CHAPTER 16

Committee 11

Diagnosis and Management of Urinary Incontinence and Encopresis in Childhood

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A. INTRODUCTION

In this chapter the diagnostic and treatment modalities of urinary incontinence and encopresis 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 innervation which is ultimately controlled by a complex interaction between spinal cord, brain stem, midbrain and higher cortical structures [1].

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

In newborns the bladder has been traditionally described as "uninhibited", and it has been assumed that micturition occurs automatically by a simple spinal cord reflex, with little or no mediation by the higher neural centres. However, studies have indicated that even in full-term 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 H_2O, 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 urge to urinate, as well as social norms and embarrassment associated with urinary incontinence. Through an active learning process, the child acquires the ability to voluntarily inhibit and delay voiding until a socially convenient time, then actively 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 and not necessarily reflect normal bladder volumes. Obviously, the relation between age and bladder capacity is not linear for all ages, nor is the relation between body weight and bladder capacity [14].

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

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

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

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

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].

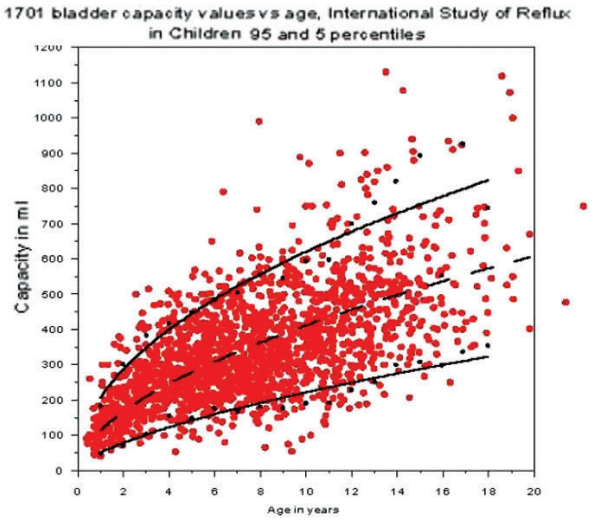

Figure 3. Bladder capacities determined by VCUG in the International Reflux Study

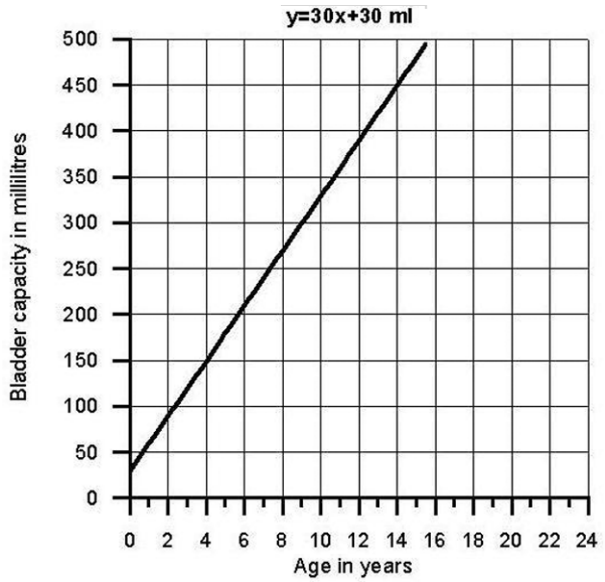

Figure 1. Bladder capacity using the formula
Y = 30 + 30 X (Y= capacity in ml, X = age in years)

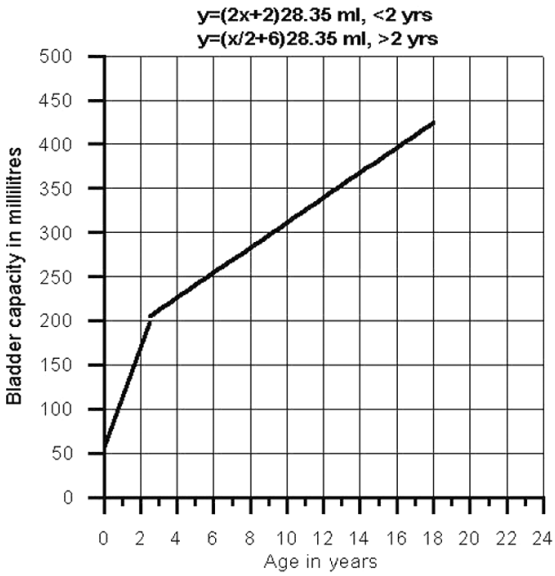

Figure 2. Bladder capacity using the formula
Y = (2 X + 2) x 28.35 ml < 2 years
Y = (X/2+6) x 28.35 ml > 2 years
(Y = capacity in ml, X is age in years)

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

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

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

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, 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-sphincter dysfunction can be diagnosed accurately in the majority of cases, and a high level of suspicion can be maintained towards incomplete bladder emptying in both neurogenic detrusor-sphincter dysfunction and structurally caused incontinence. This is important in view of the potential these conditions have to cause irreversible loss of kidney function.

In a minority of incontinent children the non-invasive assessment yields 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].

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 that which is problematic for the child.

A bladder diary is mandatory to determine the child's voiding frequency and voided volumes. Checklists and bladder dairy 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 medi-

cation 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].

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.

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

Detailed questioning of the parents' observation of the child's voiding habits is essential as is direct observation of the voiding, if possible.

Children may have their voiding dysfunction ameliorated or even eliminated by correcting anomalies of body position detected when observing the child's micturition. Children may void in awkward positions, e.g. with their legs crossed or balancing on the toilet without proper support of the legs, thereby activating the pelvic floor and obstructing the free flow of urine [7] (**Figure 4**).

III. URINALYSIS

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

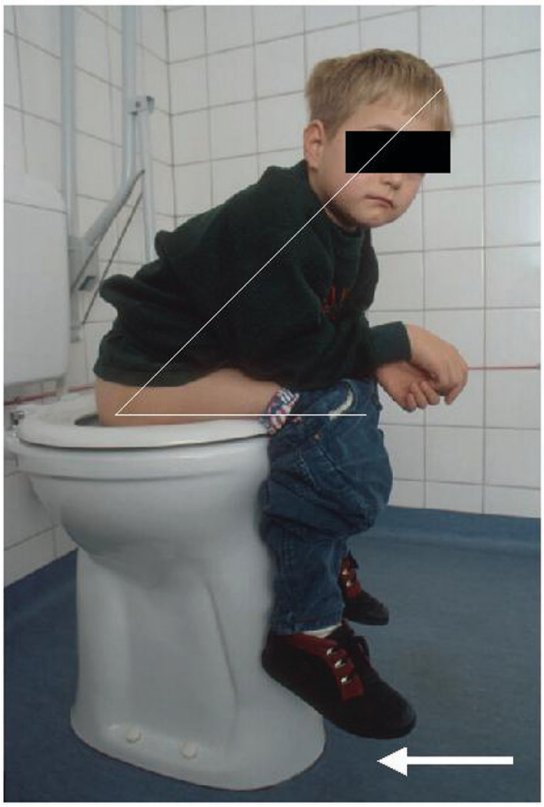

Figure 4. Improper position for voiding: the feet are not supported [unbalanced position] and the boy is bent forward. Support of the feet will correct this and will the pelvic floor muscles allow relaxing properly.

IV. NON-INVASIVE DIAGNOSTIC TECHNIQUES

1. Frequency / volume charts: bladder diary

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

From the frequency/volume chart the child's "functional" bladder capacity may be assessed as the largest voided volume, with the exception of the morning micturition, which actually represents nighttime

bladder capacity. Whenever possible, filling out the chart is the responsibility of the child: the parents provide assistance and support. Ideally the chart should cover 3 complete days, but in reality completion over a weekend restricts the record to 2 days.

The frequency volume chart is a reliable non-invasive measure of maximum bladder storage capacity and can be used as an outcome measure in children with bladder dysfunction if care is taken to minimise confounding factors and sources of error during chart completion [8].

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 [8].

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 [8-10].

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.

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 [10,11].

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. Quantification of constipation

In grading constipation, scoring a plain X-ray of the abdomen [Barr score] yields inconsistent results [12-14].

A better way to match clues from the medical history with signs and symptoms is the measurement of colonic transit time. As many children with non-neurogenic detrusor-sphincter dysfunction habitually use their pelvic floor as an "emergency brake", anomalous defecation frequency and constipation have a high prevalence in this group. Overt constipation should be dealt with before embarking on treatment of incontinence or detrusor-sphincter dysfunction [15].

4. Urinary flow

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

Graphic registration of the urinary flow rate during voiding is becoming a standard office procedure. Flow patterns and rates should be 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 [16].

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 [17]. If the bladder is still nearly empty the child should be asked to drink some water until the bladder is full enough for a reliable flow.

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

shows a interrupted flow, whereas in staccato 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 [18].

The same parameters used to characterise continuous flow may be applicable, if care is exercised, in children with intermittent, or staccato 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.

5. Ultrasound imaging of upper and lower urinary tract

In most clinical settings, ultrasound-imaging techniques are routinely used in children with incontinence. Upper tract abnormalities such as duplex kidney, dilatation of the collecting system, and gross reflux nephropathy can be readily detected, but detection of the more subtle expressions of these abnormalities require urological expertise on the part of the ultrasound operator [19].

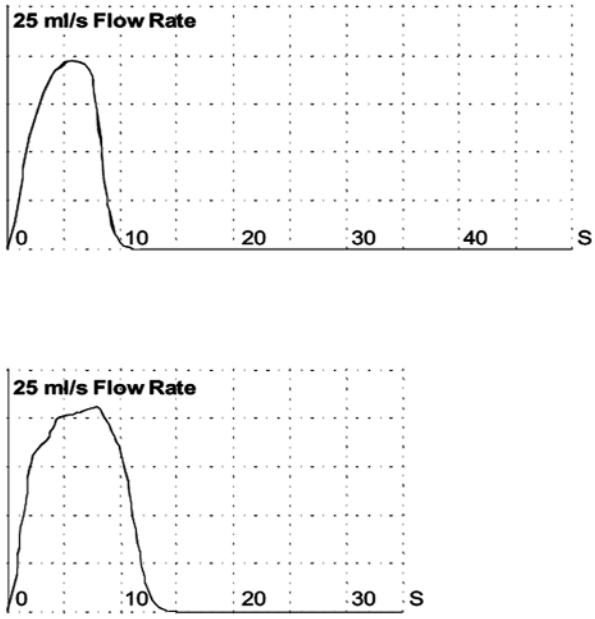

Figure 5. Normal urinary flow curves of 2 children.

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 [20,21].

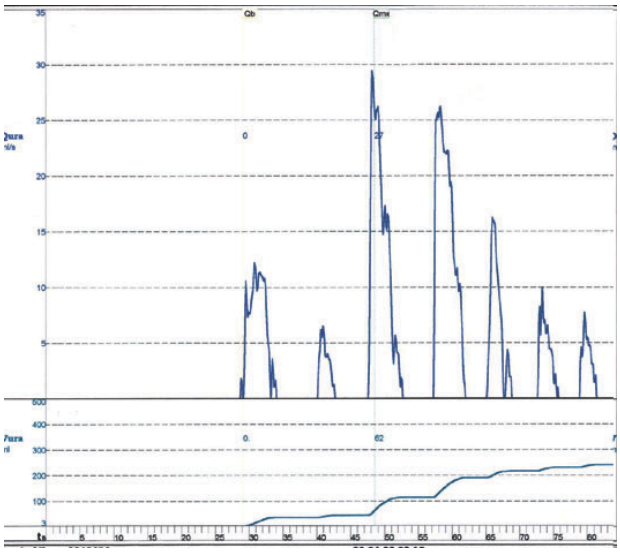

Figure 7. Intermittent flow curve in a child with disco-ordination between detrusor contraction and sphincter relaxation (pelvic floor muscles)

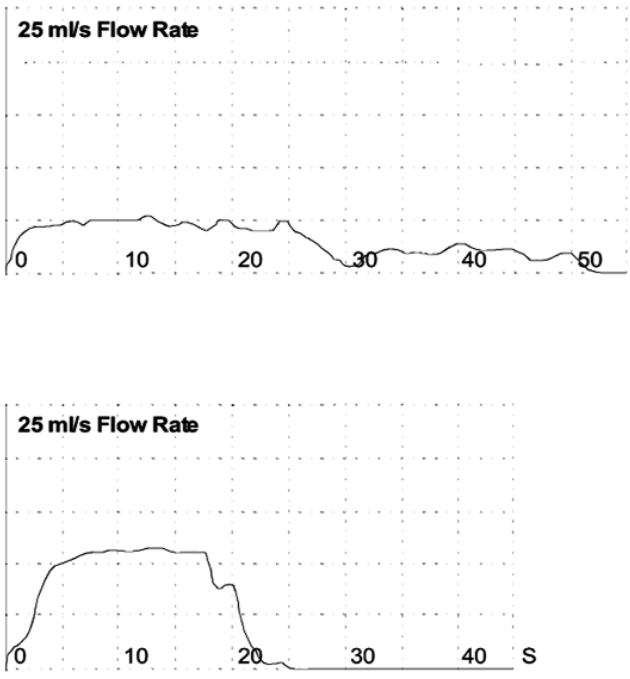

Figure 6. Flow curve of 2 children with a static, anatomic obstruction; the curve is continuous but the flow is lower than normal and extended in time.

a) Post-void residual volume

Except in small infants, the normal bladder will empty completely at every micturition [22].

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

b) Ultrasound-flow-ultrasound

This combination of imaging and non-invasive urodynamics is a standardised procedure used to obtain representative data on both flow rate and flow pattern, as well as on post-void residual volumes. With ultrasound, bladder filling is assessed and 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 [23]. Because some children have difficulty voiding in a strange environment, this option can overcome this.

6. Invasive diagnostic techniques

The important question (for the incontinent child) "whether invasive diagnostic procedures are necessary" is decided by the results of the non-invasive procedures. In general urodynamic studies will only be done if the outcome will alter the management, and this will also depend on the possible treatments available. The diagnostic information needed is that which is necessary to find the correct treatment. Indicators include voiding frequency of 3 or less per day, straining or manual expression during voiding, a weak urinary stream, previous febrile urinary tract infection, continuous dribbling incontinence or pronounced apparent stress incontinence, or previously identified dilating vesicoureteral reflux.

The finding of genitourinary abnormalities or signs of occult spinal dysraphism at physical examination also indicate the need for further diagnostics. Urinary flow registration will detect the plateau-shaped flow curve typical for structural bladder outlet obstruction, and the intermittent flow suggesting detrusor-sphincter dys-coordination [18].

A clinically significant post-void residual at repeated occasions clearly points to incomplete bladder emptying. The pad test will detect the cases with obvious stress and urge incontinence, or continuous dribbling. Ultrasound imaging will raise suspicion for extravesical ectopic ureters.

In short, invasive diagnostics are indicated when the non-invasive program 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 dysfunction [as in children with dilating vesicoureteral reflux and/or febrile urinary tract infections], or significant post void residuals.

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

a) 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 during voiding of the upper urinary tract: the degree of vesicoureteral reflux (VUR) may change with the pressure generated by the detrusor muscle during voiding. Post-void residual volumes 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.

b) 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).

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 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 [24,25].

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) Urodynamics

Especially in children urodynamic investigations should only be performed if the outcome will have consequences for treatment [26,27].

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 only do one complete filling and voiding cycle [28].

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, without additives; CO_2 is not recommended.

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 with the toes; this usually indicates voiding is imminent. In the older child, the volume may be small with the first cystometry, for fear of discomfort. This is the reason that in 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 [30].

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) [29].

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* creates a urethral segment with a small and fixed 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 during passage of urine that creates the narrow urethral segment, constantly or intermittently. To differentiate anatomical from functional obstruction, information is needed about the activity of the urethral sphincter during voiding. This information can be obtained, and recorded together with pressure and flow, by monitoring the urethral pressure at the level of the urethral sphincter, or by recording a continuous electromyogram of the striated urethral sphincter. For clinical purposes, in patients where the urethral sphincter is not readily accessible, the electromyogram of the external anal sphincter is often used to monitor activity of the striated urethral sphincter. This corresponds to activity of the pelvic floor muscles. 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 (**Figures 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 [31,32] .

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

Grade of recommendation: for all diagnostic procedures level 2

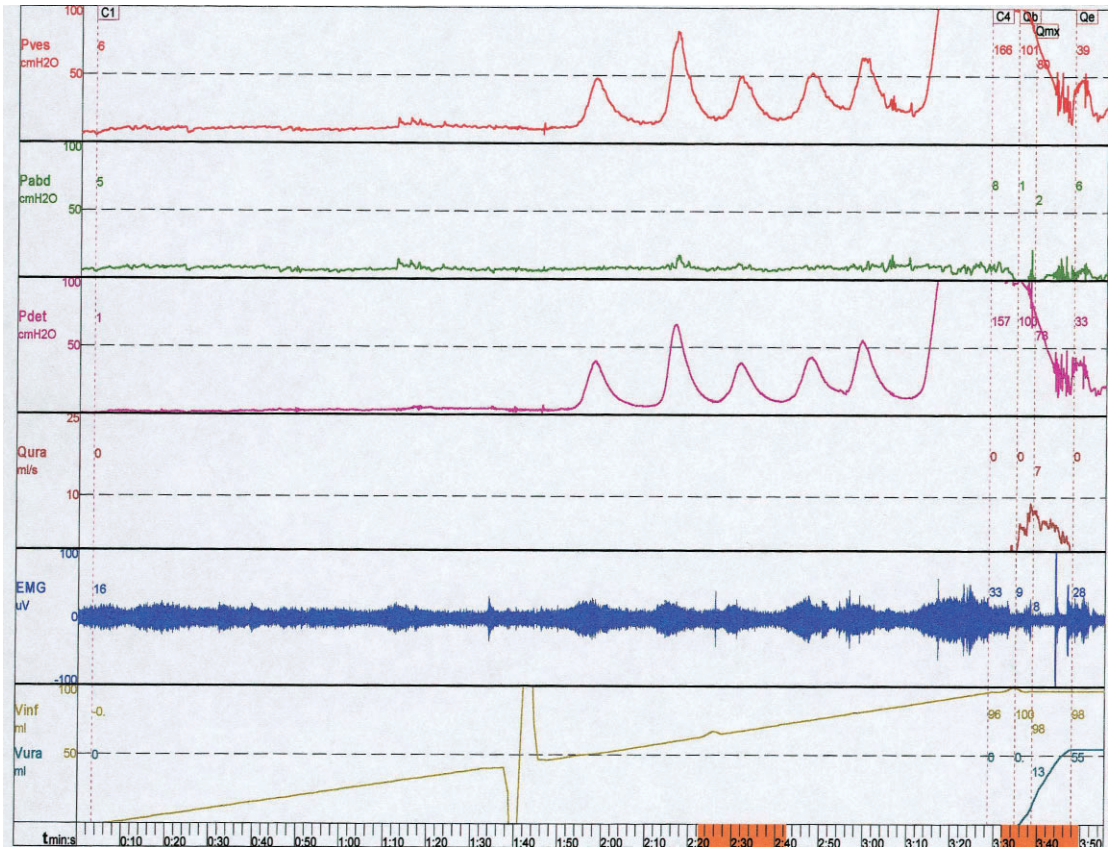

Figure 8. Urodynamic study illustrating involuntary detrusor contractions, counter action of pelvic floor muscles (guarding reflex) and incomplete relaxation during voiding resulting in post void residual urine (detrusor overactivity + dysfunctional voiding) [29].

