

# Nocturnal enuresis: Finding the treatment that fits the child

By Barton D. Schmitt, MD

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Bed-wetting is not usually a pathologic condition, but it can be traumatic for the child and requires treatment. This article examines the most common etiologies, compares available treatments, and recommends age-appropriate interventions.

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Despite centuries of bad press, involuntary urination during sleep is neither a sign of flawed character nor a disease. Enuresis is normal in infants and toddlers. The age at which children learn not to urinate during sleep is variable, ranging in our culture roughly from 3 to 6 years for 90% of children.

Many parents are upset if enuresis continues beyond age 6, and some react harshly. A survey of parental reactions in the United States found that 30% of parents dealt with enuresis by punishment. Some extreme responses--such as forcing cold showers, rubbing the child's face on the wet sheets, and spanking – qualify as emotional abuse and should be strongly denounced.

Even when parents are supportive, youngsters are often embarrassed and ashamed of their symptom – especially if they have reached the age where their peers are starting to venture on occasional sleep away experiences. They try to keep their bed-wetting a family secret and limit their activities for fear of being discovered or harassed by age-mates.

The psychologic sequelae of bed-wetting can be serious. Prolonged mishandling of enuresis can harm a child's self-concept. Reassurance alone is a disservice. Families with an enuretic child deserve information and treatment. Not surprisingly, studies show that the bed wetter's self-esteem improves with successful therapy.

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## **The reasons why**

Successful intervention requires an understanding of why the child is not able to control urination during sleep. The etiology rarely involves pathology: In almost all cases, some combination of the following, non-pathologic etiologies is involved (Table 1):

***Small bladder.*** Most children who wet the bed have a small bladder capacity, usually for genetic reasons. The bladder is too small if it is unable to hold all the urine produced during the night. Clues to small capacity are daytime frequency, wetness every night and sometimes several times at night, and presence of the problem since birth (primary enuresis). Bladder capacity is measured on a specimen taken after the child holds his urine as long as he can and then voids into a measuring cup. Normal capacity (in ounces) is the child's age plus two. Thus for a 6-year-old a capacity of eight ounces is normal, six ounces is the lower limit of normal, and five ounces or less is small. Normal adult bladder capacity is 12 to 16 ounces.

***Inability to delay the micturition urge.*** Children vary in their ability to inhibit detrusor muscle contractions following the initial urge to urinate. Some children with enuresis have daytime urgency. Those who have severe bladder spasms often have associated daytime wetting (urgency incontinence). The inability to suppress the micturition urge may explain bed-wetting in some children with normal bladder capacities. Children with both urgency and a small functional bladder capacity possibly do not have adequate time to awaken following a full bladder urge at night.

***Antidiuretic hormone (ADH) nocturnal deficiency.*** The most recently proposed etiologic theory for bed-wetting is an ADH deficit. Levels of vasopressin, the antidiuretic hormone, normally increase during the night, causing the body to produce a smaller total volume of more concentrated urine during sleep. The ratio between urine production during sleep and while awake, expressed in mL/h, is normally 1:2. In a study of 15 adolescent bed wetters, however, Norgaard and Rittig found serum vasopressin levels did not rise during sleep. Those adolescents produced larger volumes of more dilute urine while sleeping than did 11 normal adolescents in the study. Because of the sample size and age range of the patients, the findings must be considered preliminary. The frequency of nocturnal ADH deficit as a cause of primary enuresis is unknown; previous studies have shown normal nighttime urine volumes in enuretics. In addition, desmopressin reduces urine production in children with normal ADH levels.

***Evening polydipsia.*** Some children urinate in bed because they drink large amounts of fluids late in the day and produce more urine than the bladder can hold throughout the night. Inquire about the amount of fluids consumed at dinner, after dinner, at bedtime, and during the night.

***Not awakening.*** Most children with small bladder capacities or nocturnal polyuria also do not respond to the sensation of a full bladder during sleep. Ask about spontaneous awakenings at night, using the toilet at night, or awakening after clothing becomes wet. Although studies show that children with bed-wetting have normal sleep patterns, most

parents also report that it takes five to ten minutes to awaken their child and even then he acts like a “zombie”. The same is true, however, of trying to awaken a child who is not a bed-wetter from stage 3 or 4 sleep. Occasionally, the child also has sleepwalking episodes, during which he urinates in a variety of undesirable locations. Although organic pathology is present in only about 3% of bed wetters, organic conditions with enuresis as a symptom do occur and must be identified (Table 1).

