Nothing but a Pee Thing
October 4th, 2019

Jamie Neal Lewis, APRN
Disclosure

• I have no disclosures
• Intro music
Objectives

• 1. Differentiate between primary and secondary nocturnal enuresis
• 2. Differentiate between monosymptomatic and non-monosymptomatic nocturnal enuresis
• 3. Review usage of the moisture alarm
• 4. Review instructions about how to use a moisture alarm
• 5. Review medications used to treat nocturnal enuresis
• 6. Discuss research results of patients who use the moisture alarm versus medications
How common is nocturnal enuresis?

- 5 year olds 20-25%
- 6 year olds 10-12%
- 7 year olds 5-10%
- 8 year olds 7-9%
- 10 year olds 5%
- 12 year olds 3%
- 14 year olds 2%
- 16-18 year olds 1%
- More common in boys 3:2
- 15% of bedwetters outgrow it every year

Pathogenesis

- Children produce a disproportionately large amounts of urine at night (lack of ADH)
- Drinking too much fluid before bedtime
- Children do not wake up to the sensation of a full bladder (by parent report and from studies on sleep-wake arousal thresholds)
- Other - diabetes mellitus or diabetes insipidus, UTI, constipation, stress, sleep disturbances
- Unlikely to be a sign of underlying kidney disease

Neveus, 2011
Genetic component

- If 1 parent had nocturnal enuresis, there is a 42% chance each of their offspring will have it
- If 2 parents had nocturnal enuresis, there is a 77% chance each of their offspring will have it
- Likely also affects maturation and bladder control

Thurber, 2016
Why do we care about nocturnal enuresis?

- Increased risk of social/emotional problems
- Embarrassment
- Low self esteem
- May avoid certain social activities that are age appropriate (sleep overs)
- Parents may also experience emotional stress, cost/time for laundry, absorbent underwear
- More common among children with neuropsychiatric disorders, specifically ADHD
- Children and adults tend to have more depressive problems and problems at school and work

Neveus, 2011
Types of Nocturnal enuresis

- Primary - they have never outgrown the bedwetting; have never been continuously dry at least 6 months in a row
- Secondary - were dry every night for at least 6 months and then the bedwetting came back
  - Can be associated with organic or psychological causes
    - UTI
    - Sexual abuse
    - Diabetes mellitus or insipidus
    - Sleep apnea
    - Externalizing disorders such as ADHD

Harari, 2011
Self assessment 1

• Bobby is 9 years old and has always wet the bed at night. Bobby has:
  • A. Primary nocturnal enuresis
  • B. Secondary nocturnal enuresis
Other symptoms?

- Monosymptomatic - no daytime symptoms of bladder dysfunction
- Non-monosymptomatic - other symptoms concerning for bladder dysfunction such as
  - Urgency
  - Frequency
  - Leaks and accidents
  - Holding maneuvers (potty dance, St. Vincent’s curtsy)
**Do Not Pass Go if:**

<table>
<thead>
<tr>
<th>Warning signs</th>
<th>Actions to be taken</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daytime incontinence or urinary tract infections.</td>
<td>Make the family complete a frequency-volume chart before proceeding. Treat daytime incontinence before enuresis.</td>
</tr>
<tr>
<td>Faecal incontinence, hard stools, unfrequent bowel movements</td>
<td>Suspect, and treat for, constipation</td>
</tr>
<tr>
<td>Significant problems with peer relations and behavior</td>
<td>Risk for therapy-resistance and/or psychiatric comorbidity. Consider parallel psychological evaluation.</td>
</tr>
<tr>
<td>Straining, weak stream, continuous incontinence</td>
<td>Suspect neurogenic bladder or anatomic abnormalities. Send to secondary center.</td>
</tr>
<tr>
<td>Glucosuria</td>
<td>Consider diabetes mellitus. Check blood glucose immediately</td>
</tr>
<tr>
<td>Proteinuria (++ or more on urine test)</td>
<td>Consider kidney disease. Consult paediatrician</td>
</tr>
<tr>
<td>Leukocyturia or nitrite test positive</td>
<td>Take urine culture. Consider antibiotic treatment if culture is positive</td>
</tr>
<tr>
<td>Excessive thirst, need for night-time drinking</td>
<td>Consider polydipsia or kidney disease. Measure fluid intake</td>
</tr>
<tr>
<td>Nausea, weight loss, fatigue</td>
<td>Consider kidney disease. Check creatinine, hemoglobin and electrolytes and consult paediatrician.</td>
</tr>
</tbody>
</table>

Neveus, 2011
Self assessment #2

- Jenny is a 7 year old female who has bedwetting as a chief complaint. Upon further history, you discover she also has daytime incontinence, voids 15 times a day, has a lot of urgency and does not have a soft poop every day. You should:
  - A. Start treatment for bedwetting with the alarm or medications.
  - B. Do not start treatment for bedwetting, other issues need to be addressed first.
Myths about nocturnal enuresis

- Child is lazy and won’t get up at night
- Doing it on purpose
- There is a magic pill
- Punishment helps
- Medical or organic cause
- Wore Pull ups too long
- Only 1 problem causes bedwetting
- Just need to outgrow it
Bedwetting treatments through the Ages