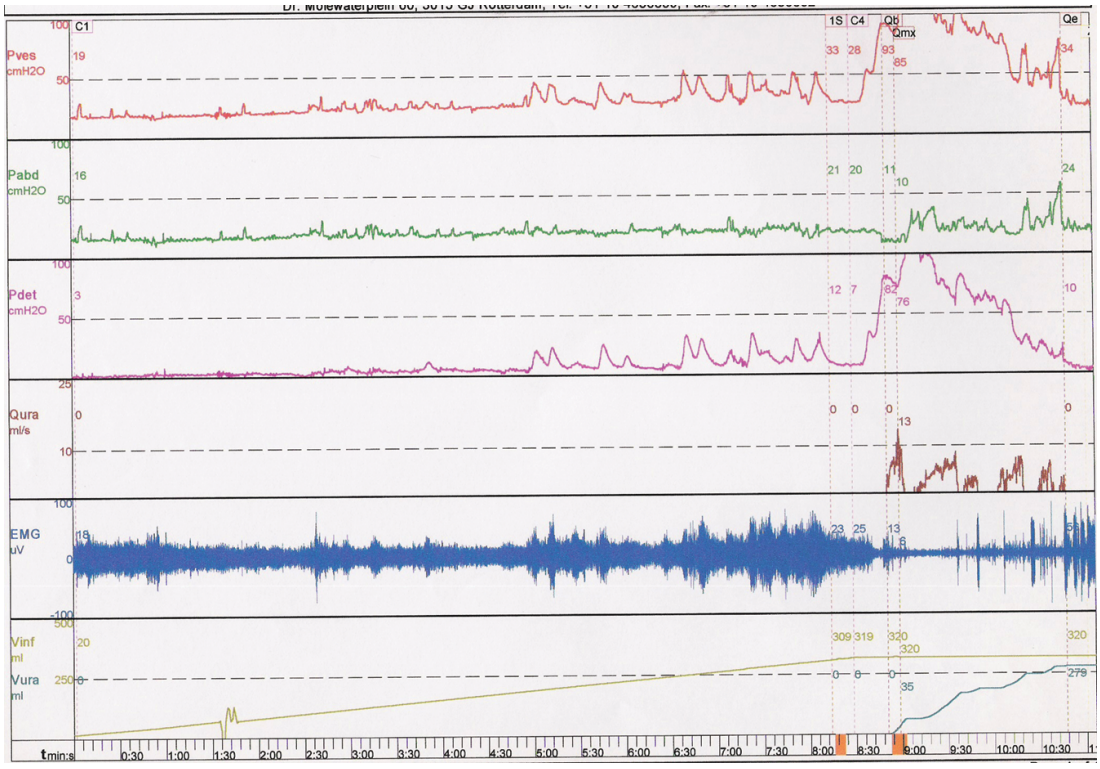

Figure 9. Interrupted voiding. Example of disco-ordination between detrusor contraction and relaxation of the pelvic floor muscles

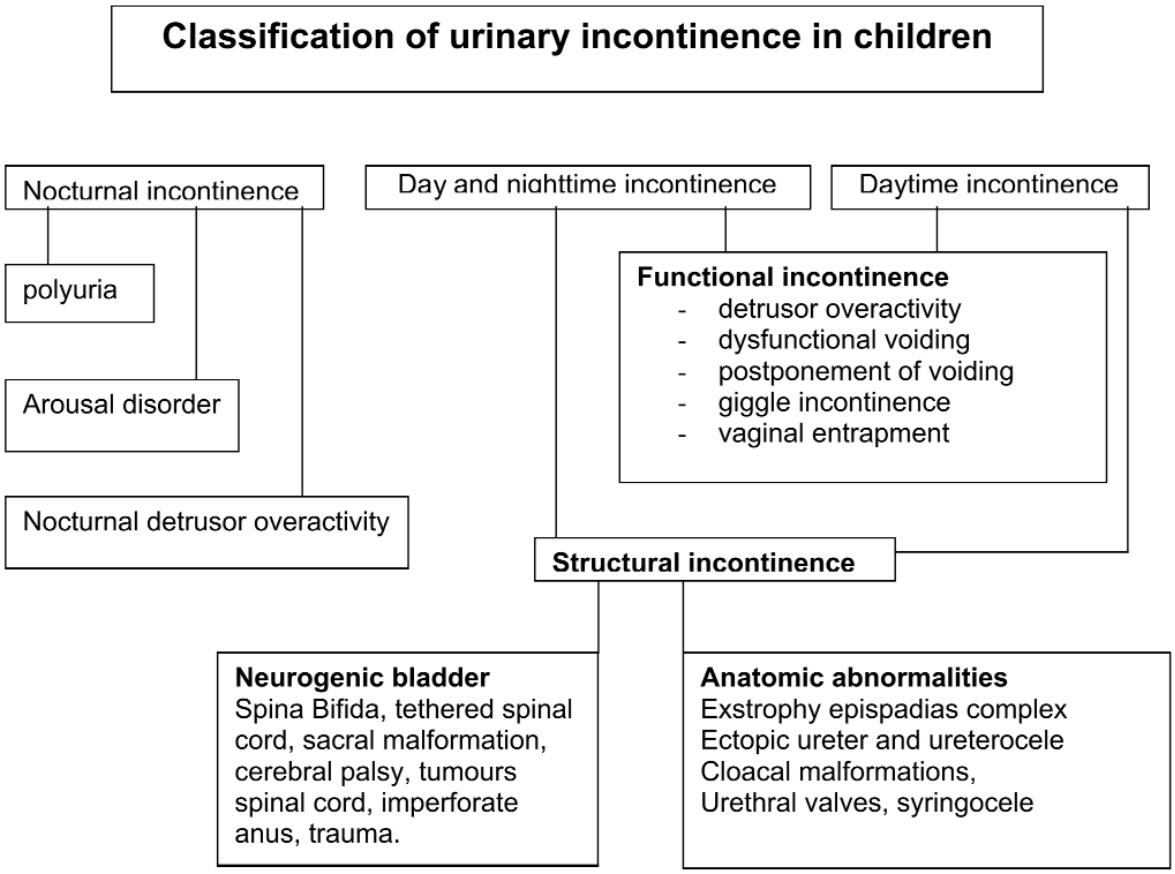

Figure 10. Classification of urinary incontinence in children.

C. NOCTURNAL ENURESIS

I. DEFINITION

Nocturnal enuresis can be defined as an involuntary voiding of urine during sleep, with a severity of at least three times a week, in children over 5 years of age in the absence of congenital or acquired defects of the central nervous system [1].

It has been argued that parental concern and child distress should also play a part in determining the clinical significance of the problem [2].

Although there is general consensus about the core descriptors of nocturnal enuresis, divergent opinions flourish over many specific aspects of the definition [3].

Age is one such issue. Most definitions refer to 5 years as the watershed although occasionally the child's 'mental age' is taken into account. The age criterion is somewhat arbitrary but reflects the natural course of achieving bladder control [4].

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

II. SEVERITY

Children manifestly vary in wetting frequency. Only some 15 percent of children with nocturnal enuresis wet every night although most children wet more than once a week [5,6].

In a population survey of nearly 1,800 Irish children aged 4 –14 year olds, Devlin found the frequency of wetting as follows: less than once per week in 33 percent, once per week in 11 percent and 2 to 4 times per week in 25 percent [7].

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

III. PREVALENCE

The extent of bedwetting is widespread. It has been argued that nocturnal enuresis is the most prevalent of all childhood problems [8]. For a more detailed description of prevalence of monosymptomatic and polysymptomatic nocturnal enuresis the chapter on epidemiology should be consulted.

In the United Kingdom estimates suggest around 750,000 children and young people over 7 years will regularly wet the bed. In the USA recent evaluations of prevalence suggest some 5 to 7 million children regularly experience primary nocturnal enuresis [9,10,11].

Epidemiological surveys tend to adopt 'lenient' criteria in defining nocturnal enuresis. They survey a sample or the whole community usually asking parents about certain voiding and wetting habits should their child wet the bed. Such surveys [including any episodes of nocturnal enuresis] undertaken in Great Britain, Holland, New Zealand and Ireland suggest that the prevalence for boys is around: 13-19% at 5 years, 15-22% at 7 years, 9-13% at 9 years and 1-2% at 16 years. For girls the prevalence rates are reported to be: 9-16% at 5 years, 7-15% at 7 years, 5-10% at 9 years and 1-2% in the late teenage years [5,7,12,13].

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

Many adults will be reluctant to come forward or admit to currently having a problem of bedwetting. Hirasing et al sampled over 13,000 adults (18-64 years) and found an overall prevalence rate of nocturnal enuresis at 0.5% [14]. Of these, 12 percent of men and 29 percent of women had daytime incontinence. Fifty percent of men and 35 percent of the women had never consulted a health professional about their bedwetting. Thirty eight percent of the men and 26 percent of the women had never done anything to try and become dry.

The enuresis prevalence of 0.5% in otherwise healthy adults in this study refers to a largely untreated population. Fifty percent of the men had primary enuresis and had never been consistently dry at night. Assuming a prevalence of enuresis of 8 percent in 7-year-old boys, this could be translated to mean that the risk for an enuretic boy to remain enuretic for the rest of his life is 3 percent if he does not receive active treatment during childhood. Three per cent equals the prevalence found in patients after the age of 20 years in the study by Forsythe and Redmond and in the Finnish 14-year-olds as described by Moilanen [15,16]. It is still not clear whether active treatment of nocturnal enuresis in childhood is able to reduce the number of adult enuretics.

Patients with ADHD and spinal muscular atrophy suffer from nocturnal enuresis and daytime incontinence more frequently [17-19].

IV. INHERITANCE

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

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

With linking analysis, foci have been found on chromosomes 8, 12, 13 and 22 [20-25]. This phenomenonis known as 'locus heterogeneity', which means that genes on different chromosomes can lead to the

same disorder. There was no clear association of any of these loci with any type of nocturnal enuresis.

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

The etiology of nocturnal enuresis is characterised by a complex interaction of genetic and environmental factors.

IV. THE GENDER DIFFERENCE

In a population survey of 706 families in London,Weir found a higher prevalence for boys than girls at age 3 years with 56 percent of boys and 40 percent of girls being wet at night more than once a week [26].

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

Historically girls have been reported as more likely to experience secondary enuresis and associated daytime incontinence, urinary frequency, emotional and behavioural problems, urinary tract infections, along with tolerant mothers, and a high level of concern about their enuresis [27-29].

Girls have also been reported to be less likely to have a family history or genetic pre-disposition to bedwetting [30,31].

V. CLASSIFICATION

The traditional classification is based on the child's history of enuresis. Children who have never achieved a period of up to 6 months free of bedwetting are considered to have primary nocturnal enuresis. There may be indications of slight maturational delay in primary nocturnal enuresis with low birth weight, soft signs of neurological delay, delayed motor development and shorter height [32-35].

However children with primary nocturnal enuresis do not have an increased likelihood of behavioural problems compared with children who are not bedwetters or former bedwetters [36-39].

Secondary or onset nocturnal enuresis is the re-emergence of wetting after a period of being dry. The time period is usually considered to be a minimum of 6 months, although some take 1 year to be the specified enuresis-free period. A birth cohort of 1265 New Zealand children studied over 10 years by Fergusson et al found an increased risk of secondary enuresis with age [40]. They found the proportion of children who developed secondary enuresis were: 3.3 percent at 5 years, 4.7 percent at 6 years, 6.2 percent at 7 years, 7.0 percent at 8 years, 7.5 percent at 9 years and 7.9 percent at 10 years.

Secondary nocturnal enuresis appears to be associated with a higher incidence of stressful events particularly parental separation, disharmony between parents, birth of a sibling, early separation of the child from parents and psychiatric disturbance in a parent [40-42].

Von Gontard and colleagues found children with secondary enuresis had significantly more emotional difficulties compared to those with primary nocturnal enuresis. Their evidence also suggests children with secondary enuresis, compared to those with primary enuresis, are significantly more likely to have behavioural problems, a finding which corresponds to that of McGee et al [43].

Both Jarvelin and Fergusson et al compellingly argue that primary and secondary enuresis are aspects of the same problem [35, 41]. They claim the two classifications share a common etiological basis. The rate at which a child acquires primary control influences his or her susceptibility to secondary enuresis. The primary form is regarded as being the consequence of a delay in maturation of the physiological mechanisms. The child's capacity to sustain and maintain nocturnal bladder control is manifest in the rate at which control is acquired. On the other hand this capacity determines the child's susceptibility to lapsing when exposed to stress.

MONO-SYMPTOMATIC VERSUS NON-MONO-SYMPTOMATIC

Mono-symptomatic nocturnal enuresis refers to those children who report no bladder or voiding problems associated with their wetting. Non-mono-symptomatic nocturnal enuresis refers to bedwetting, which is associated with detrusor overactivity or voiding problems such as urgency and postponement during the day, but no daytime wetting [44].

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

Many parents are unaware of daytime symptoms when seeking help for bedwetting and when identified these symptoms should be treated prior to intervention for the nocturnal enuresis. Between 10-28% of children with nocturnal enuresis have associated daytime problems and if they have urinary incontinence during the day these children should not be regarded as having nocturnal enuresis: they should be considered to be incontinent. The night time incontinence is not any longer an isolated phenomenon but part of the symptomatology of functional incontinence. These children are more resilient to treatment and more vulnerable to relapse [45].

VI. PATHOPHYSIOLOGY OF NOCTURNAL ENURESIS

The pathophysiology of nocturnal enuresis has been studied extensively and is still not fully understood. A conceptual model has been proposed for understanding nocturnal enuresis, envisaging it as a problem or delayed maturation in one or more of the following systems: a lack of stability in bladder function, a lack of arginine vasopressin release and an inability to wake from sleep to full bladder sensations [46].

This is supported by the work of Neveus et al, who sought to evaluate differences in sleep factors between children with wetting problems and dry children [48].

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

A unifying and simplistic concept with important clinical implications, is that nocturnal enuresis is caused by a mismatch between nocturnal bladder capacity and the amount of urine produced during the night, plus the mandatory fact that the patient does not respond to the full bladder by waking up (**Figures 11 and 12**).

1. Lack of nocturnal vasopressin release

In humans a marked circadian rhythm of urine production is developed from early childhood with a pronounced nocturnal reduction in diuresis to approximately 50% of daytime levels. [48,49]. Decrease of renal urine production during the night allows for sleep not disturbed by a full bladder. In children this is the result of nocturnal release of hormones that regulate free water excretion (arginine vasopressin, AVP) or solute excretion (angiotensin II and aldosterone). This results in increased urine concentration and reduced urine volume during sleep. This could explain why most children who are not enuretic tend to sleep through the night without being wet.

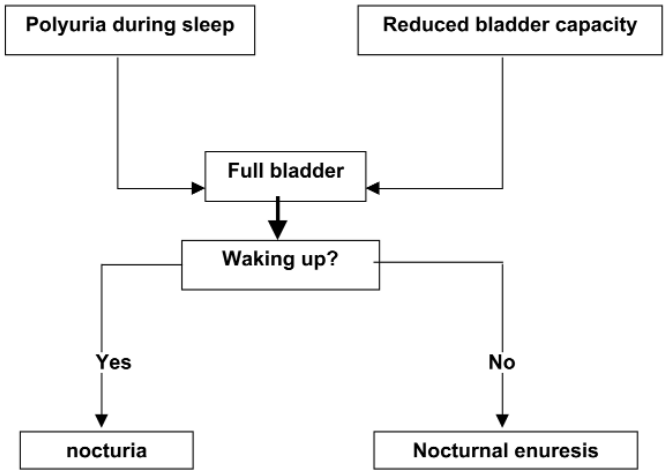

Figure 11. Basic pathophysiology of nocturnal enuresis or nocturia. When the bladder is full because of (relative) polyuria and/or a reduced bladder capacity, the child either wakes up to void (nocturia) or voids while sleeping (nocturnal enuresis).

In adolescence and adult age there is no diurnal rhythm of plasma vasopressin concentration, and the changes in urine production occur entirely owing to a decrease in the urinary sodium excretion [50].

Two thirds of patients with mono-symptomatic nocturnal enuresis have been found to have a lack of circadian rhythm of vasopressin, resulting in high nocturnal urine production, which exceeds bladder capacity [51-53].

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

Wolfish et al interestingly found that most nocturnal enuretic episodes occur in the first third of the night and many studies report that the enuretic episode is most likely to occur in the first 2 hours of sleep [45,46]. One reason for this might be that during that period waking up is most difficult.