Table 1	
<p><b>What causes enuresis?</b></p> <p><b>Non-pathological causes (97%)</b></p> <ul style="list-style-type: none"> <li>✚ Small functional bladder capacity</li> <li>✚ Inability to delay micturition urge</li> <li>✚ Nighttime polyuria because ADH levels fail to rise at night</li> <li>✚ Nighttime polyuria because child drinks too much in the evening</li> <li>✚ Child doesn't wake up when his bladder feels full</li> </ul>	<p><b>Disease states (3%)</b></p> <ul style="list-style-type: none"> <li>➤ Medically treatable               <ul style="list-style-type: none"> <li>✚ UTI</li> <li>✚ Diabetes insipidus</li> <li>✚ Diabetes mellitus</li> <li>✚ Fecal impaction or constipation</li> </ul> </li> <li>➤ Surgically treatable               <ul style="list-style-type: none"> <li>✚ Ectopic ureter</li> <li>✚ Lower urinary tract obstruction</li> <li>✚ Neurogenic bladder</li> <li>✚ Bladder calculus or foreign body</li> <li>✚ Sleep apnea secondary to large adenoids</li> </ul> </li> </ul>

### Evaluating the problem

The first step in helping the child with enuresis is a thorough evaluation to find out what lies behind the problem. A history of dysuria, intermittent daytime wetness, polydipsia, polyuria, central nervous system trauma, constipation, and encopresis may indicate medically treatable conditions. Constant wetness (dampness), an abnormal urine stream (dribbling or hesitancy), a change in gait, previous lumbar punctures, or nighttime snoring or apnea may indicate surgically treatable conditions.

These clues may be confirmed on physical examination. Abdominal examination may reveal a distended bladder or fecal impaction. Examination of the sacral area may disclose overlying birth defects. Observe the child's gait, muscle tone, strength, and deep tendon reflexes in the lower extremities. Examine the external genitals for abnormalities (meatitis, vulvitis, or signs of sexual abuse). If the urine stream sounds abnormal by history, observe it. Perform a rectal examination if the history is positive for encopresis or constipation. Check the patient for a blocked nose or obligatory mouth breathing. Such children may wet themselves during sleep apnea and may be cured by adenoidectomy.

Every child with enuresis should have a urinalysis. Absence of sugar rules out diabetes mellitus. A specific gravity of 1.015 or greater rules out diabetes insipidus. Obtain a urine culture if symptoms of a urinary tract infection (UTI) are present, the urine has a foul odor, a nitrite or leukocyte esterase dipstick is positive, white blood cells are present, or the patient has had a UTI in the past. Radiologic studies are not routinely needed, regardless of age. Children with symptoms or signs suggestive of urinary tract obstruction, ectopic ureter, or a neurogenic bladder, however, need a voiding cystourethrogram followed by either renal ultrasound or an intravenous pyelogram. Children with a past medical history of more than one UTI also need radiologic studies.

Determining the child's bladder capacity is a critical – and often overlooked – step. It's as important to the evaluation of enuresis as a rectal exam is to the evaluation of encopresis. I ask families to do at least three measurements of functional bladder capacity before their initial evaluation. If this step has been forgotten, I ask the child to drink 12 ounces of water when he arrives in my office and measure bladder size before he leaves. This information helps determine etiology, prognosis, and treatment. If the child's bladder capacity is normal, the problem usually yields to simple motivational techniques and bladder stretching exercises, or at least practicing postponing the bladder urge. If bladder capacity is smaller than the norm, treatment is more difficult, but parents and youngster are often relieved to learn that the bed-wetting has a physical explanation.

The history may also contain behavioral clues that help in planning treatment. Inquire about the amount of fluids the child consumes at dinner, after dinner, at bedtime, and during the night. Find out whether the child wakes spontaneously during the night and uses the toilet or wakes up only after his clothing becomes wet.

### **Treatment options: Self-awakening**

In a child with small bladder capacity, successful intervention must address one of three basic mechanisms. First, we can decrease urine production by reducing the child's fluid intake prior to bedtime and by prescribing desmopressin at bedtime. Second, we can increase functional bladder capacity by bladder stretching exercises during the day and by prescribing imipramine at bedtime. Third, we can teach the youngster to awaken at night using bedtime self-awakening programs and enuresis conditioning alarms (Table 2).

The most straightforward approach to bed-wetting is teaching the child to awaken at night. Theoretically, awakening is the quickest way to obtain a cure, because it can compensate for a large urine production or a small bladder size. The smaller the child's bladder, the more important it is for him to learn to

Table 2

## **Treating small-bladder enuresis**

### **The options include:**

- Decrease urine production
- Increase bladder size
- Learn to use toilet at night

awaken at night. The most important insight I have gained about bed-wetters in recent years is that most of them do not realize they need to get up at night. They go to bed telling themselves to “hold it until morning”, an impossible assignment for those with a small bladder. Instead, they need to tell themselves to “wake up every night and use the toilet”. Clarification of this goal brings a surprised response from many families.

