


# Nocturnal Enuresis

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**Nocturnal enuresis is a common problem that can be troubling for children and their families. Recent studies indicate that nocturnal enuresis is best regarded as a group of conditions with different etiologies. A genetic component is likely in many affected children. Research also indicates the possibility of two subtypes of patients with nocturnal enuresis: those with a functional bladder disorder and those with a maturational delay in nocturnal arginine vasopressin secretion. The evaluation of nocturnal enuresis requires a thorough history, a complete physical examination, and urinalysis. Treatment options include nonpharmacologic and pharmacologic measures. Contenance training should be incorporated into the treatment regimen. Use of a bed-wetting alarm has the highest cure rate and the lowest relapse rate; however, some families may have difficulty with this treatment approach. Desmopressin and imipramine are the primary medications used to treat nocturnal enuresis, but both are associated with relatively high relapse rates. (Am Fam Physician 2003; 67:1499-506,1509-10. Copyright© 2003 American Academy of Family Physicians.)**

 A patient information handout on bed-wetting, written by the author of this article, is provided on page 1509.

*Members of various family practice departments develop articles for "Practical Therapeutics." This article is one in a series coordinated by the Department of Family Medicine at the Medical University of South Carolina. Guest editor of the series is William J. Hueston, M.D.*

**N**octurnal enuresis is a common problem, affecting an estimated 5 to 7 million children in the United States and occurring three times more often in boys than in girls.<sup>1</sup> Unfortunately, only about one third of the families of children with this frequently troubling problem seek help from a physician.<sup>1</sup> Recent studies have provided more information about nocturnal enuresis, and generally effective treatments are available.

## Definitions

The International Children's Continence Society has recommended the following standardization of terminology: nocturnal enuresis is the involuntary loss of urine that occurs only at night.<sup>2</sup> It is normal voiding that happens at an inappropriate and socially unacceptable time and place.<sup>2</sup> Over the years, various terms have been used to describe wetting problems (Table 1). This practice has created confusion and impeded standardization of diagnosis.

Children are not considered enuretic until they have reached five years of age. Mentally disabled children should have reached a mental age of four years before they are considered enuretic. For the diagnosis of nocturnal enuresis to be established, a child five to six years old should have two or more bed-

wetting episodes per month, and a child older than six years of age should have one or more wetting episode per month.

## Epidemiology

At five years of age, 15 to 25 percent of children wet the bed.<sup>3</sup> With each year of maturity, the percentage of bed-wetters declines by 15 percent. Hence, 8 percent of 12-year-old

TABLE 1  
Classification Schemes for Enuresis

### According to time of day

Nocturnal enuresis: passing of urine while asleep  
Diurnal enuresis or incontinence: leakage of urine during the day

### According to presence of other symptoms

Monosymptomatic or uncomplicated nocturnal enuresis: normal voiding occurring at night in bed in the absence of other symptoms referable to the urogenital or gastrointestinal tract  
Polysymptomatic or complicated nocturnal enuresis: bed-wetting associated with daytime symptoms such as urgency, frequency, chronic constipation, or encopresis

### According to previous periods of dryness

Primary enuresis: bed-wetting in a child who has never been dry  
Secondary enuresis: bed-wetting in a child who has had at least six months of nighttime dryness

*See page 1413 for definitions of strength-of-evidence levels.*

*At five years of age, 15 to 25 percent of children wet the bed. By the age of 12 years, 8 percent of boys and 4 percent of girls are still bed-wetters.*

boys and 4 percent of 12-year-old girls are enuretic; only 1 to 3 percent of adolescents are still wetting their bed. From 15 to 25 percent of bed-wetters have secondary enuresis, but the treatment approach and anticipated response are the same.

### **Etiology**

A single explanation for nocturnal enuresis has been elusive. The current belief is that the condition is multifactorial. Numerous etiologic factors have been investigated, and various theories have been proposed.