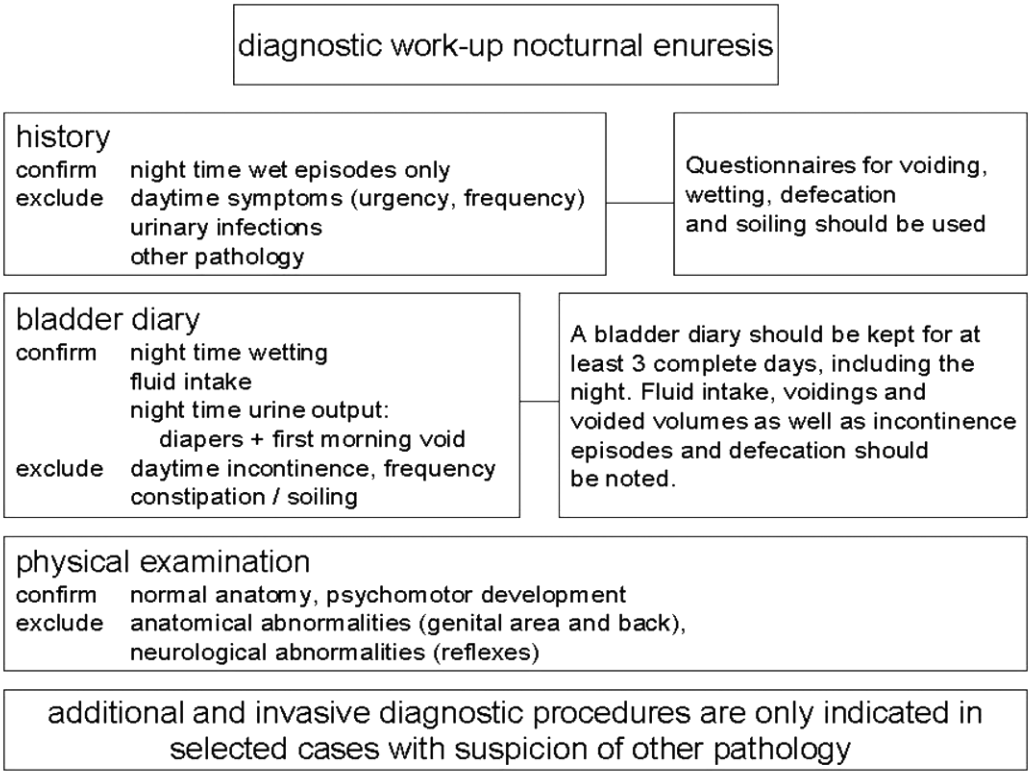

Figure 12. Schematic work-up in patients presenting with night-time wetting only.

There may be a small sub-group of children with impaired renal sensitivity to vasopressin or desmopressin [56,57]. Recent work by Devitt et al suggests that 18 percent of children have 'normal' levels of plasma vasopressin release but remain enuretic [53]. 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 (is there really nocturnal polyuria?).

The subgroup of patients with nocturnal enuresis and increased nocturnal urine output generally has a normal functional bladder capacity and a favourable response to dDAVP [58].

2. Detrusor overactivity during the night

The detrusor, in order to function appropriately, needs to be relaxed during filling and have an appropriate functional capacity. Detrusor overactivity usually causes small voided volumes resulting in a decreased functional bladder capacity [59].

Watanabe and his colleagues, employing EEG and cystometry recording during sleep, discovered that 32 percent of children with nocturnal enuresis had unvoluntary 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.

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 [65].

It is important to be aware of the possibility of detrusor overactivity as a cause of the child's nocturnal enuresis.

The following signs are indicative of detrusor overactivity [66-68]:

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

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

3. Lack of arousal from sleep

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

Whether the child has detrusor overactivity or lack of vasopressin release resulting in over production of urine, the enuresis event results from the child's inability to awaken from sleep.

Non-enuretic children are more likely to wake to void than enuretic children [66].

This might explain why the most heavily endorsed view of both children and parents, regarding the aetiology of nocturnal enuresis is a belief in deep sleep [69].

However a raft of evidence counters such a belief. Sleep patterns of children with nocturnal enuresis are no different from children who do not have nocturnal enuresis [70].

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 [71-74].

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

Wolfish et al suggest the most difficult part of the night for all children to arouse from sleep, is the first third [54].

Waking becomes easier as the night progresses. However, several authors have found that children with nocturnal enuresis are also more likely to wet in the first third of the night, often in the first two hours following sleep [71,72,75-77]. Thus the point of bladder fullness for most enuretic children coincides with a time of night where they find it most difficult to wake from sleep.

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

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

Because nocturnal enuresis is a multifactorial and complex disorder, many other risk factors have been mentioned in the literature. Although it can not be excluded that some of these factors may play a role in some patients, a solid scientific foundation is still lacking. Snoring and sleep disorders [sleep apnoea], as well as hypercalciuria and maturational delay are such factors [78-86]. In a study by Aceto et al it was found that ADH levels and nocturnal hypercalciuria correlated significantly, while daytime calciuria was not different from normal controls [82].

VII. TREATMENT OF NOCTURNAL ENURESIS

The normal annual resolution rate of monosymptomatic nocturnal enuresis is not always accounted for in cure rates reported. When reporting is done with survival analysis, the resolution rate remains visible throughout follow-up [15,16,87].

The outcome of pharmacological treatment for nocturnal enuresis is expressed as either full response or partial response, while on the prescribed medication. A ***full response*** is defined as a reduction in wet nights of at least 90%, to allow for the occasional 'accident of wetting', ***partial response*** is defined as a reduction in wet nights of 50%-90%; less than 50% reduction in wet nights is considered to be non-response [88,89]. One may argue however that curing nocturnal enuresis implies complete dryness during every night during and following successful treatment.

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

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

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

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

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

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

It is essential to explain the problem to children with mono-symptomatic nocturnal enuresis and their parents and give general advice such as to eat, drink and void regularly during the day, abstain from drinking too much during the late afternoon and evening and have relaxed routines at bedtime. It should be stressed that the condition is common and usually a benign delay in maturation without any psychopathological undertone. A positive attitude towards the child should be utilised and explained that the bedwetting eventually will cease "but nobody knows exactly when that will happen". Up to 19 percent of children will become dry within the next 8 weeks without any further treatment [48,91,92].

The management of nocturnal enuresis 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 intervention

Although treatment modalities like lifting, fluid restriction, dry-bed training, retention control training, psychotherapy, acupuncture, hypnosis all have been used, there is not sufficient data in the literature to recommend any of these [93-100].

There is only one RCT on acupuncture: of 40 children 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 12,45 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.

Besides 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 can not be recommended at this stage [101-103].

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 13**.

1. 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 nocturnal enuresis [104, 103]. 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 [105,106].

Alarm treatment is slow in the beginning so it should be continued at least 6 to 8 weeks before it is considered effective or not. Compliance remains a problem: dropout rates are rarely disclosed in reported studies. Proper guidance and instructions are mandatory.

Better results are associated with optimal motivation of the child and family, and a higher frequency of wet nights. Reduced efficacy is associated with lack of concern shown by the child, lack of supervision, inconsistent use, family stress, abnormal scores on behavioural ckecklists, psychiatric disorder in the child, failure to awaken in response to the alarm, unsatisfactory housing conditions and more than one wetting episode per night.

The mode of action of the alarm has been believed to be an amelioration of arousal to a full bladder, which may be true but lacks scientific validation. An interesting finding is that the alarm increases nocturnal

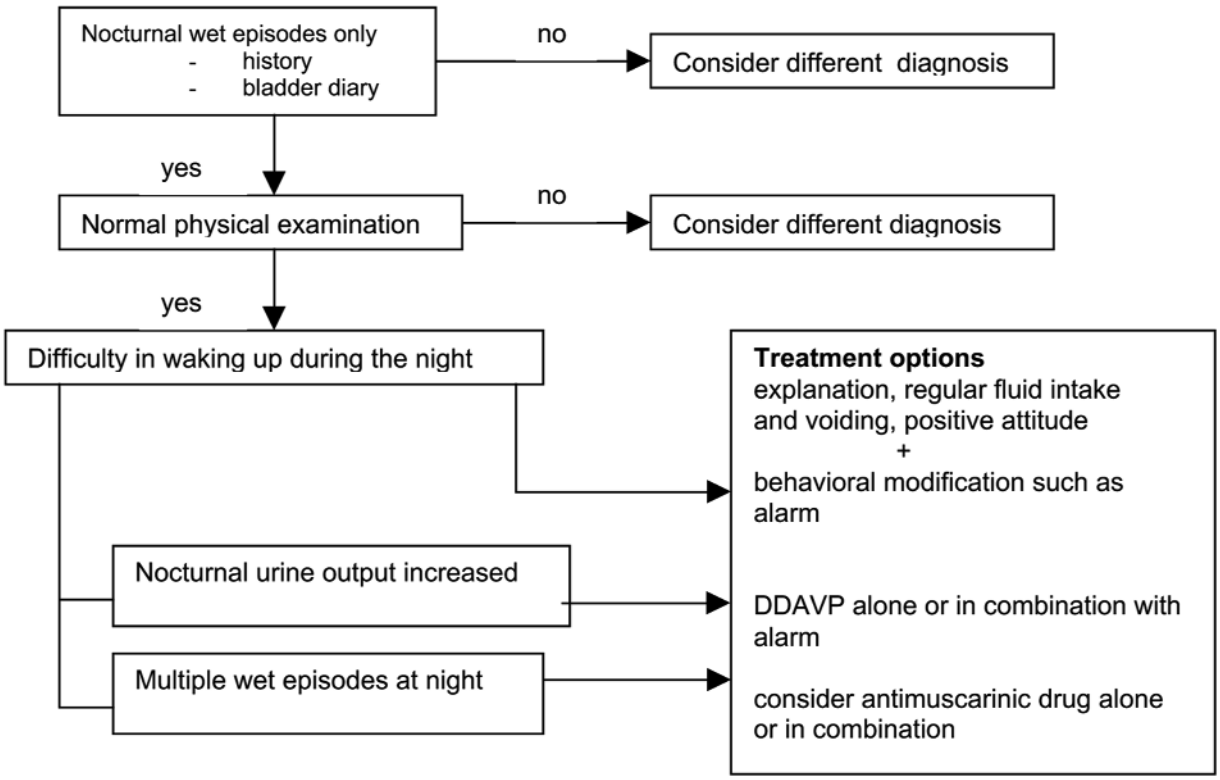

Figure 13. Pragmatic approach to the diagnosis and treatment of nocturnal enuresis

bladder capacity, which may explain why children after successful treatment are often able to sleep dry without nocturia [107,110].

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 [108,109].

Overlearning [giving extra fluids at bedtime after successfully becoming dry using an alarm] and avoiding penalties may further reduce the relapse rate [104].

Possible future alarm design could include a small ultrasound transducer to monitor bladder volume during the night, so that at a predetermined volume a sound signal is emitted, thus waking the child before the enuresis occurs [111].

Level of evidence: 1

Grade of recommendation: A

2. 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 [112].

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: 2

Recommendation: grade B

3. Dry bed training

This is a package of behavioural procedures used in conjunction with the enuresis alarm first described by Azrin et al [113]. It incorporates**:**

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

1 for the first night, waking the child each hour, praising a dry bed, encouraging the child to decide at the toilet door whether he or she needed to void, and on returning to bed the child is encouraged to have a further drink and

2 on the second night the child is woken and taken to the toilet 3 hours after going to sleep. For each dry night the waking time is brought forward by 30 minutes. If wet on any night the waking time stays at the time of the previous evening. The waking schedule was discontinued when the waking time reached 30 minutes following sleep. The waking schedule is resumed if the child begins wetting twice or more in any week, stating again 3hours after sleep.

- social reinforcement and
- increased fluid intake.

High success rates and low drop out have been reported although relapse rates are no different to enuresis alarm treatment. Modifications have been advocated to remove some of the more punitive elements of the programme but it remains a complex, time consuming and demanding procedure [114-116].

Hirasing et al found 80 percent success with group administered dry bed training. Girls responded better than boys [117]. 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 [118].

An important component analysis by Bollard & Nettelbeck found that the enuresis alarm accounted for most of the success achieved through dry bed training, that a large proportion of the components of the procedure could be eliminated without sacrificing much of its overall effectiveness and that the waking schedule coupled with the enuresis alarm was as effective as the complete dry bed training programme [119].

Level of evidence: not more effective than alarm treatment alone.

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.

4. Desmopressin

Placebo controlled studies have shown that the antidiuretic drug dDAVP is significantly more effective than placebo [120].

Patients on desmopressin were 4.6 times more likely to achieve 14 consecutive dry nights compared with placebo [121]. However, there was no difference after treatment was finished.

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

Kruse et al found that the best results were obtained in older children who respond to 20 microgr. dDAVP and who do not wet frequently [and only once per night] [122].

Relapse after short-term treatment is rather the rule, whereas long-term treatment may yield better cure rates [123]. Intermittent therapy appears to decrease the number of relapses [124].

Long-term results have been found to be 23 percent of children treated and 31 percent of those who

responded to treatment. The 23 percent is not significantly better than spontaneous resolution [125].

It has recently been shown that the chances of permanent cure may increase by adopting a 'structured withdrawal program'. This implies a gradual discontinuation of the drug (during an 8 week period) and positive reinforcement of dry nights without medication. At week 10 with complete cessation of medication 74,5 % of children remained dry [126].

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 [127-133].

Level of evidence: 1

Grade of recommendation: A

5. Combined treatment with alarm and desmopressin

Combined treatment is superior to alarm alone especially for non-responders of each individual treatment. Both treatments are started at the same time: the rapid action of dDAVP is believed to facilitate the child's adaptation to the alarm [134,135]. After 6 weeks the dDAVP is discontinued while the alarm treatment is continued until the child becomes completely dry. Compared with either therapy alone, the combination has been found to be particularly effective in children with high wetting frequencies and behavioural problems.

Combination with full-spectrum therapy may even yield higher success rates [136,137].

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 [136].

Hjälmås et al have proposed the following [not validated] protocol [48]:

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.

Level of evidence: 1

Grade of recommendation: A

6. Antimuscarinic drugs

In those children who have nocturnal enuresis due to detrusor overactivity during the night, treatment with an antimuscarinic drug should be considered [138]. 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 [139,140].

At present no studies have been performed to demonstrate its efficacy.

Level of evidence: 3

Grade of recommendation: C

7. Tricyclic antidepressants

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 [141].

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 [142].

Only in selected cases (like adolescent boys with Attention Deficit Hyperactivity Disorder and persistent nocturnal enuresis) it should be considered [143].

Level of evidence: 1

Grade of recommendation: C (cardiotoxicity)

8. Inhibitors of prostaglandin synthesis

Because nocturnal polyuria in children with nocturnal enuresis may not be entirely attributed to a defect in free water excretion, but rather to an increase in nocturnal excretion of sodium, cyclooxygenase inhi-

bitors (like diclofenac), which reduce urinary sodium excretion, have been tried and in a randomised double blind placebo controlled study proved to be effective [144-144]. Further studies need to be done to elucidate the role of these drugs.

Full response (while on medication) and Cure rates (6 months after cessation of treatment) of Nocturnal Enuresis

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

9. 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 nocturnal enuresis. These children may void more frequently than their peers or have urgency and daytime 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 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 functional 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 [147].

Some children remain non-responders to desmopressin in combination with alarm and / or anticholinergic drugs: absorptive nocturnal hypercalciuria may be responsible for the nocturnal enuresis in some of these patients. With an appropriate (low calcium) diet these patients became desmopressin responders [148].

Nocturnal enuresis 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 nocturnal enuresis.

D. DAY AND NIGHTTIME INCONTINENCE

I. INTRODUCTION

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

Micturition is modulated by higher centers from the foetal period onward, but it is not until the second or third year of life that a child is able to demonstrate bladder awareness and respond to a strong desire to void. By the fourth year the hallmarks of mature bladder function are present allowing the child to inhibit micturition, initiate a void at will regardless of bladder volume, and empty to completion. The ability to void requires interaction and co-ordination between the autonomic and somatic nervous systems. Precise motor timing ensures that the detrusor muscle contracts to initiate emptying only after urethral sphincter and pelvic floor muscle relaxation. During voiding no activity should be discernable in the sphincter or pelvic floor muscles, however at cessation of micturition tonic muscle activity is restored. The detrusor muscle then becomes silent whilst the bladder refills.

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

The desire to void is a sensation which, in the developing child, is incorporated into daily life so that voiding takes place at an appropriate time and place. Problems with training or psychological difficulties can have a great impact on the results of training: some parents send their child to the toilet many times, though his/her bladder may be empty [1].

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 [2].

Urinary incontinence in children may be due to disturbances of the filling phase, the voiding phase or a combination of both.

Overactivity of the detrusor muscle may lead to disturbances in the filling phase characterized by urgency, frequency and at times urge incontinence. Girls present with symptoms of detrusor overactivity 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 post-void residuals. Such individuals with ***dysfunctional voiding*** are also prone to constipation and recurrent urinary tract infections [3].

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

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 refractory or severe dysfunctional voiding and those not responding to treatment [4-7].

Treatment is usually a combination of 'standard therapy' ssee below), behaviour therapy, bladder training, physiotherapy and medical treatment. Rarely does surgery play a role in the management of daytime wetting in the absence of a structural abnormality. The roles of alpha-blockers, neuromodulation, botulinum toxin and intravesical therapies in the management of pediatric urinary incontinence are not well-defined.

The importance of treatment during childhood was pointed out in a general population study of 1333 adult women. Fifty percent reported symptoms of stress incontinence and 22 percent reported symptoms of urge incontinence. Eight 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 urge symptoms: occasional bedwetting was not associated with an increased risk in adult life [8].

The role of a-blockers needs to be evaluated further. Also, neuromodulation and intravesical injections with botulinum toxin may have a place in treatment but the exact indications need to be 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.

II. PREVALENCE

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 overactive bladder 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 [8].

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 [10-16].

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% when considering at least one daytime wetting episode in the prior 6 months with 16.5% having experienced more than one wetting episode and only 0.7% experienced wetting on a daily basis [17].

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 [9]. 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 [10]. Urge symptoms seem to peak at age 6–9 years and diminish towards puberty, with an assumed spontaneous cure rate for daytime wetting of about 14% per year [18,19].

Most children are toilet-trained by the age of 3 years, though there is a huge social and cultural variation. In a study by Bloom et al, the mean age ranged from 0.75 to 5.25 years, with girls being trained earlier [2.25 years] than boys (2.56 years) [13].

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 [20].

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.

The natural history of overactive bladder in children is not well understood. It is felt that idiopathic overactive bladder in children is the result of a maturational delay and resolves over time. This is in contrast to the adult population where overactive bladder is felt to be a chronic condition. There is no long-term data to determine if childhood overactive bladder predicts overactive bladder 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 [21,22].

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.

III. DETRUSOR-SPHINCTER DYSFUNCTION, RECURRENT URINARY TRACT INFECTION AND VESICOURETERIC REFLUX (VUR)

The relationship between detrusor dysfunction and VUR was first described by Allen and Koff and has been confirmed by several authors [23-26]. **Figure 14.**

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 [27].

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 urge incontinence and recurrent UTIs had reflux [28].

