

# What is the best treatment for nocturnal enuresis in children?

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## EVIDENCE-BASED ANSWER

For children with primary nocturnal enuresis, treatment with enuresis alarms reduced the number of wet nights by almost 4 per week, with almost half of patients remaining dry for 3 months after treatment (strength of recommendation [SOR]: **A**, based on a systematic review of homogeneous randomized control trials [RCTs]). Desmopressin (DDAVP) and tricyclic drugs reduce

the number of wet nights by 1 to 2 per week during treatment, although the effect is not sustained after treatment is finished (SOR: **A**, based on a SR of homogeneous RCTs). Dry bed training with an alarm results in an additional reduction of wet nights over alarms alone (SOR: **A**, based on a systematic review of homogeneous RCTs).

## CLINICAL COMMENTARY

### Alarms have a high success rate with commitment; desmopressin good for temporary reduction

Nocturnal enuresis is embarrassing to children and frustrating to parents. Even though it has a usually benign, self-limited course, many families want to hear about treatment options. Enuresis alarms have a high success rate in achieving dry nights during treatment and maintaining dry nights once treatment stops. The success of alarms requires a motivated child and family plus a significant time and effort commitment for 3 to 6 months.

Since desmopressin rapidly reduces bedwetting, it is a good choice for situational use such as

sleepovers, camping, and holidays. Desmopressin has minimal adverse reactions such as nasal irritation, nausea, and headaches, but parents should minimize evening water intake to prevent rare water intoxication side effects. The lack of benefit of desmopressin and alarm combination therapy may be partly explained by the loss of learning, if desmopressin negates the alarm needing to trigger. Since tricyclic medications do not show a benefit over desmopressin, they should be considered second-line agents due to cardiotoxic side effects and life-threatening overdose outcomes.

## ■ Evidence summary

Nocturnal enuresis is an involuntary loss of urine at night in the absence of congenital or acquired central nervous system defect among children over 5 years of age.<sup>1-4</sup> Approximately 15% of children aged >5 years wet their bed at night.<sup>5</sup> The spontaneous resolution rate is about 15% per year.<sup>5</sup> Before primary care treatment, indications for urological referral should be excluded, including daytime wetting, abnormal voiding (unusual posturing, discomfort, straining, or poor urine stream), recurrent urinary tract infections, neurological and anatomical anomalies, and urgency symptoms.<sup>4</sup>

The Cochrane Incontinence Group Trials demonstrated that enuresis alarms led to nearly 4 fewer wet nights per week compared with no treatment or placebo (weighted mean difference [WMD] = -3.65; 95% confidence interval [CI], -4.52 to -2.78).<sup>1</sup> The relative risk of failure was 0.36 compared with placebo (95% CI, 0.26 to 0.40). The number needed to treat (NNT) to achieve 14 consecutive dry nights is 2. About half the children relapse after stopping treatment, compared with nearly all children after control interventions (55% vs 99%). Evidence is insufficient to say whether the addition of dry bed training

TABLE

Nocturnal enuresis treatments and efficacy

TREATMENT	EFFICACY
Enuresis alarms	<ul style="list-style-type: none"> <li>• Reduction in 4 wet nights per week</li> <li>• NNT=2 in achieving 14 consecutive dry nights</li> <li>• 50% stay dry after treatment ends</li> </ul>
Desmopressin	<ul style="list-style-type: none"> <li>• Reduction in 1 to 2 wet nights per week</li> <li>• NNT=7 in achieving 14 consecutive dry nights</li> <li>• High relapse rate</li> </ul>
Tricyclic drugs	<ul style="list-style-type: none"> <li>• Reduction in 1 wet night per week</li> <li>• NNT=6 in achieving 14 consecutive dry nights</li> <li>• High relapse rate</li> </ul>
Dry bed training with an alarm	<ul style="list-style-type: none"> <li>• Mild additional benefit over alarms alone</li> <li>• 38% relapse rate</li> </ul>

**FAST TRACK**

**Alarms reduce the number of wet nights by almost 4 per week; adding dry bed training helps even more**

(scheduled awakenings, cleanliness training, social reinforcement, positive practice) improves the outcomes. Alarms that wake the child immediately (vs a time delay) and alarms that wake the child (instead of the parents) were slightly more effective.

A meta-analysis also showed that desmopressin (10-60 µg) at bedtime reduced bedwetting by 1 to 2 nights per week compared with placebo (WMD=1.34; 95% CI, -1.57 to -1.11 with a dose of 20 µg).<sup>6</sup> The NNT to achieve 14 consecutive dry nights is 7. However, the data suggest once treatment stops, there is little difference between desmopressin and placebo. Some evidence suggested that a higher dose was more likely to decrease the number of wet nights; however, there was no difference in cure rates. Evidence comparing intranasal with oral administration is insufficient.<sup>2</sup>

In the Cochrane review, children treated with desmopressin had 1.7 fewer wet nights (WMD=1.7; 95% CI, -2.95 to -0.45) in the first week compared with children treated with alarms.<sup>6</sup> However, at the end of 3 months, alarms were associated with 1.4 fewer wet nights per week than children treated with desmopressin (WMD=1.4; 95% CI, 0.14 to 2.66).