- 1550 BC: Juniper berries, cypress leaves and beer
- 77 AD: Eat boiled mice
- 1642: Bites of pig bladder sprinkled onto the bed
- 1709: Drink urine as punishment
- 1747: Penile clamps
- 19th century: Belladonna to paralyze the bladder
- 1904: First bell and pad alarm
- 1956: Hypnosis
- 1979: Malem alarm
- 1989: Desmopressin approved by FDA
Nocturnal enuresis treatments—general

- Wait to outgrow
  - 15% of kids get dry on their own every year
- Behavior/habit changes
  - Voiding before bedtime, managing constipation, cutting out bladder irritating drinks (caffeine, carbonation, citrus and red dyes)
- Bedwetting alarm
  - 66-75% of kids between 8 and 12 years old get dry
- Medications
  - Not a cure, considered a bridge to cover until they outgrow it
Why is treating constipation so important, even for bedwetting?

• If constipation is missed, nocturnal enuresis treatments will probably not work as well or at all
• But treating constipation by itself will not cure bedwetting in most cases (except in some teenagers – anecdotal)
• Treatment and prevention of constipation optimizes treatment for bedwetting
• Voiding dysfunction must be treated before we can treat bedwetting
• "You have to be a great poop-er before you can be a great pee-er."
# Bristol Scale

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>Separate hard lumps, like nuts or hard balls</td>
<td><img src="https://example.com/image1.png" alt="Image" /></td>
</tr>
<tr>
<td>Type 2</td>
<td>Sausage-shaped but lumpy</td>
<td><img src="https://example.com/image2.png" alt="Image" /></td>
</tr>
<tr>
<td>Type 3</td>
<td>Like a sausage or snake but with cracks on its surface</td>
<td><img src="https://example.com/image3.png" alt="Image" /></td>
</tr>
<tr>
<td>Type 4</td>
<td>Like a sausage or snake, smooth and soft</td>
<td><img src="https://example.com/image4.png" alt="Image" /></td>
</tr>
<tr>
<td>Type 5</td>
<td>Soft blobs with clear-cut edges</td>
<td><img src="https://example.com/image5.png" alt="Image" /></td>
</tr>
<tr>
<td>Type 6</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
<td><img src="https://example.com/image6.png" alt="Image" /></td>
</tr>
<tr>
<td>Type 7</td>
<td>Watery, no solid pieces</td>
<td><img src="https://example.com/image7.png" alt="Image" /></td>
</tr>
</tbody>
</table>

Moisture alarm

• Conditioning treatment
• Results in dryness in 2/3 of all children
• Sounds only when the patient gets wet, not randomly throughout the night
• Thought to improve arousal to a full bladder and increase bladder capacity
• Usually takes several weeks before efficacy can be determined
• Most research on the alarm was done on kids between 8 and 12 years of age.
• Probably ok for younger kids (6 to 7 years old), but only if child and parent are motivated!
• Consistency is crucial
• Continue treatment until at least 14 dry nights in a row

Neveus et al, 2010
Educational Alarm video
Give detailed alarm instructions!

- “The alarm is a brain trainer for deep sleepers.”
- It takes 3-4 months for most kids to get dry.
- Plan for 3-4 weeks of nightly usage before the child starts waking up to the alarm.
- Attach the sensor to dry underwear (not a pull up).
- When the alarm goes off, the parent will need to go wake the child up as the child will likely not wake up at first. Use a baby monitor if the parent is worried about not hearing the alarm.
- When the alarm goes off, parent wakes the child, but only the child should turn off the alarm.
- Go into the bathroom, check to see if any more pee comes out.
- Put on dry clothes (and sheets) and reset the alarm.
- Go back to bed. Repeat if/when the alarm goes off again.
- If the alarm goes off more than 2 times a night, call and consider a small dose of oxybutynin at bedtime to help store urine better.
Alarm general info

- Cost about $20-$30 for a basic alarm
- Can become unhooked if the move around a lot
- May go off in the child sweats heavily while asleep
- Stop the alarm after 6-8 weeks if there is no positive effect at this point

Neveus, 2011
When NOT to use the alarm

• Group home settings
• Children who are poor sleepers, may wake up and not fall back to sleep or children who wake up multiple times a night
• If the alarm is going off more than 1 time per night
Desmopressin-
1st line medication

• Analogue to antidiuretic hormone (ADH)
• Given in oral tablets
• Nasal spray had greater side effects and now not recommended for NE since 2007
• Dose is not influenced by body weight or age
• We start with 0.2mg for 1-2 weeks, then if not dry increase to 0.4mg for 1-2 weeks, max is 0.6mg
• Effect is immediate (same night)
• *Take 1 hour before bedtime but must limit fluids 2 hours before bedtime and overnight* (adverse effect is seizures from hyponatremia)
• Hold if sick (thirsty and need hydration) or done vigorous exercise that day
• We know desmopressin only gets about 50% of patients dry, no matter what dose
• Cochrane review in 2002 of 75 trials demonstrated “success” in 2/3 of children

