American Family Physician
PUBLISHED BY THE AMERICAN ACADEMY OF FAMILY PHYSICIANS MARCH 1, 1999

Primary Nocturnal Enuresis: Current Concepts

A patient information handout on bed-wetting, written by the author of this article, is provided on page 1219.

MARC CENDRON, M.D.
Dartmouth-Hitchcock Medical Center
Lebanon, New Hampshire

Primary nocturnal enuresis sometimes presents significant psychosocial problems for children and their parents. Causative factors may include maturational delay, genetic influence, difficulties in waking and decreased nighttime secretion of antidiuretic hormone. Anatomic abnormalities are usually not found, and psychologic causes are unlikely. Evaluation of enuresis usually requires no more than a complete history, a focused physical examination, and urine specific gravity and dipstick tests. Nonpharmacologic treatments include motivational therapy, behavioral conditioning and bladder-training exercises. Pharmacologic therapy includes imipramine, anticholinergic medication and desmopressin. These drugs have been used with varying degrees of success.

Currently, an estimated 5 million to 7 million children in the United States have primary nocturnal enuresis (nighttime bed-wetting). Although increasing attention has been focused on nocturnal enuresis and increasing numbers of families have sought assistance from their physicians, questions remain regarding the etiology and management of this condition.

This article reviews the current information on primary nocturnal enuresis, describes various therapies and provides an updated and comprehensive review of this common condition. In addition, the author seeks to correct several misconceptions about primary nocturnal enuresis, including the following: that a child's bed-wetting is caused by drinking too much fluid before bedtime; that bed-wetting may occur as a result of a deep sleep pattern; and that the child is too lazy to get out of bed to void. This article focuses on primary nocturnal enuresis and does not address other disorders of elimination, such as urinary tract infection and dysfunctional voiding in patients who experience both daytime and nighttime incontinence.

Causes of secondary enuresis include neurogenic bladder and associated spinal cord abnormalities, urinary tract infections, posterior urethral valves in boys and an ectopic ureter in girls.

Definition

The American Psychiatric Association has defined bed-wetters as children older than age five who are incontinent of urine at night.[1] The prevalence of nocturnal enuresis has been difficult to estimate because of variations in its definition and in social standards.[2,3] It is now generally accepted that 15 to 20 percent of children will have some degree of nighttime wetting at five years of age, with a spontaneous resolution rate of approximately 15 percent per year. Therefore, at 15 years of age only 1 to 2 percent of teenagers will still wet the bed.

Some studies report that boys wet the bed more frequently than do girls, but this finding has been disputed by other reports.[4] One study notes that 80 percent of children with enuresis wet the bed only at night, and approximately 20 percent also have some daytime wetting.[1] The latter group falls into a different category and warrants a different evaluation.

Etiology

The etiology of primary nocturnal enuresis has been widely debated but is not yet completely understood. The physician should keep in mind that primary nocturnal enuresis is a diagnosis of exclusion, and that all other causes of bed-wetting must be ruled out. Causes of secondary enuresis include neurogenic bladder and associated spinal cord abnormalities, urinary tract infections, and the presence of posterior urethral valves in boys or an ectopic ureter in girls. Posterior urethral valves cause significant voiding symptoms, such as straining to void and diminished urinary stream. An ectopic ureter causes constant wetting.

Despite numerous studies on primary nocturnal enuresis, its etiology remains elusive. Several recent reports have clarified the pathophysiology of enuresis. The condition appears to be multifactorial, thus further complicating the therapeutic approach. In addition, the well-recognized spontaneous resolution rate clouds the search for causative mechanisms. Finally, the various treatment approaches and modalities are influenced by the patient's family environment and by the background and prejudices of the patient, the parents and the physician. Possible etiologies of primary nocturnal enuresis appear in *Table 1*.

