Daytime Wetting Causes and Investigation

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RACP lecture series
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A familiar story

- 6 year old girl
- Daytime wetting
- Night-time wetting
- Urinary tract infections

What do you want to know?

- History
  - When wet?
  - Number of times, pre void, post void, unassociated with voiding
  - How wet?
  - Small / large volumes, need to change, does or doesn’t
  - Associations?
  - School, home, activities
  - Toilet training?
  - Easy/ hard/ successful
  - Observed behaviours?
    - Holding on, wiggle, “curtsey
  - Drinking?
    - How much, what, when
  - Concern?
    - Who is worried? What are they worried about?
  - Bowels

- Wet every night –difficult to rouse
- Day wetting several times per day –damp undies mainly
- Previously prescribed Ditropan by GP – worked for 2 weeks only
  - Difficulty toilet training. Posturing
  - BA 2nd daily. BSS2.
  - Wetting –preceded by urge, but not always
  - Problems with changing, school toilets, family frustration
  - Several UTI’s

What do you think she has?

- Day wetting
- Night wetting
- Urge
- Urge incontinence
- Stress incontinence
- Dysfunctional voiding
- Dysfunctional elimination syndrome
- Detrusor dyssynergia
- Unstable bladder
- ??????
Incontinence = involuntary wetting at an inappropriate time and place in a child 5 years old or more

Incontinence

Continuous incontinence

Intermittent incontinence

Daytime incontinence

Nocturnal incontinence, enuresis

Enuresis = (intermittent) incontinence while asleep

Regardless of

... whether cystometry reveals that the voiding is complete and normal or not

... whether the child also suffers from day-time incontinence or not

... what we think the cause is

Monosymptomatic enuresis = Enuresis in a child without daytime bladder symptoms

i.e. enuresis without:

- Urgency
- Incontinence
- Increased/decreased voiding frequency
- Voiding postponement
- Holding maneuvers
- Interrupted flow

Nonmonosymptomatic enuresis
Daytime wetting

- Storage/ Filling
- Voiding/ emptying

(Intermittent) nocturnal incontinence = enuresis

Children with enuresis and daytime incontinence have enuresis* and daytime incontinence

We do not change the name of the disorder just because the child also suffers from another disorder, even though it gives clues regarding pathogenesis (compare: asthma and hay-fever)

The coexistence of the two may also be just coincidence. Both conditions are common!

*Of the nonmonosymptomatic subtype

Findings related to the bladder

8 voidings or more per day = increased daytime voiding frequency
3 voidings or less per day = decreased daytime voiding frequency

More findings related to the bladder

Bladder capacity = Voided volume

"Functional bladder capacity" is substituted with maximum voided volume, as measured from a voiding diary

Maximum voided volume can be compared with expected bladder capacity, as deduced from the standard formula \[30 + (30 \times \text{age})\] ml

Terms deduced from history:

Bladder instability = Overactive bladder

Cystometric terms:

Detrusor instability = Detrusor overactivity

This is in accordance with ICS adult terminology

Instability is an ambiguous word

Lazy bladder?

Underactive bladder

Detrusor underactivity

Determined from history and voiding diary data

Determined from cystometry

We cannot speak about the detrusor without having performed a cystometry
Day-time LUT conditions

Overactive bladder: children with urgency
(increased voiding frequency and/or incontinence often present but not required for use of the term)

Urge incontinence: children with incontinence and urgency

Day-time LUT conditions

Voiding postponement: children who are observed to habitually postpone voiding using holding maneuvers
(decreased voiding frequency and urgency often present but not required for use of the term)

Underactive bladder: Children with low voiding frequency who need to use raised intraabdominal pressure to void

Dysfunctional voiding: children who habitually contract the sphincter during voiding, producing uroflow curves of a staccato type

Note:
This term says nothing about the storage phase. Dysfunctional voiding or voiding dysfunction is not the same as "any bladder disturbance"

Items to be included in a standard bladder diary, used in the research setting

Required
Voidings (timing and volumes) ≥2 days
Fluid intake ≥2 days
Daytime LUT symptoms (incontinence etc) 14 days
Enuresis and/or nocturia 14 nights

