximal urethra. The dissection around the urethra may be facilitated by a combined vaginal and abdominal approach, however, this option is limited to post-pubertal females [152].

Several technical variations of the sling have been reported. The fascial strip may be a graft or a flap based on the rectus sheath on one side. The fascial strip can be crossed anteriorly or wrapped around the bladder neck to enhance urethral compression.

Although the short-term success rate reported by most authors is encouraging, there are no series reporting detailed results at 5 years [153-154]. Most authors report a greater success when fascial slings are used in conjunction with bladder augmentation and success seems more likely in females than in males [155-158]. In patients with neurogenic incontinence postoperative CIC is recommended.

The pubovaginal sling in girls may also be placed through the vagina: in 24 girls with spina bifida this procedure was successful in 19, while another 3 became dry following additional injections with bulking agent around the bladder neck via a suprapubic needle introduction. CIC was possible in all patients. One patient developed a vesicovaginal fistula [159].

Complications of sling procedures include difficulties with intermittent transurethral catheterization, erosion of the urethra and persistent incontinence. Overall, the increase in outlet resistance provided by slings seems less than that provided by the artificial sphincter. Experience with these procedures suggests an overall success between 50 and 80% in females.

Numerous alternatives are being used nowadays: small intestinal submucosa has been used in 20 children and showed equivalent rates of continence. The advantage being that it is available off-the-shelf. Results were better in girls than in boys (85 vs 43% being dry) [160,161,162].

When combining bladder augmentation with a Gore-tex sling in 19 children the results were bad: because of erosion the sling had to be removed in 14 patients, all except one also had a bladder stone. In this respect this type of sling should not be used [163].

From the data published it presently seems that the AUS provides more consistent results in boys and for girls capable of spontaneous voiding who have not had previous bladder neck surgery. Bladder neck slings may be used for the enhancement of bladder outlet resistance in the majority of patients with neurogenic bladder who need augmentation cysto-plasty and whom we do not expect will be capable of voiding spontaneously. Sling procedures are probably equally effective for girls dependant on intermittent catheterization and in conjunction with bladder augmentation. At present, given the cost and lack of effectiveness of injection procedures, their use does not appear justified in incontinent children. The cost of the AUS may restrict its use.

Level of evidence 2. Grade of recommendation B

It is important that one should be aware of the fact that these patients who undergo bladder outlet surgery need long-term follow-up not only because of the complications but also because their bladder behavior may undergo unexpected clinically asymptomatic changes that could negatively affect their upper tracts if augmentation procedure are not performed at the same time [164].

5. BLADDER NECK CLOSURE

In 'desperate' cases the bladder neck may be closed, the indication being persistent leakage despite several attempts to enhance outlet resistance by bulking agents or other surgical procedures. Although initial results are acceptable, long-term results are usually disappointing: persistent urinary leakage, stomal stenosis and leakage or stone formation (in up to 40%) [165,166]. One of the most important factors seems to be compliance with intermittent cathe-terization and bladder irrigation.

6. BLADDER OUTLET RECONSTRUCTION

Surgical procedures to achieve urinary continence are dictated by functional and anatomic deficiencies and by the ultimate goal of either continence (with normal voiding) or dryness (dependent on intermittent catheterization).

Construction of a functional urethra for continence usually implies an anatomic defect without a neurogenic component (epispadias / esxtrophy) and includes urethral and bladder neck narrowing and urethral lengthening [167-172]..

Such procedures may initially require intermittent catheterization or occasional post voiding cathe-terization, but bladder empting by voiding is anticipated.

Urethral reconstruction for dryness, however, mandates intermittent catheterization. The goal in surgery to achieve dryness is to create a urethra suited to catheterization, which has closure such that intra-luminal pressures always exceed intravesical pressure. The most dependable procedures for dryness utilize a flap valve or tunnel to achieve urethral closure, although urethral slings, wraps and injections have also been used [173].

Level of evidence 3. Grade of recommendation C

Reconstruction to achieve **continence** is based on the principle that proximal reduction of the caliber of the

urethra supports the inherent proximal sphincteric mechanism of the bladder neck and proximal urethra. The narrowing must be dynamic to permit closure for continence and yet permit opening with funneling during voiding. Several techniques have been described to achieve this goal [3, 166-176]. Young (1922) performed a "double sphincter technique" that involved the excision of a wedge of tissue at the anterior bladder neck, as well as removal of a wedge of tissue just proximal to the epispadiac meatus (external sphincter). Dees (1949) added the concept of lengthening the urethral tube to that of narrowing. In his procedure parallel incisions were made through the existing bladder neck area which created a posterior urethral plate from what had previously been the trigone of the bladder. This is tubularized to give added length to the proximal urethra. The added length provides increased potential for urethral closure and moves the bladder neck and proximal urethra into the abdominal cavity. Leadbetter (1964) modified the Young-Dees procedure by creating muscular flaps from the area of the bladder neck and proximal urethra which were used to wrap the newly created proximal tube. This procedure was popularized by Jeffs (1983) who applied it to a staged repair of exstrophy. He supported a lengthened urethra by a suspension. They report their long term continence rate with this procedure as greater than 80%, without the need for CIC or augmentation [177].

Presently, this represents the gold standard for reconstruction for continence, however, modifications of the technique have reported similar or improved results. Most urethral lengthening procedures utilizing the posterior urethra and bladder neck require ureteral reimplantation and preservation of the posterior urethral plate. Because part of the bladder is used to create the functional lengthening of the urethra bladder capacity decreases following the procedure. It also remains to be seen whether the created urethra is actually a functioning urethra: in many patients fibrosis around the urethra prevent it from being really 'functional': in these patients it may act as an anatomic obstruction and long-term follow-up is necessary to follow not only the bladder but also the upper tract.

Surgery for **dryness** is dependent on the effectiveness of intermittent catheterization and is usually reserved for patients with neurogenic dysfunction or multiple previous surgeries. Procedures to achieve dryness usually create a urethral closure pressure that exceeds bladder pressure.

A flap valve can be constructed by using an anterior or posterior bladder flap (full thickness) to construct a tube that is placed in a submucosal tunnel [171,175,176].

The major disadvantage of these procedures (flap valves) is that the valve will not allow leakage with high intravesical pressures, potentiating renal damage. Therefore, these procedures can be dangerous to the patient who is not totally committed to follow catheterization recommendations.

Unfortunately, the ideal procedure for surgical reconstruction of the bladder neck does not exist. The surgical approach to urinary incontinence in the child must be multifaceted because of the inherent complex and varied nature of the problem.

Recent data would support the concept that very early reconstruction in the exstrophy / epispadias group may result in physiologic bladder cycling which facilitates normal bladder and urethral development. This results in higher potential for continence without the need for bladder augmentation and bladder neck reconstruction (Level 3). More work and clinical experience in this area is strongly recommended. (Grade A)

7. ALTERNATIVE CONTINENCE CHANNELS

In the surgical treatment of incontinence in children every effort must be made to preserve the natural upper and lower urinary tract. The bladder is the best urinary reservoir, the urethra the best outlet and the urethral sphincters the best control mechanism. If the bladder is partly or wholly unusable it may be augmented or replaced by a variety of techniques.

Urethral failure may occur either because the sphincters are incompetent or because it is overactive and does not allow spontaneous voiding. It would be preferable for the former to be treated by one of the techniques described above and the latter by intermittent catheterization (CIC). If all of these fail, continent supra pubic diversion is indicated.

a) The Mitrofanoff principle

Mitrofanoff's name is given to the principle of burying a narrow tube within the wall of the bladder or urinary reservoir whose distal end is brought to the abdominal wall to form a catheterizable stoma suitable for intermittent catheterization [178]. The technique is simple and familiar to all urologists who are accustomed to re-implanting ureters. Several narrow tubes are available for the Mitrofanoff conduit [179,180]. In the original description, the appendix was used. However, even if the appendix is still present, it may be unusable in 31% of patients [181].

If no suitable tube is found, a good tube can be formed by tailoring ileum transversely so that only 2-3cm of ileum can be made into a 7-8 cm conduit. This modification was originally described by Yang in humans and by Monti in experimental animals [182,183]. It is increasingly used though great care must be taken in its construction to avoid an internal fistula [184].

The ureter may be used but there may be some difficulty in achieving sufficient calibre with a previously normal ureter. Earlier reports that the Fallopian tube could be used have not stood the test of time.

The Mitrofanoff system achieves reliable continence which is maintained in long term follow-up, for a high proportion of patients. Long-term follow-up data shows that in the original series of Paul Mitrofanoff of 23 patients after a mean follow-up of 20 years, 1 patient had died, but in the other 22 patients no metabolic changes were noted. The bladder neck was closed in 21 patients. Secondary bladder augmentation had to be performed in 8, while in 4 children a non-continent diversion was created. With time the need for additional surgery decreased and after 20 years 16 patients had a good and stable continent diversion [185].

The pressure generated within the lumen of the conduit is 2 to 3 times higher than that within the reservoir so that continence is preserved even when the intra abdominal pressure is raised by straining. Conversely, the pressure in the lumen of a Kock nipple is only slightly higher than that in the reservoir so that continence is less reliable [186,187].

The conduit may be buried either between the mucosal and muscle layers of the reservoir, or may be completely imbrocated in the full thickness of the reservoir wall. Any well supported tunnel of about 2-4 cm will suffice. The choice depends both on the nature of the reservoir and on the conduit [188].

Continence rates of 90-100% with the Mitrofanoff Principle are reported, regardless of diagnosis, reservoir or conduit type [188,189]. Follow-up for at least ten years has shown that the system is resilient [190,191,192].

A modified technique of vesicostomy is described using a gastrostomy button, which could be used as a continent urinary stoma in children with incomplete voiding. Button vesicostomy is a useful addition to the options available for a catheterizable continent urinary stoma in children in the short or medium term(193).