One technique for self-awakening is to ask children to rehearse a particular sequence of events every night before going to sleep. The child lies in bed with his eyes closed and pretends that it’s the middle of the night and his full bladder is trying to wake him up by starting to hurt. He then runs to the bathroom and empties his bladder.

At the end of the rehearsal, the child can remind himself to get up in the same manner if he needs to urinate during the night. Many children are surprised to learn that their bladder sends the same signal when it becomes full at night as it does during the day. Allison Mack has recently provided a picture book called *Dry All Night* to help enuretic children learn to awaken at night. Another approach uses self-hypnosis at bedtime with the posthypnotic suggestion that the child will use the bathroom during the night. Olness reported a 77% cure rate in children over 5 years of age with this technique. Dry bed training is a more labor-intensive technique used to teach children to awaken at night. For this method to be successful, the parent must be committed and consistently available. *Give the parent the following instructions:*

- ✘ On the first night, wake the child once an hour until 1 a.m., using the minimal prompt necessary. Try a hierarchy of prompts, ranging from turning on the light to saying the child’s name to touching him. Make sure he is awake enough to walk and talk coherently. If he’s dry, praise him and ask, “Do you need to go to the toilet or can you wait another hour?” He must walk to the toilet on his own. If he’s wet, encourage him to change his pajamas and bedding. At the 1 a.m. awakening, tell the child to void even if he’s dry.
- ✘ For the next five nights, wake the child only once. The first night, wake him three hours after he falls asleep. The next night, wake him two and a half hours after he falls asleep. Keep diminishing the interval, so that on the fifth night you wake him an hour after he falls asleep. On the sixth night, tell him to wake himself from then on.
- ✘ If the child relapses—has three consecutive wet nights—repeat the six nights of awakening.

In a study of 51 children using this technique, the cure rate was 92%. The average length of time to achieve a cure, defined as 14 consecutive dry nights, was four weeks. The relapse rate was 20%, but all the children who relapsed responded to a second course of training.

## HELPING YOUR CHILD OVERCOME BED-WETTING

Bed-wetting is a very common problem—so common we consider it normal until at least 6 years of age. Some 40% of 3-year-olds urinate involuntarily in their sleep, as do 10% of 6-year-olds and 3% of 12-year-olds. The medical term for this is enuresis.

Most children who urinate in their sleep have bladders that are too small to hold all the urine produced in a night (this is an inherited characteristic), and don't awaken to the signal of a full bladder. Enuresis is rarely caused by a physical disorder, and your pediatrician can

detect those few cases that are. Emotional problems do not cause enuresis, either, but mishandling of bed-wetting can create psychological difficulties for children. Most children who wet the bed overcome the problem between 6 and 10 years of age. Even without treatment, all children eventually get over it. Therefore, treatments that might have harmful complications should not be used. Treatments without side effects, however, can be started as soon as your child has been toilet-trained for longer than six months.

### Help for children of any age -----

*Encourage your child to get up to urinate during the night.* This advice is more important than any other. Tell your child at bedtime, "Try to get up when you have to pee." Leaving a light on in the bathroom may help. Some preschoolers prefer to use a potty chair left next to the bed.

*Encourage your child to postpone urination.* If your child urinates often during the day, encourage him to go less frequently, but don't make an issue of it. Don't remind him to use the bathroom except at bedtime. Your child should start his night with an empty bladder.

*Encourage fluids during the morning and early afternoon.* The more fluids your child drinks, the more urine she will produce, and more urine leads to larger bladders.

*Discourage drinking more than two ounces of fluids during the two hours before bedtime.* Give gentle reminders about this, but don't argue about a few swallows of water.

*Protect the bed from urine.* Have your child wear extra thick underwear in addition to

pajamas. This keeps much of the urine from getting through to the sheets. By 4 years of age, your child should no longer be using diapers or plastic pants. Protect the mattress with a plastic mattress cover. Odor becomes a problem if urine soaks into the mattress or blankets.

*Establish a morning routine for wet pajamas and wet bedding.* On wet mornings, your child can rinse her pajamas and underwear in the sink until the odor is gone. If she smells of urine, she will need to take a quick shower so she won't be teased at school. You can cut down on the laundry by placing a dry towel under your child's bottom each night. This can be rinsed each morning and saved until you do your wash. If a wet bed is left open to the air, the sheets are usually dry by noon. Because of odor, the sheets may need to be washed one extra time each week.