These studies in infants and the association of 'dysfunctional elimination syndromes' with reflux and

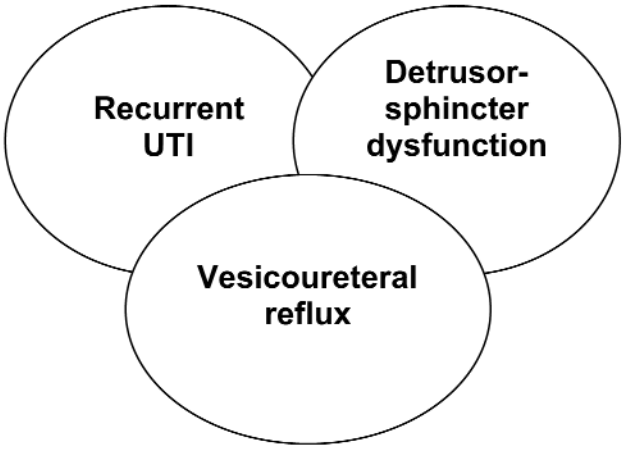

Figure 14. Association of recurrent UTI, detrusor-sphincter dysfunction and vesicoureteral reflux: each occurs separately, but the combination increases the risk of renal damage.

infection in older children strongly suggest 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 [29].

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 [30].

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 [31].

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 and decreased blood flow and relative hypoxia leading to transient bladder mucosal injury during periods of increased detrusor pressure such as during involuntary detrusor contractions,and if there is contraction of the pelvic floor muscles during voiding. Constipation is often present in children with detrusor overactivity and dysfunctional voiding and is also felt to be a risk factor for recurrent UTIs.

In a prospective non-randomised clinical series of daywetting children a strong correlation was found between recurrent urinary tract infections, detrusor overactivity and detrusor-sphincter dysfunction [32,33].

In a study by Hansson et al, symptoms of an overactive bladder, such as urgency and daytime incontinence were found in a high percentage of girls with asymptomatic bacteriuria [34].

In the majority of children with detrusor-sphincter dysfunction the recurrent infections disappeared following successful treatment of the bladder dysfunction. This finding confirms the hypothesis that detrusor-sphincter dysfunction is the main factor responsible for the infections [and to a lesser extent vice versa] [35,36].

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 [37].

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 [38-41].

IV. CLASSIFICATION

Several classifications have been used for children who present with varying degrees of 'functional' urinary symptoms, unrelated to apparent disease, injury or congenital malformation. Some are based on urodynamic patterns, others on clinical presentation. The majority of children present with frequency, urgency and infections, with or without incontinence. Although these symptoms are suggestive of underlying detrusor overactivity, urodynamic studies do not always confirm the presence of detrusor contractions.

Urodynamic investigations have provided more insight into the pathophysiology behind the symptoms and signs, and made the clinical expression of non-neurogenic detrusor–sphincter dysfunction more specific [42,43].

On the basis of urodynamic studies, the functional dysfunctions can be termed urge syndrome (detrusor overactivity), dysfunctional voiding (detrusor-sphincter dyscoordination), 'lazy bladder' (poor bladder emptying due to an underactive detrusor] and 'non-neurogenic neurogenic bladder' ('occult neurogenic bladder') [44].

The term 'non-neurogenic detrusor–sphincter dysfunction' is used in the literature to describe 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 and sphincter. However, the natural history of many of these children does not confirm this hypothesis, nor the early onset of severe pathology in some of them.

Hoebeke et al found no evidence for this dysfunctional voiding sequence: children with functional incontinence have different primary diseases, but all have a common risk of incontinence, UTI (especially in girls with a lazy bladder), VUR [15%] and constipation [17%] [45]. **Figure 15.**

1. Overactive bladder in children

The term overactive bladder is used to describe the symptom complex of urgency, which may or may not be associated with urge incontinence, often associated with frequency and nocturia that is present in the

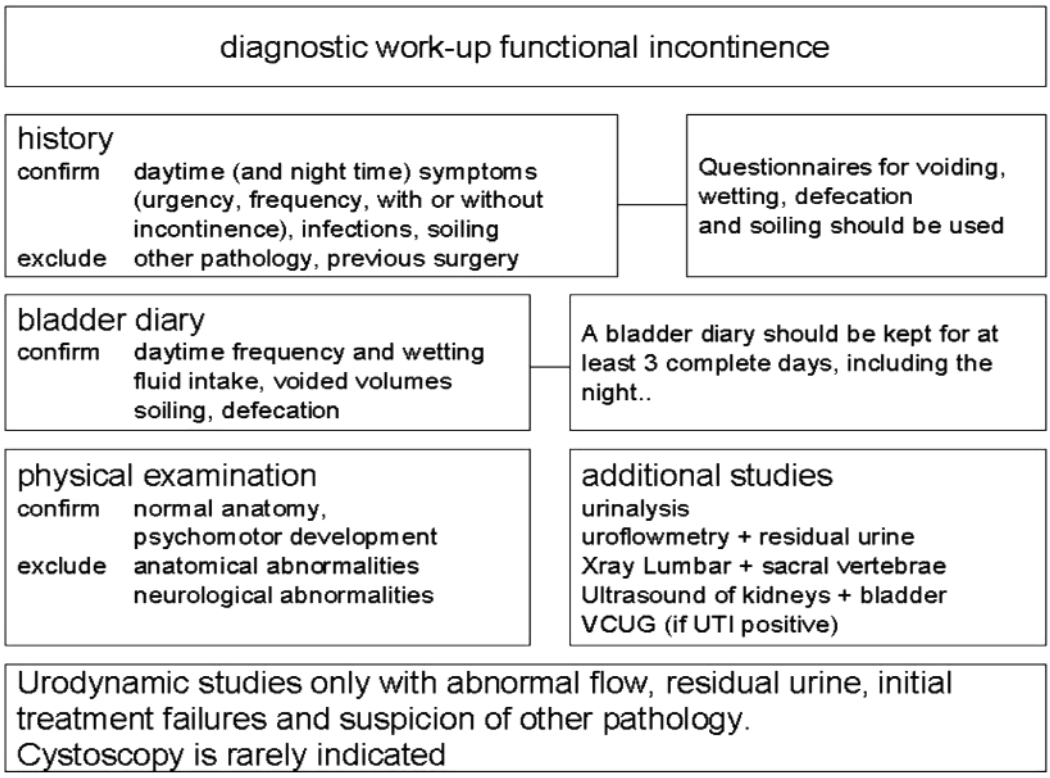

Figure 15. Workup functional incontinence

absence of pathologic or metabolic factors that may cause or mimic these symptoms. In the pediatric literature urge syndrome clinically is best characterised by frequent episodes of an urgent need to void, countered by contraction of the pelvic floor muscles (guarding reflex) and hold manoeuvres, 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 urge 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 are caused by 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 minimise wetting. The detrusor contractions can be demonstrated urodynamically, as can the increased activity of the pelvic floor muscles during each contraction. The voiding phase is essentially normal, but detrusor contraction during voiding may be extremely powerful. The flow rate reaches its maximum quickly and may level off ('tower shape').

Depending on fluid intake and urine production, the complaints of incontinence become worse towards the end of the day, due to loss of concentration and fatigue and may also occur during the night. Children usually diminish their fluid intake to minimise wetting, and therefore incontinence may not be the main complaint or symptom. Urge syndrome should also be considered in "continent" children with recurrent UTI and vesicoureteral reflux. A careful history and a bladder diary will demonstrate that they often suffer from urinary frequency, urgency and that their fluid intake is small and that their voided volumes are less than expected [46].

Some children with an overactive bladder are not incontinent during the day but suffer from nighttime incontinence. During the day they often have urgency and frequency without incontinence and should be treated accordingly. These children do not have monosymptomatic nocturnal enuresis but incontinence.

The powerful flow often seen in children with the urge syndrome can cause further problems, particularly in children who have learned to contract their pelvic floor muscles in respone to urgency. 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. 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 overactive bladder [47].

The constipation is aggravated by the decreased fluid intake. Constipation contributes to an increased risk of UTIs and may exacerbate the detrusor overactivity.

A careful history and physical examination and a bladder diary will identify those symptoms of overactive bladder. Urine flow rate registration and postvoid residual urine measurement help to further rule out 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. 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 for reflux [48,49].

The treatment of urge syndrome involves a multimodal approach. Behavioral modification is important and in some children may be all that is necessary. Others will require the addition of antimuscarinic medication. In some children, the addition of biofeedback is useful. It is important to treat other underlying and potentially complicating conditions such as constipation and UTIs.

In conclusion, the diagnosis of urge syndrome [overactive bladder in adults] may be made based on a careful history and physical examination in addition to a bladder diary. The addition of a uroflow and bladder scan postvoid residual are helpful in ruling out underlying dysfunctional voiding. Urodynamic studies are rarely required during the initial evaluation and management. Although behavioral therapy and pharmacologic therapy are the cornerstone of treatment for urge syndrome there is no strong evidence that this treatment is effective. In addition, the natural history of overactive bladder is not well understood which has an impact on determining the ideal duration of treatment [50].

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.

2. Dysfunctional voiding

Dysfunctional voiding refers to an inability to fully relax the urinary sphincter or pelvic floor muscles during voiding. Unlike, detrusor-sphincter dyssynergia there is no identified underlying neurologic abnormality in the dysfunctional voider.

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

No clear data are available on the possible causes of dysfunctional voiding. It may be that an overactive bladder eventually leads to overactivity of the pelvic floor muscles, with subsequent insufficient relaxation during voiding [51].

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 [21].

The child's environment, in particular toilet conditions and privacy issues, can trigger or exacerbate voiding anomalies [52].

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 [53].

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

Since no true structural obstruction can be identified the intermittent incomplete pelvic floor relaxation that occurs during abnormal voiding is termed a functional disorder.

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

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

Detrusor overactivity may be seen in both forms of dysfunctional voiding during urodynamic studies, but it may be absent [32,36, 43,54]

Sustained alteration of voiding is associated with subsequent filling phase anomalies such as phasic detrusor overactivity and inappropriate urethral relaxation [55]. Urinary tract infections and kidney damage are common sequelae [56].

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 underactivity of the detrusor (by some pediatricians incorrectly called the 'lazy bladder syndrome').

Urinary symptoms associated with dysfunctional voiding range from urgency to complex incontinence patterns during the day and night [57].

Urgency and incontinence of urine may result from detrusor overactivity and thus be seen in conjunction with increased urinary frequency. Alternatively, infrequent or poor bladder emptying may precipitate symptoms. Micturition is often achieved with significant abdominal activity and urodynamic investigations may show an interrupted or staccato flow pattern. 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 [45,58].

Symptoms are significantly more common in children with Attention Deficit Disorder than in 'normal' children [59].

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 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 [45, 60, 61].

The diagnosis of dysfunctional voiding should be based on a careful history and physical examination, a 48-72 hour frequency volume chart, wetness diary

and stool record. Renal and bladder wall thickness ultrasound studies along with urinary flow and residual urine measurements and urinalysis are first line investigations [62,63]. The pattern of the flow curve is usually indicative. The combination of uroflowmetry with pelvic floor electromyography [EMG], and bladder scan post-void residual determination obviate the need for an invasive urodynamic study in most cases.

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 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 [64]. A review of interventions for children with dysfunctional voiding revealed 17 studies; 8 evaluating biofeedback or pelvic floor muscle awareness training, 5 reporting alpha-blockade pharmacotherapy, 2 relating to electrical stimulation and one each describing clean intermittent catheterization and the use of anticholinergic medication. Only one study was randomized, none were controlled and 5 were retrospective.

Thus on the basis of quality, all interventions would be considered as having a level of evidence of 4 or lower. Controlled studies of the various interventions are needed.

As with overactive bladder, the natural history of untreated dysfunctional voiding is not well delineated and thus the optimum duration of therapy is not well described.

Level of evidence: 4

Grade of recommendation: C

3. Poor bladder emptying due to underactive detrusor

Children with this condition void infrequently, and usually present with urinary tract infections and incontinence. Urodynamically, the bladder has a larger than normal capacity, a normal compliance and 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 is aimed at optimising bladder emptying after each void. Clean intermittent (self) catheterisation 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 elctrostimulation 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. Non-neurogenic neurogenic bladder

Hinman and Bauman first described this condition and it was looked upon as an acquired personality disorder [65-67].

The psychogenic model has since been abandoned and it has been postulated, but not proven that the non-neurogenic neurogenic bladder may be the extreme end-stage of dysfunctional voiding.

It has been referred to as ‘occult neuropathic bladder’ [68].

A neurologic etiology must be ruled out before determining that the child’s voiding problems are consistent with the non-neurogenic neurogenic bladder.

Urodynamically, non-neurogenic neurogenic bladder is characterised by diminished bladder volume and compliance. Detrusor overactivity is often present and there is contraction of the pelvic floor muscles during voiding. Videourodynamic studies or a VCUG usually show all the features of a true neuropathic bladder. These children are at risk for upper tract damage and must be fully evaluated and seen regularly.

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

Treatment of the non-neurogenic neurogenic bladder is complex. Sometimes these children can be managed with antimuscarinic therapy and clean intermittent catheterization. Some children will require bladder augmentation to protect their upper tracts.

Level of evidence 4

Grade of recommendation C

5. Voiding postponement

A new classification of voiding dysfunction has been proposed by Lettgen et al and termed voiding postponement [69]. **Figure 16**

In this condition, children will postpone imminent micturition until overwhelmed by urgency, which makes them rush to the toilet, but often they are too late and urge incontinence occurs. Traditionally this syndrome was thought to be an acquired disorder due to detrusor overactivity and caused by voluntary overactivity of the urethral sphincter until the bladder became filled [70].

A recent study comparing children with typical urge syndrome to those with voiding postponement revealed a significantly higher frequency of clinically relevant behavioral symptoms in postponers than in children with urge syndrome, suggesting that voiding postponement is an acquired or behavioral disorder [69].

In the children with voiding postponement a staccato voiding pattern is not commonly seen, only 20% exhibiting a staccato voiding pattern. The authors concluded that the etiology of the overactive sphincter in children with voiding postponement is a behavioral maladjustment.

It remains to be determined whether or not voiding postponement can develop in the setting of a perfectly normal urinary tract or whether urge syndrome is a necessary precursor.

Level of evidence 4

Grade of recommendation C

6. Giggle incontinence

In some children giggling can trigger partial to complete bladder emptying well into their teenage years, and intermittently into adulthood [71].

The condition occurs in both boys and girls and is generally self-limiting.

The etiology of giggle incontinence is not defined. Urodynamic studies fail to demonstrate any abnor-

Figure 16. Symptoms in overactive bladder, dysfunctional voiding and voiding postponement.

Symptoms	Overactive bladder / Urge syndrome	Dysfunctional voiding	Voiding postponement
Frequency	> 7/day	varying	<5 / day
Urgency	yes	Varying, decreases with age	yes
Incontinence	+/- urge incontinence	Varying, decreases with age	Urge incontinence
Uroflow	May be tower-shaped	Staccato / interrupted	Normal or staccato
PVR	Usually <20 ml	Increased (> 20ml)	Varying
Presenting symptoms	frequency / urgency / incontinence / holding maneuvers	Recurrent UTI / incontinence	Incontinence, holding maneuvers

malities, there is no anatomic dysfunction, the upper tracts appear normal on ultrasound, the urinalysis is normal and there are no neurologic abnormalities [72,73].

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.

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 [72,74-76]. 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 4

Grade of recommendation D

7. 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 [entrapment] [77].

Vesicovaginal reflux may occur 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 to resolution of the urine leakage.

Level of evidence 4

Grade of recommendation C

8. Elimination Syndrome

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 [47,52,78].

There is also evidence to suggest that in severe cases symptoms may have 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 [79].

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 aetiological factor [80], however, recurrence of UTI in children older than 5 years is associated with the presence of ES [80,81].

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 bladder hypertrophy, detrusor overactivity, and lead to incompetence of the vesicoureteric junctions. The micturition reflex may become destabilized as a result of repeated pelvic floor recruitment aimed at controlling involuntary detrusor contractions leading to even greater detrusor hypertrophy.

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 [78].

Children with elimination syndrome commonly complain of urinary incontinence, non-monosymptomatic nocturnal enuresis, recurrent urinary tract infections, imperative urgency to void, 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.

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 the baseline characteristics of subjects were not described adequately enough to allow clear diagnosis of elimination syndromes [47,82]

The ideal study would utilize a validated symptom score, in addition to objective assessment parameters, to quantify treatment effect. Identifying a control group / treatment for children with elimination syndromes is likely to be problematic.

Level of evidence 4

Grade of recommendation C

V. TREATMENT

Many of the signs and symptoms of urge syndrome and other forms of functional urinary incontinence are the result of faulty perception of signals from the bladder and habitual nonphysiologic responses to the signals [28].

The etiology of the overactive bladder in children is unclear, but it appears to be related to a lack of ability to voluntarily inhibit the infant voiding reflex, a delay in central nervous system maturation. The pathophysiologic consequences of the overactive detrusor result from the child's voluntary efforts to try to maintain continence during the involuntary detrusor contractions. Such coping mechanisms include forceful contraction of the external sphincter and squatting maneuvers to provide perineal compression. Such maneuvers may lead to functional and morphologic changes in the bladder, which increase the child's risk of UTIs and VUR. In addition, tightening of the pelvic floor muscles leads to constipation, another risk factor for UTIs.

Older children may cope similar to adults with toilet mapping, defensive voiding and restricting fluid intake. Treatment of the overactive bladder / urge syndrome is focused 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 and dietary changes may be instituted as needed. Treatment of UTIs and constipation are also essential. More active treatment involves pharmacotherapy, 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 not randomized, are not placebo controlled, not double-blinded and have small numbers of patients enrolled making it difficult to draw conclusions. In a recent review of randomized controlled trials, for the treatment of daytime incontinence in children recorded in the Cochrane Controlled trials register, which examined Medline, Embase, reference lists of articles, abstracts from conference proceedings and contact with known experts in the field from 1996 to 2001, the authors identified only 5 trials that compared two or more

interventions using a randomized controlled design [83]. Of these 5 studies, 4 evaluated pharmacotherapy. Of the 4 pharmacotherapy studies, 2 evaluated the use of terodiline, 1 evaluated the use of imipramine and the remaining abstract the use of oxybutynin versus biofeedback [84-87].

The remaining study evaluated the use of alarm therapy for daytime incontinence [88].

Terodiline is no longer available due to its adverse effect profile, imipramine is not the first choice for daytime incontinence due to its side effects and alarm therapy is not felt to be a useful therapy for daytime incontinence. Therefore only 1 study in over 30 years was felt to be of high quality. This review highlights the need for properly designed studies to assess the impact of the various forms of therapy on daytime incontinence. The size of many existing trials means that clinically significant benefits or harms of interventions cannot be reliably ruled out. In general, published trials have not been large enough to show modest, but clinically important benefits. In addition, many of the reported studies are short-term studies and there is little data on the long-term follow-up of patients. In the adult population the importance of this is demonstrated with an initially good response to biofeedback in adult patients with overactive bladder but poor long-term results.