### **GENETIC AND FAMILIAL FACTORS**

Genetic predisposition is the most frequently supported etiologic variable. One review<sup>4</sup> found that when both parents were enuretic as children, their offspring had a 77 percent risk of having nocturnal enuresis. The risk declined to 43 percent when one parent was enuretic as a child, and to 15 percent when neither parent was enuretic. Another investigation<sup>5</sup> found a positive family history in 65 to 85 percent of children with nocturnal enuresis. If the father was enuretic as a child, the relative risk for the child was 7.1; if the mother was enuretic, the relative risk was 5.2. In addition, certain chromosomal loci (5, 13, 12, and 22) have been implicated in nocturnal enuresis.<sup>6,7</sup>

Familial factors that have been found to have no relationship to the achievement of continence include social background, stressful life events, and the number of changes in family constellation or residences.<sup>7</sup>

### **PSYCHOLOGIC FACTORS**

Nocturnal enuresis was once thought to be a psychologic condition. It now appears that psychologic problems are the result of enuresis and not the cause. Children with nocturnal enuresis have not been found to have an increased incidence of emotional problems.<sup>3</sup> For most children, bed-wetting is not an act of rebellion.

### **BLADDER PROBLEMS**

Studies attempting to establish bladder problems as the cause of nocturnal enuresis have been contradictory. Extensive urodynamic testing has shown that bladder function falls within the normal range in children with nocturnal enuresis.<sup>6</sup> However, one investigation<sup>8</sup> found that while real bladder capacity is identical in children with and without nocturnal enuresis, functional bladder capacity (the volume at which the bladder empties itself) may be less in those with enuresis.

No correlation has been found between urethral or meatal stenosis and bed-wetting. Furthermore, congenital, structural, or anatomic abnormalities rarely present solely as enuresis.

### **ARGININE VASOPRESSIN**

It has been postulated that normal development may include the establishment of a circadian rhythm in the secretion of arginine vasopressin, the antidiuretic hormone.<sup>9</sup> A nocturnal rise in this hormone would decrease the amount of urine produced at night. It may be that children with nocturnal enuresis are delayed in achieving this circadian rise in arginine vasopressin and, thus, may develop nocturnal polyuria. This nocturnal polyuria overwhelms the bladder's ability to retain urine until morning.

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## SLEEP DISORDERS

Neither nocturnal polyuria nor diminished functional bladder capacity adequately explains why children with nocturnal enuresis do not wake up to void. Controversy has existed for many years about whether enuresis reflects a sleep disorder.<sup>10</sup>

In most studies, sleep electroencephalograms have demonstrated no differences or only nonspecific changes in children with and without nocturnal enuresis. When surveyed, however, parents consistently maintain that their children with nocturnal enuresis are “deep sleepers,” compared with their offspring who are not bed-wetters. Other surveys have found that children with nocturnal enuresis are more subject to “confused awakenings,” such as night terrors or sleepwalking, than children who do not wet the bed.<sup>11</sup>

## Diagnosis

A careful history should be obtained and a thorough physical examination should be performed to look for causes of complicated enuresis in children who present with bed-wetting. Causes of complicated enuresis include spinal cord abnormalities with associated neurogenic bladder, urinary tract infection, posterior urethral valves in boys, and ectopic ureter in girls. In addition, children who have chronic constipation or encopresis may present with bed-wetting.

Parents should be questioned about their family history and the child’s medical history (Table 2). Careful questioning of parents and children can be extremely helpful in determining the type of enuresis and a possible cause or contributing factors (Table 3).

Parents often are not fully aware of their child’s daily voiding habits. Thus, a voiding diary may need to be maintained for a week or more. The family should keep track of how many times the child voids during the day and how many nights the child wets the bed.

Children with nocturnal enuresis have a normal physical examination. However, the

*The bed-wetting alarm has been shown to be the most effective treatment for nocturnal enuresis.*

physician needs to check carefully for signs that might signal other problems that can present with bed-wetting. Gait should be evaluated for evidence of a subtle neurologic deficit. The flanks and abdomen should be palpated for masses, including an enlarged bladder. The lower back should be inspected for cutaneous lesions or an asymmetric gluteal cleft, which could suggest spinal dysraphism, a variant of spina bifida.

Urinalysis is performed to assess specific gravity and urinary glucose level. It also can determine the presence of infection or blood in the urine.