Recommended
Enuresis volumes 7 days
Bed-time, wake-up time 14 days
Bowel movements 14 days

Otherwise it can be called a frequency-volume chart...
Treatment success: New terminology

- Nonresponse: <50% reduction
- Partial response: 50-89% reduction
- Full response: >89% reduction, or maximum 1 accident per month
- Relapse: >1 accident per month
- Continued success: No relapse in 6 months without treatment
- Complete success: No relapse in 2 years without treatment

Treatment success; background

*In the clinical setting,* treatment success means that the family is satisfied. *In the research setting,* treatment success is determined from a voiding chart. 1-2 wetting accidents in 14 days – as allowed by the previous ICCS definitions – does *not* mean that the problem is solved.

Treatment success and cure are not synonymous.

Prevalence population-based cross-sectional studies non-neurogenic bladder dysfunction

- 6-12 years: 0.2 - 9% daytime incontinence (Bakker 2002, Lee 2000, Swithinbank 1994)
- 1.5 – 2.8% combined day and night incontinence (Lee 2000, Gur 2004, Jarvelin 1988)
- 1.5 – 8.9% combined day and night incontinence (Butler R 2008)
- Prevalence decreases with age; 2% > 18 yrs still wet. (Bower, 1996)

Prevalence incontinence by day

The Myths…

- Incontinence is caused by...
  - the child is disturbed / expressing anger
  - The child is not expressing anger
  - the child is lazy / attention seeking
  - the child is slow to develop
  - the child is ‘not bright’
  - the family is dysfunctional
  - toilet training too early / too late / badly handled is a parenting problem

And the most prevalent of all…

- He / she will just grow out of it
Myths and beliefs still

- ‘range from “psychologisation” of childhood wetting on the one extreme to a denial of all psychological factors and an insistence on an exclusive role of somatic factors on the other’ (Abrams et al 2005)

Alexander von Gontard, 2006

- Epidemiological studies 20-30% of all I/C children show clinically relevant comorbid behavioural problems ie 2-4 times higher continent children
- Clinical studies showed 20-40%
- Lowest comorbidity MNE
- Highest 2ndary NE
- Day wetting –urge I/C lowest rate

Relationship between incontinence and behavioural disorder

- Behavioural disorder (BD) – consequence – resolves
- BD precedes I/C and might induce relapse
- BD and I/C due to a neurobiological disorder ?ADHD
- No causal relationship at all
- Therefore assess and diagnose both the type of incontinence and the behavioural disorder

Growing out of it...

- NE
  - 7 years – 8%
  - 11-12 years – 3%
  - 16 years – 0.8%
- Functional incontinence
  - 7 years – 3.2 – 6.7%
  - 15-17 years – 1.2-3%
- The association with adult continence problems

But……

- For the incontinent child there is considerable impact on self esteem, family and social relationships, so “growing out of it” is not an acceptable option
- As continence workers we need to be aware of the possible associated behavioural problems and refer to a psychologist/psychiatrist as part of the team to treat those
A familiar story

- 6 year old girl
- Daytime wetting
- Night-time wetting
- Urinary tract infections

Objective assessment

- Uroflowmetry – staccato flow. PVR=30 mls
- Bladder diary – Max and Mean voided volumes < age expected (120 and 90 mls) (EBC=270mls)
- Fluid intake – 750mls
- Voiding frequency – x8
- Nocturnal urine output (Pad weigh + 1st AM void) = 220 mls
- Moderate faecal loading LIF

Diagnosis/treatment

- OAB + voiding dysfunction
- Confounders – constipation, UTI, hygiene issues

Diagnosis/treatment

- OAB + voiding dysfunction
- Confounders – constipation, UTI, hygiene issues
- Education
- Treat constipation
- Toileting regime -“sits”
- Drink at breakfast
- Address hygiene issues
- Implement outcome measures and incentives.
- Review 2-3 weeks

Review 1

- Compliance good
- Daily BA BSS 3-4
- Day wetting little change
- NE no change
- Repeat flow/scan-staccato, PVR=25 mls