TABLE 1
Possible Etiologies of Primary Nocturnal Enuresis

Factor	Pathophysiology	Evidence
Developmental delay	Delayed functional maturation of the central nervous system causing failure of arousal	Spontaneous cure rate as children grow older, animal studies
Genetics	Unclear	Family history, gene identification, linkage analysis

Sleep disorder	Deep sleep	Sleep studies
Behavior and psychologic disorders	Unclear	Result rather than cause
Anatomy	None found	Children with primary nocturnal enuresis have normal physical examinations
Antidiuretic hormone levels	Low level of nighttime antidiuretic hormone secretion in children with primary nocturnal enuresis causes urine overproduction	Hormone studies[5,6]

Maturational Delay

The most commonly accepted cause of nocturnal enuresis, but also the most difficult to prove, is delayed functional maturation of the central nervous system, which reduces the child's ability to inhibit bladder emptying at night. The child's bladder will fill, but the sensory output resulting from the stretching of the bladder is not perceived or is not sent to the brain and, thus, central cortical control over the urinary sphincter contraction does not occur. Failure of the arousal mechanism may also contribute to the inability to inhibit micturition.

Genetic Factors

A family history of nocturnal enuresis is found in most children with the condition. One study has shown that in families where both parents had enuresis, 77 percent of children will also have enuresis. In families where only one parent had enuresis, 44 percent of children will be affected; only 15 percent of children will have enuresis if neither parent had enuresis.[7]

Heredity as a causative factor of primary nocturnal enuresis has been confirmed by the identification of a gene marker associated with the disorder. In one study,[8] Danish researchers evaluated 11 families with primary nocturnal enuresis. The trait showed nearly complete penetrance in these families. This study seems to suggest the existence of a major dominant gene for primary nocturnal enuresis. This gene appears to be located on chromosome 13. However, no specific gene locus has yet been identified. The identification of this gene marker certainly lifts the burden of guilt from children who have enuresis and helps to dispel the theory that enuresis is behavioral in origin.

Sleep Disorders

The sleep patterns of patients with enuresis have been studied extensively but are difficult to interpret because of varying findings. Investigators studying sleep electroencephalographies have reported a higher incidence of increased slow brain-wave activity in patients with nocturnal enuresis; however, this has been considered a nonspecific finding.[9] Further studies have not supported this finding and demonstrate no consistent correlation between abnormal sleep patterns and bed-wetting.[10,11] It appears that patients with enuresis may have normal sleep patterns, but a recent study[11] documented that patients with

nocturnal enuresis have difficulties in waking. Parents report that children who wet the bed usually do so earlier in the night, and some older studies[12,13] suggest that wetting episodes occur during slow-wave deep sleep. However, more recent studies[14] have shown that bed-wetting may occur at different stages of sleep. Nocturnal enuresis has also been associated with upper airway obstruction in children, and surgical relief of the obstruction by tonsillectomy, adenoidectomy or both was reported to diminish nocturnal enuresis in up to 76 percent of patients.[15]

Behavior and Psychologic Factors

Psychologic factors are an unlikely cause of primary enuresis in children. Researchers from New Zealand used a population-based model to follow children up to 15 years of age. Using specific psychiatric criteria, they found that children with primary enuresis have essentially the same behavior pattern as children without primary enuresis.[16] On the other hand, results from a Danish study[17] showed that patients with primary nocturnal enuresis seem to have a poorer sense of belonging to society and clearly have lowered self-esteem. This study suggests that enuresis itself may lead to psychologic problems in adulthood.

Anatomic Factors

In cases of isolated primary enuresis, anatomic abnormalities are not usually found. Findings from two studies[18,19] suggest that functional bladder capacity may be reduced in patients with nocturnal enuresis, but these findings have been disputed by other researchers who found a low incidence of abnormalities in bladder function and size when nocturnal enuresis was isolated.[20] While some parents report a small bladder capacity in children with enuresis, this condition usually is accompanied by daytime symptoms. A history of, or symptoms consistent with, a urinary tract infection indicate a need for further evaluation by ultrasonography and voiding cystourethrography. In the absence of symptoms of urinary tract infection, radiologic evaluation is not recommended for children with primary nocturnal enuresis.

Secretion of Antidiuretic Hormone

Diurnal and nocturnal variations in the secretion of antidiuretic hormone over a 24-hour period have been reported in humans.[21] Studies[5,6] have demonstrated that children with enuresis did not show a normal rise in the nocturnal secretion of antidiuretic hormone.

Urodynamic and radiologic evaluation are not necessary in children with straightforward primary nocturnal enuresis.