Although perfect continence seems attractive, it may not be in the child's best interests. A 'pop-off' valve may be in the interest of the child if catheterization is impossible or forgotten.

b) The Ileo-cecal valve

The ileo-cecal valve is an obvious sphincter to combine with cecum and ascending colon as the reservoir and the terminal ileum as the conduit. The early continence rate of 94% was not sustained because of high pressures in the tubular reservoir and weakness of the valve [194,195,196].

The Indiana system is based on the competence of the ileo-caecal valve but with a detubularized reservoir [197]. The valve itself is reinforced with non-absorbable plicating sutures and the terminal ileum which forms the conduit is tailored. The best reported continence rate is 96% with a 2% rate of catheterization difficulties.

In the complete Mainz I pouch a length of terminal ileum is intussuscepted through the ileo-cecal valve as a Kock nipple [198]. It is impossible to say whether the nipple or the ileocecal valve (or both) produce the continence which is reported in 96% of patients.

Both these systems work well as complete reconstructions and are widely used as bladder replacements in children. The sacrifice of the ileo-cecal valve may cause gastro-intestinal complications.

c) Kock pouch

The first workable continent diversion was the Kock pouch [42]. The reservoir is made from 40cm ileum reconfigured to reduce the intrinsic pressure. The continence mechanism is formed by intussusception of 12cm of ileum. In a complete form it requires 72cm of ileum which may be more than can be spared from the gastro-intestinal tract.

Although first described as a mechanism for a continent ileostomy in children the Kock pouch is now not commonly used in children because of the problem with large amount of bowel needed, stone formation and mediocre success with dryness of the catheterizable stoma [199,200].

d) Artificial Sphincter

As a last resort, the AUS may be considered to give continence to a reconstructed outlet. Experimental evidence suggests that AUS cuffs can be placed safely around intestine providing the cuff pressure is low [201]. The AUS has been used successfully around large bowel, in three of four children with follow-up to 11 years [202].

e) Where to place the cutaneous stoma

In patients with spina bifida, particularly non-walkers, the site must be chosen with particular care. The natural tendency is for the spine to collapse with time so that the lower half of the abdomen becomes more pendulous and beyond the range of vision. A low site may seem appropriate in the child, but will become unusable in the adult. It is best to use a high, midline site, preferably hidden in the umbilicus. The site should be determined in a sitting position and marked before surgery because in the supine position the position will change dramatically. In some patients the best position may not be in the midline at all: special care must be taken that the patient can manage bladder emptying and irrigation him/herself.

For most other patients, the site of the stoma should be chosen by cosmetic criteria. The umbilicus can be made into a very discrete stoma; the risk of stenosis is low and it is a readily identifiable landmark. Otherwise, the stoma should be as low on the abdominal wall as possible and certainly below the top of the underpants. However, many surgeons find the best results by placing the catheterizable stoma in the umbilicus.

The problem of stomal stenosis remains ever present.

It can occur at any time so that only follow up of many years could determine whether any system of anastomosis to the skin is better than any other. The published rate of stomal stenosis is between 10 and 20%. The multi-flap V.Q.Z. stoma is claimed to have the lowest rate but follow up is short and it may well not pass the test of time [203].

VIII. COMPLICATIONS OF CONTINENCE SURGERY IN CHILDREN

1. STORAGE AND EMPTYING COMPLICATIONS

In the short term, it has been shown that the continent diversions can store urine and can be emptied by clean intermittent catheterization (CIC). It is apparent that there is a constant need for review and surgical revision. This observation mirrors the late complications of augmentation cystoplasty for neuropathic bladder where the median time to revision surgery is as long as ten years [204,205].

In general, once continent, they remain continent, although there are occasional reports of late development of incontinence. The problem lies more in difficulties with catheterization, particularly stenosis and false passages which may occur in up to 34% of patients [188]. In a recent retrospective evaluation of 500 augmentations over 25 years with a median follow-up of 13.3 years, the cumulative risk of further surgery at the bladder level was 0.04 operations per patient per year of augmentation and 34 % of the patients needed further surgery for complications. Bladder perforation occurred in 43 patients (8.6%) with a total of 53 events and 125 surgeries done for bladder stones in 75 cases [206].

The principal complications arise because the reservoir is usually made from intestine. Ideally, urothelium should be used and preservation of the bladder epithelium gives fewer complications than entero-cystoplasty [207].

Combinations of detrusor myomectomy and augmentation with de-mucosalised colon have given promising results in the short term. The surgery is difficult as the bladder epithelium must not be damaged and the intestinal mucosa must be removed completely. When achieved there are no metabolic problems and many patients can void [207].

When augmentation can be done with a dilated ureter, the results are good and the complication rate low even in children with compromised renal function or transplantation [208].

All intestinal reservoirs produce mucus. The amount is difficult to measure and most estimates are subjective. No regime has been shown to dependably reduce mucus production [209].

2. RESERVOIR RUPTURE

The incidence of spontaneous rupture varies between different units. There may be delay in diagnosis although the history of sudden abdominal pain and diminished or absent urine drainage should make it obvious. The patient rapidly becomes very ill with symptoms of generalized peritonitis [210,211]. A 'pouchogram' may not be sensitive enough to demonstrate a leak. Diagnosis is best made by history, physical examination, ultrasonography and a CT cystogram. If diagnosed early, catheterization and broad spectrum antibiotics may sometimes lead to recovery. If the patient fails to respond within 12 hours on this regime or if the patient is ill, *laparotomy should be performed at once*. If there is any instability of the patient laparotomy should be considered as an immediate necessity as bladder rupture in this clinical situation can be lethal.

Level of evidence 2. Grade of recommendation A

Figures are not available on the incidence of this complication in reservoirs made only of bowel but come from patients with intestinal segments in the urinary tract. Most papers report small numbers. In a multicentre review from Scandinavia an incidence of 1.5% was noted. There were eight patients with neurogenic bladder which was said to be dispro-portionately high [210]. In a series of 264 children with any sort of bowel reservoir or enterocystoplasty, 23 perforations occurred in 18 patients with one death [211]. Therefore, as this complication is more common in children it becomes a very important consi-deration [212]. A review of 500 bladder augmentation procedures performed during the preceding 25 years, spontaneous perforations occurred in 43 patients (8.6%), for a total of 54 events. The calculated risk was 0.0066 perforations per augmentation-year [213].

Patients and their families should be warned of this possible complication and advised to return to hospital at once for any symptoms of acute abdomen, especially if the reservoir stops draining its usual volume of urine. All young patients with urinary reconstructions including intestinocystoplasty should carry suitable information to warn attending physicians of their urinary diversion in case of emergency.

3. METABOLIC COMPLICATIONS

Metabolic changes are common when urine is stored in intestinal reservoirs and must be carefully monitored. It is uncertain whether they are commoner in children or whether they just live longer and are more closely monitored.

Nurse et al found that all patients absorbed sodium and potassium from the reservoirs but the extent was variable [214]. A third of all patients (but 50% of those with an ileocecal reservoir) had hyperchloremia. All patients had abnormal blood gases, the majority

having metabolic acidosis with respiratory compensation. The findings were unrelated to renal function or the time since the reservoir was constructed.

In 183 patients of all ages at St Peter's Hospitals who had any form of enterocystoplasty, hyperchloraemic acidosis was found in 25 (14%) and borderline hyperchloraemic acidosis in an additional 40 (22%) patients. The incidence was lower in reservoirs with ileum as the only bowel segment compared to those containing some colon (9% v 16%). When arterial blood gases were measured in 29 of these children a consistent pattern was not found [215].

In a series of 23 patients, Ditonno et al found that 52% of patients with a reservoir of right colon had hyperchloraemic acidosis [216]. In ileal reservoirs, Poulsen et al found mild acidosis but no patients with bicarbonate results outside the reference range [217].

Many authors do not distinguish between patients with normal and abnormal renal function. All of 12 patients in one series with a pre-operative serum creatinine above 2.0mg% developed hyperchloraemic acidosis within 6 months of enterocystoplasty [218]. It is prudent to monitor patients for metabolic abnormalities, especially hyperchloraemic acidosis, and to treat them when found [219].

With increasing experience, it has become clear that there is a risk of developing vitamin B_{12} deficiency, sometimes after many years of follow up. It is likely that resection of ileum in children leads to an incomplete absorption defect. Stores of B_{12} may last for several years before the serum level becomes abnormal. At a mean follow up of six years, low levels of B_{12} have been found in 14% of children. There was a corresponding rise in the serum methyl malonic acid which is a metabolite that accumulates in B_{12} deficiency suggesting that the finding was clinically significant. Similarly, in adults, 18.7% have B_{12} deficiency at five years. In the adults the mean B_{12} level was significantly lower when the ileo caecal segment as opposed to ileum alone had been used (413 ng/ml compared to 257 ng/ml) [220,221]. In order to avoid the serious neurological complications, regular monitoring of B_{12} levels is essential.

In a review of 500 augmentations Starting at 7 years postoperatively, 6 of 29 patients (21%) had low B12 values, while 12 of 29 (41%) had low-normal values [222].

Pediatric patients who have undergone ileal enterocystoplasty are at risk for development of vitamin B12 deficiency. These patients are at the highest risk beginning at 7 years postoperatively, and the risk increases with time. An annual serum B12 value in children beginning at 5 years following bladder augmentation is recommended.

Level of evidence 2. Grade of recommendation B

The stomach has had a checkered career as a urinary reservoir. Its non-absorptive role in the gastro intestinal tract has made it particularly useful in reconstruction of children with inadequate intestine, such as those with cloacal exstrophy. There is little effect on gastro intestinal function. Metabolically, the acid production leading to hypochloraemic alkalosis may be positively beneficial in children with renal failure. It produces no mucus and the acidic urine is less easily infected and seldom grows stones. However about a third of children have had serious long term complications, often multiple. The quite severe dysuria / haematuria and the skin complications from the acid urine, particularly, have limited its use [223,224].

4. EFFECTS ON THE GASTROINTESTINAL TRACT

Little attention has been paid to the effects on gastro intestinal motility of removing segments of ileum or cecum for urinary reconstruction in children. In adults, disturbance of intestinal function has been found to be more frequent and more debilitating than might be expected.