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 and their caregivers are educated about normal bladder function, learning to recognize the desire to void and eradication of holding maneuvers [i.e. immediate voiding without postponement]. Micturition charts and diaries and voiding regimens are helpful in ensuring regular voiding.

Dietary changes and bowel regimens are used to treat the constipation [89].

Antibiotic prophylaxis is felt to be helpful in preventing recurrent UTIs, however, data to support this is limited.

Children with urge syndrome need to learn to recognize the first sensation of bladder filling and how to suppress this by normal central inhibition instead of resorting to emergency procedures like urethral compression.

Children with dysfunctional voiding need to learn how to void with a completely relaxed pelvic floor and to void with a detrusor contraction and not the use of abdominal pressure.

"Bladder training" is used widely, but the evidence that it works is variable [90-91].

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 [28].

More active conventional management involves a combination of cognitive, behavioural, physical and pharmacological therapy methods. Common modes of treatment include parent and child reassurance, bladder retraining (including timed toileting), pharmacotherapy, pelvic floor muscle relaxation and the use of biofeedback to inhibit rises in detrusor pressure associated with urinary incontinence [92-96].

Further treatment options include suggestive or hypnotic therapy and acupuncture.

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

Curran et al described the long term results of conservative treatment of children with idiopathic detrusor overactivity [97]. Of 30 patients follow-up was long enough to draw conclusions; it showed complete resolution in 21 and marked improvement in five patients. The average time to resolution of symptoms was 2.7 years. Children with very small or large bladders were less likely to benefit from this treatment. Age and gender were not significant predictors of resolution although girls were more likely to have resolution than boys.

1. Bladder rehabilitation / urotherapy

The concept of urotherapy dates back to the late 1970's. Despite its use for many years there is no set format to urotherapy and many clinical studies utilize combinations of therapies, which makes it difficult to evaluate the results [94,95,98]

Many of the earlier studies involved intensive inpatient programs which are less likely to be available today. The aim of urotherapy is to normalize the micturition pattern and to prevent further functional disturbances. This is done through a combination of cognitive, behavioral and physical therapy methods.

Rehabilitation of bladder and pelvic floor muscles

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

Level of evidence 3

Grade of recommendation C

2. Standard therapy

There are several key components to the nonpharmacologic approach to the management of urge syndrome and dysfunctional voiding. The main points include:

- Education regarding the function of the bladder and sphincter mechanism
- Instructions on a voiding regimen promoting regular voiding habits and proper positioning – those children with elevated post void residuals are placed on double voiding regimens in addition to timed voiding regimens
- Bladder diaries
- Treatment of underlying constipation
- Treatment of concomitant urinary tract infections and antibiotic prophylaxis in those with recurrent urinary tract infections

This standard approach is used as a first step. Although several authors have described this method, there are no prospective randomized studies available to evaluate the success rate.

Level of evidence: 3

Grade of recommendation: C

3. Biofeedback

Training with biofeedback can be used as a single treatment [101,102], or in conjunction with a comprehensive rehabilitation program [99,100].

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.

Biofeedback may be performed by a cystometrogram for those with involuntary detrusor contractions. In this situation the child is taught how to recognize and inhibit involuntary detrusor contractions by watching the pressure curve during cystometry. When an involuntary detrusor contraction occurs the child is asked to consciously suppress the contraction [central inhibition] or to contract the pelvic floor muscles.

This is invasive and time consuming and therefore has limited use as a routine treatment.

Biofeedback may be performed through the use of an EMG and uroflow for those with dysfunctional voiding. Using the flow pattern, with or without EMG of the pelvic floor muscles, will teach the child how to relax the pelvic floor during micturition: the child sits on a toilet with a flow transducer, watching the flow curve and EMG on line on a computer display, trying to empty completely in one relaxed void. Ultrasound may be used to determine the post void residual and demonstrate complete emptying. Sometimes interactive computer games are used to make it more attractive to children [103,104].

The results of biofeedback are reported in only a few studies. In one study, the results were classified as good in 68%, improved in 13% and not improved in 29%. Others confirm the positive effect of biofeedback. In most studies, no information is provided on residual urine. Inclusion and exclusion criteria and the study design vary considerably between the various studies making comparison of the results difficult [105-111].

The use of biofeedback in the child with detrusor overactivity is limited by the potentially invasive nature of the procedure and the need for repeated sessions. Limited studies with intensive training, some of which utilized inpatient training have been published. Analysis of such studies is limited by the small number of patients treated, the lack of randomization, comparison treatment or placebo arm, the absence of standardized measure of outcome, and variable patient groups being treated.

Kjolseth et al used cystometrogram assisted biofeedback in 15 children age 6-12 years with idiopathic detrusor overactivity, some of who had nocturnal wetting.The children received 1-2 inpatient sessions and then sessions were carried out depending on the severity of the child's symptoms and the ease of learning for each patient. Response rates were self-reported.The authors noted no cures, 9 (60%) with pronounced improvement, 2 [13%] with some improvement, and 4 (27%) with no improvement.

Those who had an initial improvement were followed up to 2 years after end of therapy. The beneficial effects were maintained in all but one child who relapsed 4.5 months after treatment [112].

Hellstrom et al treated 70 children with either overactive bladder, dysfunctional voiding or a combination of both with a bladder rehabilitation program for a 6 week period [113]. Biofeedback was instituted if no improvement was noted in 2 weeks. Thirty two of the 70 children required biofeedback. Follow-up was up to three years and at 3 years 71% of the children with overactive bladder, 70% of those with dysfunctional voiding and 73% of those with a combined disturbance had a normal micturition pattern.

In its most simple form biofeedback can be regarded as a self-disciplinary measure to correct a long-standing inappropriate bladder habit. The principle of "re-education" using biofeedback has also been used to train individual children to inhibit inappropriate rises in detrusor pressure during bladder filling.

The practice of biofeedback can help children learn both to inhibit increases in intravesical pressure, and to improve contraction of the pelvic floor muscles [100,114-116].

Level of evidence: 3

Grade of recommendation C

4. Physiotherapy

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

Success rates vary between 50 and 80 percent: however, all studies describe a heterogenous group of children, use more than one treatment modality [like standard therapy in combination with physical therapy and biofeedback] and outcome is defined inconsistently [97,99,117].

The finding of studies, that children who previously had been treated unsuccessfully with biofeedback or standard therapy alone responded better to a combination of treatment modalities [comprehensive package] suggests that the comprehensive program is more effective.

Level of evidence: 3

Grade of recommendation C

5. Clean intermittent (self) catheterisation

In children with an underactive detrusor, bladder emptying can be achieved with timed and double voiding. If this does not provide adequate results, clean intermittent self-catheterization (CISC) may be tried [118-120]. 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

6. Neuromodulation

Neuromodulation has been used in adults for a variety of lower urinary tract symptoms. However, the invasive nature of the procedure makes it less attractive, particularly for children.

The use of transcutaneous stimulation with surface electrodes stimulating the sacral root (S3) has shown promising results but further studies are needed [121]. Several frequencies of stimulations have been tried and stimulation of 2 Hz seems to be sufficient: it is still not clear how long the stimulation has to be given during each treatment session and for how long it needs to be continued [upto 6 weeks?]. Most studies describe children who have failed other treatment modalities: de novo patients may be included, but most studies are not explicit about this.

Different modalities [transcutaneous and intravesical stimulation] are being tested in children and the role of neuromodulation in children is not well defined [122-129]. Level of evidence: 4

Grade of recommendation D

7. 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 non-contingent alarm system (which sounded at intermittent intervals to remind the child to void) [130].

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 non-contingent alarm, the difference in the reduction in wetting between the groups was not significant (RR 0.67, 95% CI 0.29 to 1.56).

Level of evidence: 3

Grade of recommendation C

8. Conclusion

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

Most studies only state the clinical responses, and do not provide information on urodynamic parameters before and after treatment. A 'normal' flow curve 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, endoscopic investigations should be performed. Most often the abnormality can be treated at the same time. In girls, a meatal web may cause a deflection of the stream upwards [causing stimulation of the clitoris and bulbocavernosus reflex]. A meatotomy may cure this problem, though no information on the long-term effects is available [53].

VI. PHARMACOLOGICAL THERAPY

Antimuscarinic therapy remains one of the common forms of therapy for the overactive bladder. 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 overactive bladder. 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 urinary tract infections [131].

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 [98].

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 [132].

More recently, a long-acting formulation, Oxbutynin-XL, has been approved by the FDA for use in children [133]. 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 [134].

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 compa-

red to immediate release oxybutynin. Its use in the neurologically intact patient is limited by the need for catheterization [135].

There are only a few studies, that are not randomized, double blind studies assessing the efficacy of oxybutynin in overactive bladder 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 [97].

Tolterodine, a nonselective antimuscarinic is currently being used for the treatment of overactive bladder in adults. It is the first antimuscarinic agent designed specifically for use in overactive bladder 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 [140].

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 overactive bladder.

Hjålmas reported the results of an open label, dose escalation study using immediate release tolterodine in 33 children [136]. 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 [137]. 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 in children with "dysfunctional voiding" manifested as daytime wetting, frequency or urgency [138]. There was no documentation of uroflow studies to make the diagnosis of "dysfunctional voiding" and from the symptoms these children appeared to have overactive bladders. Children were started on behavioral modification for 4-6 weeks and pharmacologic therapy wasinstituted 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 [139]. 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 ($p<0.05$)

The only drug which has been investigated in a randomised placebo controlled trial is terodiline [84,85]. 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 avai-

lable in a twice a day dosing formulation. In the adult population, there is a 16% intraindividual variability in bioavailability and 36% interindividual 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 [140].

Lopez Periera et al evaluated the use of trospium in 62 children with documented detrusor overactivity and absence of 'detrusor sphincter dyssynergia' [141]. 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.

Like trospium, propiverine has been used in children, but results are variable and inclusion and outcome criteria were not in accordance with ICCS definitions which make comparison with other studies difficult [142-14].

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 [145]. The trigone should not be injected, as there is an increased risk of reflux developing. The results last about 6-9 months.

Injection is also possible into the external sphincter, but the results are more variable and last only 3-4 months [146].

Treatment of the overactive pelvic floor and sphincter is much more difficult. Treatment with α-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 [147-150]. Further studies are needed to define the place of alpha-blockers.

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 [151].

Level of evidence 3

Grade of recommendation B/C

VII. CONCLUSION

The limited number of identified randomised controlled trials does not allow a reliable assessment of the benefits and harms of different methods of management in children. Further work is required in this difficult clinical area.

The establishment of outcome measures is needed, to facilitate randomised 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 overactive bladder 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.

The term 'lazy bladder' should be changed: it has no intuitive meaning and should be dropped. It would be much better to call it 'poor bladder emptying due to detrusor underactivity or acontractile detrusor'.

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

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 neurogenic bladder. It not only made conservative management a very successful treatment option, but it also made surgical creation of continent reservoirs a very effective alternative with a good quality of life [3].

Neurogenic bladder in children with myelodysplasia presents with various patterns of detrusor-sphincter dysfunction within a wide range of severity. About 15 % of neonates with myelodysplasia have no signs of neurourological dysfunction 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 neuro-urological function at birth have a 1 in 3 risk of developing either detrusor sphincter dyssynergia or areflexia by the time they reach puberty [5].

At birth the majority of patients have normal upper tracts, but nearly 60 % of them 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 from one patient to the other. Although the last quarter century has witnessed a remarkable progress in 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 most common presentation is at birth with **myelodysplasia.** The term myelodysplasia includes a group of developmental anomalies that result from defects in neural tube closure. Lesions may include 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.

The neurologic lesions produced by myelodysplasia are variable contingent on the neural elements that have everted 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.

In **occult myelodysplasia** the lesions are not overt and often with no obvious signs of neurologic lesion, but in many patients, a cutaneous abnormality overlies the lower spine. This can vary from a dimple or a skin tag to a tuft of hair, a dermal vascular malformation, or an obvious subdermal lipoma. 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 voiding dysfunction.

Cerebral palsy patients may also present with varying degrees of voiding dysfunction usually in the form of involuntary detrusor contractions and wetting.

Detrusor sphincter dysfunction is poorly correlated with the type and spinal level of the neurologic lesion.

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 bladder may be overactive with increased contractions, have diminished 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.

These conditions may exist in any combination [8-13].

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'.

Urodynamic investigations make it possible to establish a management plan for each individual patient.

Level of evidence 3

For the very young child the combination of an overactive detrusor and sphincter is potentially dangerous because of the high intravesical pressures, which will put the upper tract at risk [vesicoureteral reflux and hydronephrosis], whereas an inactive detrusor and paralysed sphincter is relatively safe, providing a low-pressure reservoir [14,15].

Level of evidence: 2

IV. MANAGEMENT

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

In the first years of life the kidneys are highly susceptible to backpressure and infection. In this period emphasis will be on documenting the pattern of neu-

rogenic detrusor- sphincter dysfunction and assessing the potential for functional obstruction and whether or not there is vesicoureteral reflux [16,17]. Ultrasound studies and a VCUG 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 [18].

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 [18-21]. 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 [22-26].

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 [27, 28].

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 [29-31].

Level of evidence 3.

Retrospective evaluation of patients has also shown that significantly fewer augmentations were required in patients with early start of CIC [22,23].

Level of evidence 4

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%.

At present oxybutynin, tolterodine, trospium and propiverine are the most frequently used drugs: some clinical studies are available, but no randomised placebo controlled studies have been performed [31-35]. Of these drugs only oxybutynin is licensed in the USA.

Level of evidence 3. Grade of recommendation: B

A prospective controlled trial evaluating trospium in children reports that trospium is effective and safe in correcting detrusor instability in children but this study does not include patients with a neurogenic bladder [36].

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 [37].

Level of evidence 4.

Use of lidocain intravesically has been shown to be effective to improve bladder capacity and compliance and decrease overactivity in children with neurogenic bladder [38]. There are no data available on long term use.

Level of evidence 4

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 [39,40]. 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 [41,42]. 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 evidenced detrusor overactivity, while non-compliant bladders without obvious detrusor contractions are unlikely to respond to this treatment.

Level of evidence 3

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.

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, reflex activity of the external sphincter and the consequent failure to fully empty the rectum [43].

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 [44-48].

Level of evidence 3.

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 [49].

Electrostimulation of the bowel may also offer a variable improvement in some patients [50].

Level of evidence 3

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 [51-53]. 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

Patients with vesicoureteral reflux often should be placed on prophylactic antibiotics to reduce the incidence of pyelonephritis, which can potentially lead to renal damage [54,55].

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 [56]. 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 [57-61].

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 can progress slowly but may occur with startling rapidity in these children.

F. SURGICAL MANAGEMENT

Surgical intervention is usually 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. Multiple mechanisms for incontinence may coexist 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 voiding with low pressures and no 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

Bladder Exstrophy: The incidence for 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 [1-3]. Some children will develop more or less normal capacities, while other patients end up with a poorly compliant small bladder, requiring later bladder enlargement or urinary diversion [ureterosigmoidostomy] [4-7]. 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 [8,9]. Continence rates vary from center to center and may range between 43 to 87%.

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.

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.

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 [10-13].

Posterior urethral valves may cause severe hypertrophy of the detrusor with a small poorly compliant bladder [14,15].

Unfortunately, following valve ablation, these bladders may not return to normal function [16,17].

II. ABNORMALITIES OF SPHINCTERIC FUNCTION

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 [18,19].

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.

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.

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.

• Bypass of sphincteric mechanism

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 or vaginal vestibule, thus causing incontinence [20].

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.

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 [21].

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. These 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 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 blad-

der (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.

2. Sphincter function

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 at all, 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.

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 also is 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 recto-sigmoid 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.

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 [22]. 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).

2. Bladder augmentation, bladder replacement, 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 contraindications are the inability of the patient to be catheterized, or perform CIC him of 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 m2, 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).

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 these procedures may complicate transurethral catheterization.
- 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 can not be emptied through the suprapubic 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.

3. Which intestinal segment should be utilized?

a) 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 [23,24]. 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.

b) 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.

c) 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 [25,26].
- 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.

d) Bladder augmentation techniques

1. 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 well. The segment is brought down to the bladder easily in the retroperitoneal space along the great vessels.
2. 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.
3. The techniques for urinary diversion with continent stoma [Mainz pouch, Indiana pouch, Kock pouch] are covered in the chapter on urinary diversion in adults [27-29].

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 [30-35]. 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.

e) 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 or 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 [36-39], most authors have been unable to achieve previously reported success [40].

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 [41]. Similar findings have been reported by others [42,43]. 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. [44,45]. Despite the indifferent results some still suggest its consideration before a standard augmentation because of the reasons listed above [46-48]. (Grade C)

f) 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 [49-50]. The intense inflammatory response and shrinkage observed in the intestinal segment discouraged its use in humans [51]. 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 [52]. 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 [53,54]. This form of bladder augmentation was shown to prevent absorption of toxic substances like ammonium chloride [55]. 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 [56].

The initial experience in treating humans with colocystoplasty lined with urothelium were reported by Gonzales and Lima who developed a slightly different technique independently [57, 58]. 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 to contract (hey remove the balloon after 2 weeks: urine is diverted using ureteral stents): in 123 patients no ruptures were found and only 10% is regarded as failure [59]

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 conclude that this is their preferred method of augmentation when adverse bladder changes occur after implanting the AUS [60].

Although more authors have now reported their results it still remains a more complex form of augmenting the bladder and should only be done in special centres [61-64]. (Grade C)

g) 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 [65,66].

Another alternative in patients with ureteral dilation and good ipsilateral renal function, is to combine transureteroureterostomy with ureterocystoplasty [67]. Another alternative in bilateral dilated ureters with preserved renal function is bilateral reimplantation and the use of bilateral distal ends for detubularized bladder augmentation [68-69].

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 [70-73]. It has been shown that this type of augmentation can also be employed in children who require a kidney transplantation [74,75].

h) 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 can be grown by tissue culture techniques on a degradable polymer scaffold and then implanted in animal models to fashion a bladder augmentation. Clinical trials with these methods are not far away [76-80].

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 [81,82].

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 [83-85].

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 [86,87]. 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 2 years only 50% remained dry [88,89]. Others have reported success rates of 0 - 34% [90-92].

An alternate route may be the injection around the urethra using laparoscopy [93].

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 [94]. 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 [95]. 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 H2O 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 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 [96-98]

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 [99]. 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 [99-102].

The continence rate ranges from 63 to 97% [103 –107].

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 [108]. 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 [109].

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 [110].