Normal increases in the secretion of antidiuretic hormone are a typical response to extended periods of sleep. During this period, the bladder does not empty. In children who sleep between eight and 12 hours per night, the increase in the secretion of antidiuretic hormone reduces the amount of urine produced by the kidneys, thus decreasing the amount of urine stored by the bladder. There is limited evidence that some children with enuresis excrete significantly higher volumes of more diluted urine during sleep than do children without enuresis.[22] Abnormal secretion of antidiuretic hormone at night may be a significant factor in the etiology of nocturnal enuresis in some children, although studies of gene markers do not correlate with abnormalities of antidiuretic hormone function.[8]

Evaluation of Primary Nocturnal Enuresis

The most important factors to consider in the evaluation of patients with enuresis include the following: the patient's age, the severity and perceived severity of the problem within the patient's family, the spontaneous resolution rate and the patient's response to therapy. When assessing the severity and perceived severity of the problem, the physician must consider, for example, that older children tend to suffer much more than younger children from the stigma of bed-wetting. These children may warrant medical intervention that offers a quick, safe response that will allow the child to participate in peer activities. Other important factors include realistic goal setting, as well as proper follow-up.

Our experience in treating patients with primary nocturnal enuresis has shown that a consistent method of treatment and a goal-oriented approach with consistent follow-up provide the best results. After proper evaluation of the child and confirmation of the diagnosis of primary nocturnal enuresis, the expectations of the parents and the child may be assessed, and recommendations may be made.

Although the vast majority of patients who are treated for nocturnal enuresis are healthy, the evaluation should be geared toward ruling out anatomic abnormalities of the urinary tract, such as posterior urethral valves, bladder abnormalities, an ectopic ureter or an epispadiac urethra (urethral opening on the dorsum of the penis).

A careful medical history and physical examination, including urinalysis, will usually provide sufficient information for the physician to arrive at a diagnosis. The history should include an assessment of the child's history of voiding patterns and any previous work-up and therapy. The physical examination should include abdominal, genital and neurologic assessments to look for evidence of a distended bladder, spinal lesions and epispadias. Urinalysis should include urine specific gravity and dipstick tests, which might suggest the presence of diabetes insipidus. Abnormalities in renal concentrating ability should be noted. A urine culture should be obtained only if the patient has symptoms consistent with urinary tract infection or if urinalysis results are positive for the presence of red and white blood cells. Urodynamic and radiologic evaluation are not necessary in children with straightforward primary nocturnal enuresis.

Psychosocial and family histories are important, as the attitudes of the child and his or her parents are significant in selecting proper therapy for primary nocturnal enuresis.

Treatment

The first step toward proper treatment is to have the child's parents complete a questionnaire that reviews the child's history of enuresis. The physician should also consider the following points: children younger than six years of age are generally not evaluated if they have enuresis and no other ongoing urologic problems; treatment modalities will not be successful if the parents and the child do not have a cooperative attitude, and treatment will be unsuccessful if the family's social structure and home environment do not provide consistent support and care for the child.

Consistent follow-up is essential in gauging the results of therapeutic intervention. Objective documentation using a diary can help the physician, the patient and the family monitor progress. Improvement is usually defined as a 50 percent reduction in the number of nights that bed-wetting occurs. Cure or resolution of primary nocturnal enuresis is defined as only one or two wet nights over a three-month period, and documentation that the child has wakened spontaneously and gone to the bathroom to void.

Treatment of nocturnal enuresis can be divided into two broad categories: nonpharmacologic and pharmacologic. Nonpharmacologic treatment of enuresis includes motivational therapy, behavior modification (conditioning therapy), bladder-training exercises, psychotherapy, diet therapy and hypnotherapy. Because of increased awareness that primary nocturnal enuresis can be a significant psychosocial stressor, pharmacologic treatment of primary nocturnal enuresis has evolved significantly over the past 15 years, and safer, more effective medications are now available.

Nonpharmacologic Methods

Motivational Therapy. Motivational therapy for the treatment of nocturnal enuresis involves reassuring the parents and the child, removing the guilt associated with bed-wetting and providing emotional support to the child. The child should be instructed about taking responsibility for his or her bed-wetting. In other words, children with nocturnal enuresis should be helped to understand the condition and to realize that while they did not cause the problem, they do have a role in the treatment plan.