Disturbance of bowel habit does not mean diarrhoea alone. It also includes urgency, leakage and nocturnal bowel actions. It is clear that quality of life may be seriously undermined by changes in bowel habit [225].

It is known that the bowel has a considerable ability to adapt, especially in young animals, when parts are removed. Nonetheless, reconstruction should be undertaken with the smallest length of bowel possible. Particular care should be taken in children with neurologic abnormality in whom rectal control is already poor. Poorly controlled fecal incontinence may occur in a third of patients [226,227].

5. RENAL FUNCTION

Obstruction and high pressures in the bladder during storage have devastating effects on the upper urinary tract. Bladder augmentation eliminates these high pressures. Urinary diversion with recurrent urinary tract infections and stone formation also may have deleterious effects on renal function. It is therefore of utmost importance to evaluate renal function in young children who have undergone undiversion or continent diversion. In the follow-up so far available these procedures do not seem to affect renal function. When function has improved after such surgery it is likely to be the result of eliminating obstruction or high bladder storage pressure.

In rats with near complete nephrectomy the rate of progression of renal failure is no worse in those with ileocystoplasty compared to those with normal bladder [228]. This suggests, experimentally, that storage of urine in small intestine is not, on its own, harmful to renal function.

Clinically, in the longer term, renal deterioration has

been related to obstruction, reflux and stone formation. In one long-term study of Kock pouch patients, these complications occurred at the same rate as that found in patients with ileal conduits: 29% at five to 11 years [229]. Similarly, in a prospective follow-up to a minimum of 10 years, it was found that the deterioration in glomerular filtration rate (GFR), that was found in 10 of 53 patients, was due to a 'surgical' cause in all but one [230].

Although a more complicated procedure, a renal transplant can be anastomosed to an intestinal reservoir with similar long term results as those using an ileal conduit [231,232].

6. INFECTIONS AND STONES

The incidence of bladder reservoir stones varies between 12 and 25%. This is higher in children compared to adults. Palmer et al reported an incidence of 52.5% during a follow-up of four years [233]. Renal stones are uncommon, occurring in about 1.6% of patients, an incidence which would be expected in a group with congenital urinary tract anomalies.

In a series comparing the Kock pouch with the Indiana pouch (which does not have staples), 43.1% of 72 Kock reservoirs formed stones compared to 12.9% of 54 Indiana reservoirs [234]. Furthermore, no patient with an Indiana pouch formed a stone after 4 years, but patients with Kock pouches continued to do so at a steady rate up to eight years.

Apart from the presence of a foreign body, several factors have been blamed for the high stone risk. Almost all reservoir stones are triple phosphate on analysis, though Terai et al found carbonate apatite, urate and calcium oxalate in up to 50% of stones from patients with an Indiana pouch [235]. This suggests that infection rendering the urine alkaline is a key factor. Micro-organisms that produce urease and split urea to form ammonia are the main culprits. The incidence of infection in reservoirs is high, 95% in one series, and yet the majority of patients do not form stones, suggesting that there are predisposing factors other than infection and the anatomical abnormality of the urine reservoirs [236].

It has been suggested that the immobility associated with spina bifida may be responsible, but this seems to have been in series with a predominance of such patients and was not confirmed in other studies [237].

The production of excess mucus has also been blamed. The problem is that the measurement of mucus is difficult.

The finding of a spectrum of stone formation from mucus, through calcification to frank stone lends some support to this aetiology. However, it could be a secondary event, with mucus becoming adherent to a stone that has already formed. Many surgeons encourage patients to wash out their reservoirs vigorously with water two or three times a week. There seem to be fewer stones in those that claim to practice regular washing. In a prospective study a regime of weekly washouts did not improve the incidence of stones in 30 children compared to historical controls [238].

Mathoera et al found an incidence of 16% during a follow-up of 4.9 years in 90 patients: girls were more frequently affected than boys and concomitant bladder neck reconstruction, recurrent infections and difficulties with CIC were other risk factors identified, while the frequency of irrigation did not appear to be a risk factor [239].

Mucins are an important component of the epithelial barrier and protect the epithelium from mechanical and chemical erosion. Mucins are known to act as important adhesion molecules for bacteria. Mucins may also enhance the formation of crystals [240]. Mucin expression changes after incorporating the intestinal segment in the bladder. Upregulation of MUC1 and MUC4 expression occurs in transposed ileal segments resembling normal epithelium, whereas ileal segments in enterocystoplasty showed an upregulation of MUC2,3,4 and 5AC expression towards the site of anastomosis with the ileal segment. These changes which may be due to exposure to urine coincide with a change from ileal sialomucins to colonic sulfomucins by a change in glycosylation. The mucins bind calcium and may form a template resembling the crystal structure on which crystals are formed and grow. From these studies it is concluded that inhibition of bacterial adhesion (by using different irrigation fluids based on sugars) could be of eminent importance in the prevention of certain types of infection stones.

An interesting comparison has been made between children with a native bladder alone and those with an augmentation, all of whom were emptying by self catheterization. There was no significant difference in the incidence of stones with or without an augmentation [241].

Stones are associated with inadequate drainage in the sense that CIC through the urethra, the most dependent possible drainage, has the lowest stone rate. Patients with the most 'up hill' drainage, that is with a Mitrofanoff channel entering the upper part of an orthotopic reservoir have a higher incidence of stones [239].

Kronner et al made the observation, that the incidence of stones was statistically associated with abdominal wall stomas and a bladder outlet tightening procedure (21.1% compared to 6% in patients with augmentation alone) [236].

Once a bladder stone has been diagnosed it has to be removed: several methods are available, but ESWL should be avoided as it is difficult to remove all

fragments (and small particles may get trapped in mucus and the pouch wall), which may form the focus of a new calculus. Because of the recurrent nature of these stones the least invasive method should be recommended [242,243].

Because of the high incidence of stones following enterocystoplasty several measures should be recommended to the patients and their parents. Regular CIC under hygienic circumstances with adequate fluid intake and irrigation seem to be the most important [244]. It is unclear whether prophylactic antibiotics are useful, but a clinical infection should be treated adequately. Maybe in the future different types of irrigation fluid may prove helpful.

7. GROWTH

The suggestion that enterocystoplasty delayed growth in height seems to have been ill founded. In a group of 60 children reported in 1992 it was stated that 20% had delayed growth [245]. Current follow up of the same group has shown that all have caught up and achieved their final predicted height. Furthermore, measurements in a group of 123 children from the same unit have shown no significant delay in linear growth [246].

Enterocystoplasty may have an effect on bone metabolism even if growth is not impaired. At least in rats with enterocystoplasty there is significant loss of bone mineral density especially in the cortical compartment where there is endosteal resorption. These changes are not associated with HCA and are lessened by continuous antibiotic administration [247,248].

More recent follow-up data shows either no effect on growth or a decreased linear growth [249-252].

8. PREGNANCY

When reconstructing girls it is essential to have a future pregnancy in mind. The reservoir and pedicles should be fixed on one side to allow enlargement of the uterus on the other.

Pregnancy may be complicated and requires the joint care of obstetrician and urologist [253]. Particular problems include upper tract obstruction and changes in continence as the uterus enlarges.

Pregnancy with an orthotopic reconstruction appears to have a good outcome but chronic urinary infection is almost inevitable and occasionally an indwelling catheter is needed in the third trimester [254]. With a suprapubic diversion, catheter drainage for incontinence or retention may be needed in the third trimester [255].

Except in patients with an artificial urethral sphincter and extensive bladder outlet reconstruction, vaginal delivery is usual and caesarean section should generally be reserved for purely obstetric indications (distorted pelvis in spina bifida patients). During the delivery the bladder reservoir should be empty and an artificial sphincter deactivated. The urologist should be present during Caesarean section to ensure protection for the reservoir, the continent channel and its pedicles.

9. MALIGNANCY

The possibility of cancer occurring as a complication of enterocystoplasty is a constant source of worry. Currently cancer following augmentation cystoplasty is a recognized risk factor. It is known to be a frequent complication of ureterosigmoidostomy after 20 to 30 years of follow up. Animal evidence suggests that faecal and urinary streams must be mixed in bowel for neoplasia to occur. However, if it is chronic mixed bacterial infection, rather than the faeces per se, then all bowel urinary reservoirs are at risk.

In patients with colonic and ileal cystoplasties high levels of nitrosamines have been found in the urine of most patients examined [256]. Clinically significant levels probably only occur in chronically infected reservoirs [257]. Biopsies of the ileal and colonic segments showed changes similar to those that have been found in ileal and colonic conduits and in ureterosigmoidostomies. More severe histological changes and higher levels of nitrosamines correlated with heavy mixed bacterial growth on urine culture [258].

In a review by Filmer et al, 14 cases of pouch neoplasm were identified (259). Special features could be found in nearly all the cases. Ten patients had been reconstructed for tuberculosis; four tumors were not adenocarcinomas; one patient had a pre-existing carcinoma; six patients were over 50 years old. Cancer was found in bowel reservoirs at a mean of 18 years from formation. This is a few years earlier than the mean time at which malignant neoplasms are seen in ureterosigmoidostomies.

In a review of 260 patients with a follow-up of more than 10 years, Soergel et al found 3 malignancies (all transitional cell carcinoma): 2 following ileocecal and 1 after cecal augmentation. The age at augmentation was 8, 20 and 24 years respectively: the tumors were found when they were 29, 37 and 44 years old. All had metastatic desease and died. The incidence of malignancy in this group was 1.2%: considering that the development of tumors usually takes 20-25 years the probable incidence of malignancy following enterocystoplasty may be as high as 3.8 % [260].

Patients who undergo bladder augmentation with a gastric remnant are at increased risk for malignancy, probably similar to that in patients with enterocystoplasty. In a review of 119 patients underwent augmentation cystoplasty with stomach in 2 institutions, three patients had gastric adenocarcinoma, while the

other had poorly differentiated transitional cell carcinoma. Each case progressed to malignancy more than 10 years after augmentation [261,262,263].