Review 1

- Compliance good
- Daily BA BSS 3-4
- Day wetting little change
- NE no change
- Repeat flow/scan-staccato, PVR=25 mls
- Maintain “sits”
- Institute regular voiding, regular fluids.
- Teach toilet position, relaxed voiding
- Maintain outcome measures
- Review 4 weeks
### Review 2
- NE unchanged
- Day wetting x3-4/week
- Bowels daily BSS 4 (several spontaneous)
- Flow/scan – less peaks and troughs, PVR=0 mls
- Still posturing

- Maintain bowel regime
- Maintain regular voids and fluids
- Maintain toilet posture etc
- Maintain outcome measures
- Start Ditropan 2.5 mg b.d.
- Review 4 weeks

### Review 3
- 7 weeks later – family had flu!
- NE unchanged except for 1 dry night
- Day wetting as before
- Flow/scan – PVR=60 mls
- Bowels – 2nd daily BSS3

- STOP Ditropan
- Back to basics
- Repeat bladder diary
- Review 4-6 weeks

### Review 4
- NE unchanged
- Day wetting – several times per week, damp only, still reporting urgency
- Flow/scan 2 peaks, PVR= 5 mls
- Bowels \(\checkmark\)
- Regular voiding/fluids (apart from holidays)
- Voided volumes 180 and 110 mls

- Start TENS 8Hz, S3, 2 hours daily
- Continue as before
- Review 4 weeks
### Review 5
- NE unchanged
- Day wetting none, but still leaving class at times
- Flow/scan- I curve, PVR=0 mls
- Bowels
- Toileting regime

### Review 5
- NE unchanged
- Day wetting none, but still leaving class at times
- Flow/scan- I curve, PVR=0 mls
- Bowels
- Toileting regime

### Review 6
- No day wetting
- Little if any reported urgency, no observed posturing
- Flow scan – bell curve, PVR=0 mls
- Bowels (apart from 1 relapse of several days)
- Voided volumes 220 mls and 155 mls
- Stop TENS
- To start bed wetting alarm at beginning of next school holidays
- Review then
- Treatment to date 7 months—reasonably fast response—no UTIs, constant parents

### INFANT
- Pathways are intact
- Bladder capacity increases in first 2 years with improved regulation by brainstem inhibitory centre
- Frontal and parietal development allows sensation of bladder fullness, then ability to inhibit micturition, then facilitate voiding

* Mundy, AR. BJU, 1988, 62
Epidemiology of bladder control

- Usually day control first
- 20% of children become dry per year between 18 months and 4.5 years

Normal bladder function

- Bladder fundus - 3 layers of smooth muscle that criss-cross
- Internal urethral sphincter - interdigitated smooth muscle bundles around bladder neck and extending to posterior urethra
- External urethral sphincter - smooth and skeletal muscle at level of pelvic floor

Normal bladder function - nerve supply

- Autonomic nervous system
  - Sympathetic
    - Stimulates α and β receptors in smooth muscle
    - α receptors: trigone, bladder neck and distal portion urethra
    - β receptors: bladder fundus

- Parasympathetic
  - Neurotransmitter: acetylcholine
  - Receptors: bladder fundus and posterior urethra
  - Pelvic N stimulation - ACh release by postganglionic cells - detrusor contraction, inhibition of sym NS - relaxation of smooth Mm at trigone, bladder neck and posterior urethra
  - Sustained contraction of bladder until empty

Normal bladder function - nerve supply

- Neurotransmitter: noradrenaline
  - Action:
    - NA and α receptors: contraction of smooth muscle of bladder neck and posterior urethra
    - NA and β receptors: relaxation of bladder fundus
  - Regulates bladder function during filling by allowing bladder to enlarge without increasing tension within bladder wall, ie facilitates storage of urine

Normal bladder function - nerve supply

- Somatic nerves
  - From sacral cord via pelvic plexus and pudendal nerve to skeletal muscle of external urinary sphincter
Normal bladder function
- CNS role