Positive reinforcement for desired behavior should be instituted. One way to carry out a program of motivational therapy is to set up a diary and chart, with a reward system for each night the child stays dry.

The cure, or resolution rate for children receiving motivational therapy has been estimated to be only 25 percent (a figure close to the 15 percent rate of spontaneous resolution), yet up to 70 percent of children with primary noctural enuresis show marked improvement.[23] Long-term follow-up is necessary, however, and a relapse rate of approximately 5 percent has been reported.[24]

Motivational therapy appears to be a reasonable first-line approach to treating children with primary nocturnal enuresis, especially younger children. However, if therapy is not successful within three to six months, a different treatment option (e.g., behavior modification or pharmacologic therapy) should be offered.

Hypnotherapy, diet therapy and psychotherapy are treatment modalities that have not been widely used in children with primary nocturnal enuresis. Hypnotherapy has had good success rates in limited trials, but there has been no long-term follow-up. Diet therapy also may be an option for some patients. Children with a higher caffeine intake may be more prone to enuretic episodes. Foods suspected to be contributing agents for enuresis include dairy products, chocolate, and citrus fruits and juices.[25]

Behavioral Conditioning. Behavioral conditioning in the treatment of primary nocturnal enuresis is based on the use of a signal alarm device. When the child voids in bed, a moisture-sensing device that has been placed near the genitals is activated and triggers an alarm. This evokes a conditioned response of waking and inhibiting urination.

Various alarm devices are currently available. The alarm is either a sound or a vibratory device. We prefer the vibratory alarm because we have found it to be more effective than the sound devices in waking children. We do not recommend using the alarm with children younger than seven years of age.

Alarm therapy requires a cooperative and motivated child and family. Parental involvement is very important when using alarm devices. Involvement includes recording the child's responses to the device and monitoring his or her progress. Again, use of a diary and a reward system may help reinforce the desired behavior. Parents should be told that this form of therapy will require a long-term commitment as results may not be evident for several months.

Long-term success using signal alarm devices has been reported in approximately 70 percent of children with primary nocturnal enuresis.[26] We recommend that children use the alarm devices until they experience three weeks of complete dryness. Relapse rates are higher when the alarm system is discontinued after shorter dry periods. Overall, relapse occurs in 20 to 30 percent of patients. Relapse is certainly not incompatible with restarting alarm treatment, and results are generally good with consistent use.

Although alarm devices are generally safe, older buzzer systems have been known to cause buzzer ulcers. The alarm may fail if the moisture sensor is not positioned correctly. Smaller units are now available *(Table 2)*.

TABLE 2
Some Alarm Devices for the Treatment of Primary Nocturnal Enuresis

Device	Manufacturer	Cost*
Wet-Stop	Palco Labs Santa Cruz, Calif. 800-346-4488	$65.00
Nytone Enuretic Alarm	Nytone Medical Products Salt Lake City, Utah 801-973-4090	53.50
Potty Pager	Ideas for Living Boulder, Colo. 800-497-6573	49.95
Nite Train'r	Koregon Enterprises Beaverton, Ore. 800-544-4240	69.00
Sleep Dry	Star Child Labs Aptos, Calif. 800-346-7283	45.00

*--Manufacturers' prices, rounded to the nearest dollar. Shipping and handling charges are not included.

Another method of behavioral conditioning involves waking the child two to three hours after he or she has gone to sleep, eliciting a conditioned response of waking when the bladder is full. The success rate of this technique is unknown. Most parents who use this technique report having difficulties in gaining their child's cooperation with this program.

Bladder-Training Exercises. It is possible that functional bladder capacity may be reduced in children with enuresis, causing premature bladder emptying during the night.[27] As mentioned previously, urodynamic studies have not demonstrated a reduced functional bladder capacity in children with enuresis.[20]

However, in some children with a small bladder capacity, the use of bladder-retention training during the day may help increase bladder capacity at night. This training is accomplished by having the child hold his or her urine for increasing periods of time. In one study[27] of children undergoing six months of bladder-retention training, 66 percent of children reported some improvement, and 19 percent experienced complete resolution of symptoms. Bladder capacity increased significantly in patients who responded to this therapy. However, this is the only study to document such improvements, and results from this study must be validated by more data.