If cancer is going to be a common problem, there will be some difficulty in monitoring the patients at risk [264]. Endoscopy with a small instrument through a stoma may not be sufficient. Ultrasound may not be able to distinguish between tumors and folds of mucosa. Three dimensional reconstruction of computerised tomography may be helpful, though the equipment is expensive and not widely available at present (265). At present it is advised to perform an annual endoscopic evaluation in all patients following enterocystoplasty starting 10 years after surgery.

10. PSYCHOLOGICAL CONSEQUENCES AND QUALITY OF LIFE

The main justification for performing a bladder reconstruction or continent diversion is to improve the individual's Quality of Life (QoL).

It would seem logical that continent urinary diversion would be better than a bag. This is not always the case. In adults the only sure advantage is cosmetic. Validated QoL surveys in children have not been reported, primarily because of the lack of suitable instruments [266]. Our prejudice is that reconstruction does, indeed, improve the lives of children. Supporting evidence is very thin and based on experience in adults.

The ileal conduit has been a standard part of urological surgery for over 50 years. It has well known complications but few would seriously suggest that they were more troublesome than those of the complex operations for bladder replacement. In an early investigation into quality of life issues, Boyd et al investigated 200 patients, half with an ileal conduit and half with a Kock pouch: there was little difference between the groups except that those with a Kock pouch engaged in more physical and sexual contact. The only patients that were consistently 'happier' were those who had had a conduit and subsequently were converted to a Kock pouch [267].

In a recent QoL survey in adults, a wide range of complications were considered to be acceptable, although an ordinary urological clinic would be full of patients trying to get rid of such symptoms: mild incontinence (50%), nocturia (37%), bladder stones (12%), urinary infections (9%), hydronephrosis (5%). Nonetheless, their QOL was judged to be good, primarily because 70% had experienced no adverse effect on their normal daily lives [268].

Quality of life does not mean absence of disease or a level of complications acceptable to the reviewing clinician. It is a difficult concept to measure because lack of validated instruments, difficulties in translating from one culture or language to another, of the difficulties in selecting control groups and variations in clinical situations. Gerharz et al have constructed their own 102 item instrument and compared 61 patients with a continent diversion and 131 with an ileal conduit. Patients with a continent diversion did better in all stoma related items indicating that containment of urine within the body and voluntary emptying is of major importance.

In addition they had better physical strength, mental capacity, social competence and used their leisure time more actively. There was little difference in satisfaction with professional life, financial circumstances and in all interactions within the family including sexual activity [269].

CONSENSUS STATEMENT ON SURGICAL TREATMENT OF URINARY INCONTINENCE IN CHILDREN

Forms of urinary incontinence in children are widely diverse, however, a detailed history and physical and voiding diary obviate the need for further studies. These should identify that limited group that may require surgery. Many patients in this group will have obvious severe congenital abnormalities.

Because of the spectrum of problems the specific treatment is usually dictated by the expertise and training of the treating physician. The rarity of many of these problems precludes the likelihood of any surgeon having expertise in all areas. Furthermore, nuances in surgical procedures develop gradually and often are tested without rigorous statistics.

Nevertheless it may be that newer forms of very early aggressive surgical approach to severe complex anomalies such as exstrophy, myelodysplasia and urethral valves may provide a successful model for significant impact on the ultimate continence in such patients. Ultimately this may provide a basis for randomized studies to determine the most specific and effective mode of therapy.

The committee would encourage vigorous research in the molecular basis of bladder development and also support the development of surgical and treatment strategies which would utilize the natural ability of the bladder to transform in the early months of development and immediately after birth. Furthermore efforts to promote bladder healing, and protecting and achieving normal bladder function should be supported. Such studies and research may lead to earlier and more aggressive treatment of many of the complex anomalies now treated by the surgical procedures outlined in this report.

G. PSYCHOLOGICAL ASPECTS OF URINARY INCONTINENCE, ENURESIS AND FAECAL INCONTINENCE

Since the publication of the ICI report in 2005 [1] an increasing body of studies have been published on psychological factors of incontinence in children including some comprehensive reviews [2-7]. This part makes an update based on the recent literature.

I. INTRODUCTION

Children with urinary incontinence, enuresis and faecal incontinence carry a higher risk for manifest behavioural disorders, as well as for subclinical emotional and behavioural symptoms. It is important to assess and integrate psychological factors in treatment for two reasons:

1. As can be seen in the next **table 3**, the rate of comorbid behavioural and emotional disorders is much higher than possible organic causes [7]. The same care used to exclude organic causes should be applied to the assessment of behavioural aspects. Therefore, even paediatricians and urologists should have a basic understanding of psychological principles in order to treat their young patients adequately.

2. In functional elimination disorders, provision of information, cognitive therapy and behavioural modification are the most effective, first-line approaches to treatment. Medication can be helpful in many cases, but are usually not the mainstay of treatment. Surgery is rarely indicated. As most of

*Table 3. Organic causes and comorbidity of clinically relevant psychological disorders or symptom scores**

Nocturnal enuresis	
Organic causes	< 1%
Behavioural comorbidity*	20-30%
Urinary incontinence	
Organic causes	<10%
Behavioural comorbidity*	20-40%
Faecal incontinence with constipation	
Organic causes	< 5%
Behavioural comorbidity*	30-50%
Faecal incontinence without constipation	
Organic causes	< 1%
Behavioural comorbidity*	30-50%

* Comparable norms: 10%

the techniques used in "urotherapy" are based on cognitive-behavioural psychotherapy, it is, again, essential be acquainted with the basic psychological principles.

The aim of this chapter is to provide information on comorbid manifest clinical disorders, as well as symptoms which might be emotionally distressing for children and parents, but do fulfil the criteria for a disorder. Often, these will resolve upon attaining continence, while manifest disorders usually do not. In addition, children with psychological disorders are less compliant, so that the failure rate of the incontinence treatment is much higher. Therefore it is recommended that both incontinence and any comorbid psychological disorder need to be treated separately to ensure effective therapy.

Also, the relevance of psychological factors for the different subtypes of incontinence will be considered. The terminology of the ICCS for enuresis and urinary incontinence (8) as well as of the Rome-III classification (9) for faecal incontinence will be used.

II. CLINICAL BEHAVIOURAL DISORDERS

The rate of clinically relevant behavioural disorders in children and adolescents lies between 12.0% (ICD-10 criteria) [10] and 14.3% (DSM-IV) [11,12]. The rate of comorbid behavioural disorders is definitely increased in children with all types of incontinence. Comorbidity denotes the co-occurrence of two or more disorders at the same time (concurrent comorbidity) or in sequence (sequential comorbidity). The focus on comorbidity allows a descriptive approach without making reference to possible causal associations. Basically, four combinations are possible:

- A behavioural disorder can be a consequence of the wetting problem
- A behavioural disorder can precede and induce a relapse when a genetic disposition for enuresis is present, for example in secondary nocturnal enuresis
- Wetting and a behavioural disorder can both be due to a common neurobiological dysfunction (such as in nocturnal enuresis and ADHD)
- and finally, with such common disorders, no causal relationship can be present and the two may co-exist by chance.

Psychological disorders (synonyms: psychiatric, psychic, mental disturbances) indicate that there is "a clinically significant behavioural or psychological syndrome or pattern (not a variant of normal behaviour) that occurs in an individual, that it is associated with present distress, disability or impairment and carries a risk for the future development of the individual" (DSM-IV) [11].

Clinically relevant disorders can be assessed by two basic methods: the categorical and the dimensional approach. The categorical method is based on a detailed diagnostic process (including: history, observation, exploration, mental state examination, questionnaires, testing, physical examination and other procedures) and are professional diagnosis according to standardised classification schemes: ICD-10 [10] or DSM-IV [11]. Dimensional assessment is based on symptom scores by questionnaires, but do not represent diagnoses. Cut-offs are defined to delineate a clinical (and sub-clinical) range.

One can differentiate externalising or behavioural disorders with outwardly-directed, visible behaviour (examples: conduct disorders, ADHD, etc.); internalising, i.e. inwardly-directed, intrapsychic disorders such as emotional disorders (examples: separation anxiety, social anxiety, phobias, sibling rivalry, depressive disorders, etc.); and other disorders that do not fit into the two categories, such as anorexia nervosa, tic disorders, autistic syndromes, etc.

III. CLINICAL BEHAVIORAL DISORDERS IN CHILDREN WITH ENURESIS/ URINARY INCONTINENCE

Children with urinary incontinence show a higher rate of comorbid behavioural and emotional problems than non-wetting children – in both epidemiological and in clinical studies. The overall relative risk is 1.4 – 4.5 times higher (**table 4**) [7].

1. EPIDEMIOLOGICAL STUDIES

Epidemiological studies have the advantage of revealing representative associations. They often cannot differentiate well between subgroups

Not all epidemiological studies on enuresis actually assess behavioural problems in a standardised form [13]. Therefore, only those studies that clearly define the group of clinically deviant children shall be reported in table 2. If a control group is reported, the relative risk for a behavioural problem can be calculated; otherwise the normative data is used.

a) Nocturnal enuresis

In the Isle-of Wight study, 25%-28% of enuretics were seen by their parents to show problematic behaviour according to the Rutter Child Scale – 3-4 times more often than the controls [14]. Using the same instrument, the longitudinal Study from Christchurch (New Zealand) came to similar rates for the primary children with nocturnal enuresis, while the secondary children with nocturnal enuresis showed a much higher rate of 52% [15]. The same study assessed rates of DSM-III diagnoses at a later age – with marked differences between the primary and the secondary children with nocturnal enuresis [16].

In the Dutch study by Hirasing et al [18] 23% of children with enuresis scored in the clinical range of the CBCL total problem scale. In the cross-sectional Chinese study by Liu et al [17] a third of all wetting children were in the clinical range – 3.6-4.5 more often than the controls. The US-Study by Byrd et al [12] used the 32-item-BPI (Behavior Problem Index), which is modelled after CBCL. The rates are lower than in the other studies, but included infrequent wetters of as few as one wetting episode per year.