If the findings of the physical examination and urinalysis are negative and the history does not suggest a secondary cause of nocturnal enuresis, no further work-up is needed. If urinalysis reveals evidence of infection, the child should be evaluated for vesicoureteral reflux. The currently recommended work-up is a voiding cystourethrogram and renal ultrasound examination.<sup>3</sup>

## Treatment

### NONPHARMACOLOGIC TREATMENTS

*Bed-Wetting Alarm.* The concept of using an alarm that emits a sound when a child wets the

TABLE 2

### Questions to Ask About the Medical and Family History of a Child with Bed-Wetting

- Were there any complications to your child’s birth?
- Does your child have a history of problems with his or her nervous system?
- Has your child ever had any surgery or injuries to his or her nervous system or genital area?
- Did you or your child’s other parent wet the bed as a child?

**TABLE 3**  
**Questions to Ask When Taking the History of a Child with Bed-Wetting**

<i>Question</i>	<i>Significance</i>
To distinguish primary from secondary enuresis: At what age was your child consistently dry at night?	"Never dry" suggests primary enuresis
To distinguish uncomplicated from complicated enuresis: Does your child wet his or her pants during the day?	Positive answer suggests complicated nocturnal enuresis
Does your child appear to have pain with urination?	Urinary tract infection
How often does your child have bowel movements?	Infrequent stools: constipation
Are bowel movements ever hard to pass?	Constipation
Does your child ever soil his or her pants?	Encopresis
To distinguish possible functional bladder disorder from nocturnal polyuria: How many times a day does your child void?	More than seven times a day: functional bladder disorder
Does your child have to run to the bathroom?	Positive response: functional bladder disorder
Does your child hold urine until the last minute?	Positive response: functional bladder disorder
How many nights a week does your child wet the bed?	Most nights: functional bladder disorder one or two nights: nocturnal polyuria
Does your child ever wet more than once a night?	Positive response: functional bladder disorder
Does your child seem to wet large or small volumes?	Large volumes: nocturnal polyuria Small volumes: functional bladder disorder
To determine how parents have handled bed-wetting: How have you handled the nighttime accident?	Elicits information on interventions that have already been tried; be alert for responses suggesting that the child has been punished or shamed.

bed was first introduced in 1938.<sup>12</sup> The bed-wetting alarm has been shown to be the most effective treatment for nocturnal enuresis.<sup>13</sup> Compared with other skill-based or pharmacologic treatments, the bed-wetting alarm has a higher success rate (75 percent) and a lower relapse rate (41 percent).<sup>14</sup> [Evidence level B, nonrandomized clinical trial]

The alarm appears to work by negative reinforcement or avoidance. It goes off and awakens the child during voiding; the child gets out of bed and finishes voiding in the toilet or holds urine until later. For resolution of nocturnal enuresis, the bed-wetting alarm may need to be used for up to 15 weeks.

Unfortunately, treatment with bed-wetting alarms has a dropout rate of 10 to 30 percent.<sup>15</sup> Possible predictors of a poor response include an unstable or chaotic family situation, behavior deviance in the child, high level of anxiety in the mother, and lack of concern about bed-wetting on the part of the parents or child. Low parental education level and high socioeconomic status also may be predictors of a poor response.

Another cited reason for the relatively high dropout rate is that adults who used the alarms as children, even those who were cured of bed-wetting, remember the treatment period as the worst time of their life.<sup>16,17</sup> How-

ever, a study conducted at a referral center found that when parents were given a choice of treatment modality, more than 90 percent of those who selected the alarm had used such an alarm when they were children.<sup>18</sup> [Evidence level B, nonrandomized clinical trial]

Improved technology has made the bed-wetting alarm a more attractive option than in the past. Alarms are now smaller and lighter, and they can be equipped with a buzzer, rather than a sound alarm, for children who do not respond to an alarm sound or for households in which an alarm disrupts the sleep of others. A number of currently available bed-wetting alarms are listed in *Table 4*.