*Respond positively to dry nights.* Praise your child on mornings when he wakes up dry. A calendar with gold stars or "happy faces" for dry nights may also help.

*Respond gently to wet nights.* Your child does

his

not like being wet. Most bed wetters feel

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guilty and embarrassed about this problem. They need sympathy, not blame or punishment. Punishment or pressure will

delay a cure and cause secondary emotional problems. Do not allow siblings to tease a bed wetter.

**Additional help for children 6 years of age -----**

Follow the previous recommendations and add the measures outlined below:

*Help your child learn to wake up when her bladder feels full.* Children with small bladders cannot stay dry unless they get up to urinate one or more times every night. Make sure your child understands that her goal should be getting up, not holding her urine until morning. Give her a pep talk every night before she goes to sleep. Tell her she needs to practice waking up when her bladder feels full. Tell her to:

- *Lie on your bed with your eyes closed.*
- *Pretend it's the middle of the night.*
- *Pretend your bladder is full.*
- *Pretend it's starting to hurt.*
- *Pretend it's trying to wake you up.*
- *Pretend it's saying: "Get up before it's too late."*
- *Then run to the bathroom and empty your bladder.*
- *Remind yourself to get up like this during the night.*

*Encourage your child to change his own wet clothes and bedding during the night.* If your child wets at night, he should try to get up and change himself. First, if your child feels any urine leaking out, he should try to stop the flow of urine. Second, he should hurry to the toilet to see if he has any urine left in his bladder. Third, he should change himself and put a dry towel over the wet part of the bed. This step can be made easier by keeping dry pajamas and towels on a chair near the bed. The child who shows the motivation to carry out these steps is close to being able to awaken from the sensation of a full bladder.

*Find out how much your child's bladder can hold.* Ask your child to hold her urine as long as possible, then urinate into a container. Do this on at least three occasions and measure the amount of urine in ounces. The largest of the three measurements can be considered your child's bladder capacity. Normal capacity is one or more ounces for each year of age. In a 6-year-old, a capacity of five ounces or less is small; six to eight ounces is normal and means that the bladder can hold a night's urine production until morning.

*Encourage bladder stretching exercises.* These exercises gradually enlarge the size of the bladder so that it can hold more urine at night. Introduce the exercises only if your child wants to try them, however. For some children, that won't happen until age 8.

To stretch the bladder, encourage your child to hold his urine as long as possible during the daytime. Waiting ten to 15 minutes after he feels the urge to urinate during the day can help your child's bladder wait at night until he wakes from a deep sleep. Learning to resist the first urge to urinate is especially important. Whenever your child feels the urge to go, he can try to distract himself for the ten seconds or so it takes for the bladder spasms to stop. At least once a day, have your child urinate into a measuring cup to see if he has maintained or even beaten his previous record (in ounces). Mark the highest volume achieved with a piece of masking tape on the cup.

*Help your child assume responsibility.* Your child should feel responsible for solving the bed-wetting problem. The bladder exercises,

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self-awakening program, control of fluid intake, and record keeping all need her involvement and commitment. Do not routinely awaken your child at night to

As long as you are waking up your child, she is less likely to do it for herself. Your child should look upon you and her pediatrician as people who can provide suggestions and

urinate—unless you are temporarily helping her learn to respond to an enuresis alarm.

support but who do not take responsibility for the bed-wetting.

### **Additional help for children 8 years of age -----**

Follow the previous recommendations. Talk with your physician about the possibility of using alarms or drugs as well.

*Bed-wetting alarms.* Alarms are used to teach a child to awaken when he needs to urinate during the night. They have the highest cure rate (about 70%) of any available approach. They are the treatment of choice for any child with a small bladder who can't otherwise train himself to awaken at night. The new transistorized alarms are small, lightweight, sensitive to a few drops of urine, not too expensive (about \$40 to \$60), and easy for a child to set up by himself. Children using alarms still need to work on the self-awakening program. For more information, see the companion parent aid on bed-wetting alarms.

*Alarm clock.* If your child can't awaken herself at night and you don't want to use a bed-wetting alarm, teach her to use an alarm clock or clock radio. Set it for three or four hours after your child goes to bed. Put it beyond arm's reach. Encourage your child to practice responding to the alarm during the day while lying on the bed with eyes closed. Have her set the alarm each night.

Praise her for getting up at night, even if she isn't dry in the morning.