In summary, the epidemiological studies show clearly that, depending on definitions and instruments used, 20-30% of all **nocturnal enuretic children** show clinically relevant behavioural problems – 2 to 4 times higher than non-wetting children.

Children with **primary nocturnal enuresis** were not more deviant than controls in epidemiological studies [16]. **Secondary nocturnal enuresis** was preceded by a higher rate of weighted life-events [20] and was significantly associated with a higher rate of DSM-III psychiatric disorders, which can persist into adolescence [16]. By adolescence, the attainment of dryness after the age of 10 years increased the risk for behavioural problems - independently of the primary or secondary status [13].

The only epidemiological study addressing monosymptomatic nocturnal enuresis included 8242 children aged 7,5 years [21]. Though not adhering to the ICCS criteria, children with **monosymptomatic nocturnal enuresis** showed fewer behavioural symptoms than those with daytime problems (i.e. the non-monosymptomatic forms) – although the differences did not reach significance.

b) urinary incontinence (daytime wetting)

Daytime wetting has been neglected in epidemiological research. Only recently, the first study was published based on a cohort of 8213 children aged 7,5 to 9 years [19]. Children with daytime wetting had significantly increased rates of psychological problems, especially separation anxiety (11.4%), attention deficit (24.8%), oppositional behaviour (10.9%) and conduct problems (11.8%). In other words, externalising disorders predominate in daytime wetting children which, in turn, will interfere with treatment. In the same cohort, 10000 children aged 4 to 9 years were analysed. Delayed development, difficult temperament and maternal depression/anxiety were associated with daytime wetting and soiling [22].

2. CLINICAL STUDIES

Clinical studies are limited by selection biases, but allow a much more detailed assessment of patients. Overall, children with nocturnal enuresis have lower rates of comorbid disorders (33.6%) than children with daytime wetting (52.6%) (23). In another study, the rates were 29% and 46%, respectively [24]. Van

Table 4. Epidemiological studies: Percentage of children with clinically relevant behavioural problems in comparison to controls and their relative risk*

Study	Age (years)	N	Type of wetting	Incontinent children	Controls	Relative risk
				Rutter Child Scale; cut-off>13		
Rutter 1973 [14]	5-14	4481	NW/DW	Boys: 25.6% Girls: 28.6%	7.9% 7.8%	3.2 3.7
McGee 1984 [15]	7-9	1037	NW	Primary: 30.8% Secondary: 51.9% DSM-III diagnoses	21.6%	1.4 2.4
Feehan 1990 [16]	11-15	1037	NW	Total: 23.4% Primary: 0% Secondary: 42.3% CBCL Total > 90th p.	9.5%	2.5 4.5
Liu 2000 [17]	6-18	3344	NW	30.3%	9.1%	4.3
Hirasing 1997[18]	9	1652	NW	23.0% BPI > 90th p.	10.0%	2.3
Byrd 1996 [12]	5-17	10960	NW	16.5% DAWBA	10.2%	1.6 Odd's ratio
Joinson 2006 [19]	7-9	8213	DW	Separation anxiety: 11.4% Attention/activity: 24.8% Oppositional behaviour : 10.9% Conduct problems: 11.8%	6.8% 13.8% 5.8% 6.2%	1.8 2.1 2.0 2.0

*NW = night wetting (nocturnal enuresis) *DW = daytime wetting (urinary incontinence)

Hoecke et al. [25] could also show that children with daytime wetting (or combined DW/NW) had significantly higher CBCL total problem scores than pure nocturnal enuretics or controls (**Table 5**).

a) Nocturnal enuresis

In an early study of Berg et al [26] nearly 30% of children presented in a paediatric department clinic were deemed "clinically disturbed". In another study in a paediatric setting, similar rates of 26% were found 20 years later using the CBCL [27]. These rates are almost identical to our own studies in a child psychiatric setting using the same instruments [23]. The rates of a selected group of treatment-resistant children with nocturnal enuresis undergoing Dry Bed Training were 2.2 times higher [28]. In the study of Van Hoecke et al [29], internalizing symptoms predominated in a mixed group of day and night wetting children with significantly higher scores for withdrawal, physical complaints, anxious/depressed, social problems and internalising behaviour scales compared to controls.

According to the ICCS terminology, four subgroups of nocturnal enuresis can be differentiated:

• primary monosymptomatic nocturnal enuresis

• primary non-monosymptomatic nocturnal enuresis

• secondary monosymptomatic nocturnal enuresis

• secondary non-monosymptomatic nocturnal enuresis

Regarding the subtypes of nocturnal enuresis, children with primary nocturnal enuresis showed behavioural problems less frequently (19.5%) than those with the secondary type (75.0%) [23]. The group with the lowest comorbidity – no higher than in the normative population – were those with monosymptomatic nocturnal enuresis (10.0%) without any daytime symptoms such as urge, postponement or dysfunctional voiding. In a replication study, 29% of children with nocturnal enuresis had at least one ICD-10 diagnosis – 24% of those with monosymptomatic and 33% of those with non-monosymptomatic nocturnal enuresis [24].

Regarding the types of behavioural and emotional disorders, externalising disorders predominate [23]. The most specific comorbid disorders with enuresis are ADHD (according to DSM-IV) or the Hyperkinetic Syndrome (according to ICD-10). In our own studies, the rates ranged from 9.3% (HKS) to 13.5% (HKS and ADHD) [23, 31]. ADHD is not associated with any specific type of nocturnal enuresis [30].

In a retrospective study, of patients with ADHD, 20.9% wetted at night and 6.5% during the day. The odds-ratios were 2.7 and 4.5 times higher, respectively, which means that there is unspecific association of ADHD and both night/ daytime wetting [32]. 25% of

Table 5. Clinical studies: Percentage of children with clinically relevant behavioural problems in comparison to controls and their relative risk*

Study	Age (years)	N	Type of wetting	Incontinent children	Controls	Relative risk
				ICD-10 diagnoses		
von Gontard 1999 [23]	5-11	110	NW	33.6%	12.0%	2.8
von Gontard 1999 [23]	5-11	57	DW	52.6%	12.0%	4.4
Zink 2008 [24]	5-16	97	NW	29%	12.0%	2.4
	5-16	69	DW	46%	12.0%	3.8
				Rutter A questionnaire, cut off > 18 (interview)		
Berg 1981 [26]	6-13	41	NW	29.3% (26.8%)		
				CBCL Total >90th p.		
Baeyens 2001 [27]	6-12	100	NW/DW	26%	10.0%	2.6
von Gontard 1999 [23]	5-11	167	NW/DW	28.2%	10%	2.8
Hirasing 2002 [28]	6-15	91	NW	21%	10%	2.1
Van Hoecke 2004 [29]	9-12	84	NW/DW	20.4%	6.1%	3.3
Zink 2008 [24]	5-16	166	NW/DW	40%	10%	4.0

*NW = night wetting (nocturnal enuresis)

*DW = daytime wetting (urinary incontinence)

140 children with ADHD were affected by nocturnal enuresis compared to 10.8% of 120 controls [33]. The highest comorbidity rates of 40% for ADHD and nocturnal enuresis were reported by Baeyens et al. [30], possibly due to selection effects. 15% had a combined, 22.5% an inattentive and only 2.5% a hyperactive type of ADHD. In a community based sample, the prevalence rate was much lower [34]. ADHD continued to be present in 72.5% of children in a two-year follow-up indicating a high stability [34]. Children with ADHD continued to wet at follow-up much more often (65%) than controls (37%) (Odds-ratio 3.17) [34]. At a 4-year follow-up, 64% still had ADHD. Of these, 42% continued to wet at night (compared to 37% of the controls) [35].

In clinical practice, children with ADHD are more difficult to treat. In a retrospective study, 113 children with ADHD and nocturnal enuresis had a far worse outcome on alarm treatment than controls (with nocturnal enuresis only): 43% (vs. 69%) were dry at 6 months and 19% (vs. 66%) at 12 months. There was no difference if they were treated with medication, which does not require active cooperation. Non-compliance was reported in 38% of child with ADHD, but only in 22% of the controls [36]. Therefore, the comorbid diagnoses of both enuresis and ADHD require special attention – and both need to be treated separately.

b) Urinary incontinence (daytime wetting)

Far fewer studies have addressed the specific problems of daytime wetting children. In a study in a paediatric setting of 418 children aged 5 – 17 years, day wetting children were described as being more stubborn, oppositional and secretive than nocturnal enuretic children [37].

In a subgroup of 58 children, those with and without urinary tract infections were compared. 11 % of day wetting children with urinary tract infections had a CBCL total score in the clinical range, 35 % of day wetting children without urinary tract infections and 16 % of nocturnal wetters. In other words, the subgroup with a higher risk for behavioural problems were day wetting children without urinary tract infections [37]. In another study, 90 girls with recurrent UTI's had significantly more behavioural abnormalities than controls [38], so that the issue of behavioural problems in children with and without UTI's remains to be settled.

ADHD is a common problem among day wetting children, as well. Compared to controls, children with ADHD had more symptoms of incontinence, constipation, infrequent voiding and dysuria [39]. With ADHD, treatment outcome is worse. In a retrospective analysis, 68% of day wetting children with ADHD became dry compared to 91% of controls. Non-compliance was much higher for timed voiding [36].

Daytime wetting (urinary incontinence) is a heterogeneous group of disorders. According to the ICCS terminology, following subgroups can be differentiated [8].

• Over-active bladder including urgency incontinence

• Voiding postponement

• Underactive detrusor

• Dysfunctional voiding

• Obstruction

• Stress incontinence

• Vaginal reflux

• Giggle incontinence

• Extraordinary daytime urinary frequency

Only some of these subgroups have been studied regarding comorbid psychological disorders.