**Positive Reinforcement Systems.** In one positive reinforcement system, the child puts stickers on a chart or earns points for every night he or she remains dry. Once a certain number of stickers or points have been earned, the child is given a prize. Another technique uses a connect-the-dots picture. The child connects two dots for every dry night. When the picture is completed, the child receives a prize.

**Responsibility Training.** With this technique, the child is given age-appropriate responsibility, in a nonpunitive way, for the consequences of bed-wetting. Younger children may be asked to strip wet linens from the bed, whereas older children may be expected to do the laundry.

**Other Approaches.** Various nonpharmacologic treatments have been shown to have a positive effect on bed-wetting in small studies but have not been extensively evaluated (generally weak strength of evidence). These approaches include an elimination diet,<sup>1</sup> hypnosis,<sup>1</sup> retention control (i.e., holding urine for progressively longer periods),<sup>14</sup> biofeedback,<sup>19</sup> acupuncture,<sup>20</sup> scheduled awakenings,<sup>21</sup> and caffeine restriction.<sup>22</sup>

#### PHARMACOLOGIC TREATMENT

Desmopressin (DDAVP) and imipramine (Tofranil) are the primary drugs used in the treatment of nocturnal enuresis. Pharmacologic treatment is not recommended for children under six years of age.

**Desmopressin.** A synthetic analog of arginine vasopressin, desmopressin works by decreasing urine volume at night and by decreasing intravesicular pressure. The drug comes in a nasal spray or tablet. Treatment using the nasal spray is initiated with 10 mcg given at bedtime, one half of the dose in each nostril. If necessary, the dosage can be increased to 20 mcg and then 40 mcg at bedtime. The 0.2-mg tablet is taken at bedtime; if necessary, the dose can be titrated to 0.6 mg.

As a rule, desmopressin is well tolerated. Side effects, which include nasal irritation, nosebleeds, and headache, are generally mild. In one study,<sup>23</sup> however, six children withdrew because of emotional disturbances, including aggressive behavior and nightmares, which resolved when the medication was discontinued.

**TABLE 4**  
**Selected Bed-Wetting Alarms\***

Nytone Alarm
Nytone Alarms, 2424 S. 900 West, Salt Lake City, UT 84119 Telephone: 801-973-4090 Web site: www.nytone.com
Wet-Stop Alarm
Palco Laboratories, 8030 Soquel Ave., Suite 104, Santa Cruz, CA 95062 Telephone: 800-346-4488 Web site: www.palcolabs.com
Potty Pager (silent alarm)
Ideas for Living, 1285 N. Cedarbrook, Boulder, CO 80304 Telephone: 800-497-6573 or 303-440-8517 Web site: www.pottypager.com
DRI Sleeper
Alpha Consultants, 94 Selwyn Place, P.O. Box 569, Nelson, New Zealand 7001 Telephone: 877-331-2768 Web site: www.dri-sleeper.com

\*—An alarm may be covered by insurance if a physician prescribes it.

A systematic review found that desmopressin reduced the number of wet nights more effectively in children older than nine years and in children who had the fewest number of wet nights.<sup>24</sup> [Evidence level A, systematic review of randomized controlled trials] The studies examined in the review found that frequency of wetting decreased anywhere from 10 to 91 percent, but that only 24.5 percent of children achieved complete dryness.

Once desmopressin therapy is stopped, relapse rates can range from 80 to 100 percent.<sup>2,25</sup> If children respond to desmopressin, treatment is continued for three to six months. To minimize the possibility of relapse, the drug should be discontinued slowly, with the dose decreased by as little as 10 mcg per month.<sup>23</sup>

*Imipramine.* The mechanism for the benefits of imipramine in the treatment of nocturnal enuresis is not understood. One theory is that the anticholinergic effect of the drug may result in a decrease in bladder contractility that leads to increased bladder filling and improved functional bladder capacity. Imipramine provides some benefit in approximately 50 percent of children with nocturnal enuresis.<sup>14</sup> However, only 25 percent experience complete elimination of enuresis, a rate that is only slightly better than that for placebo when the 15 percent spontaneous remission rate is taken into consideration.<sup>14</sup>

Following the discontinuation of imipramine, relapse rates are high. Side effects, including cardiotoxicity at high doses, occur frequently enough that imipramine probably should not be considered a first-line treatment for nocturnal enuresis. If other treatments fail, imipramine, given once daily one hour before bedtime, can be used in the following age-related doses: 25 mg in six- to eight-year-old children, 50 mg in eight- to 12-year-old children, and 75 mg in teenagers. Depending on the patient's age, the maximum dose is 0.9 to 1.5 mg per kg.<sup>3</sup> After three to six months of treatment, imipramine should be discontinued slowly. The dose is

decreased by one half for two weeks; the reduced dose is then given every other night for an additional two weeks.