Pharmacologic Therapy

Pharmacologic therapy for the treatment of primary nocturnal enuresis is usually reserved for use in children older than seven years of age. Two approaches to drug therapy can be used. One approach is to increase bladder capacity. The other is to reduce the amount of urine produced by the kidneys. Again, a careful examination and medical history, including a history of previous treatment, should be performed before drug therapy is initiated.

Several medications are available for the treatment of primary nocturnal enuresis *(Table 3)*; however, none of these medications cures enuresis. Instead, they provide a stopgap measure until the children are able to wake on their own during the night to void. Parents should not expect immediate results and should be made aware of the potential side effects of the medications. Because both the parent(s) and the physician are generally reluctant to use medication as a first-line treatment, drug therapy is often reserved for use in children who have shown no success with other treatment modalities. In some cases, however, family circumstances and/or the need for quick symptomatic relief may make drug therapy a valuable first-line option.

TABLE 3
Pharmacologic Therapy for the Treatment of Primary Nocturnal Enuresis

Drugs	Cost*
Imipramine (Tofranil)	30 tablets, 25 mg, $14.00; generic: 30 tablets, 25 mg, $1.75 to $2.00
Oxybutynin (Ditropan)	90 tablets, 5 mg, $44.00; generic: $27.00 to $33.25; 480 mL, generic: $40.00 to $53.00

Hyoscyamine (Levsin)	90 tablets, 0.125 mg, $34.25; generic: 90 tablets, $11.75 to $14.00
Levsinex Timecaps	60 capsules, $43.75; generic: 60 capsules, $14.25 to $15.00†
Desmopressin acetate (DDAVP)	5-mL nasal spray, $121.25‡; 0.1 mg, 60 tablets, $96.75; 0.2 mg, 60 tablets, $156.25

*--Estimated cost to the pharmacist based on average wholesale prices, rounded to the nearest quarter dollar, in Red book. Montvale, N.J.: Medical Economics Data, 1997. Cost to the patient will be higher, depending on prescription filling fee.

†--Check product for generic equivalency.

‡--Not available in generic form.

Tricyclic Antidepressants. Tricyclic antidepressants, including imipramine (Tofranil), have been used extensively during the past 25 years in the treatment of primary nocturnal enuresis. Imipramine's exact mechanism of action has not been well established, but it may have an impact on enuresis on several levels. Studies linking enuresis to rapid-eye-movement sleep suggest that tricyclic antidepressants alter the sleep and arousal mechanism.[28] However, more recent studies[29] have failed to demonstrate a relationship between sleep stage and enuresis.

Imipramine may also have a weak peripheral anticholinergic effect, as well as a possible effect on the sympathetic nerves in the bladder. Furthermore, imipramine has been hypothesized to alter secretion of antidiuretic hormone.[30]

The initial dosage of imipramine is 25 mg taken one hour before bedtime. Response should be monitored and, if response is not satisfactory after one or two weeks, the dosage can be increased to 50 mg one hour before bedtime in children seven to 12 years of age, and up to 75 mg before bedtime in older children. Initial success rates of between 10 and 15 percent have been reported, and a large study[30] combining data from eight controlled double-blind trials reported a long-term cure rate of 25 percent. The optimal duration of therapy has not been determined, but the empiric approach is to treat children for three to six months and then wean them from the medication by reducing the dosage in increments of 25 mg over three to four weeks. Clinical response with imipramine has been shown to correlate with plasma levels.[31]

Although imipramine has been prescribed extensively with significant results, its use continues to decrease because of the potential for major side effects, including anxiety, insomnia, dry mouth, nausea, personality changes, sleep disorders, tiredness and nervousness. Imipramine has also been associated with severe accidental overdose in both patients and their siblings.

No pharmacologic method cures enuresis, but pharmacology can be used as a stopgap measure until patients are able to wake and void on their own.

Anticholinergic Therapy. Anticholinergic medications, such as hyoscyamine (Levsin) and oxybutynin (Ditropan), have a direct effect on smooth muscle relaxation and therefore reduce or decrease the bladder's ability to contract. Extensive use of anticholinergic agents for the treatment of uninhibited bladder contraction has been reported, but experience with anticholinergics for the treatment of enuresis is limited.

