PRIMER

Nocturnal enuresis

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Nighttime incontinence, otherwise known as nocturnal enuresis, is a common condition that can cause substantial psychological distress in children with the condition. Nocturnal enuresis is defined as nighttime bedwetting in children five years of age or older.[1] The prevalence of bedwetting (≥ 2 nights per week) in one large British study was 8% at 9.5 years.[2] There is a strong genetic component to bedwetting; in one large study, the odds of a child being a "severe" bedwetter were 3.6 times higher when there was maternal nocturnal enuresis.[3] Gender also plays a role in bedwetting. In a large American study of children between 8 and 11 years of age, the prevalence of bedwetting was 6.21% among boys and 2.51% among girls.[4] Boys have also been found to have more severe bedwetting than girls.[5]

Although very little progress has been made recently in the treatment of bedwetting, there is a greater understanding of the pathophysiology of this condition, in particular, the role of the central nervous system. Here we discuss the proposed pathophysiology behind bedwetting, investigations and evidence for current treatments.

Why does nocturnal enuresis occur?

There are three commonly proposed mechanisms to bedwetting. These include excessive nocturnal urine production, bladder overactivity and a failure to awaken in response to bladder sensations. Each mechanism can be supported by various studies, and no one theory is likely to explain bedwetting in all children. Excessive nocturnal urine production in some children is based on abnormal nocturnal plasma vasopressin release.[6,7] Other children may have an "overactive bladder;" however, these children typically have daytime symptoms including urgency, frequency and incontinence. Yeung performed ambulatory cystometries and found that bladder overactivity is an important cause of therapy-resistant nocturnal enuresis.[8]

Newer theories point to the role of the central nervous system in bedwetting. Parents of children who wet the bed often claim that they are "deep sleepers." Children with nocturnal enuresis may, however, have sleep disruption. In one recent study of children with bedwetting, sleep was significantly more fragmented and there was excessive daytime sleepiness.[9] Sleep disruption may result in a loss of the physiologic inhibitory signals to the bladder seen in animal studies.[10] This may also be the mechanism behind nocturnal enuresis in children with obstructive sleep apnea.[11]

KEY POINTS

- Bedwetting is a common condition and in isolation is not associated with a major illness.
- A thorough history and physical examination can prevent the need for further investigations.
- The bed alarm has the highest long-term success rate but can be labour intensive for children and their families.
- Although desmopressin can improve bedwetting, the effects are not sustained when the medication is stopped.

Which conditions need to be ruled out?

A thorough history and focused physical examination are important for all children who present with incontinence. The history should focus on the presence of daytime symptoms, which may suggest bladder dysfunction. Life stressors have, in some studies, been linked to bedwetting; however, for most children with bedwetting, there have not been any major life events. It is reasonable to ask about any stressors (e.g., new baby in the home, recent move, loss of a loved one), particularly in children with secondary enuresis (i.e., who were previously continent at night). More importantly, physicians should ask about the impact of bedwetting on the child's quality of life.

Physical examination should include an abdominal examination to palpate for stool and a back examination to look for signs of congenital spinal malformations such as dimples or hairy patches. A history of recurrent urinary tract infections or day-

time symptoms such as urinary frequency, incontinence or constipation suggests that further investigation is required. Investigations may include bladder pressure monitoring for those with daytime symptoms and magnetic resonance imaging of the spine to exclude spinal malformations.

If the sole symptom is urinary incontinence at night, urinalysis and urine culture may be the only investigations that are necessary. This approach is supported by the literature. Cayan and colleagues reported that the findings of ultrasonography and uroflowmetry were no different in children with nocturnal enuresis than in children without the condition.[12] Performing more than a urinalysis and culture for children with nocturnal enuresis would not be cost effective nor helpful to the child. Some argue that even urinalysis may be unnecessary.[12]

Which treatments work?

Treatment options for bedwetting include lifestyle modification, medications and alternative therapies. The most critical aspect of treatment is reassurance for the child, who may experience low self-esteem.[13] Parents must understand that, unlike daytime behaviour, nighttime incontinence is not within the child's control. Children may come up with ways to live with the incontinence and still participate in normal childhood activities. One option for sleepovers is placing pullups and plastic bags in the child's sleeping bag so that the other children do not know about the incontinence. Fluid limitation after dinner may decrease the volume of incontinence but is unlikely to stop it. Caffeinated beverages should be avoided in general, but particularly in the evening.

The medical treatments for bedwetting have not changed recently; however, we now have better evidence as to their effectiveness. Commonly accepted treatments include the bed alarm, desmopressin and tricyclic antidepressants. The bed alarm is believed to address the difficulty children may have in waking in response to bladder sensations; however, many children who are successful using the alarm may remain dry without waking. It is the only treatment that has been shown to treat bedwetting with long-lasting effect. A systematic review found that after 10–20 weeks, 66% of children maintained 14 consecutive dry nights compared with only 4% of children with no treatment (relative risk [RR] for failure 0.38, 95% confidence interval [CI] 0.33–0.45).[14] The effect lasts even after the bed alarm is stopped. Success with the bed alarm depends on active involvement of the parents. If children do not wake with the noise or vibration, it is important for their parents to wake them. This can cause stress within the family and may not be practical if children share rooms. The bed alarm can be a very effective treatment in motivated families for children who are distressed by the bedwetting.

Desmopressin (synthetic vasopressin) acts on the renal collecting duct and distal tubules to enhance reabsorption of water. This treatment addresses excessive nocturnal urine production, which is likely to be the cause in only a subset of children who wet the bed. A Cochrane systematic review found that children taking desmopressin had a greater chance of cure (RR for failure with 60 μg 0.94; 95% CI 0.89–0.99).[15] This effect was not maintained once the medication was stopped. Desmopressin is available in tablets or melts. There have been no trials comparing the formulations; however, makers of the melts advertise the ease of delivery for children and the ability to take it without a liquid. Adverse effects from the medication are uncommon and were primarily related to nasal discomfort from the nasal spray, which is no longer available.

Tricyclic antidepressants are thought to act via the brainstem through their noradrenergic action. In a Cochrane review, 20% of children who took a tricyclic antidepressant became dry (RR for failure 0.77, 95% CI 0.72–0.83).[16] However, the result was not sustained once the medication was stopped. Parents must be warned about the cardiotoxic and hepatotoxic effects of a tricylic overdose. Minor adverse effects include postural hypotension, dry mouth, constipation, tachycardia, nausea, lethargy and insomnia. Few parents choose this form of treatment. It may, however, be beneficial for teenagers who are also experiencing depression.

Alternative therapies that have been tried for bedwetting include hypnotherapy, acupuncture, chiropractic treatment and psychotherapy. To date, there is very weak evidence to support any of these for the successful treatment of bedwetting.[17]

When does bedwetting usually stop?

There is a substantial yearly natural cure rate to bedwetting. Fifteen percent of children per year will stop bedwetting without treatment.[18,19]

Conclusion

Nocturnal enuresis is a common condition that can affect a child's self-esteem. Reassurance and minimizing the number of investigations are critical to address parents' concerns. The bed alarm has the most long-lasting success rate and is worthy of consideration if children are truly dis-

tressed by bedwetting. Desmopressin can be effective for improving quality of life; however, it only masks the condition until the child outgrows it. Alternative therapies have not been shown to improve bedwetting.

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