*Medications.* Most children who have trouble staying dry at night need extra help for slumber parties, camping trips, vacations, or other overnights. Some take an alarm clock with them and stay dry by awakening once at night. Some are helped by temporarily taking medication at bedtime. One medication, desmopressin (DDAVP), comes in the form of a nasal spray. Desmopressin decreases urine production at night and is quite safe. Another drug, imipramine (Janimine, Tofrarily), is a tablet. Imipramine temporarily increases bladder capacity. It is safe at the correct dosage, but dangerous if too much is taken or a younger sibling gets into it. If you do use either medication, be very careful about the amount you use and where you store it—and be sure to keep the safety cap on the bottle. The drawback of these medications is that bed-wetting usually returns when your child stops taking them. They do not cure bed-wetting. Therefore, children who take medication for enuresis should also be using an alarm and learning to wake themselves up at night.

### **Call your physician during regular hours if: -----**

- Bed-wetting is a new problem (your child used to be dry at night).
- Urination (at any time) causes pain or burning.
- The urine stream is weak or dribbly.
- Your child also has daytime wetting.
- Your child is over 12 years of age.
- Your child is over 6 years of age and is not better after three months using this treatment program.

### **Enuresis alarms**

Several portable, transistorized conditioning alarms that are worn on the body (Nite-Train'r, Nytone, Wet-Stop) are now available to help teach children to awaken to the sensation of a full bladder. They are convenient, comfortable, inexpensive, and easy for

the child to set up without help and should supersede the use of older, bell-and-pad types.

Enuresis alarms have the highest cure rate of any available approach to enuresis. Long-term cures in unselected patients from 5 to 15 years of age were 67% with the Nytone alarm and 72% with the Wet-Stop. A recent review of six studies of the transistorized mini-alarms described above found a combined initial cure rate of 68%. Relapse rates ranged from 10% to 15%, and these children usually responded to a second short course of treatment.

The disadvantage of enuresis alarms is that they are time-intensive. They require motivated patients and parents who are willing to learn how to use them properly and continue to use them for two to three months. An alarm is especially frustrating in situations where the child does not awaken when the buzzer goes off. Parents must remind the child at bedtime to wake up before the buzzer sounds and use programs that teach self-awakening along with the alarm. By awakening as quickly as possible to the alarm, the child eventually learns by conditioning or approximation to awaken to the internal stimulus of a full bladder.

Meadow found that half his patients using alarms learned to awaken at night and half learned to hold their urine until morning. I suspect that most of the children in the latter group had normal bladder size and normal increase in nocturnal ADH production. In my experience, most children who are successful with an alarm learn to awaken at night. Most of the patients referred to me, however, have very small bladders. Clearly, children with nighttime polyuria, whether from an ADH deficit or other cause, also need to learn to awaken themselves, as do children with diabetes insipidus and diabetes mellitus.

The parent aid on page 10 describes how to use an enuresis alarm. Suppliers usually can provide a demonstration model, pamphlets, and order forms on request; the parent aid includes suppliers' addresses. These alarms cost from \$42 to \$60. Warn parents about companies that advertise widely and charge more than \$1,000 for enuresis programs.

Some pediatricians rent alarms to parents or provide bulletin board space for parents who want to resell an alarm when they are finished with it. If the pediatrician writes a prescription that includes the words "medical device", health insurance sometimes covers the cost. For families who can't afford an enuresis alarm, recommend a clock radio or alarm clock set for three hours after going to sleep.

Almost all children who wet the bed need to get up during the night to urinate. A bed-wetting (enuresis) alarm, which is activated

by moisture, can help your child learn to awaken in time to go to the bathroom. The new models are lightweight and easy for the child to operate.

# HOW TO USE A BED-WETTING ALARM

## What to tell your child -----

Give your child the following instructions:

- This is your alarm. It can help you wake up if you use it correctly. Remember, the alarm won't help you unless you listen for it carefully and respond to it quickly.

- Hook up the alarm system by yourself.

Trigger the buzzer a few times by touching the sensors with a wet finger and practice going to the bathroom as you will do if it goes off during the night.

- Turn on your nightlight before you go to sleep

or keep a flashlight near your bed so you can see what you are doing when the alarm sounds.

- Try to beat the buzzer. Wake up when your bladder feels full, but before any urine leaks out and sets off the alarm. If the buzzer does go off, try to wake up and stop urinating as soon as you think you hear it (even if you think you are hearing it in a dream).

- As soon as you hear the alarm, jump out of bed

and stand up. Once you are standing and awake, turn off the buzzer by removing the metal trip from the little pocket in your underwear (if you

have a Wet-Stop) or disconnect the clips (if you have a Nytone) and dry them off.

- Hurry to the bathroom. Empty your bladder to see how much urine you were able to hold back.

- Put on dry underwear and pajamas, and reconnect the alarm. Put a dry towel over the wet spot on your bed. Remind yourself to get up before the alarm buzzes next time and review your plan.