Hyoscyamine, which has been used to treat irritable bowel syndrome and primary nocturnal enuresis, is available in timed-release capsules and is reported to be effective for at least eight to 10 hours. To our knowledge, no studies reporting the success rate of hyoscyamine for the treatment of enuresis have been published. Anecdotal reports and our own experience, however, indicate a favorable response; this preparation may be effective in children with nocturnal enuresis.[32]

Evidence from a prospective, double-blind study[33] of 30 children with enuresis showed no difference in the response of children who were given 10 mg of oxybutynin at bedtime compared with children who were given placebo.

Oxybutynin is administered in dosages of 5 mg at bedtime in children older than five years of age. The dosage may be increased to 10 mg in older children. The dosage of hyoscyamine is based on weight; however, the extended-release form is given as 0.375 mg at bedtime. The most commonly reported side effects of anticholinergics in children are dry mouth, facial flushing, drowsiness, constipation, dizziness and occasional tremulousness. In the summer, hyperpyrexia can also be a concern.

Desmopressin Acetate. Desmopressin acetate (DDAVP), a synthetic analog of arginine vasopressin (antidiuretic hormone), has a highly specific antidiuretic effect, a relatively long half-life and an extended duration of action. Desmopressin is administered through nasal insufflation. It is rapidly absorbed by the nasal mucosa and achieves maximum plasma concentration in about 45 minutes. The biologic half-life of desmopressin acetate is four to six hours.[34]

The use of desmopressin is based on the finding that a subgroup of patients with enuresis had lacked the normal diurnal rhythm of antidiuretic hormone production. In patients without enuresis, production of antidiuretic hormone increases during the night and reduces the amount of urine produced, allowing the child to sleep for extended periods. In one study,[35] 15 patients with enuresis produced a decreased amount of antidiuretic hormone, compared with 11 children without enuresis.

Patients included in several double-blind, randomized trials[36-39] evaluating the effectiveness of desmopressin therapy (10 to 40 µg administered intranasally at bedtime) for the treatment of enuresis showed significant improvement in enuresis, with a long-term response rate of 10 to 70 percent.

The initial recommended dosage of desmopressin nasal spray is 20 µg (one spray into each nostril) at bedtime. Response should be evaluated after two weeks of therapy and, if no response is noted, the dosage can be increased to 40 µg at bedtime. Some patients older than 12 years of age can be treated with up to 60 µg intranasally. Interestingly, some patients will respond to as little as 10 µg per day. Patients should receive desmopressin for at least three to six months and should be monitored carefully for response. The dosage can be tapered slowly after three to six months. Because abrupt discontinuation of therapy can

result in a high incidence of relapse, the dosage should be reduced slowly by increments of 10 µg per month. Long-term therapy with desmopressin appears to be safe.

Desmopressin may be used on an as-needed basis in patients who have responded to it in the past and need temporary relief of enuresis, such as when visiting a summer camp or going on sleepovers. Because of desmopressin's rapid onset of action and good safety profile during the past 10 years, children can benefit from intermittent therapy to help them overcome difficult psychosocial situations. Parents who are reluctant to have their children take medication for extended periods of time may also feel more comfortable with this approach.

When compared with placebo, the side effects of desmopressin have been negligible in all studies reviewed. Occasional epistaxis and abdominal pain have been reported. Two reports[32,40] of symptomatic hyponatremia in children using desmopressin have been published. These reports prompted recommendations that serum electrolyte levels be checked after two weeks of therapy, but this practice has not been carried out universally.

Combination Therapy

Combination drug therapy may be tried in older patients with refractory primary nocturnal enuresis when neither the alarm nor pharmacologic therapy has been effective. A recent study[41] evaluated the use of combination therapy to treat primary nocturnal enuresis. Twenty-three patients (17 boys and six girls from nine to 16 years of age) in whom prior medical therapy had failed were treated with desmopressin acetate and hyoscyamine therapy for an average of eight months. Patients were monitored monthly, and the dosage of medication was adjusted as needed. Medications were tapered and discontinued when patients did not experience nighttime bed-wetting for at least 80 percent of the time. Twelve patients (52 percent) were considered dry and off all medications. Eight patients showed improvement and three patients showed little or no response. Drug therapy can be combined with the use of alarms to optimize effectiveness.[42]

Marc Cendron, M.D., is a member of the speaker's bureau for Rhône-Poulenc Rorer Pharmaceuticals, Inc.