Montaldo et al, 2012
Alarm versus desmopressin

- Open label, randomized, multi center trial
- Age 5-16 years with MNE with >6 wet nights a week
- Never been treated or were treated > 1 year ago and/or for < 4 weeks

- Alarm group:
  - 25 patients completed
  - Treated ≤ 6 months until 14 consecutive dry nights or treatment no longer beneficial

- Desmopressin group:
  - 114 patients completed
  - Treated for 3 months, then stopped the med for 2 weeks, restart for 3 months if not dry
  - 0.2mg desmopressin 1 hour before bedtime, could drink only to satisfy thirst 1 hour before and 8 hours after desmopressin
  - If more than 1 wet night, increased to 0.4mg

Alarm versus desmopressin

- **ALARM**
  - Lower compliance 50-75%
  - 56% got dry
  - After 12 months, 38% responded
  - Over half of the patients originally assigned to this group dropped out

- **DESMOPRESSIN**
  - Higher compliance 80-91%
  - 34% got dry
  - After 12 months if not dry during study, 54% got dry later

Evans et al, 2010
Self assessment #3

• Bobby has primary monosymptomatic nocturnal enuresis. He and his family appear motivated. You recommend the following as first line treatment:
  • A. The alarm, he is too young for medication
  • B. Medication, he is too old for the alarm
  • C. Give the patient and family the choice of what they would like to try first
Anticholinergics

- Oxybutynin and tolterodine
- Suppress detrusor overactivity (bladder muscle)
- Multiple studies- including randomized, placebo controlled studies conducted
- Use when standard therapy has failed (alarm or desmopressin)
- Adverse effects: constipation, dry mouth, dry eyes, flushing of skin, increased post void residual which could contribute to urinary tract infections (UTIs),
- Some risk of mood/behavior changes (more common with oxybutynin)

Neveus et al, 2010
Desmopressin + oxybutynin (randomized, double blinded, placebo controlled)

- 206 children between 6 and 13 (mean 10.6+- 2.9 years), 117 males and 89 females
- Had bedwetting only, no daytime symptoms, constipation or encopresis
- 120ug (101) versus 240ug (105)
- 120ug= 35 got dry every night, 64 did not get dry every night (12 more got dry when increasing dose to 240ug)
- 240ug= 38 got dry every night, 67 did not get dry every night
- 120 patients did not get dry every night with desmopressin at either dose (85 partial dry, 35 no response)
- 61 of these patients added oxybutynin 5mg, 13 more got dry, 15 partial dry and 33 no response
- 59 patients got placebo, 3 got dry, 7 partial dry, 49 no response

Montaldo, 2012
Another study: Combo therapy with desmopressin and anticholinergic (tolterodine LA)

- Randomized, double-blind, placebo controlled study
- 6-17 years old
- Monosymptomatic NE was only symptom
- Refractory to desmopressin alone up to 0.6mg (max dose)
- Excluded for daytime bladder concerns and/or constipation (via Rome II criteria)

Desmopressin + tolterodine results

### TABLE 2: Treatment Outcome Response Rates

<table>
<thead>
<tr>
<th></th>
<th>Desmopressin + Placebo</th>
<th>Desmopressin + Long-Acting Tolterodine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full response</td>
<td>1 (6)</td>
<td>3 (17)</td>
</tr>
<tr>
<td>Partial response</td>
<td>4 (25)</td>
<td>5 (26)</td>
</tr>
<tr>
<td>Nonresponse</td>
<td>11 (69)</td>
<td>10 (56)</td>
</tr>
<tr>
<td>Marginal response</td>
<td>4 (25)</td>
<td>7 (36)</td>
</tr>
<tr>
<td>No change</td>
<td>7 (44)</td>
<td>3 (17)</td>
</tr>
</tbody>
</table>

Full response = >90% decrease in wet nights
Partial response = 50-89% decrease in wet nights
Nonresponse = 0% to 49% decrease in wet nights

Higher dose oxybutynin + desmopressin for refractory NE

• Retrospective chart review of 61 kids ages 7-18 years
• Both MNE and NMNE (but daytime symptoms controlled) initially treated with desmopressin
• All patients who failed desmopressin 0.6mg were started on oxybutynin 5mg then titrated to 10mg of oxybutynin
• Results: use of escalating doses of oxybutynin with desmopressin got 96% of their kids dry
• Low dose (desmo 0.6mg and oxy 5mg) still got 68% of kids dry
• Advanced dose (desmo 0.6mg with oxy 7.5mg) got 75% of kids dry
• No adverse events with desmopressin, no drop outs due to adverse effects
• Kids with ADHD/ADD and/or daytime symptoms had decreased response to desmo

Berkenwald, Pires & Ellsworth 2016
Tricyclics

- Specifically imipramine
- No more effective than desmopressin
- Higher relapse rate
- Overdose can cause life threatening cardiotoxicity
- Definitely considered 3rd line therapy

Harari, 2011


Thank you

• Amanda Porter, CLS
• Janet Austin, RN
• Hannah Wooten, RN
• Lora Bear, APRN
• Leslie Malle, APRN
• Uri Alon, MD
• Brandon Newell, MD