- In the morning, write on your calendar DRY (no alarm), WET SPOT (you got up after the alarm went off), or WET (you didn't get up).

- Use the alarm every night until you go three or four weeks without bed-wetting. This program usually takes two to three months, so try to be patient.

While your child is using the bed-wetting alarm, it's very important that he also practice a self-awakening program at bedtime. For instructions on teaching your child self-awakening, see the companion parent aid, "Helping your child overcome bed-wetting".

## The parent's role -----

If your child doesn't awaken immediately to the sound of the buzzer on the bed-wetting alarm, she needs your help. You may need to be involved every night for the first two or three weeks. Here's what to do:

- Go to your child's room as soon as you hear the buzzer. Turn on the light and say loudly, "Get out of bed and stand up."

- If that doesn't work, sit her up in bed and run a cold washcloth over her face to bring her out of deep sleep.

- When she is on her feet, remind her to turn off

the alarm. Don't do it for her. Your child must learn to carry out this step herself.

- Make sure the child is wide awake and walks into the bathroom before you leave her. If necessary, ask her questions to help her wake up.

- Your goal is to help your child awaken immediately and get out of bed when the buzzer goes off. Phase yourself out of the alarm program as soon as possible. Making sure your child goes to bed at a reasonable hour, with the radio off and a night light on, can help her respond faster to the alarm.

## How to order an alarm -----

Alarms and parent information flyers can be ordered from:

- Nytone Alarm: Nytone Medical Products, 2424 S 900 W, Salt Lake City, UT 84119, or call 1-801-973-4090.
- Nite Train'r Alarm: Koregon Enterprises, 9735 SW Sunshine Ct, Beaverton, OR 97005, or call 1-800-544-4240
- Wet-Stop Alarm: Palco Laboratories, 5026 Scotts Valley Dr, Scotts Valley, CA 95066, or call 1-408-476-3151.

Health insurance policies sometimes cover these alarms when they are prescribed by your pediatrician.

## Increasing bladder capacity

Functional bladder size can be increased by prolonging the intervals between daytime urinations. Encourage the child to hold his urine as long as possible during the day. Voluntarily contracting the pelvic floor muscles inhibits bladder detrusor contractions. You can teach the child to do this by having him tighten the muscles in his buttocks. Learning to resist the first urge to urinate is especially important. Instruct the parents to have the child urinate into a measuring cup once a day to see if he has maintained or passed his previous record in ounces.

In a study of 110 children, Starfield found a 25% cure rate after six months of bladder exercises reinforced by home visits from a public health nurse. Interestingly, the children who were cured had increased their bladder capacity significantly more than the children who were still enuretic.

Exercises have also been successfully combined with incentives in a program called retention control training. In this system, the child drinks eight ounces of water and receives a monetary reward for every three minutes he successfully holds his urine after the initial urge to micturate.

## Drug therapy

Drugs are an appealing form of therapy because they bring immediate results. If the child is going to respond at all, he does so after the first or second dose. The cure rates of the drugs used to treat enuresis vary from one study to another, however. The main reason is that children with enuresis are a heterogeneous group, with problems of varying etiology and intensity. Around 95% of the patients referred to me, for example, are wet every night and have a bladder capacity about half normal size. This group is difficult to treat and usually responds only to awakening at night. By contrast, most of the studies showing exceptional cure rates have knowingly or unknowingly enrolled patients with a mean of three dry nights per week. Any of us using any approach would succeed with this group. When you compare study results, examine the severity of the subjects' enuresis.

The two drugs that have been most extensively studied for enuresis are desmopressin acetate (DDAVP) and imipramine hydrochloride (Janimine, Tofranil). A third drug, oxybutynin chloride (Ditropan) has an antispasmodic effect that reduces uninhibited detrusor muscle contractions. Only one controlled study has evaluated oxybutynin for nocturnal enuresis, however, and it found that oxybutynin did not

significantly increase the number of dry nights for 30 children with primary nocturnal enuresis.