Evidence is conflicting for increased efficacy for combining desmopressin with enuresis alarms. There is some limited

evidence that children receiving combination treatment with desmopressin and alarms had fewer wet nights than children treated with alarms and placebo.<sup>6</sup> This combination treatment did not show a benefit with failure rates (not attaining 14 consecutive dry nights) or a statistically significant difference in failure and relapse rates once treatment stopped. In addition, one RCT in which desmopressin nonresponders were supplemented with alarms showed no added benefit in remission rates compared with conditioning alarms plus placebo (51% vs 48% in achieving 28 dry nights).<sup>7</sup> Neither was there added benefit in relapse rates once treatment stopped.

Children treated with tricyclic drugs compared with those treated with placebo had approximately 1 less night of enuresis per week (WMD=1.19; 95% CI, -1.56 to -0.82).<sup>8</sup> More children achieved 14 dry nights while on imipramine compared with placebo (21% vs 5%; NNT=6); however, this advantage was not sustained once treatment finished (96% vs 97% relapsed). Little evidence exists to compare desmopressin with tricyclic drugs.<sup>2,8</sup>

Simple behavior methods may be more effective than no treatment, but there is little evidence for how these methods compare with one another, or with

more successful means of treatment.<sup>9</sup> Behavior techniques include lifting (taking a sleeping child to urinate in the bathroom), waking, rewards, and evening fluid restriction.

Dry bed training refers to comprehensive regimes, including enuresis alarms, waking routines, positive practice, cleanliness training, and bladder training in various combinations. A meta-analysis examining dry bed training including an enuresis alarm showed children had fewer wet nights compared with children receiving no treatment (relative risk [RR] of failure=0.17; 95% CI, 0.11–0.28).<sup>2,10</sup> Additionally, more children remained dry after treatment stopped (RR of relapse=0.25; 95% CI, 0.16–0.39). However, evidence was not sufficient to show a remission benefit for dry bed training without an alarm (RR of failure=0.82; 95% CI, 0.6–1.02), highlighting the key role for alarm therapy. On the other hand, dry bed training including bed alarms may reduce the relapse rate compared with alarm monotherapy (RR for failure or relapse=0.5; 95% CI, 0.31–0.8)

### Recommendations from others

A recent evidence-based practice parameter from the American Academy of Child and Adolescent Psychiatry states once the history and physical suggest primary nocturnal enuresis, treatment should include education demystification and withholding punishment.<sup>4</sup> Although insufficient evidence exists to recommend behavioral interventions such as journal keeping, fluid restrictions, and night awakenings, these supportive approaches are acceptable, benign starting points. Conditioning with an enuresis alarm and overlearning, which involves giving extra fluids at bedtime after successfully becoming dry and intermittent reinforcement before ending treatment, is a highly effective first-line management approach. Medication choices include desmopressin and imipramine, although relapse rates are high. Short-term use of desmopressin may be used for sleepovers or camping trips. ■

### REFERENCES

1. Glazener CM, Evans JH, Peto RE. Alarm interventions for nocturnal enuresis in children. *Cochrane Database Syst Rev* 2003; (2):CD002911.
2. Lyth N, Bosson S. Nocturnal enuresis. *Clin Evid* 2004; (11):468-477.
3. Butler RJ. Childhood nocturnal enuresis: developing a conceptual framework. *Clin Psychol Rev* 2004; 24:909-931.
4. Fritz G, Rockney R; American Academy of Child and Adolescent Psychiatry Work Group on Quality Issues. Summary of the practice parameter for the assessment and treatment of children and adolescents with enuresis. *J Am Acad Child Adolesc Psychiatry* 2004; 43:123-125.
5. Mammen AA, Ferrer FA. Nocturnal enuresis: medical management. *Urol Clin North Am* 2004; 31:491-498.
6. Glazener CM, Evans JH. Desmopressin for nocturnal enuresis in children. *Cochrane Database Syst Rev* 2002; (3):CD002112.
7. Gibb S, Nolan T, South M, Noad L, Bates G, Vidmar S. Evidence against a synergistic effect of desmopressin with conditioning in the treatment of nocturnal enuresis. *J Pediatr* 2004; 144:351-357.
8. Glazener CM, Evans JH. Tricyclic and related drugs for nocturnal enuresis in children. *Cochrane Database Syst Rev* 2003; (3):CD002117.
9. Glazner CM, Evans JH. Simple behavioural and physical interventions for nocturnal enuresis in children. *Cochrane Database Syst Rev* 2004; (2):CD003637.
10. Glazener CM, Evans JH, Peto RE. Complex behavioural and educational interventions for nocturnal enuresis in children. *Cochrane Database Syst Rev* 2004; (1):CD004668

### FAST TRACK

**Desmopressin and tricyclics reduce wet nights by 1 or 2 per week, but the effect stops after treatment ends**