Children with **urgency incontinence** have previously been considered to have few behavioural problems [40]. 29 % of children with urgency incontinence had an ICD-10 diagnosis and 14% had an internalizing disorder. 13.5 % had a clinical total problem score in the CBCL – again mainly internalizing problems [41, 42]. The children are distressed by their wetting and family functioning is intact [42]. In a new study, 35% of children with urgency incontinence fulfilled the criteria for an ICD-10 diagnosis [24]. In summary, children with urgency incontinence have only a slightly increased rate of comorbid psychiatric disorders. If they are affected, emotional, introversive symptoms predominate.

Children with **voiding postponement**, on the other hand, fall into two groups: in some it represents an acquired habit, in others, it is associated with externalising psychological disorders, especially oppositional defiant disorder (ODD). In a systematic study of children with voiding postponement in a paediatric and child psychiatric setting, 53.8 % fulfilled the criteria for at least one ICD-10 diagnosis [41]. These were mainly externalizing disorders in a third of all children such as Oppositional Defiant Disorder (ODD). Also, 37.3 % of children had a CBCL total score in the clinical range, again, with externalizing symptoms predominating. In addition, family functioning was impaired [41,42]. In a new sample, 53% of children with voiding postponement had at least one ICD-10 diagnosis [24]. In summary, children with voiding postponement have highly increased psychiatric risks.

Systematic studies on comorbid behavioural problems in children with underactive bladder **have not been performed, although by clinical impression the rate of associated problems is high. In the original article, the "lazy bladder syndrome" was described as an acquired behaviour: it has "developed from the habitual neglect of the patient to empty the bladder on getting the urge to micturate" [43].**

Systematic investigations of psychological aspects of **dysfunctional voiding** are rare. Again, in some children it represents an acquired habit, in others severe psychological disturbances are present [44]. Also, dysfunctional voiding following severe sexual abuse and deprivation as well as other familial stressors such as migration has been described in case reports [45].

There have been no systematic investigations of children with **giggle incontinence**. From clinical experience, they are highly distressed by the symptom and try to avoid situations in which they might be forced to laugh. Social withdrawal, not going to parties and meeting with friends have been observed. It is not known if the rate of behavioural disorders is increased, however.

Regarding the **other subtypes of urinary incontinence**, not even anecdotal data is available.

IV. CLINICAL BEHAVIORAL DISORDERS IN CHILDREN WITH FECAL INCONTINENCE (FAECAL INCONTINENCE)

According to the Rome-III classification, two subtypes of faecal incontinence can be differentiated [9]:

• Functional constipation (with or without incontinence)

• Nonretentive fecal incontinence.

1. EPIDEMIOLOGICAL STUDIES

In the large Alspac study of 8242 children aged 7-8 years, children with faecal incontinence had significantly increased rates of separation anxiety, specific phobias, generalised anxiety, ADHD and ODD (**Table 6**) [46]. In other words, soiling children show a completely heterogeneous pattern of both internalising and externalising disorders. Again, these will require assessment in the individual child, as they will interfere with treatment of the incontinence.

2. CLINICAL STUDIES

As many studies have used the Child Behaviour Check List (CBCL) [47], the results can be compared easily. As shown in table 4, 35% to 50% of all children with faecal incontinence had a total behavioural score in the clinical range in this parental questionnaire. Compared to the normative population (10%), 3.5 to 5 times more children with faecal incontinence have total behaviour scores in the clinical range. As all studies were conducted in a paediatric setting, this rate

Table 6. Epidemiological and clinical studies: Percentage of children with clinically relevant behavioural problems in comparison to controls and their relative risk *

Study	Age (years)	N	Type of faecal incontinence	Incontinent children	Controls	Relative risk
Epidemiological studies				DAWBA		
Joinson 2006 [46]	7-8	8242	Not specified	Separation anxiety: 4.3%	0.8%	5.4
				Specific phobia: 4.3%	1.0%	4.3
				Generalised anxiety: 3.4%	0.4%	8.5
				ADHD: 9.2%	1.9%	4.8
				ODD: 11.9%	1.9%	6.3
Clinical studies				CBCL Total >90th p.		
Gabel 1986 [49]	6-11	55	Not specified	49%	10.0%	4.9
Young 1995 [50]	5-17	76	Not specified	51%	10.0%	5.1
Nolan 1991 [48]	4-16	169	Not specified	43%	10.0%	4.3
Loening-Baucke 1987 [51]	6-11	38	Functional constipation	42%	10.0%	4.2
Benninga 1994 [52]	5-17	111	Functional constipation	39%	10.0%	3.9
Benninga 2004 [53]	5-17	135	Functional constipation	37%	10.0%	3.7
Benninga 1994 [52]	5-17	50	Nonretentive faecal incontinence	44%	10.0%	4.4
Van der Plas 1997	5-17	71	Nonretentive faecal incontinence	35%	10.0%	3.5
Benninga 2004 [53]	5-17	56	Nonretentive faecal incontinence	39%	10.0%	3.9

cannot be due to selection effects of mental health clinics. Children with behavioural maladjustment are less compliant than children without psychological disorders (71% vs. 38% non-compliant) – so if these problems are not addressed treatment will be less successful [48].

Encopretic children with constipation have the same rate of behavioural scores in the clinical range as children without constipation (39% vs. 44%, Benninga et al 1994; and 37% vs. 39%, Benninga et al., 2004). In other words, the two major types of faecal incontinence cannot be differentiated according to the behavioural comorbidity. More importantly, regarding the aetiology, there's no evidence that one type (i.e. with constipation) has more somatic, while the other type (i.e. without constipation) a more psychogenic aetiology. Also, there is no specific psychopathology typical for faecal incontinence – all

types of behavioural and emotional disorders can co-exist.

Internalising clinical behavioural scores (32%) were twice as common as externalizing ones (17%) in one study (54). In others, single behavioural items, denoting oppositional behaviour and attentional problems predominate [49, 55]. Compared to controls, children with faecal incontinence rated significantly higher regarding anxious/depressed behaviour, attentional difficulties and disruptive behaviour on the CBCL subscales. For example, the rate of children with attentional problems in the clinical and borderline range was 6-7 times higher than in controls (20% vs. 3%; norms 5%) [56]. Again, the heterogeneity of behavioural symptoms is apparent.

Only few studies have assessed behavioural and emotional disorders according to standardized child psychiatric criteria. They also show a high general

rate and heterogeneity of comorbid disorders. Thus, 34% of 41 children with faecal incontinence had an emotional disorder, 12% a conduct disorder and 10% a hyperkinetic syndrome according to ICD-criteria [57]. In another study of highly selected 85 child psychiatric inpatients with faecal incontinence, 83 % fulfilled the criteria for at least one ICD-10-diagnosis. 32% had a hyperkinetic syndrome, 21% an emotional disorder and 9% a conduct disorder [58]. Children with faecal incontinence and urinary incontinence have an even higher rate of behavioural and emotional disorders than children with wetting problems alone [59].

The co-occurrence of faecal incontinence and sexual abuse has been described by several authors [60]. In one study, 36% of abused boys had faecal incontinence [61], but other symptoms can co-exist [62,63]. However, in a retrospective analysis of 466 children having experienced sexual abuse, 429 children with externalising disorders and 641 controls, the occurrence of faecal incontinence did not differ between groups (faecal incontinence in 10.3%, 10.5% and 2%, respectively) (64).

V. SUBCLINICAL SIGNS AND SYMPTOMS

Subclinical behavioural signs and symptoms are common, understandable, adequate reactions towards the wetting problem and not disorders. Many studies have addressed the impact of wetting on children.

1. IMPACT ON CHILDREN

Most children are distressed by enuresis. For example, 35% said that they felt unhappy, 25% even very unhappy about wetting at night in one study (40 children aged 5-15 years) [65]. In a Finnish population-based study, 156 day and night wetting children (from 3375 7-year olds) showed significant differences compared to 170 controls regarding following personality traits [66]: they were more fitful (vs. peaceful), more fearful (vs. courageous), more impatient (vs. calm), more anxious (vs. does not worry) and had more inferiority feelings (vs. feels equal). In a large population-based British study of 8209 children aged 9 years, 36.7% of children consider bed-wetting to be "really difficult" – ranking 8th behind other stressful life-events [67].

In a clinical study, 70.3% of day and night wetting children aged 5 to 11 years could clearly indicate that the wetting was of disadvantage [68]. The types of disadvantages or negative consequences were: social (I can't sleep at friends' house, friends can't stay over night – in 32.1%), affective (I feel sad, ashamed, annoyed – in 16.4%), of isolation (I feel like a baby, nobody is allowed to know about it, I feel different from other children – in 6.7%), of sensation (it feels

unpleasant, cold, wet, itchy, nasty – in 32.1%) or referred to direct consequences (I have to take a shower, sleep in pampers, won't get a bicycle – in 17.6%). Only 4.9% reported any advantages of the wetting at all (I like the wet feeling, get more attention from mother).

One construct of special importance is that of **self-esteem**. In one study, lower self-esteem in children with enuresis disappeared upon attaining dryness [69]. In another, global self-esteem was significantly lower in children with nocturnal enuresis than in controls [70] and in yet another, the self-esteem total score was higher among enuretics than norms [71]. Therefore, it was concluded that there is no clear evidence that bedwetting leads to lower self-esteem [72] – but there can be no doubt that self-esteem can improve upon attaining dryness [71]. Self-esteem even increases even if treatment of enuresis is not successful [73], showing that care and "good doctoring" for children and parents is of great help – regardless of outcome. Recently, a focus has been on **quality of life**, which is reduced in children with urinary incontinence [74].

In a population-based study of 75 boys with **faecal incontinence** were compared to 73 matched controls as shown in table 16.9 [75]. Specifically, encopretic boys showed higher rates of food refusal, general negativism, strong anxiety reactions, lack of self-insurance, poor tolerance to stress, both inhibited and aggressive behaviour, a strong fixation to their mother and difficulties in relationships. Also, children with faecal incontinence tended to feel less in control of positive life events and had a lower sense of self-esteem than children with other chronic conditions [76]. However, in a more recent study, self-esteem did not differ between children with faecal incontinence and controls on the Piers-Harris questionnaire [77]. Although some of these subclinical symptoms will diminish under successful treatment [53,54], it is not known which ones will persist and chronify.