- Bladder distension - impulses along afferent pathways via pelvic nerves to sacral cord with stimulation of Sympathetic, Parasympathetic and somatic nerves back to bladder.
- Messages between sacral and thoracolumbar areas and brainstem
- Communication between brainstem and frontal and parietal lobes

EVALUATION

- History
  - General
  - Perinatal
  - Developmental including toilet training history
  - Wetting
    - When - day/night/both
    - How much - ? Quantify with pad test
    - Primary/secondary
    - How often
    - Pattern of wetting
    - Urinary stream, strain during voiding
    - Family history, family function
    - School toileting routines
    - Diet and fluid intake

- Physical examination
  - BP
  - Genitalia
  - Perineal and perianal sensation
  - Spine and sacrum
  - Anal tone
  - Reflexes
  - Gait/limb asymmetry
  - Urinalysis and culture

NOCTURNAL ENURESIS
Nocturnal enuresis

- Normal void at inappropriate or socially unacceptable time or place
- Void in bed whilst asleep
- Usually not roused by voiding
- Monosymptomatic
- Often familial

Nocturnal enuresis

- Age: after 5 years
- Frequency
  - Number of wet nights/week
  - Number of wetting episodes /night
  - Time of wetting
- Amount
- Arousability
- Family history

Nocturnal Enuresis - definitions

- Primary
- Secondary
  - Bedwetting that affects child who has been dry for > 6 months
- Monosymptomatic
  - No day time symptoms

Epidemiology

- Australia
- 2290 families
- 5% wetting more than once/week
  - Bower W, Br J Urology 1996

PATHOPHYSIOLOGY

- Genetics
- Nocturnal polyuria
- Arousal
- Detrusor hyperactivity
- Psychological factors
Genetics

- Heredity has major influence
- Nocturia
- Subjectively high arousal thresholds common in enuretic families
- Gene linkage studies have identified 4 genes
- Phenotype does not clearly correspond with genotype

Chromosomes Involved in PNE

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Genetic markers</th>
<th>Study</th>
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</thead>
<tbody>
<tr>
<td>13</td>
<td>D13S263, D13S291</td>
<td>Eiberg et al. 1995</td>
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<tr>
<td>12</td>
<td>D12S80, D12S43</td>
<td>Dahl et al. 1995</td>
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<td>8</td>
<td>D8S260</td>
<td>Eiberg et al. 1996</td>
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<tr>
<td>22</td>
<td>D22S446, D22S343</td>
<td>Eiberg et al. 1997</td>
</tr>
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</table>

Nocturnal Polyuria

- Nocturnal deficiency of ADH
- Nocturnal urine production exceeded functional bladder capacity
- Nocturnal polyuria not exclusive to bedwetters
- 12% of dry children produce more urine at night than during day

Diurnal Variation in Plasma Vasopressin (p-AVP)

- J.P. Nørgaard et al. 1985
- S. Rittig et al. 1989

Pathophysiology – urine production

- Urine production rate vs. Urine osmolality

S. Rittig et al. 1989

Detrusor overactivity

- Sleep cystometrograms in NE
  - 30% have uninhibited detrusor contractions in sleep -
  - More common in children with NE unresponsive to therapy
- Hyperactive bladder is usually small bladder
- Smaller bladder capacity in NE is functional
Impaired Arousal

- Subjective observation that children with NE are harder to wake and rarely wake spontaneously to any stimulus
- EEG and polysomnography studies inconclusive
- Some experimental support for enuretic children sleeping more deeply and being harder to rouse

Psychology

- Most psychological problems are secondary to enuresis and not causative
- NE more common in children with ADHD or learning problems

Management - PNE

- Wait - 15% of children become dry every year
- Conditioning with bell and mat alarm
- DDAVP (Minirin)
- Combination of DDAVP and alarm
- Imipramine
- ? anticholinergics

Daytime Wetting

- Epidemiology
  - Australia
    - 2292 children, 5 – 12 year olds
    - 458 had wetting
    - Prevalence
      - Nocturnal enuresis alone 15% (60% M)
      - Isolated day wetting 2% (50% M)
      - Combined day and night wetting 4%
      - Marked wetting (>2/week)
        - Day 1.4% of sample (34), night 5.1% (119)