### **Desmopressin therapy**

Desmopressin, the synthetic analog of the ADH vasopressin, has been used for nocturnal enuresis for more than ten years. It reduces nocturnal urine production by increasing water retention and urine concentration in the distal tubules. The tasteless, odorless drug is administered intranasally using a unit-dose, spray-pump delivery

TABLE 3

## **Treating enuresis with drugs**

	<b>Desmopressin (DDAVP)</b>	<b>Imipramine</b>
How supplied	5-mL spray bottle (delivers 10 ug/spray)	25-mg tablets
Dosage	2 sprays hs Increase by 1 spray weekly to maximum of 4 sprays/night	8-12 yr. 25-50 mg hs >12 yr. 50-75 mg hs
Cautions	Avoid excessive fluids to prevent hyponatremia	Overdose can be lethal Keep out of reach of younger siblings
Tapering	By 1 spray q2wk	By 25 mg q2wk
Enuresis alarm	Use simultaneously	Use simultaneously

system. The starting dosage for all ages is 20 ug, or one spray is each nostril, at bedtime (Table 3). The dosage can be increased by 10 ug weekly to a maximum of 40 ug if the patient is unresponsive and decreased if nasal or abdominal discomfort occurs. Any patient who remains completely dry on 20 ug should be tried on 10 ug. The drug's duration of action is ten to 12 hours. Children with allergic rhinitis need to take an antihistamine concomitantly to promote adequate absorption of the vasopressin.

Klauber's review of 12 placebo-controlled studies of desmopressin therapy for nocturnal enuresis showed improvement rates that ranged from 10% to 65%. The improvement rate was defined as the percentage reduction in wet nights when the subjects were taking desmopressin, compared to wet nights when they were taking the

placebo. Most of the studies involved children who were resistant to other treatment regimens, including imipramine and alarms. The two studies of children who were not previously treated showed improvement rates of 62% and 65%. The best response was seen in children over age 10, these with nocturnal polyuria, and those with urine osmolality over 1,000 mosm/kg after desmopressin therapy.

Most studies indicate that over 80% of patients relapse immediately when desmopressin is discontinued, after periods ranging from two to 12 weeks. Prolonging therapy may be effective, however. Some 27% of Miller's patients who started with a 40-ug dosage for two months and tapered off the drug gradually over a three- to six-month period remained cured. Further studies of the optimal duration of therapy are needed.

No serious side effects were reported in the 516 patients followed in the 12 controlled studies reviewed by Klauber. Since desmopressin causes water retention, hyponatremia is a possible complication but was not reported in any of these studies. Symptomatic hyponatremia is prevented by compensatory polyuria the following day when the drug's effect has worn off. Desmopressin is contra-indicated in patients with habitual polydipsia, hypertension, or heart disease. Mild symptoms that have been reported with the drug include headache, abdominal discomfort, nausea, and nasal discomfort. They occur in less than 5% of patients. The main side effect of desmopressin is financial; it costs about \$1.50 per spray.

### **Imipramine therapy**

Imipramine has been used extensively for nocturnal enuresis, despite considerable concern about the drug's toxicity (discussed below). Its mechanism of action combines an anticholinergic effect that increases bladder capacity with a noradrenergic effect that decreases bladder detrusor excitability. Imipramine also significantly reduces the amount of time spent in rapid-eye-movement sleep but does not decrease the time spent in stage 3 and 4 (deep) sleep.

Imipramine is taken one hour before bedtime. The starting dosage is usually 25 mg per day (Table 3). The maximum dosage is 50 mg per day for children from 8 to 12 years of age and 75 mg per day for children over 12. The drug's duration of action is eight to 12 hours. Larger doses do not increase the success rate.

Blackwell reviewed the eight controlled, double-blind studies on imipramine that include long-term follow-up results. Cure rates for patients who had been off the drug for over three months ranged from 5% to 40%, with the combined data showing an overall cure rate of 25%. Initial cure rates for patients currently on imipramine ranged from 10% to 60%. Most cures were attained when imipramine was prescribed for three to four months, then gradually tapered off over three to four weeks. Kolvin found an immediate return to baseline bed-wetting levels following abrupt withdrawal of the drug. The best results have been reported in children with normal-size bladders who are already occasionally dry. The worst results are seen in children with small bladders and older adolescents.

Few drugs are as toxic or potentially lethal in low doses as imipramine. In other words, it has a low toxic/therapeutic ratio. The symptoms of overdosage are ventricular tachycardia, coma, and seizures. In Great Britain, imipramine is one of the most common causes of fatal poisoning in children under 5 years of age. Older children also

have died from accidental overdose. Many school-age children do not realize the potentially hazardous consequences of taking extra amounts of prescription medications. If imipramine is prescribed, both parents and patient should be made aware of its unusual toxicity,\* and the prescription label should carry a typed warning such as, "Keep out of children's reach; highly dangerous if taken in overdose." The milder side effects of the drug are anxiety, nervousness, insomnia, uncontrollable crying and other personality changes.

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\*See Poison Pen: "Imipramine overdose – Prejudiced and proud," Contemporary Pediatrics. August 1988

### **Comparing treatments**

Most studies of enuresis therapy compare a treatment to a placebo. Only a few have compared one treatment to another. Wille compared desmopressin to a buzzer-and-pad enuresis alarm in 46 children. The improvement rate at the end of three months was 86% in the group treated with the alarm and 70% in the group treated with desmopressin. One patient with the alarm relapsed after treatment was discontinued, compared to more than half the patients on desmopressin.