2. IMPACT ON PARENTS

Enuresis and urinary incontinence may be just as distressing for parents as for children. Generally, parents are very concerned about the welfare of their child. In a population based study, 17% worried a great deal and 46% some or a little [78]. In one study, the greatest maternal concerns were: emotional impact, social relationships, smell, extra washing and financial aspects [79]. Mothers of children with nocturnal enuresis had a reduced quality of life scores (bodily pain and emotional role) and more depressive symptoms [80].

Parents also believe that their child should be dry at a very early age, which can induce anxiety and stress: the mean anticipated age of dryness was 3.18 years in one study [81] and 2.75 years in another [82]. Also,

many parents think that emotional factors are the cause of nocturnal enuresis and forget that they might be the effect of the wetting problem instead [81,82].

A minority of parents show an attitude that was described as "maternal intolerance" by Butler et al [79]. Convinced that their child is wetting on purpose, the risk for punishment is increased. The reported rates of punishment varied from 37% [85], 35.8% [81], 23% [82] to 5.6% [84]. In other cultures, punishment is even more common: 42% of Turkish children were spanked and 13% beaten [85]. Chinese parents show a high level of parenting stress associated with externalising behavioural problems or their child [86]. These parental attributions and experiences have to be taken into account in all treatment plans for enuresis, as they can decisively influence the outcome.

Parents of children with **faecal incontinence** are also stressed and worried the problem (87). In one study, children with faecal incontinence had family environments with less expressiveness and poorer organisation than controls (77). In another study of 104 families, nearly half (51%) had no unusual family problems; 23 had severe and widespread difficulties including sexual abuse; 11 families described moderate difficulties and 18 a single traumatic event [88]. In other words, the atmosphere was warm and supportive without major difficulties in at least half of the families.

VI. GENERAL PRINCIPLES: ASSESSMENT

1. SCREENING QUESTIONNAIRES

Due to this high comorbidity of psychological symptoms as well as disturbances, every child should be screened as part of the routine assessment. The best screening instrument is still a good history and careful clinical observation, which requires some training and experience. The second best approach is screening questionnaires, such as the Child Behavior Check List (CBCL) [47], which contains 113 empirically derived behavioural items. These are checked on a three-point scale and are formulated in simple wording. From these items, eight specific syndrome scales and three general scales can be calculated.

Recently, even shorter screening instruments have been derived from the CBCL. Thus, Van Hoecke et al. (89) validated a short questionnaire consisting of 7 items for emotional problems, 3 for attention problems and 3 for hyperactivity/impulsivity. This is an extremely useful short questionnaire both for clinical and research uses.

Also, other useful questionnaires addressing specific aspects of **enuresis** have been developed [90]. These assess the subjective views and attributions of parents and children, such as parental intolerance. Another

potentially useful questionnaire addresses aspects of everyday burden of enuresis on children and their families [91]. Other non-validated questionnaires for the assessment of children with all types of incontinence can be found in von Gontard and Neveus [8]. For children with **faecal incontinence**, the Virginia-Faecal incontinence-Constipation-Apperception Test (VECAT), a validated, picture-based questionnaire for children and parents was shown to differentiate well regarding bowel-specific problems [92].

One construct of special interest in children with elimination disorders is that of **self esteem**.

Well-known self-esteem questionnaires include the Piers-Harris Children's self – concept scale [93] as well as others [94]. Another important construct is that of health related **quality of life** (HQOL). This is a complex construct that tries to assess health related wellbeing in different domains of daily life. Generic HQOL questionnaires allow comparison between children with different medical disorders [95,96]. These range from short screening to longer, more detailed questionnaires (such as the KINDL-questionnaire) [97]. Recently, the first specific quality of life questionnaire for children with wetting problems was developed by Bower et al. [98]. These have the advantage that the specific, elimination-related effects on daily life can be assessed. For children with faecal incontinence, health-related quality of life questionnaire with good psychometric properties was described. The Defecation Disorder List (DDL) consists of 37 items and can be used in children with all types of faecal incontinence and/or constipation [99].

2. CHILD PSYCHIATRIC ASSESSMENT

A child psychiatric assessment is a professional procedure with the goal to come to a categorical decision: to see if a diagnosis according to the standardised classification schemes (ICD-10 or DSM-IV) is present in the child or not.

The first step is a detailed developmental, behavioural and family history in much greater detail than provided in the outline in the appendix. The next step is to observe the child as well as the parent-child-interaction, followed by an active exploration of the child. The information gained from history, observation and exploration forms the basis of the mental state examination. This is a descriptive, phenomenological assessment of mental and behavioural signs and symptoms (for example: CASCAP-D) [100].

Questionnaires are always an essential part of child psychiatric assessment. They are a time-economical way to gather information from different informants. They can contribute towards but do not provide a diagnosis. Behavioural questionnaires can again be divided into general and specific questionnaires. The best known, most widely used general parental questionnaire is the Child Behavior Check List, which

has been translated into many languages (CBCL/4-18) [47]. In the meantime, Achenbach and co-workers have produced a whole "family" of questionnaires for different age groups (infants, children – adolescents, young adults) and different informants (parents, teachers and for children themselves starting from age 11). In addition, other specific questionnaires address circumscribed areas such as depressive symptoms or ADHD problems.

An intelligence test is not routinely indicated in the assessment of children with elimination disorders, as the IQ is in the normal range for most children with wetting, as well as soiling problems. However, the rate of elimination disorders is clearly increased in children with general developmental disorders, with mental and physical handicap [101-103]. If a lower intelligence is suspected, one-dimensional tests (such as the CFT or CPM/SPM tests) or multidimensional tests such as the Kaufman or the Wechsler tests can be performed. If specific developmental disorders such as dyslexia or dyscalculia are suspected, specific tests for these circumscribed disorders are indicated. Disorders of speech or language (such as articulation, expressive and receptive speech disorders) require a detailed assessment by an audiologist and speech therapist.

Motor disorders can be assessed clinically by including soft neurological signs in the physical examination of children or by standardized tests such as the Zurich Motor Tests [104,105].

After the diagnostic process has been completed, the child's disorder is diagnosed according to standardized classification schemes. The two standard classification systems are the ICD-10 [10], which is widely used in Europe and in other parts of the world and the DSM-IV [11] employed in the United States. In child psychiatry, a multiaxial classification is used. Six different axes denoting different domains are used, including:

1. Axis: clinical psychiatric diagnosis (such as anorexia nervosa, depressive episodes, etc.)

2. Axis: specific developmental disorders (such as dyslexia)

3. Axis: intelligence (such as dyslexia, speech and motor disorders)

4. Axis: somatic diagnosis (such as epilepsy and other paediatric diagnoses)

5. Axis: psychosocial risks occurring within the last six months (such as distorted intrafamilial interaction, isolated family and other stressful life events)

6. Axis: the global severity of a disorder (ranging from mild incapacitation to disorders requiring constant supervision and guidance)

Only after the diagnostic process has been completed and discussed with parents and children, should therapeutic interventions be planned.

VII. GENERAL PRINCIPLES: TREATMENT OF PSYCHOLOGICAL DISORDER

For most children with elimination disorders, a symptom-oriented approach is sufficient. If, however, another, co-occurring child psychiatric disorder is present, additional types of treatment will be necessary. In these cases, a differential indication for therapy is mandatory. The question is: which treatment is most effective for this child in this family at this moment?

For some disorders (such as ADHD), medication plays a major role. For most others, psychotherapeutical interventions are the first-line treatment. There can be no doubt that psychotherapy in children is effective. In one of the best and largest meta-analysis of 150 studies, Weisz et al. [106] conclude that "psychotherapy with young people produces positive effects of respectable magnitude" (i.e. effect sizes in the medium to large range - 0.5 to 0.8). It has been estimated that over 500 different types of psychotherapies exist in the USA for children and adolescents alone [107]. Of those which have been evaluated, four basic schools of psychotherapy can be differentiated: 1. depth psychology (or psycho-analysis), which addresses and works with unconscious aspects of the psyche; 2. Client-(or child) centred-psychotherapy, which focuses on the current conscious experience of the child and the healing aspects of their therapeutic relationship; 3. Family therapy, which focuses on the interaction between family members but not the individual person; 4. Cognitive-behavioural therapy, focussing on cognitions and observable behaviour.

Before initiating any psychotherapy, a differential indication for therapy as to be made. The first basic question should be: is treatment needed at all? In many cases counselling of parents and child is all that is required. In other cases, changes in the child's environment (such as changing school) or help from social services can be more useful than psychological treatment in the narrower sense.

The modality has to be considered. Although parents are nearly always included, the focus can be on an individual, group or family therapy. The intensity and duration have to be addressed: is a short focal therapy focussed on one specific problem needed or a longer, more general treatment? The age of the patient plays an important role: while older children and adolescents can be reached verbally, younger children require play or other non-verbal media in their therapy.

Psychotherapies can be combined with other methods, such as pharmacotherapy, but also with speech, occupational, physio-, music- and other types of therapies – if indicated. The decision should no longer be based on personal inclinations. Instead, empirically based "practice parameters" or "guidelines" have been

developed in many countries. These interventions are usually performed on an out-patient basis. Day clinic treatment can be indicated in more severe disorders, which require a more intense approach and management. Finally, in-patient child psychiatric treatment is indicated in severe disorders, in which a more intense type of treatment is possible.

VIII. GENERAL PRINCIPLES: UROTHERAPY

A major part of therapy of incontinence in children is non-pharmacological and non-surgical. The term **urotherapy** is used in some countries. It is an umbrella term which has been defined as a "type of training which makes use of cortical control of the bladder, teaching children to recognize and employ conscious command over their lower urinary tract. Its main ingredients are information about normal lower urinary tract function and the specific dysfunction in the child, instruction about what to do about it and support and encouragement to go through with the training program" [108].