Neveus et al, Scand J Urol Nephrol, 2000

Detrusor hyperactivity

Nocturnal polyuria

Nocturia, incontinence, urgency

Deep, uninterrupted sleep

Good DDAVP response

Poor DDAVP response

High arousal threshold
Epidemiology

- Belgium
- 4332 children 10-14 years
- Prevalence
  - MNE 1% (n = 62, 47 M)
  - Isolated daytime wetting 4% (192, 68 M)
  - Day and night wetting 3.5% (151, 89 M)
  - Soiling 3% (120, 45 M)

Investigation

- Urine culture and analysis
- Renal US
- Bladder US with pre and post micturition volumes
  - Residual volume <20 ml
  - Or < 10% of CBC

Investigations

- 2 day frequency volume chart or voiding diary
  - Time and volume of drinks
  - Time and volume of voids
  - Time and amount of wetting
  - Presence of urgency
  - Provides
    - Voiding frequency
    - Total volume voided in 24 hours
    - Average volume voided
    - Largest and smallest volume voided
    - Distribution of urine volume over day and night
    - Urine loss
    - Fluid intake

Frequency Volume Chart

<table>
<thead>
<tr>
<th>Date</th>
<th>Drinks - time</th>
<th>Drinks (mL)</th>
<th>Void - time</th>
<th>Void (mL)</th>
<th>Urgency</th>
<th>Wet Dry</th>
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<tbody>
<tr>
<td>0800</td>
<td>150</td>
<td>0730</td>
<td>200</td>
<td>N</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>0930</td>
<td>50</td>
<td>N</td>
<td>D</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1100</td>
<td>50</td>
<td>N</td>
<td>D</td>
<td></td>
<td></td>
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<tr>
<td>1200</td>
<td>150</td>
<td>1230</td>
<td>30</td>
<td>Y</td>
<td>W</td>
<td></td>
</tr>
<tr>
<td>1500</td>
<td>150</td>
<td>1400</td>
<td>60</td>
<td>Y</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>1600</td>
<td>30</td>
<td>Y</td>
<td>W</td>
<td></td>
<td></td>
<td></td>
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<td>1630</td>
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<td>D</td>
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<td></td>
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<tr>
<td>1700</td>
<td>25</td>
<td>Y</td>
<td>W</td>
<td></td>
<td></td>
<td></td>
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Summary

Cystometric Bladder Capacity

- CBC (ml) = $30 + (30 \times \text{age (yrs)})$
- OR = $(\text{age (yrs)} + 2) \times 30$

Investigation

- Urine flow study
- Bladder scan
- Urodynamics
- ? MCU
- ? MR spine

Uroflow

- Measurement of urine flow during voiding
- Rate and pattern
- Least invasive
- Age > 4 years, 3 curves prior to interpretation
- Appropriate sitting position

Uroflow patterns

(a) Normal
(b) Interrupted
(c) Obstructive
(d) 'Tower' - urgency

Lazy Bladder Syndrome

Norgaard et al ICCS, BJU, 1998, 81, S3
Uroflow
lowest acceptable max flow rates

Table 1. Lowest acceptable maximum uroflow rates according to age and sex for males and females.

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Minimum (ml)</th>
<th>Male</th>
<th>Female</th>
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<tbody>
<tr>
<td>4-7</td>
<td>180-195</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>8-13</td>
<td>185-195</td>
<td>14</td>
<td>15</td>
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<tr>
<td>14-45</td>
<td>200-210</td>
<td>21</td>
<td>16</td>
</tr>
<tr>
<td>46-65</td>
<td>210-220</td>
<td>22</td>
<td>19</td>
</tr>
<tr>
<td>66-80</td>
<td>200-220</td>
<td>9</td>
<td>10</td>
</tr>
</tbody>
</table>