The Author

MARC CENDRON, M.D.,
is an associate professor of surgery and pediatrics in the Section of Urology, Department of Surgery, at Dartmouth Medical School, Lebanon, N.H., and a pediatric urologist at the Children's Hospital at Dartmouth Medical School. He received a medical degree from Tufts University School of Medicine, Boston, and completed a residency at the Hospital of the University of Pennsylvania, Philadelphia. He also completed a fellowship at the Brady Urological Institute at the Johns Hopkins Hospital, Baltimore. Dr. Cendron has a special interest in voiding dysfunction, bladder physiology and reconstructive surgery of the urinary tract, as well as the prenatal diagnosis of anomalies.

Address correspondence to Marc Cendron, M.D., Section of Urology, Dartmouth-Hitchcock Medical Center, One Medical Center Dr., Lebanon, NH 03756-0001; e-mail: Marc.Cendron@Hitchcock.org.

Reprints are not available from the author.

REFERENCES

1. Friman PC, Warzak WJ. Nocturnal enuresis: a prevalent, persistent, yet curable parasomnia. Pediatrician 1990;17:38-45.
2. Fergusson DM, Horwood LJ, Shannon FT. Factors related to the age of attainment of nocturnal bladder control: an 8-year longitudinal study. Pediatrics 1986;78(5):884-90.
3. Rushton HG. Nocturnal enuresis: epidemiology, evaluation, and currently available treatment options. J Pediatr 1989;114(4 Pt 2):691-6.
4. Howe AC, Walker CE. Behavioral management of toilet training, enuresis and encopresis. Pediatr Clin North Am 1992;39(3):413-32.
5. Norgaard JP, Pedersen EB, Djurhuus JC. Diurnal anti-diuretic-hormone levels in enuretics. J Urol 1985;134:1029-31.
6. Rittig S, Knudsen UB, Norgaard JP, Petersen EB, Djurhuus JC. Abnormal diurnal rhythm of plasma vasopressin and urinary output in patients with enuresis. Am J Physiol 1989;256(4 Pt 2):664-71.
7. Backwin H. The genetics of enuresis. In: Colvin I, McKeith, RC, Meadow, SR, eds. Philadelphia: Lippincott, 1973.
8. Eiberg H, Berendt I, Mohr J. Assignment of dominant inherited nocturnal enuresis (ENURI) to chromosome 13q. Nat Genet 1995;10:354-6.
9. Watanabe H, Azuma Y. A proposal for a classification system of enuresis based on overnight simultaneous monitoring of electroencephalography and cystometry. Sleep 1989;12:257-64.
10. Norgaard JP, Hansen JH, Wildschiotz G, Sorensen S, Rittig S, Djurhuus JC. Sleep cystometries in children with nocturnal enuresis. J Urol 1989;141:1156-9.
11. Robert M, Averous M, Bessett A, Carlander B, Billiard M, Guiter J, et al. Sleep polygraphic studies using cystomanometry in 20 patients with enuresis. Eur Urol 1993;24:97-102.
12. Broughton RF. Sleep disorders: disorders of arousal? Enuresis, somnambulism, and nightmares occur in confusional states of arousal, not in "dreaming sleep." Science 1968;159:1070-8.
13. Evans JI. Sleep of enuretics. Br Med J 1971;3:110.
14. Bhatia MS, Kaur N. The problem of bed-wetting. Nurs J India 1989;80(7):193.
15. Weider DJ, Sateia MJ, West RP. Nocturnal enuresis in children with upper airway obstruction. Otolaryngol Head Neck Surg 1991;105:427-32.
16. Feehan M, McGee R, Stanton W, Silva PA. A six-year follow-up of childhood enuresis: prevalence in adolescence and consequences for mental health. J Paediatr Child Health 1990;26:75-9.
17. Stromgren A, Thomsen PH. Personality traits in young adults with a history of conditioning-treated childhood enuresis. Acta Psychiatr Scand 1990; 81:538-41.
18. Mayo ME, Burns MW. Urodynamic studies in children who wet. Br J Urol 1990;65:641-5.
19. Weerasinghe N, Malone PS. The value of videourodynamics in the investigation of neurologically normal children who wet. Br J Urol 1993;71:539-42.
20. Whiteside CG, Arnold EP. Persistent primary enuresis: a urodynamic assessment. Br Med J 1975;1:364-7.
21. George CP, Messerli FH, Geneset J, Nowaczynski W, Boucher R, Kuchel Orofo-Oftega M. Diurnal variation of plasma vasopressin in man. J Clin Endocrinol Metab 1975;41:332-8.
22. Norgaard JP. Urodynamics in enuresis 1: reservoir function pressure-flow study. Neurourol Urodynam 1989;8:119-24.
23. Marshall S, Marshall HH, Lyon RP. Enuresis: an analysis of various therapeutic approaches. Pediatrics 1973;52:813-7.
24. Rushton HG. Nocturnal enuresis: epidemiology, evaluation and currently available