The second most common problem is the development of reduced bladder compliance with time. This may result from an error in the preoperative evaluation, the reaction of the detrusor to obstruction (a reaction noted in some patients with spina bifida). Or 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% [103]. For this reason AUS implantation may be better considered as the initial treatment in selected cases [111].

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 [112].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 [113].

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 [114,115]

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 [116-119].

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 [120].

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 equal results compared to rectus fascia. The advantage being that it is available off-the-shelf. Results were better in girls than in boys (85 vs 43% being dry) [121,122].

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 [123].

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. 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.

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%) [124,125].

One of the most important factors seems to be compliance with intermittent catheterization 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 [126-131].

Such procedures may initially require intermittent catheterization or occasional post voiding catheterization, 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 intraluminal 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 [132]. [Grade 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 [126-136]. 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 [137].

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 [131,135,136].

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)

VII. 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.

1. 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 [138]. 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 [139,141]. In the original description, the appendix was used. However, even if the appendix is still present, it may be unusable in 31% of patients [140].

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 [142,143]. It is increasingly used though great care must be taken in its construction to avoid an internal fistula [144].

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. [145]

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 [146,147].

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 [148].

Continence rates of 90-100% with the Mitrofanoff Principle are reported, regardless of diagnosis, reservoir or conduit type [148,149].

Follow-up for at least ten years has shown that the system is resilient [150,151].

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.

2. 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 [152-154].

The Indiana system is based on the competence of the ileo-caecal valve but with a detubularized reservoir [155]. 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 [156]. 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.

3. Kock pouch

The first workable continent diversion was the Kock pouch [157]. 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 [158,159].

4. 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 [160]. The AUS has been used successfully around large bowel, in three of four children with follow-up to 11 years [161].

5. 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 [162].

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 [163,164]

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 [148].

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 enterocystoplasty [165].

Combinations of detrusormyomectomy 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 [165].

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 [166].

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 [167]

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 [168,169] . 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.

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 disproportionately high [168]. In a series of 264 children with any sort of bowel reservoir or enterocystoplasty, 23 perforations occurred in 18 patients with one death [169]. Therefore, as this complication is more common in children it becomes a very important consideration [170].

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 [171]. 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 [172].

In a series of 23 patients, Ditonno et al found that 52% of patients with a reservoir of right colon had hyperchloraemic acidosis [173]. In ileal reservoirs, Poulsen et al found mild acidosis but no patients with bicarbonate results outside the reference range [174].

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 [175]. It is prudent to monitor patients for metabolic abnormalities, especially hyperchloraemic acidosis, and to treat them when found [176].

With increasing experience, it has become clear that there is a risk of developing vitamin B12 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 B12 may last for several years before the serum level becomes abnormal. At a mean follow up of six years, low levels of B12 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 B12 deficiency suggesting that the finding was clinically significant. Similarly, in adults, 18.7% have B12 deficiency at five years. In the adults the mean B12 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) [177,178] . In order to avoid the serious neurological complications, regular monitoring of B12 levels is essential.

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 [179,180].

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 [181].

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 [182,183].

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 [184]. 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 that has been found 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 [185]. 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 [186].

Although a complicated procedure, a renal transplant can be anastomosed to an intestinal reservoir with similar long term results as those using an ileal conduit [187,188].

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 [189]. 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 [190]. 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 [191]. 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 [192].

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 [193].

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 [194].

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 [195].

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 [197]. 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 [196].

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 [195].

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] [192].

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 [198, 199].

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 [200]. It is unclear whether prophylactic antibiotics is 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 [201]. 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 [202].

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 [203, 204].

More recent follow-up data shows either no effect on growth or a decreased linear growth [205-207].

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 [208]. 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 [209]. With a suprapubic diversion, catheter drainage for incontinence or retention may be needed in the third trimester [210].

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. 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 [211]. Clinically significant levels probably only occur in chronically infected reservoirs [212]. 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 [213].

In a review by Filmer et al, 14 cases of pouch neoplasm were identified [214]. 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 % [215].

If cancer is going to be a common problem, there will be some difficulty in monitoring the patients at risk [216]. 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 [217]. 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 [218]. 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 [219].

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 [220].

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 [221].

IX. 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. FECAL INCONTINENCE IN CHILDREN

I. INTRODUCTION

Fecal incontinence during childhood may be a symptom of delayed acquisition of toileting skills or may reflect serious underlying organic or functional pathology. Whatever the cause, the social and psychological consequences for the child and their family are often profound.

There are considerable cultural differences in toilet training and across the world children acquire bowel control at anytime between 1 year and 4 years of age [1,2,3]. Children tend to be trained earlier when the carer is able to immediately respond to signals that the child is about to defecate. The trend in Western cultures has changed in the past 30 years to allow a more child oriented approach in which the behavior of the child dictates when toilet training is introduced [4]. In the USA the average age at which bowel control is gained is 28 months and the vast majority of children will have acquired bowel control by 4 yrs of age [5].

The pattern of bowel actions changes during early life from an average of 3 stools per day in the neonate to 1.7 stools per day at 1 year of age. 97% of preschool children in the UK will pass stool within the range 3 times per day to alternate day [6].

Epidemiological data on fecal incontinence in the normal childhood population is variable. Bellman observed a prevalence of 1.5 % among 7 yr old Swedish children, and Rutter in the UK reported a similar prevalence in 10-11 year olds [7,8]. It accounts for 3% of referrals to a medical clinic in Boston [9] and 25% of referrals to specialist gastroenterology clinics.

It is now generally accepted that by far the most common cause (around 95%) for fecal incontinence in childhood is secondary to functional fecal retention (FFR) or constipation.

There is a smaller group of children where there are other causes, such as delayed acquisition of toileting skills, often related to neuro-developmental difficulties or delay, or organic pathology such as anorectal anomalies and spina bifida. Finally a group with functional non-retentive soiling where the soiling appears deliberate and associated with significant emotional disturbance.

Whatever the cause, soiling is responsible for profound social and psychological consequences for the child and results in behavior disturbance in 40% of affected children [10]. Resolution of soiling makes a huge difference in improving the child's self-esteem, family and school relationships. Achieving this is best done using a multi-disciplinary team approach making sure parents and children are fully informed and engaged with the management strategy.

Levels of evidence and research into the most common cause of fecal incontinence in children – functional retentive soiling - are generally poor although combined laxative and behavioral toileting programs have been shown to be more effective than either alone.

II. DEFINITIONS

Differences in definition can lead to confusion when comparing the literature.

In the USA encopresis is defined as "involuntary fecal soiling in the presence of functional constipation, in a child over the age of 4 years". Within the UK and Australian literature this is usually called "soiling" with the term encopresis being reserved for those where there appears to be voluntary passage of stool into a socially unacceptable place, implying a large emotional and behavioral element. This is a far less common cause of incontinence.

A Multinational Consensus Document On Functional Gastrointestinal Disorders: Rome II [11] identifies functional fecal retention and functional non-retentive soiling as separate entities with the following descriptions:

"Functional fecal retention [FFR] is the most common cause of constipation and fecal soiling in children. It consists of repetitive attempts to avoid defecation because of fears associated with defecation. Consequently, a fecal mass accumulates in the rectum."

The Rome II criteria for FFR is of a history of > 12 weeks, passage of less than 2 large diameter bowel movements a week, retentive pushing and accompanying symptoms such as fecal soiling. Unfortunately this is likely to be too restrictive and does not identify all children with FFR [12]. Additional items are suggested: – large stools, history of chronic abdominal pain relieved by laxatives and presence of an abdominal or rectal fecal mass.

"Functional non-retentive soiling may be a manifestation of an emotional disturbance in a school-aged child. Soiling episodes may have a relationship to the presence of a specific person [e.g., a parent] or time of day, and may represent impulsive action triggered by unconscious anger."

III. CAUSES AND ASSOCIATIONS OF CONSTIPATION AND FECAL INCONTINENCE

1. Organic causes of constipation

The first role of the pediatrician is to identify those few children with underlying organic disease such as Hirschprung's disease, anorectal anomaly and those with a neuropathic bowel (**Figure 17**). 1 in 5000 children is born with Hirschprung's disease. Reports of fecal incontinence after surgery for Hirschprung's disease vary widely. Several studies show a prevalence of 10 – 20% [13,14] but Catto-Smith and colleagues in Melbourne have described soiling in 80% of 60 patients followed up by questionnaire and interview [15].

Figure 17. Organic causes of constipation

Neurogenic
meningomyelocele, spinal dysraphism, spinal tumor, sacral agenesis, cerebral palsy, dystrophia myotonica
Anorectal anomaly
anal atresia, stenosis, ectopic anus
Acquired anal conditions
anal fissure, Group A streptococcal infection, lichen sclerosis et atrophicus, anal sexual abuse
Congenital bowel disorders
Hirschprung's disease, neuronal intestinal dysplasia, chronic intestinal pseudo-obstruction
Miscellaneous medical conditions
Hypothyroidism
Hypercalcaemia
Cow's milk protein intolerance
Drugs
Opiate analgesia
Loperamide
Anticonvulsants
Antimuscarinics

Ninety percent of those with meningomyelocele will experience fecal incontinence of some degree [16]. It is important to identify children with less overt spinal abnormalities, such as spinal dysraphism and sacral agenesis as the majority in this group will also have a neurogenic bladder. Preservation of the upper renal tract from reflux and infection is a priority in order to protect future renal function.

There seems to be no obvious connection between symptoms, degrees of difficulty in controlling bowel movements and laxatives needed to treat, with the cause of constipation except the suggestion that some children with early onset constipation and little or no soiling may have Intestinal Neuronal Dysplasia [17,18].

Another interesting observation in a group of 89 children with generalised hypermobility of the joints is the association of an increased incidence of constipation and soiling in boys. The girls were more likely to have day and night wetting problems [19].

A systematic review of the treatment of anal fissures in all ages with a variety of therapies including glyceryl trinitrate, botulinum toxin, diltiazem, placebo and surgery has shown that the medical therapies were only marginally better than placebo and for chronic fissures surgery gave the most effective results [20].

2. Functional fecal retention / functional retentive soiling

95% of children who soil have no inherent bowel or neurological abnormality but are incontinent as a result of functional constipation. There has been considerable debate as to the relative influences of psychological, behavioral and physical factors in the development of constipation but the cause of severe constipation is probably multifactorial.

In young children, stool holding is a common antecedent of constipation seen in 13 % of 480 children followed through the toilet training process by Taubman [5]. Parents may describe manoeuvres and postures adopted by the child that almost certainly represent avoidance of defecation. Such behavior is reinforced by episodes of painful defecation, as with anal fissure. In older children, reluctance to use toilet facilities at nursery and school may also precipitate stool holding and subsequent constipation .

There are still problems in identifying children with this condition at an early stage as 10-20% parents may misinterpret the soiling as normal passage of stool and do not appreciate there is underlying fecal retention [21,22]. However in these children, the fact that they have little sensation of the passage of this stool should alert the pediatrician to the likelihood of constipation as the underlying cause of the soiling.

Assessment of these children requires a detailed history and examination to exclude any organic cause. No recent changes to the process have been suggested and in general, few if any, initial investigations are necessary provided no other potential condition is discovered on assessment. The key to management following initial clearout remains a combination of a toilet training behavioral program with laxatives to keep the bowel clear. Increasing clear fluids and attention to diet to increase fibre content and reduce milk intake if necessary, is also important.

Over the last few years osmotic laxative treatment with macrogols (polyethylene glycol variations, with and without electrolytes) have been shown to be effective and safe both in large doses for initial clear out and smaller doses for maintenance [23, 24, 25, 26, 27].

These medications are well tolerated and thus improve compliance. Most children can now be cleared out at home and no longer require hospital admission although families need to be warned that the process can take 5 days or more to complete. If hospital admission for clear out is necessary, oral treatment for disimpaction using Kleen Prep® by nasogastric tube is usually effective and avoids the use of rectal enemas or suppositories that can upset younger children.

Although macrogols are effective for maintenance, some children will not be completely controlled and require additional stimulant laxatives such as Senna or Sodium Picosulfate – the latter being more effective and better tolerated than Senna.

Parents / carers still require encouragement to continue with medication for a long time, often well over a year, only reducing it slowly. Any recurrence of soiling is usually an indication that fecal retention has occurred and medication should be increased or changed accordingly. This should be written into care plans (where they exist) so there is no delay in re-establishing bowel control.

3. Functional non-retentive soiling

Children over 4 years who do not have underlying constipation and have no organic or anatomical abnormality are defined as having "non-retentive soiling". They often pass normal stools into clothing at normal stool frequencies. Day and night time urinary incontinence is commonly associated. Attention to signs of toilet training readiness is important with specialist help in devising programs to encourage continence for both urine and stools.

Soiling may result from loose stools in some children. Care needs to be taken to make sure this is not overflow soiling and to identify any underlying inflammatory bowel disease. Anti-diarrhoeals may help in achieving continence.

Primary and involuntary soiling may be due to delayed toilet training. Children with neuro-developmental disorders such as autism, attention deficit hyperactivity disorder and developmental co-ordination disorder are more likely to have problems with constipation. They are more likely to have difficulties in establishing normal toilet training routines because of problems with poor attention, motivation, fine motor skills and sequencing [28]. Functional constipation is also common in this group.

There are now some useful publications to help parents and professionals available through ERIC (Education and Resources for Improving Childhood Continence) and the assistance of a pediatric nurse specialist continence advisor is useful in making sure home/school programs are appropriately arranged and properly coordinated [29].

Secondary or voluntary soiling is more likely to have an underlying psychological cause especially when it is related to specific and identifiable triggers. Children with a history of abuse or neglect often have continence problems with soiling in 26% [30]. However chronic fecal retention needs to be excluded.

Children who appear to have a major social and behavioral element underlying deliberate soiling of normal stools in unacceptable places need more intensive help from Child & Adolescent Mental Health teams where the whole family situation can be addressed.

4. Anorectal malformations

These conditions are often associated with urological congenital anomalies. In high anorectal malformation this reaches 25-50%. In a series of 47 children without concomitant meningomyelocele, a variety of urological abnormalities were found with an association of fecal incontinence in over 50% [31]. It is thus important that both urinary tract and bowel are investigated and treated appropriately in these conditions.

The surgical treatment of these conditions and Hirschsprung's disease is not within the remit of this review.

IV. SECONDARY EFFECTS

1. Psychological and behavioral effects

Whatever the cause of fecal incontinence, loss of bowel control is one of the most devastating symptoms a child can suffer. Soiling results in increased anxiety and loss of self-esteem. There are significant negative effects on relationships with family members and at school where bullying can become a serious problem. Children are often blamed for being "lazy" as it is not understood that they have little or no bowel control. Many children respond by denial and will hide soiled pants rather than admit to an accident. The whole family, not just the affected child, can experience guilt and failure with associated shame and secrecy leading to isolation [32]. Parents and other carers often give confusing messages by being cross and punitive at times but encou-

raging and forgiving at others. Continuing problems can lead to "learned helplessness" as all attempts to control the soiling fail [33-35]. Behavior problems defined by parents are found in up to 40% of children with soiling but these are not generally as severe as in children referred to child mental health services [34,36]. Most of these behavior difficulties resolve with successful treatment of soiling indicating they are likely to be secondary. However some children with severe behavioral difficulties associated with poor intra family relationships do not have good outcomes [37]. Breaking these negative cycles by engaging the child and family with appropriate explanations in a non-blaming fashion is vital. It should generate the motivation to cooperate with the management of the condition.

2. Educational aspects

Although up to 40% of children will not have gained full bowel control by entry into nursery at 3 years of age, lack of adequate provision for these children can cause difficulties. In the UK, Department of Health guidance suggests that schools should "recognize the need for unrestricted access to non-threatening toilet facilities". However, school toilets are often unsatisfactory or viewed as such by children [38].

V. ASSESSMENT

The aim of assessment is to identify the cause of fecal soiling and especially identify those children where there may be an underlying organic condition. Other related problems need exploring and an appropriate management plan developed that takes into account the whole child and family.

1. History

A careful history is vital. The following areas should be covered:

	Reason
Age of onset, any initiating factors. Primary or secondary	Constipating event?
Present stool habits – interval, size [any huge] and consistency	
Soiling – interval, amount, consistency, when and where.	
Coping strategies. Hiding soiled pants? School involved?	
Attitude of child, parent, school friends etc.	
Co existing conditions. Congenital or acquired disorders	Neuropathy?
Atopy	Cow's milk intolerance?
Medication [e.g. antimuscarinics, anticonvulsants, opiates]	Constipating effect
Learning or attentional difficulties, language impairment.	Delayed toileting
Behavioral problems	1° or 2° to soiling?
Previous surgery – especially related to GI tract	Possibly related
Previous GI symptoms	Constipation associated
Birth history – delay in passage of meconium, early constipation	Hirschsprung's disease
Family history of bowel related difficulties	Genetic or dietary
Social history, any past history of any type of abuse	Abuse associated
Toilet training history – delay, holding, toilet refusal.	Constipation
Age when could identify need to pass stool without prompting	1° or 2° soiling
Nocturnal enuresis, day wetting, frequency, urgency	Frequently associated
Diet [fibre content and balance]	Very low fibre, restricted
Fluid intake and type.	Poor total intake or milk in excess

2. Physical examination

Special attention should be paid to:

- growth and general overview to exclude failure to thrive and neglect,
- abdomen – distension, palpable fecal mass
- anus and genitalia – careful inspection for abnormality
- perianal sensation, inspection of lower back, spine and buttocks, lower limb reflexes to exclude any suggestion of neuropathy
- rectal examination is not usually necessary and may cause distress to younger children.

Where there is doubt and perhaps when parents need convincing evidence, a plain abdominal X-ray can show significant fecal loading and gross rectal enlargement. A recto-pelvic ratio greater than 0.61 has been suggested as demonstrating enlargement. [39]. Scoring systems have been devised in an attempt to quantify fecal loading [40,41]. Measurement of bowel transit time using radiological markers may contribute to the clinical picture [42]. A simple method to determine fecal impaction is the use of ultrasound: a fecal mass behind the bladder can easily be detected.

3. Anal manometry

Anal manometry is an invasive investigation and is not regarded as routine. It may contribute useful information in children suspected of having a neurological abnormality or where response to conventional treatment is poor.

Children with chronic constipation have significantly increased rectal volume and rectal myohypertrophy [43,44]. 50% of 34 constipated children studied by Loening-Baucke had an abnormal increase in external sphincter activity during attempts to pass a balloon [43]. There is no evidence for any underlying abnormality in rectal sensation or rectal wall compliance in children with fecal impaction [39]. Anal manometry abnormalities have been shown to persist even after effective treatment of constipation and encopresis (or soiling) [43].