Although not a psychotherapy in a narrow sense, it employs many psychotherapeutical techniques borrowed especially from counselling and cognitive-behavioural therapies. As these approaches have been shown to be most effective, basic principles and findings shall be outlined.

1. UNSPECIFIC APPROACHES

The first step in any diagnostic and therapeutical process is to **create a good relationship** to both the child and the parent. One should enquire and talk about all relevant facts, signs and symptoms openly. It is also important to ask about the subjective meanings and connotations. Next, the **provision of information** is essential, because many facts are not known. It is often forgotten that not only parents but each child needs information, as well. This should be provided in words and concepts that a child understands and in a format that is attractive. Increasing motivation and alleviation of stress and guilt feelings are also part of all patient contacts.

2. COUNSELLING

Counselling is already part of the treatment process, which has been defined as the provision of assistance and guidance in resolving personal, social, or psychological difficulties. For many children, even with psychological disorders, counselling is, in fact, sufficient. Sometimes, it can be helpful to enhance the verbal counselling by other techniques. One simple technique is that of "demonstration", e.g. actively showing how an alarm works. In "coaching", parents and children take an even more active role, e.g. they set and activate an alarm themselves. They can be observed and corrected. Other techniques might include "modelling" and "role-playing". The learning effect is much greater in these active forms of teaching than in solely verbal counselling.

3. COGNITIVE-BEHAVIOURAL THERAPY

Cognitive-behavioural therapy (CBT) is a subtype of psychotherapy that has shown to be effective for many disorders. Cognitive therapy focuses on irrational, dysfunctional conditions, thoughts and beliefs. Cognitive therapy encompasses a whole variety of techniques such as "self-monitoring" (observation and registration), "activity scheduling" (organisation of activities) and "labelling" (using positive suggestive statements). Behavioural therapy concentrates on observable behaviour, which it aims to modify with a variety of techniques. These include "classical conditioning" and "operant conditioning", which basically means learning by success, which can be achieved by different strategies using positive or negative reinforcement.

4. BASELINE AND OBSERVATION

Baseline and **observation** are effective techniques used in cognitive-behavioural therapy. Children (and parents) are advised to observe a defined symptom. Different parameters such as frequency (how often it occurs), severity (how marked it is), symptomatology (in what form it occurs) and in which situation (associated factors) can be registered, e.g. in an observation chart. The mere observation and registration actually has a therapeutic effect and many symptoms actually diminish simply if they are observed.

In **nocturnal enuresis, c**hildren are asked to fill out a calendar or chart depicting the wet and the dry nights symbolically for two to four weeks [109,110]. These non-specific measures have been shown to be successful and are associated with fewer wet nights [3,111]. In one clinical trial, for example, 18% became dry after an 8-week baseline [112]. The authors of the recent Cochrane Review conclude that "simple methods could be tried as first line therapy before considering alarms or drugs, because these alternative treatments may be more demanding and may have adverse effects" [3, 5].

In **urgency incontinence**, the cognitive aspects are stressed in treatment: children are asked to register feelings of urgency, refrain from using holding manoeuvres, to void and register the voiding (or any wetting) in a chart [113,114]. For children with **voiding postponement**, timed voiding 7 times a day and registration in a chart is recommended [114].

For all children with **faecal incontinence**, stool regulation is an essential part of treatment. Children are asked to sit on the toilet three times a day after meal-times in a relaxed mode for five to ten minutes

[115]. This is documented in a chart and can be reinforced positively. In one study, 15 % of children were cured within six weeks by simple methods such as these [54]. If **constipation** is present and the large amount of faecal masses has accumulated, disimpaction has to be performed at the beginning of treatment. To avoid re-accumulation of faecal masses, maintenance therapy with oral laxatives (such as Polyethylenglycol) is recommended for at least six and up to twenty-four months [116]. The preferred oral laxatives are osmotic laxatives such as (PEG). "These behavioural interventions when used together with laxative therapy may improve continence" according to a Cochrane review of 18 RCT's and 1168 children [6] and other reviews [117].

5. BIOFEEDBACK

Biofeedback has been shown to be effective in some elimination disorders such as **dysfunctional voiding** [118]. It is defined as a variety of techniques, by which physiological activity is registered, enhanced and presented to the patient in real time by visual and acoustical signals [118]. In **faecal incontinence**, biofeedback is no more effective than standard behavioural techniques in faecal incontinence both with [119] and without constipation [120] and is not recommended in a systematic Cochrane Review [6].

6. ALARM TREATMENT

Alarm treatment for **nocturnal enuresis** is also a type of cognitive behavioural therapy. It worksby positive reinforcement, as well as aversive, negative experiences and has been shown to be highly effective and was introduced by Mowrer and Mowrer [121].

It is the most effective form of treatment of nocturnal enuresis with the best long-term results (grade I level of evidence according to reviews and meta-analyses). Houts et al. [122] compiled a systematic review and meta-analysis on 78 randomised studies on nocturnal enuresis. 62% were dry at the end of treatment and 47% at follow-up. The authors conclude that "urine alarm treatments should not only be considered the treatment of choice, but the evidence from this review suggests that cure rather than management is a realistic goal for the majority of children suffering from nocturnal enuresis".

Lister-Sharp et al [111] provided a systematic review, including only RCT's on nocturnal enuresis. The likelihood for 14 consecutive dry nights was13.3 times higher than without treatment. The authors conclude that "in the long term, alarm treatment would appear to be the most clinically effective and because the cost of drug therapy, also the most cost effective intervention". Mellon and McGrath's [123] compiled a systematic review on 70 well-controlled outcome studies. With a dryness rate of 77.9%, alarm treatment is deemed clearly efficacious. A comprehensive narrative review was written by Moffat [124] concluding

that "all the current evidence suggests that conditioning gives the best long-term outcomes for bed wetters". Finally, a Cochrane review of 50 RCT's involving 3257 children concluded: "Alarm interventions are an effective treatment for nocturnal enuresis. Alarms appear more effective than Desmopressin or tricyclics because around half of the children remain dry after alarm treatment stops" (2).

Therefore, when indicated, alarm has been endorsed as a first line treatment by multidisciplinary European [125], world-wide [126], German [110] and American child psychiatric guidelines [109], as well as various individual authors [127].

The effect of alarm treatment can be enhanced by adding additional behavioural components to the treatment. Programmes that include alarm in addition to other behavioural components showed following general effects: 72% of children became dry at the end of treatment, and 56% remained so at follow-up (meta-analysis) [122], so that combinations were considered as "probably effective" [123].

These specific programmes including alarm are all essentially cognitive-behavioural techniques. **Arousal training is** a simply and easily performed [128,129]. Children are instructed to turn off the alarm within three minutes, go to the toilet and reset the alarm. This goal is reinforced positively with two tokens. If the goal is not reached, one token has to be returned. The initial success rate (89 %) and the rate of dryness after 2 ? years (92 %) were higher than with alarm treatment alone (73 % and 72 % respectively) [128].

Dry Bed Training is a complicated program starting with an intensive night and maintenance treatment and using positive, as well as negative reinforcers [130]. Despite high success rates reported in early studies [130], recent meta analysis have shown that DBT is no more effective than alarm treatment alone [111]. The likelihood to attain 14 consecutive dry nights was 10 times higher than in controls without treatment – but not different from alarm treatment alone. Also, alarm is the most important component of DBT. DBT without alarm showed only a 2.5 times higher likelihood of attaining dryness than controls. The relapse rates were not improved by DBT compared to alarm treatment alone [111]. As it is a cumbersome treatment, it nowadays it is reserved for children and especially adolescents with therapy-resistant nocturnal enuresis, as it "may augment the effect of an alarm" and "might reduce the relapse rate" (3). Thus, Hirasing et al. [28] could show that behavioural problems were reduced in children with persistent nocturnal enuresis treated with DBT.

Other programmes include the **Full spectrum home treatment**. This is a combination package including a written contract, full arousal, overlearning and bladder retention exercises [122]. 78.5% of children became

dry in 2 studies [123], but the alarm exerts the main effect [3]. **Overlearning** is a relapse prevention programme: after attaining dryness, increasing fluids are given before sleep to stabilise the achieved effects [131]. The relapse rate could be reduced from 20-40% to 10% through this "provocation method".

Finally, alarm treatment can be combined with **pharmacotherapy**, although the evidence for combination treatment is conflicting. The combination of **desmopressin** and alarm treatment has been reported in several studies [132-135]. The combination with **anticholinergics** plays an important part in clinical practice, but has not been investigated systematically.

CONCLUSION AND SUMMARY

This review summarised the most important psychological aspects in children with enuresis, urinary incontinence and faecal incontinence.

The rate of comorbid clinical behavioural disorders is increased. Children with urinary incontinence are more affected than those with nocturnal enuresis. Children with secondary and non-monosymptomatic nocturnal enuresis have especially high rates of comorbid psychological disorders. The most common single diagnosis is ADHD.

Children with daytime wetting have mainly externalising behavioural disorders. Children with urgency incontinence have a low comorbidity, those with voiding postponement are characterised by oppositional behaviour. Children with faecal incontinence have the highest rate of associated disorders – both internalising and externalising.

These disorders will not disappear upon attaining dryness. They have to be addressed, as they will interfere with the incontinence therapy due to low compliance.

Even if comorbid disorders are not present, children and parents are highly stressed by the incontinence. These subclinical symptoms will often recede upon successful treatment.

Questionnaires are useful as screening instruments in the assessment process. If a psychological disorder is suspected, a full child psychiatric assessment and treatment or needed. The basic principles, including those of psychotherapy, are outlined. Psychothe-rapeutic techniques are used in urotherapy, especially cognitive-behavioural elements. Non-pharmacological and non-surgical techniques are most effective for most forms of incontinence based on systematic reviews. Therefore, it is important that psychological aspects are integrated into the treatment of children with incontinence problems.

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B. EVALUATION IN CHILDREN WHO WET

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D. CHILDREN WITH BOTH DAY AND NIGHT TIME INCONTINENCE

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