Available by gender and body size

Urodynamics

- Measure pressure/volume relationship of bladder
- Continuous study of filling and emptying
- Transurethral or suprapubic approach
- Rectal probe for abdominal pressure
- Combine with fluoroscopy – video UD
  - Provides VCUG
    - Anatomical info – bladder shape, VUR, configuration and behaviour of bladder neck and pelvic floor
- EMG – assess sphincter activity
- OR
- Intraluminal urethral pressure

Uroflow percentiles

Urodynamics - indication

- Neuropathic bladder-sphincter dysfunction
- Non neuropathic bladder – sphincter dysfunction
  - Dysfunctional voiding ?? Fail to respond to treatment
  - Lazy bladder syndrome
  - Failure to respond to traditional treatment ??
  - Guide to treatment – pharmacotherapy or urotherapy
  - Recurrent UTI

Urodynamics

- Filling
  - Detrusor activity
  - Bladder sensation
  - Bladder capacity
  - Bladder compliance
  - Detrusor pressure
- Emptying
  - Contractility of detrusor
  - Pressure flow relationship
Urge incontinence

- Involuntary loss of urine associated with urgency
- Imperative urge to void
- Frequency
- Holding on – squat, curtsey
- Worse in afternoon
- Usually small volume incontinence
- Can have night wetting
- UTI
- Constipation

Urge incontinence - pathogenesis

- Habitual non physiological responses to signals from bladder and urethra
- Fail to obtain, or lose CNS control
- Detrusor instability – involuntary phasic detrusor contraction of any pressure during filling phase whilst attempting to inhibit micturition - no relevant neuropathy
- (if neuropathy present, same phenomenon is detrusor hyperreflexia)

Urge incontinence - Investigations

- FVC
  - Small bladder capacity
  - Frequency
- US – small bladder capacity, complete emptying
- Flow, PVR - Normal micturition with complete emptying
- UD - Overactive detrusor contraction in early filling phase

Dysfunctional voiding

- Abnormality of voiding
- Overactivity of pelvic floor during voiding

Dysfunctional voiding

- Staccato voiding
  - Incomplete relaxation of urethral sphincter during voiding
  - Bladder emptying prolonged and incomplete
  - Flow – dips in flow rate
  - UD – dips in flow rate coinciding with high bladder pressure
  - Pathophysiology – flow rate above certain threshold triggers pelvic floor contraction. Contraction reduces flow rate so pelvic floor relaxes
Dysfunctional voiding

- Fractionated voiding
  - Hyperactivity of pelvic floor that stops flow rate so voiding occurs in portions.
  - Detrusor hypotonic, flow due to weak detrusor contraction. Strain to increase speed of micturition. Incomplete voiding.
  - Bladder instability present but easily inhibited
  - Incontinence due to overflow

- Lazy bladder syndrome
  - Long term dysfunctional voiding
  - Absent detrusor contractions
  - Empty by abdominal pressure – straining
  - Absent normal bladder sensation
  - Recurrent UTI
  - Large residual volumes
  - Low voiding frequency – micturition postponed

Management incontinence

- Address
  - UTI
  - Fluid intake
  - Voiding frequency
  - Constipation

Management – Day Wetting

- Pharmacotherapy (mainly urge syndrome)
  - Anticholinergics – oxybutinin, propantheline, tolterodine
- Urotherapy (mainly dysfunctional voiding)
  - Voiding frequency
  - Bladder training incl cognitive bladder training school
  - Pelvic floor relaxation
  - Biofeedback
- Others
  - Psychologist
  - CIC
  - TENS
  - PENS

Outcome

- Treatment begun at an earlier age seems to have greater chance of success with fewer complications
  - Moilanen at el Br J Urol 1998 81
- Incontinence is a very stressful event leading to behavioural problems
  - Hellstrom Lancet 2000 85
- Self esteem after treatment improves and attains the same levels as in healthy children
  - Hagglof et al, Eur Urol 1998 33
- Very few parents spontaneously search for medical help
### Outcomes

- Sureshkumar et al J Urol, 2003, 170
- Systematic review of RCT
- Only 5 trials suitable for review – all with inherent errors
- Terodiline - ? Most effective

### Outcomes - reality

- Frustrating
- Slow
- Intensive