Two studies have compared imipramine to a buzzer-and-pad enuresis alarm. The alarm gave better results in both cases. The first study defined a cure as 14 consecutive dry nights. The cure rate was 83% for patients using the alarm and 33% for those using imipramine. The corresponding relapse rates were 50% and 100%. A second study of 94 children, 8 to 10 years of age, defined successful treatment as an 80% improvement in dry nights over baseline. The treatment period was two months. At two months, the buzzer-and-pad alarm had a 52% success rate and imipramine a 45% rate. After two additional months without any treatment, the alarm group had maintained a 50% success rate. The success rate of the imipramine group dropped to 30%, no better than that of the children who had been treated with a placebo. Clearly, alarms are much better than drugs if the goal is a permanent cure.

TABLE 4

**Comparing enuresis treatments**

	<b>Enuresis alarm</b>	DDAVP	Imipramine	Self-awakening
Cure rate	70%	12%-65%	10%-60%	92%*
Relapse rate	10%	>90%	>90%	20%*
Risks	None	Mild	Serious	None
Cost	\$42-\$60	\$90/mo	\$5/mo (generic)	Free

\*With dry bed training.

Only one study has compared desmopressin to imipramine; it found the efficacy of the two drugs to be similar. Since desmopressin and imipramine have different mechanisms of action, a combination of the two may be useful for a few children, but no study has yet looked at their combined effects.

The drug of choice in terms of safety is desmopressin. The drug of choice in terms of cost is imipramine, \$5 a month (generic) vs. \$90 a month for desmopressin.

My approach in children over 3 years who have daytime bladder control is to put a potty chair in the child's room and tell him it's a good idea to get up and use the potty at night. The child needs to wear easily removable training pants or diapers.

By age 6, most children with normal bladder capacities can be cured by giving them responsibility for solving the problem and providing appropriate consequences for being wet or dry. For dry nights, the consequences should be praise, a star on a calendar or chart, and a reward, such as 25 cents, in the morning. For wet nights, the consequence should be helping clean up. When Marshall and Marshall used this "active role" approach with 90 patients, they achieved a decrease of 80% or more in wet nights in 70% of the children. Punishment, blame, criticism, and pressure are demotivating and have no place in treating bed-wetting. Six-year-olds with small bladders can go through a more formal bedtime self-awakening ritual along with the consequences already described. Occasionally, children are interested in the alarm at this age and respond to it.

By age 8, more vigorous intervention is in order. Most children of this age are sufficiently motivated to stay dry because bed-wetting begins to interfere with their social development—staying overnight at a friend's house, for example. For these children, the most effective treatment is an enuresis alarm and bladder stretching exercises. Enuresis alarms have been the treatment of choice in Europe for some time, but have not been widely used in the US. Foxman reported in a multisite study that alarms were prescribed for only three of 92 bed-wetting children who saw a physician.

However, a 990 survey to be published later this month in the *Contemporary Pediatrics* special issue on technology indicates that more than half of US pediatricians are recommending alarms.

For children over 8 years of age who are using an alarm and striving toward a permanent cure, you may want to prescribe intermittent medication for special occasions such as summer camp, vacations, slumber parties, or visits to relatives. Most physicians agree that this is the proper indication for using medication. Even though drugs usually produce improvement on the first night they are used, they should be tried at home for a few nights before the child goes away to allow proper adjustment of dosage.

To minimize the emotional side effects of enuresis, youngsters who continue to wet the bed frequently after age 11 or 12 despite such broad-based interventions as enuresis alarms, bladder stretching, and incentives may need long-term medication. For adolescent enuretics who have become discouraged or desperate, medication may restore hope. While most controlled studies have prescribed desmopressin for eight weeks, a recent study prescribed it safely for six months. After the youngster is dry on medication for two months, the dosage should be gradually tapered. Enuretic youngsters should continue using an alarm while they are taking medication and should be told at bedtime that they need to get up during the night. A recent study of 28 children with enuresis found that the combination of an alarm and desmopressin was significantly more effective (5.1 dry nights per week) than the alarm alone (4.1 dry nights per week).

Nocturnal enuresis is a difficult problem for the pediatrician to treat. Biofeedback advocates swear by enuresis alarms. Chemotherapists tout drugs. Behaviorists endorse self-awakening programs and consequences. My viewpoint is, "When in doubt, join forces." When enuresis is severe, the smart pediatrician prescribes a combined approach.