VI. MANAGEMENT

Most advocate a multidisciplinary approach in which psychosocial and biological issues are both addressed [47,34]. Nolan and colleagues, in a large randomized trial found a multimodal approach [disimpaction, maintenance laxatives and behavior modification] to be superior to behavior therapy alone [48].

There are various components to a successful treatment plan:

1. Explanation / "demystification"

It is crucial that parents, carers and the child understand the reason why soiling is occurring. The child is likely to have little or no sensation of soiling episodes. Acknowledging this is a relief for children who previously have not been believed although it may cause guilt for those parents.

2. Toileting program

Establishing a normal and regular pattern of bowel evacuation is central to eventual success for children with soiling from any cause. Star charts and reward systems can be used to reinforce this behavior. Externalization of the bowel problem by using ideas such as goal scoring charts or beating that "sneaky poo" can be helpful. Behavioral programs like these on their own have been shown to be of benefit but are even more successful when used in conjunction with appropriate laxative medication [48,49]. Continuing follow up and support to maintain motivation is important.

3. Diet and fluid intake

A well balanced diet with a reasonable fibre intake is likely to be helpful. Experimental studies have shown that increasing fibre results in shorter bowel transit times and stool with greater volume and water content [50]. Mean daily fibre intake in constipated children was statistically lower than that of controls in a series from Greece but low fibre intake is not thought to be the only causative factor [51]. Excessive consumption of milk or poor fluid intake probably contributes.

4. Laxatives

There is general consensus that the child with constipation and overflow soiling requires laxative treatment with the aim of evacuating retained stool and maintaining regular bowel actions thereafter [31, 52, 53].

The evidence base to support the choice of laxatives is however small. Within the UK and Australia the common practice is to combine osmotic laxatives such as lactulose with stimulants such as senna, sodium picosulphate or sodium dioctyl. There are however very few relevant clinical trials and none which contribute significantly to the debate. Lubricants such as mineral oil provide the mainstay of

treatment in USA often in combination with laxatives such as senna. Lipoid pneumonia has been described with mineral oil treatment and this should be used with caution in a child at risk of aspiration [54].

Fecal impaction can often be cleared with oral laxatives and lubricants in adequate doses, but in more resistant cases, enemas may be required. Many children find these distressing and effective evacuation of stool is often possible without resorting to rectally administered treatment [55].

Isotonic intestinal lavage with polyethylene glycol is effective and clears retained feces in severe refractory constipation [56,57].

Once retained stool is cleared soiling will dramatically reduce. Various approaches have been used to maintain regular bowel actions – the mainstay being laxative treatment with behavioral approaches, designed to establish a regular toiletting routine, enhance compliance and maintain motivation.

5. Biofeedback

Biofeedback training appears to have short term benefits but more recent controlled studies have not demonstrated that these are greater than the success following standard combined behavioral and laxative therapy with supportive follow up [58,59,60,61]. There is some evidence it may be helpful in children who have non-retentive soiling [62].

6. Complementary therapies

Abdominal massage with or without aromatology, reflexology, homeopathy and acupuncture can all be helpful, sometimes in conjunction with standard management, where they assist in establishing a regular toileting routine. Evidence base for these therapies is poorly established.

7. General support

Fecal incontinence has socially isolating effects for the whole family. The network of support is generally less than for other chronic conditions but appropriate literature and advice can be very helpful. Within the UK, the Enuresis Resource and Information Centre, has done much to raise the profile of this disabling childhood problem [63].

8. Specialist Psychology and Psychiatry Services

Children whose soiling is associated with complex family functioning difficulties may need the expertise of a child and family mental health team.

VII. ASSOCIATED DISABILITIES

In those with structural or neurogenic abnormalities, the aim is to achieve social continence. The treatment approach, once corrective surgery is complete, is remarkably similar – namely to remove fecal impaction and maintain regular bowel actions. Laxatives and regular toileting plans [with physical aids for those with additional disabilities] may be sufficient but in those with inadequate bowel emptying additional techniques such as use of enemas or rectal washouts may be required to prevent overflow soiling. Malone in 1990 introduced the surgical technique of the antegrade colonic enema [ACE] whereby the large bowel is irrigated via a caecostomy tube or appendix stoma [64,65]. By keeping the large bowel empty in this way overflow soiling can be largely abolished. This technique has also been used in severe intractable functional constipation with megacolon [66].

1. Medical management of bowel dysfunction in neurological disorders

A recent prospective evaluation has shown no association between spina bifida occulta and bowel or lower urinary tract dysfunction [67]. This is useful information for advising parents / carers of children where this has been a chance finding on abdominal X-Ray and should help prevent further unnecessary investigations.

Conditions including spina bifida, sacral agenesis, cerebral palsy and spinal injury are commonly associated with bowel dysfunction.

There are multiple and complex factors governing bowel emptying in these conditions which include loss of anal sensation, loss of inhibitory regulation of the anorectum and left colon with lack of ability to voluntarily contract the external sphincter [68]. In Upper Motor Neuron lesions the bowel usually empties [by reflex activity] in response to suppositories or digital stimulation, while in a Lower Motor Neuron lesion the bowel becomes flaccid and requires artificial regular evacuation. Concomitant urological problems are likely and any suggestion of a neurogenic bladder requires urgent investigation and appropriate management to prevent long term renal damage.

Toilet training should start at the usual time using stimulant laxatives, mini enemas or suppositories to maintain regular evacuation and prevent constipation. Starting this early is important to establish the routine and avoid the child's resentment and difficulties adapting at a later age. Fecal softeners such as

lactulose or high dietary fibre are best avoided as soft stools are more difficult to evacuate.

Information for parents and professionals is available from Education, Resources and Information for Childhood Continence (ERIC) in the form of booklets and advice [29].

If constipation does occur it may be signaled by 'over-flow' diarrhea. Clear out using Polyethylene Glycol based osmotic laxative granules suitably mixed with flavored drink is usually satisfactory. If the diarrhea is secondary to an overactive bowel then attention to dietary factors with the addition of anti-diarrheals may be effective.

Anal tampons are useful when swimming but should only be used with a bowel evacuation program.

When fecal incontinence is associated with urgency and/or frequency or urge incontinence, intravesical electrical stimulation to decrease involuntary detrusor contractions and increase bladder capacity / sensation has also shown to decrease the number of episodes of fecal incontinence although not the number of bowel movements [45].

As soon as the child is able to understand and cooperate they should be taught the anatomy and basic functions of bladder and bowel. Showing pictures and using a small mirror can help them to identify their urethra and anus. They need to be able to identify these structures accurately with their eyes closed and then can practice inserting mini-enemas or suppositories while lying back on pillows with their legs apart. After 10 minutes they can transfer to the toilet to allow evacuation to take place.

Problems are related to associated lack of co-ordination, poor spacial awareness and fine motor difficulties and in spinal lesions with impaired sensation in the lower half of the body. Care needs to be taken regarding the position of the child on the toilet, making sure the child's feet are supported and he or she is comfortable. The child should not be left too long in this position.

Some children have memory and attentional problems and prompts with a bleeper device may be useful to ensure regular toileting. They may respond well to continual encouragement with rewards for sticking to a regular daily routine that is carefully broken down into step by step manageable stages.

If this conventional management fails or becomes unworkable for any reason, then a caecostomy with regular daily or alternate day ante colonic enemas are known to work well although there is the inevitable possibility of leakage or stenosis at the stoma site for some [46]. Children do need to be able to sit for up to an hour on the toilet to allow their bowel to empty completely using this method and this factor needs to be considered in the pre-op assessment. Sometimes additional aids may be needed if the child has an associated handicap such as a severe scoliosis.

Supervision from a multidisciplinary team in both home and school environments is imperative to establish care plans and ensure a smooth transition if the child should move house or school. Pediatrician, Occupational Therapist, Physiotherapist and Specialist Pediatric Continence Advisors all have a role to play.

To ensure support is provided at school a special statement may be required and this should reflect in detail the support the child requires for his/ her continence needs in school. Individual care plans need to be revised at important change over periods and in particular when transition to adult services is planned.

If children do require intimate help with their continence needs in school, training of staff and consent issues become important and must be resolved to the satisfaction of care staff, child and family.

2. Failure of medical management program

When the mega rectum becomes so large that it is impossible to keep clear with oral laxatives or even with regular enemas or suppositories then consideration of a caecostomy to allow antegrade continence enemas [ACE] is now a well recognized alternative. Results from this procedure are generally good with 85% attaining continence and can sometimes allow the mega rectum to resolve [59]. However, this approach does not suit all children with the most common complication being stoma stenosis. The child also needs to be able to co-operate with the enema routine (see under practical management points).

A further approach has been to surgically reduce the affected bowel. This has also shown good results [69] but has only been undertaken in older children who are not responding to a conservative treatment.

Another new avenue of approach may be to tackle the hypertrophy of the internal anal sphincter either by internal anal myectomy or with injections of intrasphincteric botulinum toxin injections. Early evidence from a randomized control trial suggests both may be effective in allowing better and more complete emptying of the rectum with the advantage that the toxin injections should be without the long term potential side effects resulting from surgery [70].

VIII. OUTCOME OF CHILDHOOD FECAL INCONTINENCE

Several studies have demonstrated the chronicity of this condition. The prognosis seems better in those diagnosed before the age of 4 years with recovery in 63% of children followed up by Loening Baucke [71]. In older children approximately 50% will have discontinued laxatives at 12 month follow-up, with a further 20% coming off laxatives in the next 2 years [72,73,74]. In Clayden's series of over 300 children with severe constipation, laxative treatment was required by 56 % for over 12 months [31]. At a mean of 6.8 years after treatment nearly 70% of 43 constipated children reviewed by Sutphen were entirely asymptomatic. Mild constipation persisted in 13. Fecal incontinence persisted in 3 of the 17 children who first reported it [75].

IX. CONCLUSION

Most children have gained bowel control by 4 years of age.

The prevalence of fecal incontinence is around 1.5% at 10 – 11 years of age.

A comprehensive and holistic assessment is necessary with consideration of family, psychological and educational issues.

The few children with organic causes of fecal incontinence must be identified, investigated and managed appropriately. Children with a neurogenic bowel or congenital bowel anomalies should be managed within specialist pediatric units.

Functional results of reconstruction of congenital anorectal anomalies (e.g. imperforate anus and Hirschsprung's disease) may be poor. These children require long term follow-up.

The vast majority of soiling children have functional retentive soiling secondary to constipation with no underlying organic abnormality. Stool holding is a common antecedent of constipation.

Psychological and behavioral problems are common and are usually secondary to the soiling. These improve when the child becomes continent.

Functional non-retentive soiling is less common and may be due to delay in establishing bowel control or to significant psychological and behavioral problems associated with other family and relationship difficulties.

Biofeedback training has been found useful for some children with functional non-retentive soiling.

A multidisciplinary team approach engaging both parents/carers and school staff is important in the management of any child with fecal incontinence of any cause but essential for children with a neurogenic bowel.

Parents and children need a clear understanding of the reasons why soiling is occurring in order to prevent intolerance and encourage compliance with the program. Behavioral issues need to be addressed in conjunction with a combined laxative and toileting program.

A number of reports indicate that treatment with macrogols (based on polyethylene glycol) is proving useful for both "clear out" and maintenance in children with functional fecal retention.

Laxative therapy may be needed for many months to maintain regular bowel actions.

Outcome is generally better when the condition is diagnosed early.

Ante-colonic-enemas [ACE] are showing good long term results in both neurogenic bowel and refractory chronic constipation.

(See algorithm for management of fecal incontinence in children (**Figure 18**).

X. RECOMMENDATIONS

There is often a considerable delay before children with fecal incontinence present to knowledgeable health professionals indicating a need for general health promotion and professional training in this area.

Definitions and classification of fecal incontinence are not yet universally agreed and would benefit from clarification. Classification needs to take into account the development of further subdivisions by causal mechanisms within this group, which will assist research.

The research base in this common and important condition is still generally poor with no recent trials of laxative therapy suitable for a systematic review.

Levels of evidence and research into the most common cause of fecal incontinence in children – functional retentive soiling - are generally poor although combined laxative and behavioral toileting programs have been shown to be more effective than either alone.

FLOW CHART FOR MANAGEMENT OF FAECAL INCONTINENCE IN CHILDREN

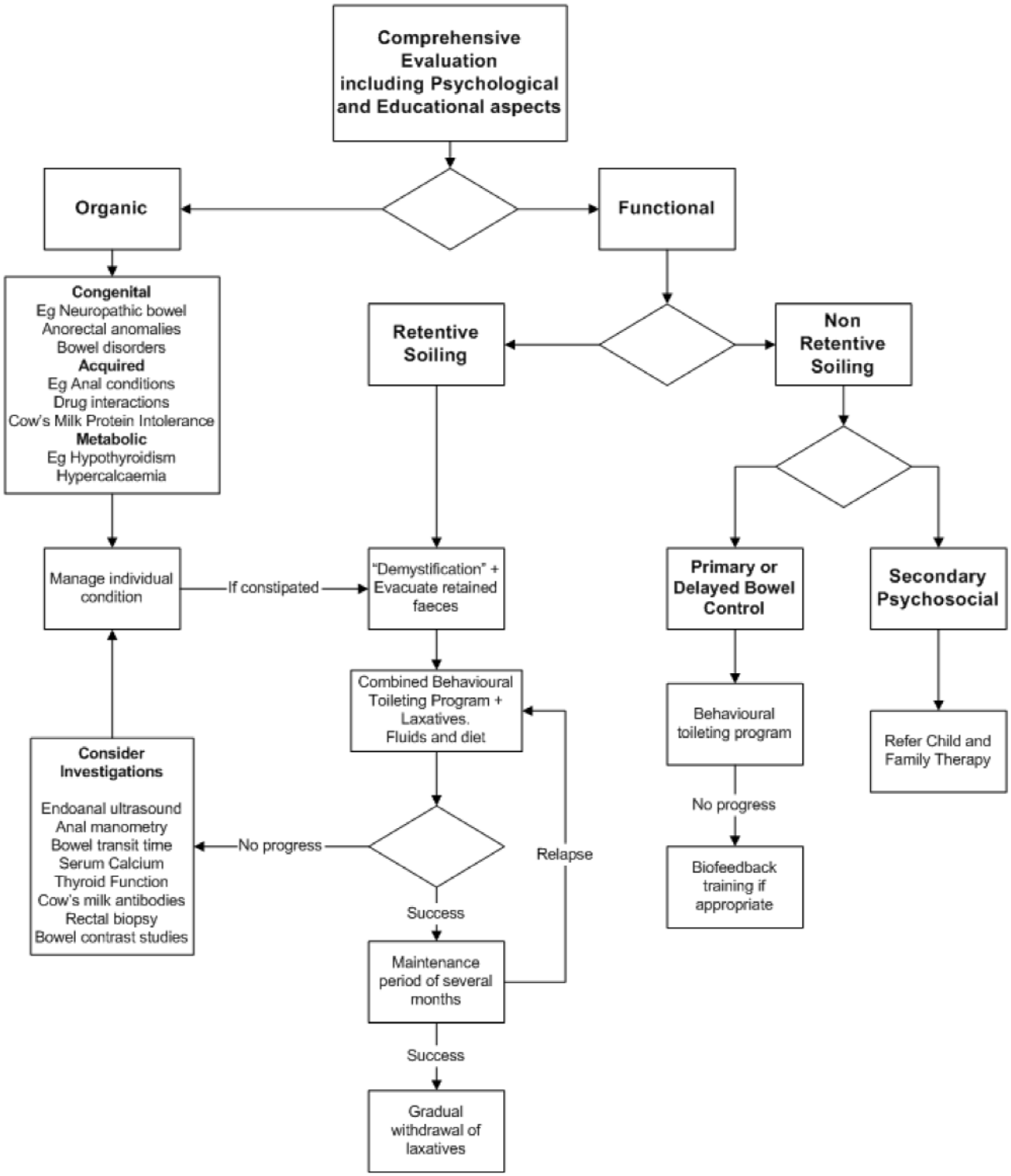

Figure 18. Treatment algorithm of fecal incontinence in children

H. PSYCHOLOGICAL ASPECTS OF URINARY INCONTINENCE AND ENURESIS IN CHILDREN

I. INTRODUCTION

Children with urinary incontinence and enuresis carry a higher risk for (sub-) clinical emotional and behavioral symptoms. In epidemiological, as well as clinical studies, the rate of comorbid behavioral disorders lies between 20-30% (max. 40%), i.e. 2-4 times higher than in non-wetting children. Secondary nocturnal enuresis and voiding postponement have a higher comorbidity, while urge incontinence and primary nocturnal enuresis, especially the monosymptomatic forms, have a low risk for comorbid behavioral disorders. The association between nocturnal enuresis and urinary incontinence and behavioral disorders are complex. While subclinical symptoms will often improve upon attaining dryness, obvious psychological disorders require additional counselling and treatment. This substantial group of nearly a third of all wetting children requires professional attention.

Children with wetting problems [nocturnal enuresis or urinary incontinence] represent a risk group for additional comorbid psychological symptoms and disorders. Even though an increasing body of literature is available on this topic, many myths and unsubstantiated beliefs still flourish. These range from a "psychologisation" of childhood wetting on the one extreme, to a denial of all psychological factors and insistence on an exclusive role of somatic factors, on the other. The aim of this chapter is to provide a review of current empirical data on psychological aspects of enuresis and urinary incontinence in children.

II. CLINICAL BEHAVIORAL DISORDERS

Clinically relevant behavioral problems and disturbances can be defined by two methods: by a categorical and a dimensional approach.

The ***categorical method*** is similar to the process of diagnosis-finding in other fields of medicine: a diagnosis is either present or not, i.e. is exclusive. After the diagnostic process, which includes a thorough history, observation, exploration, mental state examination, questionnaires, testing, physical examination and other procedures, a diagnosis is found according to standardized classification schemes. Currently, two major classification manuals are in use: the ICD-10 by the WHO, which is in wide use in Europe and the DSM-IV by the American Psychiatric Association, which is the standard in North America [1,2]. Both are quite similar for many disorders, but do show considerable differences for some child psychiatric disorders like ADHD [attention deficit hyperactivity disorder- DSM-IV] which is a much wider concept than the more stringently defined Hyperkinetic Disorders of ICD-10. Therefore, in diagnosing a childhood disorder, one should always add which classification is being used. In population-based epidemiological studies, the rate of clinically relevant behavioral disorders in children and adolescents lies between 12.0% [ICD criteria] and 14.3% [DSM criteria] [3]. This overall rate is almost the same in most cultures. One should always consider that diagnoses are professional assessments of a child's behavior, which requires special training. For research purposes, a standardized interview or, alternatively, symptom lists and diagnostic consensus conferences are required to ensure adequate reliability.