### Developing a Treatment Plan

One study<sup>1</sup> found that 23 to 36 percent of parents had used punishment as their primary means of dealing with bed-wetting. Hence, family education is crucial. Parents and the affected child need to know that bed-wetting is a common problem, and parents should be instructed not to blame or shame the child. The physician can foster a sense of optimism about the potential for improvement while at the same time giving the child responsibility for achieving urinary control at night.

Sometimes the very process of seeking help leads to improvement of nocturnal enuresis. One study<sup>26</sup> comparing the use of desmopressin plus behavior therapy, placebo plus behavior therapy, and desmopressin therapy alone found improvement in all three groups in the first weeks after enrollment, before the actual study had even begun.

The timing of treatment should be individualized. It is important that the child be motivated to take an active role. The younger the child, the more fragile his or her motivation may be. The depth of this motivation can be assessed by assigning the child the task of keeping the voiding log. If the child seems inadequately motivated, it may be best to ask the family to postpone treatment until the child is ready.

All treatments should be explained carefully. One study<sup>18</sup> found that when choices were well explained, slightly more parents selected no treatment at all than treatment with desmopressin, indicating that many parents simply want reassurance.

Information obtained in the initial voiding diary may give clues about the best choice of initial treatment.<sup>6</sup> The child who voids frequently during the day (seven times or more), voids small amounts, has few or no dry nights during the week, and wets the bed more than once a night is more likely to have low func-

**TABLE 5**  
**Comparison of Treatment Modalities for Nocturnal Enuresis**

<i>Treatment</i>	<i>Advantage</i>	<i>Disadvantage</i>	<i>Cost for brand name product (generic)*</i>
Bed-wetting alarm	Effective, low relapse rate	Takes weeks for results; can be disruptive to family	\$50 to \$75, plus shipping and handling charges
Desmopressin (DDAVP)	Rapidly effective, few side effects	High-relapse rate with discontinuation	5-ml nasal spray: \$149 for 5-mL bottle 0.1-mg tablets: \$72 for 30 tablets 0.2-mg tablets: \$85 for 30 tablets
Imipramine (Tofranil)	Inexpensive, works quickly	High-relapse rate with discontinuation; side effects, including cardiotoxicity at high doses	25-mg tablets: \$28 (8) for 30 tablets

\*—Prices for desmopressin and imipramine were obtained from [www.drugstore.com](http://www.drugstore.com) (January 13, 2003) and reflect what patients' families are likely to pay.

tional bladder capacity. This child may benefit most from the use of a bed-wetting alarm. On the other hand, the child who has a normal voiding pattern during the day, voids large amounts at night, and wets only one to two nights per week may have nocturnal polyuria and therefore may be an appropriate candidate for desmopressin therapy. A child who fails one treatment modality is likely to benefit from another treatment.

Financial resources, the family's motivation, and the stability of the home situation are factors to consider in deciding on the best treatment for a child with nocturnal enuresis. Continence training should be part of any treatment plan. Given its higher success rate and lower relapse rate, an alarm system should be considered as first-line treatment for many children (Table 5). Desmopressin is rapidly effective, but sole use of the drug neglects continence skills. The alarm system and desmopressin can be used in combination.

Whatever the treatment plan, follow-up, support, and encouragement are important

components. One study<sup>27</sup> of the psychological benefits of treatment for nocturnal enuresis found that children rated their self-concept as being improved after all treatments (even placebo) and that parents' perception of their child's behavior improved, no matter what treatment was used or how successful it was.

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