treatment options. J Pediatr 1989;114(4 Pt 2):691-6.
25. Esperanca M, Gerarrd JW. Nocturnal enuresis: comparison of the effect of imipramine and dietary restriction on bladder capacity. Can Med Assoc J 1969;101:65-8.
26. Schmitt BD. Nocturnal enuresis. An update on treatment. Pediatr Clin North Am 1982;29:21-36.
27. Starfield B, Mellits ED. Increase in functional bladder capacity and improvements in enuresis. J Pediatr 1968;72:483-7.
28. Kales A, Kales JD, Jacobson A, et al. Effect of imipramine on enuretic frequency and sleep stages. Pediatrics 1977;60:431-6.
29. Mikkelsen EJ, Rapoport JL, Nee L, Gruenau C, Mendelson W, Gillin JC. Childhood enuresis. I. Sleep patterns and psychopathology. Arch Gen Psychiatry 1980;37:1139-44.
30. Rapoport JL, Mikkelsen EJ, Zavadil A, Nee L, Gruenau C, Mendelson W, et al. Childhood enuresis. II. Psychopathology, tricyclic concentration in plasma and anti-enuretic effect. Arch Gen Psychiatry 1980;37:1146-52.
31. Jorgenson OS, Lober M, Christiansen J, Gram LF. Plasma concentration and clinical effect in imipramine treatment of childhood enuresis. Clin Pharmacokinet 1980;5:386-93.
32. Bamford MF, Cruickshank G. Dangers of intranasal desmopressin for nocturnal enuresis [Letter]. J R Coll Gen Pract 1989;39:345-6.
33. Lovering JS, Tallet SE, McKendry JB. Oxybutynin efficacy in the treatment of primary enuresis. J Urol 1966;96:718-20.
34. Richardson DW, Robinson AG. Desmopressin. Ann Intern Med 1985;103:228-39.
35. Norgaard JP, Rittig S, Djurhuus JC. Nocturnal enuresis: an approach to treatment based on pathogenesis. J Pediatr 1989;114(4 Pt 2):705-10.
36. Rittig S, Knudsen UB, Sorensen S, et al. Long-term double-blind crossover study of desmopressin intranasal spray in the management of nocturnal enuresis. In: Meadows SR, ed. Desmopressin in nocturnal enuresis: proceedings of an international symposium. Sutton Coldfield, England: Horus Medical Publications, 1988:43-55.
37. Miller K, Klauber GT. Desmopressin acetate in children with severe primary nocturnal enuresis. Clin Ther 1990;12:357-66.
38. Terho P. Desmopressin in nocturnal enuresis. J Urol 1991;145(4):818-20.
39. Mark SD, Frank JD, Mark SD. Nocturnal enuresis. Br J Urol 1995;75:427-34.
40. Simmonds EJ, Mahony MJ, Little JM. Convulsion and coma after intranasal desmopressin in cystic fibrosis. BMJ 1988;297:1614.
41. Cendron M, Klauber J. Combination therapy in the treatment of persistent nocturnal enuresis. In press.
42. Wille S. Comparison of desmopressin and enuresis alarm for nocturnal enuresis. In: Meadows SR, ed. Desmopressin in nocturnal enuresis: proceedings of an international symposium. Sutton Coldfield, England: Horus Medical Publications, 1989.

March 1, 1999 Contents | Subscribe | Search | *AFP* Home Page