In this context, "psychiatric" or "behavioral" disorders or disturbances are used interchangeably. Specifically, two broad types of disorders can be differentiated:

- externalizing [or behavioral in a narrower meaning] disorders with manifest, outwardly directed behavior such as in conduct disorders and ADHD
- internalizing [or emotional] disorders, which denote a disturbance of intrapsychic processes, such as in depressive and anxiety disorders.

The other type of approach is a ***dimensional assessment*** of symptom scores generated by questionnaires. These symptom scores are calculated for specific or general scales. The scores represent a spectrum and can range from low to high values. Based on population norms, cut-offs are defined, which delineate a clinical [and sub-clinical] range. For many scales, a cut-off at the 90th percentile is considered best to define clinical range. This would mean that in the population 10% of all children would be considered to show this behavioral problem. If a higher proportion of incontinent children show pro-

blems in the clinical range, this would be indicative of a higher behavioral comorbidity.

Symptom scores never represent diagnoses – these are professional assessments – but reflect the view of the informant. Most questionnaires are parent questionnaires, who, from their point of view, can tend towards both under-reporting, as well as over-reporting. It is well-known that for some problems the concordance between different informants such as children, parents and teachers can be quite poor. As questionnaires are an economical way of procuring information and are widely used, it is important to know their limitations.

The best-known parental questionnaire is the CBCL [Child Behavior Checklist] [4]. It consists of competence items, as well as of 118 problem items. From the latter, 8 specific syndrome scales, as well as three composite scales: internalizing, externalizing and total problem behavior scores can be calculated. The clinical range is defined by the 90th percentile. The Child Behavior Checklist is used in both clinical, as well as in epidemiological studies.

III. CLINICAL BEHAVIORAL DISTURBANCES IN CHILDREN WITH ENURESIS / URINARY INCONTINENCE: EPIDEMIOLOGY

Not all epidemiological studies on enuresis actually assess behavioral problems in a standardized form. The famous studies of Fergusson et al. unfortunately do not address the question of comorbidity [5]. Others report raw or mean T-values, which might not be easily understood if one is not familiar with the questionnaire. Therefore, only those studies that clearly define the group of clinically deviant children shall be reported. If a control group is reported, the relative risk for a behavioral problem [odds ratio] can be calculated, otherwise the normative data is used. The most important epidemiological studies are summarized in **table 1.**

In the famous Isle-of Wight study the 31-item Rutter Child Scale, a standard instrument at the time of the study, was filled out by parents [6]. At the defined cut-off, 14-44% of enuretics were seen by their parents to show problematic behavior – 3-4 times more often than the controls. Using the same instrument, the longitudinal Study from Christchurch came to similar rates for the primary nocturnal enuretics, while the secondary nocturnal enuretics showed a much higher rate of up to 52% [7]. As the controls also showed higher rates, the relative risk was 1.3 to 2.4 times higher. The same study was the only one to assess rates of DSM-III diagnoses at a later age – with marked differences between the primary and the secondary nocturnal enuretics [8].

In the cross-sectional Chinese study by Liu et al a third of all incontinent children were in the clinical range – 3.6-4.5 times more often than the controls [9]. The US-study by Byrd et al used the 32-item-BPI [Behavior Problem Index], which is modeled after CBCL [10]. The rates are lower than in the other studies, but included infrequent wetters with 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 incontinent children show clinically relevant behavioral problems – 2 to 4 times higher than continent children. This is a substantial number of children, considering that the comorbidity of chronically ill children, some with severely incapacitating illnesses, have a 2-3 fold higher comorbidity of behavioral disorders [11,12].

IV. CLINICAL BEHAVIORAL DISTURBANCES IN CHILDREN WITH ENURESIS/URINARY INCONTINENCE: CLINICAL STUDIES

The epidemiological studies are important, because they report general prevalences in the population without selection biases. On the other hand, they usually rely on questionnaires as their only source of information. Thus, the type, frequency and associated symptoms of wetting are often not assessed. Clinical studies with smaller groups of examined children, can address these questions in greater detail – but can reflect possible recruitment biases. Important studies are summarized in **table 2.** As many did not have controls, but were designed as intergroup comparisons, normative values are provided.

In an early study of Berg et al, nearly 30% of children presenting to a pediatric department clinic were deemed “clinically disturbed” by non-standardized interviews and by the Rutter questionnaire (using a different cut-off) [6,7,13]. In another study in a pediatric setting, similar rates of 26% were found 20

Table 1. Epidemiological studies: Percentage of children with clinically relevant behavioural problems in comparison to controls and their increased risk (odd-ratios)

Study	Measure	Enuretics	Controls	Higher risk (odds ratio)
Rutter 1973, U.K., Isle of Wight, n=4481, cross-sect., 5-14 years	Rutter Child Scale [parent]; cut-off>13			
	Age 5 years	Boys: 30.8% Girls: 14.3%	8.1% 4.4%	3.8 3.2
	Age 7 years	Boys: 25.6% Girls: 28.6%	7.9% 7.8%	3.2 3.7
	Age 9/10 years	Boys: 27.4% Girls: 16.3%	6.5% 5.3%	4.2 3.1
	Age 14 years	Boys: 27.6% Girls: 43.8%	10.2% 6.8%	2.7 6.8
McGee et al., 1984, New Zealand, longitudinal, n=1037	Rutter child scale [parent]; cut-off>13			
	Age 7 years	Primary: 30.8% Secondary: 51.9%	21.6%	1.4 2.4
	Age 9 years	Primary: 23.1% Secondary: 37.0%	17.5%	1.3 2.1
Feehan et al. 1990, New Zealand, longitudinal, n=1037	DSM-III, age 11years	Total: 23.4% Primary: 0% Secondary: 42.3%	9.5%	2.5 4.5
	DSM-III, age 13 years	Total: 17.5% Primary: 10.5% Secondary: 23.8%	9.1%	1.9 1.2 2.6
	DSM-III, age 15 years	Total: 13.3% Primary: 10.5% Secondary: 20.0%	9.8%	1.4 1.1 2.0
Liu et al., 2000, China, cross-sect., n=3344, 6-18 years	CBCL Intern. >90th p. CBCL Extern.> 90th p. CBCL Total > 90th p.	31.0% 29.0% 30.3%	10.4% 9.3% 9.1%	4.5 3.6 4.3
Byrd et al. 1996, USA, cross-sect., n=10960, 5-17 years [includes infrequent bedwetting > 1x/per year]	BPI > 90th p.	16.5%	10.2%	1.6
Feehan et al. 1990, New Zealand, longitudinal, n=1037	DSM-III, age 11years	Total: 23.4% Primary: 0% Secondary: 42.3%	9.5%	2.5 4.5
	DSM-III, age 13 years	Total: 17.5% Primary: 10.5% Secondary: 23.8%	9.1%	1.9 1.2 2.6
	DSM-III, age 15 years	Total: 13.3% Primary: 10.5% Secondary: 20.0%	9.8%	1.4 1.1 2.0

Table 2. Clinical studies: Percentage of children with clinically relevant behavioral problems in comparison to controls and their increased risk (odd-ratios)

Study	Measure	Enuretics	Normative values	Higher risk (odds ratio)
Berg et al., 1981, U.K., n=41, 6-13 years, pediatric clinic, nocturnal enuresis	Rutter A questionnaire Cut off > 18	29.3%		
	Interview: "clinically disturbed"	26.8%		
Bayens et al., 2001, Belgium, n=100, 6-12 years, pediatric clinic, nocturnal and mixed D/N wetting	CBCL Total >90th p. CBCL Intern. >90th p. CBCL Extern. >90th p.	26% 25% 14%	10.0% 10.0% 10.0%	2.6 2.5 1.4
Von Gontard et al., 1999, Germany, n=167, 5-11 years, child psychiatric clinic	CBCL Total>90th p. CBCL Intern. >90th p. CBCL Extern. >90th p. ICD-10	28.2% 20,9% 22,1% 40.1%	10% 10% 10% 12%	2.8 2.1 2.2 3.3
	CBCL Total >90th p. ICD-10	Primary nocturnal enuresis 20.0% 19.5%	10.0% 12.0%	2.0 1.6
	CBCL Total>90th p. ICD-10	Primary mono symptomatic nocturnal enuresis 14.3% 10.0%	10.0% 12.0%	1.4 0.8
	CBCL Total >90th p ICD-10	Primary non-. monosymptomatic nocturnal enuresis 29.0% 34.4%	10.0% 10.0% 12.0%	2.9 2.9 2.9
	CBCL Total>90th p. ICD-10	Secondary nocturnal enuresis 39.3% 75.0%	10.0% 12.0%	3.9 6.3
Von Gontard et al., 1998; Lettgen et al., 2002, Germany, n=94, 5-11 years, two centres: pediatric and child psychiatric clinics	CBCL Total>90th p. ICD-10	Urge incontinence 13.5% 28.6%	10.0% 12.0%	1.4 2.4
	CBCL total>90th p. ICD-10	Voiding postponement 37.3% 53.8%	10.0% 12.0%	3.7 4.5

years later [14]. These rates are almost identical as the results from von Gontard [15].

In addition, the behavioral comorbidity using the CBCL and ICD-10 diagnoses were analyzed for specific subtypes of incontinence [15]. Primary nocturnal enuretics showed behavioral problems less frequently than secondary nocturnal enuretics. The group with the lowest comorbidity – no higher than in the normative population – were monosymptomatic nocturnal enuretics without any daytime symptoms such as urge, postponement or dysfunctional voiding.

In a two-centre study in a pediatric and child psychiatric clinic, of the children with daytime incontinence, those with urge incontinence were less 'deviant' than those with voiding postponement [16,17]. The data on children with dysfunctional voiding is even more sparse. In the study by von Gontard, 10 of 167 children showed dysfunctional voiding [15]. The absolute rate of behavioral disorders was higher than in other forms of urinary incontinence, thus only 40% had an ICD-10 diagnosis and 40% a CBCL total score in the clinical range.

In summary, clinical studies came to remarkably similar results as those in the general population with 20-40% being affected for most types of incontinence– independent of the type of institution. They do, however point to the fact, that the comorbidity differs greatly between different forms of incontinence: the lowest comorbidity is found among primary monosymptomatic nocturnal enuretics, the highest among the secondary nocturnal enuretics. Among the children with daytime incontinence, those with urge incontinence have the lowest rate of concomitant problems.

V. WHAT TYPE OF BEHAVIORAL DISORDER ?

These global findings from epidemiological and clinical studies do not reveal what type of behavioral disorder is most common. Contrary to common belief, children with incontinence problems are prone to show externalizing disturbances more often than internalizing disorders. As shown in **table 3**, 21% had externalizing disorders according to the ICD-10 criteria [15]. Of these 9.6%, had hyperkinetic disorders, characterized by hyperactivity, impulsivity, short concentration span and distractibility. 11.4% showed conduct disorders, defined by a transgression of norms and rules, most of which were oppositional-defiant disorders. Only 12% showed internalizing, emotional disorders such as depression, anxiety and phobias.

Hyperkinetic disorders (ICD-10 criteria; affecting 1.7% of the population) are more stringently defined than ADHD (DSM-IV criteria; affecting at least 5% of the population). ADHD seems to be a common type of co-morbid disorder. Thus, in a retrospective analysis of 153 children with ADHD and 152 controls, the risk for nocturnal enuresis in a 6-year old child with ADHD was 2.6 times higher, for daytime incontinence the risk was even 4.5 times higher [18]. The causal, possibly neurobiological relationship between nocturnal enuresis and ADHD is not known, but according to formal genetic analyses, the two disorders are not inherited together [19].

Table 3. ICD-10 diagnoses (multiple diagnoses possible) in 167 children aged 5-11 years with noctural enuresis and functional urinary incontinence [15]

Type of diagnoses	Percentage (n)
Externalizing disorders	21.0% (35)
Hyperkinetic Syndrome	9.6% (16)
Conduct Disorder	11.4% (19)
Internalizing (Emotional) Disorders	12.0% (20)
Encopresis	12.0 (20)
Others	6.0% (10)
ICD-10 diagnoses	40.1% (67)

VI. RELATIONSHIPS BETWEEN BEHAVIORAL DISORDERS AND INCONTINENCE

Theoretically four different types of associations between behavioral disorders and incontinence have to be considered [20]:

- The behavioral disorder might be a consequence of the incontinence problem – and might recede upon attaining dryness.
- The behavioral disorder might precede and thus induce a relapse, which has been shown in epidemiological studies [8]. Often, a genetic disposition for enuresis is present even in these secondary forms [21].
- Incontinence and behavioral disorder might be due to a common neurobiological disorder, which has

to be considered in the association of ADHD and nocturnal enuresis.

- There might not be a causal relationship at all. As behavioral disorders and enuresis/urinary incontinence are so common they might simply co-exist by chance. In these cases one should critically review, if the need for a causal explanation might not be induced by parents and professionals.

In summary, there are no simple causal relationships between enuresis and behavioral disorder. The different possibilities have to be considered, even though it might not be possible to clarify the associations in the individual case. Therefore, it is important to assess and diagnose both: the type of incontinence and the behavioral disorder.

VII. SUBCLINICAL BEHAVIORAL SIGNS AND SYMPTOMS

In addition to manifest behavioral and emotional disorders, many children show subclinical symptoms, These are often understandable reactions towards the wetting problem and do not represent a disturbance. This is very important to differentiate,

Thus, in a study of 40 children aged 5-15 years with a structured interview and questionnaires, 35% said that they were unhappy and 25% very unhappy about the incontinence [22]. In von Gontard's studies, based on a structured interview by Butler, 70.3% experienced disadvantages through their incontinence, only 4.9% advantages [23,24]. The type of disadvantage and typical explanations by children are shown in **table 4**. Again, these do not represent a disturbance, but reflect the subjective predicament and suffering many incontinent children endure.

In one of the few population based studies, Moilanen et al compared 156 enuretics and 170 controls (from a population of 3375 7-year old school entrants in Finland) [25]. In a parental interview and questionnaire (non-standardized), the enuretic children differed significantly on most personality traits. The greatest difference with a p<.01 were: the children were more fitful (vs. peaceful), more fearful (vs. courageous), and more impatient [vs. calm], more anxious [vs. does not worry) and had more inferiority feelings (vs. feels equal). Again, these constructs are not to be seen as disturbances per se.

One of the most analyzed construct is that of "self-esteem", which can be used interchangeably with

Table 4. Subjective view of wetting – structured interview of the child [n=165]; ages 5-11 years, nocturnal enuresis and urinary incontinence [24]

Consequences of wetting	Percentage
DISADVANTAGES	70.3%
SOCIAL: I can't sleep at friends' house, friends can't stay over night	32.1%
AFFECT: I feel sad, ashamed, annoyed	16.4%
ISOLATION: I feel like a baby, nobody is allowed to know about it, I feel different from other children	6.7%
SENSATION: it feels unpleasant, cold, wet, itchy, nasty	32.1%
DIRECT CONSEQUENCES: I have to take a shower, sleep in pampers, won't get a bicycle	17.6%
ADVANTAGES: I like the wet feeling, get more attention from mother	4.9%

"self-regard" and "self-concept". It is defined as a "relatively stable set of self-attitudes reflecting both a description and an evaluation of one's own behavior and attitudes" [26]. It is an important attribute thought to be associated with mental health. In their critical review, Redsell and Collier, point out that the evidence does not indicate conclusively that nocturnal enuresis leads to lower self-esteem [27]. In one study, the self esteem total score was even higher among enuretics [58.5] than the original norms [51.8] [28].

But evidently, self-esteem can improve upon attaining dryness. In a population-based study of 6-8 year old enuretics, self esteem was higher in controls than in patients, higher in girls and in children from higher socio-economic background. After 6 months of treatment, self-esteem was similar to controls in those children who achieved dryness and remained low in those with persisting urinary problems [29].

In the study of Moffat et al, 66 children randomly received alarm treatment, while 55 were assigned to a 3-month waiting list [28]. Using the 80-item Piers-Harris questionnaire, the total score increased significantly from 58.5 to 61.5 in the treatment group [26]. Self-esteem increased in children with total success and those with a greater than 25% improvement, but not in those with treatment failure (less

than 25% success). At the same time, parents rated an improvement of their child's behavior, with the CBCL total T-values dropping from 60.1 to 55.2 (n.s.).

In a second study, 182 children were randomly assigned to alarm, placebo and dDAVP treatment [30]. After 6 months – independent of any improvement - self esteem [measured with the Piers-Harris questionnaire] increased significantly for the alarm and dDAVP groups, but not for the placebo group. Regardless of outcome, children feel better with treatment. For those with 75% or more dryness, the CBCL scores improved significantly for placebo and dDAVP, but not for alarm. The authors conclude that frequent follow-up and emotional support and encouragement appear to be important components of an efficacious intervention for children with nocturnal enuresis.

In summary, subclinical behavioral symptoms are common in children with enuresis/urinary incontinence and can improve with successful treatment. It is important to differentiate between these and manifest disorders, which will not recede, but require additional treatment.

VIII. CONCLUSIONS

Epidemiological, as well as clinical studies show conclusively that up to a third of all incontinent children have clinical relevant behavioral scores or manifest behavioral disorders. This rate is at least as high as in children with chronic medical illness [11, 12]. In addition, subclinical behavioral and emotional symptoms can coexist. This rather substantial group of incontinent children need professional attention.

The first recommendation would be to screen children with enuresis/urinary incontinence with questionnaires such as the CBCL. As many subclinical symptoms will diminish and self-esteem will increase – the main aim should always be directed towards getting the child dry. This is all that is needed for many children. If, however, a manifest behavioral disorder is present, this will not disappear upon symptomatic treatment and may even impede or jeopardize the treatment of the wetting problem. In these cases, a multidisciplinary approach is mandatory with a detailed diagnostic child psychological work-up and treatment recommendation. In many cases, counseling will suffice, in others, more intense treatment is needed.

It would be desirable that all professionals involved with these children and families should have a basic knowledge of behavioral disorders in childhood – just as all mental health workers should have a basic understanding of urodynamics, for example. In larger teams, the inclusion of a psychologist or a urotherapist trained in psychotherapy would be optimal. Consultation / liaison with child psychiatric services would be desirable for more severe cases. In any case, a multidisciplinary approach should become the standard for this group of patients.

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G. FEACAL INCONTINENCE

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H. PSYCHOLOGICAL ASPECTS OF URINARY INCONTINENCE AND ENURESIS IN CHILDREN

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